Justus-Liebig-Universität Gießen
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Spinale durale arteriovenöse Fistel –

pathogenetische und therapeutische Aspekte einer seltenen Erkrankung

Habilitationsschrift

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Abkürzungsverzeichnis

AV	arteriovenös
ASA	Arteria spinalis anterior
CE-MRA	kontrastverstärkte MR-Angiographie
DSA	digitale Subtraktionsangiographie
Dyna-CT	angiographische Computertomographie
ICG	Indocyaningrün-Videoangiographie
sdAVF	spinale durale arteriovenöse Fistel
PSA	Arteriae spinales posterolaterales
seAVF	spinale epidurale arteriovenöse Fistel

1 Einleitung

1.1 Definition

Spinale durale arteriovenöse Fisteln (sdAVF) sind pathologische arteriovenöse (AV) Kurzschlüsse zwischen einem oder mehreren radikulomeningealen Ästen einer spinalen Segmentarterie und einer intraduralen Vene.[1, 2] Mit einer Inzidenz von ca. 5/1 000 000/Jahr stellen sdAVF die häufigste spinale Gefäßmalformation dar.[3]

Obwohl sdAVF bisher als erworbene Malformationen im Erwachsenenalter gelten, ist die genaue Ätiologie bis heute unbekannt.[4, 5] Betroffen sind meistens Patienten* männlichen Geschlechts zwischen 50 und 70 Jahren.[3, 6] Die meisten sdAVF sind in der thorakolumbalen Region lokalisiert und deutlich seltener am kraniozervikalen Übergang oder in der tiefen lumbosakralen Region zu finden.[7]

Erste genauere Beschreibungen der Pathophysiologie dieser Fisteln gelangen Aminoff und Logue im Jahr 1974 sowie Merland et al. im Jahr 1980.[1, 8] Daraufhin folgten mehrere Fallserien über klinische sowie diagnostische und therapeutische Aspekte dieser Erkrankung.[6, 9]

In der Mehrheit der bisher repräsentativen Studien wird über einen chronisch progredienten Verlauf von unspezifischen, aber auch typischen Symptomen myelopathischer Genese berichtet.[6, 10] Bei den meisten Patienten wird zum Zeitpunkt der korrekten Diagnose sowohl über eine spinale Ataxie, eine Paraparese und Hypästhesien der unteren Extremitäten als auch eine über Blasen-Mastdarm-Funktionsstörung und Erektionsstörungen in unterschiedlicher Ausprägung berichtet.[9, 10] Seltener werden lumbale Rückenschmerzen oder Radikulopathien beschrieben.[7, 10]

* Aus Gründen der besseren Lesbarkeit wird in dieser kumulativen Habilitationsschrift auf die gleichzeitige Verwendung der Bezeichnungen männlich, weiblich und divers (m/w/d) verzichtet. Sämtliche Personenbezeichnungen sollen gleichermaßen für alle Geschlechter verstanden werden.

1.2 Diagnostische Besonderheiten

Die Mehrheit der Patienten beschreibt häufig unspezifische Beschwerden im Sinne von spinaler Ataxie mit asymmetrischen sensomotorischen Defiziten der unteren Extremitäten.[3, 6] Daher ist eine Diagnosestellung von sdAVF ohne weitere bildmorphologische Untersuchungen nicht möglich.[11]

Der häufigste diagnostische Fehler in der klinischen Vorfelddiagnostik ist die Annahme einer Polyneuropathie oder einer Spinalkanalstenose bzw. eines Bandscheibenvorfalls.[12] Weitere Rückenmarkserkrankungen wie entzündliche Pathologien, intramedulläre Gliome, eine Syringomyelie oder Rückenmarksischämie können ebenfalls als mögliche Differentialdiagnosen in Frage kommen.[12, 13]

Die hohe Rate an initialen Fehldiagnosen und die darauf basierenden Therapien führen bei den meisten sdAVF-Patienten zu einer erheblichen Verzögerung der Diagnosestellung und Therapie.[10] Bei den meisten Patienten erfolgen bis zum Zeitpunkt der korrekten Diagnose ein- oder mehrfache operative Therapieversuche bei bestehendem Verdacht auf eine andere Pathologie.[3, 10]

Bleibt eine sdAVF unerkannt und/oder unbehandelt, kann die resultierende progressive kongestive Myelopathie zu einer irreversiblen Schädigung des Myelons und einer vollständigen Querschnittslähmung führen.[12] Aminoff et al. stellten in ihrer Analyse fest, dass 50 % der unbehandelten sdAVF-Patienten innerhalb von drei Jahren nach dem Auftreten der ersten Beschwerden rollstuhlpflichtig werden.[14]

Die adäquate Diagnose und suffiziente Therapie einer sdAVF erfordern vor allem ein fundiertes anatomisches Verständnis der spinalen vaskulären Anatomie und ihrer Variationen.[15] An dieser Stelle ist zu erwähnen, dass mehrere klinisch relevante Aspekte der spinalen vaskulären Anatomie bisher ungeklärt sind und teilweise kontrovers in der

Literatur beschrieben wurden.[16, 17] Dies ist vor allem auf die Komplexität, aber auch auf die Seltenheit der spinalen Gefäßmalformationen zurückzuführen.

1.3 Klinische spinale vaskuläre Anatomie

1.3.1 Arterielle Versorgung

1.3.1.1 Segmentarterien

Zervikal stammen die Segmentarterien überwiegend aus den Arteriae vertebrales, Arteriae cervicales profundae und Arteriae cervicales descendens.[18] Am zervikothorakalen Übergang (C8 bis T3) können mehrere Segmentarterien über einen gemeinsamen Abgang aus dem Truncus costocervicalis der Arteria subclavia oder direkt aus dem Aortenbogen oder einer Arteria vertebralis verfügen und werden als Arteria intercostalis suprema bezeichnet.[19]

Im Bereich der Brust- und Lendenwirbelsäule versorgen die Segmentarterien aus der Aorta den Wirbelkörper, die paraspinalen Muskeln, die Dura spinalis, die Nervenwurzeln und das Myelon mit Blut.[19, 20] Im thorakolumbalen Bereich (T3 bis L4/seltener L5) gehen sie paarweise aus dem dorsalen Bereich der Aorta descendens ab.[20]

Die Segmentarterien der tiefen lumbosakralen Region stammen aus Ästen der Arteria iliaca interna (Arteriae iliolumbales und Arteriae sacrales laterales) oder aus der Arteria sacralis mediana.[7]

Die Rami spinales aller Segmentarterien sind klinisch von Bedeutung. Sie treten durch die Foramina intervertebralia in den Spinalkanal ein und teilen sich in (a) ventrale und dorsale epidurale Arterien, auch als retrokorporale bzw. prälaminäre Arterien bekannt, und (b) Radikulararterien, die radikulomeningeale, radikulopiale und radikulomedulläre Äste abgeben können.[20]

Die retrokorporalen und prälaminären Äste (a) stellen sowohl die Blutversorgung intraspinaler, extraduraler, ossärer und discoligamentärer Strukturen als auch jene des

epiduralen Fett- und Bindegewebes sicher. Sie nehmen bei der arteriellen Versorgung spinaler epiduraler AV-Malformationen eine zentrale Rolle ein.[21]

Die radikulomeningealen Arterien (b) versorgen hauptsächlich die Dura im Bereich der Nervenwurzelabgänge, sind über durale longitudinale Anastomosen miteinander verbunden und in der Regel die arteriellen Versorger der sdAVF.[20]

Die radikulomedullären Arterien (b) stellen eine Verbindung entlang der vorderen oder hinteren Nervenwurzel zu den perimedullären Arterien her und versorgen dadurch das Myelon arteriell mit.[17, 18] Während der embryonalen Entwicklung sind sie anfangs auf der Höhe aller Segmente der spinalen Achse bilateral nachweisbar.[18] Ihre Anzahl verringert sich jedoch noch intrauterin auf fünf bis acht radikulomedulläre Arterien.

Die kaliberstärkste radikulomedulläre Arterie wird nach dem ersten Beschreiber Adamkiewicz benannt und befindet sich bei 75 % der Menschen linksseitig zwischen den Segmenten T8 und L2.[20]

Die Identifizierung der radikulomedullären Arterien ist bei der Therapieplanung einer spinalen Gefäßmalformation obligatorisch.[22] Ein iatrogener Verschluss der Adamkiewicz-Arterie kann zum Beispiel zu einer ausgedehnten Rückenmarksischämie mit schwerwiegenden neurologischen Defiziten führen.[18]

1.3.1.2 Perimedulläre Arterien

Die direkte arterielle Versorgung des Myelons erfolgt über die perimedullär verlaufende Arteria spinalis anterior (ASA) und die paarigen Arteriae spinales posterolaterales (PSA).[18, 20] Die Versorgung der zervikalen ASA erfolgt überwiegend auf der Höhe des Foramens magnum aus absteigenden Ästen der intrakraniellen Segmente der Arteriae vertebrales und kann interindividuell stark variieren.[23] Die ASA läuft subpial entlang des Sulcus medialis anterior bis zum Conus medullaris, wo sie die sogenannte Conusarkade mit den PSA bildet und in die Arteria des Filum terminale übergeht.[23]

Über die oben genannten anterioren radikulomedullären Arterien wird die Durchblutung über die ASA entlang der spinalen Achse verstärkt. Daher sollte die ASA nicht als eine einzige gerade Arterie, sondern als eine aufeinanderfolgende Reihe von anatomischen Gefäßschleifen betrachtet werden.[19]

Die paarigen PSA beginnen auf der Höhe des Foramens magnum und werden zervikal, ebenfalls mit verschiedenen Variationen, von Ästen der Arteriae vertebrales oder der Arteria cerebelli posterior inferior gespeist.[23] Die PSA verlaufen subpial entlang der rechten und linken posterolateralen Fissur des Myelons und werden auf verschiedenen Ebenen von den posterioren radikulomedullären Arterien versorgt.[18, 23]

Neben der direkten Verbindung zwischen der ASA und den PSA am Conus medullaris (Conusarkade) besteht auf der gesamten Oberfläche des Rückenmarks ein ausgedehntes Anastomosennetz zwischen diesen Arterien.[20]

