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Success of dental implants in compromised patients

"Erfolg dentaler Implantate bei kompromittierten Patienten"

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1 Introduction

1.1 Dental implants

The main goal of modern dental treatment is to restore function and aesthetics to patients who have lost hard and soft tissue in their oral cavity. Dental implants can achieve this goal due to their unique properties [1], including biocompatibility and osseointegration, which are essential characteristics of modern endosseous implants [2]. Such implants are a minor percentage of the total amount of foreign materials inserted in patients across all medical specialties [2]. The demand for implantation materials is based on the fact that most damaged or missing structures in the human body cannot regenerate [2].

The nature of implants must be appropriate to the oral cavity's physiological conditions, specifically to withstand high pressure and bending forces during chewing [3]. In addition, implants must be corrosion resistant and biocompatible, as they are introduced into vital tissue and exposed to different fluids, such as blood, saliva, and drinks with different pH values. Finally, osseointegration is essential for the stability and long-term success of implants [4]. Thus, successful treatment with predictable and lasting function is the primary goal of modern implantology [5]. Titanium meets these requirements and, therefore, is widely used in this field [6].

Modern implants are an excellent alternative to conventional prosthodontic treatments (e.g., dental bridges and removable prostheses), mainly because they increase patients' quality of life and self-confidence [7].

Bone atrophy affects the procedure of dental implant placement, and as a result, bone augmentation may be required [8]. Many studies have been conducted in the last decades to improve the augmentation procedures before implantation [9]. The focus of such scientific work has been either the augmentation material itself or enhancing material such as platelet-rich plasma (PRP) or platelet-rich fibrin [10–12]. While the use of autografts is the gold standard of augmentation, donor-site morbidity is of great

importance [13–15]. The size and type of augmented bone affect the dental implant's success and can cause complications, especially in patients with compromised bone quality [16]. Long-term implant evaluation is an essential tool to ensure the success of prognostic strategies [17]. However, dental implant survival does not indicate success [18]. Therefore, the use of standardized success criteria for implant assessment studies is necessary [19].

The current work elucidates the function of and patient satisfaction with oral rehabilitation in patients with compromised dental and medical conditions, asserting the necessity of bone augmentation for implant success.

1.1.1 History and development

The idea of replacing missing teeth has existed for a long time and extends back to 6000–4000 BC [20]. The earliest evidence of dental implantology is the amazingly detailed dental work on an ancient Egyptian mummy that archaeologists have dated to 2000 BC. The results show intricate gold work around the teeth. The two donor teeth had holes drilled into them; wires were strung through these holes and then around the neighboring teeth. This finding was made by Egyptologist Hermann Junker in 1914 and is still the most widely recognized evidence of the advanced dentistry that flourished in those days [21].

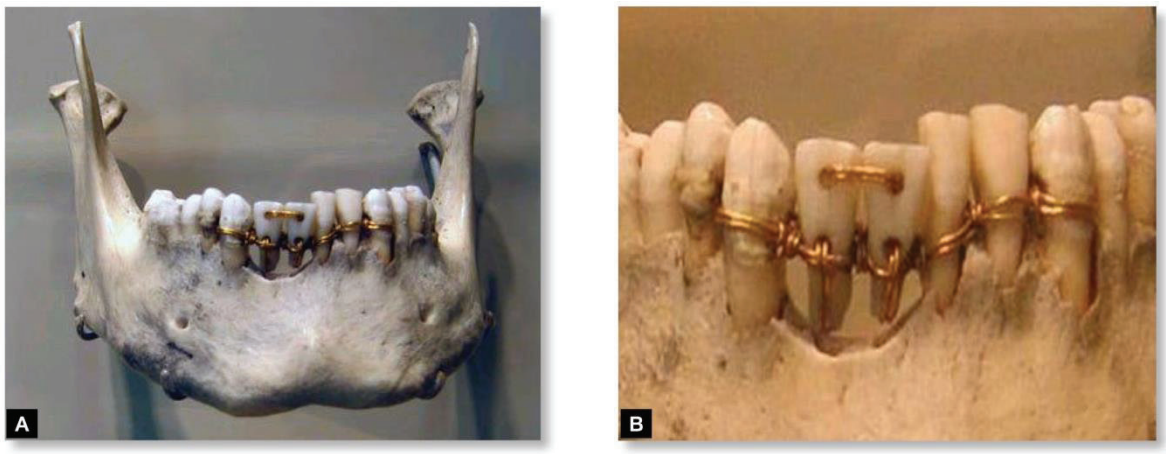

Figure 1. The earliest evidence of implantology art shows the use of a gold wire bridge to resort the lower right first and second incisors and was discovered in an old Egyptian mummy: A) the whole mandible; B) magnification of the lower anterior area (both photographs are from Ancient Egyptian Dentistry, written by Venice Attia; they were used with her permission) [22].

In the classical age, Hippocrates reported replacing missing teeth using artificial teeth fixed with gold thread [23]. In the early nineteenth century, Maggiolo and Jourdan were the first to anchor an alloplastic material consisting of conical gold wire in the lower jaw [20]. The first step of modern implantology dates back to 1947, when Formiggini developed helio-colloidal screws made of tantalum. These screws were inserted into the alveolar bone to replace missing teeth [20]. Between the 1970s and 1980s, Brånemark presented osseointegrated dental implants, which was the final step in developing today's implantology [24]. Brånemark established the concept of osseointegration [20, 24], i.e., the structural and functional connection between the living bone and the implant's surface [24, 25]. The bone is fused directly to the implant surface without any connective tissue transition [4]. Successful osseointegration is a prerequisite for dental implant functionality [26]. Implant healing can be defined as direct bone attachment that occurs on the implant's surface, i.e., "functional ankylosis" [26, 27]. The formation of bone in close proximity to the implant surface is described as primary bone-to-implant healing. The result is a fixed and absolutely immobile implant within the surrounding bone, described as osseointegration [28, 29]. Several prerequisites are required for successful osseointegration, including primary bone healing, a precise fit, primary stability, and immobilization during the healing phase [30].

1.1.2 Clinical requirements for dental implants

Sufficient bone quantity is essential for the successful insertion of an endosseous dental implant [31]. An alveolar ridge width of 6–7 mm in the mesiodistal direction and 5–6 mm in the bucco-oral direction is required [32]. The mandible consists mainly of compact bone, while the maxilla comprises more cancellous bone. After tooth loss, atrophy of the alveolar ridge occurs over time. This is a chronic, progressive, and irreversible process that occurs mainly in the first six months after tooth extraction [33]. Atrophy of the edentulous alveolar ridges of the mandible has been well described in the literature [33, 34]. The alveolar ridge height decreases, resulting in an

approximation of the mandibular canal and the inferior alveolar nerve to the alveolar ridge. If the implant insertion is not adequately planned, complications such as nerve lesions might occur [35]. Maxillary atrophy has also been documented; this leads to inadequate alveolar bone height until the maxillary sinus is reached, causing implant insertion complications [36]. Therefore, the bone height should be determined radiologically prior to implant placement. The usable bone height is the distance between the alveolar ridge and the anatomical boundaries, such as the maxillary sinus or mandibular canal [37]. If bone resorption in the mandible toward the buccal surface and the palatal direction in the maxilla occurs, an unfavorable maxillary/mandibular relation can develop.

Bone quality is another essential parameter for successful osseointegration of dental implants [38]. This can be determined by the bone density, which can be evaluated by three-dimensional radiological analysis. However, a reliable statement regarding bone quality can only be achieved via a surgical procedure [39]. The bone quality of the alveolar ridge is one of the most critical factors for the primary stability of an inserted implant [40].

The quality of the soft tissue surrounding an implant can also affect its success. A well-known beneficial factor in preserving soft tissue health is the presence of keratinizing mucosa around an implant [41–43]. Several studies described the importance of healthy mucosa, indicated by less plaque aggregation and mucosal inflammation, for implant success. Therefore, bone resorption is correlated with an adequate band of keratinized mucosa around implants [42, 43]. Several variables, including tooth location, an elevated frenulum, and gingival recession due to inflammation or traumatic reasons, have been suggested to influence the width of the attached gingiva around natural teeth [44]. Wang et al. performed a retrospective analysis of 726 patients with 1,252 dental implants, determining the quality and width of the keratinized mucosa around the implants. The average amount of keratinized mucosa was significantly higher in the maxilla compared to the mandible [45]. Implants inserted after periodontitis-caused tooth loss showed a lower keratinized mucosa

width. Implants inserted after bone augmentation showed a higher risk of insufficient keratinized mucosa than those inserted without prior bone augmentation surgery. The longer the follow-up time, the greater the chance of the implants losing keratinized mucosa [45].

To conclude, sufficient bone volume and healthy mucosa are the most critical factors influencing dental implants' short- and long-term success.

1.1.3 Methods to assess dental implant treatment outcomes

Primary implant success depends on the quality and quantity of the newly formed bone adjacent to the implant surface [46]. This requires optimal surgical implantation, mechanical anchorage, and primary stability without excessive heat generation [47]. Micromovement higher than 150 μm at the implant interface can result in entire or partial fibro-integration and impair an implant's success [48]. An implant healing period of about 3–6 months without functional loading is required to ensure successful osseointegration [49]. However, waiting too long for functional loading can lead to bone resorption around implants, as mastication forces stimulate bone remodeling and maturation [50]. Different implant surface treatments have been introduced in recent years, aiming to reduce the healing time for early or even immediate implant loading without affecting osseointegration success [28, 51]. The assessment of implant success is, in brief, the assessment of lasting implant osseointegration. Histomorphometric investigation is the gold standard to evaluate osseointegration [52]. However, histological analysis cannot be done in routine clinical practice to assess implant osseointegration due to its invasiveness. Therefore, it is used in experimental and preclinical studies only [53]. Radiological -investigations, such as panoramic and periapical x-rays and cone-beam computed tomography, are widely used for this purpose [54]. However, such investigations are neither standardized nor calibrated and produce metal artifacts that do not allow accurate evaluation of dental implants, especially in the proximal areas [55].

Another way to assess successful implant osseointegration is the vibration method, with either transient impulsive or stationary force [55]. The percussion test is based on applying a transient force and is widely used in the dental field [56]. By applying a controlled vertical force on the dental implant, the sound produced will either be defined or dull according to the presence or lack of osseointegration [57]. However, this test is not standardized because it is a subjective evaluation method and the outcome depends on the experience of the evaluators [57]. Another problem with using this test is the accuracy, as 20% successful osseointegration of the implant surface can be enough to produce a high sound that does not reflect the actual implant treatment outcome [58]. Based on the same principle, a device has been developed to standardize and calibrate the percussion test. Periotest® (Siemens, Bensheim, Germany) can be used to assess implants' osseointegration [59]. The device taps the implant with a plunger and measures how strongly the plunger is damped by the implant [60]. This process provides the user with numerical values between –10 and +50 (Table 1).

Table 1: The meaning of the numerical Periotest® (PT) values

PT value	**Meaning**
-10 to 0	Satisfactory osseointegration
+1 to +9	Clinical examination of the implant necessary
+10 to +50	Insufficient osseointegration

Implant osseointegration can also be determined using devices focused on stationary force. In this case, the vibrations of the bone–implant system can be recorded using steady sinusoidal pressure at a defined frequency or over a given frequency range [61]. Based on this principle, resonance frequency analysis has been introduced to assess the degree of implant stability at any point during implant treatment and after functional loading, so changes in implant stability can be tracked over time [62]. The

method is available commercially as Osstell® (Integration Diagnostics, Savedalen, Sweden), and a unit has been developed to define implant stability. An implant stability quotient has been generated; the numbers range between 1 and 100, with 100 representing the highest implant stability coefficient [63].

1.1.4 Implant survival

A dental implant in the oral cavity that has not been removed regardless of its clinical status is considered to have survived [64]. The implant survival rate is the most straightforward data presentation of implant treatment outcomes. However, depending only on this method to evaluate dental implants can be misleading, especially in a clinical situation wherein the implants are unstable or located in severely inflamed tissue, as shown in Figure 2 [65]. An implant's success is not a given.

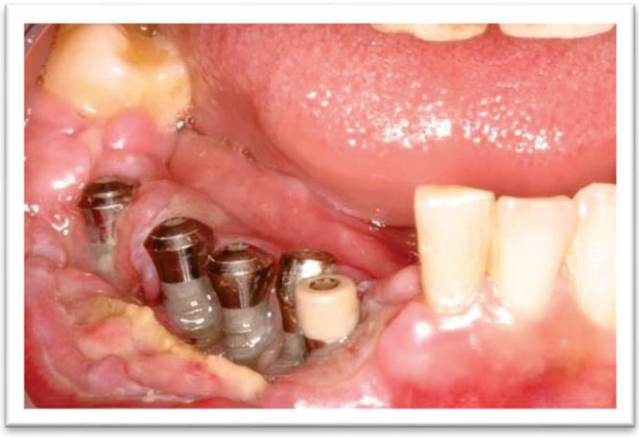

Figure 2. The compromised clinical situation of dental implants with peri-implantitis rated as having survived as they are still in situ. Clinical case of the Department of Oral and Maxillofacial Surgery, University Hospital Giessen.

Conditions such as sleeping implants, fractured implants, and implants in a non-ideal prosthetic location are rated as survived dental implants and may give the impression of success. For these reasons, some authors encourage applying the implant success rate according to defined success criteria to evaluate implants' treatment outcomes [18, 19, 66, 67]. Furthermore, patients' satisfaction with their dental implants, either functionally or aesthetically, cannot be obtained from survival data alone [68]. Ettl et al. concluded that implant survival varies considerably from implant success in patients with head and neck cancer [69]. Moreover, infection around dental implants

cannot be evaluated using the survival rate. Peri-implant infections are usually associated with bone resorption and, over time, will lead to loss of osseointegration. Mucositis and peri-implantitis are terms used to describe inflammation of the peri-implant tissue [70]. While mucositis is limited to the soft tissue and is a reversible process, peri-implantitis is infection of both the soft and hard tissue and, therefore, irreversible [71, 72]. Bone resorption around dental implants may have other causes, such as residual cement from fixing the superstructure and implant overloading, which can act occlusally and/or laterally on implants [73, 74]. Parafunctional habits, such as bruxism, are also a risk factor wherein excessive and uncontrolled mastication forces overload the implants [73]. Additionally, oral hygiene plays an essential role in local infection around dental implants as well as in their success [75].

In summary, the survival rate of implants at a particular time point is determined by the ratio of explanted implants to all inserted implants; in the literature, this rate is called the "in situ rate" [76]. Here, only "input–output statistics" are used to determine whether an implant has been lost [77–79]. According to Kaplan and Meier, the survival time analysis is determined using the proportional hazard rate [80]. According to this statistical method, implants' survival probability is assessed based on their loss rate over a defined period [81]. The probability of an implant's loss is calculated according to its retention time; therefore, this analysis is more meaningful than the input–output statistic. The disadvantage, however, is that radiological, clinical and functional aspects are not considered [18].

1.1.5 Implant success

Implant survival analysis does not require any assessment of the hard and soft tissue condition around an implant. Thus, multiple success criteria have been defined by various authors. To determine the success of an implant, clinical parameters are used to assess the peri-implant tissue. All implants are considered in situ, and the success rate can then be concluded from the success criteria.

In the field of dental implantology, the criteria and classifications of successful implantation have been the subjects of controversial statements. Multiple non-homogenous and non-standardized criteria have been introduced over the last decades, allowing clinical "implant success" to become objective and assessable [82]. In 1979, Schnitman et al. introduced the first set of implant success criteria [83]. Since then, the lists that determine success have continued to multiply. The following summary categorizes implant success by author:

The National Institute of Health Criteria (1979)

- Implant mobility should be less than 1 mm in any direction.
- Bone loss around the implants should not exceed one-third of the bone's vertical height.
- Neighboring teeth should not be symptomatic, demonstrate odontogenic inflammation, or be damaged.
- The mandibular canal, maxillary sinus, and nasal floor should be free of paresthesia and uninjured.

Three years after their introduction, these success criteria were revised to include the following aspects: implants should be retained for 60 months or longer in the oral cavity, and there should be definitive loss of mobility [84]. The parameters included the absence of radiograph radiolucency and bleeding around the implant shoulder. Additionally, the patients should be free of pain, granulomatosis, gingival hyperplasia, or expanding peri-implant space on radiograph [84].

In 1984, a new revision of the criteria was performed, with several subjective aspects included: proper chewing, lack of discomfort or pain, and improvement of patients' aesthetic and psychological state [85]. However, applying these criteria meant that any implant that does not function for five years or more could not be rated as successful. Therefore, these criteria are no longer used as guidelines [86].

Albrektsson's Implant Success Criteria (1986)

In 1986, Albrektsson et al. published newly defined success criteria [87]:

- The implant should be clinically firm on examination.
- There should be no radiological translucency around the implant.
- Vertical bone loss should be less than 0.2 mm/year after the first year under loading.
- There should be no evidence of infection, pain, neuropathy, paresthesia, or mandibular canal injury.
- The success rate should be 85% within a five-year observation period. At the end of a 10-year observation period, the success rate should be 80% [87].

Buser's Implant Success Criteria (1990)

Buser et al. published additional success criteria in 1990 [88]:

- No persistent pain, foreign body sensation, or dysesthesia.
- No recurrent purulent peri-implant infection.
- No implant mobility.
- No continuous peri-implant radiolucency.
- Possibility of prosthetic restoration (superstructure) [88].

Success Criteria According to Jahn and d'Hoedt (1992)

- The sulcus depth at the mesial, distal, buccal, and oral sides must not exceed 4 mm in two consecutive controls.
- Clinical mobility must not exceed loosening grade I.
- The implant must not have a continuous bilateral gap with a width greater than 0.5 mm on radiograph.
- The angular bone defect (mean value of the mesial and distal measurements on radiograph) must not exceed 3/10 of the constructively endosseous implant section.

- The patient's subjective evaluation of the implant must not be worse than three according to the German school grading system [89].

Implant Success Criteria According to Karoussis et al. (2003)

In general, one of the limitations of the criteria listed above is that they primarily assess the peri-implant hard tissue. Criteria that examine the soft tissue around implants are not precisely listed. This is exactly what the working group of Karoussis et al. observed in 2003 [90]. They introduced new success criteria that included a combination of the previously published criteria, as follows:

- No implant mobility (Buser et al., 1990 [88]).
- Absence of pain, foreign body sensation, or dysesthesia (Buser et al., 1990 [88]).
- Probing depths not >5 mm (Mombelli & Lang, 1994 [91]; Brägger et al., 2001 [92]).
- No bleeding on probing (BOP) (Mombelli & Lang, 1994 [91]).
- Absence of persistent radiolucency around the implant (Buser et al., 1990 [88]).
- After the first year under loading, the vertical bone loss should not exceed 0.2 mm/year (Albrektsson et al., 1986 [87]).

Health Scale for Dental Implants (2008)

A conference funded by the International Congress of Oral Implantologists established categories for the success, survival, and failure of dental implants [65]. Implant success is described as the optimal therapeutic state exhibited by an implant and should be combined with prosthetic survival. For at least 12 months, the implant should act as a prosthetic abutment. The criteria for survival are classified into two categories: adequate and impaired survival. Implants that do not show optimal circumstances are categorized in both of these groups. However, to avoid implant failure, adequate implants do not need professional care, and compromised implants require clinical therapy to prevent implant loss [65]. Implant failure is described as an implant that has already been lost or needs removal [65] (Table 2).

Table 2: The implant quality scale, as suggested by the International Congress of Oral Implantologists (2007) [65].

Implant quality scale group	Clinical findings
I. Success	-Absence of pain -No mobility -Bone loss less than 2 mm -Absence of pus
II. Satisfactory survival	-Absence of pain -No mobility -Bone loss between 2 and 4 mm -Absence of pus
III. Compromised survival	-Sensitivity on function -No mobility -Bone loss more than 4 mm but not exceeding half the implant's length -Probing depth (PD) less than 7 mm -History of pus
IV. Failure	-Pain -Mobility -Bone loss more than half the implant's length -Pus (active) -Explanted implant

1.1.6 Implant failure

The success or failure of osseointegration is multifactorial and may depend on anatomical conditions, genetic predisposition, oral health status, and the presence of systemic diseases, including the immune system's status [93]. There are two reasons

loss of osseointegration and, thus, implant loss may occur depending on the time of occurrence. Regarding failed osseointegration during the healing phase (also called early implant loss or primary failure), the reasons may be overheating of the peri-implant bone during the surgical procedure or no primary stability after implant placement [73]. Thus, constant water cooling with sterile saline during implant surgery was recommended and, meanwhile, became mandatory [25, 94, 95]. Too-early loading of an implant during the healing phase may also lead to primary failure [73] as well as lack of primary stability and poor bone quality. Incorrect choice of implant length or diameter is also an essential factor that may cause primary implant loss.

The loss of existing osseointegration is called later implant loss or secondary failure [96]. A foreign body reaction after implant placement is unavoidable [97]. Successful implant healing comes from the balanced equilibrium between the foreign body and surrounding tissue. If the balance is disturbed due to one or several reasons, such as an unsuitable implant, poor implant healing, patient factors, cement remnants, or overloading, marginal bone loss around the implant may occur, which may lead to implant loss [98].

Peri-implantitis is an infection around an implant that is associated with irreversible bone loss. The term was defined at the First European Workshop on Periodontology in 1993 and stands for a destructive inflammatory process around a functioning osseointegrated implant. This results in deep pocket formation and bone resorption [91, 99]. The prevalence of peri-implantitis reported in the literature varies from 12.9% to 56% [100, 101]. The inflammatory process of peri-implantitis is visible based on clinical appearance, e.g., redness, swelling, BOP, deep pocket formation, and bone resorption [101]. The course of peri-implantitis is usually painless, and the peri-implant bone evaluation can be measured radiologically [101]. Crater-shaped defects can be seen in a circular pattern around the implant.

Destruction of the bone may progress without loosening the implant for many months. Consequently, the inflammatory process remains unnoticed until complete loss of osseointegration occurs and, thus, leads to implant loss [91]. However, vertical bone

resorption around an implant is not necessarily caused by an inflammatory process [91]. Other reasons for bone resorption are subcrestal placement of the implant, placing two implants too close to each other, and implant overloading [102, 103]. Peri-implantitis is associated with polymicrobial aerobic and anaerobic infection [104, 105]. The inflammatory process is favored by the presence of a biofilm [70]. It has been demonstrated that the following indicators are associated as the main risk factors for peri-implantitis: poor oral hygiene, positive family history, positive smoking behavior, alcohol consumption, and diabetes mellitus [101].

Furthermore, a rough implant surface, remnants of the cement used to attach the superstructure, and the absence of keratinized gingiva around the implant favor the development of peri-implantitis [70]. There are several therapeutic approaches to treat this, including conservative and surgical methods. Non-surgical peri-implantitis treatment includes administration of systemic antibiotics and anti-infective mouthwash. In contrast, surgical management utilizes access flap debridement with several approaches, such as laser disinfection of the implant surface, implantoplasty to smooth the surface, resective procedures, and regeneration therapies [106].

Optimal therapy for complete bone healing after peri-implantitis is a challenge, and therefore, surgical removal remains the definitive therapy of choice, especially in delayed cases (Figure 3).

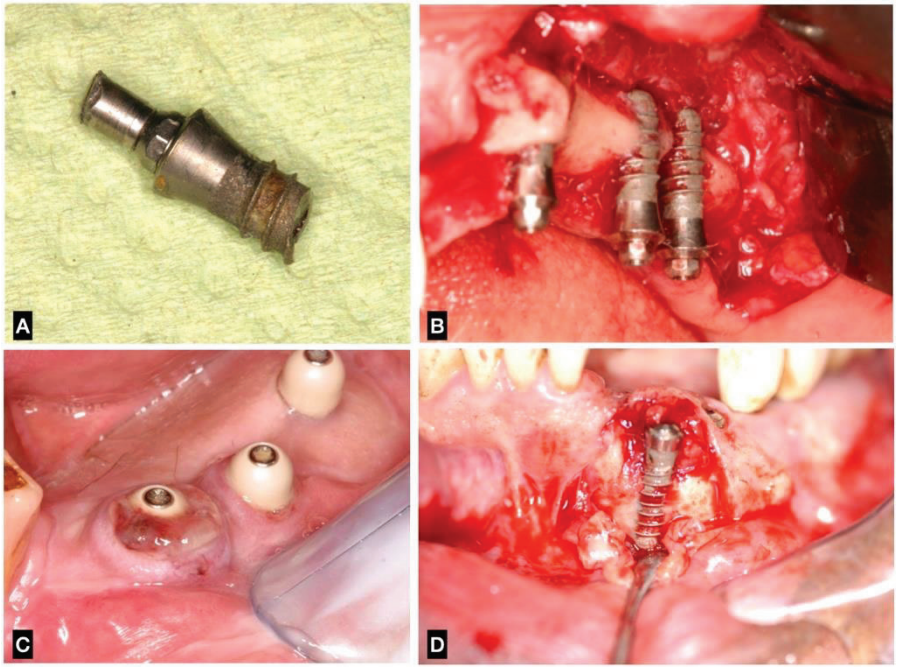

Figure 3. Implant-related inflammation and failure: A) implant fracture; B) peri-implantitis in the upper jaw with loss of bone at the alveolar ridge; C) mucositis with exudate around implant in the premolar region of the mandible; D) bone resorption around the implant in the lower jaw. Clinical cases of the Department of Oral and Maxillofacial Surgery, University Hospital Giessen.

1.2 Dental implants beyond established indication limits

The number of dental implant insertions is growing worldwide, as are such insertions' various indications. It is expected that by 2022, the North American and European implant markets will hit nearly 4.2 billion United States dollars [107]. The primary established indication for the placement of dental implants is to replace missing teeth to avoid grinding healthy tooth substances and prevent local bone loss resulting from missing mastication forces [108]. The indication for dental implant placement must be determined by a detailed history of patients' problems, related habits, and medical and dental records. Certain medical conditions, such as preexisting and untreated disorders, are likely to play a role in implant failure [109]. Patients' expectations must also be evaluated adequately during treatment planning to obtain an optimal patient satisfaction treatment outcome. However, some clinical situations in medically or dentally compromised patients require urgent oral and dental rehabilitation [19, 110, 111]. In such cases, dental implant insertion is a must. Therefore, the number of contraindications in implant dentistry has decreased over the last few years [112].

1.2.1 Medically compromised patients

Successful dental and oral rehabilitation with dental implants depends on proper case selection and a good evaluation of patients' medical and dental history [113–115]. However, dental implants are often used to treat people with one or more risk factors [18, 19, 67, 110, 111]. Risk factors for implant placement are diseases of the bone system, hemorrhagic diatheses, diseases of the hematopoietic system, and deficient immune defenses. In addition, psychotic syndromes, alcohol, drug, or medication abuse, and lack of compliance are also presented as risk factors. In applying bisphosphonates, a distinction must be made between low-dose oral and high-dose intravenous (IV) administration. It is not recommended to insert implants in patients who have received bisphosphonate medication via IV administration because of the risk of bisphosphonate-associated bone necrosis [116, 117].

Patients who undergo tumor ablative surgery and jaw reconstruction are also considered a risk group, especially if exposed to adjuvant radiochemotherapy [118]. After jaw resection, tumor patients suffer from disfigurement, which leads to social isolation. Functional and aesthetic impairment is also one of the results of tumor ablative surgery [119]. Therefore, dental and oral rehabilitation of these patients is essential to ensure their reintegration into society and everyday life and healthy nutrition [120]. Oral rehabilitation depends mainly on dental implants as the anchor of the prosthetic therapy [121]. Dental implant insertion requires sufficient bone tissue and healthy keratinized mucosa to ensure the osseointegration process and long-term treatment outcomes [122]. Patients who undergo tumor surgery with jaw resection need urgent jaw reconstruction with bony and soft tissue flaps, which enables implant insertion and prosthetic rehabilitation [123]. “Jaw in a Day” is a modern approach to performing all surgical procedures in one operation: tumor resection, jaw reconstruction, implant placement, and insertion of the dental prosthesis [124] (Figures 4–6). The fibula flap is considered a standard flap for jaw reconstruction, which can be performed immediately after tumor resection via a two-team approach [125].

Previous studies have reported comparable implant success inserted in fibula to those inserted in normal jawbone; the patients were satisfied with the functional and aesthetic treatment outcomes [110, 111, 126].

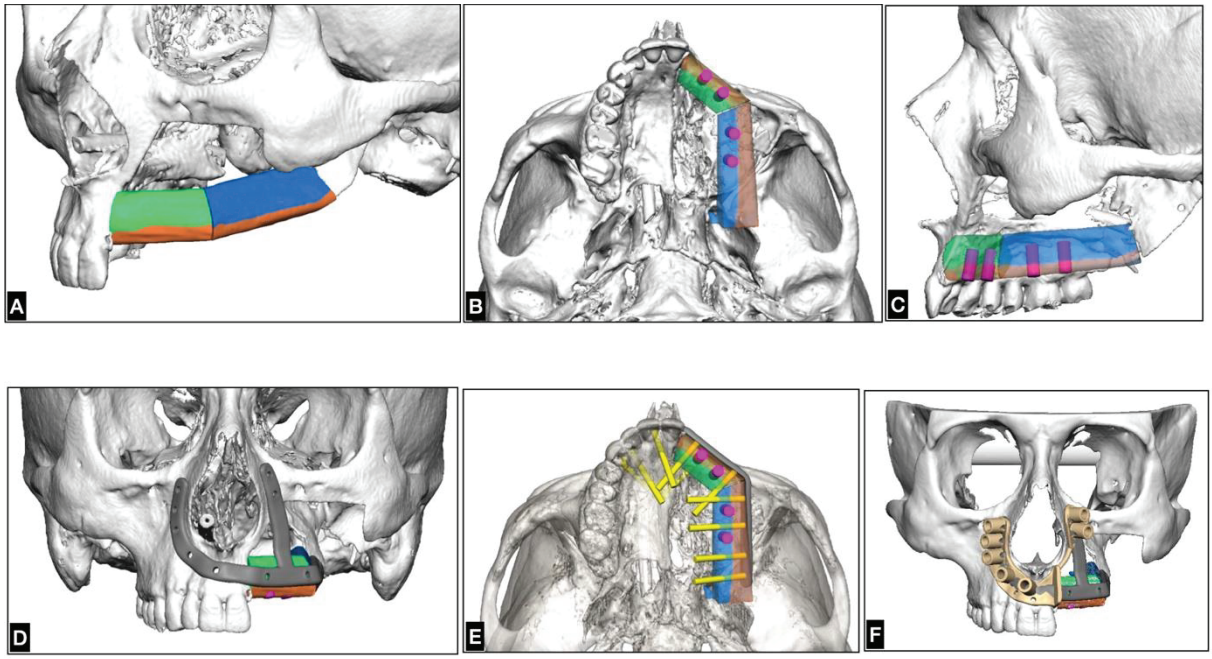

Figure 4."Jaw in a Day" planning: virtual planning (KLS Martin, Group, Germany): A) fibula adaptation to the maxilla; B–C) three-dimensional implant planning; D) patient-specific plate planning; E) occlusal view of the planning, including dental implants and patient-specific plate; F) planning of the cutting guide.

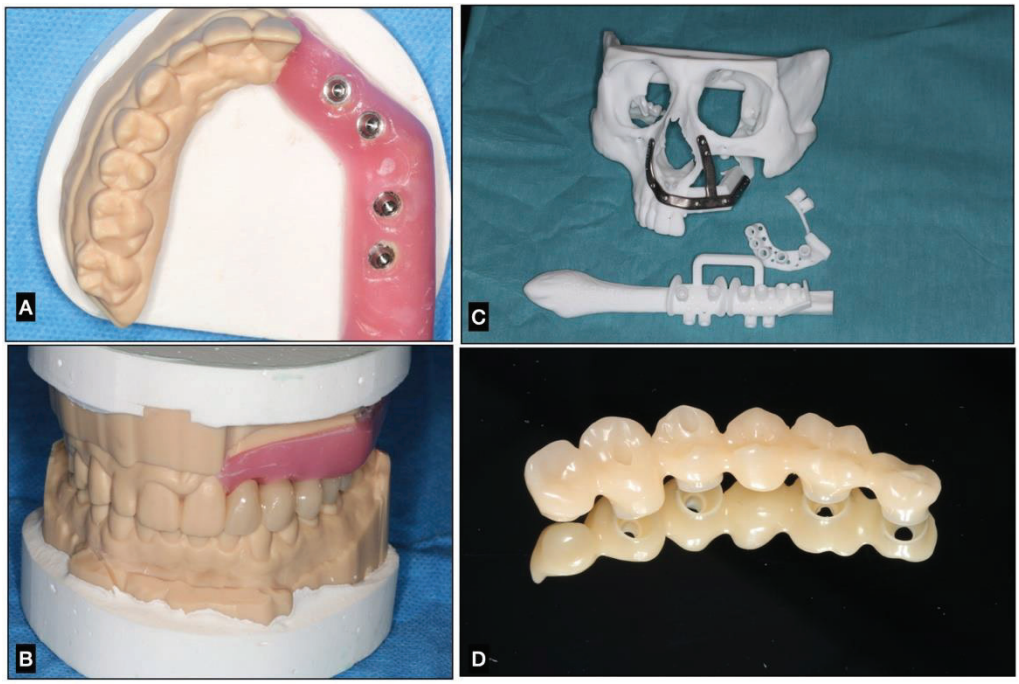

Figure 5."Jaw in a Day" prefabrication of A+B+D) dental prosthesis and C) patient-specific plate, implant, and cutting guide.

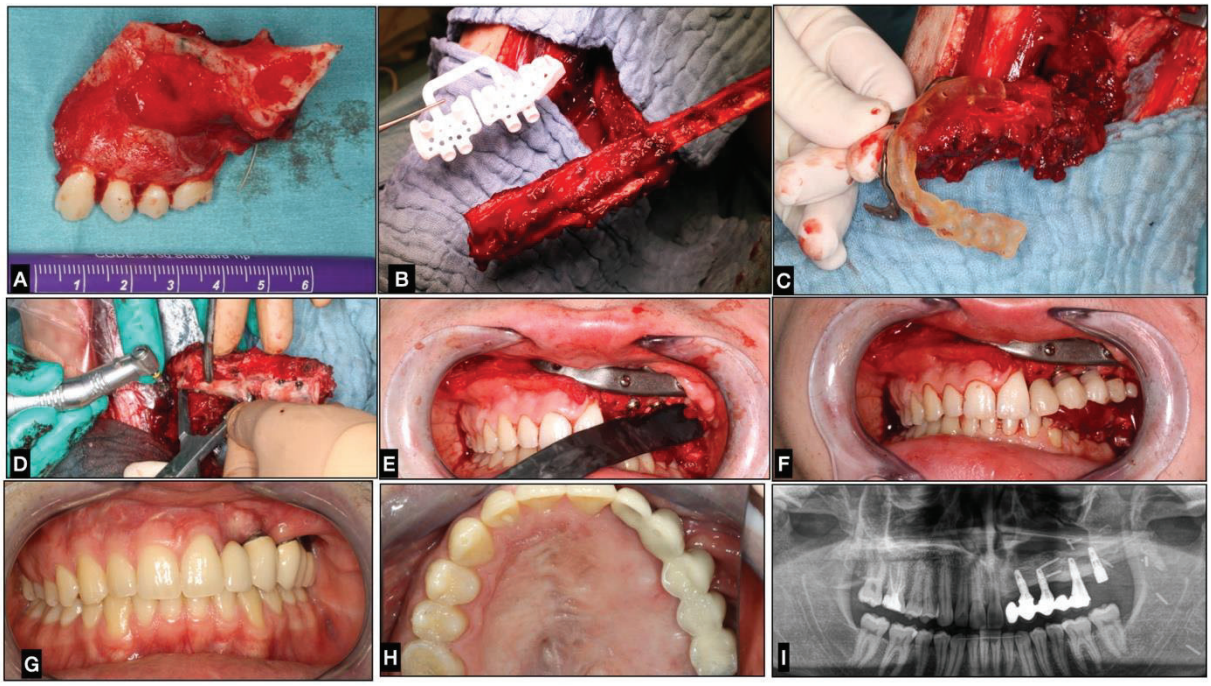

Figure 6."Jaw in a Day" surgical procedures: A) maxillary resection of keratocystic odontogenic tumor; B) fibula raising and the cutting guide; C–D) implant insertion with guiding splint; E) fibula flap fixation to the maxilla; F) insertion of the temporary bridge with moderate aesthetic results; G–H) after insertion of the final bridge; I) panoramic x-ray after prosthetic treatment. The implant in the second molar region could not be included in the prosthetic treatment and remained a sleeping implant. Clinical case of the Department of Oral and Maxillofacial Surgery, University Hospital Giessen.

Dental aplasia is a tooth anomaly in which the number of teeth reduces. It is considered the most common dental anomaly in tooth development [127–129]. The severity of dental aplasia ranges from hypodontia (missing 1–5 teeth) and oligodontia (missing 5+ teeth) to anodontia (missing all teeth, excluding the wisdom teeth) [127, 130]. The etiology of hypodontia may be either non-syndromic or associated with certain syndromes such as ectodermal dysplasia, cleft lip and palate, and Down's syndrome [129–131]. Many studies have reported that patients with hypodontia have a narrower alveolar ridge than patients with normal dentition [132]. Such patients are considered medically compromised and a risk group for dental implants (Figure 7).

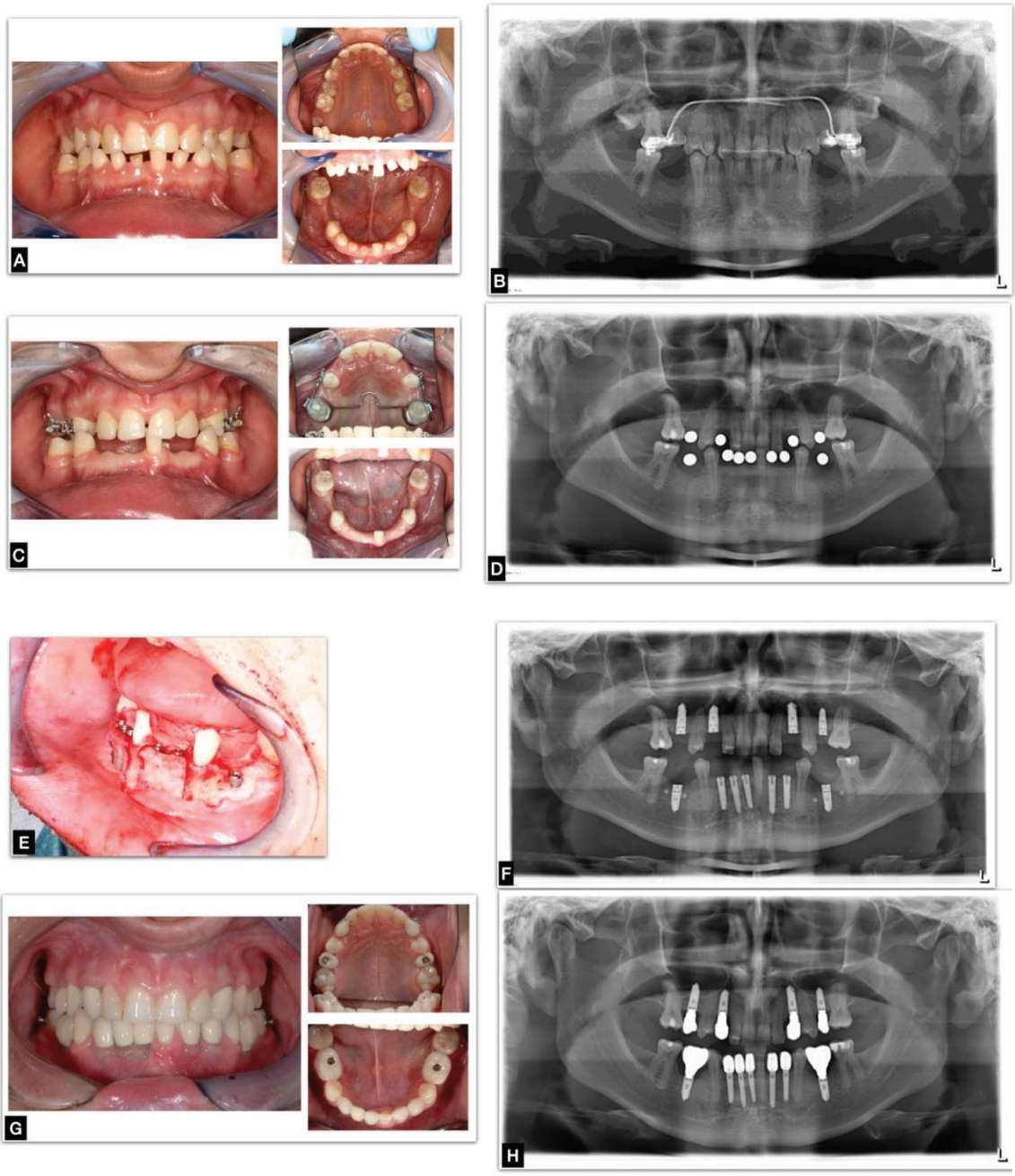

Figure 7. Patient with oligodontia: A) initial situation with some deciduous teeth still in situ (55, 53, 63, 65, 73, 72, 81, 82, 83); B) panoramic x-ray related to the initial situation; C) condition after extraction of the deciduous teeth. There was a crossbite in the posterior region due to the size discrepancy between the upper and lower jaws. To create space for the subsequent implants, orthodontic gap opening was performed. D) Panoramic x-ray for implant planning with references; E) intra-operative photo showing the implant insertion with the bone-splitting technique; F) panoramic x-ray after implant placement; G) the situation after prosthetic rehabilitation; H) panoramic x-ray after crown insertion. Clinical case of the Department of Oral and Maxillofacial Surgery, University Hospital Giessen.

1.2.2 Dentally compromised patients

There is no clear definition in the literature to describe dentally compromised patients in correlation to dental implants. However, evidence has been reported that patients

treated for periodontitis might experience more frequent implant loss and implant complications than patients without periodontitis [133].

As mentioned before, successful implantation depends on sufficient bone and healthy gingiva. Patients who do not have an adequate amount of bone to ensure implant insertion require bone augmentation. These patients can be considered dentally compromised. Jawbone atrophy is always correlated with missing teeth (acquired or congenital), as no mastication forces are transferred through the roots to the bone. In the first year of tooth loss, the bone loss in the region is the worst; after that, the loss of bone tissue slows down over time [134]. Bone loss can also be associated with trauma and neoplasia or surgical procedures to remove benign or malignant tumors [135]. The type of augmentation material is selected depending on the etiology, extent, and dimension of the bone atrophy. Detailed information about the augmentative procedures for atrophied or resected jaws is listed in the next section.

Soft tissue plays a vital role in dental implants' long-term success, not only for the aesthetic results but also for the complete long-term treatment outcomes. Healthy oral mucosa acts as a tight seal around the implant shoulder and prevents bacterial infiltration (and its destructive effects) into the bone [136]. High-polished titanium in the implant neck area reported to result in an ideal soft-tissue seal to protect implants from bacterial infection [136]. Adequately keratinized mucosa is essential to reducing plaque accumulation and preventing gingival infection, especially in implants inserted in the area of the molars [137]. Absent or inadequate keratinized mucosa (<2 mm) requires surgical augmentation using free gingival grafts [138]. The ideal donor site for these grafts is the hard palate. This is considered the most effective treatment for augmenting the attached gingiva around dental implants [139].

In some cases, there is a combination of bone and soft tissue atrophy. In these complex situations, proper diagnostics and case selection have to be performed to avoid complications. The soft tissue condition has to be improved first to ensure tension-free sutures at the bone-augmented areas to prevent wound complication or graft loss.

Osmotic soft tissue expanders may help generate more soft tissue and reduce postoperative complications after bone augmentation procedures [140] (Figures 8, 9).

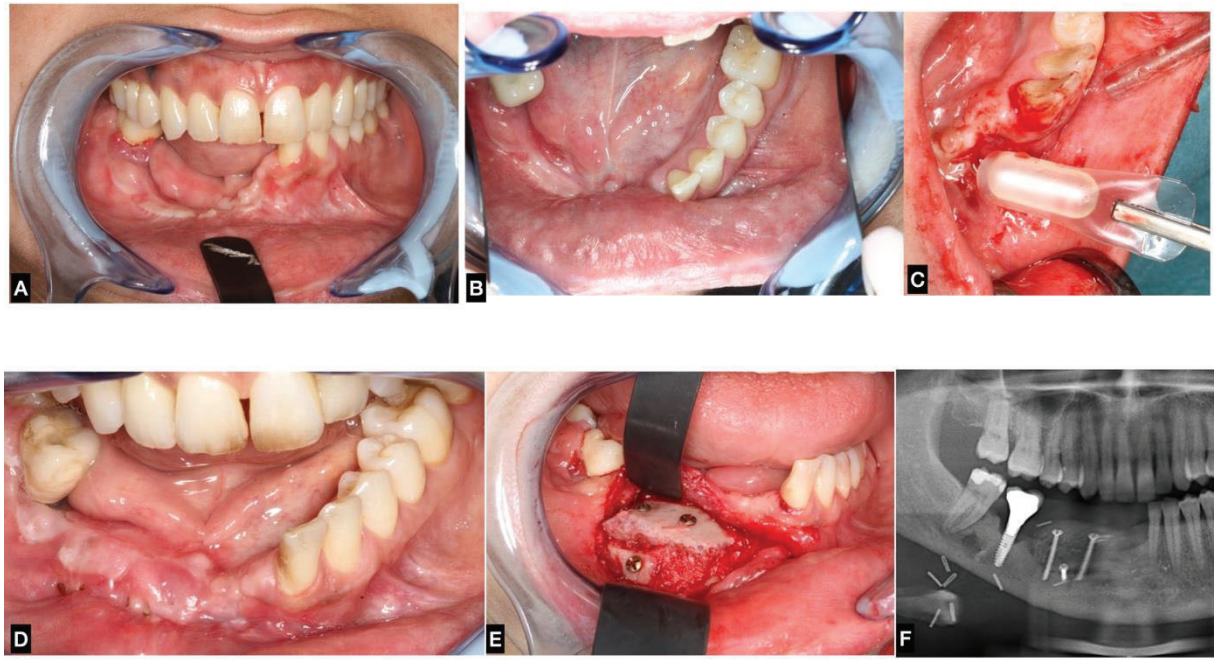

Figure 8. Clinical case with soft and hard tissue atrophy: A–B) patient with bone and gingival atrophy in the lower jaw; C) insertion of osmotic soft tissue expander; D) the situation after soft tissue generation; E) bone augmentation from iliac crest; F) postoperative panoramic x-ray.

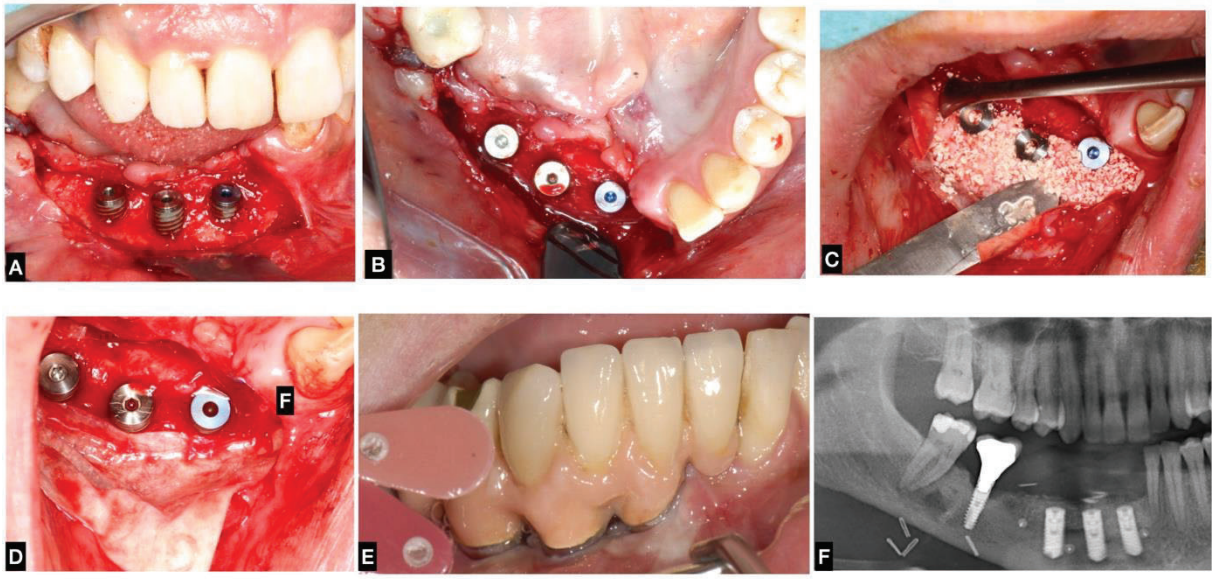

Figure 9. Previous clinical case: A–B) implant insertion with bone deficiencies; C–D) the use of plasma-rich growth factor, bone substitution, and membrane to augment the implant surfaces outside the bone; E) the situation after prosthetic restoration; F) panoramic x-ray after implant insertion. Clinical case of the Department of Oral and Maxillofacial Surgery, University Hospital Giessen.

The soft tissue situation of patients who undergo tumor ablative surgery and reconstruction using free flaps and, later on, dental implants is challenging. The skin paddle of the free flaps plays an essential role in closing wounds after tumor resection,

prevents the development of saliva fistulas, and measures good protection for dental implants during the healing period [110]. However, after implant reopening, the skin paddle, based on its mobility and thickness, is no longer suitable as peri-implant soft tissue. The mobility leads to food accumulation between the implant and bone and may lead to mucositis and peri-implantitis. The high skin thickness leads to difficulties in taking impressions of the implant for prosthetic rehabilitation. In this case, the skin paddle has to be replaced with keratinized mucosa using a free palatal mucosa graft. This surgery is performed alongside the implant exposure, and a vestibuloplasty, if required, can also be performed [110, 111] (Figure 10).

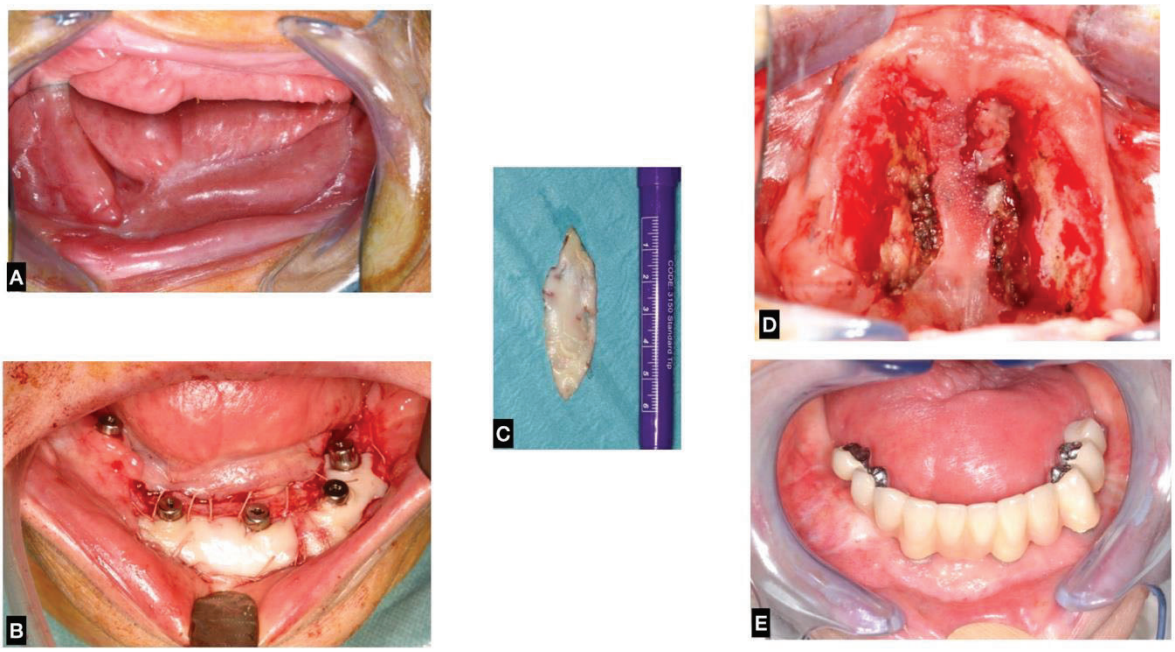

Figure 10. Improvement of the soft tissue condition around dental implant: A) patient with ablative tumor surgery in the mandible reconstructed with a fibula free flap (FFF); B–D) palatal mucosa graft transplanted to the implant site to replace the skin from the FFF with keratinized mucosa; E) after insertion of the dental prosthesis. Clinical case of the Department of Oral and Maxillofacial Surgery, University Hospital Giessen.

1.3 Maxillofacial autograft material

Autogenous bone grafting is still the gold standard regarding augmentation and reconstruction of atrophied and resected jaws [141]. Successful autograft augmentation relies on grasping the wound healing fundamentals, material properties, rigid fixation, and correct graft type selection for the jaw atrophy. The

ultimate aim of grafting is to promote the bone regeneration to be as efficient as the original situation. These goals can be achieved by stimulating the formation of healthy, well-vascularized bone with typical bone properties such as remodeling and physiological healing. These properties allow for adequate insertion of dental implants and lead to proper osseointegration. Via implant-supported prostheses, functional and aesthetic rehabilitation can be well performed. Autogenous non-vascularized bone grafts also offer many advantages over allogenic and xenogeneic materials. They not only serve as placeholders, as most alloplastic materials do, but are permanently integrated into the surrounding tissue and are part of constant bone remodeling of the skeleton. In addition, the risk of an immune reaction is eliminated, and there is a significantly lower risk of wound infection, making them superior to foreign materials in their ability to reconstruct defects. However, additional surgery is required to remove osteosynthesis material, which creates another wound and is a burden on the patient [142]. Furthermore, autogenous bone transplantation requires harvesting procedures, with the risk of donor-site complication. The cost–benefit relationship of such an operation has to be evaluated to validate its indications. This requires follow-up evaluation to report any donor-site morbidity.

1.3.1 Bone grafts from the retromolar area

The extent and dimension of a bone defect influence the type of graft selected. In small and medium defects, a bone graft from the mandibular angle can be performed [15, 143]. These bone grafts show a low complication rate. The advantages of intraoral bone graft harvesting are that the procedure can be performed under local anesthesia and the operating time is short [143]. The surgical principle is to create a standardized bone cavity from the individual horizontal bone defect using a grinding burr with diameters of 5.5, 6.5, or 7.5 mm. Then, adapted trephine drills with corresponding diameters are used to harvest the standardized bone cylinder from the donor side. After the bone harvesting, a guide hole is drilled centrally or in the apical third of the graft, which is

then fixed by lag screw fixation. The screw can be removed three months after augmentation, and implantation can occur [144] (Figures 11, 12).

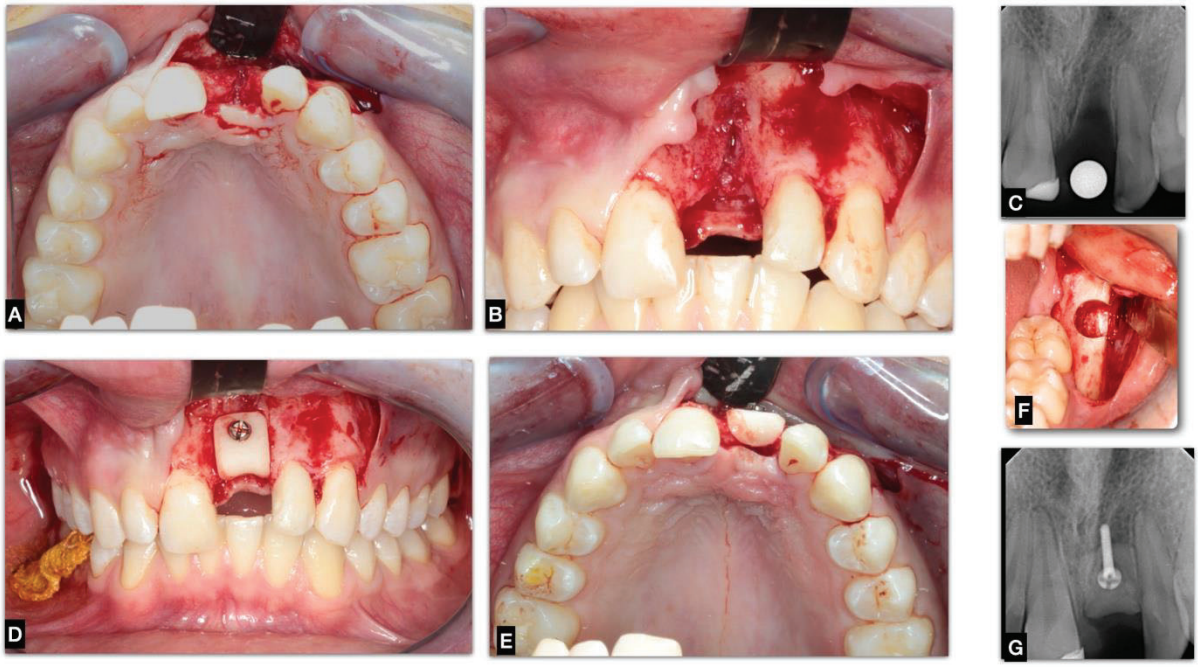

Figure 11. Small alveolar bone atrophy augmented with a bone graft from the retromolar area using standardized osseotransfer: A–B) intra-operative bone atrophy illustration; C) single-tooth radiograph showing atrophy of the left first maxillary incisor alveolar ridge; D–F) harvesting of the bone graft from the mandibular angle and fixation to the atrophied alveolar ridge using a micro-lag screw; G) radiograph after bone transplantation. Clinical case of the Department of Oral and Maxillofacial Surgery, University Hospital Giessen.

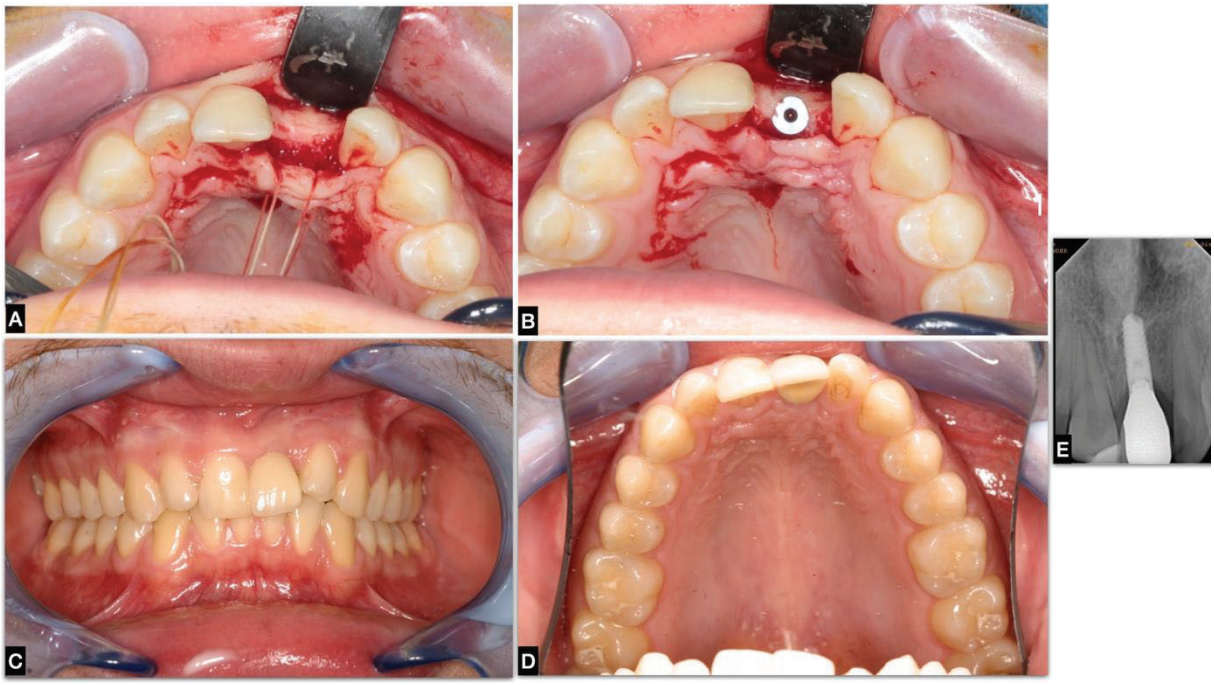

Figure 12. Previous clinical case: A, B) ideal bone healing three months after the augmentation surgery and implant insertion; C–E) Photos and radiograph after insertion of the dental crown. Clinical case of the Department of Oral and Maxillofacial Surgery, University Hospital Giessen.

1.3.2 *Bone grafts from the iliac crest*

In the case of large bone defects due to atrophy after multiple tooth loss, a non-vascularized iliac crest graft is considered the gold standard. Reconstruction of a severely atrophied jaw with iliac crest grafts and endosseous implant placement is a common technique for long-term jaw rehabilitation. Bone loss around an implant placed in the iliac crest is comparable to bone loss in a non-augmented jaw [145, 146]. One of the most important advantages described for iliac crest grafts is that the greatest amount of high-quality cancellous and cortical bone can be harvested with low donor-site morbidity (Figures 13, 14).

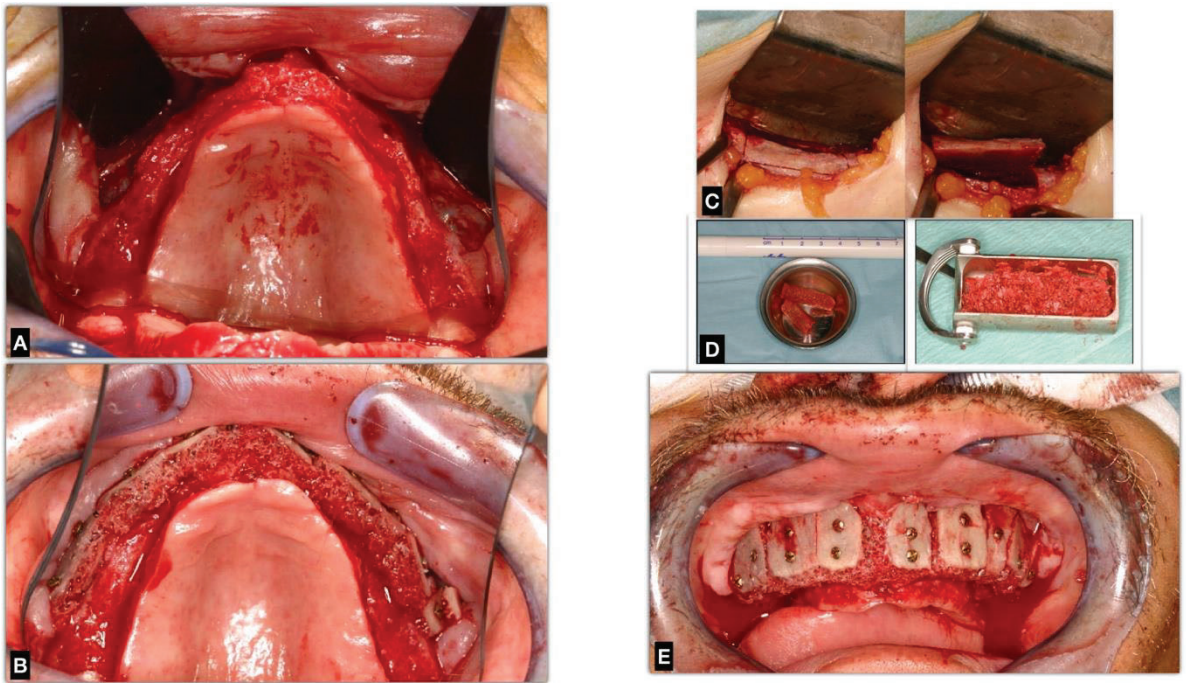

Figure 13. Bone augmentation of atrophied maxilla with iliac crest bone graft: A) intra-operative photos of severe atrophied maxilla; B–D) Cortico-spongiosa bone transplantation from the iliac crest; E) the maxilla after autograft fixation using mini screws. Clinical case of the Department of Oral and Maxillofacial Surgery, University Hospital Giessen.

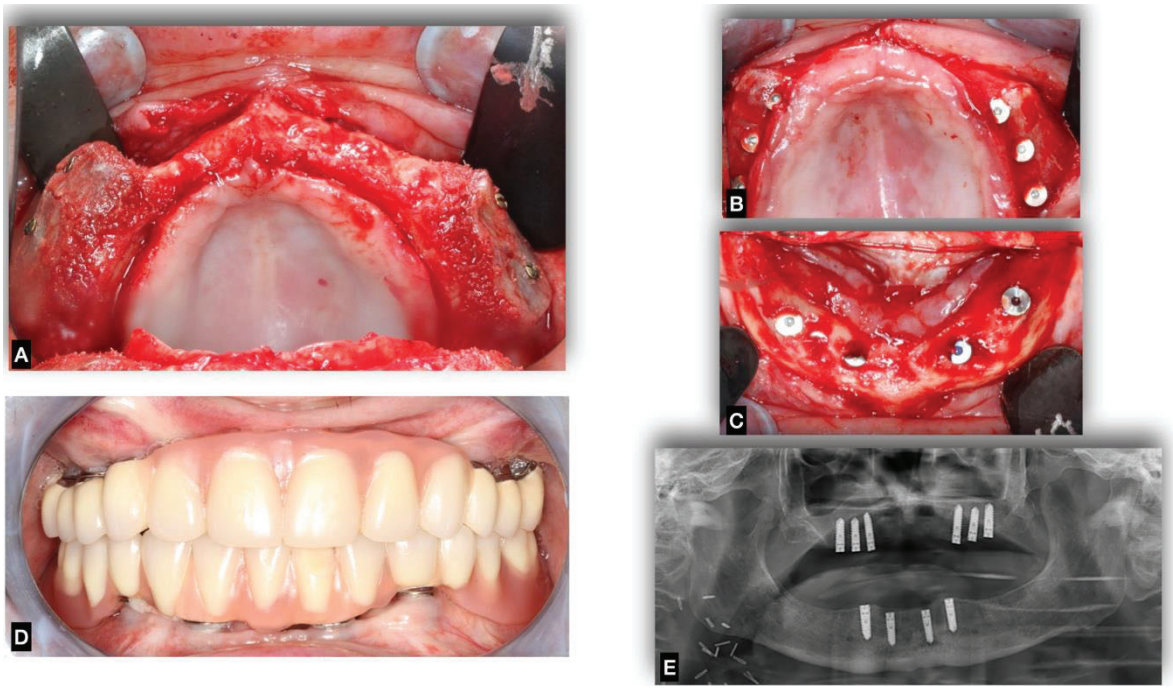

Figure 14. Clinical case after bone augmentation with iliac crest autograft: A) intra-operative photo showing the situation three months after the bone graft, with good healing results; B–C) intra-operative dental implant insertion, six in the maxilla and four in the mandible; D) photos after prosthetic rehabilitation; E) panoramic x-ray after implant insertion. Clinical case of the Department of Oral and Maxillofacial Surgery, University Hospital Giessen.

1.3.3 Microvascular fibula flaps for jaw reconstruction

All abovementioned forms of bone or tissue replacement have an indication limited to small to large defects within the original jawbone. After ablative tumor resection of the jaw, microvascular grafts are an adequate treatment. Of the different free flaps, the fibula flap has proven to be an effective method to reconstruct resected jaws [123, 147]. It is a long-bone flap that can be transferred with skin paddles. Flap raising can be performed with a two-team approach, which reduces the operation time significantly. Endosseous dental implants can be inserted with high primary stability due to the large quantity of cortical bone. Implantation is possible because the thickness of the fibular diaphysis is always at least 1 cm and the bi-cortical bone provides good fixation for the implants. Dental implants inserted in the fibular bone show a high survival rate

and lead to good functional and aesthetic rehabilitation [110, 111] (Figure 15).

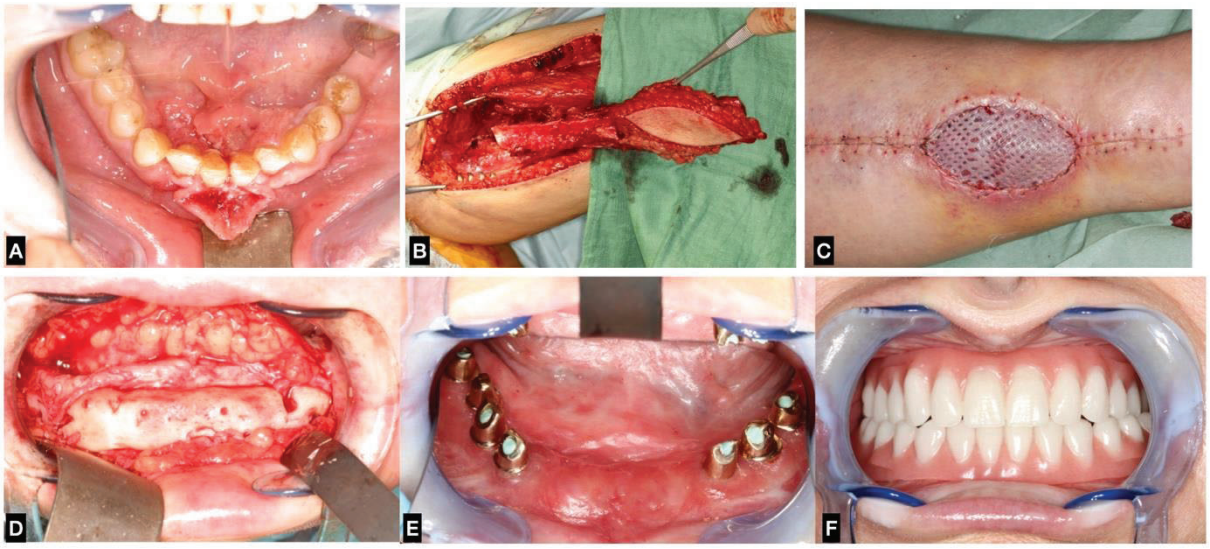

Figure 15. Clinical case of jaw reconstruction with FFF: A) squamous cell carcinoma of the anterior mandible; B) raising of the FFF; C) result at donor site with well-healed skin graft being mashed; D) after bone graft healing; E–F) dental and oral rehabilitation with a dental implant and overdenture prosthesis. Clinical case of the Department of Oral and Maxillofacial Surgery, University Hospital Giessen.

1.3.4 Deep circumflex iliac artery (DCIA) flaps for jaw reconstruction

Vascularized iliac crest free flaps, also known as DCIA flaps, were initially reported by Taylor et al. in 1979 [148]. Over time, DCIA flaps have proven to be reliable and successful for jaw reconstruction [149]. One of their particular advantages is the bone quantity and quality, as a large mass of bone, including cancellous, monocortical, and bicortical bone, can be harvested [150]. This allows for excellent functional and aesthetic treatment outcomes with the help of dental implants, as shown in Figure 16. Other advantages are relatively easy access, the feasibility of a two-team surgical approach, and comparatively low donor-site morbidity [148] (Figure 16).

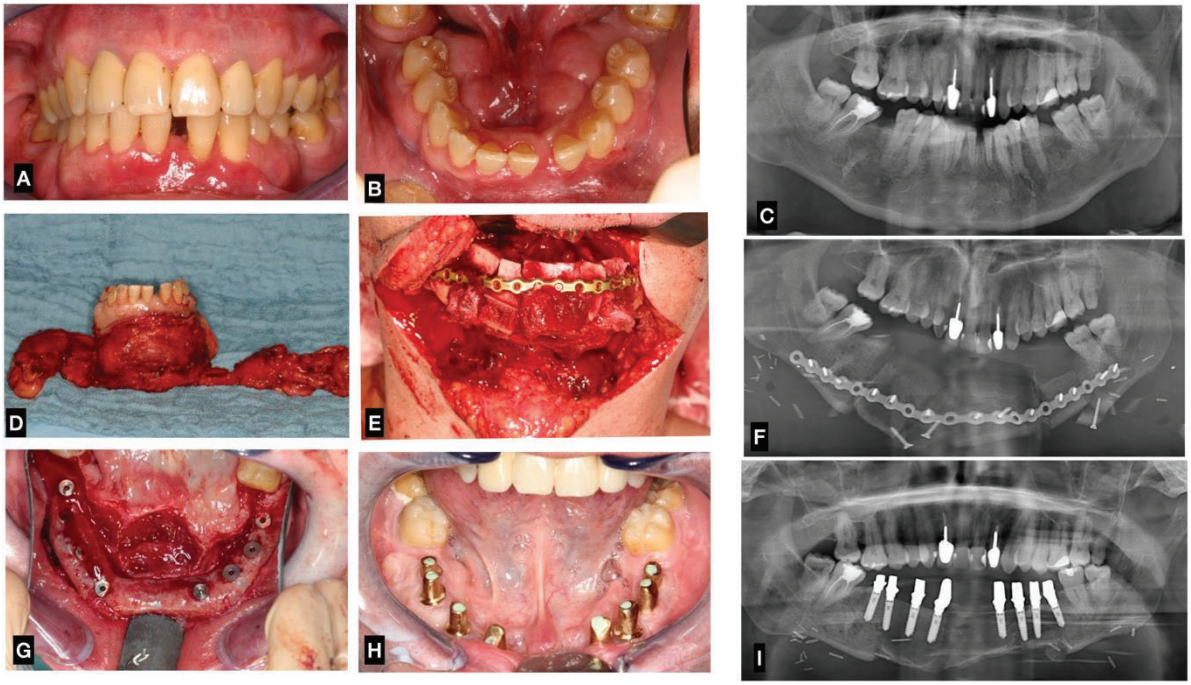

Figure 16: Jaw reconstruction by means of a DCIA flap: A–C) initial intra-oral photos and radiograph of patient diagnosed with osteosarcoma in the anterior of the mandible; D) tumor resection; E) jaw reconstruction; F) postoperative panoramic x-ray; G) implant insertion; H–I) intra-oral photo and radiograph after prosthetic rehabilitation. Clinical case of the Department of Oral and Maxillofacial Surgery, University Hospital Giessen.

1.3.5 PRP and autograft

Many new approaches have been presented in recent years to improve the autograft healing process. Platelet-rich plasma is one such method to improve existing augmentation techniques and make them more efficient [151]. Since the introduction of the positive healing effect of PRP on autologous bone grafts, many studies have been conducted to investigate PRP's effects in this context [152, 153]. Platelet-rich plasma is an autologous concentrate of human platelets in a small amount of plasma [154]. Due to the high concentration of the growth factors contained in the platelets, it is believed that PRP improves bone regeneration, accelerates bone healing, and counteracts resorption processes [151, 155]. In addition, it is assumed that PRP causes faster and better new bone formation, increased ingrowth of blood vessels into the grafts, and, ultimately, a shortened treatment time [156]. Many studies have examined the influence of PRP on augmented autologous bone with controversial results [12, 66, 67, 152, 153, 157].

2 Classification of the present work

A reliable and reproducible system should be developed to identify implant success criteria, which increase proportionally to dental rehabilitation possibilities, technical advancements in clinical treatments, and material sciences. Implant success is also associated with nutritional and dental hygiene habits. It can be appraised by assessing two different aspects. The first aspect is objective and reviews the results of implant survival clinically and radiologically; the second is based on patients' satisfaction with the aesthetics and personal expectations related to the functional outcomes, which are subjective. Both objective and subjective criteria are crucial determinants applicable to healthcare research, as is reflected in this thesis.

The present work hypothesizes that the objective aspects of assessing implant success are more reliable than the subjective aspects. Thus, it provides valuable input to develop clinical healthcare outcomes. This thesis investigates the long-term subjective and objective success outcomes of dental rehabilitation with dental implants in patients with comorbidities considering various aspects/scoring criteria. The clinical data address the following points: 1) oral rehabilitation with and without augmentative materials to enhance bone healing, 2) patients with oral and underlying systemic diseases, and 3) prosthodontic design.

Furthermore, the work also addresses the donor-site morbidity in autograft-aided oral rehabilitation and the outcomes of dental implants in the grafted areas.

The data reflect the limitations in the existing guidelines and current criteria known to determine the success of dental implants and their lack of crucial determinants required to provide better oral care for patients previously suffering from tooth loss (Figure 17).

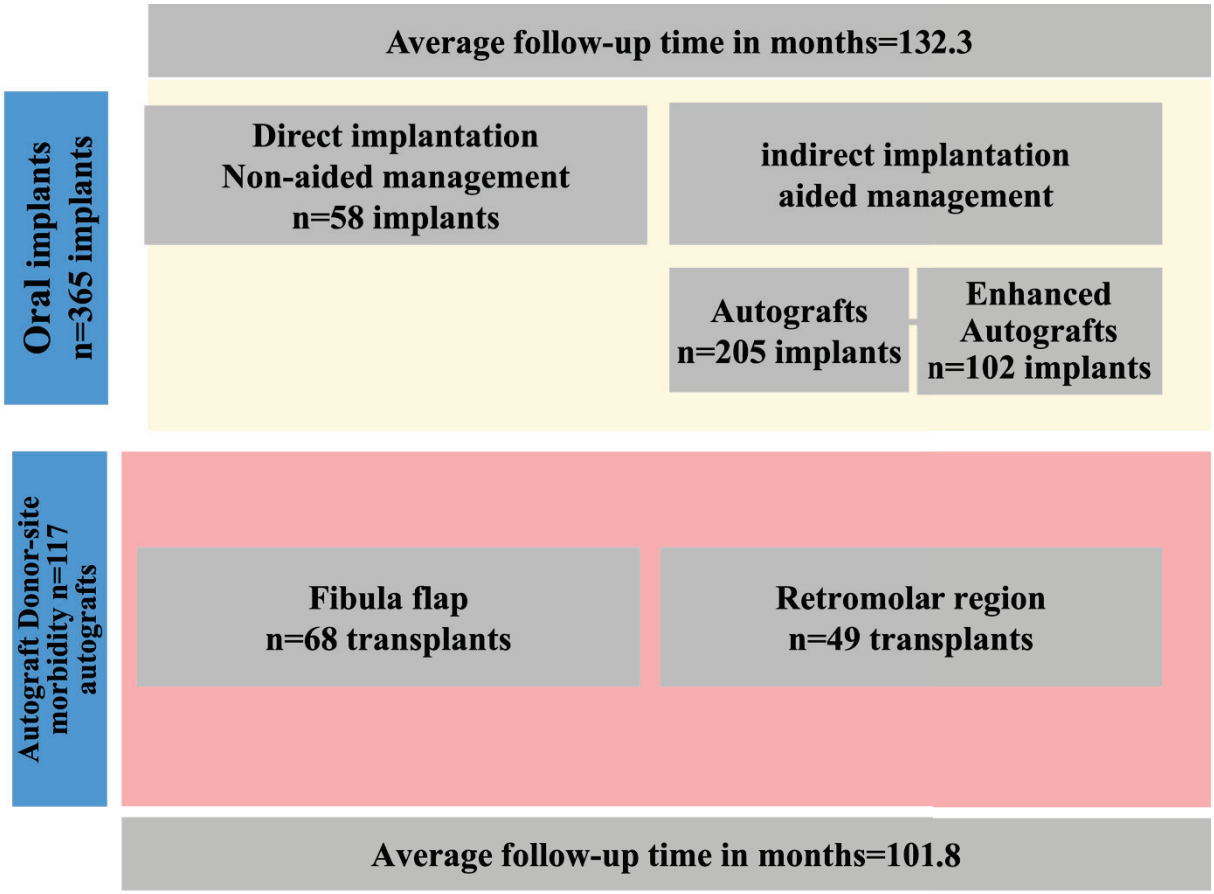

Figure 17. Overview of patient subgroups investigated in this thesis.

2.1 Aims

Dental implants installed in medically and dentally compromised patients do not have an ideal prerequisite for success. Therefore, it has been proposed that an additional surgical procedure may be necessary to optimize the procedural outcomes to allow for implant insertion and long-term success, as these surgeries may cause compilations that can influence the planning phase.

In the light of the gain–risk concept in healthcare research, providing a better understanding of the following aspects, the present thesis aims to do the following:

1. Evaluate the long-term implant success in medically and dentally compromised patients
2. Evaluate the functional and aesthetic treatment outcomes by assessing patient satisfaction as part of the implant success determinants

3. Critically appraise the reasons behind complications that might result after jaw reconstruction or augmentation and donor-site morbidity, highlighting their impact on procedural decision-making.

2.2 Overview of the objectives in this work

1. To evaluate and analyze dental implant survival and success according to defined criteria in patients with hypodontia (Original Article 1)

2. To assess the functional and aesthetic treatment outcomes of patients with hypodontia after dental and oral rehabilitation using endosseous implants (Original Article 2)

3. To analyze the donor-site morbidity and patient satisfaction after alveolar ridge augmentation with standardized cylindrical bone grafts from the mandibular angle via the Osseo Transfer System (Original Article 3).

4. To evaluate implants' long-term success and survival in patients who undergo sinus lifting and jaw augmentation using iliac crest bone with and without PRP (Original Article 4).

5. To evaluate the long-term impact of PRP on clinical and radiological implant outcomes after sinus lifting using iliac crest bone with and without utilization of PRP (Original Article 5).

6. To assess donor-site complications in a split-leg study after fibula transplantation in patients who undergo reconstructive jaw surgery (Original Article 6).

3 Original papers on the topic

3.1 Evaluation of Implant Success in Patients with Dental Aplasia

Attia, S.; Schaper, E.; Schaaf, H.; Pons-Kühnemann, J.; Schlenz, M.A.; Streckbein, P.; Böttger, S.; Howaldt, H.P.; Wilbrand, J.F. Evaluation of Implant Success in Patients with Dental Aplasia. *Biomed Res Int* **2019**, *2019*, 1680158, doi:10.1155/2019/1680158.

Summary

Dental implants are widely depicted as an effective treatment modality for young patients with a reduced number of teeth (hypodontia). However, given the prolonged service period of these implants, a wide array of complications may emerge throughout implants lifetime, requiring good planning and proactive management. Therefore, this retrospective study aimed to evaluate dental implants' survival and success rates in dentally compromised patients with hypodontia.

From November 2000 to February 2016, 43 patients presented with hypodontia or oligodontia at the Department of Oral and Maxillofacial Surgery, University Hospital Giessen, Germany, and received dental implants for functional and aesthetic rehabilitation. While 25 (58%) were females, 18 (42%) were males. The mean age of the patients was 21.44 (17–44) years old, and the majority (76.7%) were young. In 13 (35.1 %) patients with 89 (57.4 %) implants, iliac crest bone grafts were used.

The implants were evaluated using several variables: plaque level, BOP, PD, implant mobility, implant stability, and implant loss. Out of 155 inserted implants, two failed, indicating a survival rate of 98.7%. While the success rate was 96.8%, according to Buser et al.'s criteria, it was 88.4% according to Albrektsson's criteria; such a difference was possibly due to vertical bone loss.

Overall, the dental implants in patients with hypodontia seem to have similar survival and success rates as those placed in an unaffected population [18].

Original Article 1

Hindawi
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Research Article

Evaluation of Implant Success in Patients with Dental Aplasia

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Guest Editor: Maria Sartori

Introduction. Dental aplasia is an anomaly in which the number of teeth is reduced. It is the most commonly occurring dental anomaly during tooth development. Treatment management of patients with dental aplasia is challenging. *Objectives.* The aim of this retrospective clinical study was to analyze the survival and success rates of dental implants placed in hypodontic patients, rated with different criteria. *Methods.* Forty-three patients were diagnosed with dental aplasia and treated with dental implants between November 2000 and February 2016. The variables assessed included the plaque level, bleeding on probing, probing depth, implant mobility, implant stability, and implant loss. To analyze the peri-implant bone level, a panoramic X-ray of each patient was taken. The results were compared with X-rays taken immediately after implantation. *Results.* Thirty-seven patients (16 males; 21 females) participated in this study. In total, 155 implants (86 maxillary; 69 mandibular) were inserted. Two of the 155 implants failed; the *in situ* survival rate was 98.7%. The success rate according to the criteria of Buser et al. was 96.8%, and that according to the criteria of Albrektsson et al. was 88.4%. *Conclusion.* The survival and success rates of dental implants in patients with congenitally absent teeth were very high and did not differ significantly from results achieved in an unaffected population. Dental implants are a reliable therapy for patients with dental aplasia.

1. Introduction

Types of dental aplasia include hypodontia, oligodontia, and anodontia. Hypodontia is the absence of one to five teeth, and oligodontia is the absence of more than five teeth, excluding the wisdom teeth [1]. Anodontia is characterized by the partial or complete absence of deciduous and permanent dentition [2]. The prevalence of dental aplasia in the deciduous dentition varies among countries, with a reported range of 0.2% to 0.9% [3, 4]. Agenesis of the primary dentition is associated with an increased risk of tooth absence in the secondary dentition [5]. The prevalence of hypodontia in the permanent dentition is 2–10% [6, 7]. Several studies have documented an uneven sex distribution for dental aplasia, with a greater prevalence among females than among males [8–10]. The most frequently absent teeth in the permanent dentition are the mandibular second premolars (1–5%), maxillary lateral incisors (0.5–3%), maxillary second premolars (1–2.5%), and mandibular lateral incisors (0.5%). The prevalence of wisdom tooth absence is 10–35% [6]. Dental aplasia is associated with several syndromes, such as ectodermal dysplasia, cleft lip, cleft palate, Rieger syndrome, and Down's syndrome [11]. The etiology of hypodontia may involve genetic (nonsyndromal) factors [12]. Seven genes are known to be associated with the development of dental aplasia: *MSX1*, *PAX9*, *AXIN2*, *EDA*, *EDARADD*, *NEMO*, and *KRT17141* [13]. However, the exact etiopathogenesis of dental aplasia is not completely clear [14]. Although there is no clear relationship between dental aplasia and bone metabolic disease recorded, many clinical signs are generally observed.

Table 1: Summarize the clinical and radiological parameters with the selected scoring system.

Clinical/Radiological Parameters	Scoring system
Plaque index	the modified Mombelli plaque index [31]: (i) Grade 0: no plaque detected by inspection and probing. (ii) Grade 1: accumulation of plaque that is visible only by probing the sulcus with a probe but not with the eye. (iii) Grade 2: visible plaque deposition. Grade 3: massive plaque deposition.
Probing depth	measured using the Click-Probe (Kerr Corporation, Orange, CA, USA) The measurement takes place in four sites around the implant - mesial, vestibular, distal and oral. The maximum measurements in mm were recorded.
Bleeding on probing	The bleeding index is determined parallel to the probing depths. If bleeding occurs during probing, this is indicated in the patient's sheet with a plus sign [+]
Mobility grade/Osseointegration	Periotest® device (Gulden, Modautal, Germany) The manufacturer specifies a scale from -08 to +50. The smaller the measured value is, the better the osseointegration is assessed: (i) Values from -08 to 00: good osseointegration of the implant (ii) Values +01 to +09: A clinical review is needed to investigate osseointegration (iii) Values from +10 to +50: Insufficient osseointegration of the implant
Vertical bone loss	the difference in alveolar bone height between panoramic X-rays taken immediately after implantation and at the follow-up examination in millimeters

These clinical features include tooth morphology (microdontia) and tooth malposition in different manner such as infraocclusion of primary molars, ectopia, and transposition of permanent teeth [15, 16]. Dental aplasia can seriously affect young patients physically and psychologically, particularly during puberty. Interdisciplinary cooperation among dental practitioners is important to achieve optimal treatment outcomes for these patients [2]. Therapeutic options for dental aplasia depend on the number and location of absent teeth, dental implants, resin-bonded or conventionally fixed dental prostheses, autotransplantation sites, and sites of orthodontic tooth gap closure [14, 17–19]. Dental implant placement is a reliable and effective method for the rehabilitation of even augmented jaws [20]. A deciduous tooth can serve as a space maintainer until cranial bone growth is complete and a dental implant can be inserted [21].

Many studies have evaluated dental implants in patients with dental aplasia, with a focus on the implant survival rate [22–27]. Soft-tissue parameters were not evaluated in most of these studies, and implant success was evaluated with self-defined parameters. Standard success criteria were not used in any of these studies. The aim of the present retrospective study was to determine the success and survival rates of dental implants in patients with dental aplasia. Implant success was evaluated using the Buser and Albrektsson criteria [28, 29]. An individual questionnaire was used to collect general patient data and record patient satisfaction.

2. Materials and Methods

Forty-three patients with dental aplasia were treated with endosseous implants at the Department of Oral and Maxillofacial Surgery, University Hospital Giessen, Germany, during 2000–2016. Data collected from patient records included age, sex, number and location of absent teeth, and implant- and prosthetic-based rehabilitation. All selected patients who fulfilled the inclusion criteria were invited to undergo clinical and radiological examinations and an interview that included the administration of a customized questionnaire. The main purpose of the assessment was to evaluate implant success according to the criteria of Albrektsson and Buser [29, 30]. Implant success was defined as the fulfillment of all criteria, and implant failure was defined as the failure to satisfy at least one criterion. Explanted implants, regardless of the reason for removal, were also considered to have failed.

The following clinical parameters were recorded in the assessment of dental implant success: the modified Mombelli plaque index [31], probing depth measured using the Click-Probe (Kerr Corporation, Orange, CA, USA) [32], bleeding on probing (*the mobility grade inferred the osteointegration and stability and was calculated for each dental implant* using the Periotest® device (Gulden, Modautal, Germany)), and the absence or presence of keratinized gingiva (Table 1).

The presence of peri-implant infection was assessed clinically and radiologically at the same time and defined as the presence of a pocket depth ≥ 4 mm, bleeding on probing, and/or exudate and vertical bone loss $> 1.5\,\text{mm} + [0.2\,\text{mm} \times (\text{years} - 1)]$.

Vertical bone loss was determined by calculating the difference in alveolar bone height between panoramic X-rays taken immediately after implantation and at the follow-up examination. The presence of radiolucency around dental implants was assessed on the panoramic X-rays. To exclude measurement error, all panoramic X-rays were obtained with the same device (Sirona®, Bensheim, Germany) and evaluated by the same examiner. The data were collected from the patients' digital files (KAOS software, University Hospital Giessen clinical administration system) and categorized using Microsoft Excel® software (version 2017; Microsoft Corporation, Redmond, WA, USA).

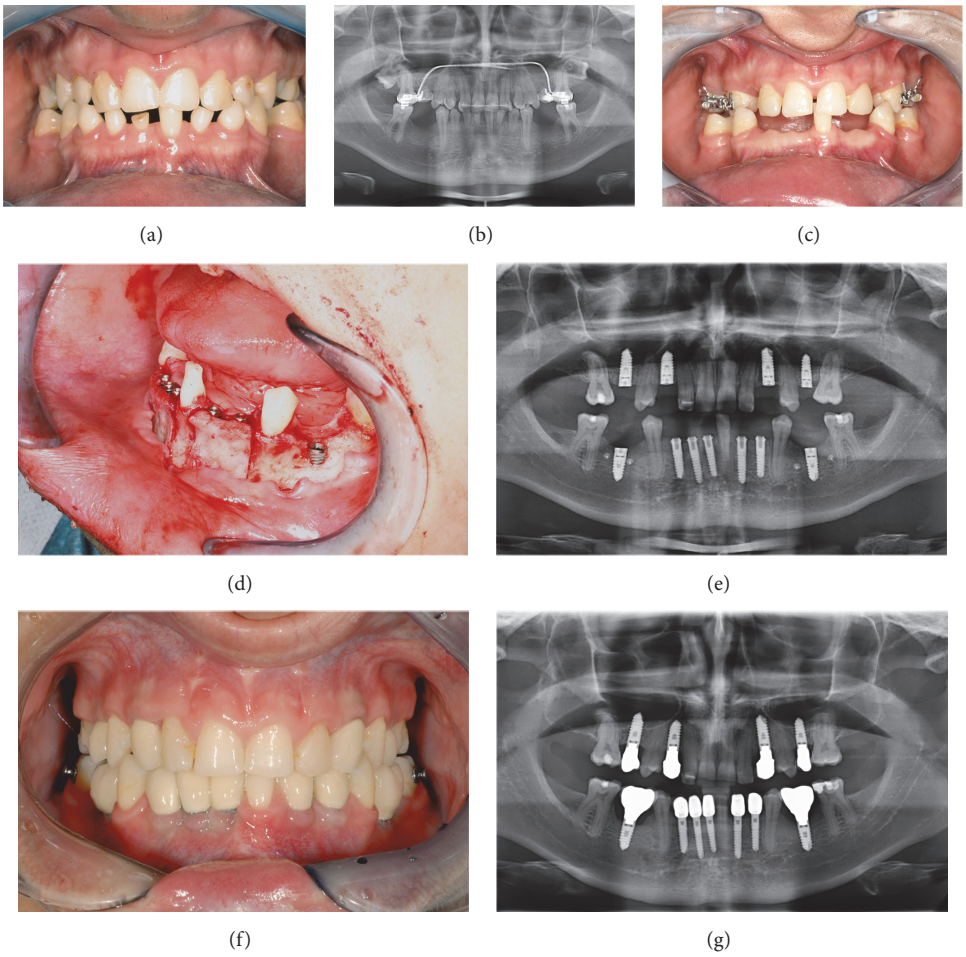

Figure 1: Treatment procedures of patient with oligodontia until oral rehabilitation. (a) Initial condition, patient with oligodontia (13 teeth absent). (b) Panoramic X-ray of the initial case. (c) After deciduous tooth extraction. (d) Intraoperative surgical view, insertion of implant and bone splitting. (e) Postoperative panoramic X-ray showing implant position. (f) Prosthetic rehabilitation with single tooth crowns. (g) Panoramic X-ray, 3 years after implantation.

The research ethics committee of the Faculty of Medicine, Justus Liebig University Giessen, approved this study (no. 209/15).