1.3.1.3 Tiefes arterielles System

Das tiefe arterielle System wird wiederum in ein zentrales und ein peripheres unterteilt.[23] Das zentrale System besteht aus den von den ASA ausgehenden zentralen Arterien, die in die Fissura mediana anterior gelangen und als sulcale oder sulcocommisurale Arterien bezeichnet werden.[17] Nachdem sie entweder links oder rechts in das Myelonparenchym eindringen, verzweigen sie sich vorwiegend zentrifugal innerhalb der grauen Substanz.[17] Das periphere System wird von kleinen Ästen der ASA und PSA gespeist (Vasocorona) und versorgt über kleine Perforatoren die oberflächlich gelegene weiße Substanz.[23]

Infolgedessen versorgt die ASA ungefähr zwei Drittel der Querschnittsfläche des Myelons, wobei die PSA das hintere Drittel versorgen. Die kortikospinalen Bahnen werden von beiden Systemen versorgt.[19]

1.3.2 Venöse Drainage

Aus dem Rückenmarksparenchym wird das venöse Blut über kleinere intrinsische horizontal verlaufende Venen in die Peripherie drainiert.[24] Auf der Ebene der spinalen Pia mater drainiert das Blut im Wesentlichen in zwei longitudinal verlaufende Venensysteme: die Vena spinalis anterior und posterior. Die longitudinalen Venensysteme des Rückenmarks sind in Bezug auf Verlauf, Größe und Lokalisation variabler als das benachbarte Arteriensystem.[24, 25]

Die Vena spinalis anterior befindet sich zur ASA unmittelbar dorsal und liegt somit subpial. Bei etwa 80 % der Menschen läuft sie zusammen mit dem Filum terminale als teilweise äußerst große terminale Vene bis zum Ende des Duralsacks.[18, 24] Die Vena spinalis posterior liegt subarachnoidal, variiert stark in ihrer Morphologie und zeigt perimedullär am thorakolumbalen Übergang eine ausgeprägte Vernetzung.[25]

Weitere intraparenchymale transmedulläre venöse Anastomosen verbinden die Venae spinales anteriores und posteriores.[24] Diese venösen Anastomosen sind im thorakalen Bereich am stärksten ausgebildet und können das venöse Blut dadurch bei hämodynamischen Veränderungen rasch von einer Seite zur anderen drainieren.[25]

Am kraniozervikalen Übergang gehen die Venae spinales anteriores und posteriores in die Hirnstammvenen sowie in die großen venösen intrakraniellen Blutleiter über.[25]

Zusätzlich wird das venöse Blut über radikuläre Venen drainiert, die entlang der vorderen und hinteren Nervenwurzel verlaufen und die Dura epidural durchqueren.[18, 24]

Die Anzahl dieser Venen ist generell hoch und kann ebenfalls stark variieren. In einigen Studien wurde eine durchschnittliche Anzahl von 25 radikulären Venen gezählt, die das Blut in den spinalen Epiduralraum drainieren.[24] Wenn jedoch kleinere Venen (< 0,25 mm Durchmesser) ausgeschlossen werden, beträgt die Anzahl dieser Venen sechs bis elf für die vordere und fünf bis zehn für die hintere Nervenwurzel.[24, 25]

Die Anzahl dieser Venen kann mit zunehmendem Alter aufgrund von fibrotischen Veränderungen abnehmen, was von einigen Autoren als begünstigender Faktor bei der Entstehung von sdAVF betrachtet wird.[26]

Der epidurale venöse Plexus erstreckt sich als kontinuierliches System vom Kreuzbein bis zur Schädelbasis und befindet sich im Fett- und Bindegewebe des spinalen Epiduralraums.[23] Dieses ventillose Venensystem besteht aus dünnen elastischen Wänden und ist im zervikalen Bereich mit den tiefen Halsvenen und thorakolumbal durch Segmentvenen mit den Azygos- und Hemiazygos-Venensystemen verbunden.[24]

2 Fragestellungen und Zielsetzungen der Arbeit

Aufgrund der insgesamt niedrigen Inzidenz der sdAVF sind in der Literatur bisher noch viele Details der Ätiologie, des klinischen Verlaufs, der optimalen Diagnostik und der Behandlung umstritten und ungeklärt.

Zunächst werden in dieser kumulativen Habilitationsschrift die bisher in der Literatur diskutierten ätiologischen und pathogenetischen Aspekte dargestellt und anhand unserer eigenen Datenbank diskutiert. Insbesondere werden in dieser Schrift folgende Fragen bearbeitet:

- Wenn davon ausgegangen wird, dass eine sdAVF eine im Erwachsenenalter erworbene Gefäßerkrankung ist, stellt sich die Frage, ob sich systemische vaskuläre Risikofaktoren wie arterielle Hypertonie, Diabetes mellitus, Fettstoffwechselstörungen und Nikotinabusus auf die Entstehung und den Verlauf dieser Erkrankung auswirken.
- Sind mögliche anatomische Variationen der spinalen Blutversorgung auch ein weiterer prädisponierender Faktor bei sdAVF-Patienten?

Aufgrund der komplexen Anatomie der spinalen arteriellen Versorgung und der bisher unerforschten hämodynamischen Aspekte der spinalen venösen Drainage werden im nächsten Abschnitt dieser Habilitationsschrift die anatomischen und neuroradiologischen Merkmale seltenerer Untergruppen der spinalen AV-Shunts mit folgenden Zielsetzungen diskutiert:

- Es erfolgt eine Erläuterung der komplexen klinischen vaskulären Anatomie der tiefen lumbosakralen Region sowie eine Demonstration der diagnostischen und therapeutischen Herausforderungen der sdAVF in diesem Bereich.

- In einem weiteren Schritt werden die diagnostischen und therapeutischen Algorithmen von Patienten mit tiefen lumbosakralen Fisteln sowie die Ergebnisse im Langzeitverlauf präsentiert.
- Die anatomischen und neuroradiologischen Merkmale der bisher selten beschriebenen multiplen sdAVF werden separat bearbeitet. Insbesondere wird die ätiologische und pathogenetische Bedeutung ihrer Angiomorphologie diskutiert.
- Zuletzt werden in diesem Abschnitt die epiduralen AV-Shunts mit einer retrograden Drainage demonstriert. Diese Untergruppe der spinalen AV-Shunts ist in zahlreichen beteiligten Disziplinen bisher noch unbekannt. Der genaue Pathomechanismus der spinalen epiduralen arteriovenösen Fisteln (seAVF) wurde in der Literatur bisher ebenfalls nicht beschrieben.

Im nächsten Abschnitt der Arbeit werden die therapeutischen Optionen erläutert. Insbesondere wird die frühpostoperative Verschlechterung der Symptome trotz erfolgreicher Ausschaltung des AV-Shunts diskutiert. Hier werden folgende Fragen bearbeitet:

- Wie ist der genaue Pathomechanismus einer frühen postoperativen Verschlechterung trotz adäquater Ausschaltung der sdAVF zu verstehen?
- Ist eine routinemäßige therapeutische Heparinisierung bei allen sdAVF-Patienten postoperativ sinnvoll?
- Hat eine postoperative Heparinisierung im Allgemeinen einen Einfluss auf den klinischen Langzeitverlauf bei sdAVF-Patienten?

Im letzten Abschnitt wird der klinische Langzeitverlauf der sdAVF-Patienten untersucht. Hier werden im Rahmen einer retrospektiven Analyse alle demographischen, klinischen und neuroradiologischen Befunde erfasst und zur Bearbeitung folgender Fragen analysiert:

- Geben die in den spinalen MRT-Untersuchungen nachweisbaren Veränderungen des Rückenmarks, beispielsweise Ödem oder Kontrastmittelaufnahme, Hinweise auf eine irreversible medulläre Schädigung, die den klinischen Langzeitverlauf beeinflussen kann?
- Ist die Lokalisation der sdAVF prognostisch von Bedeutung?
- Wie ist der prognostische Stellenwert weiterer demographischer und klinischer Befunde zum Zeitpunkt der Diagnosestellung im Langzeitverlauf zu sehen?

3 Zusammenfassung der Ergebnisse der wichtigsten Arbeiten zur Thematik

3.1 Evaluation eines möglichen Einflusses systemischer vaskulärer Risikofaktoren auf die Entstehung und Aufrechterhaltung einer spinalen duralen arteriovenösen Fistel (Anlage 1)

Spinale durale arteriovenöse Fisteln sind die häufigsten vaskulären Pathologien der spinalen Achse und machen ca. 70 % aller spinalen Gefäßmalformationen aus.[3] Ihre klinischen und radiologischen Merkmale waren in den letzten zwei Jahrzehnten Gegenstand verschiedener Studien.[9] Dennoch ist über ihre genaue Ätiologie bisher wenig bekannt.[5] Nach dem aktuellen Stand wird davon ausgegangen, dass sdAVF eine erworbene Erkrankung ist.[19, 27] Klinische Risikofaktoren, die eine sdAVF induzieren oder ihre Symptome hervorrufen bzw. verstärken können, sind derzeit nicht bekannt.