2.1. Statistical Analysis. Implant survival probability was calculated in a Kaplan–Meier analysis performed in collaboration with the Institute of Medical Informatics of Justus Liebig University Giessen using SPSS software (version 24.0; IBM Corporation, Armonk, NY, USA). *The Chi-square test (χ^2)- or Fischer's more accurate test for categorical variables was applied to investigate the correlation between implant systems used, the type of graft, and age or sex of patients.*

3. Results

Forty-three patients with hypodontia or oligodontia (25 females; 18 males) received dental implants for functional and aesthetic rehabilitation during November 2000–September 2016. All patients were treated surgically at the Department of Oral and Maxillofacial Surgery and prosthodontically at the Department of Prosthodontics of the University Hospital Giessen, Germany. Data on the patients' general condition and personal habits were collected at the time of the follow-up examination. Treatment outcomes were evaluated in 37 patients using a customized questionnaire during the clinical examination. Six patients refused to participate in the study and were counted as dropouts. Patient age at the time of implantation ranged from 17 to 44 years (mean, 21.4 years). The majority (n = 33) of patients treated with dental implants were young. Bone augmentation from the mandibular angle was performed in five (13.5%) patients with eight (5.2%) implants. Iliac crest bone grafts were used in 13 (35.1%) patients with 89 (57.4%) implants. Figure 1 shows a patient with oligodontia and treatment procedures until oral rehabilitation.

3.1. Dental Implants and Survival. In total, 155 implants (86 maxillary; 69 mandibular) were inserted (94 in males; 61 in females; Figure 2).

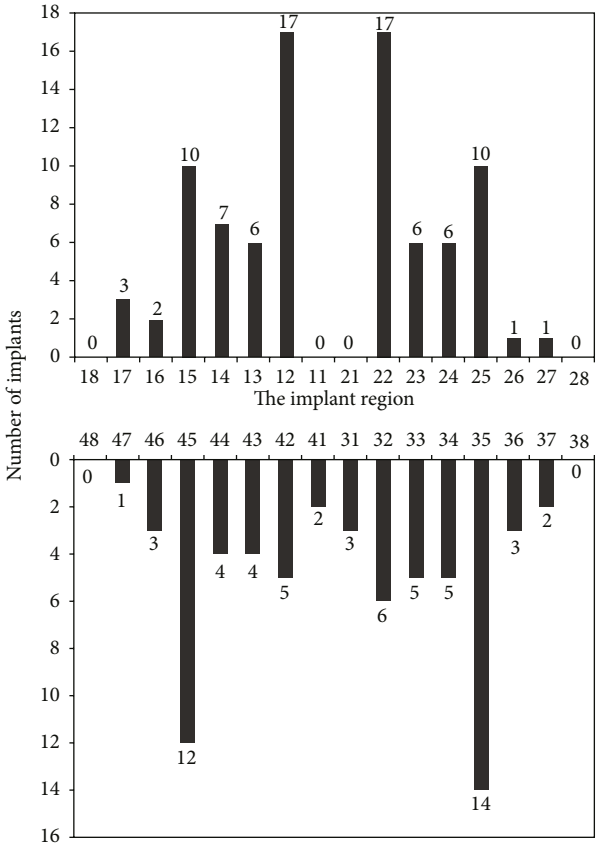

Figure 2: Implant distribution according to dental region.

Three different implant systems were used over the time of observation. In the beginning (Year 2000) mainly Straumann Standard® Implants with a parallel macrogeometry (Straumann, Basel, Switzerland; $n = 10$) were inserted. Within the following years (until 2016) mainly two different implant systems (Xive Plus® with a parallel and self-cutting shape, Friadent, Mannheim, Germany, $n = 105$, and Bego Semados® RI with a conical and condensing shape $n = 28$, and Bego Mini $n = 12$, Bego Implant Systems, Bremen, Germany; total $n = 40$) were inserted. Two implants were explanted at 6 (BEGO-Mini) and 34 months (Xive) after implantation, respectively. The overall implant survival rate over 189 months as determined by Kaplan–Meier Analysis was 98.7% (Figure 3).

3.2. Clinical and Radiological Characteristics of Dental Implants. Clinical and radiological evaluation was performed for 155 implants. Two implants were lost due to explanation. The following parameters were examined: plaque index, probing depth, bleeding on probing, implant mobility, and keratinized gingiva.

Inspection and probing revealed no plaque on 67 (43.8%) implants, grade 1 plaque according to the Mombelli index [31] on 48 (31.4%) implants, grade 2 plaque on 32 (20.9%) implants, and grade 3 plaque on 6 (3.9%) implants.

In total, 128 implants had maximum probing depths of 1.0–4.0 mm, which are considered to be physiologically normal. Probing depths were ≥ 4 mm for 24 implants. At the follow-up examinations, most ($n = 93$) implants did not bleed on probing. None of the 153 dental implants examined showed mobility, as measured manually. Periotest® values for 122 implants ranged from −7 to 0, indicating good osseointegration. Twenty-five implants had scores of 1–9, indicating the requirement for clinical reevaluation. One implant had a score of 13, which represents insufficient osseointegration. Keratinized gingiva was observed around the crowns of most ($n = 137$) implants.

Bone loss was determined radiologically for each implant by comparing bone levels on postoperative and follow-up panoramic X-rays. Bone loss of 0–0.5 mm was recorded for 33 implants, and loss of 0.5–3.5 mm was recorded for 103 implants. Bone loss > 3.5 mm was observed around 17 implants. *No correlation was found between implant systems used, the type of graft, and age or sex of patients in Fischer's exact test, and bilateral correlation testing of all parameters resulted in a p-value <= 0.05.*

3.3. Implant Success according to the Buser Criteria. According to Buser's success criteria, five implants in our sample failed due to explantation ($n = 2$), radiolucency ($n = 2$), and dysesthesia ($n = 1$). Thus, the implant success rate according to these criteria was 96.8%.

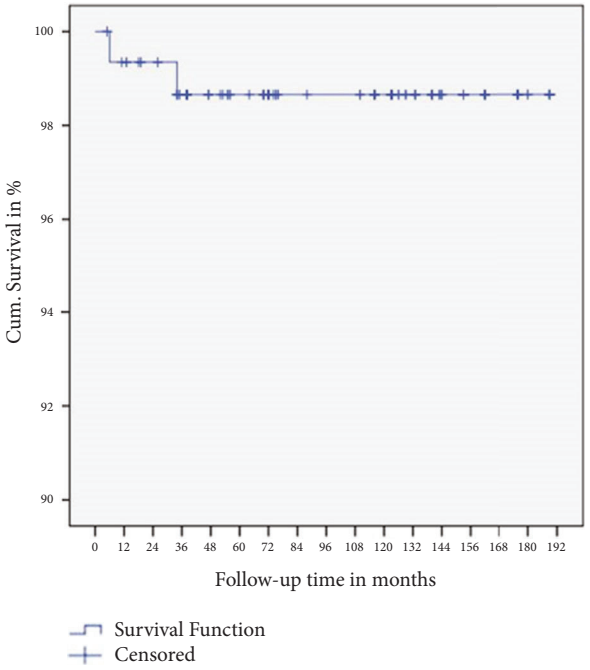

Figure 3: Cumulative Kaplan–Meier survival curve for dental implants.

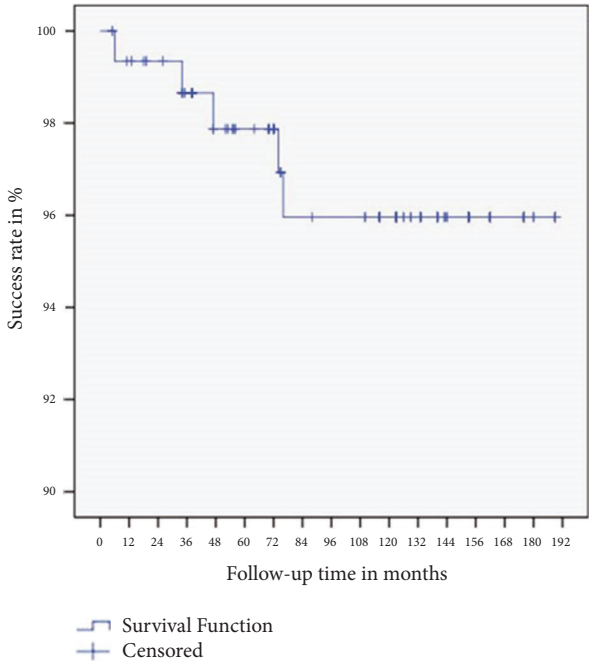

Figure 4: Cumulative success rate according to the Buser criteria.

The Kaplan–Meier curve for these data (Figure 4) shows that five of 155 implants failed during the 189-month (15.75-year) observation period, resulting in a cumulative success rate of 96%.

3.4. Implant Success according to the Albrektsson Criteria. One or more parameters (explantation, radiolucency, dysesthesia, vertical bone loss, and infection) led to the failure of 18 implants. Thus, the implant success rate according to the Albrektsson criteria was 88.4%.

The Kaplan–Meier curve for these data (Figure 5) shows that 18 of 155 implants failed during the 189-month (15.75-year) observation period, resulting in a cumulative success rate of 61%.

4. Discussion

This study considered patients who had received dental implants due to dental aplasia, regardless of whether the condition was hypodontia, oligodontia, ectodermal dysplasia, or cleft lip or palate. Limitations of this study were related to the numbers of patients (n = 37) and dental implants (n = 155) included. This relatively small sample is not representative of a larger population. Due to the rareness of dental aplasia, smaller numbers of patients and implants were included in previous studies [27, 33, 34]. The sex distribution in this study was 43.2% male and 56.8% female patients (ratio, 1:1.3). Similar distributions have been reported in the literature [8, 9]. Patient age at the time of implantation in this study ranged from 17 to 44 years (mean, 20 years), and 89.2% (n = 33) of patients were aged 17–23 years. Other studies have included similarly young patient groups [35, 36]. A possible explanation for the predominance of young patients is that early implant treatment planning commences at the age of 17–21 years, when cranial growth is complete. The most frequently absent teeth replaced with dental implants in this study were the maxillary lateral incisors and maxillary and mandibular second premolars. This prevalence distribution is comparable to results from the literature [7, 9]. The implant loss rate in this study was 1.3% (n = 2), and the *in situ* implant survival rate was 98.7% (n = 153/155). One implant was lost after 34 months due to osseointegration failure, and another was lost after 6 months due to peri-implantitis. Notably, the latter was a mini-implant with a diameter of 2.9 mm and length of 11.5 mm. Becelli et al reported a survival rate of 96.6% for 60 implants in 8 oligodontic patients [34]. In a review and meta-analysis of 19 articles on this topic, survival rates ranged from 76.6% to 100%, and the overall survival rate was 95.3% [37]. Comparable results were recorded in the present study.

4.1. Implant Success Criteria. The survival of dental implants is not necessarily equivalent to their success. The assessment of implant success in addition to survival is very important in the evaluation of treatment outcomes. Many similar studies of dental implants in patients with dental aplasia did not involve the use of implant success criteria [37]. In studies assessing implant success, self-defined criteria or the sole criterion of the marginal bone level had been applied [38–40]. Therefore, comparison of implant success rates between this study and previous studies is not meaningful. In this study, implant success was evaluated using the criteria of Buser et al. [30] and Albrektsson et al. [29]. Two sets of

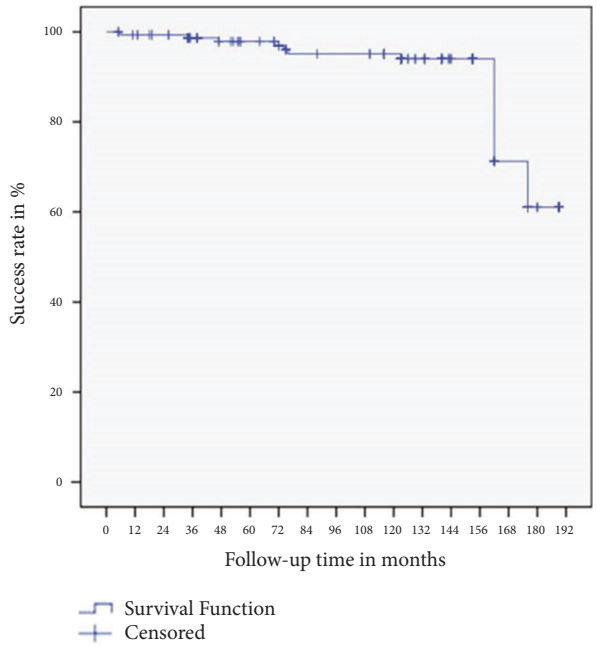

Figure 5: Cumulative success rate according to the Albrektsson criteria.

criteria were used to enable the consideration of differences in implant success in an identical patient sample resulting from the use of different measures. Depending on the criteria used, the implant success rate in the same patient sample may vary. According to the Buser criteria, five implants in this study were considered to have failed (two due to radiolucency and one due to paresthesia). According to the Albrektsson criteria, an additional 13 implants from the same sample failed (total, n= 18). Unlike the Buser criteria, the Albrektsson criteria include vertical bone loss and the presence of infection (peri-implantitis). As a result, the peri-implant hard and soft tissues were evaluated more stringently, which explains the lower success rate. However, neither of these criteria includes subjective assessment of dental implants. Only the success criteria of Jahn and d'Hoedt [41] consider patient satisfaction. Buch et al. criticized the use of only hard- and soft-tissue evaluations for the assessment of implant success and recommended additional subjective assessment of patient satisfaction [42]. About 30 years ago, researchers used primarily measurable clinical parameters to detect disease-related impairments and evaluate therapeutic success; today, patients' perceived satisfaction has become focal [43]. For this reason, patient satisfaction should be taken into consideration in the future establishment of success criteria. The Buser and Albrektsson criteria also neglect the assessment of prosthetic outcome, which should be considered in future development of success criteria. A new implant success assessment tool could also employ score calculation in which criteria (clinical and radiological parameters, prosthetic outcome, and patient satisfaction) are differentially weighted statistically. The classification of implant success should be graded (e.g., very good, good, medium, and bad), so that a less successful implant does not necessarily mean complete failure.

5. Conclusion

In this retrospective study, 155 implants were inserted in patients with dental aplasia (risk group) and examined during a median observation period of 10.25 years. The survival rate (98.7%) was comparable to those of other studies conducted with normal cohorts. Patient satisfaction parameters are planned to be acquired, addressed, and discussed in a future manuscript. In this study, two sets of criteria were used to measure implant success. The implant success rate was higher according to the Buser criteria (96.8%) than according to the Albrektsson criteria (88.4%). The main reason for the lower Albrektsson implant success rate is the assessment of marginal bone loss. Further development of a complex implant success scoring system might be useful for standardized follow-up evaluation of dental implants.

Data Availability

The data used to support the findings of this study are available from the corresponding author upon request.

Conflicts of Interest

The authors declare no conflicts of interest.

Acknowledgments

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3.2 Oral Rehabilitation of Hypodontia Patients Using an Endosseous Dental Implant: Functional and Aesthetic Results

Attia, S.; Schaaf, H.; El Khassawna, T.; Malhan, D.; Mausbach, K.; Howaldt, H.P.; Streckbein, P. Oral Rehabilitation of Hypodontia Patients Using an Endosseous Dental Implant: Functional and Aesthetic Results. Journal of Clinical Medicine 2019, 8, 1687, doi:ARTN 168710.3390/jcm8101687.

Summary

Oral rehabilitation of dental and additionally medically compromised patients diagnosed with severe hypodontia is challenging. In this retrospective study, the functional and aesthetic treatment outcomes were investigated, and the results were correlated with the implant success according to Albrektsson's criteria. Here, 37 patients with 155 dental implants and a follow-up time varying between 5 and 189 months were reinvestigated concerning the following variables: positive family history of hypodontia, patient satisfaction, functionality, and aesthetic outcome. The patients' ages ranged from 17 to 44 years old (mean ± SD: 21.4 ± 5.6). Moreover, 28 patients were missing 1–5 teeth, whereas 9 were missing more than 6 teeth. Dental aplasia was previously detected in at least one family member of 24 of the patients (64.9%). Most of the study subjects (32 patients, 86%) had an orthodontic treatment prior to the implant treatment. An average of 1–2 implants was inserted in 62% of the included patients, whereas 38% had between 3 and 15 implants. Eighteen implants were unsuccessful according to Albrektsson's criteria; two of them had already been removed. For the dentally compromised patients with alveolar ridge atrophy, autografts (either from the iliac crest or retromolar region) were used for bone augmentation of 97 implants. Most of the study subjects were satisfied with their chewing function (69.4%) as

well as pronunciation (80.6%). The aesthetic result was given an excellent rating by 17 patients (47.2%).

With interdisciplinary treatment planning and dental implants, dentally compromised patients with dental aplasia can undergo dental and oral rehabilitation, leading to satisfactory, functional, and aesthetic treatment outcomes [19].

Original Article 2

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Article

Oral Rehabilitation of Hypodontia Patients Using an Endosseous Dental Implant: Functional and Aesthetic Results

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Abstract: Hypodontia often leads to limited bone availability of the alveolar ridges. Oral rehabilitation of severe hypodontia patients is challenging. In this retrospective study, we evaluated the functional and aesthetic results after dental implants in hypodontia patients, corroborated by Albrektsson implant success criteria. Over a period of 15 years (2000–2015), a total of 43 patients were diagnosed with hypodontia and 165 dental implants were inserted. Six patients who received 10 implants were lost in the follow-up. We examined 155 implants in 37 patients between December 2015 and May 2017. Besides family history, patients evaluated the general satisfaction, functionality, and aesthetics of the implants. Study subjects were between 17 and 44 years old (mean ± SD: 21.4 ± 5.6). Hypodontia patients were missing one to five teeth (n = 28), whereas patients diagnosed with oligodontia (≥6 missing teeth, n = 9). In this study, 24 patients (64.9%) with hypodontia had a positive family history; the remaining 13 patients had no family member with hypodontia. The final follow-up time ranged between 5 and 189 months after implant placement. Orthodontic treatment was performed in 32 patients (86%) before implant placement. Rehabilitation resulted in 62% of the cases being treated with 1–2 implants and 38% treated with 3–15 implants. However, out of 155 inserted dental implants, 18 implants failed to meet Albrektsson criteria, under which two implants were removed. Only autografts were used for bone augmentation with 97 implants. More than two-thirds of the patients showed high general satisfaction and masticatory function (69.4%) as well as phonetic ability (80.6%). The aesthetic outcome was rated as excellent by 17 patients (47.2%). The findings emphasize the importance of interdisciplinary treatment of hypodontia, leading to a satisfactory, functional, and long-term fixed prosthodontics using dental implants.

Keywords: tooth agenesis; hypodontia; dental implants; quality of life; implant success

1. Introduction

Hypodontia is the most common congenital anomaly in tooth development [1–3] that results in tooth agenesis. A cut-off of five missing teeth differentiates between hypodontia and severe hypodontia (oligodontia) [4]. Studies reported a 2–10% incidence rate of hypodontia in the secondary dentition, with women being more affected than men [5–7]. Although tooth agenesis be associated with other

syndromes or occur as a result of genetic factors [8–12], the exact mechanism of hypodontia is not fully understood [13].

Hypodontia may result in complex sociopsychological problems, especially during puberty and in the case of face disproportion. Therefore, treatment options with good long-term functional and aesthetic rehabilitation results are urgently needed [1]. However, a multidisciplinary team is often required with different competences, including maxillofacial surgeons, orthodontists, prosthodontists, speech pathologists, and psychologists, to treat severe hypodontia [14–18].

Patients with face disproportion and with either class II or III malocclusion need a combination of orthodontics and orthognathic treatment before teeth replacement [14,16]. Conservative prosthetic treatment options have limitations in severe hypodontia cases and might lead to unsatisfactory results [15,19]. Besides patient dissatisfaction, removable partial dentures have a short life span of 3.5–4 years due to wear and fracture [17,20]. In contrast, replacing missing teeth with dental implants in hypodontia and other indications has been shown to achieve adequate success in terms of function, aesthetics, dental rehabilitation, and long-term survival [5,18,21–23].

Adequate alveolar bone and keratinized gingiva have been implicated in successful implant insertion [24]. The presence of remaining deciduous teeth preserves the buccal bone, and their early loss leads to alveolar bone atrophy [10]. However, the surgical removal of an ankylosed deciduous tooth is often associated with local bone loss. Therefore, augmentation before dental implant placement is often required in such situations [25]. Iliac crest bone graft is the gold standard for jaw augmentation and is mainly used in patients with large amounts of alveolar bone atrophy [26]. Alternatively, intraoral bone harvesting from the retromolar area, chin, or maxilla can be performed to rebuild the atrophic area [27,28]. Autografts provide important properties for bone formation, such as osteogenesis, osteoconduction, and osteoinduction [26]. Besides autografts, an allograft, xenograft, or a combination of grafts have been successfully implemented [29].

Long-term aesthetic, functional, and satisfaction results in hypodontia patients are not adequately addressed in the literature [23]. The survival of dental implants is not an indication of their success [30]. Therefore, a comparison between implant survival and patient satisfaction as a success criterion has, to the best of our knowledge, not yet been addressed. The new generations of implants are designed with improved material, geometry, and concepts in comparison with the early models.

Taken together, these reasons inspired us to revisit the decades-old standards of implant success criteria by including not only survival but also functionality and aesthetics as defined by patients. Thus, clinically qualified personnel can improve approaches to meet the needs of patients within the limits of successful treatment prerequisites. Therefore, we reassessed the same subjects reported in a recent study addressing implant survival and success in patients [30] to evaluate aesthetic and functional treatment results. In this retrospective study, we compared these results with implant success according to the Albrektsson criteria.

2. Materials and Methods

2.1. Ethics and Privacy

This study was approved by the ethics committee of the Faculty of Medicine at Justus-Liebig University (Giessen, Germany; approval no. 209/15). The anonymity of the patients was ensured by assigning each patient a number; the statistical evaluation then occurred only with the assigned numbers.

2.2. Study Design

This retrospective, clinical, observational study included all hypodontia patients (n = 43) treated with dental implants in the period from January 2000 to December 2016 at the Department of Oral and Maxillofacial Surgery, University Hospital Giessen, Germany.

2.3. Exclusion Criteria

The following exclusion criteria were considered in this study: (1) patients physically unable to respond to the questionnaire; (2) patients with a disease or take a medicine that direct influences osseointegration; and (3) female patients who were pregnant at the time of the follow-up.

2.4. Surgical Procedures

Recommended and standardized surgical protocols were followed for oral implants. The dental implant site and size were based on preparatory diagnostic aids and clinical assessment including bone quality. Drilling was maintained below 800 rpm under constant irrigation with normal saline. Implant placement was attempted using an electrical micro motor with a maximum torque of 50 N·cm.

2.5. Measured Variables

We interviewed 37 (21 women and 16 men) of the 43 (25 women and 18 men) patients using a customized questionnaire: 28 with hypodontia and nine with severe hypodontia. The questionnaire was used to collect data regarding the patients' sex, general diseases, family history related to hypodontia, smoking behavior, general satisfaction with dental implants, chewing ability, pronunciation, and aesthetic outcome.

General satisfaction, chewing ability, pronunciation, and aesthetic outcomes were assessed using the German grade ranking: grade 1 = excellent, grade 2 = good, grade 3 = acceptable, grade 4 = adequate, grade 5 = poor, and grade 6 = unsatisfactory. Types of prosthetic restorations and their complications (e.g., crown and abutment loosening, screw fracture, and ceramic chipping) were recorded.

Photographic documentation was recorded for all cases at the follow-up examination. This included a frontal image as well a picture of the upper and lower jaw. If removable dentures were present, a photo was captured with and without dentures. Implant loss was defined as the complete removal of an implant.

Implant success was evaluated using the Albrektsson implant success criteria [31], as reported in a previous study [30]. In the present study, we analyzed the Albrektsson criteria for successful and failed dental implants with regard to: augmentation, augmentation type, prosthetic type, implant company, general satisfaction, aesthetics, speech, and chewing function.

2.6. Statistical Analysis

Statistical analysis for this study was conducted using the statistical package PASW 24.0 (IBM Corporation, Armonk, NY, USA). Data were examined for their Gaussian distribution and were found to be non-parametric. Frequency analysis was conducted using the chi-square test to compare the implant success and failure. Data are presented as bar graphs with whiskers of the standard error of means.

3. Results

A total of 43 patients (25 women and 18 men) were diagnosed with hypodontia and treated with 165 dental implants. Six patients did not respond to follow-up. Therefore, 37 patients (21 women and 16 men) were included in this analysis. Twenty-eight patients were diagnosed with hypodontia when missing one to five teeth, whereas the nine patients diagnosed with severe hypodontia were missing 6–20 teeth.

The final follow-up time was recorded per implant (not patients). The follow-up ranged between a minimum of 5 and maximum of 189 months, with a mean ± SD of 109.92 ± 54 and a median of 123 months.

A total of 155 dental implants were inserted in hypodontic areas. Two implants were rated as failures and were removed (1.3%); this resulted in a survival rate of 98.7% (Table 1). The implant success according to Albrektsson criteria was 88.4% with 18 implant failures [30]. Figure 1 shows the

number of inserted implants in each patient. The medical conditions of patients were recorded prior to treatment (Table 2). Inserted dental implants in relation to missing teeth were categorized as follows: 50 incisors, 21 canines, 68 premolars, and 16 molars (Supplementary Table S1).

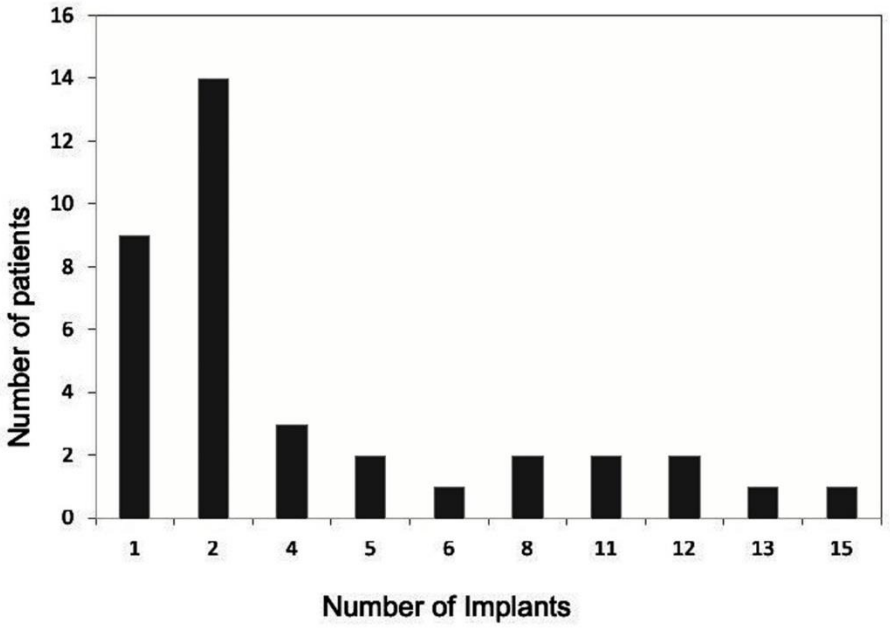

Figure 1. Number of inserted implants per patient (n = 155).

Table 1. Overview of patients regarding number, sex, drop-outs, and implant removal.

	Number of Patients	Number of Implants
Total number of patients	43	165
Men	18	97
Women	25	68
Drop-outs	6	10
Investigated patients	37 *	155
Removed implants	2	2
Implant failure (Albrektsson)	7	18

* A total of 42 patients were selected with the inclusion criteria; however, only 37 patients who responded to the questionnaire and follow-up were investigated. Those six patients were considered drop-outs; therefore, they were not included in the statistical analysis. The removed implants were considered only in the investigated patients.

The following representative case reflects the diagnostic and treatment procedure and outcome. A 23-year-old female patient was referred to our department with hypodontia and gaps in the left maxillary: first premolar and lateral incisor regions. The patient had class III malocclusion and was orthodontically and orthognathically treated. Clinical and radiographical investigation showed bone atrophy in the maxillary lateral incisor region, meaning that we augmented this area with bone harvested from the retromolar region. Three months later, we inserted two Xive Plus® dental implants (Dentsply Friadent, Mannheim, Germany). In February 2013, the implants were exposed and two single ceramic crowns were inserted. A follow-up investigation, including the assessment of functional and aesthetic outcomes, was performed 56 months later (Figure 2).

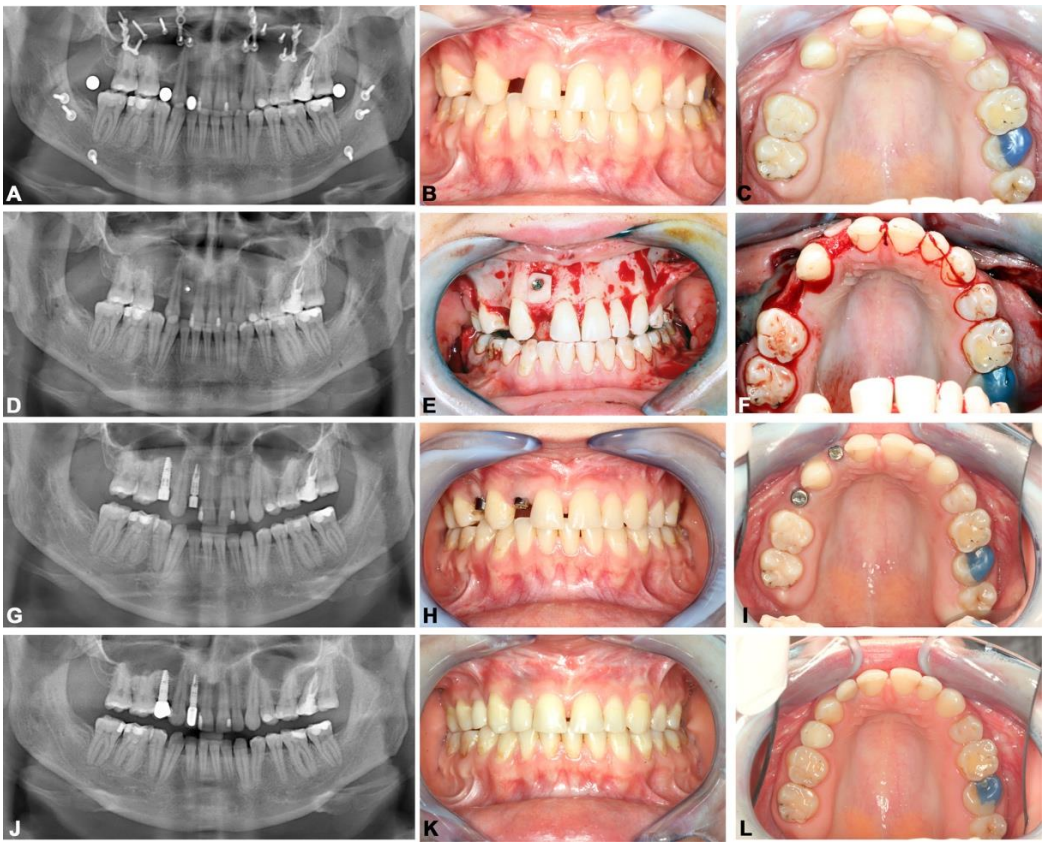

Figure 2. Dental rehabilitation of patient with hypodontia. (**A**–**C**) Panoramic radiograph and intraoral photos showing the situation after orthognathic surgery and teeth gaps in the left maxillary: first premolar and lateral incisor region. (**D**–**F**) Panoramic radiograph and intra-operative photos showing bone augmentation in the left maxillary lateral incisor region. (**G**–**I**) Panoramic radiograph and intraoral photos after the exposure of the implants. (**J**–**L**) Panoramic radiograph and intraoral photos after 54 months of prosthetic rehabilitation.

The general condition of patients, as well as existing allergies at the time of follow-up, were documented. The smoking behavior of the patients was also noted. Table 2 lists the patients with general conditions, allergies, and regular nicotine consumption.

Table 2. Patients' medical condition, allergies, and smoking behavior recorded prior to treatment.

General Disorders, Allergies, and Smoking Behavior	No. Patients
Cleft lip/palate	2
Diabetes Type 2	2
Bronchial asthma	1
Blood clotting disorder	1
Ectodermal dysplasia	2
Hypothyroidism	3
Allergy: penicillin	1
Smoking	10

Overall, four patients had syndromes associated with hypodontia. To assess possible genetic factors related to the presence of hypodontia, patients were asked about family history of hypodontia (parents, grandparents, siblings, and siblings of the parents). A total of 24 patients (64.9%) with hypodontia had a positive family history in this study; the remaining 13 patients had no family member with hypodontia. The age of the 37 patients at the time of implant placement ranged from 17 to

44 years, with a mean ± SD of 21.4 ± 5.6 and a median of 20 (Figure 3). Predominantly young patients (17–23 years, n = 33) received dental implants after the completion of cranial bone growth.

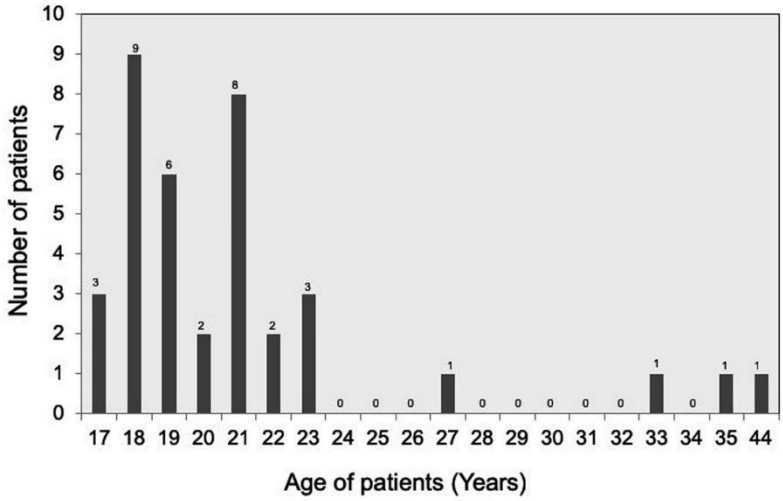

Figure 3. Age distribution of the 37 patients at the time of implant insertion.

Patients with hypodontia either have class I, II, or III malocclusions. In this study, 30 patients reported with class I, one with class II, and six with class III malocclusion. Surgical management was necessary in seven patients who had class II and III, including bimaxillary advancement (four patients) and Le Fort 1 osteotomy (two patients), whereas bisagittal split osteotomy of the mandible was performed in one patient. Thirty-two patients received orthodontic treatment prior to implant placement (Table 3).

Table 3. The relationship between the aesthetic treatment outcomes and the orthodontic treatment prior to implant placement.

No. of Patients (%)	Aesthetics	Orthodontic Treatment Prior to Implant Placement?	
		No	Yes
17 (47.22%)	Very good	2 (5.55%)	15 (41.66%)
16 (44.44%)	Good	2 (5.55%)	14 (38.88%)
2 (5.55%)	Satisfactory	1 (2.77%)	1 (2.77%)
1 (2.77%)	Unsatisfactory	0	1 (2.77%)

In 18 patients, alveolar ridge augmentation was performed either from the retro molar region (five patients (13.5%) and eight implants (5.2%)) or from the iliac crest (13 patients (35.1%) and 89 implants (57.4%)). Three different implant systems were used: 40 implants (25.8%) with Bego® Semados (28 implants with Semados RI and 12 with Semados Mini/Bego Implant Systems, Bremen, Germany), 10 implants (6.5%) with Straumann Standard® (Straumann AG, Basel, Switzerland), and 105 implants (67.7%) with Xive Plus® (Dentsply Friadent, Mannheim, Germany). The time between implantation and follow-up was 5–189 months. The difference between follow-up examinations at the time of implantation constituted the in situ time of the implants (n = 155; mean age = 9.16 years, SD = 4.5 years, and median = 10.25 years).

Two implants were removed (1.3%): one after 6 months and one after 34 months due to periimplantitis. This resulted in survival rates of 97.7% and 100% for the upper and lower jaw, respectively. Survival rates for each implant company were as follows: Bego®, 97.5% (Bego Implant, Bremen, Germany); Xive®, 99% (Dentsply Friadent, Mannheim, Germany); and Straumann®, 100% (Straumann AG, Basel, Switzerland).

3.1. Patient-Related Parameters

Functional and aesthetic outcomes were evaluated using a questionnaire. Of 37 patients, one could not answer the questionnaire because the dental implant was removed before the study. Figure 4 summarizes the patients' answers using pie graphs in the categories of general satisfaction, chewing ability, pronunciation, and aesthetic outcome (n = 36) in percentages using the German School grading system.

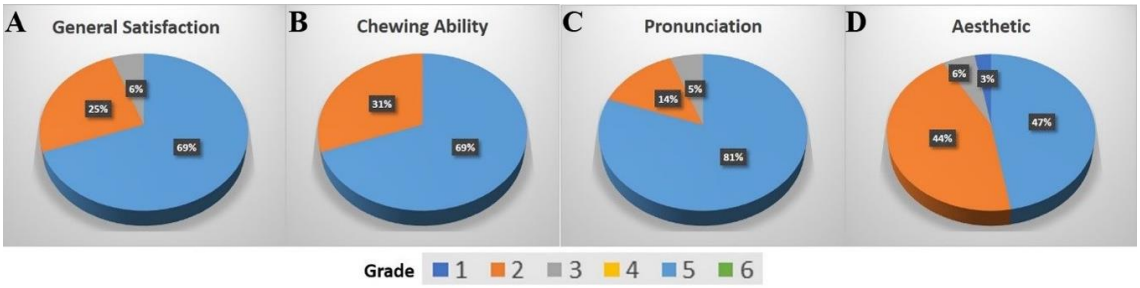

Figure 4. Satisfaction parameters of patients at the follow-up time graded using the German school grading system, in which 1 is the best and 6 is the worst. Left to right: (**A**) general satisfaction, (**B**) chewing ability, (**C**) pronunciation, and (**D**) aesthetics of patient (n = 36).

Most of the patients (n = 25, 69.4%) reported general satisfaction with the dental implant, assigning an excellent grade; nine (25%) patients rated it good; and two (5.6%) patients rated it as acceptable. The chewing ability was rated excellent by 25 patients (69.4%) and good by 11 (30.6%). The pronunciation quality was rated excellent by 29 patients (80.6%), good by five patients (13.8%), and two (5.6%) rated it acceptable. In the aesthetic category, 17 (47.2%) patients rated the outcome excellent, 16 (44.4%) patients rated it good, and two (5.6%) rated it acceptable. Only one patient (2.8%) did not like the aesthetic outcome. In this patient, the implant surface was present under the mucosa. Regarding an improvement in quality of life due to the use of implants, patients provided very good and medium ratings (29 patients very good and eight medium).

Single-tooth crowns were used for 100 implants. In one patient with 15 implants, a double crown prosthesis was used for prosthetic reconstruction. Prosthetic restoration for 37 implants was an implant-supported bridge. Prosthetic complications were documented: crown loosening was observed in four implants, abutment loosening in one implant, and a screw fracture in one implant. All problems were reversible and could be repaired.

3.2. Analysis of Implant Success Using Albrektsson Criteria

The overall success of implants (n = 155) among patients (n = 37) was evaluated using Albrektsson criteria [31]. We evaluated 21 women and 16 men. Only two of 61 implants (3.27%) in women and 16 of 94 implants (17%) in men failed to meet the Albrektsson criteria. Frequency analysis was performed, and the results are presented as bar graphs with the standard error of the mean (Figure 5).

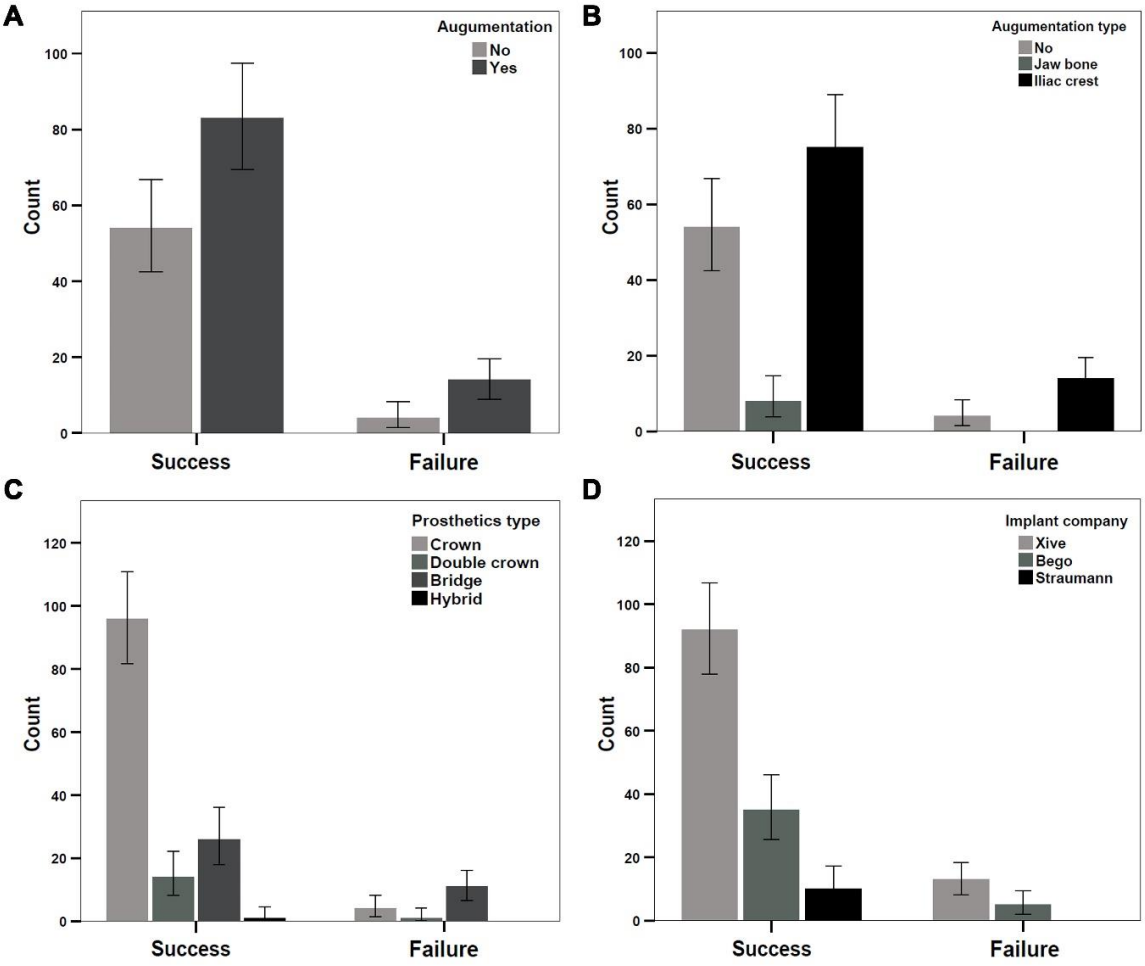

Figure 5. Frequency analysis revealed differences in the success and failure of implant materials based on the Albrektsson criteria. Implant success among patients was investigated through (**A**) the use of augmentation, (**B**) the choice of augmentation material, (**C**) the use of prosthetics, and (**D**) the choice of implant material.

Bone augmentation was performed for 97 of 155 implant sites prior to implant placement. According to Albrektsson criteria, 14 implants failed in patients with augmented bone defects, and four implants failed in patients without bone augmentation (Figure 5A). Bone was harvested either from the jaw bone (eight implant sites) or iliac crest (89 implants sites); the use of the jaw bone as a grafting material showed no implant failure (Figure 5B), whereas implant failure was exclusively observed in areas grafted with iliac crest (14 of 89 = 15.7%; Figure 5B).

Four different prosthetic designs were used to treat the patients: crown, double crown, bridge, and hybrid. A dental crown was applied in 100 implants, of which three showed failure (Figure 5C). Bridge prosthetics were applied in 37 implants, of which 11 showed failure. Double crown prosthetics were applied in 15 implants, of which two implants showed failure (Figure 5C).

We analyzed four different implant systems in the patients: one system from Xive (Dentsply Friadent, Mannheim, Germany), two systems from Bego (Bego Implant, Bremen, Germany), and one system from Straumann (Straumann AG, Basel, Switzerland). Most patients (n = 22) were treated using Xive implants (n = 105); 10 of these implants showed failure (Figure 5D). A total of 13 patients were treated with 40 Bego implants, whereas two patients were treated with 10 Straumann implants. Implant failure was observed in five Bego implants, whereas no implant failures were observed in Straumann implants (Figure 5D).

Individual implant performance was evaluated among patients based on general satisfaction (with or without pain), aesthetics, speech, and chewing function (Figure 6). General satisfaction levels among patients were graded as satisfactory, good, and very good; 77 and 71 implants were graded as good and very good, respectively, whereas six implants were graded as satisfactory (Figure 6A). Of the 72 implants, 17 that were graded as very good showed implant failure according to the Albrektsson score. Only one implant failure was observed in implants graded as good; no implant failures were observed in the implants graded as satisfactory. The reliability of new implants was further tested by comparing aesthetic outcomes reported by patients (Figure 6B); these outcomes were categorized as unsatisfactory, satisfactory, good, and very good. Two implants were evaluated by the patients as unsatisfactory in their aesthetics, neither of which failed according to Albrektsson criteria. A total of 27 patients reported satisfactory aesthetics with one failure in implant success (Figure 6B). We found that 74 implants were graded as having good aesthetics and 47 implants were graded as having very good aesthetics. Of the 74 implants with good aesthetics, 16 implants showed failure. However, no implant failures were observed in the implants with very good aesthetics (Figure 6B). Speech and chewing functions were assessed among patients with implants. Speech function was graded as satisfactory, good, and very good. Of the implants, 97 were graded as very good, and no implant failures were observed (Figure 6C); 49 implants were graded as good, and 13 of these showed implant failure; the remaining three implants showed satisfactory speech function with no implant failures (Figure 6C). Chewing function was graded as good and very good (Figure 6D). Of the implants, 87 were graded as very good and 67 implants were graded as good; of the 87 implants, only two showed failure per the Albrektsson criteria, whereas 15 of the 67 implants showed failure (Figure 6D).

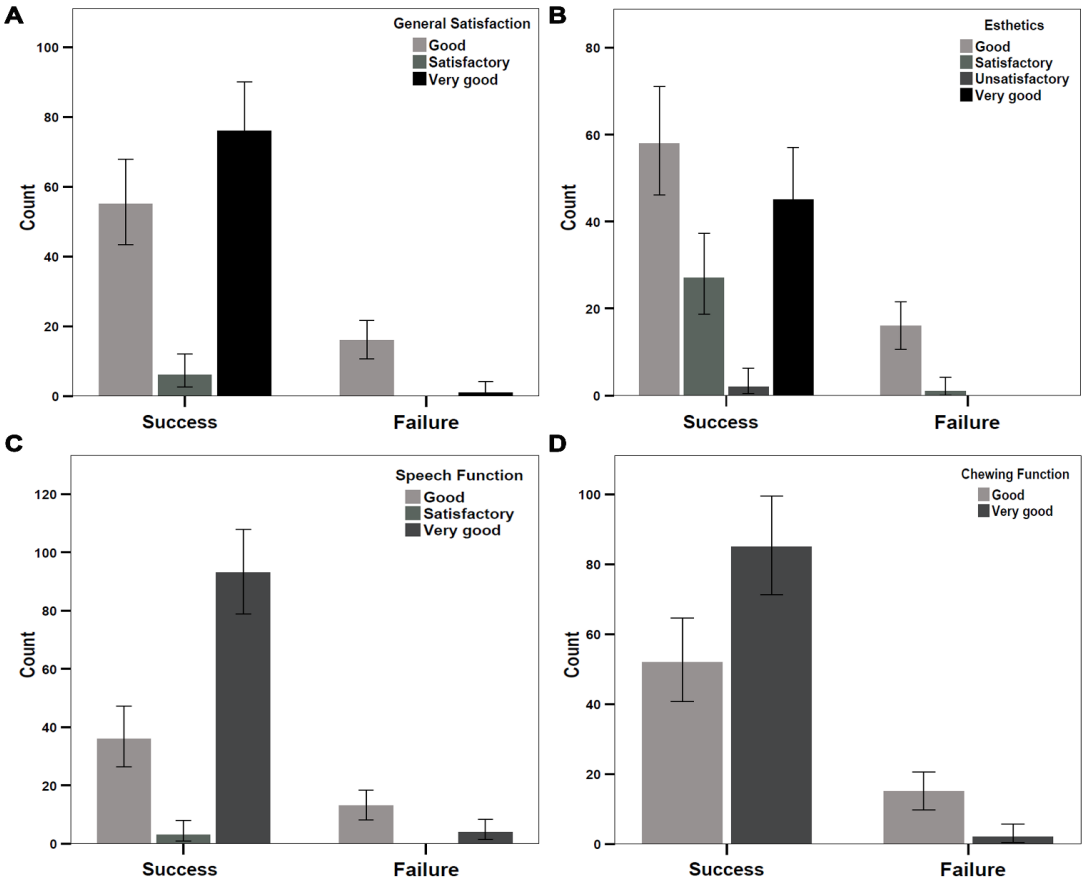

Figure 6. Frequency analysis revealed the implant success level in patients after rehabilitation. Implant performance and success was evaluated based on (**A**) the general satisfaction of patients, (**B**) the grading of aesthetics, (**C**) speech function, and (**D**) chewing ability after implantation.

4. Discussion

The aim of treatment of hypodontia patients by replacing missing teeth is to restore functions such as chewing and speech. However, patients strongly value the aesthetic restoration of missing teeth. Aesthetics in the anterior region are invaluable for patient satisfaction. Unfortunately, conventional prosthetics solutions often yield unsatisfactory results and depend on preparing healthy teeth next to those that are missing. Therefore, patients with a large pulp chamber might need further treatment [19]. Although the use of adhesive bridges might avoid the preparation of healthy teeth [5], this is usually limited to managing a single missing tooth [32]. However, to lessen the bone loss that can result from bridge restoration, dental implantation is a useful alternative [33]. One advantage of dental implantation is the use of existing dental implants as an anchor for prosthetic choices in cases of further tooth loss next to the implant [5].

In this study, orthodontic treatment was performed in 32 patients (86%) before the implant placement. Early and proper orthodontic intervention can prevent bone loss in the hypodontic areas and create root parallelism to facilitate implant insertion surgery [16]. The most common orthodontic strategy for bone and keratinized mucosa preservation include orthodontic extrusion of primary teeth in infra-occlusion, delayed orthodontic space opening, orthodontic gap closure in risky implant regions, and the use of a rigid retainer to maintain the implant sites [16,34–37].

Bone augmentation surgeries in selected patients can be substituted using the orthodontic implant site switching (OISS) technique. The technique results in moving the tooth to the adjacent atrophic alveolar ridge to leave a gap with adequate bone, thereby leaving the original tooth position as a good quality region for successful implant placement and avoiding bone augmentation [35,38–40]. Although this is time-consuming and might result in the alteration of the periodontal support of the moved tooth, OISS can be used in hypodontia patients in the case of atrophic alveolar ridges. In such cases, donor-site morbidity of the autologous bone graft surgery can be avoided [35,40–42].

One of the limitations in this study is the missing information regarding orthodontic treatment. Many patients were referred to the university hospital from different orthodontists, and this led to difficulties in data collection.

Orthognathic surgeries to treat malocclusion were found in seven out of 37 patients (six class III and one class II). This result aligns with other studies that reported a high prevalence rate of hypodontia in patients with class III malocclusion [41].

Although difficult to interpret, the subjective assessment of patient satisfaction is important. In the context of implant success criteria, patient satisfaction is valuable [43]. To the best of our knowledge, only two studies regarding patient opinion of dental implants in cases of hypodontia have been published. Finnema et al. assessed patient satisfaction using a 10-point score (1 = very poor, 10 = excellent). The results showed that the patients were satisfied (seven to nine points) and more self-confident [44]. Zou et al. examined patient satisfaction, including aesthetics, denture comfort, and speech, using a three-point score (0 = unsatisfied, 1 = satisfied, and 2 = very satisfied); none of the patients were unsatisfied in that study [45]. However, neither study correlated the subjective satisfaction score with a well-known and dependable score of implant success. In the present study, implants were evaluated in terms of success according to Albrektsson criteria [31]. The subjective satisfaction of patients was obtained using questionnaires based on the literature [22,46–49]. Success criteria were then corroborated with patient satisfaction. Chewing function, speech ability, and aesthetics were assessed. The evaluation was based on the German school grade system (grade 1 to 6). In these categories, no grade was worse than satisfactory, except in a patient who was dissatisfied with aesthetics due to the visibility of implant material through the mucosa. In general, patient satisfaction in this study was high and comparable to that reported in similar studies [44,45].

Recently, we showed that dental implant survival did not necessarily constitute success, although only when Albrektsson criteria are applied to the investigated dental implants [30]. The augmentation procedure used to insert the implants (n = 97) was either from the retromolar region (n = 8) or from the iliac crest (n = 89). The area used for harvesting bone was selected based on the severity and

size of bony defects. In case of a small and medium bone atrophy with two or fewer missing teeth, autografts were taken from the angle of the mandible [28]. However, bone from the iliac crest was used for augmentation if more than two teeth were missing and/or a combination of vertical and horizontal atrophy was diagnosed [50]. However, hypodontia commonly exhibits multiple missing teeth and complex atrophy, resulting in a higher number of implants inserted in iliac crest-augmented jaw bone. This may also explain why no unsuccessful implants were found in augmented jaws from the retromolar region. Each augmentation procedure involved different bone characteristics. Whereas iliac crest bone has more cancellous bone with higher bone resorption potential [51,52], compact bone (e.g., mandible and tabula externa) has slower resorption rates, which is preferable for long-term implant success [53].

One objective of this study was to correlate the type of prosthetics with implant success. Of 18 unsuccessful implants, 11 were bridges (61%), three were crowns (16.6%), and two were double crowns (11%). Altogether, 100 crowns, 37 bridges, and 15 telescopic crowns were designed for all patients. The pronounced failure incidence in the bridge design may be an indication of the difficulty in the maintenance of good oral hygiene [54].

Although patient satisfaction is important for assessment of procedural outcome [30], purely objective assessments are generally used as success criteria. We compared patient satisfaction with Albrektsson criteria for implant success. Of 18 unsuccessful implants, 17 of the patients reported very good satisfaction with the implant. Similar results were found in the subjective aesthetics component from the patient perspective, where 16 failed implants received good aesthetic evaluations. Speech and chewing functions showed similar results with 13 and 15 implant failures, respectively; all were rated as good by the patients. These results suggest that the objective success criteria used by professional dental implantologists may differ from the subjective consideration of patients. Therefore, a success scale is needed for dental implants that combine both aspects.

5. Conclusions

Despite unfavorable conditions with limited bone availability for the placement of dental implants in patients with hypodontia, we found a very good implant survival and success rate. Patients' general satisfaction rates were high. All patients could eat a normal diet with good chewing ability. Pronunciation ability and aesthetics were acceptable for all patients. Dental implants constitute a standard therapy with high clinical, functional, and aesthetic treatment outcomes in patients with hypodontia. The current study suggests the need for a new assessment system of dental implants, which corroborates clinical parameters with patient contentment.

Supplementary Materials: The following are available online at http://www.mdpi.com/2077-0383/8/10/1687/s1, Table S1: Number of implants per region and type of replaced tooth.

Author Contributions: Conceptualization, S.A., H.S., H.-P.H., and P.S.; Methodology, S.A.; Validation, S.A., H.S., H.-P.H., and P.S.; Formal Analysis, T.E.K., D.M., and K.M.; Investigation, S.A.; P.S., H.S., and K.M.; Writing—Original Draft Preparation, S.A., T.E.K., D.M., and K.M.; Writing—Review and Editing, H.S., H.-P.H., and P.S.; Visualization, T.E.K. and D.M.; Supervision, H.S., H.-P.H., and P.S.

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3.3 Donor-Site Morbidity After Retromolar Bone Harvesting Using a Standardised Press Fit Cylinder Protocol

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Summary

Patients with small and medium-size alveolar ridge atrophy are considered dentally compromised in relation to dental implants. Therefore, their alveolar ridges need to be augmented with an autograft from the oral cavity. One favorable donor site is the retromolar region. However, the technique used plays an essential role in the site's healing and, therefore, the success of the transplanted bone. Accurate bone fitting into the recipient site and stable fixation are the most critical factors for complication-free healing. The standardized Osseo Transfer System is designed to fulfill all the criteria mentioned above by ideally preparing the recipient site to receive the adjusted bone graft. This study aimed to evaluate the donor-site complications after bone transplantation from the mandibular angle using the Osseo Transfer System.

Additionally, patient satisfaction with the surgery was assessed. All patients who received a bone graft using the Osseo Transfer System between 2006 and 2013 were included here. The complications, success, and subjective patient satisfaction were documented with a questionnaire and clinical and radiological follow-up investigations.

Overall, 54 patients with 64 transplanted bone grafts were included. All transplanted bones received dental implants after bone healing. One implant loss was reported in relation to bone graft failure, and six patients had neurological disorders in locally limited areas without any complete damage to the inferior

alveolar nerve. Thus, 94% (n = 52) of the study subjects were either "very satisfied" or "satisfied" and would recommend this surgical treatment to other patients.

It was concluded that dentally compromised patients with small or medium-size alveolar ridge atrophy can successfully be treated using a bone graft from the retromolar area with the standardized Osseo Transfer System. Furthermore, the donor-site morbidity is very low, and the successful healing rate is satisfactory [15].

Original Article 3

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Article

Donor-site Morbidity after Retromolar Bone Harvesting Using a Standardised Press Fit Cylinder Protocol

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Abstract: Precise fitting and immobilisation of bone transplants at the recipient site is of utmost importance for the healing process. With the help of the standardised Osseo Transfer System, the recipient site is adjusted to the graft, rather than vice versa as it is typically done. The aim of this study was to analyse donor-site morbidity after harvesting cylindrical bone grafts from the retromolar region using the Osseo Transfer System. The patient satisfaction with the surgical procedures was also evaluated. All patients treated with this standardised reconstruction method between 2006 and 2013 at the Department of Cranio-Maxillofacial Surgery, University Hospital Giessen, were included in this study. Complications were recorded and evaluated. Bone graft success and patient satisfaction were documented with a questionnaire, and then confirmed by clinical and radiological follow-up examinations. Fifty-four patients were treated and 64 harvested cylindrical autologous bone grafts were transplanted. In all cases, dental implants could be inserted after bone healing. One patient lost an implant, associated with failure of the bone graft. Six patients who were examined continued to show neurological disorders in locally limited areas. No complete or long-term damage of the inferior alveolar nerve occurred. More than 94% (n = 52) of the patients were 'very satisfied' or 'satisfied' with the results and would recommend this surgical treatment to other patients. The standardised Osseo Transfer was an effective treatment option for small and mid-sized alveolar ridge augmentations. A low donor-site morbidity rate and a high transplant success rate were verified. The Osseo Transfer System demonstrated to be a reliable surgical technique without major complications. We highly recommend this surgical augmentation procedure as a surgical treatment for local bone defects.

Keywords: alveolar ridge augmentation; bone reconstruction; horizontal bone defect; press fit; autologous bone graft; trephine drill

1. Introduction

The lack of teeth is usually a result of tooth extraction or trauma, but some patients may have dental aplasia [1,2]. Missing teeth for more than three months can lead to a local atrophy of the alveolar ridge due to the lack of chewing forces and a functional stimulus [3,4]. Dental implants can only be inserted if adequate bone volume is available to ensure the primary stability of implants

and stable osseointegration [2]. Implants must be inserted into the bone so that the rough surface is completely surrounded by well-perfused bone to allow long-term success without peri-implantitis [5]. Depending on the implant system, a minimum of 6–7 mm mesiodistal and 5–6 mm buccolingual alveolar bone widths are suggested for successful implant placement [6]. Otherwise, alveolar bone augmentation before dental implant insertion is required [2]. Autologous bone grafts (e.g., from the iliac crest) are considered the gold standard for augmentation and used mainly to restore large volumes of alveolar bone atrophy [7]. In small- and medium-sized bone defects, an intraoral bone graft can be used to augment the atrophic areas. Bone can be harvested either from the retromolar area of the mandible, chin, or maxilla [8,9]. Other than autografts, allografts, xenografts, or for some indications a combination of both can be used for bone reconstruction [10]. Autografts are preferably used due to their biocompatibility and osteogenesis properties which lead to better bone regeneration [2,7]. Autologous bone grafts from the retromolar region of the mandible have some significant advantages: they can be harvested in local anaesthesia, the amount of available bone can be easily estimated in a standard panoramic X-ray, and minimal resorption of the mainly compact bone can be expected [9].

Bone harvesting can be performed using various instruments, such as drills, chisels, a saw or via piezosurgery [8,9]. With the Osseo Transfer System (BEGO Implant Systems, Bremen, Germany), cylindrical bone grafts can be harvested by using trephines. Three cylindrical burrs with three different diameters are available to harvest a piece of bone that precisely fits to the local defect (Figure 1). This set of instruments was introduced in 2006 as a new augmentation tool for minimally invasive reconstruction of small- and medium-sized jaw defects [11]. The uniqueness of the procedure is that the recipient region can be modulated according to the transplant, not vice versa. The Osseo Transfer System can transform alveolar ridge defects to standardised recipient site defects which enable a perfect geometric matching of the press fitting graft to the defect. Fixation of the graft is performed by using a single lag screw. This leads to high retention and stability of the transplanted bone and maximizes the surface contact to the residual bone for an optimal healing process. When using this standardised procedure, there is no need for manual graft moulding, therefore, the operation time will be reduced [11]. The Osseo Transfer System is mainly used for horizontal augmentation of the alveolar ridge but vertical deficiencies can also be addressed [11]. The standardised procedures have been applied routinely as a minimal invasive surgical procedure in the Department of Cranio-Maxillofacial Surgery, Giessen, Germany. To date, no relevant data concerning complications or transplantation success of this procedure have been published yet.

The aim of this retrospective study was to analyse donor-site complications associated with this procedure. The data obtained are intended to demonstrate the success of the augmentation procedure and patient satisfaction.

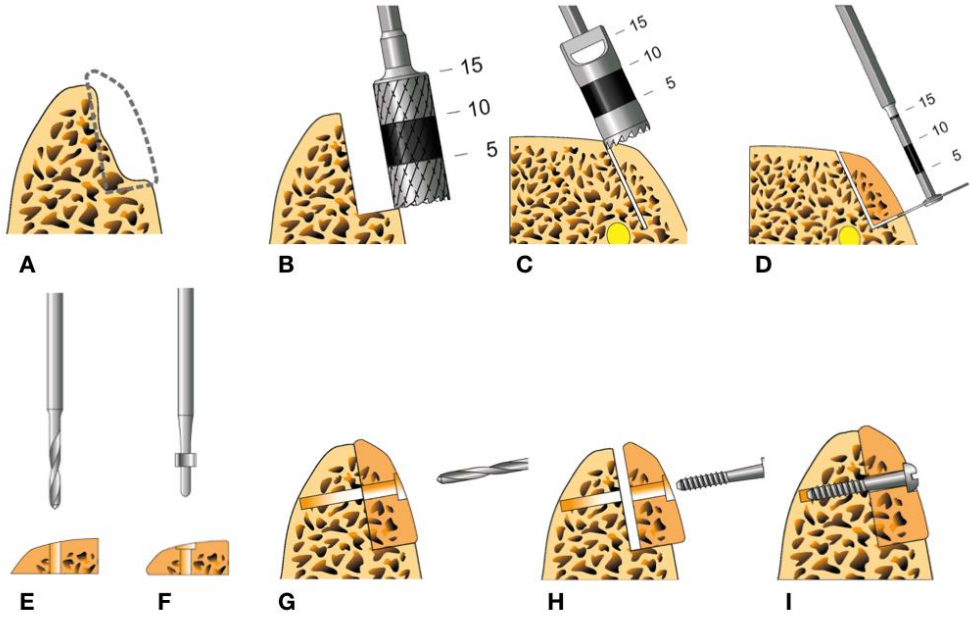

Figure 1. Schematic illustration of the Osseo Transfer System protocol: (**A**) The recipient site. (**B**) Extending the bone defect on the recipient site with a grinding burr to obtain a standardised bone defect. (**C**) Cutting out a bone cylinder from the donor site using a trephine drill to harvest a matching piece of bone. (**D**) Transection the bone cylinder using a micro saw. (**E**) Drilling of a gliding hole in the centre of the bone graft. (**F**) Drilling countersink to avoid extending the screw head outside the graft. (**G**) Adapting the graft to the standardised defect on the recipient's site and drilling through the graft. (**H**,**I**) Graft fixation using micro-lag-screw.

2. Material and Methods

This retrospective, clinical, observational study includes all patients treated in our Department of Cranio-Maxillofacial Surgery, University Hospital Giessen, Germany, from April 2006 to February 2013, who received a standardised bone graft of the retromolar region by using the Osseo Transfer System. A total of 54 patients with bone defects were augmented with press fit bone cylinder. Fifty-two patients completed the questionnaire and 48 patients accepted the follow up examination. In one patient, bone was harvested from both mandibular angles, hence we count a total of 49 bone donor sites. Surgical protocols recommended by the manufacturer were followed for all transplanted bone. Data were collected from patient charts including age, sex, indication for treatment, defects and bone cylinder size. Information about antibiotic administration, surgery duration and intraoperative complications were also recorded. All included patients were scheduled for follow-up examinations and asked to fill out a customized questionnaire. The main purpose of the assessment was to determine the complications and to describe the rate of donor-site morbidity. Postoperative complications include wound infection, wound dehiscence, secondary haemorrhage, haematoma, pain, nerve injury and limitations of speech and swallowing. Duration and intensity of the complications were also specified. Furthermore, the success rate of the bone grafting procedure and patient satisfaction were evaluated. A visual analogue scale (VAS) was used to determine: A) the degree of pain, with the endpoints of 'no pain' (VAS 1) and 'maximum pain' (VAS 10); and B) the presence of nerve injury with 'no sensory disorder' (VAS 1) and 'absolute deafness' (VAS 10).

Subsequently, patients were followed-up in terms of clinical status and radiological imaging. Radiographs and photographs were acquired for the documentation and analysis of abnormalities. The two-point discrimination test was performed on patients who developed nerve injury to record any irreversible nerve lesion.

This study was approved by the Ethics Committee of the Faculty of Medicine, Justus Liebig University Giessen, under the approval number (201/11).

Data from the questionnaires and the follow-up examinations were anonymised and coded in an Excel spreadsheet (Excel 2007; Microsoft Corp., Redmond, WA, USA). The data were descriptive, and were analysed using SPSS software (IBM SPSS Statistics, version 22; IBM Corp., Armonk, NY, USA).

3. Results

In a period of almost 13 years, a total of 54 patients with 64 bone cylinders were surgically treated with the here described standardised bone transfer. Fifty-two patients completed the questionnaire, and 48 (92.3%) agreed to clinical follow-up consultations, where 49 bone transplantation sites could be observed. Figure 2 outlines the clinical course of a patient with bone atrophy in the left maxillary central incisor region who was treated with a standardised bone graft from the left retromolar region of the mandible.

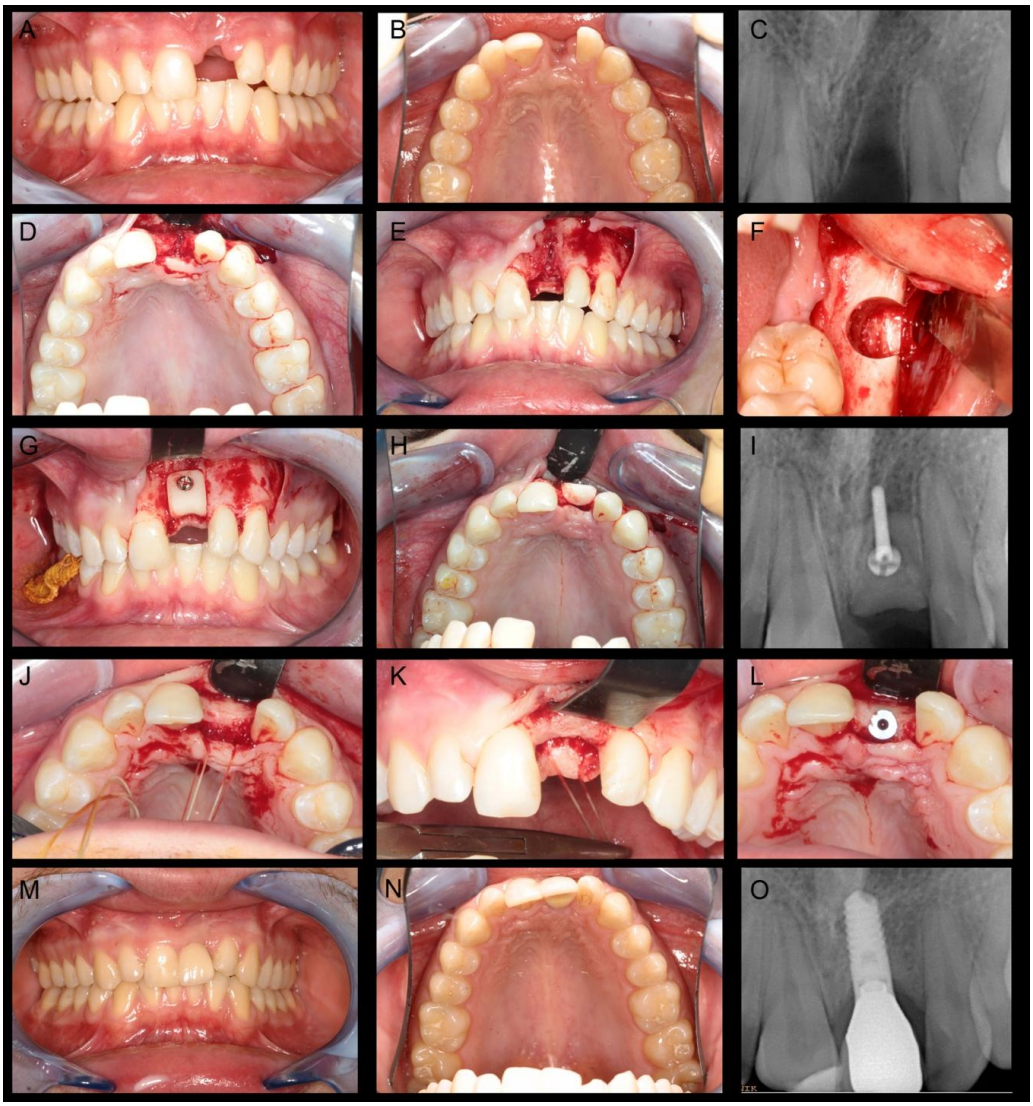

Figure 2. Clinical case report of patient with bone atrophy in the left maxillary central incisor region: (**A**–**C**) Intraoral photos and radiograph show the initial situation; (**D**,**E**) intraoperative photos shows bone defect; (**F**) intraoperative photos after the removal of the standardised bone graft from the left retromolar area of the mandible; (**G**–**I**) Intraoperative photos and radiograph after bone graft fixation using micro-lag-screw; (**J**–**L**) Intraoperative photos 3 month show the bone healing and implant insertion; and (**M**–**O**) intraoral photos and radiograph after prosthetic rehabilitation using ceramic crown.

For feasible statistical analysis, only the number of bone transplantation were be considered. The pre-therapeutic statistical analysis in this study included data from all treated cases (54 patients, 64 bone cylinders) whereas the follow-up evaluation is based on 48 patients and 49 bone harvesting sites.

In 49 bone transplantations, 26 procedures (53.1%) were performed in females and 23 (46.9%) in males. The patient age at the time of bone graft surgery ranged between 15 and 75 years (mean 35.18 years) (Figure 3). In one patient, the bone transplant was not successful and the necrotic bone graft with the already inserted dental implant at this region had to be removed. This amounts to a 98% success rate of the transplanted standardised bone graft.

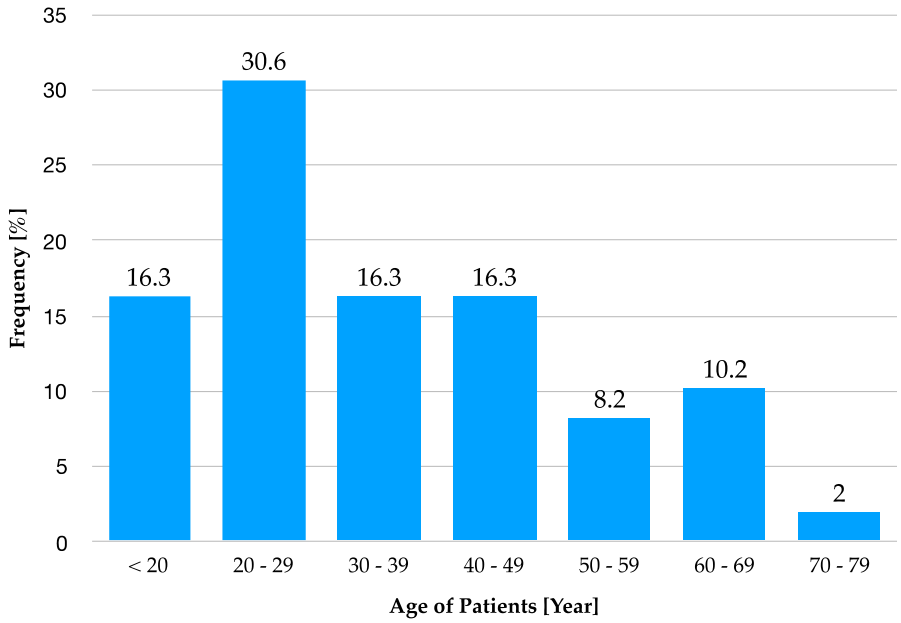

Figure 3. Age distribution of the included patients at the time of the bone graft surgery.

Forty-six (93.9%) procedures were performed in the outpatient clinic, and three (6.1%) procedures were done in hospitalized patients because additional surgical procedures were performed. The most frequent indication for press fit bone cylinder was alveolar crest atrophy in a single tooth area (n = 46; 93.9%). Two (4.1%) patients underwent sinus lifting surgeries, and one (2%) patient underwent defect filling after a cystectomy.

The average duration of surgeries was 83.7 (± 27.06) min. The shortest procedure lasted 46 min, the longest 153 min. Nearly two-thirds of interventions (65.4%) lasted less than 90 min (see Figure 4).

The surgical bone harvesting was carried out by a total of ten different surgeons, three of them made 71.4% of all interventions. The bone harvesting was performed predominantly from the right mandibular angel (n = 31, 63.3%). In 18 cases (36.7%), the left side was selected.

The average length of the harvested bone cylinders was 8.69 mm. A total of 60.9% of bone transplants were used to augment the upper jaw, and 39.1% were placed in the lower jaw. Almost half (49.9%) of all harvested bone cylinders were transplanted into the anterior teeth region of the upper jaw (Table 1).

Table 1. Recipient regions (FDI) of bone grafts (frequencies in percent).

-	-	1.6	-	-	1.6	7.8	18.6	17.2	3.1	1.6	6.3	1.6	1.6	-	-
18	**17**	**16**	**15**	**14**	**13**	**12**	**11**	**21**	**22**	**23**	**24**	**25**	**26**	**27**	**28**
48	**47**	**46**	**45**	**44**	**43**	**42**	**41**	**31**	**32**	**33**	**34**	**35**	**36**	**37**	**38**
-	-	7.8	12.5	-	3.1	1.6	3.1	3.1	-	-	1.6	4.7	1.6	-	-

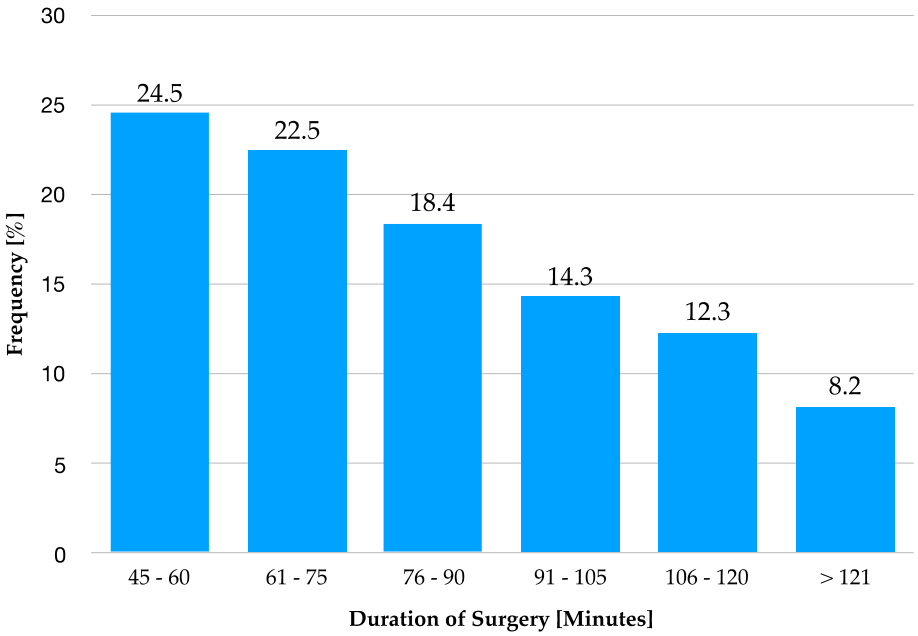

Figure 4. The frequency of the surgery time in minutes.

3.1. Intraoperative Antibiotic

In 37 procedures (75.5%), patients received an intravenous single-dose antibiotic prophylaxis intraoperatively. Sultamicillin was used in most cases (n = 30, 81.1%). Clindamycin was administered in five cases (13.5%), in two interventions (5.4%), the drug used could no longer be determined. The remaining 12 cases (24.5%) did not receive intraoperative antibiotics.

3.2. Complications

Intraoperative complications were described in two cases. The mandibular canal was opened after bone harvesting in both procedures. Postoperative complications were recorded at four different time points: one and ten days after surgery, before implant insertion, and at the follow-up examination. At the time of the first postsurgical follow-up (one day after surgery): No patient had experienced wound infection, wound dehiscence, fracture or postoperative bleeding. However, 48 (98%) procedures resulted in haematomas of the buccal mucosa. Thirty-two patients (65.3%) reported pain episodes. Hypoesthesia of the inferior alveolar nerve at the operation site was reported in 12 (24.5%) cases. Ten days after surgery: Wound dehiscence was reported 10 days postoperatively, at the time of suture removal, in four (8.2%) cases. Haematomas were present in 15 (30.6%) cases. Hypoesthesia in the operative area was reported in 11 (22.4%) cases. Pain episodes at this point were reported in six (12.2%) cases. Pre–implant insertion: Three (6.1%) cases still had wound dehiscence at the pre–implant insertion surgical site about three months later, and nine (18.4%) patients reported hypoesthesia. Follow-up examinations: Nine (18.4%) patients reported locally limited hypoesthesia, at the follow-up examinations. No other complication (wound dehiscence, pain episode, or fracture) was reported. The complications recorded at the various postoperative time points are summarised in Figure 5.

On follow-up radiographic examination, the harvest area on the mandibular angle remained visible after 2.5 years in one (2.0%) patient. Delayed re-ossification was seen in the retromolar region due to lower bone density. No radiological abnormality was seen in the rest of the patients (98%). The harvested areas were compared to the pre-surgical sites and were not elevated, lowered, or reduced in density. The intraoral mucosal scar in the operated area was not irritated in any patient.

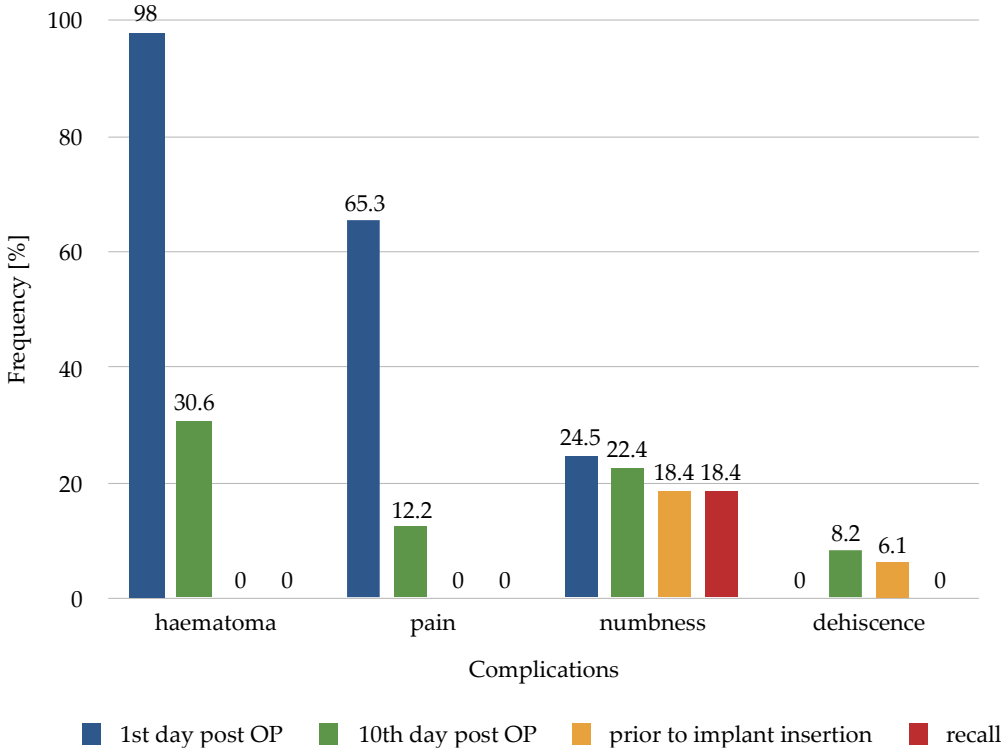

Figure 5. Postoperative complications at different time points.

3.3. Patients Related Parameters:

3.3.1. Pain

Postsurgical pain in the harvest area was reported in 37 (69.8%) cases and denied in 16 (30.2%) cases. On average, the patients reported a pain intensity of 4.67 (2.17) of 10 points on the VAS. Of those patients who reported postsurgical pain episodes, 80% were pain free within one week.

3.3.2. Hypoesthesia

Hypoesthesia in the chin region as a result of injury to the inferior alveolar nerve was reported in six (11.3%) cases. Hypoesthesia at the chin persisted in two cases.

After the conversion of patients' VAS responses to corresponding numerical values, we concluded that the objectification of disturbance magnitude was difficult.

3.3.3. Functional limitations

The various functional limitations documented are presented in Table 2.

Table 2. Functional limitations.

Functional limitations	NO	YES (total)	YES (temporary < 3 months)	YES (permanent)
Chewing	35.8	64.2	62.3	1.9 *
Speech	90.6	9.4	9.4	-
Swallowing	96.2	3.8	3.8	-
Dysgeusia	98.1	1.9	1.9	-
Mouth opening	37.7	62.3 **	60.4	-

* Consequences of a trauma; independent of standardised Osseo Transfer. ** One patient stated that the functional restriction at mouth opening lasted six months.

3.3.4. Patient satisfaction

More than 94.0% of the patients were very satisfied or satisfied with the general outcome of bone transplantation from the mandibular angle using the Osseo Transfer technique. The average score was 1.58 points (1= very satisfied, 5 = completely unsatisfied). Most (94.2%) patients indicated that they would recommend this procedure in a completely unreserved or reserved way to other patients with similar clinical and surgical indications.

3.4. Summary of Results

In summary, no postsurgical complication occurred in 31 (63.3%) of the 49 bone transplantations from the mandibular angle. In the remaining 18 (36.7%) cases, the documented complications (particularly the neurological problems) need to be differentiated between (1) problems that arose due to the use of the Osseo Transfer technique, and (2) those that were independent of the bone transfer method. The latter problems may have existed prior to the transfer or may have developed after bone rebuilding due to other factors. Table 3 shows the documented complications and their causal relationships to the Osseo Transfer surgery.

Table 3. Summary of postoperative complications.

Complications [post OP]	**Frequency [n]**	**Frequency [%]**
No abnormality	31	63.3
Temporary abnormality, Osseo Transfer **(causal)**	7	14.3
Permanent abnormality, Osseo Transfer **(causal)**	8	16.3
Abnormality, Osseo Transfer **(not causal)**	3	6.1

4. Discussion

This study designed to be a retrospective, clinical, observational study. Due to the fact that no other comparable procedure for bone harvesting was applied in the same hospital, direct comparison of this standardised bone transfer to a control group was not possible. Comparison with another method of operation seems hardly possible. The procedure presented here is performed with a standardised set of instruments and a certain surgical protocol followed common practice to obtain bone through sawing, milling, and chiselling which fit into the size of the anatomical defect. The advantage of the standardised bone transfer is that the recipient area is prepared to fit to the graft, not vice versa as with classical augmentation procedures [11]. Therefore, a direct comparison of this standardised method with other non-standardised methods is not meaningful.

One of the limitations of this study is the subjective assessment of some data which was collected after their occurrence. Patients have different memory skills which can lead to deviations in the information such as pain and its strength. Such data should, therefore, be viewed with caution. This process is also called "recall bias" and should always be considered in the interpretation of results [12].

Surgical procedures in the cranio-maxillofacial field always carry a risk of nerve injury complications [13]. The inferior alveolar nerve is the most affected nerve during bone harvesting from the retromolar area of the mandible [14]. Drilling to an extended depth into the retromolar region may expose the mandibular canal. Partial damage or complete transection may follow. Clinical symptoms include reduced sensibility if the nerve is partially damaged, and complete anaesthesia if it is fully severed. However, the symptoms can range from dysesthesia to hyperesthesia [15,16]. The seriousness of this complication and the need to open the mandibular canal during surgery in two of our cases emphasise the importance of pre-surgical radiological diagnostics to estimate the

maximum possible drilling depth above the mandibular nerve canal. Basic diagnostic modalities (i.e., orthopantomography) should be complemented by cone-beam computed tomography in critical borderline cases [17].

In this study, no significant complication was recorded for 31 (63.3%) of the 49 bone transplantations from the retromolar region. In the remaining 18 (36.7%) cases, the sources of documented complications (particularly neurological; i.e. related to or independent of the surgical procedure) need to be differentiated accurately. In three (6.1%) cases, the documented nerve injuries were independent of bone transplantation. Fifteen (30.6%) postoperative complications were related directly to the surgical procedure. Amongst those 15 complications, seven (14.3%) complications were temporary and improved over time, with complete rehabilitation. These observations correspond to reports in the literature that hypoesthesia improves over time, and ultimately can disappear completely [18–20]. Persistent manifestation occurred in eight (16.3%) patients, six (12.2%) of them described small, local sensibility deficits.

Another complication can occur when the graft does not properly adapted to the receipt site. This may lead to reduced perfusion of the graft site and therefore to the loss of graft [21]. Success of bone graft significantly depends on the close and tight contact between graft and recipient region [22,23]. Faupel et al. found a complete bony connection between graft and receipt site without formation of intermediate soft tissue in areas of high contact pressure. In areas with lower pressure, connective tissue between graft and bearing bone was formed [24]. In extreme cases, this could lead to sequester formation and consequently to graft loss. The proper use of the Osseo Transfer System produces a press fit junction between original bone and graft preventing such complications [11].

Almost all (97.0%–100%) functional restrictions were temporary. In general, the problems lasted for a few days and no more than a few months.

The patients described postsurgical pain as comparable to pain after other oral surgical procedures in the dento-alveolar area (e.g., extraction of wisdom teeth). This result corresponds to the observations of other authors [25].

Lower bone density in the retromolar region was detected during the clinical follow up examination in only one patient after 2.5 years. The reduced density was a result of delayed re-ossification at the bone cylinder harvest site and might be related to the patient's advanced age (70 years). However, as the patient was completely free of symptoms, no clinical relevance was attributed to this finding. Jensen and Sindet-Pedersen et al. made a similar observation. They described delayed bone regeneration at harvest sites in patients aged > 60 years at one year after bone transfer surgery [26]. None of the remaining patients in this study had a radiologic abnormality. This finding concurs with the results of Misch et al. and Nkenke et al., who described complete regeneration of retromolar bone harvest sites six months postoperatively [9,27]. Refilling of the bone cavities with artificial bone substitute after bone transfer was not necessary, although other authors have recommended this approach [28]. The retromolar region of the mandible where the bone grafts are harvested consists of very solid bone which is strengthened by trajectory lines derived from the main mastication forces. According to the common understanding of bone healing, functional remodelling takes place and allows for quick and effective healing after removal of limited cylindrical bone grafts [29].

As all donor regions examined in this study were intraoral, no functionally or aesthetically relevant scarring was visible, which significantly increased patient satisfaction. Other authors have also described this advantage of intraoral bone harvesting [9,30].

Application of the Osseo Transfer System is not limited to bone harvesting from the mandibular angle or augmentation of the alveolar bone. The procedure can be used wherever bone regeneration after customised transplantation is desired. Limiting factors are the size of the area that needs to be regenerated and the availability of bone in the donor region.

5. Conclusions

Standardised press fit bone cylinder using the Osseo Transfer System surgical kit is a safe, practical, and promising option for the treatment of small and medium-sized alveolar ridge bone defects. This procedure presents good feasibility for the surgeon and impose little stress on patients. Standardised bone transfer surgery has a low rate of complications and is considered as a reliable procedure for patients and surgeons. This method should be applied whenever suitable indications exist.

Author Contributions: Conceptualization: P.S., R.S., and S.A.; data curation: M.M.; formal analysis: J-F.W., T.L., and H.S.; investigation: P.S., M.M., R.S., and S.A.; methodology: P.S. and H.S.; project administration: C.K., T.L., and H-P.H.; supervision: P.S., H-P.H., and R.S.; validation: H.S., H-P.H., and S.A.; visualization: C.K., J-F.W., and T.L.; writing—original draft: P.S., M.M. and S.A.; writing—review and editing: P.S.

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Conflicts of Interest: The kit of surgical instruments named Osseo Transfer System (BEGO Implant Systems, Bremen, Germany) was developed by P.S. and R.S., who also performed hands-on courses related to the surgical protocol. Despite this, all authors declare no conflict of interest.

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3.4 Long-Term Influence of Platelet-Rich Plasma on Dental Implants after Maxillary Augmentation: Implant Survival and Success Rates

Attia, S.; Narberhaus, C.; Schaaf, H.; Streckbein, P.; Pons-Kühnemann, J.; Schmitt, C.; Neukam, F.W.; Howaldt, H.P.; Böttger, S. Long-Term Influence of Platelet-Rich Plasma on Dental Implants after Maxillary Augmentation: Implant Survival and Success Rates. *J Clin Med* **2020**, *9*, 391, doi:10.3390/jcm9020391.

Summary

Patients with large-size maxillary bone atrophy are dentally compromised and need ridge augmentation prior to implant insertion for dental rehabilitation. In a previous randomized controlled trial (RCT), the impact of PRP during maxillary augmentation was evaluated. The short-term findings did not report any positive effects of PRP on bone healing via histological and radiological investigations. The present study aimed to reinvestigate the previous study's cohort to document the long-term impact of PRP on the implants' survival and success rates.

A total of 53 subjects from the previous study who underwent ridge bone augmentation from the iliac crest and received dental implants were included here. Of these, 34 patients had this intervention conducted with a split-mouth design, in which bone enhancement with PRP was used on a randomly chosen side while the other side was the control side of bone enhancement without PRP. The remaining 19 study subjects were operated on the same side only and randomly assigned to the PRP or control group.

Implant reinvestigation was performed after an average time of 13 years. Implant success was reported according to Buser's and Albrektsson's criteria. In total, 37 patients (25 females, 12 males) were reevaluated, with 17 (12 females, 5 males) in

the PRP group and 20 (13 females, 7 males) in the control group. Out of the 210 implants placed, 102 (48.57%) were inserted in the PRP group and 108 (51.42%) in the control group. The 102 investigated implants in the PRP group showed six cases of implant loss (survival rate 94.1%). In the control group, two cases of implant loss were recorded (survival rate 98.1%). This resulted in a cumulative survival probability of 94.1% in the PRP group and 98.1% in the control group, with no statistically significant difference between the groups. A higher considerable difference for the control group was found in the cumulative success probability using Albrektsson's criteria ($p = 0.05$). A positive impact of PRP on the long-term implant survival and success was not evident [66].

Original Article 4

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Long-Term Influence of Platelet-Rich Plasma (PRP) on Dental Implants after Maxillary Augmentation: Implant Survival and Success Rates

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Abstract: The atrophic maxilla often requires bone augmentation before implant placement to ensure long-term implant success. A previous prospective clinical trial examined the use of platelet-rich plasma (PRP) during maxillary augmentation. The short-term results showed no positive effect of PRP. The aim of this study was to evaluate the same patient collective of the previous study regarding the PRP long-term impact on the survival and success of dental implants. Fifty-three patients from the previous study diagnosed with maxillary atrophy and augmented with autologous bone grafts from the iliac crest and dental implants, were included in this study. Treatment was carried out on both sides in 34 patients with a split-mouth-design in which one randomly chosen side was treated additionally with PRP, the other side was the control-side. Nineteen patients were treated only on one side and were assigned to the PRP—or the control group randomly. Implant follow-up of the patients from the previous study was performed after an average time of 13 years. Implant success was evaluated using two different success criteria. Thitry-seven patients (25 women and 12 men) were investigated in this study. Seventeen patients (12 female, 5 male) were included in the PRP group, while 20 patients (13 female, 7 male) participated in the control group. A total of 210 implants were inserted. Of these, 102 implants (48.57%) were placed in the PRP group and 108 implants (51.42%) in the control group. Out of 102 investigated implants in the PRP group, 6 were removed (survival rate 94.1%). While two of the 108 implants in the control group were loss (survival rate 98.1%). In the PRP group, the cumulative probability of survival after 15.1 years was 94.1% and in the control group, was 98.1%, with no significant difference between the two groups. Higher significant difference for the control group was found in the cumulative success probability using Albrektson criteria ($p = 0.05$). Positive impact of PRP on long-term implant survival and success could not be found.