Zum Entstehungsmechanismus von duralen AV-Fisteln im Zentralnervensystem wurden bereits verschiedene Theorien aufgestellt.[28] Beispielsweise wurde die Hypothese aufgestellt, dass eine intrakranielle Venenthrombose mit assoziierter intravenöser Hypertonie und die Obstruktion des venösen Abflusses die Öffnung von kleinsten AV-Shunts hervorrufen.[28] Eine im Verlauf progrediente entzündlich-reaktive Angiogenese in den betroffenen Arealen wurde als zusätzlicher Auslöser dieser Fisteln vermutet.[28]

In Bezug auf sdAVF gingen Merland et al. davon aus, dass ein vorbestehender unzureichender venöser Auslass des Rückenmarks die Entwicklung dieser Fisteln und ihre klinischen Symptome zusätzlich hervorrufen könnte.[8]

Zwischen einer Venenthrombose und einer sdAVF wurde jedoch kein Zusammenhang nachgewiesen. Es wird allgemein angenommen, dass anatomische Veranlagungen und lokale hämodynamische Veränderungen die Entstehung einer sdAVF im Erwachsenenalter begünstigen.[16, 29, 30]

Das Ziel unserer Studie bestand darin, den Einfluss von systemischen vaskulären Risikofaktoren auf die Entstehung oder Aufrechterhaltung einer sdAVF im Rahmen einer epidemiologischen Analyse zu eruieren.[4]

Hierfür wurde die Rolle von systemischen vaskulären Risikofaktoren wie arterieller Hypertonie, Diabetes mellitus, Fettstoffwechselstörungen und Nikotinabhängigkeit durch einen Vergleich der Prävalenzen dieser Risikofaktoren in einer sdAVF-Kohorte von 59 Patienten mit jenen der Allgemeinbevölkerung verglichen.[31]

Die alterskorrigierte Prävalenz der arteriellen Hypertonie in der sdAVF-Kohorte war signifikant höher als jene der Allgemeinbevölkerung ($P < 0,001$). Die Prävalenzen von Diabetes mellitus ($P = 0,150$), Nikotinabhängigkeit ($P = 0,561$), Adipositas ($P = 0,217$) und Fettstoffwechselstörungen ($P = 0,125$) in der sdAVF-Kohorte unterschieden sich nicht von der Prävalenz dieser Erkrankungen in vergleichbaren Kohorten in der Allgemeinbevölkerung.

Da die meisten Patienten mit arterieller Hypertonie keine sdAVF entwickeln, ist es unwahrscheinlich, dass die arterielle Hypertonie die einzige Ursache für sdAVF ist. Es ist aber denkbar, dass es sich bei der arteriellen Hypertonie um einen zusätzlichen Faktor handelt, der die Symptome von sdAVF aggravieren oder deren Entwicklung beim Vorhandensein anderer prädisponierender Faktoren begünstigen könnte. Diese Hypothese sollte im Rahmen anatomischer und histopathologischer Studien weiter untersucht werden.

3.2 Klinische und radiologische Besonderheiten der spinalen duralen arteriovenösen Fisteln in der tiefen lumbosakralen Region (Anlage 2)

Spinale durale arteriovenöse Fisteln in der tiefen lumbosakralen Region sind selten und stellen sowohl eine diagnostische als auch therapeutische Herausforderung dar. Spezifische klinische und neuroradiologische Merkmale dieser Fisteln wurden in der Literatur bisher nicht beschrieben und waren ein Gegenstand dieser Studie.[7]

Hierzu wurden retrospektiv alle Daten der sdAVF-Patienten ausgewertet, die an der Uniklinik Aachen zwischen 1990 und 2017 behandelt wurden. Zwanzig Patienten mit tiefen lumbosakralen sdAVF konnten in diese Studie eingeschlossen werden. Ein Patient starb drei Monate nach der Behandlung an einer Lungenembolie und wurde aus der Analyse ausgeschlossen. Die epidemiologischen und klinischen Daten wurden aus den elektronischen Patientenakten entnommen.

Präoperative kernspintomographische und angiographische Aufnahmen mittels spinaler digitaler Subtraktionsangiographie (DSA) wurden ebenfalls für diese Studie evaluiert. In den präoperativen MRT-Aufnahmen wurde sowohl das Ausmaß der Hyperintensität in den T2-Sequenzen als auch der medullären Kontrastmittelaufnahme in den T1-Sequenzen anhand der Anzahl der betroffenen Segmente bewertet. Die Erweiterung der perimedullären Venen wurde anhand der T1- und T2-Sequenzen als nicht vorhanden, mild oder ausgeprägt eingestuft. Des Weiteren wurden die angiographischen Befunde wie Lokalisation der Fistelzone, arterielle Blutversorgung und Drainagevene in diese Studie eingeschlossen.

Der häufigste neurologische Befund zum Zeitpunkt der Aufnahme in unserer Einrichtung war eine subjektive und objektive Gangstörung. Bei 17 (85 %) Patienten war in den unteren Extremitäten eine Parese nachweisbar. Die restlichen drei Patienten (15 %) hatten eine langsam progrediente Ataxie ohne manifeste motorische Defizite.

Sensorische Symptome in unterschiedlichen Ausprägungen wurden bei 18 (90 %) Patienten in Form einer diffusen Hypästhesie und/oder Parästhesie in den unteren Extremitäten dokumentiert. 14 (70 %) Patienten hatten zum Zeitpunkt der Aufnahme eine Blasenfunktionsstörung.

Die durchschnittliche Zeit zwischen den ersten Symptomen und der Diagnosestellung betrug bei allen 20 Patienten 15 Monate. Insgesamt erhielten neun (45 %) Patienten auswärtig eine andere Behandlung bei Verdacht auf eine degenerative, entzündliche oder tumoröse Pathologie in der Wirbelsäule.

Bei allen Patienten waren eine medulläre T2-Hyperintensität und eine intramedulläre Kontrastmittelanreicherung in den spinalen MRT-Aufnahmen nachweisbar. Die Vene des Filum terminale und/oder eine lumbale Radikularvene waren bei 19/20 (95 %) Fällen deutlich erweitert in den MRT-/MRA-Aufnahmen ersichtlich. Zudem konnte eine bilaterale arterielle Versorgung der Fistel bei fünf (25 %) Patienten angiographisch identifiziert werden.

Zusammengefasst ist zu betonen, dass ein medulläres Ödem in Kombination mit einer Erweiterung der Filumvene oder anderer lumbaler Radikularvenen ein charakteristischer kernspintomographischer Befund der lumbosakralen sdAVF ist. Eine adäquate spinale MRA erleichtert die Identifikation der Drainagevene und Lokalisation der Fistelzone in der tiefen lumbosakralen Region.

Eine ausreichende bildmorphologische Darstellung der Angiomorphologie und eine suffiziente intraoperative Identifizierung dieser Fisteln erfordern ein fundiertes anatomisches Wissen über die vaskuläre Anatomie der tiefen lumbosakralen Region.

3.3 Behandlungsstrategie und Analyse des Langzeitverlaufs bei Patienten mit tiefen lumbosakralen arteriovenösen Fisteln (Anlage 3)

Nachdem wir in unserer ersten Studie die klinischen und radiologischen Besonderheiten dieser speziellen Untergruppe der sdAVF diskutiert hatten, analysierten wir in der folgenden Arbeit die Ergebnisse unserer Behandlungsstrategie sowie den Langzeitverlauf bei diesen Patienten.[32]

Alle Patienten in unserer Kohorte wurden chirurgisch behandelt. Ein Patient starb drei Monate nach der Behandlung an einer Lungenembolie und wurde von unserer Ergebnisanalyse ausgeschlossen.

Die operative Versorgung erfolgte über eine Hemilaminektomie in der zuvor mittels DSA identifizierten Lokalisation der sdAVF. Die intraoperative Dopplersonographie wurde bis 2012 routinemäßig zur Identifizierung und Verifizierung der arterialisierten Drainagevene verwendet. 2012 wurde diese Technik durch die Indocyaningrün-Videoangiographie (ICG) ersetzt. Postoperativ erhielten alle Patienten eine frühe MRT-Kontrolle. Eine frühe postoperative DSA wurde nur in besonderen Fällen durchgeführt (n = 6), wenn sich intraoperativ Unklarheiten über die genaue Lokalisation der Fistelzone ergeben hatten. Weitere klinische und radiologische Verlaufskontrollen erfolgten im ambulanten Rahmen.

Die klinischen Daten zum Zeitpunkt der Aufnahme, der Entlassung sowie ein Jahr nach der Entlassung und bei der letzten Nachuntersuchung wurden in dieser Studie evaluiert. Das Durchschnittsalter in unserer Kohorte betrug 65 ± 7 Jahre, 16 (84 %) Patienten waren männlich. Die durchschnittliche Symptomdauer bis zur Diagnosestellung betrug 15 Monate. Zum Zeitpunkt der Entlassung hatte sich eine Verbesserung des neurologischen Status bei drei (16 %) Patienten gezeigt. Der neurologische Status der restlichen 16 (84 %) Patienten war weitestgehend unverändert. Die Miktionsstörung war bei allen Patienten unverändert.

Bei der Analyse des einjährigen Langzeitverlaufs fehlten Daten von vier Patienten, die daraufhin von der Analyse ausgeschlossen wurden. Bei der Verlaufskontrolle ein Jahr nach der Entlassung (n = 15) hatte sich der neurologische Status bei insgesamt sechs (32 %) Patienten gebessert, war bei acht (42,1 %) unverändert und bei einem (5,3 %) Patienten verschlechtert. Die Miktionsstörung hat sich nur bei einem Patienten gebessert.

Aufgrund der neurologischen Verschlechterung bei einem Patienten und des progredienten medullären Ödems bei zwei weiteren Patienten wurden spinale Gefäßdarstellungen mittels DSA durchgeführt. Bei allen drei Patienten zeigte sich ein Rezidiv der sdAVF, das erneut chirurgisch behandelt wurde.

Für die Analyse des Langzeitverlaufs (länger als ein Jahr) fehlten Daten von zwei weiteren Patienten, die daraufhin ebenfalls von der Analyse ausgeschlossen wurden. Die mittlere Dauer zwischen Entlassung und letzter Untersuchung betrug bei den 13 Patienten 86 Monate.

Insgesamt zeigte sich sonst bei acht (62 %) Patienten keine weitere Befundänderung. Bei den restlichen sechs (38 %) Patienten war eine leichte Verschlechterung ohne den Nachweis eines Rezidivs der sdAVF zu beobachten.

Zusammengefasst bietet die chirurgische Behandlung der tiefen lumbosakralen Fisteln eine sichere und effektive Therapieoption. Die Rezidivrate betrug in unserer Kohorte 27 %.

Eine engmaschige und längerfristige Verlaufskontrolle ist bei diesen Patienten aufgrund der insgesamt höheren Rezidivrate im Vergleich mit den häufigeren thorakolumbalen sdAVF erforderlich. Eine routinemäßige angiographische Verlaufskontrolle ist bei diesen Patienten zwar nicht indiziert, sollte aber aufgrund der besonders komplexen Anatomie dieser Fisteln bei jedem klinischen oder kernspintomographischen Verdacht auf ein Rezidiv durchgeführt werden.