Keywords: implant survival; implant success; PRP; platelet-rich plasma; long-term result; sinus lift

1. Introduction

Facial bone loss due to trauma, disease, aging or congenital abnormalities can lead to deficiencies of maxillary bone. Depending on its extent, it remains a challenge for both health professionals and

patients. Furthermore, bone loss has a high psychological impact on patients. Therefore, aesthetic and functional reconstruction have the same importance in the maxillofacial region [1]. Tissue engineering is increasingly being used to reach excellent aesthetic and functional results of facial reconstruction. In this context, also platelet-rich plasma (PRP) is used to enhance autologous bone grafts [2]. The last years showed a staggering development concerning the use of tissue engineering and biomaterials such as decellularized matrix, nanoparticles, stem-cell therapies, scaffolds, and even the engineering of a whole tooth. This has shifted our beliefs and expectations regarding the results of bone reconstruction [3]. But the development of such new strategies has not yet been completed and therefore, older approaches such as PRP and platelet-rich Fibrin (PRF) still require validation or disproof of their clinical efficacy through long-term follow-ups [3–5].

Successful clinical implantation can only be performed with sufficient bone supply [6]. Enough bone in vertical and horizontal direction is necessary for the primary implant stabilization and lead to successful osseointegration [7,8]. Implants should be at least 10 mm in length and 3 mm in diameter [8]. Extensive, individualized prosthetic and surgical planning before implantation is desired as implants should be placed where they are needed for prosthetic rehabilitation [9,10]. However, the ideal implant site may be located in atrophic jaw areas. In such cases, bone augmentation is necessary prior to implantation [6]. In order to achieve better results of bone augmentation surgery and to reduce the impairment of the patients, a constant attempt is made to improve augmentation techniques and efficiency [11].

Marx et al. reported for the first time in 1998 that the intraoperative use of platelet-rich plasma (PRP) leads to faster bone healing in autologous graft transplantation [2]. Since then, many other studies have been conducted to investigate the effect of PRP in this context [12,13]. PRP is an autologous concentrate of human platelets in a small amount of plasma [14]. It has a 3 to 5-fold higher platelet concentration than normal blood [15]. The growth factors contained in platelets play a major role in wound healing and have been used in implantology to improve bone regeneration [12].

To demonstrate these effects, many studies examined the influence of PRP on augmented autologous bone. Aimetti et al. involved four patients undergoing bilateral bone augmentation in the upper jaw. Using split-mouth design, PRP was used on one side of the maxilla. The authors were able to demonstrate higher bone regeneration at the PRP side [16]. Consolo et al. investigated the effect of PRP on bone regeneration in 17 patients. Patients received bilateral sinus lift surgery with autologous bone graft. This was enriched with PRP on one side. Radiological and histological evaluation of bone density was performed. The authors documented increased bone density and activity on the PRP side. However, they also observed a diminished positive effect of PRP approximately six months post intervention [17]. The same design of the previous study was used by Khairy et al. in 15 patients. After three months, the authors could not find a positive effect of PRP, but they were able to detect increased bone mineral density in the PRP group after six months [18]. The clinical question of Bettega et al. was whether the use of PRP in sinus lift surgeries with autologous bone leads to higher bone formation [19]. Bilateral treatment of 18 split-mouth patients was performed. The histological and radiographical bone examination did not show statistically significant differences between the two groups [19]. The research by Raghoebar et al. examined the effect of PRP on the remodeling of autologous bone grafts. Two-sided jaw bone augmentation was performed in five patients using PRP on a randomly selected jaw side. The authors were unable to document any improvement in wound healing or bone remodeling when using PRP [20]. Consequently, the presented studies could not clearly demonstrate the efficacy of PRP in augmentation surgery of jaws. According to Aurora et al., this is mainly due to the lack of standardization of the study structure and small population sizes [21].

In order to investigate the influence of PRP on bone density, a bi-centric clinical randomized study was conducted at the Departments for Craniomaxillofacial Surgery in Giessen and Erlangen, Germany. Between 2001 and 2004, 53 patients with maxillary atrophy were included in the study. Sinus lift operation was performed, if necessary, in combination with an on-lay graft osteoplasty. Patients were randomly assigned to the study group (sinus lift augmentation with PRP) or to the control group

(augmentation without PRP). Nineteen patients underwent unilateral surgery and the remaining 34 were treated bilaterally (split-mouth design). PRP concentrations added to the cancellous bone used to fill the maxillary sinus were measured. The intraoperative procedure is as follows:

1. 3 mL PRP (drops) on 3 cm^3 of cancellous bone;
2. 0.5 mL calcium gluconate 10% (drops) on 3 cm^3 of cancellous bone;
3. 0.5mL of native wound blood (drops) on 3 cm^3 of cancellous bone.

The substance was gently resuspended with a plastic pipette until, after about four minutes, a homogenous gel-like consistency was formed. This allowed better handling of the bone graft. After a healing period of four months, the implants were inserted using a drilling template. This was created by 3D planning with CT scans made during the healing period. During implant surgery, biopsies were taken from the graft region on each side treated. The biopsies were evaluated histomorphometrically for bone density. Bone density was also examined on CT by means of the Hounsfield scale in the augmented regions. The results showed no significant differences between the study groups. Neither the histomorphologically nor the radiographically assessed bone density was significantly higher with the use of PRP. Similarly, the rate of short-term implant loss, graft resorption, and clinical parameters did not vary significantly between the groups. Implant loss was evenly distributed in both groups. Schaaf et al. concluded that PRP has no short-term effect on bone density and bone regeneration [22,23].

Long-term effects of the use of PRP in combination with autologous bone augmentation has on implantation success is not well reviewed in literature. To date, few studies can be found which only marginally address this topic [24–28]. Between 2004 and 2017, many studies dealing with the long-term impact of PRP on implant survival and success were published. Velich et al., 2004, examined the long-term results of various augmentation materials during sinus lift operations. In one out of ten investigated groups, bone augmentation was carried out with alloplastic bone substitute material and PRP. The follow-up period for this study was up to five years. An implant loss rate of 3.6% was recorded in the PRP group but this was not statistically significant in comparison to the other groups. Robiony et al., 2008, investigated the use of PRP after distraction osteogenesis, autologous bone transplantation and insertion of dental implants. Twelve patients who received such treatment were examined; there was no control group. At a follow-up time of five years post dental implants, a survival rate of 97.9% and a success rate of 91.5% were recorded according to Albrektsson. In a split mouth design examined by Dasmah et al. in 2013, dental implants which were inserted after iliac bone graft with and without PRP were examined. After an observation period of five years, there was no implant loss and therefore no statically significant data between the groups could be found. Long-term implant survival after maxillary bone augmentation using intraorally obtained autologous bone and xenogeneic bone substitute mixed with PRP was presented by Schwartz-Arad et al. in 2014. The study was conducted without a control group and stated an implant survival rate of 93.4% after an average observation time of 3.3 years. Finally, in 2017, the study published by Khouly et al. stated a cumulative survival of dental implants inserted after sinus lift augmentation with xenogeneic bone and PRP of 89.9% at an average of 7.2 years post-surgery. The study did not contain a control group.

The existing literature findings do not allow a valid statement on the long-term results of implant survival and implant success after the use of PRP. The aim of this study was to determine whether the use of PRP during augmentation of the maxilla has a long-term impact on implant treatment outcome. Implant survival and success rates were assessed. From the multitude of success criteria available in the literature, the criteria according to Albrektsson et al. [29] and Buser et al. [30] were considered to be most useful. They represent the most frequently used criteria for assessing implantation success [31]. This allows a comparison of implant success results with other studies using the same criteria. To date, an official uniform and international agreement on how to define success in implantology and related criteria is still lacking [32]. In this study, we hypothesized that implants placed in PRP-enriched augmented bones lead to higher survival and success rates.

2. Materials and Methods

2.1. Study Design and Patient Population

The study was conducted as a two-center, controlled randomized single-blind retrospective study which builds on the research of Schaaf et al. [22,23]. The inclusion criterion of this study was the participation in the previous randomized controlled trial (RCT). However, patients with pregnancy and reduced general medical and physical condition were excluded. All investigated implants were assigned to either the study (inserted in PRP treated bone) or control (without PRP) group. Due to the identicality of patients' factors, implants inserted bilaterally in a split mouth design were evaluated separately.

2.2. Examiner Blinding and Calibration

The clinical examinations and radiological evaluations were carried out by one examiner who did not know the patients' research group assignment, so blinding was ensured. In order to ensure the validity of measurements, the examiner was trained prior to data collection. For randomly selected patients, all clinical and radiological parameters to be recorded in the study were measured on a total of 50 implants and compared with the results of an experienced oral surgeon.

2.3. Study Parameters

The main parameter was the long-term survival and success rate of the implants. Implants that remained in situ were defined as surviving implants. To calculate the survival rate, the existing implants were noted during the clinical examination and the number and time of removed implants were documented. Since implant survival is not equivalent to implant success [33,34], success criteria of Buser et al. [30] and Albrektsson et al. [29] were evaluated in this study. Albrektsson et al. defined dental implant success as a state of no clinical implant mobility or radiographic radiolucency, annual vertical bone loss of less than 0.2 mm after the first year post surgery, and absence of irreversible symptoms such as pain, infection, neuropathy, paranesthesia or mandibular canal injury [29]. Buser et al. include the following aspects to rate an implant as a success: no subjective complaints (pain, foreign body sensation or dysesthesia), no recurrent purulent infection, no mobility, no continuous radiolucency around the implant, and possibility of prosthetic loading [30]. The main difference between the two known criteria is considering the vertical bone loss as a success factor. In order to assess implant success, the implants were examined with regard to the corresponding criteria. If one or more of the negative criteria were present, the implant was considered a failure. Already explanted implants were also rated as a failure.

2.4. Statistical Analysis

Collected data was divided into two groups (bilaterally and unilaterally treated patients) prior to statistical analysis. In each group, results of the PRP-group were compared with the results of the control group. Group similarity was compared by using the rank sum test according to Mann–Whitney and Wilcoxon. In order to compare frequencies, Fisher's exact test or the chi-square test was used, depending on the available data. Survival and success rates were analyzed with the Kaplan–Meier method. Implants that were in situ or successful during the observation period are censored and thus included in the calculation of survival and success probabilities [35]. The survival and success probabilities were compared with the logrank test. For all statistical tests applied, the significance level was defined as $\alpha = 0.05$. Therefore, for a p-Value above 0.05, the null hypothesis was retained, for values below 0.05, the alternative hypothesis was adopted.

2.5. Ethics and Privacy

The study protocol was presented and approved by the ethics committee of Justus-Liebig University Giessen (approval number 129/15). The patients consented that their intraoral pictures and X-ray images may be used anonymously in the publications. In addition, all data in the Excel spreadsheet was pseudonymized.

3. Results

Out of 53 participants, 37 patients in two centers (Giessen 31 out of 41, Erlangen six out of 12) were available for follow-up examination and included in this study. Reasons for the drop-out of 16 patients were: rejection of participation (n = 7), failure to reach patients (n = 5), poor medical condition (n = 2), and decease (n = 2). Out of the 37 examined patients, 25 (67.6%) were female and 12 (32.4%) male. Patient age ranged between 30 and 90 years, the median was 65 years. In the study by Schaaf et al., 306 implants were originally placed. Due to the withdrawal of 16 patients, 96 implants could not be examined. Consequently, 210 implants were considered in the statistical evaluation, which represents 68.6% of the original implant number. Due to eight implant losses, 202 implants were clinically and radiographically examined. Reasons for implant loss (n = 8) were documented as follows: periimplantitis (n = 5, 4 PRP side,1 control side), removal of implant at the PRP side due to intra-operative complication (perforation of the maxillary sinus, n = 1), and failure of osseointegration (n = 2). The implant observation period was between 11.3 and 15.1 years. The median and mean age of implants was 13 years. Regardless of control or PRP group, a survival rate of 96.2 percent could be calculated.

A case presentation of one of the included patients can be seen in Figure 1.

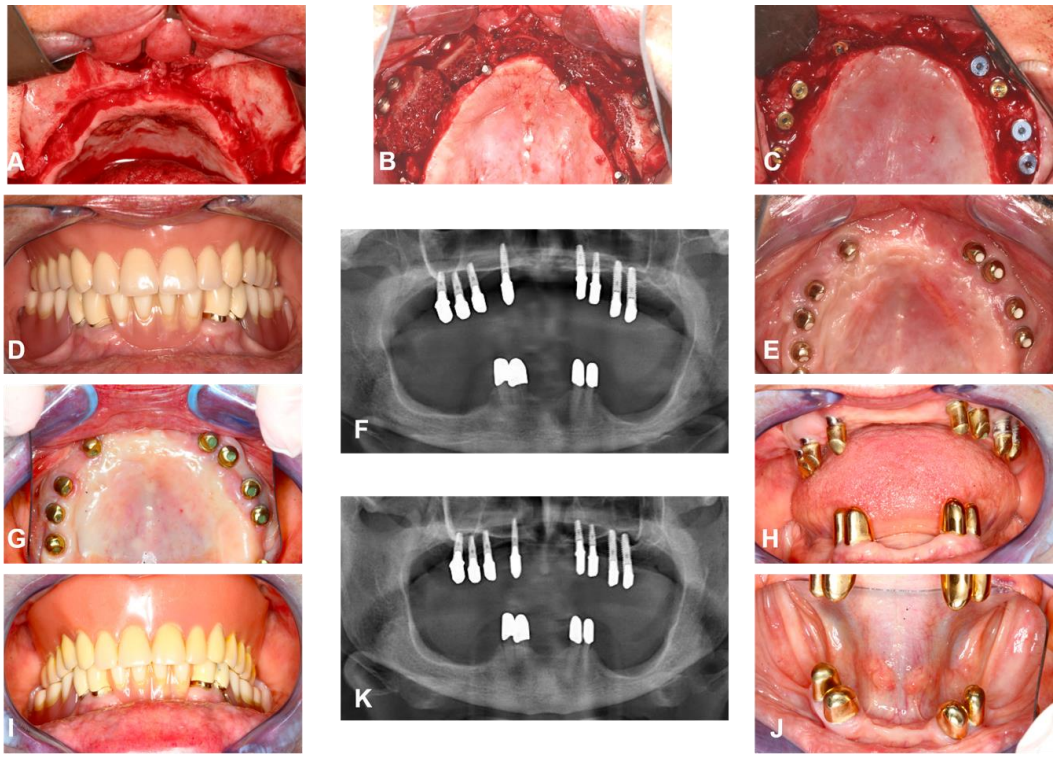

Figure 1. Clinical case included in the study. (**A**,**B**) intra-operative images show extrem maxillary atrophy before and after autologus bone transplantation from the iliac crest and bilaterial sinus lift, on one side platelet-rich plasma (PRP) was used, (**C**) intra-operative image, six months post implant placement (n = 8), (**D**–**F**) intra-oral image and panoramic radiograph after prosthetic rehabilitation, (**G**–**J**) intra-oral images and panoramic X-ray at long-term follow-up examination at 13 years post-surgery.

3.1. General Implants Evaluation

The general implants evaluation includes all inserted implants in 37 patients: 23 bilaterally treated patients and 14 patients treated on one side. Implants were assigned either to PRP or control group.

3.1.1. Patients Gender, Age, and Smoking Behavior

Seventeen patients (12 female, 5 male) were included in the PRP group, while 20 patients (13 female, 7 male) participated in the control group. Uniform gender distribution between the groups was demonstrated with Fisher's exact test ($p = 1.0$). The age similarity of the patients in the PRP (mean 65.9, SD 16.6, median 68) and control group (mean 60.1, SD 15.8, median 63.5) was given ($p = 0.25$). Patient's information about smoking behavior was evenly distributed as Fisher's exact test indicated $p = 0.67$ for the structural similarity of the two groups.

3.1.2. Implant Numbers and Survival Age

A total of 210 implants were inserted. Of these, 102 implants (48.57%) were placed in the PRP group (mean 12.5, SD 2.7, median 13.0 years) and 108 implants (51.42%) in the control group (mean 12.9, SD 1.6, median 13.0 years). Fisher's exact test demonstrated homogeneity of the two groups with respect to the number of implants per group ($p = 0.16$). The structural similarity between the groups was proven by Fisher's exact test ($p = 0.16$). The rank sum test according to Mann–Whitney and Wilcoxon with $p = 0.76$ proved the structural similarity between the PRP and the control group.

3.1.3. Survival Rate of Implants

Out of 102 investigated implants in the PRP group, 6 were removed (survival rate 94.1%). While two of 108 implants in the control group were lost (survival rate 98.1%). According to Fisher's exact test with $p = 0.16$, no difference between the two groups could be found. The Kaplan–Meier curve in Figure 2 shows the survival time analysis for all implants assigned to the PRP and control group. In the PRP group, the cumulative probability of survival after 15.1 years was 94.1%. In the control group, the cumulative probability of survival was 98.1%. The comparison of survival times using the logrank test resulted in $p = 0.08$ and therefore, no significant difference between the two groups was observed.

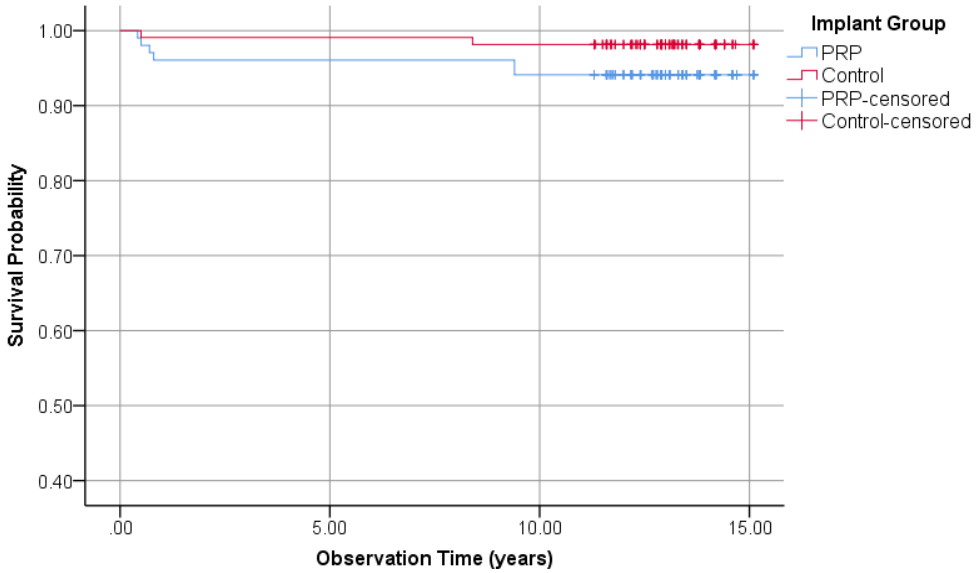

Figure 2. Kaplan–Meier survival probabilities of 210 investigated implants, 102 PRP, and 108 control group.

3.1.4. Implant Success Rate Regarding Buser

Regarding the Buser implant success criteria, 7 implants in the PRP group and two implants in the control group failed to fulfill the success requirements and were rated as failures. This led to a success rate of the PRP and control group of 93.1% and 98.1%, respectively (Fisher's exact test: $p = 0.94$). Kaplan–Meier cumulative success probabilities of the PRP group after an observation period of 15.1 years is 90.9%. The last variable in the control group after 15.1 years was 98.6%. The logrank test was used to compare the success probabilities. A difference between the PRP and the control group could not be determined ($p = 0.13$, Figure 3).

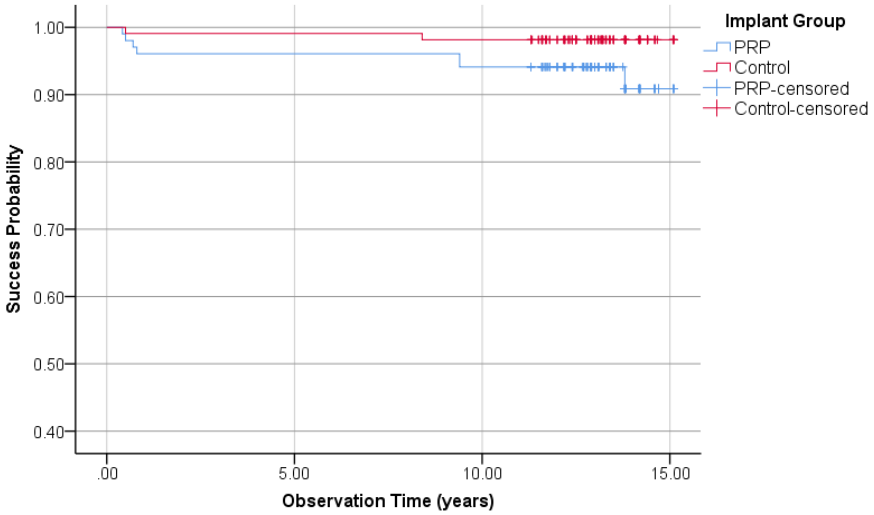

Figure 3. Kaplan–Meier success probabilities of 210 implants according to Buser implant success criteria.

3.1.5. Implant Success Regarding Albrektsson

By applying the Albrektsson implant success criteria on the PRP and control groups, 23 and 12 implants were unsuccessful, respectively. This results in success rates of 77.5% in the PRP group and 88.9% in the control group (Fisher's exact test: $p = 0.04$). Kaplan–Meier cumulative success probability in the PRP group after 15.1 years was 44.5%, whereas the cumulative success probability in the control group was 80.3% (Figure 4). The logrank test showed a significant difference at borderline level between the PRP and control groups ($p = 0.05$).

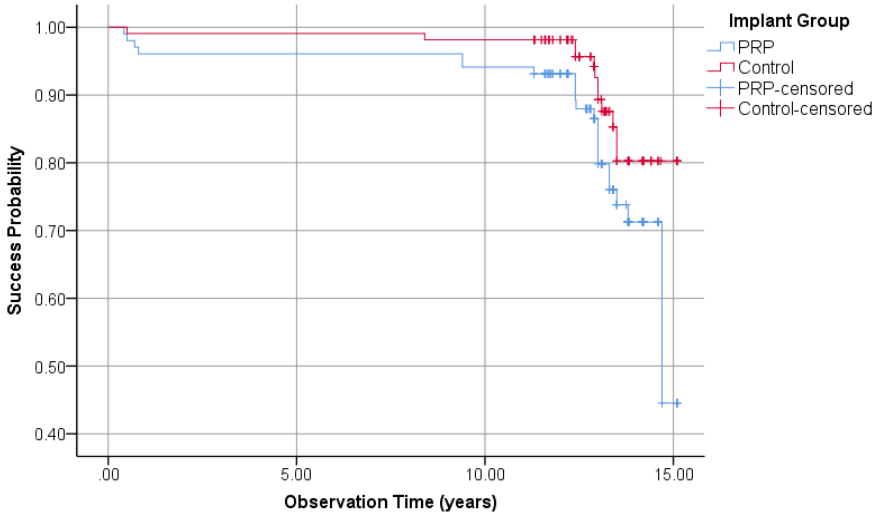

Figure 4. Kaplan–Meier success probabilities of 210 implants according to Albrektsson implant success criteria.

3.2. Split-Mouth Evaluation

The split-mouth evaluation included only the 23 patients who were treated on both sides of the maxilla. One hundred and seventy-one implants were inserted (90 PRP side and 81 control side). Fisher's exact test represents a uniform distribution ($p = 1.0$).

3.2.1. Survival Rate of the Implants (Split-Mouth)

Altogether, seven implants were lost on the PRP-side, 5 out of 90 implants were removed (survival rate 94.4%). On the control-side, two out of 81 implants were lost (97.5% survival rate). The cumulative survival probability according to Kaplan–Meier after an observation period of 15.1 years in the PRP and control side was 94.4% and 97.5%, respectively. The logrank test with $p = 0.31$ showed no statistically significance between the PRP and the control side regarding survival rates of the implants (Figure 5).

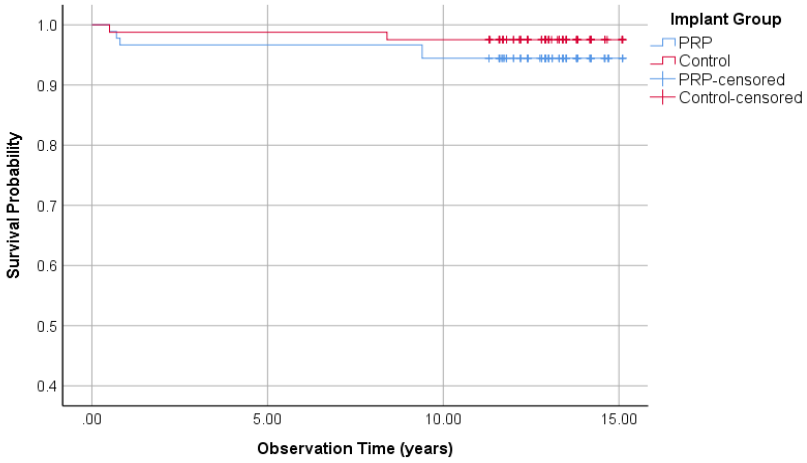

Figure 5. Survival rate of 171 implants in PRP and control side (split-mouth).

3.2.2. Implant Success Rate Regarding Buser (Split-Mouth)

On the PRP side, six implants failed to meet the success criteria of Buser and were rated as failure, resulting in a success rate of 93.3%. The control side had two unsuccessful implants (97.5 % success rate). Kaplan–Meier success probability after an observation period of 15.1 years in the PRP and control side was 91.1% and 97.5%, respectively. Despite better results on the control side, there was no statistically significant difference between the two sides regarding Buser implants success tested by the logrank test ($p = 0.20$) (Figure 6).

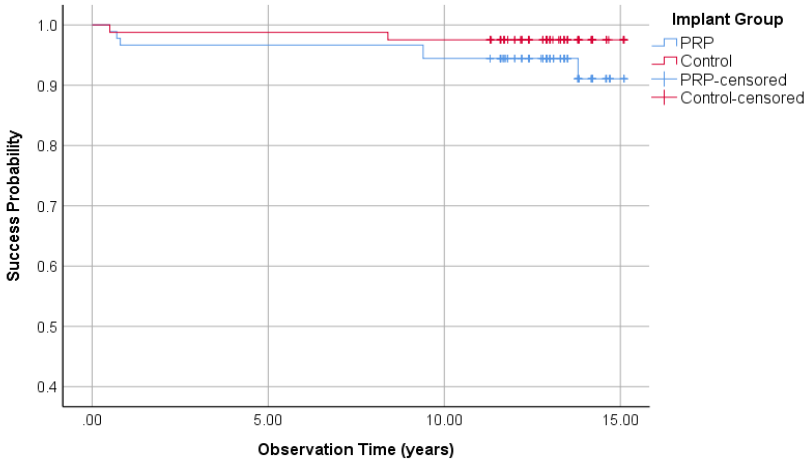

Figure 6. Kaplan–Meier success probabilities of 171 implants regarding the Buser implant success criteria in the split-mouth evaluation.

3.2.3. Implant Success Regarding Albrektsson (Split-Mouth)

On the PRP side, 22 implants were unsuccessful versus eleven implants on the control side referring to the Albrektsson implant success criteria. Consequently, the success rates of implants at the PRP and control side are 75.6% and 86.4%, respectively. Figure 7 visualizes the Kaplan–Meier success probabilities regarding to the Albrektsson criteria. On the PRP side, the 5-, 10-, and 15-year success probability was 96.7%, 94.4%, and 43.7%, respectively. The results on the control side were 98.8%, 97.5%, and 77%. Within the logrank test, a p-Value of $p = 0.13$ showed no significant difference of success rate between the PRP and the control side.

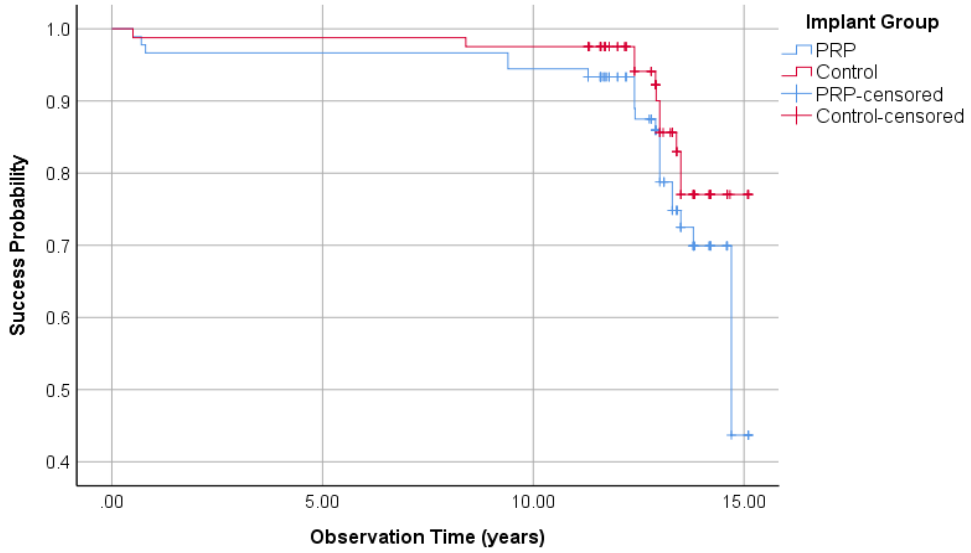

Figure 7. Kaplan–Meier success probabilities of 171 implants regarding the Albrektsson implant success criteria in the split-mouth evaluation.

3.3. Overall Evaluation

Table 1 presents the 12 examined parameters of the general and split-mouth evaluation. Overall, the values from the PRP group were worse than the control group.

Table 1. Summary of test results and comparison of PRP and control group based on tested parameters.

Parameter		PRP-Group		Control-Group	
		Value	Rating	Value	Rating
General-Evaluation	Survival rate	94.1%	-	98.1%	+
	Cumulative survival rate	94.1%	-	98.1%	+
	Success according to Buser	93.1%	-	98.1%	+
	Cumulative success according to Buser	90.9%	-	98.6%	+
	Success according to Albrektsson	77.5%	-	88.9%	+
	Cumulative success according to Albrektsson	44.5%	-	80.3%	+
	Mean years of Evaluation	12.53		12.90	
Split-Mouth-Evaluation	Survival rate	94.4%	-	97.5%	+
	Cumulative survival rate	94.4%	-	97.5%	+
	Success according to Buser	93.3%	-	97.5%	+
	Cumulative success according to Buser	91.1%	-	97.5%	+
	Success according to Albrektsson	75.6%	-	86.4%	+
	Cumulative success according to Albrektsson	43.7%	-	77%	+
	Mean years of Evaluation	13.1		13.1	

+: Value is better than in the other group, -: Value is worse than in the other group.

4. Discussion

The aim of this study was to examine whether PRP has a positive influence on the long-term survival and success of dental implants when used in combination with maxillary bone augmentation. This could not be confirmed by the evaluation of the three parameters (survival rate, success rate according to Buser criteria, and Albrektsson criteria). Most parameters did not show any significant difference between the PRP group and the control group. Kaplan–Meier cumulative success probability according to Albrektsson criteria was statistically significantly higher in the control group than the PRP group. Thus, the hypothesis could not be proven.

Results presented in this study follow the findings of the previous study by Schaaf et al. and prove (in the same patient collection) that PRP has no positive effect in the use of maxillary augmentation on short-term and long-term results. The goal of bone augmentation is to create an optimal bone situation for implant placement and osseointegration, thus ensuring long-term implant success. This study did not show any positive influence of PRP on the long-term implant results. However, it should be noted that the implant success rates of both groups can be regarded high, and thus very satisfactory after an average of 13 years. To see any beneficial effect for any treatment modality, a high number of patients are needed which is a challenge to achieve. It is therefore without surprise that no significant difference in treatment outcome was found.

The most evaluated variable in literature concerning the long-term implant outcome after jaw augmentation and PRP treatment is implant survival. Only one study (Robiony et al.) evaluated the implant success according to Albrektsson criteria and reported an implant success rate of 91.5% after five years. Bone augmentation prior to implantation was performed in combination PRP [27]. In this study, the results regarding long-term survival of the PRP group are inferior. Two reasons might cause this effect. First, the longer follow-up period of this study has to be considered. Second, in the study by Robiony et al., no control group was included. This represents a significant disadvantage because only with a controlled and randomized study design the benefit of a treatment modality, here PRP, can be validly proved as effective [36].

The overall analysis (Table 1) shows that the values of all parameters in the PRP group is inferior to the control group. Therefore, the question arises whether PRP may have a negative impact on long-term outcome. The failure rate probabilities according to Albrektsson criteria were distinctly higher in the PRP group. In order to clarify whether PRP had a negative influence on long-term implant outcome, further controlled trials with larger numbers of test subjects might prove this hypothesis.

In the present study, the two internationally recognized success criteria of Buser and Albrektsson were used. The success rates differed depending on which success criterion was applied. Generally, Albrektsson success criteria presented lower success rates as the one of Buser. The reason may be the assessment of the peri-implant bone loss. However, both success criteria have deficits because they do not reflect the condition of the implant and the surrounding tissue sufficiently. Furthermore, patient satisfaction is not addressed in either success criteria. Some papers suggested the development of a success score [34,37] to assess clinical, radiological, prosthetic and patient satisfaction parameters, as well as implant survival. In addition, an internationally recognized score to measure implant success is highly beneficial to compare the success rates in different studies.

Recently published meta-analysis concerning long-term implant survival after sinus lift surgery and augmentation using different bone grafts conclude that there is no significant difference between autologous and substitute bone graft [38,39]. The current study results also confirm this finding. Therefore, further clinical trials dealing with other regenerative therapy strategies should be conducted. Many of these strategies were described in recent literature [3,4,40]. Most of them aim to avoid surgical complications such as donor-site morbidity in case of autologous bone transplantation and limitations of PRP-technique. Practical considerations regarding feasibility, ethics, and specialization are also relevant when planning a new therapeutic regimen.

The recent discovery of generating mesenchymal stem cells from periapical tissue is a promising concept and might be available for dental practitioners in the future [41]. Due to the good porosity at

low costs, scaffolds are often used in cases of disturbed bone healing and in setting of tumorous bone disease [40]. Furthermore, the use of mineral agents like calcium phosphate cement added with active ingredients such as strontium or nanoparticles loaded on scaffolds such as nanosilicates (poly (glycerol sebacate)) showed an improved mineralization in vivo and in vitro [4,42]. Beside the long way until becoming a certified product, all the above-mentioned technologies are still in the early stages of development with many unknown factors. Long-term follow-up studies are required to demonstrate their clinical effectiveness. Probably it will be time-consuming and hard to prove the benefit of these treatment modalities in RCT. Thus, even older techniques like PRP should be further developed and revalidated. This long-term follow-up study aims to assess the value of autologous bone augmentation in combination with and without PRP, which has been a state-of-the-art approach for many decades.

5. Conclusions

Long-term survival and success rates of dental implants placed after sinus-lift surgery using autologous bone is high and similar to various other bone substitute materials. PRP shows no positive impact with a tendency to a slightly negative effect on implant survival and other success criteria. Therefore, upcoming biologic regenerative therapies to improve bone healing and implant-tolerance should be investigated further.

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3.5 Long-Term Influence of Platelet-Rich Plasma on Dental Implants after Maxillary Augmentation: Retrospective Clinical and Radiological Outcomes of a Randomized Controlled Clinical Trial

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Summary

The long-term clinical and radiological results of dental implants placed in PRP-treated enhanced bone have yet to be properly addressed in the literature. This research was based on a group of patients who participated in an RCT that found no short-term benefits of PRP on bone healing following sinus lift surgery with autologous iliac crest bone transplant. The goal of this trial was to determine how long PRP had an effect on the clinical and radiological results of the implants placed in the previous RCT. The plaque index, PD, bleeding index, mobility grade, PT scores, and radiographic bone loss were all parameters examined in this analysis. We were able to reinvestigate 37 patients (n = 210 implants) in two centers out of the 53 individuals (n = 306 implants) in the prior trial (31 in Giessen, Germany, and 6 in Erlangen, Germany). The clinical and radiological characteristics revealed that the peri-implant tissue was in good health. Most variables between the PRP and control groups were not significantly different. In 64% of the analyzed parameters, the PRP group's outcome data were inferior to those of the control group according to the overall evaluation. The current study was unable to demonstrate that PRP had a positive impact on the long-term

implant clinical and radiological outcomes. In the PRP group, there was a trend toward poorer long-term outcomes, although this did not reach a statistically significant level. To further study this connection, further controlled experiments are required [67].

Original Article 5

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Long-Term Influence of Platelet-Rich Plasma (PRP) on Dental Implants after Maxillary Augmentation: Retrospective Clinical and Radiological Outcomes of a Randomized Controlled Clinical Trial

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Abstract: The long-term clinical and radiological outcomes of dental implants inserted in augmented bone treated with platelet-rich plasma (PRP) has not been well addressed in the literature yet. This study is based on a collection of patients from a randomized controlled trial (RCT) that did not report any short-term positive effects of PRP on bone healing after sinus lift surgery using autologous iliac crest bone graft. This study aimed to evaluate the long-term impact of PRP regarding clinical and radiological outcomes on the inserted implants in the previous RCT. For this evaluation, we considered the following variables: plaque index, probing depth, bleeding index, mobility grade, Periotest® values, and radiological bone loss. Out of 53 patients (n = 306 implants) included in the previous study we were able to reinvestigate 37 patients (n = 210 implants) in two centers (31 in Giessen, Germany and 6 in Erlangen, Germany). Clinical and radiographic parameters suggested overall healthy conditions of the peri-implant tissue. The PRP-group and the control group did not differ significantly in the majority of the parameters. The overall evaluation showed that result data of the PRP-group was inferior to the control group in 64 percent of the evaluated parameters. The present study cannot provide evidence of a positive effect of PRP on the long-term implant clinical and radiological outcomes. In fact, a tendency towards inferior long-term results in the PRP-group was detected without reaching a significant threshold. Further controlled trials need to be conducted to investigate this correlation.

Keywords: dental Implant; PRP; Long-term result; Sinus lift; clinical outcome; radiological outcome

1. Introduction

Dental implants have high survival probabilities with good clinical and radiological findings [1]. Long-term studies documented a survival rate of approximately 95% over a study period of at least ten years [2,3]. One of the important factors leading to late implant loss is peri-implantitis, which is a combination of mucositis and bone resorption around implants [4–6]. Pain, implant mobility, crestal bone loss over a half of implant length, and persistent exudate from the peri-implant tissue

are the most common reasons for implant removal [7]. Studies have reported a correlation between autologous cancellous bone grafts and long-term bone resorption, which leads to peri-implantitis and consecutive implant loss [8,9].

Bone loss resulting from trauma, disease, aging, or congenital abnormalities, remains a global challenge for health professionals and patients. Maxillofacial or craniofacial bone loss has a high psychological impact on patients. Therefore, aesthetic reconstruction is as valuable as functional reconstruction in this region [10].

Tissue engineering is a feasible method which can be pursued to perform aesthetic reconstruction. This implies the enhancement of autologous bone grafts using PRP [11]. In recent years, a staggering development on the use of tissue engineering and biomaterials has shifted beliefs and expectations [12]. Although recent strategies, such as decellularized matrix, nanoparticles, stem-cell therapies, scaffolds, and the engineering of a whole tooth, have shown some success, older approaches such as platelet-rich plasma (PRP) and platelet-rich fibrin (PRF) still require validation or disproof of their clinical efficacy through long-term follow-ups [12–14].

Since the first introduction of the use of PRP in augmentation techniques [11], various studies have been conducted to evaluate its effectiveness [15–20]. Optimized bone healing with enhanced bone mineral density was the most tested hypothesis in these studies. Results were controversial, with positive effects [15,18] and no effects [17,21] of PRP. Following initial positive effects of PRP, Consolo et al. reported a decrease of the bone mineral density after six months [18]. In another study, the same period was needed to report the first improvement of bone density by using PRP [22]. The fact is, if the bone density improves after augmentation using a mainly cancellous bone graft, such from the iliac crest bone, the long-term bone resorption around dental implants will be reduced [23]. Although the literature has addressed augmentation with and without PRP, long-term follow up has been rarely discussed. Thor et al. compared implant survival, marginal bone level, and implant stability after one year of mastication function of inserted dental implants in the maxilla, following autogenous bone grafting with or without PRP in a split mouth design [24]. The implant survival and marginal bone level revealed no statistically significant differences. Implant stability was tested by using resonance frequency analysis (RFA). Only implants in the anterior maxilla proved to be more stable on PRP sites [24]. Recent studies focused on the effect of PRP have had some limitations, such as a lack of a control group or only mid-term follow-up time [25–27]. Clinical practitioners judge the validity and feasibility of a given procedure more through a randomized controlled trial with long-term results. To the best of our knowledge, long-term clinical and radiological implant assessments after using an autologous iliac crest bone graft and PRP have not been well addressed in the literature. To investigate the long-term influence of PRP, we used the same collection of patients from the prospective randomized clinical trial (RCT) by Schaaf et al. [19]. The RCT was conducted between 2001 and 2004 in two centers (Oral and Maxillofacial Departments at the Universities of Giessen and Erlangen, Germany). 53 Patients (34 split-mouth, 19 unilateral) with maxillary atrophy underwent sinus lift surgery and iliac crest augmentation with and without PRP. That study could not determine any significant differences between the test and control group regarding bone density [19]. In this study, we hypothesized that dental implants placed in PRP-augmented bones have better clinical and radiological outcomes.

2. Materials and Methods

2.1. Study Design and Patient Groups

The study has been designed as a randomized controlled single-blind retrospective study. 53 patients from the Schaaf et al. study were included in this retrospective clinical and radiological study. The majority of the patients were examined in the Department of Cranio-Maxillofacial surgery in the University Hospital of Giessen. In addition, some examinations were carried out at the University Hospital in Erlangen. Due to the long journey from their place of residence, some patients were examined at the offices of their family dentists. Nevertheless, all examinations were carried out

by the same evaluator. Patients were divided into two groups: split-mouth and unilateral groups to make the results comparable. Pregnancy and bad general condition were the exclusion criteria. Examiner preparation was done before starting the follow-up investigation. The evaluator prepared by investigating 50 dental implants clinically and radiologically from randomly selected patients. None of these patients were part of the study. Independently, an experienced oral surgeon evaluated the same implants and patients. The results of both evaluators were then compared. Agreement between the evaluators was measured by Kappa and Bland-Altman analysis. For the plaque index, Kappa values were 0.940 ($p \leq 0.001$), for probing depth 0.870 ($p \leq 0.001$), for bleeding index 0.919 ($p \leq 0.001$), and the Periotest® was 1.000 ($p \leq 0.001$). In the mobility test, no variation was detected, therefore no Kappa calculation was possible. Agreement of bone loss measurement was proven by Bland-Altman analysis. We detected a bias of 0.04 with limits of agreement from -0.6 to 0.52. This calibration method was aimed at improving the accuracy of the diagnostic tasks as previously reported and recommended [28]. Radiographs were evaluated independently in a random fashion by the evaluator and an experienced oral surgeon to avoid investigation bias. The current study re-examined patients who participated in a randomized controlled prospective study after a mean follow-up period of 13 years. In this follow-up study, the single evaluator of the clinical examination and both evaluators of the radiological examination were blinded to the treatment with PRP. A number of 23 patients were treated bilaterally in a split-mouth design and 14 patients were treated on one side only. The patients who were treated unilaterally were randomly assigned to the study or control group depending on the side treated. The bilaterally treated patients were classified to the following subgroups "right with PRP, left without PRP" or "right without PRP, left with PRP ". This was done with adaptive stratification using central telephone randomization for both treatment centers. This study follows the CONSORT 2010 checklist developed for reporting a randomized trial [29].

2.2. Measured Variables

2.2.1. Clinical Parameters:

Clinical parameters used to evaluate dental implants include the following.

Plaque Index

To document the plaque colonization on the implant, the Mombelli plaque index was used with these characteristics:

Grade 0: No plaque detectable
Grade 1: Plaque only detectable by probing
Grade 2: Visible plaque deposit
Grade 3: Massive plaque deposition [30].

Probing Depth

The probing depths around the implants were measured at four sites (mesial, vestibular, distal, and palatal) using a plastic Click Probe ™ (Kerr Dental, Bioggio, Switzerland).

Bleeding Index

The bleeding tendency of the gingiva during probing was measured parallel to the probing depths. Existing or missed bleeding was also documented at four sites per implant.

Mobility Grade

The degree of clinical loosening was determined for each implant. The different grades were categorized into the following grades:

Grade 0: No increased mobility
Grade 1: Perceptible and visible horizontal mobility ≤1 mm
Grade 2: Visible horizontal mobility >1 mm
Grade 3: Movement through tongue or lip pressure.

Periotest® Values

The Periotest® Classic device (Medizintechnik Gulden, Modautal, Germany) can be used to evaluate the osseointegration of implants [31]. The device taps the implant with a plunger and measures how much the plunger is dampened by the implant. The results are classified into the following values:

−8 to 0 Satisfactory osseointegration
+1 to +9 Clinical examination of the implant required
+10 to +50 Insufficient osseointegration.

2.2.2. Radiological Parameters:

Bone loss of the augmented bone region in the upper jaw was also determined. The alveolar crest height in the upper jaw was measure in a panoramic X-ray. The difference in bone resorption was determined using the post-augmentation alveolar crest height in the previous study. The Sidexis 4 Viewer® program was used to measure the alveolar ridge height. The measurement was performed as carried out in the study by Schaaf et al., right and left upper second premolar and first molar. To eliminate the magnification factors in the panoramic X-ray, calibration using the implant diameter was used (Figure 1). Subsequently, the distance from the sinus floor to the alveolar crest was measured in second premolar and first molar regions and calculated with the previously calculated magnification factor. To calculate bone loss, the calculated alveolar crest height was subtracted from the value measured in the previous study prior to implant surgery.

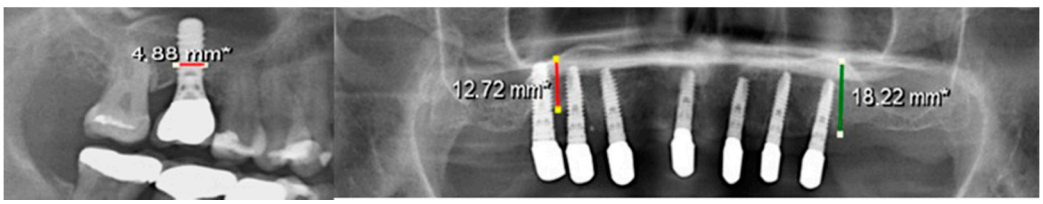

Figure 1. Calibration of the panoramic X-ray for accurate measurement of the bone resorption. *: calibrated according to scale bar.

Smoking
Patients should provide information on their smoking behavior in the following increments:

- 1–5 cigarettes a day
- 5–15 cigarettes a day
- > than 16 cigarettes a day.

2.3. Statistical Analysis

Data recorded from the patients were divided to unilateral and bilateral groups of patients and were analyzed separately. The evaluation of the clinical and radiological parameters was performed mainly on the inserted implant in the two groups. A Fischer's exact test or a chi-square test was used to analyze the qualitative variables. Quantitative variables were compared using the Mann-Whitney and Wilcoxon rank sum test. SPSS 25 was used for data analysis (IBM Corp. Released 2017. IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY: IBM Corp.). Normality distribution of quantitative variables was verified by graphical methods (Histogramm, QQ-Plots).

2.4. Ethics Approval

This study was approved by the ethical committee of the medical faculty at Justus-Liebig University of Giessen (Approval number 129/15).

3. Results

Out of 53 patients (n = 306 implants) included in the previous study by Schaaf et al., we were able to investigate 37 patients (n = 210 implants) in two centers (31 in Giessen, Germany and 6 in Erlangen, Germany). Various reasons lead to the drop-out of 16 patients such as: deceased or bad physical condition (n = 4), rejection of participation (n = 7), and patients not reachable (n = 5) (Figure 2).

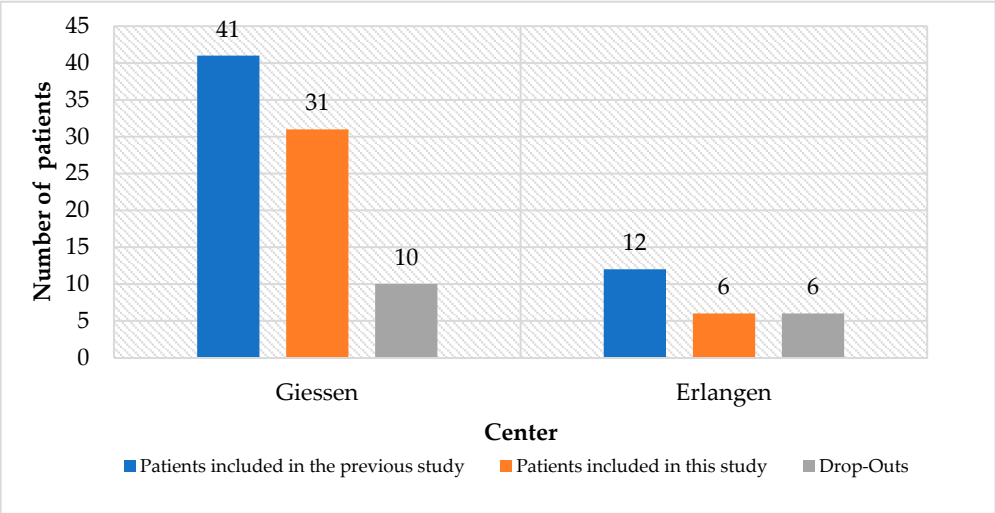

Figure 2. Number of patients included in this study versus number of drop-outs in the two clinics.

25 female (67.6%) and 12 male (32.4%) patients with ages ranging between 30 and 90 years (median 65 years) and 210 implants were included. Out of 210 inserted dental implants, eight implants were lost and removed. Time between implant placement and follow-up examination ranged between 11.3 and 14.1 years (mean 13 years). The survival rate for all inserted implants was 96.2%. The statistical analysis was divided into two evaluation groups depending on the treatment design. Patients who were treated bilaterally (n = 23) were included in the split-mouth evaluation. The unilateral evaluation included the unilaterally treated patients (n = 14) and the 23 patients from the split-mouth evaluation, which were randomly included with one side of the body in the evaluation, so that the participants belonged to either the PRP or the control group.

3.1. Split-Mouth Evaluation

All 23 patients who were treated bilaterally, one side with PRP and the other one only with bone, referred to as control side, were included in this evaluation. The gender distribution was 15 (65.2%) female and 8 (34.7%) male patients. The age range of the patients was 30–90 years. Altogether 171 dental implants were inserted, 90 implants in the PRP and 81 in the control group. The implant systems used were: Xive® implants (Dentsply Sirona, York, USA), Straumann® Standard Plus (Straumann, Basel, Swizerland), Brånemark MK III TiUnite® Implants (Nobel Biocare, Kloten, Switzerland), and Osseotite® implants (Biomet 3i, Munich, Germany) (Figure 3). The average time between the implant insertion and follow-up examination was 13 years. Since the clinical parameters of the seven already-lost implants could not be determined, the number of implants evaluated decreased from n = 171 to n = 164.

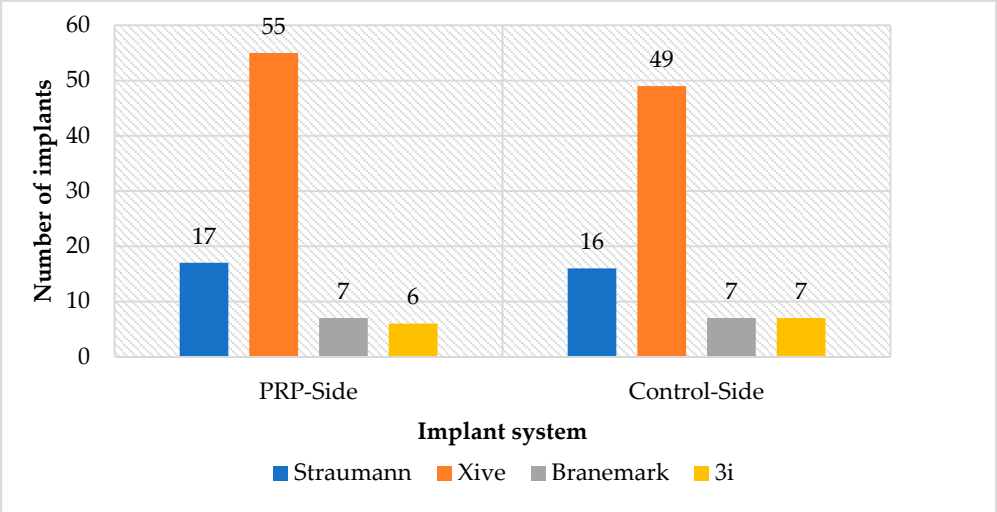

Figure 3. Number of implant in each implant system in both the platelet-rich plasma (PRP) and control sides.

3.1.1. Plaque index

Table 1 shows the results of the clinical examination for plaque accumulation on the implants. On average, a plaque index of 1 on the PRP and 1.2 on the control side was documented. Fisher's exact test ($p = 0.57$) showed no statistically significant difference between the PRP and the control side.

Table 1. Distribution of the plaque index on the implants (split-mouth evaluation).

Plaque Index According to Mombelli	Platelet-rich plasma (PRP) Side		Control Side	
	Number of Implants	Percent	Number of Implants	Percent
Grade 0: No Plaque	26	30.6%	19	24%
Grade 1: Plaque visible by probing	38	44.7%	33	41.8%
Grade 2: Visible plaque accumulation	17	20%	21	26.6%
Grade 3: Massive plaque accumulation	4	4.7%	6	7.6%
Total	85	100%	79	100%

3.1.2. Probing Depth

The maximum probing depth measured on each implant was recorded (Table 2). On average, the maximum probing depths were 4.1mm (Standard Deviation (SD) 1.3) on the PRP side and 3.8 mm (SD 1.2) on the control side, with a median of 4 (min.: 2, max.: 7) on both groups. The Mann-Whitney and Wilcoxon test showed no statistically significant difference between the PRP and the control side ($p = 0.11$).

Table 2. Distribution of the maximum probing depth in both the PRP and control sides (split-mouth evaluation).

Maximum Probing Depth	PRP Side		Control Side	
	Number of Implants	Percent	Number of Implants	Percent
2 mm	8	9.4%	7	8.9%
3 mm	22	25.9%	29	36.7%
4 mm	27	31.8%	27	34.2%
5 mm	11	12.9%	8	10.1%
6 mm	16	18.8%	5	6.3%
7 mm	1	1.2%	3	3.8%
Total	85	100%	79	100%

3.1.3. Bleeding Index

On the PRP side, 51 implants (60%) did not bleed on probing and 35 (40%) did bleed. On the control side, bleeding occurred in 22 implants (27.8%), but 57 implants (72.2%) did not bleed. There was no difference with Fisher's exact test ($p = 0.14$) between the PRP and control sides.

3.1.4. Mobility Grade

None of the examined implants in both PRP and control sides showed any signs of mobility.

3.1.5. Periotest® Value

Table 3 shows the Periotest® measurements. The values were summarized in three value ranges. With two implants, one on the PRP and one at the control side, the Periotest® measurement was more than 10. One of the implants had a loose superstructure, the other implant had no other clinical or radiographic abnormalities other than the remarkable Periotest® value. On average, a Periotest® value of 1.3 was determined on the PRP and the control side. Fisher's exact test with p = 0.69 showed no statistically significant difference between the PRP and the control side.

Table 3. Distribution of Periotest® value ranges (split-mouth evaluation).

Periotest®	PRP Side		Control Side	
	Number of Implants	Percent	Number of Implants	Percent
Values between −8 and 0: Satisfactory osseointegration	64	75.3%	54	68.3%
Values between 1 and 9: Clinical examination is necessary	20	23.5%	24	30.4%
Values ≥10: Insufficient osseointegration	1	1.2%	1	1.3%
Total	85	100%	79	100%

3.1.6. Alveolar Ridge Height

The distance from the sinus floor to the alveolar crest in the panoramic X-ray in the augmented region was measured as the height of the alveolar ridge. This ranged in the PRP side between a minimum of 9.6 mm and maximum of 21.9 mm, with a mean SD of +/- 3.4 mm and a median of 13.3 mm. In the control side, the distance ranged between minimum of 9.4 mm and maximum of 23.9 mm, with SD of 4.1 mm and median of 12.7 mm. The rank sum test according to Mann-Whitney and Wilcoxon with $p = 0.72$ indicates no difference between the PRP and the control side (Figure 4).

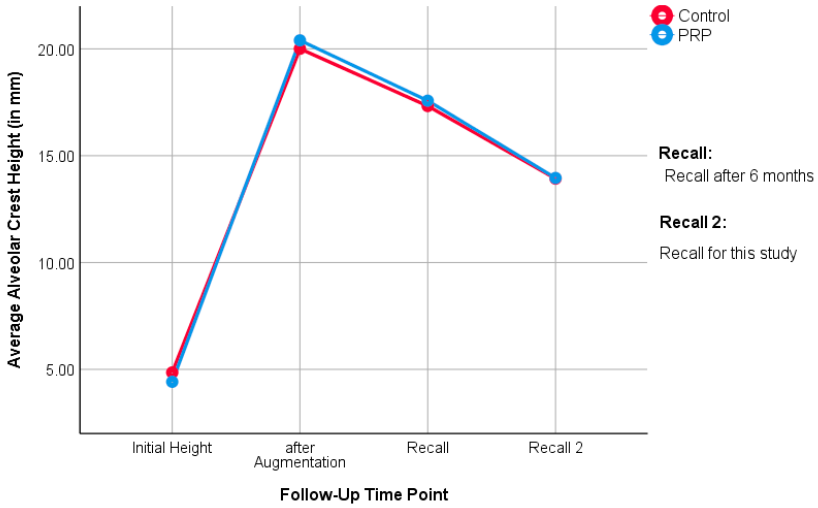

Figure 4. The alveolar crest height at the follow-up examination between the PRP and control side (split-mouth evaluation).

3.1.7. Bone Loss at Augmented Areas

Absolute bone loss represents the difference in alveolar crest height after augmentation (post-operative) and measured alveolar crest height in this study (follow-up). The Mann-Whitney and Wilcoxon rank sum test showed no difference between the median bone loss values of the PRP side and the control side ($p = 0.88$). The percentage of bone loss represents the ratio of absolute bone loss to bone height after augmentation. There was no significant difference between the two sides with the rank sum test according to Mann-Whitney and Wilcoxon ($p = 0.53$) (Table 4).

Table 4. Absolute bone loss of the augmented region/percentage of bone loss of the augmented region (split-mouth evaluation).

Patients.	PRP Side		Control Side	
Number of Patients	23		23	
Mean	6.4391 mm	29.6%	6.0783 mm	27.3%
Standard deviation	4.48135 mm	13.5%	5.49545 mm	18%
Minimum	1.30 mm	8.6%	0.40 mm	2.5%
Median	5.4000 mm	31.5%	4.6000 mm	25.6%
Maximum	19.30 mm	64.3%	21.30 mm	66.6%

3.2. Unilateral Evaluation

The unilateral evaluation includes 14 unilaterally treated patients and the 23 bilaterally treated patients that were randomly included with one side of the maxilla in the evaluation, so that the participants belonged to either the PRP or the control group. In conclusion, of the 37 patients, 20 (13 female, 7 male) were in the control group and 17 patients (12 female, 5 male) belonged to the PRP group. Fischer's exact test demonstrated the even gender distribution between the groups ($p = 1.0$). The age of the patients in the PRP group was 31–90 years with SD, median, and mean of 16.6, 81, and 60.1 years respectively. The age of the patients in the control group was 30–81 years, with SD of 15.8, median of 68, and mean of 65.9 years. The rank sum test according to Mann-Whitney and Wilcoxon with $p = 0.26$ showed that the two study groups were not different in terms of median age. Table 5 illustrates how the patients' data on smoking behavior was distributed. Fischer's exact test indicated $p = 0.53$ for the structural similarity of the two groups. A total of 127 implants were inserted. Of these, 58 implants (45.7%) were placed in the PRP group and 69 implants (54.3%) in the control group. The homogeneity of the two groups was proven by using Fisher's exact test ($p = 0.53$) with respect to the number of implants per patient. Figure 5 shows the distribution of the implant systems used in the two groups. The structural similarity between the groups was proven by Fischer's exact test ($p = 0.37$). Time between implant placement and follow-up examination in the PRP group was between 11.6 and 14.6 years, with a mean of 13.0 (SD 0.9) years and median of 13 years. In the control group, the follow-up time ranged between 11.3 and 15.1 years, with a mean of 12.9 (SD 1.1) years and median of 13 years. The rank sum test according to Mann-Whitney and Wilcoxon with $p = 0.96$ proved the structural similarity between the PRP and the control groups. Due to the four implants lost, the number of implants was reduced from $n = 127$ to $n = 123$ in the evaluation of clinical and radiological parameters.

Table 5. Distribution of smoking behavior in PRP and control groups (unilateral evaluation).

Smoking Behavior	PRP Group		Control Group	
	Number of Patients	Percent	Number of Patients	Percent
Non-smoker	12	70.6%	15	75%
Smoker and ex-smoker	5	29.4%	5	25.0%
Total	17	100%	20	100%

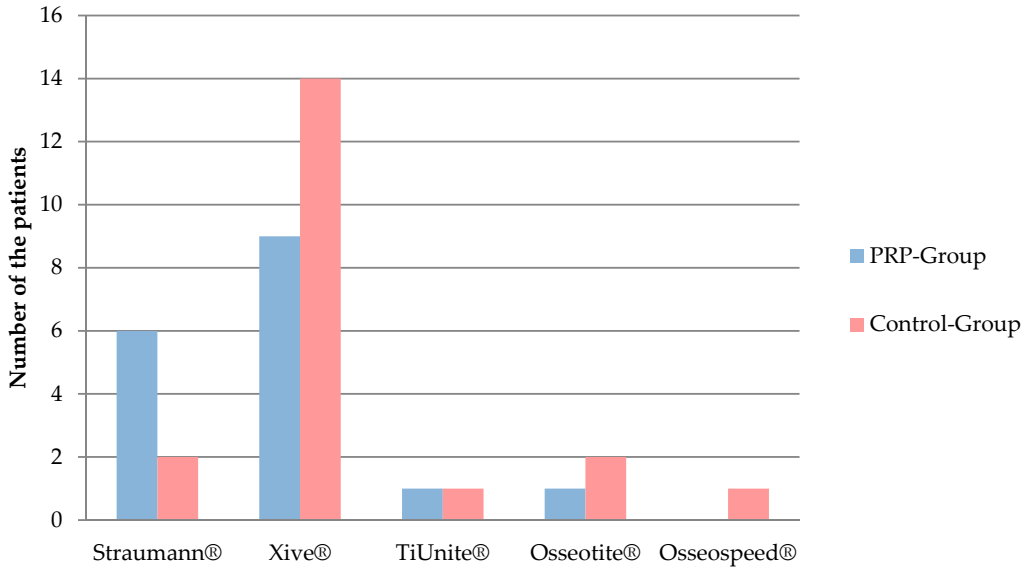

Figure 5. Distribution of implant systems used in PRP and control groups (unilateral evaluation).

3.2.1. Plaque Index

Table 6 shows the distribution of the Mombelli plaque index in the PRP and control groups. On average, the plaque index was found to be 0.9 in the PRP group and 1.1 in the control group. Fisher's exact test demonstrated no difference between the two groups ($p = 0.28$).

Table 6. Distribution of the plaque index on the implants (unilateral evaluation).

Plaque Index According to Mombelli	PRP Side		Control Side	
	Number of Implants	Percent	Number of Implants	Percent
Grade 0: No Plaque	21	38.2%	15	22.1%
Grade 1: Plaque visible by probing	22	40%	34	50%
Grade 2: Visible plaque accumulation	10	18.2%	16	23.5%
Grade 3: massive plaque accumulation	2	3.6%	3	4.4%
Total	55	100%	68	100%

3.2.2. Probing Depth

Table 7 shows the distribution of the maximum probing depths measured on the implants in the PRP and control groups. The average probing depth for the PRP group was 4.2 mm (SD 1.37), and 3.6 mm (SD 1.06) for the control group (median PRP: 4, range: 2–8; median control: 3, range: 2–7). The Mann-Whitney and Wilcoxon test of $p = 0.005$ proved a statistically significant difference between the two groups.

Table 7. Distribution of the maximum probing depth in both PRP and control groups (unilateral evaluation).

Maximum Probing Depth	PRP Side		Control Side	
	Number of Implants	Percent	Number of Implants	Percent
2 mm	5	9.1%	8	11.7%
3 mm	13	23.6%	28	41.2%
4 mm	17	30.9%	24	35.3%
5 mm	9	16.4%	3	4.4%
6 mm	9	16.4%	4	5.9%
7 mm	1	1.8%	1	1.5%
Total	1	1.8%	0	0%

3.2.3. Bleeding Index

Peri-implant tissue bled upon probing in 22 implants (40%) of the PRP group, 33 (60%) did not bleed. In the control group, bleeding occurred in 19 implants (27.9%), and did not occur in 49 (72.1%). Fischer's exact test could not prove any statistically significant difference between the two groups ($p = 0.18$).

3.2.4. Mobility grade

All examined implants had a degree of loosening of 0.

3.2.5. Periotest® value

Table 8 gives an overview of the distribution of recorded Periotest® values. The values are displayed in value ranges. On average, a Periotest® value of 1.3 was measured in the PRP group, 1.2 in the control group. Fischer's exact test with $p = 0.84$ showed no statistically significant difference between the PRP and the control group.

Table 8. Distribution of Periotest® value ranges (unilateral evaluation).

Periotest®	PRP Side		Control Side	
	Number of Implant	Percent	Number of Implant	Percent
Values between -8–0: Satisfactory osseointegration	41	74.5%	52	76.5%
Values between 1–9: Clinical examination is necessary	14	25.5%	16	23.5%
Total	55	100%	68	100%

3.2.6. Alveolar Ridge Height

The distance from the sinus floor to the alveolar ridge was measured by a panoramic X-ray in the augmented region. The distance in the PRP group ranged between 7.1 to 21.9 mm, with SD of 4.2 and a median of 12.8. The alveolar ridge height in the control group ranged between 8 and 23.9 mm, with SD of 3.2 and median of 12.8 mm. The rank sum test according to Mann-Whitney and Wilcoxon did not prove any statistically significant difference between the PRP and the control groups ($p = 0.96$). Figure 6 shows mean alveolar crest height over time from the beginning of the previous study to the follow-up in this study.

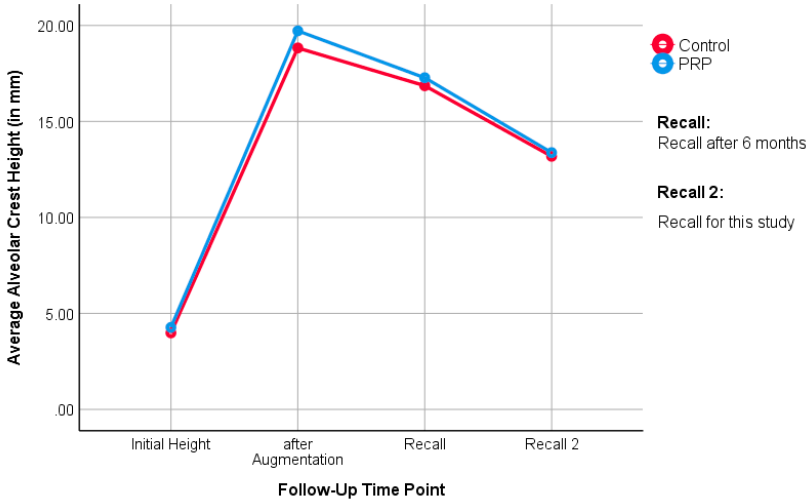

Figure 6. The alveolar crest height at the follow-up examination between the PRP and control sides (unilateral evaluation).

3.2.7. Bone Loss of the Augmented Region

The absolute bone loss, calculated from the difference in alveolar crest height after augmentation, and the measured alveolar crest height in the course of this study were recorded.

A comparison of the median bone loss values of the PRP and control groups with the Mann-Whitney and Wilcoxon rank sum test failed to show any difference between the two groups with $p = 0.46$.

The ratio of absolute bone loss to bone height after augmentation was calculated as percentage of bone loss. There was no difference between the PRP and the control group with the Mann-Whitney and Wilcoxon rank sum test ($p = 0.70$) (Table 9).

Table 9. Absolute bone loss of the augmented region/percentage of bone loss of the augmented region (unilateral evaluation).

Patients	PRP Side		Control Side	
Number of patients	17		20	
Mean	6.3412 mm	31.3%	5.6450 mm	28.2%
Standard deviation	3.86831 mm	15%	4.57032 mm	16.3%
Minimum	1.30 mm	8.6%	0.40mm	2.5%
Median	5.4000 mm	35%	4.9000 mm	27.2%
Maximum	16.70 mm	60.6%	21.30 mm	66.6%

3.3. Overall Evaluation

Table 10 presents the clinical and radiological parameters ($n = 14$) of the split-mouth and the unilateral evaluation in a general overview. Overall, the values of the PRP group exceeded the control group in three parameters. The values of the control group exceeded the values of the PRP group in nine parameters. For two parameters, the values of both groups were the same.

Table 10. Summarizing the result of the tested parameters between the PRP and control groups in both evaluations.

Parameter		PRP-Group		Control-Group	
		Value	Rating	Value	Rating
Split-Mouth Evaluation	Plaque index (mean)	1.0	+	1.2	-
	Probing depth (mean)	4.1 mm	-	3.8 mm	+
	Bleeding index	40%	-	27.8%	+
	Periotest® (mean)	1.3	=	1.3	=
	Alveolar ridge height (median)	13.3 mm	+	12.7 mm	-
	Absolute bone loss (median)	5.4 mm	-	4.6 mm	+
	Percentage bone loss (median)	31.5%	-	25.6%	+
Unilateral Evaluation	Plaque index (mean)	0.9	+	1.1	-
	Probing depth (mean)	4.2 mm	-	3.6 mm	+
	Bleeding index	40%	-	27.9%	+
	Periotest® (mean)	1.3	-	1.2	+
	Alveolar ridge height (median)	12.8 mm	=	12.8 mm	=
	Absolute bone loss (median)	5.4 mm	-	4.9 mm	+
	Percentage bone loss (median)	35%	-	27.2%	+

+: value is better than in the other group, -: value is worse than in the other group, =: value is similar to the other group.

4. Discussion

This study aimed to investigate the long-term impact of PRP on the clinical and radiological treatment outcomes of dental implants. A comparison to the treatment outcome without PRP was established by the evaluation of a control group or a control side. The distribution of the patients to the study groups was randomized and the investigators were blinded (patients' group affiliation was unknown to the investigator). This study represents a non-experimental therapeutic study with

retrospective data collection and thus shows a lower level of evidence compared to other prospective studies. Nevertheless, it must be emphasized that there is currently no controlled study reporting the influence of PRP on long-term clinical and radiological outcomes, therefore, this study provides important information in this regard. The randomization and stratification of the previous trial achieved a structural equality within the individual groups. Since the present study is based on the same patient collection, structural equality, despite the drop-outs, was maintained. Additionally, this study was designed as a bicentric study, as patients from both Giessen and Erlangen were examined. Using several centers increased the external validity and improved the comparability of the results of the study [32]. One limitation of this study is the number of 37 included patients. Statistically, this represents a small population of patients. A greater quantity of patients allows for higher statistical power and can be better communicated to the general public [33]. However, as this is a long-term follow-up study in which patient population was dependent on the previous study, it is obvious that contact would not be possible for several patients.

The clinical and radiological implant parameters were hard to compare with the current literature, as there is a lack of equivalent research already published. Therefore, studies disregarding PRP were considered and contrasted with the results of the control group. The plaque index according to Mombelli et al. [30] was recorded in all investigated implants. In the PRP group, 75.3% (split-mouth evaluation) and 78.2% (unilateral evaluation) of the implants showed no or low plaque accumulation (Grade 0 or 1). In the control group, similar results were reported in 65.8% (split-mouth evaluation) and 72.1% (unilateral evaluation) of the implants. This suggests that good oral hygiene was maintained by the majority of patients in both groups. Moderate to massive plaque (Grade 2 or 3) was found in 24.7% (split-mouth evaluation) and 21.8% (unilateral evaluation) of implants in the PRP group, and 34.2% (split-mouth evaluation) and 27.9% (unilateral evaluation) in the control group. There was no significant difference between the groups. Average plaque index was 1 in the PRP group (split-mouth evaluation) and 0.9 (unilateral evaluation) and in the control group it was 1.2 (split-mouth evaluation) or 1.1 (unilateral evaluation). The implants' plaque index in the study by Attia et al. reported Grade 0 or 1 in 75.2% of cases, while 24.8% of the implants were Grade 2 or 3 [34]. This corresponds to the results of the control group from the present study. Simonis et al. investigated 131 implants after an observation period of 10 to 16 years [35]. The average plaque index documented in this study was 1.1, which is comparable with the data of the control group from the present results.

On average, the measured pocket depth in the PRP group was 4.1 mm and 4.2 mm, and in the control group 3.8 mm and 3.6 mm in split-mouth evaluation and unilateral evaluation, respectively. Probing depths of more than 4 mm were considered pathological for implants [36]. In the present study, 67.1% (split-mouth evaluation) and 63.6% (unilateral evaluation) of the implants had probing depths of up to 4 mm in the PRP group. In the control group, a probing depth exceeding 4 mm was present in 79.8% (split-mouth evaluation) and 88.2% (unilateral evaluation) of implants. Pathological pocket depths of more than 4 mm were documented in the PRP group in 32.9% (split-mouth evaluation) and 36.4% (unilateral evaluation) of total implants, in the control group in 20.2% (split-mouth evaluation) and 11.8% (unilateral evaluation) of total implants. No statistically significant differences between the groups could be demonstrated in the split-mouth analysis with respect to the probing depths. In the unilateral evaluation, however, the PRP group had significantly higher probing depths. Here, it must be taken into consideration that the measurement of probing depths due to pseudo pockets and the design of the crown can be falsified. In case of pseudo pockets, there is no equivalent marginal bone loss despite increased probing depth. In the evaluation of crestal bone loss, no significant difference between the groups was detected in the unilateral evaluation. It can therefore be assumed that the results of the probing depths were worsened by pseudo pockets. In the study by Attia et al., 84.1% of the implants had probing depths of up to 4 mm. Pocket depths of more than 4 mm were measured on 15.7% of all implants. These values confirm the results from the control group of this study [34]. In addition, Van Velzen et al. reported in their prospective study of 177 patients probing depths of

3.7 mm with 374 implants after 10 years. This result is also comparable with the results of the control group in this study [37].

In both end points of the PRP group, 60% of implants showed no bleeding on probing. In the control group, 72% of implants did not bleed in both evaluations. No significant difference was found between the two study groups. Becker et al. examined 388 implants after an average of 14 years. They were clinically unable to detect bleeding in 79.1% of the implants. This result is similar to the values of the control group from this study [38].

No implant loosened at the time of follow-up. Thus, there is no difference between the PRP and the control group with respect to the degree of loosening. Other studies in the literature indicate the same results [34,39].

Periotest® values of −8 to 0 indicate a satisfactory osseointegration of the tested implant. Values of up to 9 should be clinically re-evaluated and values of 10 and above indicate a lack of osseointegration [40]. In the present study, values ranging from -8 to 0 (68.3 to 76.5%) were observed in both groups in approximately half of the implants. Between 23.5% and 30.4% of the implants, the Periotest® device delivered values of 1 to 9. Values above 10 were only determined for a maximum of 1.3% of the implants. In the two evaluations, no statistically significant difference could be detected between the PRP and the control group. Periotest® measurements in this study are not very objective, however, because the supra constructions were not removed. Due to the similar study design, a comparison is merited with the results of Attia et al., who investigated implants in hypodontia patients, and they state that only one of the 148 implants tested had a Periotest® value greater than 10 [34]. This corresponds to 0.7%, which is consistent with the values of the control group in the present work.

The median alveolar crest height in the PRP group was 13.3 mm (split-mouth evaluation) and 12.8 mm (unilateral evaluation), while it was 12.7 mm (split-mouth evaluation) and 12.8 mm (unilateral evaluation) in the control group. Here, it can be seen that the PRP group had slightly more bone height than the control group, until the first follow-up in the study of Schaaf et al. [19,20]. Over time, the groups ended up at equal heights. This is also noticeable when looking at the medians: in the split-mouth evaluation, the medians of the study groups are close to each other. In the unilateral evaluation, they are even identical. This suggests that the influence of PRP on the bone level of the augmented region is, if present, a short-term result. No statistical differences between the groups could be determined in the long-term follow-up.

The percent of bone loss of the augmented region relates absolute bone loss to the baseline. As a result, the percentage change is a meaningful measure for the resorption of the augmented jaw region. The median percentage of bone loss in the PRP group was 31.5% (split-mouth evaluation) and 35% (unilateral evaluation). In the control group, the values were 25.6% (split-mouth evaluation) and 27.2% (unilateral evaluation). The statistical analysis did not show any significant difference between the groups. Schmitt et al. examined 25 patients who had received augmentations in the upper jaw. After ten years, the authors found that 30.2% of augmented bone was resorbed. These findings can be regarded as equivalent to this study [41].

The majority of the clinical and radiological parameters did not show any difference between the PRP group and the control group. Thus, the hypothesis defined in this study could not be proven. Most of these results correspond to current literature and follow the findings of the previous study by Schaaf et al. [19,20]. In the same patient collection, there was no positive effect of PRP in the use of autologous bone grafts at the upper jaw in the short-term outcomes. Now, in this long-term clinical and radiological follow-up, no change could be observed, either.

Ample evidence on the use of regenerative therapy approaches are present in the literature, most of which circumvent one or more limitation of autologous bone grafts and PRP enhancement. Nonetheless, many, if not all, alternative methods open other issues in terms of ethics, feasibility, and specialization.

Using scaffolds in their various forms, decellularized matrix, hydrogels, or spun collagens have certain advantages in handling, and there is the possibility of loading them with mesenchymal stem cells (MSCs). Such scaffolds have shown enhanced osteogenic properties in vitro and enhanced differentiation of loaded stem cells [27]. In dental treatment, the recent discovery of periapical cyst-mesenchymal stem cells will advance this concept as a local source for stem cells [42]. To benefit from the scaffolds properties, such as porosity and low coast, osteoconductive rather than osteoinductive approaches have been addressed, especially in disturbed bone healing in cases of tumorous bone such as multiple myeloma [43], or systemically diseased bone such as in osteoporosis [44]. Different compounds could enhance osteoblasts or inhibit osteoclasts in vitro such as Donepezil [45]. The use of minerals such as calcium phosphate cements doped with active ingredients such as strontium [46] or nanoparticles loaded on scaffolds such as nanosilicates poly(glycerol sebacate) [13], showed enhanced mineralization in vivo and in vitro.

There are new upcoming development towards smart biomaterials and a faster implementation and integration of materials in patient treatment by modulating the immune response [47,48]. The main idea is to implement biomaterials to regulate inflammatory response, one of the major challenges in tissue grafts and an often neglected effect by clinicians. The future aim is to use the immune reaction to manage drug release temporarily and locally according to the need [49]. One of the methods to regulate the immune response is the regulation of oxidative stress, which is involved in the response to pathogen infection and inflammation [50,51]. However, these procedures are still far from daily clinical applications and are costly for the patient.

This paper aimed to fairly assess bone augmentation with PRP after a long-term follow-up, bone augmentation having been the state-of-the-art approach 20 years ago. Besides there being a long way until becoming a certified product, all the above-mentioned technologies are still in the early stages of development with variable unknown factors. Further long-term follow-up studies will be necessary to prove their validity.

5. Conclusions

Long-term clinical and radiological follow-up of dental implants inserted in autologously augmented maxillary bone was proven satisfactory, with stable results after an average of 13 years. No statistically relevant differences between the PRP and control groups regarding peri-implant parameters or remnant bone height of the alveolar ridge could be observed. Despite an expectable significant drop-out rate in this retrospective study after 13 years, the long-term results confirm the previously published RCT short-term results.

Since PRP, as an autologous adjuvant for bone regeneration, did not lead to promising results in comparison to standard surgery control groups, new approaches should be investigated. Decellularized bone, extracellular matrix, and human dental pulp stem cells as a construct for bone regeneration need to be tested in future randomized prospective clinical trials.

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3.6 Donor-Site Morbidity After Fibula Transplantation in Head and Neck Tumor Patients: A Split-Leg Retrospective Study with Focus on Leg Stability and Quality of Life

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Summary

Given the low prevalence of donor-site complications among head and neck cancer patients, free fibula flaps have been the gold standard for orofacial reconstruction for the last 30 years. Nevertheless, donor-site complications have been inconsistently reported, with high heterogeneity, especially in the reporting methods, complication severity, and associated risk factors. In addition, patients' quality of life can be significantly impacted by the restricted stability and reduced balance of the involved leg. Therefore, this study aimed to retrospectively evaluate the stability and balance of the affected leg using a split-leg design.

In total, 119 patients underwent ablative jaw tumor surgery and free fibula flaps between December 2014 and January 2018. Of these, 51 were either excluded or depicted as drop-outs because of limited physical condition (n = 7) or lack of response to phone calls or emails (n = 9). A total of 68 patients (57%) were clinically examined for donor-site morbidity. In addition to the commonly reported complications, the Star Excursion Balance Test (SEBT) and the Foot and Ankle Disability Index (FADI) were used to assess their ankle function and lower leg–related quality of life, respectively.

The SEBT showed a mean value of 55.3 cm in the operated leg as the supporting leg, corresponding to 95.5% of the 57.9 cm scored by the healthy leg as the supporting leg. The median FADI score was 96.0,% indicating that 72.1% of the patients suffered from limitations due to donor-site morbidity. Therefore, the SEBT and FADI seemed to be appropriate instruments for evaluating patients after fibular transplantation, with minimal restrictions of the involved legs compared to the healthy legs. Overall, the reported limitations were clinically irrelevant and had a very slight impact on the patients' quality of life and daily routine [13].

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Donor-Site Morbidity after Fibula Transplantation in Head and Neck Tumor Patients: A Split-Leg Retrospective Study with Focus on Leg Stability and Quality of Life

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Abstract: The free fibula flap has been one of the most important microvascular grafts for orofacial reconstruction for more than 30 years. The complication rates at the donor-site reported in literature are considered to be low, but the published data vary greatly in some cases. In particular, restrictions in the stability and balance of the involved leg and their effects on the quality of life have been described very inconsistently to date. Therefore, this study mainly focuses on the stability and balance of the affected leg in a split-leg design. Between December 2014 and January 2018, out of 119 subjects who underwent mainly jaw ablative tumor surgery and reconstruction using a fibula flap, 68 subjects were examined for donor site morbidity. Besides reporting general types of complications, two specific test procedures were used. The Star Excursion Balance Test (SEBT) as a practical test for ankle function and the Foot and Ankle Disability Index (FADI) as a questionnaire in order to assess quality of life, depending on the lower leg function. SEBT revealed an average of 55.3 cm with the operated leg as the supporting leg, which corresponds to 95.5% of 57.9 cm achieved with the healthy leg as the supporting leg. An average FADI score of 89.4% was recorded. SEBT and FADI seem to be suitable methods of examination for subjects post fibular transplantation and pointed out minimal limitations of the involved legs in comparison to the unaffected legs. These limitations were clinically not relevant and they had minor influence on the subjects' quality of life and their daily activities.

Keywords: fibula flap; donor-site morbidity; SEBT; FADI; maxillofacial surgery; head and neck cancer; microvascular flaps

1. Introduction

Since its first description over 40 years ago, the fibular graft has become one of the most important grafts in oral and maxillofacial surgery [1]. It is used for a wide range of indications, but, by far, the largest and most demanding part of fibula transplants in the orofacial area still relates to reconstructive surgery after ablative tumor resection [2]. A fibula flap was proven to be a reliable method for

bone reconstruction of the jaws and it can be regarded as the workhorse for functional and aesthetic rehabilitation in oncologic patients [3,4] suffering from head and neck cancer. Worldwide, more than 300,000 patients a year are diagnosed with head and neck cancer [5]. The most common head and neck tumor is the squamous cell carcinoma, accounting for approx. 90% of cases, followed by adenocarcinoma, accounting for approx. 5% of cases [6]. The tumorigenesis has several risk factors, such as alcohol abuse, smoking, poor oral hygiene, as well as genetic aspects in rare cases [7]. Furthermore, infections with human papilloma viruses (HPV) are increasingly recognized as a key tumorigenic factor, especially when located in the area of the throat [8]. The main goals of cancer treatment are the removal of the entire tumor and subsequent reconstruction of the resected tissues [9]. Oral cancer patients often undergo extensive surgical excision of the tumor, including mandibular and/or maxillary resection. These hard and soft tissue defects lead to a series of functional and aesthetic problems [10]. The best time for jaw reconstruction in oncologic head and neck patients is the time of resection [11]. The immediate reconstruction provides perfect access to the bone margin after the ablative surgery, leading to the prompt assessment of the hard and soft tissue defects. It also reduces the number of surgical procedures and achieves oral rehabilitation in a shorter amount of time [12]. In this setting, there is also the best opportunity to find suitable vessels for the microanastomosis required for a fibular flap or any other microvascular flap. Frozen-section analysis and flat-panel volume computed tomography of the resected tissues ensure high reliability in terms of the complete removal of the tumor [13]. The immediate reconstruction of the complex soft-tissue and bone defects caused by the tumor ablative surgery requires free vascularized tissue transplant [14].

Microvascular techniques were first introduced in the 1970s and, from this time forward, several autologous grafts for reconstructive head and neck surgery have been proposed [15]. In 1975, Taylor et al. performed the first microvascular fibular bone transfer [16]. In 1983, Chen and Yan were the first to use an osteocutaneous fibula flap for the reconstruction of bone and soft tissue defects [17]. By using osteotomies in the fibular bone, Hidalgo performed the first lower jaw reconstruction to simulate the form of the mandible [18,19]. Since 1990, the fibula flap is widely used for facial reconstruction [17,20]. To overcome the limited height of the fibula, Jones et al. introduced a double barrel technique, which postulates that two osteotomized bone segments of fibula can be folded in order to cover a greater height [21].

The fibula flap is widely used and preferred in the head and neck reconstructive surgery due to several advantages. Besides the considerable length of available bone, the fibula transfer is a feasible technique and it can be performed as a two-team approach leading to a significant reduction of operation time [18]. Furthermore, the flap possesses a sufficiently long and high-caliber vascular pedicle, making microsurgical anastomoses feasible to perform [22]. Cortical bone allows for the insertion of primary stable dental implants required for dental rehabilitation [3].

Various studies in literature report on the use of fibula grafts for orofacial reconstruction in general and the associated donor-site morbidity in particular. Although these studies describe the limitations that are associated with fibula removal as minor [23–25], complications can still occur with severe consequences for patients [26–28]. The methods often differ greatly between individual studies. On the one hand, limitations were recorded subjectively by the patients in individual questions or by means of questionnaires; on the other hand, there were various practical test methods. These range from simple sensomotoric examinations of the N. fibularis and walking tests, to complex optical and kinetic analyses of leg function [29–33]. However, data regarding donor site morbidity after lifting of the fibula flap in a split-leg design are rare in literature [34]. The here presented study mainly focuses on the stability and balance of the affected leg. The upper ankle, including fibula, tibia, and talus in particular seemed to be an interesting indicator. To date, the effect of fibular transplantation has not been examined in detail. We have selected a specific test procedure to objectively investigate the donor-site morbidity. To determine ankle stability, we selected the Star Excursion Balance Test (SEBT), which is a clinical balance test. The Foot and Ankle Disability Index (FADI) questionnaire was selected to additionally examine the influence of ankle function on quality of life. Both tests are highly reliable

and they have been proven in orthopedics and sport medicine [35–37]. The hypothesis of this study is that fibula transplantation only slightly restricts leg function and that the loss of quality of life due to donor site morbidity is minor/acceptable. Additionally, this study aims to answer the following questions:

- How is the ankle function and thus the balance and stability of a leg restricted by the removal of a fibular graft?
- How much does the aforementioned restriction affect daily activities and quality of life?

Answering the study questions should help to further improve patient selection and the surgical procedure itself and reduce donor site morbidity in the future.

2. Results

2.1. Basic Data

A total of 119 subjects were included according to the previously defined inclusion criteria. Fifty-one subjects could not be examined and were considered as drop-out due to the following reasons: 30 subjects had deceased; two subjects lived abroad; three subjects were in hospital care; seven subjects found themselves unable to participate due to their limited physical condition; and, nine subjects could not be reached by phone or mail. A total of 68 subjects, 22 female (32.4%) and 46 male (67.6%), were examined and included in the study, which corresponds to a rate of 57%. The mean age of the subjects at surgery was 55.4 years (median 57 years), with the youngest patient being 17 years old and the oldest patient being 80 years old. The mean time between the fibula transplantation surgery and follow-up for study subjects (n = 68) was 1428 days (minimum 51, median 809, and maximum 5083 days).

Height, Weight and Body Mass Index (BMI)

The average height was 1.74 m (median 1.78 m) and varied between 1.5 and 1.92 m, the average body weight was 73.8 kg (median 75 kg) and varied between 43 and 118 kg. On average, a body mass index of 24.3 (median 23.6) was calculated. The values fluctuated between 16.4 and 39.1 (Table 1).

Table 1. A demographics table illustrate the collected data and subject population. Data are given as mean (standard deviation) or as percentage % (absolute frequency).

Variable	Mean (Standard Deviation) or Percentage % (Absolute Frequency)
Age (years) at surgery	55.4 (12.5)
Gender (m/f)	67.6% (n = 46)/32.4% (n = 22)
Height (cm) at surgery	174 (11)
Weight (kg) at surgery	74 (17)
BMI at surgery	
underweight	8.8% (n = 6)
normal weight	54.4% (n = 37)
pre-obesity	25.0% (n = 17)
obesity grade I	8.8% (n = 6)
obesity grade II	2.9% (n = 2)
Indication of fibula transplantation	
squamous cell carcinoma	69.1% (n = 47)
ameloblastoma	8.8% (n = 6)
keratocystic odontogenic tumor	7.4% (n = 5)
jaw atrophy	2.9% (n = 2)
adenoid cystic carcinoma	2.9% (n = 2)
acinar cell carcinoma	1.5% (n = 1)

Table 1. *Cont.*

Variable	Mean (Standard Deviation) or Percentage % (Absolute Frequency)
adenosquamous carcinoma	1.5% (n = 1)
mucoepidermoid carcinoma	1.5% (n = 1)
myoepithelial carcinoma	1.5% (n = 1)
hemangiopericytoma	1.5% (n = 1)
osteoradione necrosis	1.5% (n = 1)
Operated Leg (left/right)	25% (n = 17)/ 75% (n = 51)
Type of transplant	
osseomyocutan	76.5% (n = 52)
osseomuscular	14.7% (n = 10)
prefabricated	8.8% (n = 6)
Wound closure	
graft from thigh region	73.5% (n = 50)
primary sutured	26.5% (n = 18)
Hospitalisation time	
up to 1 week	1.5% (n = 1)
>1 up to 2 weeks	35.3% (n = 24)
>2 up to 3 weeks	27.9% (n = 19)
>3 up to 4 weeks	14.7% (n = 10)
>4 up to 5 weeks	13.2% (n = 9)
more than 5 weeks	7.4% (n = 5)

2.2. Surgical Information

2.2.1. Indications and Localization of Defects

The most common indication for a fibula transplantation was cancer resection. As the most common tumor in the head and neck area, squamous cell carcinoma clearly predominates, with 69%. From our cohort of 68 subjects, 65 had tumors, three subjects underwent surgery due to atrophy (n = 2) and osteoradionecrosis (n = 1). Almost three-quarters of the defects were located in the lower jaw (73.5% n = 50), less than one quarter in the upper jaw (26.5%, n = 18). The distribution can be explained by the fact that the fibular graft is particularly well suited for the reconstruction of the lower jaw (Table 1).

2.2.2. Donor-Site, Type of Fibula Transplantation, and Wound Closure

The transplants were harvested from the left lower leg in precisely 25% of cases (n = 17) and from the right lower leg in 75% of cases (n = 51). If preoperative diagnostics, especially femoral angiography, does not conflict with this, the right leg is usually chosen for ergonomic reasons. We distinguished between three different types of grafts:

- osseomyocutan graft (bone, muscle tissue, and skin island);
- osseomuscular graft (bone and muscle tissue); and,
- prefabricated fibula graft (bone covered with pre-transplanted skin graft and already inserted dental implants) (Table 1).

Tumor reconstruction was the main indication for a fibula graft (Table 1). The operated tumors, mainly squamous cell carcinomas, usually also infiltrate adjacent tissue, which makes resection with a sufficiently large safety margin necessary. The resulting bone and soft tissue defects can be best reconstructed with a graft containing soft tissue and skin in addition to bone. For this reason, most fibular grafts are raised as osseomyocutaneous grafts. Most of the wounds at the donor site were closed using skin grafts from the thigh region (n = 50, 73.5%), and the remaining cases, primary wound closure could be performed (n = 18, 26.5%).

2.2.3. Inpatient Stay

Subjects included in this study were hospitalized for an average of 20 days. The duration of inpatient stay after a fibula transplant varied between seven and 52 days with a median of 17 days (Table 1).