3.4 Anatomische Aspekte und neuroradiologische Besonderheiten der multiplen spinalen duralen arteriovenösen Fisteln (Anlage 4)

Spinale durale arteriovenöse Fisteln sind in der Mehrheit der Fälle solitäre Läsionen, die bei Männern im Alter zwischen 50 und 70 Jahren zu finden sind. In allen bisherigen Studien wurde eine erworbene Pathogenese dieser Erkrankung vermutet.[28]

Die Fistelzone befindet sich überwiegend in der Dura am Abgang einer Nervenwurzel, die von meningoradikulären Ästen einer Segmentarterie versorgt wird und transdural in den perimedullären Venenplexus drainiert.[5, 18, 23]

Es bleibt jedoch weiterhin unklar, warum sdAVF bei fast allen Patienten ein einmaliges Ereignis sind. Es wurde bisher über keine Patienten berichtet, die nach einer suffizienten Behandlung einer sdAVF eine erneute Fistel an einer anderen Stelle entwickelten. Aufgrund dessen haben wir in dieser Studie unsere Datenbank nach Patienten mit multiplen sdAVF evaluiert und die klinischen und radiologischen Merkmale dieser Patienten separat ausgewertet. Des Weiteren wurde im Rahmen dieser Studie eine Literaturrecherche zu Patienten mit multiplen sdAVF durchgeführt.[33]

Von 209 sdAVF-Patienten, die zwischen 1990 und 2017 in unserer Einrichtung behandelt wurden, zeigten nur drei (1,4 %) Fälle multiple sdAVF. Alle drei Patienten waren Männer und das Durchschnittsalter betrug zum Zeitpunkt der Diagnose 68 Jahre. Die neurologischen Befunde der drei Patienten waren mit jenen von Patienten mit einer solitären sdAVF vergleichbar. Alle drei Patienten zeigten Paresen, Gangataxie und Sensibilitätsstörungen in den unteren Extremitäten. Bei einem dieser drei Patienten zeigte sich zudem eine neurogene Miktionsstörung.

Alle sdAVF befanden sich bei diesen Patienten in der thorakolumbalen Region zwischen T7 und L2. Ein T2-hyperintenses Signal sowie eine Erweiterung der perimedullären Venen waren bei allen drei Patienten nachweisbar. Bei zwei dieser drei Patienten war eine intramedulläre Kontrastmittelaufnahme darstellbar.

Alle drei Patienten unterzogen sich einer chirurgischen Behandlung beider Fisteln in einem Eingriff. Postoperative Kontrollen zeigten eine suffiziente Ausschaltung der Fistelzonen bei allen Patienten.

Unsere Literaturrecherche ergab insgesamt 25 Fälle mit multiplen sdAVF. Epidemiologische und klinische Daten waren mit jenen unserer Kohorte vergleichbar. Interessanterweise befanden sich die Fisteln in der Mehrheit der bisher beschriebenen Fälle (67 %) in einem Abstand von weniger als drei Segmenten ipsi- oder kontralateral. Diese Beobachtung könnte durch die bisher vermutete Ätiologie der sdAVF erklärt werden. Da die Entwicklung einer sdAVF bisher als Folge einer Venenthrombose und/oder einer Auslassstörung des spinalen Venensystems angesehen wird, könnte die resultierende venöse Hypertension durch hämodynamische Verschiebungen des Blutflusses, der Gewebeperfusion und der venösen Drainage in unmittelbarer Nachbarschaft zur Entwicklung einer weiteren Fistel führen. Weitere Fragen im Hinblick auf den genauen Aufbau des perimedullären venösen Systems sollten anhand unserer Beobachtungen in der Zukunft jedoch durch anatomische Studien erforscht werden.

3.5 Spinale epidurale arteriovenöse Fisteln mit perimedullärer venöser Drainage: Klinische und radiologische Merkmale einer unterschätzten vaskulären Pathologie (Anlage 5)

In den letzten Jahrzehnten wurden verschiedene Klassifikationen für spinale Gefäßmalformationen erstellt. Die am häufigsten verwendete Klassifikation wurde 1988 von Oldfield und Doppman entwickelt.[34] Sie klassifizierten diese vaskulären Läsionen der spinalen Achse in vier Typen: durale AV-Shunts, intradurale glomuläre AV-Pathologien, juvenile AV-Malformationen und perimedulläre AV-Fisteln. Die selteneren und in den letzten Jahren häufiger diagnostizierten seAVF wurden sowohl in dieser Klassifikation als auch in den anderen jedoch nicht berücksichtigt.[21, 35–37]

Im Gegensatz zu den klassischen sdAVF befindet sich die Fistelzone der seAVF im spinalen Epiduralraum. Die venöse Drainage dieser AV-Shunts kann sowohl extraspinal als auch intradural erfolgen.[38]

Bei einer retrograden intraduralen venösen Drainage der seAVF kommt es wie bei den klassischen sdAVF zu einer kongestiven Myelopathie mit unspezifischen Symptomen. Da diese Pathologien jedoch in der Literatur bisher nur in wenigen Fallberichten präsentiert worden sind, wurden in dieser Studie die anatomischen, klinischen und radiologischen Charakteristika dieser Fisteln ausführlich demonstriert.

Insgesamt wurden Daten von 13 Patienten mit einer seAVF mit einer perimedullären venösen Drainage in unserer Datenbank identifiziert und für diese Studie evaluiert.

Demographische und klinische Daten wie der neurologische Status zum Zeitpunkt der Aufnahme in unserer Einrichtung, die Dauer der Symptome bis zur Diagnosestellung sowie frühere Fehldiagnosen und Behandlungen wurden in unsere Analyse eingeschlossen. Des Weiteren wurden alle MRT- und DSA-Befunde der 13 Patienten nochmals bewertet.

Das Durchschnittsalter in unserer Kohorte betrug 72 Jahre. Eine Paraparese trat bei zwölf (92 %) Patienten auf. Blasenfunktionsstörungen und sensorische Defizite der

unteren Extremitäten wurden bei der Aufnahme bei sieben (54 %) bzw. sechs (46 %) Patienten dokumentiert. Die durchschnittliche Dauer der Symptome bis zur Diagnosestellung betrug sechs Monate. Eine kongestive Myelopathie war in der MR-Bildgebung bei allen Patienten nachweisbar. Prominente arterialisierte perimedulläre Venen wurden in nur drei Fällen gezeigt. Die CE-MRA zeigte bei 9/10 (90 %) Patienten arterialisierte perimedulläre Venen mit einem assoziierten arterialisierten epiduralen Konvolut, das meist ventrolateral lokalisiert war. Spinale DSA-Aufnahmen zeigten eine multisegmentale Ausdehnung des arterialisierten ventrolateralen epiduralen Konvoluts in sechs (46 %) Fällen. Die intradurale drainierende Radikularvene wurde bei drei (23 %) Patienten mit einer deutlichen Entfernung vom ursprünglichen Fistelpunkt lokalisiert.

Im Wesentlichen unterschieden sich die Symptome der seAVF nicht von jenen der sdAVF. Ein wesentlicher klinischer Befund in unserer Kohorte war jedoch der relativ akute/subakute Verlauf der Symptome im Vergleich zum chronisch progressiven Verlauf der Symptome bei sdAVF.

Die Angioarchitektur der seAVF unterscheidet sich wesentlich von jener der klassischen sdAVF. Die arterielle Blutversorgung der seAVF erfolgt aus mehreren Ästen der Segmentarterien im spinalen Epiduralraum, während sie bei den sdAVF im Gegensatz über die radikulomeningealen Äste stattfindet.

Die venöse Drainage der seAVF stellt eine weitere anatomische Besonderheit dar, die zunächst über ein epidurales Konvolut und im weiteren Verlauf intradural in den perimedullären Venenplexus erfolgt.

Das arterialisierte epidurale Konvolut war bei den meisten Patienten ventral/ventrolateral lokalisiert und kann durch die ausgeprägte Anastomosenbildung des epiduralen Venenplexus im ventralen thorakolumbalen Epiduralraum erklärt werden.

Ungeachtet dessen bleibt der genaue Pathomechanismus der retrograden venösen Drainage von epi- nach intradural weitestgehend unklar. Der sogenannte Anti-Reflux-

Mechanismus des spinalen venösen Systems wurde bereits in einigen anatomischen Studien diskutiert. Insbesondere der transdurale Verlauf der Radikularvenen sollte bei diesem Mechanismus dementsprechend eine entscheidende Rolle einnehmen.
Solange dieser Anti-Reflux-Mechanismus jedoch intakt bleibt, kann eine pathologische Arterialisierung des perimedullären Venensystems bei seAVF nicht stattfinden und sie verlaufen daher asymptomatisch.
Eine intravenöse Stase und/oder akute hydrostatische Veränderungen dieser erweiterten arterialisierten epiduralen Konvolute könnten zur Entwicklung einer Venenthrombose in dem Areal führen. Dies kann wiederum in einer akuten Störung des duralen Anti-Reflux-Mechanismus und einer retrograden venösen Drainage resultieren, wodurch der häufig akute/subakute Verlauf der Symptome bei diesen Patienten erklärt werden könnte.

3.6 Antikoagulative Therapie nach chirurgischer Behandlung spinaler duraler arteriovenöser Fisteln – Analyse der Effektivität und des Langzeitverlaufs (Anlage 6)

Eine frühe postoperative neurologische Verschlechterung trotz der erfolgreichen Behandlung einer sdAVF ist ein bekanntes, wenn auch seltenes Phänomen.[16] Als Ursache hierfür wurde bisher die Bildung von Mikrothromben in den zuvor erweiterten und elongierten perimedullären Venen nach der Ausschaltung des AV-Shunts vermutet.[16, 29]

Basierend auf dieser Hypothese wurde in einigen Studien eine postoperative Antikoagulation der sdAVF-Patienten als präventive Maßnahme gegen eine mögliche frühpostoperative Verschlechterung oder sogar auch zur Beschleunigung der neurologischen Besserung empfohlen.[16] Die Effektivität und Sicherheit dieser postoperativen Antikoagulation bei sdAVF-Patienten wurden bisher jedoch nicht untersucht und waren daher unter anderem Themen dieser Studie.[39]

In unserem Zentrum wurden die Patienten nach der Präferenz des jeweiligen Operateurs entweder prophylaktisch mit niedrig dosierter Heparinisierung oder therapeutisch mit einer Ziel-PTT von 40–50 Sekunden postoperativ antikoaguliert. Infolgedessen wurde unsere Patientenkohorte in zwei Gruppen dichotomisiert.

- Gruppe A: postoperative therapeutische Heparinisierung (Ziel-PTT: 40–50 Sekunden)
- Gruppe B: routinemäßige thromboembolische Prophylaxe mit niedrig dosierter Heparinisierung

Insgesamt konnten 53 Patienten in diese Analyse eingeschlossen werden. In Gruppe A (n = 11) wurde frühpostoperativ über keine akute Verschlechterung berichtet. In Gruppe B (n = 42) entwickelten vier Patienten eine akute frühpostoperative Ver-

schlechterung. Alle vier Patienten wurden daraufhin mittels therapeutischer Heparinisierung (Ziel-PTT: 40–50 Sekunden) antikoaguliert und zeigten im weiteren stationären Verlauf eine vollständige Regredienz der postoperativ aufgetretenen neurologischen Verschlechterung.

Zwischen den beiden Gruppen war kein signifikanter Unterschied der frühpostoperativen Verschlechterungsrate nachweisbar. Des Weiteren unterschied sich der neurologische Status der beiden Gruppen zum Zeitpunkt der Aufnahme ($p = 0{,}093$), der Entlassung ($p = 0{,}723$) und der letzten Verlaufskontrolle ($p = 0{,}222$) nicht signifikant.

Unabhängig von der therapeutischen Modalität (chirurgisch/endovaskulär) kann sich der klinische postinterventionelle Verlauf variabel gestalten. Die prä- oder postoperative Gabe von Steroiden wurde bereits in mehreren Studien diskutiert und zeigte keinen ausreichenden Erfolg. In mehreren Fallberichten wurde sogar eine Verschlechterung der kongestiven Myelopathie nach einer Steroidgabe demonstriert.

Der Pathomechanismus der frühpostoperativen Verschlechterung bei sdAVF-Patienten wurde bisher nicht vollständig erforscht. Criscuolo et al. stellten die Hypothese auf, dass durch die Bauchlagerung der Patienten für die Operation eine Übertragung des erhöhten intraabdominalen und intrathorakalen Drucks auf die spinalen Venen erfolgt, wodurch die bestehende venöse Hypertension verstärkt wird und die resultierenden Symptome ebenfalls verschlechtert werden.[40] Darüber hinaus wären die hämodynamischen Veränderungen der spinalen venösen Drainage nach einem Verschluss der Drainagevene ein zusätzlicher Risikofaktor für die frühe postoperative Verschlechterung.[40]

Wären diese Hypothesen korrekt, wäre auch eine höhere Inzidenzrate der frühen postoperativen Verschlechterung erwartbar. Wir vermuten, dass noch komplexere anatomische Prädispositionen und lokale hämodynamische Veränderungen zu diesem Phänomen beitragen können. Eine verminderte arterielle Versorgung durch Vasospasmen

in den intraduralen Arterien oder der Adamkiewicz-Arterie im thorakolumbalen Bereich durch operative Manipulationen könnte sich darauf ebenfalls auswirken. Auch auf der venösen Seite kann es durch den Verschluss des AV-Shunts zu einer Stase und Thrombenbildung in den zuvor erweiterten Venen kommen. Eine intraoperative Dopplеruntersuchung dieser Venen zeigte, dass der Blutdruck in den zuvor arterialisierten Venen unmittelbar nach dem Verschluss des AV-Shunts zwar deutlich absinkt, die Venen aber dennoch nicht vollständig kollabieren.[16, 29] Es wird daher vermutet, dass diese Situation das Risiko einer Thrombenbildung zusätzlich erhöht.

Zusammengefasst stellt eine akute frühpostoperative Verschlechterung bei Patienten mit sdAVF eine klinisch relevante Komplikation dar. Sie trat bei insgesamt 7,5 % der Patienten in unserer Fallserie auf.

Obwohl die routinemäßige therapeutische Heparinisierung die Rate der frühpostoperativen Verschlechterung in unserer Kohorte nicht signifikant verringert hat, deuten unsere Ergebnisse darauf hin, dass die therapeutische Heparinisierung in Fällen einer akuten postoperativen Verschlechterung eine sichere und effiziente Behandlungsoption darstellen könnte.

3.7 Analyse des prognostischen Stellenwerts verschiedener klinischer und radiologischer Parameter auf den Langzeitverlauf von Patienten mit spinalen duralen arteriovenösen Fisteln (Anlage 7)

Der prognostische Stellenwert typischer radiologischer und klinischer Befunde bei Patienten mit sdAVF wurde in der Vergangenheit kontrovers diskutiert. Die Aussagekraft dieser Analysen bleibt jedoch durch verschiedene Störfaktoren eingeschränkt.[6, 9] Die niedrige Inzidenz dieser Erkrankung und die daraus resultierenden niedrigen Fallzahlen in den Studien stellen hierbei die größte Herausforderung dar.[6] Gleichzeitig ist die Erfassung von Daten zum Langzeitverlauf einer überwiegend älteren und oft multimorbiden Patientenpopulation mit mehreren logistischen Schwierigkeiten verbunden.[3, 9]

Ungeachtet dessen erzielten wir in dieser Studie die Erfassung aller verfügbaren demographischen, klinischen und radiologischen Befunde und untersuchten deren prognostischen Einfluss auf die funktionelle Erholung der Patienten im Langzeitverlauf.[10]

Wir analysierten retrospektiv alle Patienten in unserer Datenbank, die in unserer Einrichtung zwischen 2006 und 2016 aufgrund einer sdAVF behandelt wurden. Hierzu wurden das Alter des Patienten, der neurologische Status zum Zeitpunkt der Diagnosestellung, die Dauer der Symptome vom Beginn bis zur Diagnosestellung sowie die klinischen Befunde im Langzeitverlauf erfasst.

Sowohl das Ausmaß der medullären T2w-Hyperintensität, der intramedullären Kontrastmittelaufnahme und der Erweiterung der perimedullären Venen in der MR-Bildgebung zum Zeitpunkt der Diagnosestellung als auch die Fistellokalisation in der DSA wurden zusätzlich analysiert.

Daten für die Langzeitergebnisse lagen bei 40 Patienten mit einer mittleren Nachbeobachtungszeit von 52 Monaten vor. Das Durchschnittsalter zum Zeitpunkt der Diagnosestellung betrug 69,3 ± 9 Jahre mit einer deutlichen männlichen Dominanz (n = 32;

80 %). Die durchschnittliche Dauer der Symptome bis zur Diagnosestellung betrug 20,2 Monate.

Für diese Analyse standen präoperative MR-Bildgebungen (n = 40) und zusätzliche kontrastmittelverstärkte MRA-Untersuchungen (CE-MRA) (n = 34) zur Verfügung. Ein medulläres Ödem wurde bei 35/40 (88 %) festgestellt und erstreckte sich im Durchschnitt über 5,5 Segmente. Eine intramedulläre Kontrastmittelaufnahme wurde bei 30/40 (75 %) beobachtet und erstreckte sich im Durchschnitt über vier Segmente. Bei allen 40 Patienten wurden erweiterte perimedulläre Venen im thorakalen und/oder thorakolumbalen Bereich mit einer mittleren Ausdehnung von 7,5 Segmenten beobachtet. In der DSA befanden sich 17 sdAVF im thorakalen Bereich und 19 im thorakolumbalen Bereich. Vier weitere sdAVF befanden sich in der tiefen lumbosakralen Region.

In der aktuellen Analyse konnte kein Zusammenhang zwischen den initialen neuroradiologischen Befunden und dem klinischen Langzeitverlauf nachgewiesen werden. Es zeigte sich jedoch eine signifikante Korrelation zwischen einer kürzeren Dauer der Symptome ($\leq$ 6 Monaten) und einer Verbesserung der Symptomatik bei der letzten Verlaufskontrolle ($p < 0,05$). Alle anderen untersuchten demographischen und klinischen Parameter zeigten in dieser Hinsicht keine statistisch signifikante Korrelation.

Erstaunlicherweise unterschied sich die Dauer der Symptome in unserer aktuellen Kohorte nicht wesentlich von jener einer vorigen Kohorte unseres Zentrums aus den Jahren 1988 bis 2002 (20 vs. 19 Monate; $p = 0,533$).

Trotz der heutzutage deutlich höheren Verfügbarkeit moderner spinaler MRT-/MRA- und DSA-Untersuchungen lässt sich diese Verzögerung der Diagnosestellung am ehesten durch eine weiterhin unzureichende Erfahrung der primären behandelnden Ärzte erklären. Es sollte nach unserer Erfahrung bei jedem Patienten mit einer unkla-

ren Gangunsicherheit eine kernspintomographische Darstellung der gesamten spinalen Achse erfolgen. Bei Zeichen für intraspinale Gefäßpathologien sind weitere Gefäßdarstellungen mittels adäquater spinaler MRA oder DSA indiziert.

Zusammengefasst sind sdAVF generell durch interindividuell variable klinische Darstellungen gekennzeichnet, die die Bestimmung spezifischer prognostischer Faktoren erschweren. Unsere aktuelle Analyse verdeutlicht den Einfluss der raschen Diagnosestellung auf den Langzeitverlauf dieser Erkrankung. Trotz der technischen Entwicklungen und der deutlich höheren Verfügbarkeit der neuroradiologischen nicht-invasiven Untersuchungstechniken in den letzten Jahrzehnten erfolgt die Diagnosestellung von sdAVF jedoch weiterhin verzögert. Unsere Beobachtungen spiegeln daher am ehesten einen anhaltenden Mangel an Wissen und Erfahrung im Umgang mit dieser seltenen Krankheit in den beteiligten Fachdisziplinen wider.