2.3. Follow-Up Examination

2.3.1. Complications at the Donor-Site

Post-operatively, 36 subjects (53%) experienced complications at the donor-site, mainly delayed wound healing and paresthesia, as shown in Figure 1 Seven subjects with wound healing disturbance suffered from a second complication, two in each case from paresthesia and persisting pain and one in each case from edema, hallux rigidus, and eczema. In 18% of subjects (n = 12), one or more surgical procedures were necessary at the donor site following the primary operation, mainly due to delayed wound healing and infection (Figure 1).

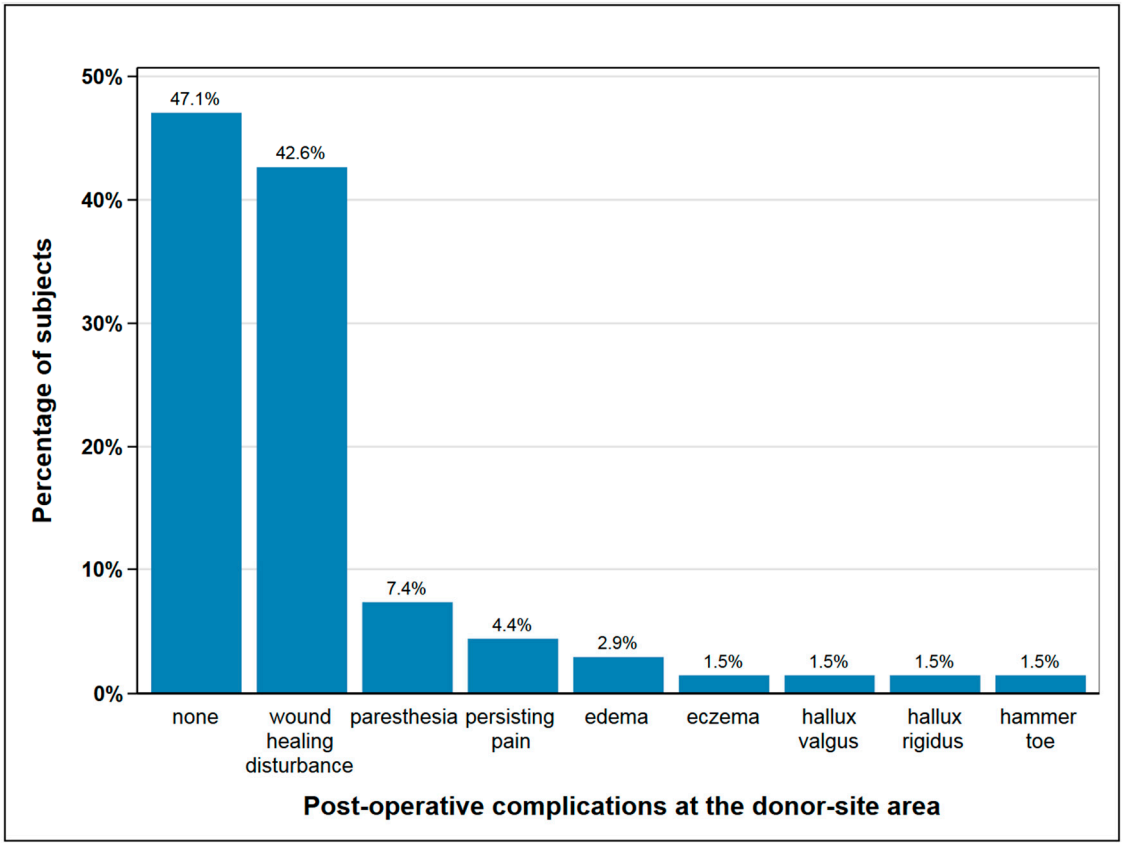
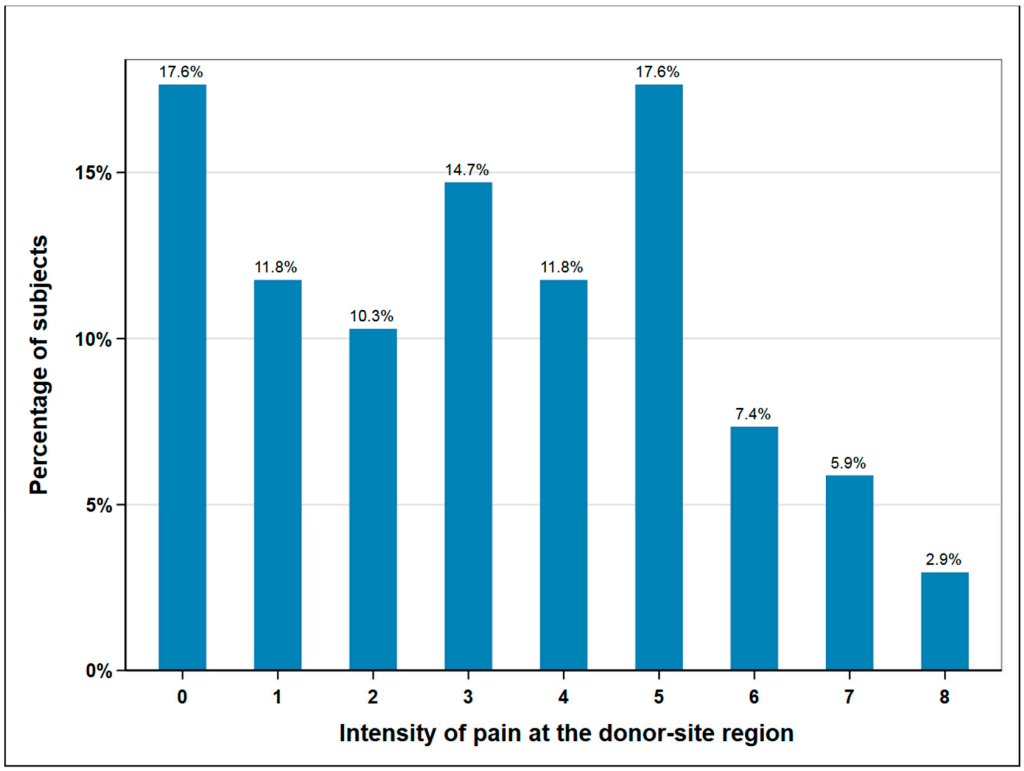


Figure 1. Post-operative complications at the donor-site area; seven subjects suffered from a second complication besides wound healing disturbance, which is paresthesia and persisting pain (each n = 2), edema, hallux rigidus and eczema (each n = 1); with seven cases of double complications this figure depicts n = 75 complications in total.

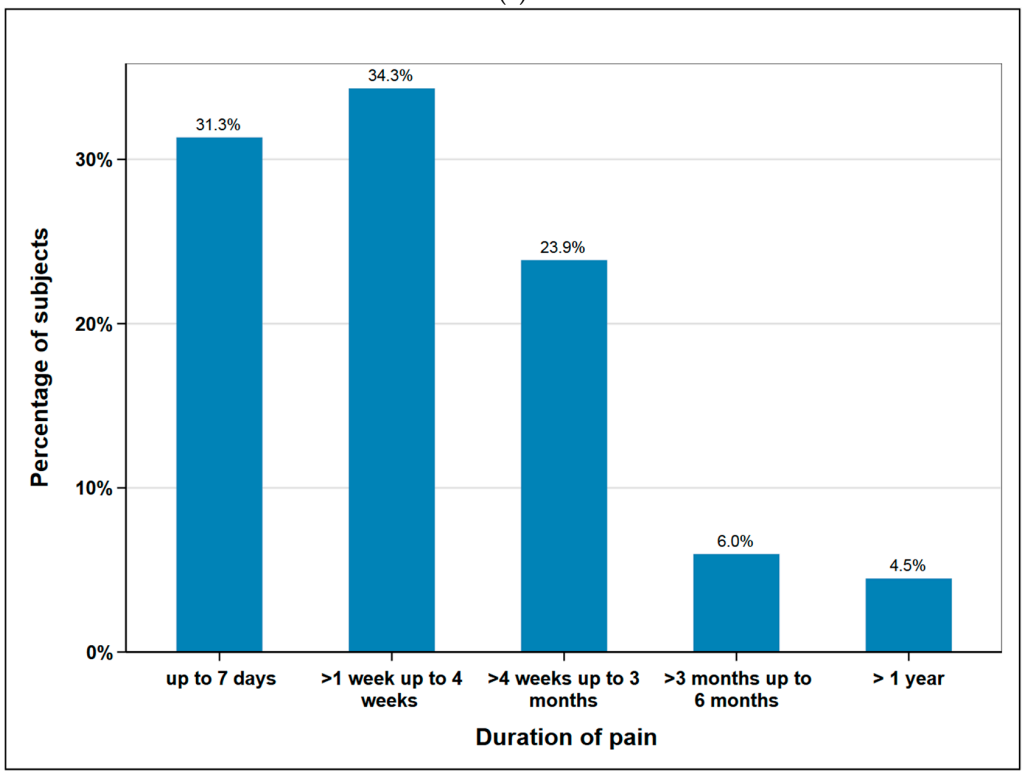
2.3.2. Post-Operative Pain

The subjects rated postoperative pain sensation at the donor-site region on a numeric rating scale (NRS) from 0 to 10 (0 no pain, 10 most intense pain imaginable). The mean was 3.2 (median 3) and the maximum values 9 and 10 were not given by any patient. Additionally, post-operative pain duration was documented. 88% of the subjects were free of pain after three months at the latest. One subject stated to have persisting pain at a short follow-up time of just three months. As this subject had

unfortunately died when we tried to assess the pain duration at a later date, it was excluded from this figure. Therefore, Figure 2b shows the data of $n = 67$ subjects (Figure 2).



(**a**)



(**b**)

Figure 2. Responses of subjects regarding donor site pain: (**a**) intensity in scale 0 (no pain) to 10 (maximum imaginable pain), $n = 68$; (**b**) duration of pain (weeks, months, >1 year), $n = 67$.

2.3.3. Fibular Nerve Function and Sensitivity Disorder

A total of 10.3% (n = 7) of the subjects experienced a disturbance in the foot elevation, which indicates a lesion of the fibular nerve. The superficial sensitivity was tested in the area of the surgical scar by means of sharp-blunt discrimination test. A total of eight sharp or blunt stimuli were placed on the skin in the same area using a dental probe. Normal sensitivity was assumed if the patient was able to correctly assign seven or eight of the stimuli. Less recognized stimuli corresponded to hypesthesia. According to this classification, normal sensitivity was found in 62% (n = 42) of subjects and impaired sensitivity in 38% (n = 26) (Figure 3).

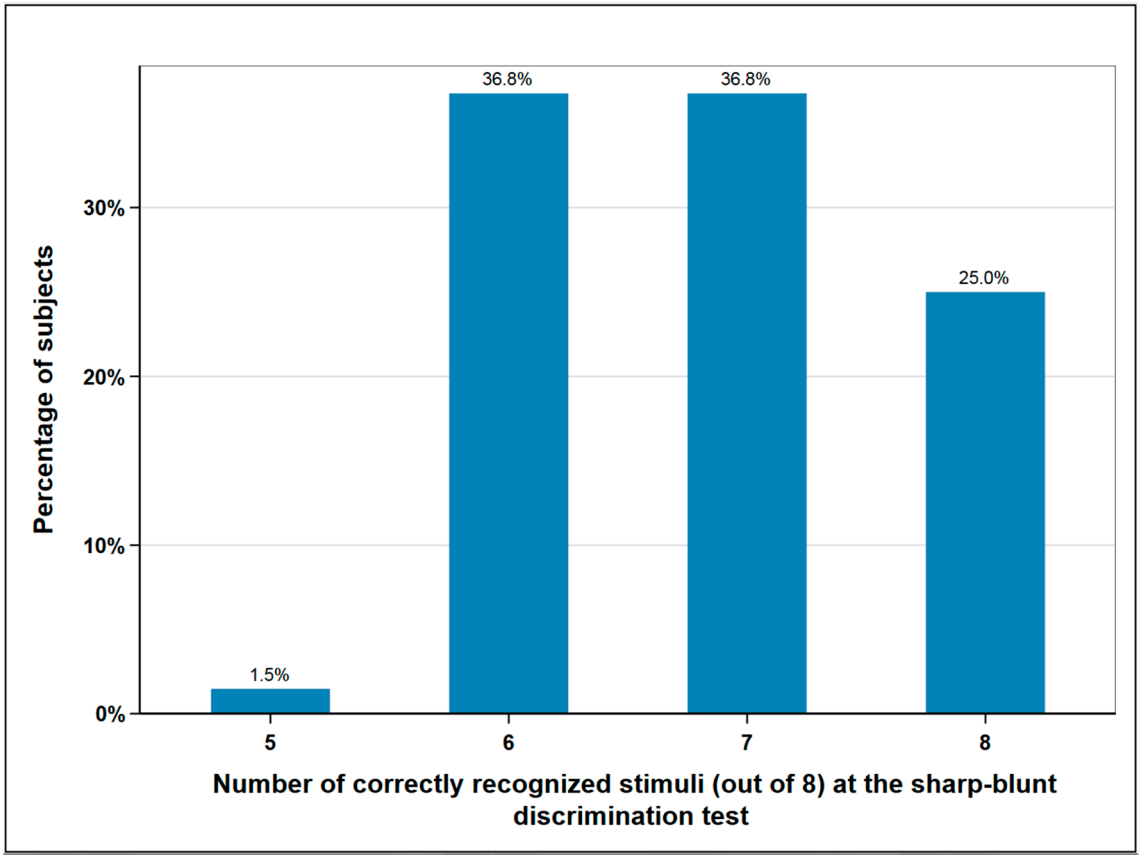


Figure 3. Sharp-blunt discrimination test at the donor-site; eight and seven correctly recognized stimuli correspond to normal sensation, six and lower to impaired sensation; n = 68.

2.3.4. Scar

The size of the scar was measured with a tape measure and the skin color of the scar area was determined and documented by a picture. The mean average scar length was measured at 32.7 cm, with 40 cm being the maximum and 25 cm the minimum length. In terms of width, we distinguished between donor site scars with and without skin island removal. In the 16 subjects without skin island removal, the average width was measured at 0.63 cm. In the 52 remaining subjects, the scar area of the skin island measured at an average width of 6.4 cm. The skin color of the scar was compared to the surrounding skin and classified as lighter, darker, the same, or reddened (Figure 4).

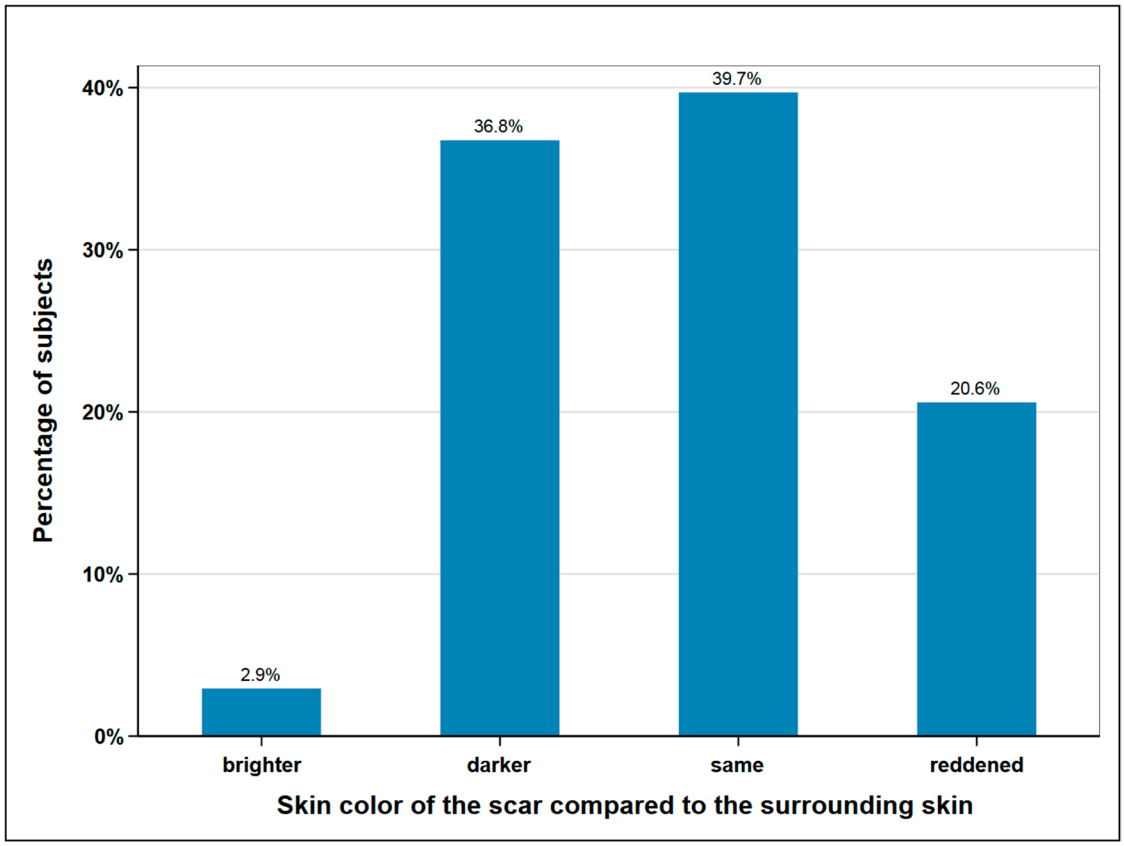
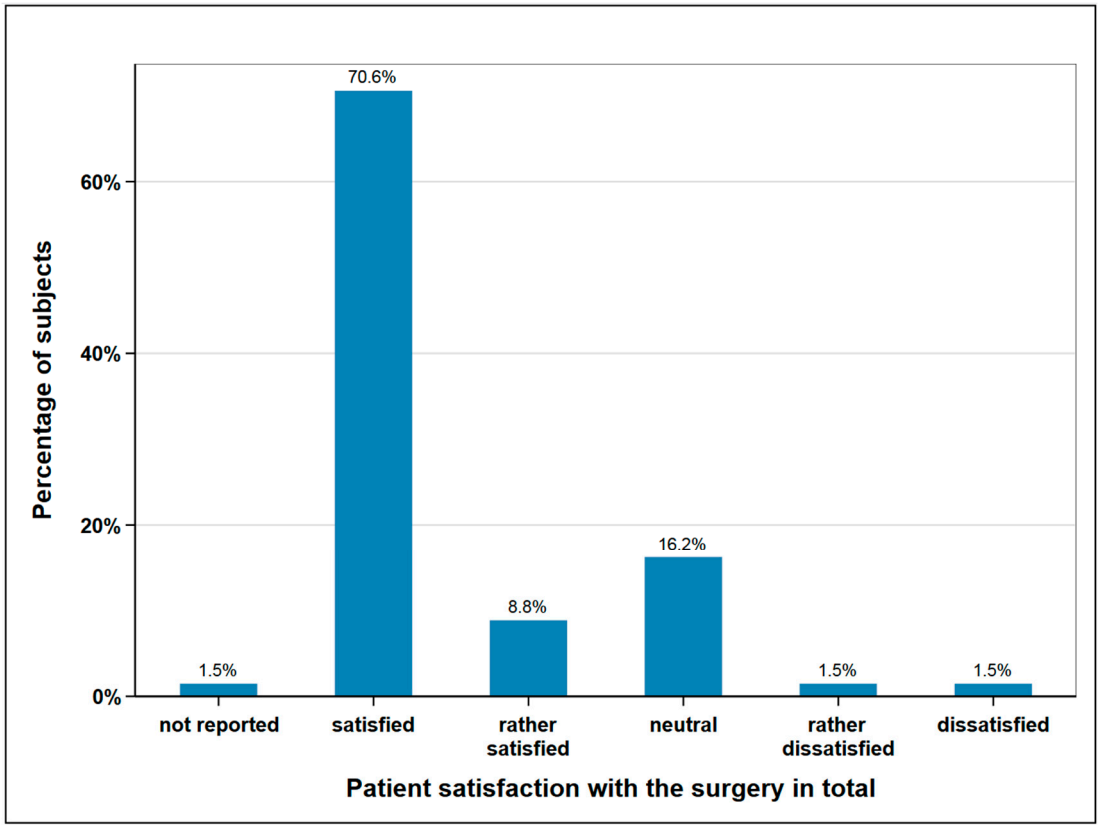


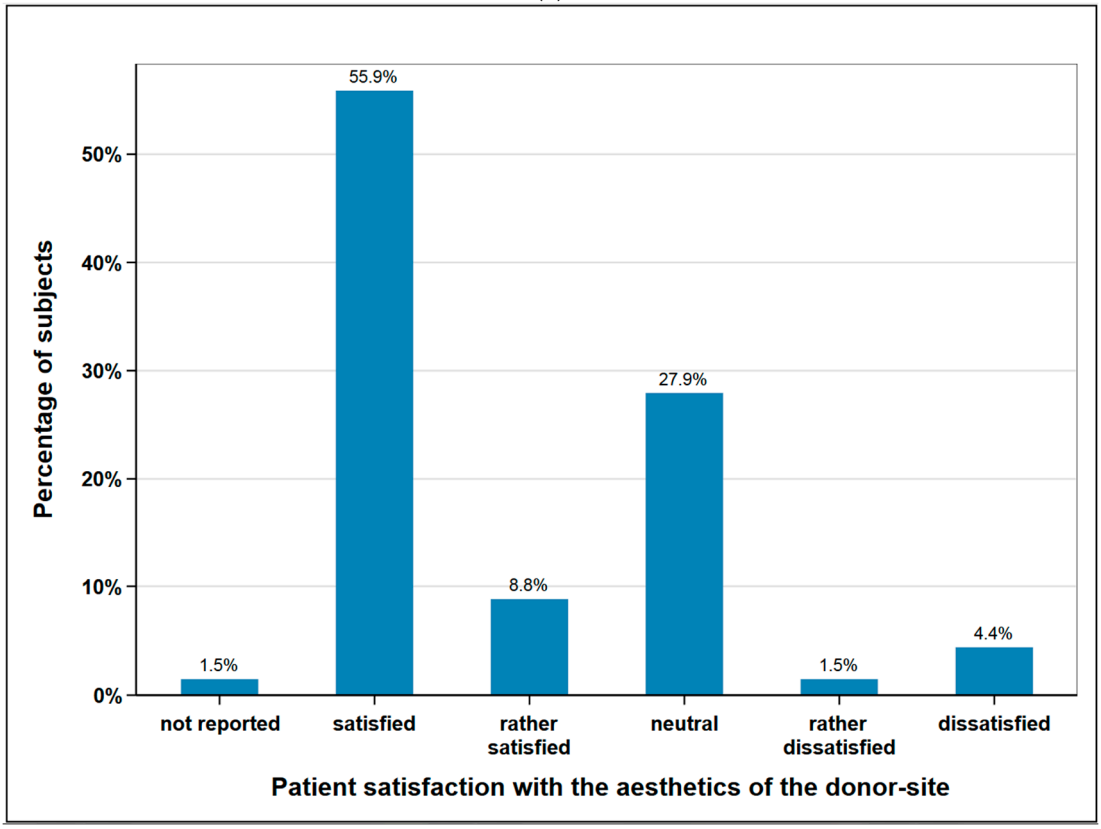
Figure 4. Skin color of the scar compared to surrounding skin; $n = 68$.

2.3.5. Level of Patient Satisfaction

The subjects were asked about their satisfaction concerning the aesthetics of the donor-site and the overall operation. 64.7% of the subjects ($n = 44$) were satisfied or rather satisfied regarding aesthetics of the donor site, 5.9% ($n = 4$) were unsatisfied or rather unsatisfied, and 27.9% ($n = 19$) remained neutral. With regard the operation in general, 79.4% of the subjects ($n = 54$) were satisfied or rather satisfied, 2.9% ($n = 2$) unsatisfied or rather unsatisfied, and 16.2% ($n = 11$) remained neutral. One patient did not provide any information on either aspect (Figure 5).



(**a**)



(**b**)

Figure 5. Subjects satisfaction with (**a**) the surgery in total (n = 68); (**b**) aesthetics of the donor-site (n = 68).

2.4. Star Excursion Balance Test—SEBT

Of the total 68 participating subjects, seven subjects were unable to perform the SEBT, even after several attempts. This was mainly due to balance problems when standing on one leg. To evaluate the SEBT data, the mean of each of the remaining 61 subjects was taken from the three values achieved per axis of movement as the starting value. The mean values of SEBT of the donor-legs and the non-operated legs from all eight directions (A, AM, M, PM, P, PL, L, AL) were calculated. An average of 55.3 cm was achieved with the operated leg as the supporting leg, which corresponds to 95.7% (0.95 confidence interval: [94.4%; 97.0%]) of 57.9 cm achieved with the healthy leg. The lowest lengths were reached in the lateral direction with both legs. A significant difference between the healthy and operated leg in all eight directions was determined using a paired *t*-test ($p < 0.01$). The differences between the average SEBT values of unoperated and operated legs for each of the 61 subjects were recorded. In the median values, the greatest lengths were measured in the medial direction for the healthy leg and in the anteromedial direction for the operated leg. As in the mean values, both legs reached the lowest lengths in the lateral direction. The mean absolute difference is largest in the posterolateral direction with 4.1 cm and smallest in the medial direction with 1.8 cm (Table 2; Figure 6).

Table 2. Distribution of the Star Excursion Balance Test (SEBT) values (mean of three measurements) (cm), operated versus healthy legs ($n = 61$).

Direction	Operated Leg				Healthy Leg				Difference Operated—Healthy Leg				*p* Value [1]
	Min	Max	Mean	Std	Min	Max	Mean	Std	Min	Max	Mean	Std	
A	39.3	78.0	56.7	8.1	41.0	81.0	58.8	8.5	−15.0	9.7	−2.1	3.9	0.001
AM	40.3	81.0	60.8	8.7	46.0	82.7	62.8	9.0	−18.0	8.2	−2.0	4.6	0.001
M	39.7	82.7	62.1	8.5	43.7	85.0	63.9	8.6	−15.0	8.7	−1.8	4.0	<0.001
PM	44.0	87.0	61.8	9.4	41.2	89.3	64.6	9.4	−14.0	7.7	−2.7	4.3	<0.0001
P	22.3	89.3	56.3	11.1	27.5	90.3	59.5	11.1	−11.7	7.3	−3.2	4.0	<0.0001
PL	23.7	75.7	48.9	11.5	21.3	86.0	53.0	12.1	−22.0	7.7	−4.1	5.9	<0.0001
L	21.7	70.7	43.6	8.3	20.7	69.0	46.5	8.5	−19.0	8.0	−2.8	4.4	<0.0001
AL	36.7	77.0	52.3	7.9	37.0	78.3	54.2	8.0	−14.0	11.0	−2.0	4.5	0.001

[1] paired *t*-test.

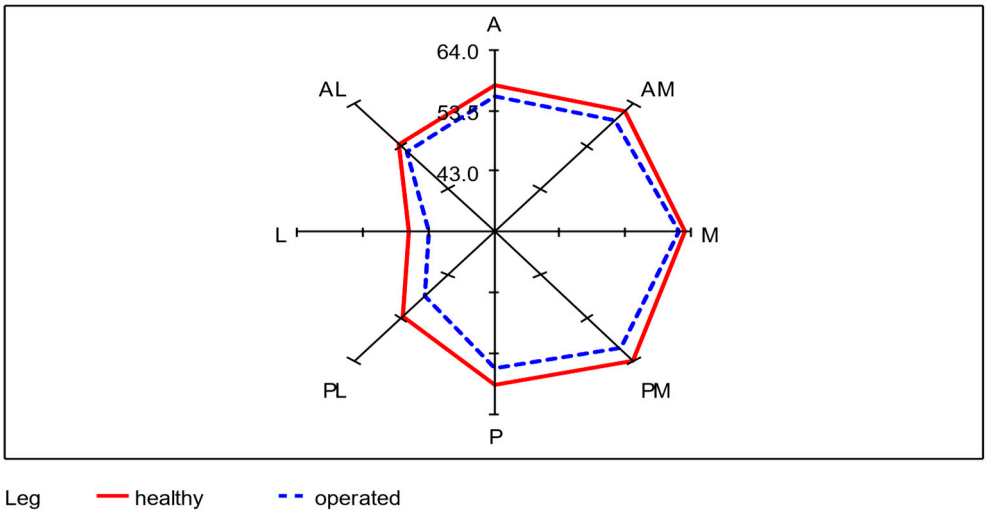


Figure 6. Radar plot for the visualization of the differences of the mean values between healthy and operated leg in each of the eight directions; $n = 61$.

2.5. Foot and Ankle Disability Index—FADI

The FADI questionnaire included all 68 participants. A median FADI score of 96.0% (0.95-confidence interval: [92.3%; 98.1%]) was recorded (mean: 89.4%). Becasue the score only shows the

overall average, but not the distribution of points for the 26 individual items, it is worthwhile to present them individually. Thus, one can see, in detail, to which extent the fibula removal affects the subjects in the respective activities as well as their pain sensation. Figure 7 illustrates an overview about each of the 26 items of the FADI questionnaire. The maximum of four points corresponds to 100% in the figure, which states "no difficulty/no pain at all". Subjects were restricted due to other causes than fibula harvesting and were thus removed from the respective score.

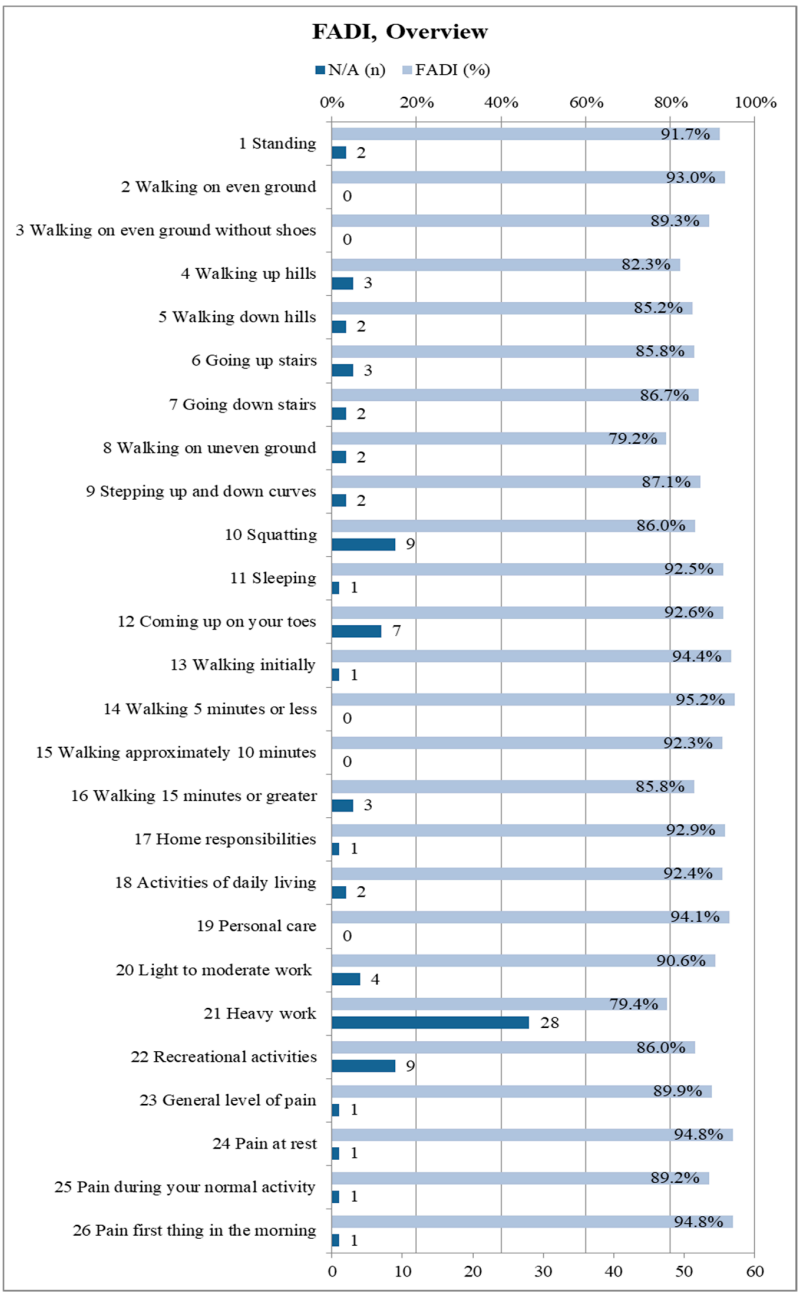


Figure 7. Summary of the Foot and Ankle Disability Index (FADI) results in detail for all 26 items (n = 68); depicted percentages are mean values; the maximum score of 100% corresponds to 4 points and represents "no difficulty/pain", 75% corresponds to three points and represents "slight difficulty/mild pain", 50% corresponds to two points and represents "moderate difficulty/pain", 25% corresponds to one point and represents "extreme difficulty/severe pain", 0% corresponds to one point and represents "unable to do/unbearable"; if subjects were limited by something else than their lower leg condition resulting from fibula flap harvest the related item is marked as "N/A" and excluded from the total score.

27.9% of the subjects always scored the full four points on each FADI item. Accordingly, 72.1% of the subjects had some kind of limitation due to the donor site morbidity following fibula transplantation. The majority of limitations were minor (Figure 7).

3. Discussion

In this study, the donor-site morbidity after fibula transplantation was examined with particular focus on the extent of restrictions regarding stability and balance of the operated leg as well as quality of life of the patient. To date, the donor-site morbidity was described as low in literature. However, fluctuations between 1–19% were found in comparable studies [23].

3.1. Evaluation of Material and Methods

The number of 68 subjects included in this study corresponds to the values of comparable studies [31] or is significantly higher [34,38,39]. The average age of the subjects in this study was 55 years and 68% of the subjects were of male sex. Both correspond to the main indication of the fibular graft, the oral tumors and especially squamous cell carcinomas [27,31,40–45]. Examination sheets and questionnaires used in this study were obtained from similar studies that have been tried and tested in literature [23,27,46,47]. The two main parameters of the study, the SEBT and FADI, were both described as reliable tools to examine ankle injury [36,48–50]. SEBT was used in the sense of a "split leg" design. In each patient, the operated supporting leg served as the group to be examined, and the healthy supporting leg the control group. General differences between the left and right leg were already ruled out in literature, hence both sides can be regarded as equivalent [49,51]. In order to avoid errors due to inaccuracies in the axis cross, it was printed on a tarp. Seven subjects were unable to perform the SEBT; therefore, the number of participants was reduced to $n = 61$. A simplified variant of the SEBT, e.g., the Y-Balance Test (YBT) consisting of three direction axes, was not used due to the assumed limited significance [52]. FADI as a retrospective questionnaire has a very low error margin. All of the items of the FADI questionnaire were explained to the subjects by the examiner, any questions answered, and the questionnaires were filled out together with the examiner [35]. There are alternatives to SEBT and FADI in comparable literature. The American Orthopedic Foot and Ankle Society's index (AOFAS) and the 36-items short form (SF-36) are the most frequently described questionnaires, but they are not validated for populations with ankle instability [26,53,54]. In addition to the FADI, the Foot and Ankle Outcome Score (FAOS), and the Foot and Ankle Ability Measure (FAAM) also meet this requirement. Because our subjects no longer practiced any sports activities, FADI seemed the most suitable method for the study subjects [54,55]. As an alternative to the SEBT, the 6-min. walk test (6MWT) has also been mentioned in literature as a physical test after fibula removal, but is only suitable to compare different collectives or a collective at different times [32,56].

In this study, pain severity was determined on a numerical scale from 0–10, which is equivalent to the visual analog scale (VAS) that was used in other studies [57,58]. However, the retrospective assessment of pain after a long follow-up time of 46 months can be inaccurate. Damage to the nerve root of the fifth lumbar nerve can be recorded using the sharp-blunt discrimination with the aid of a dental probe [59,60]. Here, further sensory checks are useful to determine the severity and location of nerve damage.

3.2. Discussion of the Results

The main indication for fibula transplantation in this study subjects was tumor (95,6%, $n = 65$), most of them squamous cell carcinomas with 69% ($n = 47$). In literature, the indication rates due to a tumor diagnosis are described at lower rates 62–89% [30,34,40,45,61].

3.2.1. Subjects Collective and Surgical Procedures

The body mass index (BMI) in our study determined an average value of 24.3 kg/m^2, which is in the upper range of normal weight and it is similar to values from comparable studies [38,53,62,63]. For

better comparability with other studies, we summarize our graft types to fibula grafts with skin (76%) and without skin island (24%). In similar studies, the values for grafts with a skin island are usually between 47 and 90% [27,31,64–66], but there is also a study with only 18% [67]. A general classification of the grafts could improve the comparability between future studies. Wound closure in this study was mainly performed using skin grafts (73.5%), and the rest was primarily sutured. In literature, the values fluctuate strongly between 11.3% [31], 31% [1], 51% [40], 64% [27], 66% [68], and 84% [39] specified for skin graft closure. The subjects in our study were hospitalized for an average of 20 days postoperatively. In the setting of primary wound closure, the average stay lasted 16 days, in the setting of a split skin graft 22 days. Only a few studies provide specific information on in-patient stays that fluctuate between 12 and 26 days [30,53,65,68,69].

3.2.2. Surgical Complications

The total post-operative surgical complication rate was 53% of all study subjects. This seems to be very high when compared to 1–19% of the comparative study by Ling et al. [23], whereas individual studies also give high values of complications [34,65,70]. However, if the temporary complications, such as delayed wound healing and edema, were excluded, the long-term complication rate is 16%. In the case of temporary complications, wound healing disorders with 38% (n = 26) and edema with 3% (n = 2) are in the range of values from the literature of 4–38 and 1.5–8% [23,24,30,43]. Long-term complications reported in this study were mainly paresthesia with 7.3% (n = 5). In literature, higher values of 21 to 37% were described [41,71]. Unfortunately, there are no uniform categories regarding nerve injuries. Hyp-, par-, and anesthesia are often summarized as sensory deficits. A comparable study by Ling and Peng calculated an average frequency of 6.95% for sensory deficits, but the values vary between 1.7–76% [23]. Other studies reported values up to 48% [26], Shah et al. mentioned 23% (n = 6) for numbness in the area of the fibular and Sural nerve [34]. For hypesthesia, the sharp-blunt discrimination test in this study resulted in a value of 38%, which is higher than the results in two comparable studies (11–20%) [39,72]. In this study, damage to the fibular nerve was found in 10.3% (n = 7) of subjects. However, only foot lifting was examined, which makes the value susceptible to errors and it only indicated an affection of the deep fibular nerve. In literature, the values range between 1.7 to 31% [30,71,73]. In our study, persistent pain was reported at a rate of 4.4% (n = 3) of the subjects, which approximately corresponds to the value of 5% in Schardt et al. [39]. In literature, different data on donor-site pain can be found, varying between 0–100%. Ling and Peng et al. reported a mean pain value of 6.5%, the main source being ankle pain [23]. Further studies presented rates of 7, 9, and 21% for moderate pain [72,74,75], 43% for severe pain [72], 51% for load-dependent pain [26], and up to 73% for persistent pain [29]. A total of n = 3 subjects (4.4%) developed a complication affecting the toes, including hallux valgus, hallux rigidus, and hammer toe (n = 1 each). Hallux valgus is only reported in a comparable study, the incidence here is 16%, which seems very high [76]. Hallux rigidus is described in two studies, with values between 10 and 18% [77,78]. Hammer toes were explicitly stated in only one study (6%) [79]. Surgical revision due to persistent wound infection was necessary in 12 out of our subjects (18%), including n = 2 subjects (3%), who needed a second wound revision. In these subjects, skin graft was performed in 91.6% (n = 11). Only Sieg et al. found comparable values of 13% (n = 9) for a surgical revision, including n = 5 subjects with split skin coverage [31]. In our collective, the average pain severity was postoperatively rated on a numerical scale from 0 to 10, with an average of 3.2. In two studies, an equivalent visual analogue scale (VAS) was described at 3.7 postoperatively, and 1.3 and 1 after a minimum of one year of follow-up [39,57,62]. 88% (n = 60) of the subjects in this study stated lengths of up to three months at the pain duration at the donor-site area.

3.2.3. SEBT und FADI

The SEBT and FADI recorded in this study show significant restrictions due to fibula flap harvesting. However, these restrictions did not seem to have any serious disadvantages for subjects. The SEBT had an average difference of 2.6 cm or 4.5% between the reach of a healthy and operated leg. A comparison

of the differences in length of the SEBT to values from literature can be found in the following overview that is delineated in Table 3.

Table 3. SEBT literature comparison, percentage differences between affected leg and control group; SEBT = overall percentage difference, mean value; A, AM, M PM, P, PL, L, AL = differences percentages for each reach direction, mean value; CAI = chronic ankle instability; AD = ankle distortion; CL = cruciate ligament surgery (Lig. cruciforme anterior); FT = fibula transplantation SL = "Split Leg" (comparison between legs of the same person).

Literature Review	Age (y)	SEBT Ø (%)	A (%)	AM (%)	M (%)	PM (%)	P (%)	PL (%)	L (%)	AL (%)
Olmsted 2002 *n* = 20 CAI, SL [36]	19.8	5.5	3.9	5.4	3.8	6.3	3.8	3.1	10.6	4.2
Gribble 2004 *n* = 30 CAI [80]	22.3	-	5.6	-	5.9	-	7.4	-	-	-
Hertel 2006 *n* = 48 CAI, SL [81]	20.9	3.3	3.8	2.4	3.4	4.5	2.4	2.5	4.3	2.8
Hale 2007 * *n* = 29 CAI,SL [82]	21.4	4.2	2.8	3.9	3.5	4.7	3.2	5.2	6.4	3.8
Delahunt 2013 *n* = 17 CL [83]	20.8	-	3.8	-	-	8.6	-	9.4	-	-
Kalichmann 2016 *n* = 20 *AD*, SL [84]	25.4	2.2	2	2.4	1.6	3.7	2.8	1.7	0.6	3
Ko 2018 *n* = 24 CAI, SL [85]	15.5	-	11.3	-	-	9.4	-	7	-	-
Kobayashi 2019 *n* = 50 *CAI* [86]	20.8	8.8	7.3	7.1	7.2	7.7	9.7	13	10	8.3
Hadadi 2019 *n* = 44 CAI [87]	22.9	-	-	5.3	9.3	6.4	-	-	-	-
average	*22*	*5.1*	*5.8*	*4.5*	*5.2*	*6.3*	*5.2*	*6.3*	*6.4*	*4.6*
our study *n* = 61	55.4	4.5	3.6	3.2	2.8	4.2	5.4	7.8	6.1	3.6
Shah 2017 * *n* = 26 FT SL [34]	49.4	−0.2	−1.6	3.1	−1.6	−3.3	0	0	1.6	0

* = FADI also used.

The average differences between affected and healthy leg in SEBT in this study were comparable to other publications (2.2 to 8.8%) [84,86]. However, only five other studies had a split-leg design and the SEBT values were completely measured for all eight directions [34,36,81,82,84]. Interestingly, the only study that did not report significant differences between the involved and uninvolved limbs was the study of Shah et al., which also examined donor-site morbidity after fibula transplantation [34]. Only in the study published by Kobayashi et al., the distribution of values is similar to ours with the greatest differences in the posterior (P), posterolateral (PL), and lateral (L) directions [86]. The study by Karagiannakis et al., in which electromyography during SEBT was used, showed that in the three aforementioned directions, there is significantly higher activity. The fibularis brevis muscle has a connection to the fibular bone; in addition, both muscles could also be restricted by lesions of the deep fibularis and superficialis nerve [88]. This could explain the large differences in the posterior, posterolateral, and lateral directions [32,89]. With the exception of the study by Shah et al., the main cause of the different SEBT results is likely to be the younger collectives and different medical conditions. Chronic ankle instability, in particular, seems to have a similar impact on SEBT as a fibula transplant.

In our study the subjects achieved 89.4% of the FADI, which corresponds to values for the chronic ankle instability (CAI—Chronic Ankle Instability). This indicates an average of 89.3% for the FADI. Shah et al. also give similar values for the FADI, with 89% after fibula transplantation [34]. The following overview Table 4 shows a comparison with selected literature:

Table 4. FADI literature comparison; FADI = Foot and Ankle Disability Index; CAI = Chronic ankle instability; score shows mean value of all 26 FADI items as percentage; CAI average = mean value of all depicted studies involving subject with CAI; FADI average = overall mean value of all compared studies.

Literature Review	Medical Condition	*n*	Age (y)	Score (%)
Hale & Hertel 2005 [35]	CAI	30	21.5	89.6
Hale 2007 * [82]	CAI	29	21.4	89.7
McKeon 2008 [90]	CAI	31	20.9	84.2
Cook 2010 [91]	severe arthritis	79	63.9	46
Hubbard-Turner 2012 [92]	CAI	120	20.6	87.6
Wikstrom 2012 [93]	CAI	24	21.7	95.2
Kim 2013 [94]	professional athletes	85	19.8	88.9
Shah 2017 * [34]	Fibula Transplant	26	46.4	89
Sanders 2019 [95]	Fibula fracture surgery	103	39.5	91.4
Carter 2019 [96]	Tibia Pilon fracture	99	-	76
CAI average	CAI	46,8	21.2	89.26
FADI average		62,6	30.6	83.8
Our study *	Fibula transplant	68	55.4	89.4

* = SEBT also used.

In general, it turns out that our FADI averages correspond to studies on chronic ankle instability (CAI). However, our collective is significantly older than in the CAI studies, which mainly examine young and athletic subjects. Only the study conducted by Shah et al. resembles our study with regard to the average age of 46.4 years and the FADI of 89%, but the SEBT values stand in stark contrast to our values.

3.3. Limitations of This Study

The retrospective design and the relatively high drop-out rate are limitations of the study. As the patient questionnaires were filled out years after the surgical procedure, the accuracy and, hence, validity can be limited.

4. Materials and Methods

4.1. Study Design and Examiner Blinding and Calibration

This study was conducted as a retrospective clinical split-leg study at the University Hospital Giessen, Germany, Department for Oral and Maxillofacial Surgery. One examiner was responsible for the entire investigation and data acquisition. Previous training and calibration for the examiner was performed prior to patient examination.

4.2. Patient Inclusion and Exclusion Criteria

All of the subjects who underwent fibula transplantation for orofacial reconstruction between January 2002 and November 2017 were included in the study. The subjects who needed walking aids were excluded as the only exclusion criteria. Because these were mainly cancer subjects, an increased drop-out rate due to deceased and physically impaired subjects was to be expected. A number of 68 subjects could be recruited for the study.

4.3. Study Parameters

The basic and surgical data, such as patient age, sex, and diagnosis, were taken from existing files; in individual cases, the data was verified with the patient during the follow-up examination. The study parameters were assessed in one follow-up examination per subject. These included the permanent complications such as pain and nerve lesions. BMI classified according to the world health organization

(WHO) classification to: underweight below 18.5, normal weight 18.5–24.9, pre-obesity 25.0–29.9, obesity grade I 30.0–34.9, and obesity grade II 35.0–39.9. Table 5 summarizes all documented data.

Table 5. The collected study parameters divided into basic, surgical, and follow-up data.