4 Diskussion

4.1 Ätiologische und pathophysiologische Aspekte

Über die Jahrzehnte wurden verschiedene Theorien zur Pathogenese von sdAVF aufgestellt und intensiv diskutiert.[1, 8, 34, 40] Im Jahr 1972 berichteten Manelfe et al. im Rahmen einer anatomischen Studie von vaskulären glomerulusähnlichen Strukturen, die sich physiologischerweise zwischen zwei Schichten der spinalen Dura mater befinden.[41] Die genaue Funktion dieser glomerulusähnlichen Strukturen konnte bisher jedoch nicht ermittelt werden; es wird angenommen, dass sie möglicherweise eine regulierende Funktion haben und einen konstanten Venendruck im Rückenmark gewährleisten.[41]

Des Weiteren konnten Tadie et al. in einer histologischen Studie keine Venenklappen in den spinalen Venen nachweisen.[42] Ihre Untersuchungen zeigten jedoch eine auffällige zickzackförmige Verengung der Radikularvenen an der Stelle, an der sie die spinale Dura mater überqueren.[42] An dieser Stelle verliert die Vene ihre eigene Wand, die durch eine Arachnoidalmanschette und durch die Dura selbst ersetzt wird.[5, 42]

Basierend auf diesen Beobachtungen wurde postuliert, dass der zickzackartige Verlauf und der eigenartige Aufbau dieser Venen unter normalen physiologischen Bedingungen weitestgehend einen retrograden Blutfluss aus dem epiduralen in den intraduralen Raum verhindern.[5, 43]

In einer Kadaverstudie wurde von Thron et al. wurde der transdurale Verlauf der spinalen Venen radioangiographisch und histologisch genauer erforscht.[5] Anhand dieser Analyse konnten sie den transduralen Verlauf der Radikularvenen hauptsächlich in zwei histomorphologische Typen unterteilen: 1) der ‚Slit'-Typ in ca. 60 % der Untersuchungen und 2) der ‚Bulge/Nodular'-Typ in 35 % der Fälle. Die restlichen 5 % machten in den Untersuchungen einen Mischtyp aus den beiden o. g. Formen aus. Sowohl der

schmale (Typ 1, ‚Slit') als auch der noduläre (Typ 2, ‚Bulge/Nodular') Verlauf der Radikularvenen schienen eine retrograde Füllung von epi- nach intradural zu verhindern. Durch diese anatomischen und histologischen Beobachtungen wurde der Begriff ‚Anti-Reflux-Mechanismus der spinalen Dura mater' in der Literatur etabliert.[43] Ein Versagen dieses Anti-Reflux-Mechanismus würde eine retrograde Füllung der Radikularvenen unter bestimmten Umständen begünstigen.[5, 21] Infolgedessen kann dieser pathologische retrograde Blutfluss zur Bildung von Mikrothromben und zu weiteren umschriebenen Gefäßverschlüssen in dem betroffenen Areal führen.[16] Dies kann über entzündliche reaktive Veränderungen der Dura wie eine Angioneogenese die Entwicklung und Aufrechterhaltung einer sdAVF befördern.[4]

Wenn das Versagen des Anti-Reflux-Mechanismus der spinalen Dura mater jedoch der einzige Pathomechanismus der sdAVF wäre, wäre auch eine deutlich höhere Inzidenz erwartbar. Daher müssen auch zusätzliche Faktoren zu der Entwicklung dieser Fisteln beitragen.

Basierend auf dieser Hypothese wurde im Rahmen der kumulativen Habilitation der Einfluss von systemischen vaskulären Risikofaktoren auf die Entstehung oder Aufrechterhaltung einer sdAVF im Rahmen einer epidemiologischen Analyse erstmalig wissenschaftlich erforscht.[4] Hierfür wurden systemische vaskuläre Risikofaktoren wie arterielle Hypertonie, Diabetes mellitus, Fettstoffwechselstörungen und Nikotinabhängigkeit durch einen Vergleich der Prävalenzen dieser Risikofaktoren in einer sdAVF-Kohorte von 59 Patienten mit jenen der Allgemeinbevölkerung verglichen.[31]

Interessanterweise lag die alterskorrigierte Prävalenz der arteriellen Hypertonie in der sdAVF-Kohorte signifikant höher als jene der Allgemeinbevölkerung ($p < 0{,}001$). Die Prävalenzen der restlichen vaskulären Risikofaktoren unterschieden sich nicht von jenen der Allgemeinbevölkerung.

Eine plausible denkbare pathophysiologische Korrelation zwischen arterieller Hypertonie und sdAVF wäre aus unserer Sicht, dass ein länger bestehender arterieller Bluthochdruck zur Aufrechterhaltung und Erweiterung eines duralen AV-Shunts in der Fistelzone beitragen könnte. Diese Hypothese kann auch durch die klinische Beobachtung bekräftigt werden, da viele Patienten eine vorübergehende Verschlechterung der Symptome bei körperlicher Anstrengung wie schnellem Treppensteigen, psychischer Aufregung oder sportlichen Aktivitäten beschreiben, die normalerweise mit einem Anstieg des arteriellen Blutdrucks einhergehen.

Bei der Aufrechterhaltung des AV-Shunts verringert die resultierende venöse Hypertension den AV-Druckgradienten und reduziert somit sowohl die Blutversorgung als auch die Gewebeperfusion des Myelons, was als kongestive Myelopathie bezeichnet wird.[13] Die medulläre Autoregulation in den betroffenen Arealen wird dadurch progressiv ausgeschöpft.[29]

Es kommt im weiteren Verlauf zu einer unkontrollierten Gefäßerweiterung, die die Kapillaren erreicht und eine intraparenchymatöse Ödembildung verursacht. Schreiten diese unkontrollierten Prozesse fort, kommt es im späteren Stadium der Erkrankung zu einem irreversiblen, ischämisch nekrotisierenden Prozess im Myelon (Foix-Alajuannine-Syndrom).[40, 44]

Darüber hinaus konnten wir im Rahmen einer weiteren Studie feststellen, dass das perimedulläre Venensystem bei Patienten mit einer kürzeren Symptomdauer in der MRT-Bildgebung deutlich prominenter erscheint.[45] Diese Beobachtung wurde in der Literatur bisher nicht beschrieben. Interessanterweise zeigten diese Patienten zudem in der Langzeitanalyse ein signifikant größeres Potential zur Erholung und Rückbildung der Symptome.[45]

Die Ergebnisse unserer Studie deuten darauf hin, dass die pathophysiologischen Veränderungen des Myelons über die Zeit verschiedene Stadien durchlaufen. In der frühen Phase kommt es als Reaktion auf den erhöhten intravenösen Druck zu einer Erweiterung des perimedullären Venenplexus. In diesem Stadium der Erkrankung ist die venöse Drainage des Myelons wahrscheinlich noch erhalten und suffizient, wodurch die deutlich bessere Erholung dieser Patienten im Langzeitverlauf bei erfolgreicher Behandlung erklärt werden kann.[45] Im weiteren Verlauf der Erkrankung kann es durch die progressive venöse Hypertonie zu Gefäßverschlüssen und der Bildung von Mikrothromben kommen, die wiederum die spinale venöse Drainage irreversibel beeinträchtigen und durch die die Verschlechterung der Langzeitergebnisse bei diesen Patienten erklärt werden kann.[29]

Es konnte jedoch bisher nicht nachvollzogen werden, wann und unter welchen Umständen das medulläre Gewebe bei bestehender venöser Hypertension dekompensiert und wann die irreversiblen Schäden des Myelons auftreten.

4.2 Diagnostische Verfahren und Besonderheiten

In der Primärdiagnostik ist vor allem die spinale MRT von Bedeutung.[11, 19] Typische MRT-Befunde, die häufig gleichzeitig auftreten, sind bei sdAVF-Patienten zu beachten:

- Die betroffenen Areale des Myelons erscheinen als Ausdruck eines zentromedullären Ödems bzw. einer Mischung von Ödem und Nekrose in der T1-Wichtung leicht hypo- und in der T2-Wichtung deutlich hyperintens.[46]

- Eine irreguläre Kontrastmittelaufnahme in der T1-Wichtung kann ebenfalls häufig beobachtet werden und dient als Hinweis auf das Vorliegen einer subakuten oder chronischen Infarzierung.[11]

- Die typischerweise erweiterten und geschlängelten perimedullären Venen sind in unterschiedlicher Ausdehnung und Lokalisation in den T2-Wichtungen oftmals als Flow-Voids zu erkennen. Diese pathologisch erweiterten Venen lassen sich in der T1-Wichtung nach Kontrastmittelgabe noch deutlicher darstellen.[11]

Die endgültige Diagnose, Lokalisierung und Beschreibung der hämodynamischen Aspekte einer sdAVF bleiben jedoch eine Domäne der selektiven spinalen DSA.[19]

Dessen ungeachtet kann sich die Darstellung der Fistelzone in vielen Fällen, auch in den Händen von erfahrenen Untersuchern, als schwierig gestalten. Nicht wenige Patienten unterziehen sich mehreren spinalen DSA-Untersuchungen, bis die korrekte Diagnose einer sdAVF gestellt werden kann, was der komplexen Angioarchitektur des Rückenmarks geschuldet ist.[15, 33]

Vor allem die Erkennung einer sdAVF in der tiefen lumbosakralen Region erfordert ein exzellentes Wissen über die Blutversorgung und die venöse Drainage dieser Areale.[7] Diese Untergruppe der sdAVF wurde in der Literatur bisher nur in wenigen Fallberichten beschrieben und im Rahmen dieser kumulativen Habilitation daher durch mehrere Analysen ausführlich erforscht.

Zunächst wurden die anatomischen, neuroradiologischen und klinischen Charakteristika dieser Patientengruppe analysiert. Ein charakteristischer kernspintomographischer Befund der lumbosakralen sdAVF in unserer Kohorte war ein medulläres Ödem in Kombination mit einer Erweiterung der Filumvene oder anderer lumbaler Radikularvenen. Darüber hinaus war bei 25 % der Patienten mit einer sdAVF in der tiefen lumbosakralen Region eine bilaterale Blutversorgung der Fistelzone nachweisbar. Eine solche multiple arterielle Versorgung dieser Fisteln wurde in der Literatur bisher nicht

beschrieben. Anhand unserer Beobachtung stellt diese eine weitere Besonderheit und gleichermaßen diagnostische Herausforderung sowie ein ernsthaftes Risiko eines Therapieversagens dar. Basierend auf unseren aktuellen Ergebnissen sollten bei bestehendem Verdacht auf eine sdAVF in der lumbosakralen Region alle versorgenden Arterien der tiefen lumbosakralen Region angiographisch suffizient mit seitlichen, anterior-posterioren und schrägen Aufnahmen dargestellt werden.

In einer weiteren Analyse untersuchten wir unser Therapiemanagement und den klinischen Langzeitverlauf bei dieser Untergruppe von sdAVF separat und ebenfalls erstmalig in der Literatur. Alle Patienten mit einer lumbosakralen sdAVF wurden in unserer Klinik operativ behandelt. Bei diesen Patienten wurde in unserem Therapiealgorithmus bewusst von einer endovaskulären Therapie aufgrund der relativ häufigen komplexen arteriellen Versorgung der Fistelzone und des resultierenden erhöhten Risikos einer insuffizienten endovaskulären Ausschaltung abgesehen. Eine suffiziente Ausschaltung der sdAVF konnte bei 95 % der Fälle erreicht werden, wodurch die Effizienz unserer neurochirurgischen Versorgung dieser Fistel bestätigt werden konnte.

Interessanterweise unterscheidet sich der postoperative Verlauf dieser Patienten nicht wesentlich von jenem der Patienten mit den häufigeren thorakolumbalen sdAVF. Dies ist am ehesten durch den ähnlichen Pathomechanismus dieser Fisteln, die kongestive Myelopathie, zu erklären.

Da diese Untergruppe von sdAVF in der Literatur lediglich in wenigen Fallbeispielen beschrieben wurde, war ein Vergleich mit einer ähnlich großen endovaskulär behandelten Patientengruppe leider nicht möglich.

Darüber hinaus stellen die seAVF weitere klinische und therapeutische Herausforde-

rungen dar und wurden in der Literatur ebenfalls nur selten beschrieben. Die klinischen, anatomischen und neuroradiologischen Aspekte der seAVF wurden im Rahmen dieser Habilitationsschrift ausführlich analysiert.[21]

Eine kongestive Myelopathie mit einem akuten/subakuten klinischen Verlauf war in unserer Kohorte der dominierende Befund bei seAVF. Im Gegensatz zur klassischen sdAVF wurden prominente arterialisierte perimedulläre Venen nur bei wenigen seAVF festgestellt. Die initiale MRA-Bildgebung zeigte dahingegen bei 90 % dieser Patienten ein langstreckiges arterialisiertes epidurales Konvolut, das meist intraspinal ventrolateral lokalisiert war. Spinale DSA-Aufnahmen bestätigten die multisegmentale Ausdehnung dieses arterialisierten epiduralen Konvoluts bei diesen Patienten, das als eine Fistelzone angesehen werden kann. Des Weiteren war die intradurale drainierende Radikularvene bei 23 % der Patienten mit einer deutlichen Entfernung vom ursprünglichen Fistelpunkt lokalisiert. Aufgrund dieser komplexen Anatomie und der häufigen langstreckigen Ausdehnung des venösen Konvoluts sehen wir eine operative Versorgung dieser Patienten als effiziente Modalität.

Wir konnten hier ebenfalls keine vergleichbaren Studien über seAVF in der Literatur finden, sodass unsere aktuellen Daten als Grundlage für zukünftige Analysen, aber auch als Referenz bei der diagnostischen und therapeutischen Planung dieser Entität dienen können.

Neben dem MRT und der DSA sind moderne Untersuchungstechniken wie die spinale kontrastverstärkte MR-Angiographie (CE-MRA) und die angiographische Computertomographie (Dyna-CT) im Rahmen der spinalen Angiographie hervorragende diagnostische Mittel in der neuroradiologischen Darstellung spinaler Gefäßmalformationen, die bei unseren Patienten standardmäßig durchgeführt wurden.[11, 47]

Am Beginn des Jahrhunderts wurde die CE-MR entwickelt.[11, 48] Diese zeitlich und

räumlich hochaufgelöste MR-Angiographie-Technik ermöglichte die exzellente nicht-invasive Darstellung der spinalen Gefäße sowie die Identifizierung und Lokalisierung eines AV-Shunts mit hoher Sicherheit. Mull et al. veröffentlichten im Jahr 2007 eine Serie mit 19 Patienten mit einem klinisch kernspintomographischen Verdacht auf eine sdAVF.[11] Bei all diesen Patienten wurde vor der spinalen Angiographie eine CE-MRA durchgeführt. In 14 Fällen ließ sich die sdAVF anhand der CE-MRA erkennen und präzise lokalisieren. In nur fünf Fällen kam es zu einer Differenz bezüglich der Höhe um ein Segment. Diese Technik wurde in den folgenden Jahren deutlich verfeinert und gehört in den Referenzzentren inzwischen zur nicht-invasiven Standarddiagnostik bei spinalen Gefäßmalformationen.[49]

Die genaue Identifizierung und Lokalisation des Fistelpunkts in der spinalen Angiographie erfolgt in der Regel anhand eines deutlichen Kalibersprungs von der kleinkalibrigen Arterie in die dickere Vene.[19, 46] Im Rahmen der Angiographie kam in den letzten Jahren häufiger eine Dyna-CT zur Anwendung, die eine exzellente Visualisierung der Gefäße in Bezug auf die knöchernen Strukturen bietet und daher in unserem diagnostischen Algorithmus etabliert wurde.[47] Die Darstellung der benachbarten knöchernen Strukturen bietet dem Operateur eine exzellente Möglichkeit, um die Fistelzone intraoperativ lokalisieren zu können. Der Stellenwert dieser Technik wird im Rahmen weiterer Analysen noch erforscht, insbesondere im Hinblick auf die begleitende Strahlenbelastung und die mögliche Analyse der dynamischen Aspekte einer spinalen Gefäßmalformation.

4.3 Therapeutische Modalitäten

Das Ziel der Behandlung einer sdAVF sollte die Unterbindung des AV-Shunts an der Fistelzone sein, um eine Reduktion der venösen Hypertension des Myelons zu erreichen.[6, 26]

Bei der Behandlung der sdAVF haben sich über die letzten Jahrzehnte zwei Therapiemöglichkeiten etabliert: a) ein chirurgischer Verschluss des proximalen Abschnitts der Drainagevene mittels Clipping oder bipolarer Koagulation oder b) eine endovaskuläre Embolisation im Rahmen superselektiver (Mikro-)Katheterisierung der versorgenden radikulomeningealen Arterie.[9]

In unserer Kohorte erhielten alle Patienten eine chirurgische Behandlung und die Verschlussrate lag bei 98 %.[39] Während die intraoperative Dopplersonographie in den 90er Jahren und noch zu Beginn des 21. Jahrhunderts zur Erkennung der arterialisierten Venen verwendet wurde, wird die ICG-Videoangiographie seit 2015 standardmäßig bei allen Patienten verwendet.[7, 50]

Bei der operativen Behandlung von spinalen Gefäßmalformationen, insbesondere von sdAVF und seAVF, ermöglicht diese Technik eine suffiziente intraoperative Echtzeitdarstellung der Gefäße, des Blutflusses und der Gewebeperfusion der untersuchten Areale.[47] Sie bietet zudem eine unmittelbare, noch intraoperative Kontrolle des Behandlungserfolgs.[32]

Die ersten operativen Therapieversuche zielten auf eine komplette Resektion sämtlicher erweiterter perimedullärer Gefäße ab, was in der Mehrzahl der Fälle zu einer erheblichen irreversiblen Schädigung des Myelons führte.[50, 51] Anhand der Ergebnisse von anatomisch-histologischen Untersuchungen in den 1970ern und 1980ern wurde zunehmend klar, dass bereits eine Okklusion der Drainagevene mit/ohne Koagulation der Fistelzone eine suffiziente Behandlung darstellt.[34, 50, 52]

In Fallserien über operativ behandelte sdAVF wurde über eine Verschlussrate der Fisteln von 95 % mit relativ wenigen perioperativen Komplikationen berichtet.[6, 9] Die Operationsverfahren bei sdAVF haben von der über die letzten Jahrzehnte fortschreitenden technischen Entwicklung der neurochirurgischen Operationen deutlich profitiert.[39]

In den 1980ern und frühen 1990ern war eine multisegmentale Laminektomie ein Standardverfahren bei der operativen Behandlung einer sdAVF.[50] Durch die weitere Entwicklung und Einführung moderner Techniken in der neuroradiologischen Diagnostik und die daraus resultierende optimale Darstellung der Fistelzone und der Drainagevene ist heutzutage in der Regel eine unisegmentale Hemilaminektomie über der Fistelzone als operativer Zugangsweg in den meisten Fällen völlig ausreichend.[39]

Die erste endovaskuläre Embolisation einer sdAVF wurde von Doppman et al. im Jahr 1968 beschrieben.[19, 53] Aufgrund der geringen Invasivität und der Möglichkeit, die Embolisation der sdAVF im Rahmen der diagnostischen DSA durchzuführen, etablierte sich die endovaskuläre Therapie zunehmend in den 1980ern und 1990ern.[54–56] Bereits in den ersten Fallserien mit endovaskulär behandelten Patienten wurde jedoch von einer deutlich höheren Rezidivrate im Vergleich mit den chirurgisch behandelten Fällen berichtet.[9] Trotz der Verwendung moderner Embolisate wie Isobutyl- und N-Butylcyanoacrylat oder Onyx in den letzten Jahren blieb diese weiterhin relativ hoch.[57] Auch kombinierte endovaskulär-neurochirurgische Therapiekonzepte wurden diskutiert.[53] Bei diesem Therapiekonzept erhalten die Patienten bereits während der diagnostischen Angiographie, wenn eine sdAVF dargestellt wird, einen endovaskulären Therapieversuch.[58] Beim Versagen der endovaskulären Behandlung werden die Patienten chirurgisch behandelt, ohne weitere Embolisationsversuche durchzuführen. Die Rezidivraten solcher Therapiekonzepte lagen jedoch im Vergleich zu der rein chirurgischen Behandlung ebenfalls deutlich höher.[6, 58]

Unabhängig von der Behandlungsmodalität ist eine frühpostoperative Verschlechterung trotz adäquater Okklusion der sdAVF ein bekanntes und bisher ungeklärtes Phänomen.[16] Eine frühpostoperative Verschlechterung trat bei insgesamt 7,5 % der Patienten in unserer Fallserie auf.[39]

Als Ursache hierfür wird in der Literatur vermutet, dass es durch den Verschluss der AV-Fistel und der dadurch abrupt eintretenden hämodynamischen Veränderungen im intraspinalen venösen System zu einer Thrombenbildung in den perimedullären Venen kommen könnte.[29] Basierend auf dieser Vermutung wurde in vielen Zentren in den letzten Jahrzehnten eine postoperative Heparinisierung dieser Patienten routinemäßig durchgeführt.