Basic Data	Surgical Data	Follow-Up Ex
Follow-up time	Indication for surgery	Subjective pain intensity (harvested leg)
Age of the patient (surgery)	Localisation of the harvested flap (right or left leg)	Duration of pain
Height	Type of graft removed (osseocutaneus, osseomuscular, prefabricated)	Fibular nerve lesion
Body weight	Type of wound closure	blunt sharp discrimination test (harvested leg)
Body Mass Index (BMI)	Hospitalization time	Scar length and width (harvested leg)
	Post-operative complications	Skin color (harvested leg)
		Subjects satisfaction aesthetics (harvested leg)
		Subjects general satisfaction

4.4. Star Excursion Balance Test—SEBT

The Star Excursion Balance Test (SEBT) is mainly used in orthopedics and sports medicine to determine ankle function/leg function [97]. It was first described in its current form in 2000 by Hertel et al. [98]. Previously, it had already been described in a simplified form as a "star excursion test" with four instead of eight movement axes [99]. It can be used to record various restrictions, diseases, and injuries to the lower extremity and ankle [49]. It is often used in the assessment of ankle injuries, particularly chronic ankle instability (CAI—Chronic ankle instability), where it has a high degree of reliability [35,37,49,100]. This is of particular importance for the present study, since the fibula is directly involved in the upper ankle joint. Overall, the Star Excursion Balance Test is widely described in literature as a reliable method for determining the stability of the lower extremity and the ankle [48,51,99]. The SEBT measures the maximum range of one leg while standing on the other one. The subject stands in the middle of an eight-section cross, with all of the axes orientated at an 45° angle to each other. The axes are referred to clockwise from the right leg, counterclockwise from the left leg, as anterior (A), anterolateral (AL), lateral (L), posterolateral (PL), posterior (P), posteromedial (PM), medial (M), and anteromedial (AM). During the test, the complete balance must be kept on the supporting leg, the other leg must not carry any weight. The subject tries to move the contralateral leg as far as possible in each of the eight directions without losing balance. The examiner marks the furthest point where the foot touches the axis. These values are marked for each of the eight axes, with a total of three passes per left and right leg. A slightly adapted variant of the SEBT was used in the study [101]. The test setup was printed on a tarp for better feasibility.

All eight directions were continuously scaled to a length of 100 cm and the individual values were easy to read. After the subjects had been informed and a demonstration had taken place, the foot of the supporting leg was placed centrally on the center of the cross in the anterior direction. This was followed by four practice runs for each leg. Thereafter, starting with a randomly selected standing leg, three runs were carried out per leg with the standing leg being changed after each round. The achieved lengths were noted on the axes with a wipeable marker in blue (right leg) and red (left leg). The values, rounded to the nearest centimeter, were then noted in a table. The mean value was calculated from the three values noted for each axis and supporting leg, which resulted in 16 values for eight axes and two legs. These values were used for the subsequent statistical analysis SEBT set as the primary endpoint in this study (Figure 8).

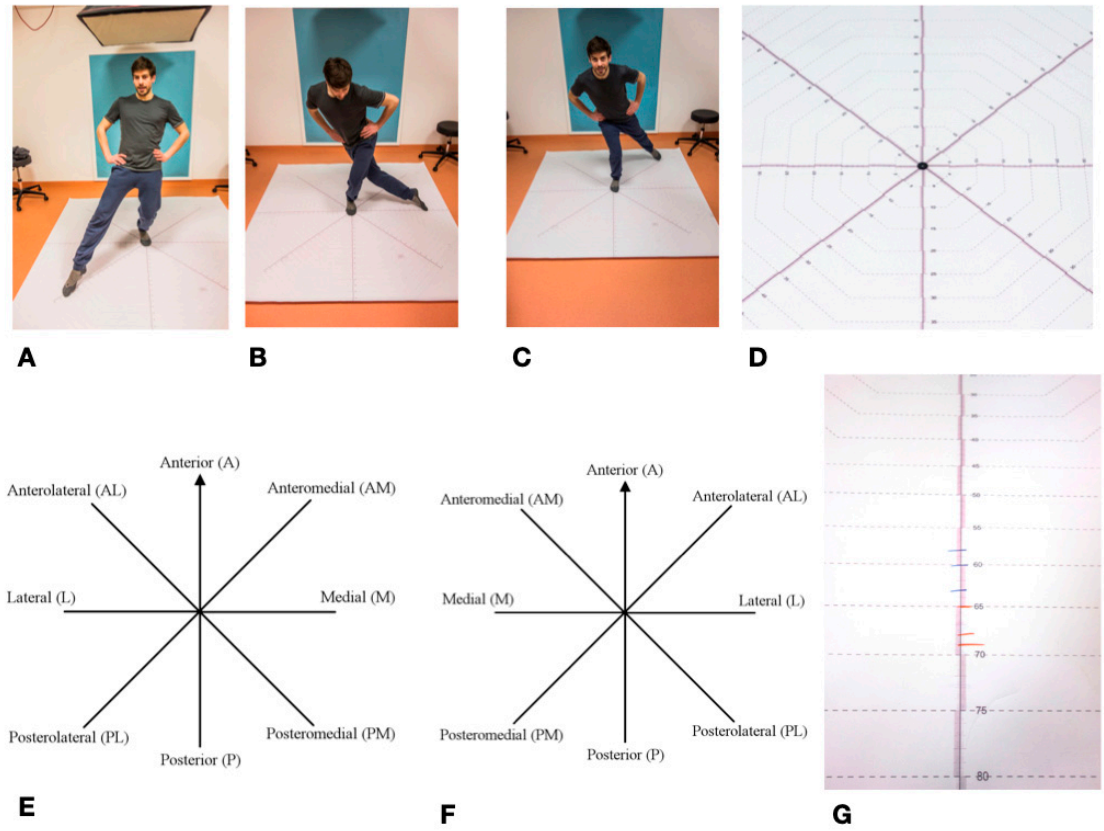


Figure 8. Star Excursion Balance Test—SEBT: (**A**–**C**) Mainstay left, towards Posterolateral; Lateral; and, Posteromedial; (**D**) SEBT detailed view of measuring cross; (**E**) SEBT stand on the left; (**F**) SEBT mainstay on the right; and, (**G**) Length marking as an example; blue = right leg; red = left leg.

4.5. Foot and Ankle Disability Index—FADI

The Foot and Ankle Disability Index (FADI) was first mentioned in literature in 1999 [55]. It is a questionnaire, in which subjects with ankle injuries can assess their injury-related limitation in terms of movement, everyday activities, and pain. Similar to the SEBT, the FADI is particularly suitable for the assessment of chronic ankle instability (CAI) [102]. Therefore, it is often used in studies with the SEBT and it is particularly suitable for evaluating rehabilitation after ankle injuries [35,90,103]. In addition to the basic form of the FADI, there is an extension consisting of eight additional questions regarding sport activities, the so-called "FADI Sport".

The basic form of the Foot and Ankle Disability Index (FADI) consists of 26 items. For 22 of these questions, the patient has to rate different activities of daily life (ADL) and the following points can be assigned: four points (no difficulty), three points (slight difficulty), two points (moderate difficulty), one point (extreme difficulty), or 0 points (unable to do). The four remaining questions are about pain intensity; here the points can be assigned, as follows: four points (no pain), three points (slight pain), two points (moderate pain), one point (severe pain), 0 points (unbearable). Overall, a maximum score of 104 points (26 × 4 points) is possible. It is particularly important that the only cause of the complaints must come from the disease or injury to the ankle. If another illness is the cause of the restrictions or pain, the respective question is marked with "N/A" and taken off the total score and the total score is adjusted. In this case, the examined disease or injury to the ankle corresponded to the raising of the fibular graft. The original test can be expanded to include the "FADI Sport" subscale for a young and active athletic collective, in which eight questions about sporting activities have to be answered in the same scheme [50]. The structure of the questionnaire used was taken from Hale et al. [35]. The FADI questionnaire was explained to each patient by the examiner, who took special care that each patient understood the questions and above-mentioned assessment requirements. The questions were

answered together with the patient, and the score was noted. The overall result was then determined in absolute terms and as a percentage value.

4.6. Ethics, Privacy and Statistical Analysis

The ethics committee at the Medical Faculty of Justus-Liebig University Giessen approved the study under the approval number 232/14. The collected patient data were pseudonymized before statistical analysis was performed. Each patient could only be assigned to the respective data record using a key. The statistical evaluation was carried out together with the Institute for Medical Informatics at University Hospital Giessen, Germany. Continuous variables are expressed as mean ± standard deviation (std), median, minimum, and maximum, categorical variables are reported as absolute and/or relative frequencies. Normal distribution of continuous variables were evaluated by QQ-Plot, group comparison was executed by *t*-test. No adjustment for multiple testing was performed. All obtained parameters were listed in a combined Excel table and then evaluated using SAS (version 9.4 SAS Institute, Cary, NC, USA).

5. Conclusions

Donor-site morbidity after fibula transplantation is relatively low and, compared to the outstanding benefits of the fibula graft in the reconstructive facial surgery, the complications are still well justifiable. The vast majority of subjects are satisfied with both the functional and aesthetic result. The most common complications identified were transient wound healing disorders as well as paresthesia.

The examinations using SEBT and FADI showed a small but significant, lower stability, and ankle function due to the operation, similar to a chronic ankle instability (CAI). However, the limitations of quality of life and daily activities were minimal for most subjects. SEBT and FADI both seem to be suitable methods to examine patients after fibula transplantation. In general, future studies on donor-site morbidity after fibula transplantation should use uniform test methods. This is the only way to effectively compare the abundant data in literature.

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Donor-Site Morbidity after Fibula Transplantation in Head and Neck Tumor Patients: A Split-Leg Retrospective Study with Focus on Leg Stability and Quality of Life

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4 Discussion

Oral rehabilitation using dental implants is an established treatment option for a broad spectrum of clinical indications [158]. However, in patients compromised both medically and dentally, a surgical procedure may need to be performed to allow for predictable implant placement, primary stability, and osseointegration. Therefore, the main focus of this work was to assess the clinical success and survival rates of the dental implants inserted in compromised patient collectives. Survival is defined as when the implant remains in the oral cavity regardless of the clinical and radiographic assessment results [18, 19, 66, 67].

Patients with dental aplasia are dentally compromised through their congenitally missing teeth and the resulting alveolar bone atrophy. In certain cases, dental aplasia can be accompanied by systemic medical diseases, such as ectodermal dysplasia, cleft lip or palate, Rieger syndrome, and Down's syndrome [159]. In healthcare research, it is essential to assess the implant success of this compromised group of patients and their dental rehabilitation [18]. The relatively low number of patients (n = 37) and dental implants (n = 155) was a limiting factor when pursuing this research [18]. However, due to the rareness of tooth agenesis, previously published papers in this field have also included smaller numbers of patients and implants [160–162]. Here, the gender prevalence ratio of hypodontia was 1:1.3 (43.2% male and 56.8% female), comparable to the previously published ratio [163, 164]. The mean age of the included patients was 20 years (17–44) at the time of implantation, with 33 patients aged between 17 and 23. This report was similar to other studies [165, 166]. The reason for the predominance of young patients was that maxillofacial surgeons start to replace congenitally missing teeth after complete cranial growth at the age of 17–21 years. The maxillary lateral incisors and maxillary and mandibular second premolars were the most frequently missing teeth replaced with dental implants in the sample population (Original Articles 1 and 2). The implant survival rate was 98.7% (n = 153/155). One

implant was lost after 34 months due to osseointegration failure, and another was lost after six months due to peri-implantitis.

A survival rate of 96.6% for 60 implants in eight patients was reported by Becelli et al. [162], and a previously published meta-analysis found an implant survival rate of 95.3% [167]. Alveolar ridge atrophy requires bone augmentation before dental implant insertion. In 97 dental implant sites, bone augmentation was performed from either the retromolar region (n = 8) or iliac crest (n = 89). The area used for harvesting bone was selected based on the severity and size of the bone defects. In the case of small and medium bone atrophy with two or fewer missing teeth, autografts were taken from the mandibular angle [15, 144]. Each augmentation procedure involved different bone characteristics. Whereas iliac crest bone has more cancellous bone with higher bone resorption potential [168, 169], compact bone (e.g., the mandible and tabula externa) has slower resorption rates, which is preferable for long-term implant success [170]. According to Albrektsson's criteria, out of 18 unsuccessful implants, 11 were bridges (61%), 3 were crowns (16.6%), and 2 were double crowns (11%). These findings represent a correlation between prosthetic design and unsuccessful dental implants. Altogether, 100 crowns, 37 bridges, and 15 telescopic crowns were designed for all patients. The pronounced failure incidence in the bridge design may have indicated difficulty in the maintenance of optimal oral hygiene [171].

Furthermore, patient satisfaction was compared with Albrektsson's criteria for implant success. Out of 18 unsuccessful implants, 17 of the patients reported very high satisfaction with their implants. Similar results were found in the subjective aesthetics component from the patients' perspective, where 16 failed implants received good aesthetic evaluations. Although all were rated as good by the patients, the speech and chewing functions had similar results, with 13 and 15 unsuccessful implants, respectively. Furthermore, high general patient satisfaction encompassing mastication, pronunciation, and aesthetic parameters was reported. These results suggest that the objective success criteria used by specialist implantologists may differ

from the subjective considerations of patients. Therefore, a success scale that combines both aspects is needed for dental implants [19].

The long-term effect of PRP combined with autografts from the iliac crest in sinus lifting procedures on implant survival and success was evaluated. The overall analysis showed that the values of all parameters in the PRP group were inferior to those in the control group. Therefore, the question arose as to whether PRP has a negative impact on the long-term outcomes. Furthermore, the failure rate probabilities according to Albrektsson's criteria were distinctly higher in the PRP group. To clarify whether PRP has a negative influence on long-term implant outcomes, further controlled trials with more significant numbers of test subjects could help prove this hypothesis [66, 67].

The definition of dental implant success is not standardized in dentistry [172]. Many authors have tried to conceive objective implant success criteria to evaluate treatment outcomes [82]. The two most popular implant success criteria used in the literature were considered here to describe our patient collective [87, 88]. The primary purpose of this double assessment in the same patient collective was to achieve an accurate success judgment by comparing the criteria with each other. Generally, the success rate in the evaluated subjects was similar to that in the literature. However, the success rates observed using Albrektsson's criteria were lower than those calculated from Buser's criteria. This difference may have been due to the strict evaluation of bone resorption around implants in Albrektsson's criteria [18, 67].

Despite the reduced bone available for dental implant insertion in patients hypodontia and maxillary atrophy, the implant survival and success rates were comparable to those of non-compromised patients [19, 66, 67]. These results were possible following bone atrophy compensation using an autologous bone graft [15]. Intriguingly, autologous bone graft enhancement by PRP did not induce any significant improvement in the short-term bone healing [152]. In the long-term implant follow-up, the implants inserted in the jaw area augmented with iliac crest and PRP had lower

survival and success rates and clinical findings. Therefore, the clinical benefit of adding PRP during bone augmentation surgery was not validated [67].
Dental implants have proven to be a recommended therapy with desirable clinical, functional, and aesthetic treatment outcomes in medically and dentally compromised patients who have received autologous bone augmentation [19, 111].

The donor-site morbidity after fibula transplantation and bone harvesting from the retromolar area is relatively low [13, 15]. Compared to the outstanding benefits of optimizing the oral condition for better healing and long-term implant success, the complications are still justifiable. Most patients who undergo these surgical procedures are satisfied with the results. These outcomes should encourage oral and maxillofacial surgeons to perform augmentative and reconstructive jaw surgeries to provide successful dental implant placements. The patients' benefits include functional and aesthetic oral rehabilitation exceeding the low donor-site complication rate.

4.1 Development of a new assessment method for implant success

The current study considered the two most popular implant success criteria according to Albrektsson [87] and Buser [88]. The treatment outcomes from the two criteria vary not only from each other but also from real clinical situations and individuals' characteristics. The application of Buser's criteria in the present study must be critically questioned considering a single aspect: the absence of recurrent purulent infection. In this study, a single follow-up was planned to assess implant success. Thus, it was not possible to determine whether purulent suppuration occurred once or repeatedly. If pus leakage from the sulcus occurred within an implant site, the implant was classified as unsuccessful. Therefore, this evaluation may be considered too strict and exclusive. Moreover, Buser's criteria might not be useful for patients who have undergone

complex jaw reconstruction and radiotherapy because of their compromised oral mucosa and gingiva as a result of the radiation exposure.

Albrektsson's criteria considers the bone resorption loss per year around implants. If the bone resorption rate around an implant is above a defined limit, the implant is classified as unsuccessful. However, complete bone resorption affecting the entire implant body was not necessary for the current assessment. Thus, the failure criteria according to Albrektsson are more stringent compared to Buser's criteria.

Albrektsson's success criteria are not all clearly defined, making widespread implementation difficult. For example, according to Albrektsson: "There should be no irreversible peri-implant infection in a successful implant." [87]. However, the exact definition of such inflammation is not stratified.

In the present work, such infection was interpreted as peri-implantitis because peri-implantitis involves inflammation of the peri-implant tissue and crestal bone. Thus, Albrektsson's two criteria regarding inflammation and bone resorption could be combined for clinical purposes. The investigators assumed infection in the presence of selected common criteria, such as gingival bleeding, PDs greater than 4 mm, and crestal bone loss above the calculated threshold. There is no international consensus on when peri-implantitis should be diagnosed, so other limits could be potentially set.

To summarize, the two sets of existing implant success criteria showed limitations in the following points:

A- Formulation is less concrete, focuses only on the hard tissue and assessment of omitted soft tissue

For example, implants in patients with persistent complaints, such as pain, foreign body sensation, or dysesthesia, are considered unsuccessful. However, this can be misleading, as seen in Figure 18, which shows a patient diagnosed with hypodontia and implant insertion in regions 14, 12, 22, and 46. The implant in region 46 was rated unsuccessful regarding both criteria as the patient had hypoesthesia in the right inferior alveolar nerve. The patient's satisfaction and the implants' functional, clinical, radiological assessment results were very good.

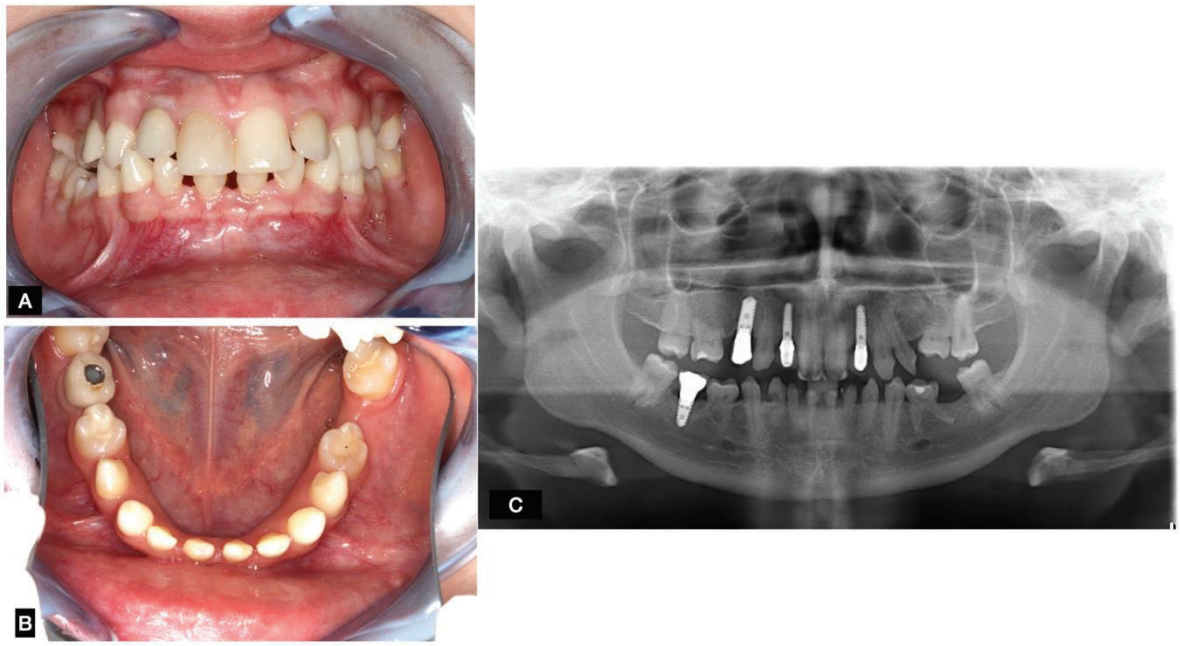

Figure 18. Clinical case with an unsuccessful dental implant in the right mandibular first molar region according to Albrektsson and Buser: A–B) intra-oral photos; C) panoramic x-ray. Subjective assessment of patient satisfaction is missing. Clinical case of the Department of Oral and Maxillofacial Surgery, University Hospital Giessen.

B- No assessment of subjective criteria, including patient satisfaction

Both classifications use purely objective criteria without considering patient satisfaction. In one of the studies included in this thesis, we compared patient satisfaction with implant success according to Albrektsson's criteria. Regarding the 17 unsuccessful implants, the patients were still functionally and aesthetically satisfied with the implants. These results proved the need to supplement the objective success criteria used to assess the implant treatment outcomes with the subjective considerations of patients.

C- No evaluation of the implant–prosthesis suprastructure as a unit

The assessment of prosthetic outcomes and complications is ignored in the success criteria. A dental implant comprises a sub-crestal implant screw and supra-crestal

prosthetic part. Therefore, the prosthetic treatment outcome is an integral part of the implant success assessment.

To overcome the limitations mentioned above in the implant treatment outcomes, the current study revealed the need for a new assessment system dedicated to dental implants. The proposed system should be in the form of a three-point scoring system and include clinical and radiological parameters, prosthetic outcomes, and patient satisfaction. According to the suggested scoring, implant success is graded into different levels, e.g., very good, good, satisfactory, and bad/failure. The main goal of such a score is to prevent premature diagnosis of implant failure. The suggested implant score includes four groups of criteria:

1- Knockout criteria: In the presence of the following criteria, the implant is definitively considered unsuccessful, and no further investigation is required: implant mobility, implant fracture, and implant in the wrong position. Therefore, prosthetics cannot be provided.

2- Implant-related findings, which include the following:

a) Absence of pain detected by percussion and palpation tests

b) Annual peri-implant crestal bone resorption does not exceed the value calculated ("y = 1.5 mm + 0.2 mm * (x – 1)"; y: allowed bone loss, x: age of the implant in years) when compared to the time of implant insertion.

c) The mean PD from four sides does not exceed 4 mm

d) Absence of BOP

These criteria are essential for the treatment outcomes of dental implants; therefore, each of the abovementioned sub-criteria is given two points.

2- Soft tissue and prosthodontics: These criteria evaluate the absence of plaque and prosthetic complications, such as crown fracture or debonding, and the presence of healthy mucosa. For every fulfilled sub-criterion, one point is given.

3- Patient satisfaction, which includes the following aspects: no foreign body sensation, no paresthesia, aesthetic satisfaction, masticatory function satisfaction, and speech ability satisfaction. For every fulfilled sub-criterion, one point is given.

The maximum number of points that can be collected by applying this score is 18. The score is analyzed as follows: 0 failure, 1–6 satisfactory, 7–12 good, and 13–18 very good (Figure 19).

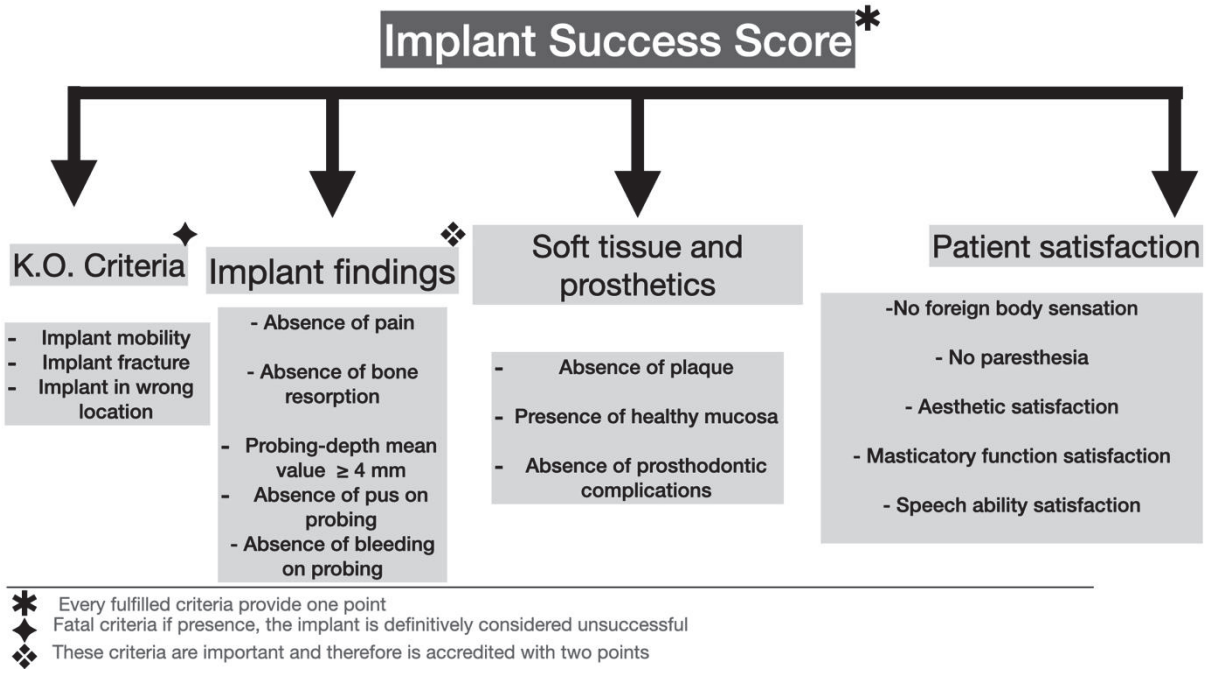

Figure 19. A flowchart explaining the proposed implant success scoring system.

4.2 Limitations of the present work

In order to identify the strengths and weaknesses of Albrektsson's and Buser's implant success criteria, the study should include the same patient collective to be investigated by a statistically acceptable number of dentists. Therefore, designing the study as a prospective randomized controlled study to assess those two routinely used criteria can be difficult, because a high number of dentists and implants must be guaranteed. Moreover, the dentists might implement the criteria differently than in their daily routine if they are compelled to complete detailed questionnaires for a study rather than just perform their routine work according to their experience and best judgment. Therefore, several of the projects included in the present thesis were conducted as retrospective clinical follow-up studies, which present a lower level of evidence when compared to the prospective observations [173]. Nevertheless, every patient included

in any of the cumulative studies was recruited for a follow-up examination that reported clinical and radiological findings, separately or combined.

Thereby, the data of the retrospective cases were strengthened through the follow-up re-examination, which provided a more concurrent representation of the treatment results.

However, this resulted in a lack of multicenter cooperation, which could decrease the study's external validity [174].

A standardized method for recording patients' oral health–related quality of life was not included in this work, and no corresponding documentation was done before treatment commencement. However, for future studies, the Oral Health Impact Profile could be implemented [175, 176]. This is a questionnaire that provides information on orofacial pain, psychosocial influences, orofacial aesthetics, and oral function [176].

Another limitation associated with the present work is the collection of subjective data many years after actual treatment and symptom occurrence. For example, the patients were asked about the intensity of their pain after their bone graft transplantation. Since patients have varying memory capabilities, they could have reported details on the pain and its severity differently. Therefore, "recall bias" should be considered to compensate for these weaknesses, and the subjective data should be interpreted cautiously [177].

5 Summary and perspective

Dental implants play a vital role in the oral and dental rehabilitation of patients with complex medical needs. Contraindications to implants are decreasing over time as a result of modern evidence-based clinical protocols, enhanced implant materials, and improved procedural strategies, such as augmentation of small and large defects. The present work aimed to evaluate dental implants' success and survival in medically and dentally compromised patients.

Sufficient quality and quantity of bone and soft tissue are the essential requirements for implant placement, and atrophy of this tissue requires augmentation. However, donor-site complications should not be neglected when assessing the risk prevalence. Therefore, this thesis also evaluated the donor-site complications of two methods of augmentation used for compromised patients.

In Original Articles 1 and 2, the survival and success rates of 155 implants inserted in 37 patients (21 females, 16 males) diagnosed with dental aplasia were evaluated. The implant success was assessed according to Albrektsson's (1986) and Buser's (1990) criteria. The clinical and radiological examinations included the following parameters: plaque index, PDs, BOP, degree of mobility, PT, presence of keratinized gingiva, presence of infection, implant loss, and peri-implant bone loss. The patient satisfaction was reported and included masticatory function, speech, aesthetic aspects, and overall satisfaction. Out of the 37 patients included, 4 were medically and dentally compromised with the following additional diagnoses: ectodermal dysplasia (n = 2), cleft lip or palate (n = 2), and/or oligodontia (n = 9). Moreover, 24 were only dentally compromised with hypodontia. A total of 155 implants were inserted (n = 86 in the maxilla and n = 69 in the mandible). Two implants in the maxilla had to be explanted, resulting in a dental implant survival rate of 97.7% for the maxilla and 100% for the mandible. Overall, the survival rate of the dental implants was 98.7%. The success rate, according to Buser's criteria, was 96.8%, while the success rate according to Albrektsson's criteria was 88.4%. The patient satisfaction at follow-up was very high.

All patients were able to intake food normally and testified to an uncompromised chewing ability. The speech ability was acceptable for all patients. The aesthetic outcome was unsatisfactory for only one patient (2.7%).

The survival and success rates of dental implants in medically compromised patients with dental aplasia are high and comparable to those in non-compromised patients. Therefore, dental aplasia should not be considered a risk factor for implant placement. Original Article 3 reported the donor-site morbidity of dentally compromised patients with small and medium alveolar ridge atrophy augmented with an autologous bone graft from the retromolar area using a standardized bone graft transfer. The augmentation, dental implant success after insertion in the augmented areas, and patient satisfaction were assessed; 54 patients with 64 bone graft cylinders were included. Only one implant loss was observed in a patient who received bone grafting, and six patients reported a localized neurological disorder (hypoesthesia) associated with the inferior alveolar nerve. Most of the patients were "very satisfied" or "satisfied" with the standardized bone graft transfer results and would recommend this operation to other patients. Thus, autologous bone grafting from the retromolar area proved to be a reliable method with a low complication rate to compensate for alveolar ridge atrophy and dental implant rehabilitation.

In Original Articles 4 and 5, the long-term implant survival and success were investigated in the dentally compromised patients with maxillary/mandibular atrophy who underwent sinus lift surgery and autologous bone grafting (iliac crest) with and without PRP in a previous RCT, which aimed to evaluate the short-term impact of adding PRP to the iliac crest autograft in sinus lift surgery. The present articles investigated the long-term impact of PRP on implant survival and success based on clinical and radiological findings. The implant success was assessed using Albrektsson's and Buser's criteria. In total, 37 patients (25 females, 12 males) were included, covering 23 patients treated bilaterally with a split-mouth design and 14 patients treated unilaterally. The median age of the patients at examination was 65 years. A total of 202 implants were examined, and a total of eight implant losses were

documented. The survival rates were 94.4% (split-mouth evaluation) and 94.8% (unilateral evaluation) in the PRP group and 97.5% (split-mouth evaluation) and 98.6% (unilateral evaluation) in the control group. The success rates according to Buser's criteria were 93.3% (split-mouth approach) and 93.1% (unilateral evaluation) in the PRP group and 97.5% (split-mouth evaluation) and 98.6% (unilateral evaluation) in the control group. The success rates according to Albrektsson criteria were 75.6% (split-mouth evaluation) and 75.9% (one-sided evaluation) in the PRP group and 86.4% (split-mouth evaluation) and 89.9% (one-sided evaluation) in the control group. No statistically significant difference between the two study groups was found in terms of the survival and success rates. The clinical and radiographic parameters suggested mostly healthy conditions of the peri-implant tissue. For the majority of these parameters, the PRP and control groups did not differ significantly, but the overall evaluation showed that the PRP group scored worse than the control group in over 80% of the 28 parameters. A high level of patient satisfaction was determined. The article could not demonstrate a favorable effect of PRP on the long-term success of implants. Thus, the use of PRP in maxillary augmentation is not recommended. In fact, there was a tendency toward worse long-term results in the PRP group; further controlled studies need to be warranted to verify this relationship.

In Original Article 6, the donor-site morbidity of medically compromised patients who underwent ablative jaw surgery and reconstruction using FFFs were evaluated. The study focused on leg stability (with a split-leg design), patient satisfaction, and quality of life. The ankle joint was selected as an indicator of balance and stability, in which the fibula is involved as one of three bones. Two test procedures specific to this purpose were used: the SEBT as a practical test of ankle function and the FADI as a questionnaire to assess the quality of life regarding the ankle joint. The majority of patients (97%) underwent surgery for tumors, 69% of which were squamous cell carcinomas. An osteocutaneous graft was harvested in 76.4%, and the donor site was closed with a split-skin graft in 73.5%. The inpatient stay length averaged 20 days and was prolonged for the squamous cell carcinomas and osteocutaneous grafts. The

postoperative pain intensity was reported as 3.2 on average on a scale of 0–10, with 88% of patients pain-free after three months at the latest. With split-skin coverage, the pain lasted longer, and wound healing problems occurred more frequently. Temporary donor-site complications, mainly related to the wound healing process, occurred in 41% of patients, and long-term complications, mostly paresthesia and chronic pain, were observed in 16%. Foot lift weakness was noted in 10.3% of patients, suggesting damage to the fibular nerve. Only 3% of patients were dissatisfied with the overall surgery, and 6% were dissatisfied with the aesthetics of the donor site. On the SEBT, the participants scored significantly shorter in all eight directional axes with the operated leg as the support leg. On average, the healthy leg discrepancy in this regard was 4.5%, consistent with chronic ankle instability studies. The FADI score of 89.4% was also within the range of such studies, meaning limitations were present that impaired the quality of life only slightly. Overall, the donor-site morbidity was low and comparable to the literature results. The benefits obtained from the transplanted flap, including jaw reconstruction, function, and aesthetic rehabilitation, superseded the morbidity risk for the abovementioned compromised patients.

The current work demonstrated the limitations associated with the established implant success criteria, which can only be circumvented by designing a new success score that includes objective and subjective parameters. Nonetheless, such a score should be initially revised by experts in the appropriate clinical field to ensure its acceptance by the community, after which the score shall be evaluated for accuracy by examiners in different dental centers. The previous points should be addressed through the formation of consortia supported by national and international associations, such as the German Association of Implantology.

6 Zusammenfassung und Ausblick

Dentale Implantate spielen eine wichtige Rolle im Rahmen der oralen und dentalen Rehabilitation von Patienten mit komplexen medizinischen Bedürfnissen. Die Zahl der Kontraindikationen in der modernen Implantologie nimmt im Laufe der Zeit ab, was auf moderne evidenzbasierte klinische Protokolle, verbesserte Implantatmaterialien und optimierte Verfahrensstrategien wie die Augmentation kleiner und großer Defekte zurückzuführen ist. Die vorliegende Arbeit bewertet den Erfolg und das Überleben von dentalen enossalen Implantaten bei allgemein- und zahnmedizinisch kompromittierten Patientenkollektiven.

Ausreichend Hart- und Weichgewebe sind wichtige Voraussetzungen im Rahmen von Implantatversorgungen. Sind diese Gewebe atrophiert, sollte vor oder nach der Implantatinsertion eine entsprechende Augmentation durchgeführt werden. Zur Bewertung von Risiken chirurgischer Verfahren haben Untersuchungen von Komplikationen im Bereich der Entnahmestelle eine besondere Bedeutung. In der vorliegenden Arbeit wurden hierfür zwei klinisch relevante Augmentationstechniken bezüglich ihrer Komplikationen an der Entnahmestelle bei kompromittierten Patientenkollektiven untersucht.

In den Originalarbeiten 1 und 2 wurden die Überlebens- und Erfolgsrate von 155 inserierten Implantaten bei 37 Patienten (21 weiblich, 16 männlich) mit diagnostizierter Zahnaplasie ausgewertet. Der Implantaterfolg wurde nach den Kriterien von Albrektsson (1986) und Buser (1990) bewertet. Die klinische und radiologische Untersuchung umfasste die Parameter: Plaqueindex, Sondierungstiefen, Blutung beim Sondieren, Grad der Lockerung, Periotest®, Vorhandensein von keratinisierter Gingiva, Vorhandensein einer Infektion, Implantatverlust und periimplantärer Knochenverlust. Die Patientenzufriedenheit wurde untersucht und umfasste die Kaufunktion, Sprache, ästhetische Aspekte und die Gesamtzufriedenheit. Von den 37, in der Studie eingeschlossenem Patientenkollektiv, waren vier Patienten medizinisch und zahnmedizinisch kompromittiert mit den

folgenden zusätzlichen Diagnosen: ektodermale Dysplasie (n = 2), Lippen-Kiefer-Gaumenspalte (n = 2), Oligodontie (n = 9) und bei 24 Patienten lag eine Hypodontie vor. Es wurden insgesamt 155 Implantate inseriert (n=86 im Oberkiefer und n=69 im Unterkiefer). Zwei Implantate im Oberkiefer mussten explantiert werden. Daraus ergab sich eine Überlebensrate der Zahnimplantate für den Oberkiefer von 97,7 % und für den Unterkiefer von 100 %. Insgesamt lag die Überlebensrate von Zahnimplantaten bei 98,7 %. Die Erfolgsrate nach Buser betrug 96,8 %, während die Erfolgskriterien nach Albrektsson eine Erfolgsrate von 88,4 % ergaben. Die Patientenzufriedenheit bei der Nachuntersuchung war sehr hoch. Alle Patienten waren in der Lage, normal zu essen und zeigten eine gute Kaufähigkeit. Die Sprachfähigkeit war bei allen Patienten akzeptabel. Das ästhetische Ergebnis war nur bei einem Patienten (2,7%) unbefriedigend.

Die Überlebens- und Erfolgsrate von Zahnimplantaten bei medizinischen und kompromittierten Patienten mit dentaler Aplasie ist hoch und vergleichbar mit den Raten bei nicht kompromittierten Patienten. Daher kann eine dentale Aplasie nicht als Risikofaktor für die Implantation angesehen werden.

In Originalarbeit 3 wurde die Entnahmemorbidität bei zahnmedizinisch kompromittierten Patienten mit kleiner und mittlerer Alveolarkammatrophie berichtet, die mit autologen Knochentransplantaten aus dem retromolaren Bereich unter Verwendung einer standardisierten Knochenentnahmetechnik augmentiert wurden. Zusätzlich wurden der Augmentations- und Implantaterfolg nach der Insertion in die augmentierten Bereiche sowie die Patientenzufriedenheit bewertet. Es wurden 54 Patienten mit 64 Knochentransplantatzylindern eingeschlossen. Es wurde lediglich über einen Implantatverlust im Zusammenhang mit dem Versagen des Knochentransplantats berichtet. Sechs Patienten berichteten über eine neurologische Störung (Hypästhesie) des Nervus alveolaris inferior. Die meisten Patienten waren mit den Ergebnissen des standardisierten Knochentransfers "sehr zufrieden" oder "zufrieden" und würden diese Operationstechnik anderen Patienten empfehlen. Das autologe Knochentransplantat aus dem retromolaren Bereich erwies sich als

zuverlässige Methode mit geringer Komplikationsrate zur Kompensation der Alveolarkammatrophie und der dentalen Implantatrehabilitation.

In den Originalarbeiten 4 und 5 wurde das langfristige Überleben und der Erfolg von Implantaten bei Patienten mit einer Atrophie der Kiefer untersucht. Das Kollektiv hat sich einer Sinusliftoperation mit autologen Knochentransplantaten (Beckenkamm) jeweils mit und ohne PRP im Rahmen einer vorangegangenen randomisierten Untersuchung unterzogen. Ziel der früheren Studie war es, die kurzfristigen Auswirkungen der Zugabe von PRP zum Beckenkamm-Autotransplantat bei der Sinuslift-Operation zu bewerten, während in der vorliegenden Studie die langfristigen Auswirkungen von PRP auf das Überleben und den Erfolg von Implantaten sowie auf klinische und radiologische Befunde untersucht wurden. Der Implantaterfolg wurde anhand der Kriterien nach Albrektsson und Buser beurteilt. 37 Patienten (25 Frauen und 12 Männer) wurden in diese Studie eingeschlossen. Darunter waren 23 Patienten, die bilateral in einem Split-Mouth-Design behandelt wurden, und 14 Patienten, die unilateral behandelt wurden. Das mediane Alter der Patienten bei der Untersuchung betrug 65 Jahre. Insgesamt wurden 202 Implantate untersucht und es wurden insgesamt acht Implantatverluste dokumentiert. Die Überlebensrate betrug 94,4 % (Split-Mouth-Auswertung) und 94,8 % (unilaterale Auswertung) in der PRP-Gruppe und 97,5 % (Split-Mouth-Auswertung) und 98,6 % (unilaterale Auswertung) in der Kontrollgruppe. Die Erfolgsrate nach Buser betrug 93,3 % (Split-Mouth-Auswertung) und 93,1 % (unilaterale Auswertung) in der PRP-Gruppe und 97,5 % (Split-Mouth-Auswertung) und 98,6 % (unilaterale Auswertung) in der Kontrollgruppe. Die Erfolgsrate nach Albrektsson lag bei 75,6 % (Split-Mouth-Auswertung) und 75,9 % (einseitige Auswertung) in der PRP-Gruppe und 86,4 % (Split-Mouth-Auswertung) und 89,9 % (einseitige Auswertung) in der Kontrollgruppe. Es zeigte sich kein statistisch signifikanter Unterschied zwischen den beiden Studiengruppen in Bezug auf die Überlebens- und Erfolgsraten. Die klinischen und röntgenologischen Parameter deuteten auf einen überwiegend gesunden Zustand des periimplantären Gewebes hin. In der Mehrzahl dieser Parameter unterschieden sich die PRP-Gruppe

und die Kontrollgruppe nicht signifikant. Die Gesamtauswertung zeigte, dass die PRP-Gruppe in über 80 % der insgesamt 28 Parameter schlechter abschnitt als die Kontrollgruppe. Es konnte ein hohes Maß an Patientenzufriedenheit festgestellt werden. Die vorliegende Studie kann keinen positiven Effekt von PRP auf den Langzeiterfolg von Implantaten nachweisen. Im Gegenteil, es zeigte sich eine Tendenz zu schlechteren Langzeitergebnissen in der PRP-Gruppe. Weitere kontrollierte Studien müssen durchgeführt werden, um diesen Zusammenhang zu verifizieren.

In Originalarbeit 6 wurde die Morbidität der Entnahmestelle bei Patienten nach ablativer Tumorchirurgie und einer Rekonstruktion mit freien Fibulatansplantaten bewertet. Die Studie konzentrierte sich auf die Beinstabilität in einem Split-Leg-Design sowie auf die Zufriedenheit und Lebensqualität der Patienten. Als Indikator für Gleichgewicht und Stabilität wurde das Sprunggelenk ausgewählt, an dem die Fibula als einer von drei Knochen beteiligt ist. Es wurden zwei spezifische Testverfahren verwendet, der Star Excursion Balance Test (SEBT)- als praktischer Test der Sprunggelenksfunktion- und der Foot and Ankle Disability Index (FADI)- als Fragebogen zur Beurteilung der Lebensqualität in Abhängigkeit vom Sprunggelenk. Die Mehrheit der Patienten (97 %) wurde aufgrund eines Tumors im Kieferbereich operiert, 69 % davon waren Plattenepithelkarzinome. Ein osteomyokutanes Transplantat wurde in 76,4 % entnommen und die Spenderstelle wurde in 73,5 % mit einem Spalthauttransplantat verschlossen. Der stationäre Aufenthalt betrug im Durchschnitt 20 Tage und war bei Plattenepithelkarzinomen und osteomyokutanen Transplantaten länger. Die postoperative Schmerzintensität wurde mit durchschnittlich 3,2 auf einer Skala von 0-10 angegeben, wobei 88% der Patienten nach spätestens drei Monaten schmerzfrei waren. Bei der Spalthautdeckung hielten die Schmerzen länger an und es traten häufiger Wundheilungsstörungen auf. Vorübergehende Komplikationen an der Spenderstelle, hauptsächlich Wundheilungsstörungen, traten bei 41 % der Patienten auf. Langfristige Komplikationen, wie Parästhesien und chronische Schmerzen, traten bei 16 % auf. Eine Fußheberschwäche wurde bei 10,3 % der Patienten festgestellt, was auf eine

Schädigung des Nervus fibularis hindeutet. Nur 3 % der Patienten waren mit dem gesamten Eingriff unzufrieden, 6 % waren mit der Ästhetik der Entnahmestelle unzufrieden. Im Durchschnitt betrug der Unterschied zum gesunden Bein in dieser Hinsicht 4,5 %, was mit Studien zur chronischen Knöchelinstabilität (CAI) übereinstimmt. Auch der FADI-Score von 89,4 % liegt im Bereich der CAI-Studien, wonach zwar Einschränkungen vorhanden sind, diese aber die Lebensqualität nur geringfügig beeinträchtigen. Insgesamt ist die Morbidität der Spenderstelle gering und vergleichbar mit Ergebnissen aus der Literatur. Die operative Tumortherapie mit plastischer Rekonstruktion ist auch nach Abwägung der Risiken von Komplikationen im Bereich der Spenderregion einer konservativen Therapie überlegen. Es überwiegen die Vorteile besonders im Hinblick auf die Funktion und ästhetische Rehabilitation von kompromittierten Patienten.

Die aktuelle Arbeit zeigt die Grenzen der etablierten Implantaterfolgskriterien auf, welche nur durch die Entwicklung einer neuen Erfolgsbewertung, die objektive und subjektive Parameter enthält, verbessert werden können. Zunächst sollte eine überarbeitete Scorebewertung von Experten auf dem klinischen Gebiet der Implantologie beurteilt werden, um deren Akzeptanz durch die Gemeinschaft zu gewährleisten. Im Anschluss ist eine multizentrische wissenschaftliche Überprüfung der Methodengenauigkeit notwendig. Diese Weiterentwicklung sollte durch Konsortien betrieben werden, die von nationalen und internationalen Verbänden wie beispielsweise der Deutschen Gesellschaft für Implantologie (DGI e.V.) unterstützt werden.

7 Attachment

7.1. Abbreviations

PRP : platelet-rich plasma

mm : millimeter

µm : micrometer

PT : Periotest value

PD : probing depth

BOP : bleeding on probing

IV : intravenous

FFF : fibula-free flap

DCIA : deep circumflex iliac artery

RCT : randomized controlled trial

SEBT : Star Excursion Balance Test

FADI : Foot and Ankle Disability Index

7.2. List of figures

Figure 1. The earliest evidence of implantology art shows the use of a gold wire bridge to resort the lower right first and second incisors and was discovered in an old Egyptian mummy: A) the whole mandible; B) magnification of the lower anterior area (both photographs are from Ancient Egyptian Dentistry, written by Venice Attia; they were used with her permission) [22]…… 2

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8 References

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