Die Effektivität und Sicherheit der frühpostoperativen Heparinisierung bei operativ behandelten sdAVF-Patienten wurde in der Literatur bisher noch nicht untersucht und war der Gegenstand einer Analyse im Rahmen dieser kumulativen Habilitation.

In unserem Patientengut wurde nach der Präferenz des jeweiligen Operateurs entweder prophylaktisch mit niedrig dosierter Heparinisierung oder therapeutisch mit einer Ziel-PTT von 40–50 Sekunden postoperativ antikoaguliert. Dadurch gelang es, den möglichen Effekt der therapeutischen Heparinisierung gegenüber der routinemäßigen thromboembolischen Prophylaxe bei diesen Patienten zu untersuchen. Unsere Ergebnisse zeigten keinen signifikanten Unterschied der frühpostoperativen Verschlechterungsrate bei beiden Gruppen. Des Weiteren unterschied sich der neurologische Status der beiden Gruppen zum Zeitpunkt der Entlassung ($p = 0,723$) und der letzten Verlaufskontrolle in der Langzeitanalyse ($p = 0,222$) nicht signifikant.

Es ist jedoch anzumerken, dass eine rasche Erholung bei Patienten mit einer frühpostoperativen Verschlechterung nach dem Ansetzen der therapeutischen Heparinisierung beobachtet wurde. Auch wenn die routinemäßige Heparinisierung keinen Einfluss auf die funktionelle Erholung im Langzeitverlauf zeigte, bietet diese im Fall einer frühpostoperativen Verschlechterung jedoch eine effektive Behandlungsoption und ist anhand unserer Daten einzusetzen. Da diese Fragestellung in der Literatur bisher nicht bearbeitet wurde, kann unsere Analyse als Grundlage für weitere anatomische und mög-

licherweise auch prospektive Studien dienen, um diese bisher ungeklärten Phänomene besser zu verstehen und die Therapiekonzepte in den verschiedenen Zentren zu optimieren.

4.4 Klinische und radiologische Prädiktoren für den Langzeitverlauf

Aufgrund der insgesamt unspezifischen Symptomatik und der niedrigen Inzidenz der sdAVF ist bisher nur wenig über mögliche prädikative Faktoren für den Langzeitverlauf nach dem Abschluss der Therapie bekannt.[6] Zahlreiche Faktoren wurden in der Literatur kontrovers diskutiert, ohne dass ein Konsens gefunden werden konnte.[3, 9, 59]

Wir analysierten unsere Datenbank sowohl im Hinblick auf den prädikativen Stellenwert verschiedener epidemiologischer und klinischer Aspekte als auch auf MRT- und DSA-Befunde.[10] Die Ausdehnung der medullären Veränderungen in den MRT-Aufnahmen wie bei einem Ödem und einer Kontrastmittelaufnahme sowie das Ausmaß der Erweiterung der perimedullären Venen wurden ausgewertet. Des Weiteren evaluierten wir den Einfluss des Patientenalters, der neurologischen Befunde sowie der Symptomdauer bei allen Patienten.

Bei einer mittleren Nachbeobachtungszeit von 52 Monaten korrelierte bei 40 Patienten eine kürzere Symptomdauer (≤ 6 Monate) als einziges statistisch signifikantes Ergebnis mit einer besseren Prognose. Alle weiteren untersuchten klinischen Befunde zeigten interessanterweise keinen Einfluss auf den Langzeitverlauf.

Unabhängig von der Therapieoption ist der prognostische Einfluss der initialen neuroradiologischen Befunde auf den klinischen Langzeitverlauf bei Patienten mit sdAVF weiterhin umstritten.[9, 60, 61] Hetts et al. beobachteten bei einer Kohorte von 31 Patienten eine positive Korrelation zwischen der frühen funktionellen Erholung nach der Behandlung und dem Ausmaß der erweiterten perimedullären Venen zum Zeitpunkt der

Diagnosestellung.[62] In einer anderen Kohorte von 65 Patienten von Cenzato et al. war eine lumbale Lokalisation der sdAVF mit einem deutlich geringeren Erholungspotential assoziiert.[63] Im Gegensatz dazu berichteten Dhandapani et al. bei 22 mikrochirurgisch behandelten Patienten über eine höhere Verbesserungsrate bei Patienten mit sdAVF unterhalb von Th9 innerhalb einer mittleren Nachbeobachtungszeit von sieben Monaten.[61]

Im Gegensatz zu diesen Studien zeigte unsere aktuelle Analyse keine Korrelation zwischen den initialen neuroradiologischen Befunden und dem klinischen Langzeitverlauf. Zusammengefasst heben unsere Ergebnisse die Notwendigkeit einer rascheren Diagnosestellung einer sdAVF hervor. Trotz mehrerer auswärtiger aufwendiger spinaler MRT- und DSA-Untersuchungen blieb die sdAVF bei vielen Patienten in unserer Kohorte lange Zeit unerkannt. Bei der heutzutage hohen Verfügbarkeit moderner diagnostischer Mittel ist diese Verzögerung der Diagnose am ehesten auf einen Mangel an Wissen über diese Erkrankung unter den Ärzten der beteiligten Disziplinen zurückzuführen. Um solche klinisch relevanten Verzögerungen zu vermeiden, sollte aus unserer Erfahrung bei jeder unspezifischen Symptomatik der unteren Extremitäten oder Gangataxie mit ungeklärter Genese eine MRT-Untersuchung der gesamten spinalen Achse veranlasst werden. Beim Nachweis medullärer Veränderungen oder ungewöhnlicher Gefäßerweiterung sind hier weitere Gefäßdarstellungen mittels spinaler CE-MRA oder DSA obligatorisch. Eine adäquate Diagnose und ein rascher Therapiebeginn bieten den Patienten die besten prognostischen Aussichten.

5 Zusammenfassung

Trotz der technischen Fortschritte in den letzten Jahrzehnten gelten die spinalen Gefäßmalformationen weiterhin sowohl diagnostisch als auch therapeutisch als komplexe Pathologien. Es wurden zwar verschiedene Theorien zur Pathogenese dieser AV-Malformationen aufgestellt, eine ausreichende Erklärung des Entstehungsmechanismus blieb bisher jedoch aus.

Basierend auf der Annahme, dass die Erkrankung eine erworbene vaskuläre Pathologie ist, wurden im Rahmen dieser kumulativen Habilitation erstmalig in der Literatur die häufigsten vaskulären Risikofaktoren in einer großen Fallserie statistisch epidemiologisch untersucht. Interessanterweise zeigten unsere Daten, dass Patienten mit einer sdAVF signifikant häufiger als die Gesamtbevölkerung an einer therapiebedürftigen arteriellen Hypertonie leiden. Aufgrund unserer Analyse nehmen wir an, dass die arterielle Hypertonie als ein begünstigender Faktor in der Pathogenese der sdAVF angesehen werden kann. Diese Korrelation zwischen sdAVF und arterieller Hypertonie erklärt zudem einige bisher nur unvollständig geklärte klinische Phänomene. Dabei handelt es sich um die Fragen, warum sdAVF fast ausschließlich bei Patienten im mittleren bis fortgeschrittenen Alter (50–60 Jahre) auftreten und warum die Symptome der unbehandelten sdAVF-Patienten bei körperlicher Anstrengung wie psychischer Aufregung oder sportlichen Aktivitäten akut zunehmen. Andererseits stellt unsere Hypothese sicherlich einen Anreiz für weitere histologische und anatomische Studien der bisher wenig erforschten spinalen Dura und spinalen vaskulären Anatomie dar.

Darüber hinaus ist ein fundiertes Wissen über die vaskuläre Anatomie des Rückenmarks, deren Varianten und pathologische Prozesse eine obligatorische Voraussetzung für ein suffizientes diagnostisch-therapeutisches Konzept.

Im Rahmen dieser kumulativen Habilitation wurden erstmalig klinische, angiomorphologische sowie auch neurochirurgische Aspekte seltener Untergruppen der spinalen AV-Fisteln ausführlich erforscht.

Sowohl die klinisch-bildmorphologischen Besonderheiten als auch die Therapieoptionen und der Langzeitverlauf von neurochirurgisch behandelten Patienten mit einer sdAVF in der tiefen lumbosakralen Region wurden in mehreren Analysen bearbeitet. Unsere Daten zeigten, dass die venöse Drainage dieser Fisteln sowohl über eine Radikularvene als auch über die Vene des Filum terminale erfolgen. Der AV-Shunt in diesen Fisteln zeigt einen besonderen Low-Flow-Charakter.

Unsere Analysen ergaben zudem, dass sdAVF in der tiefen lumbosakralen Region durch eine relativ häufige multiarterielle/bilaterale Versorgung im Vergleich zu den häufigeren sdAVF in der thorakolumbalen Region gekennzeichnet sind. Einen weiteren Unterschied stellt die Lokalisation der Fistelzone dar, die sich bei diesen sdAVF im Gegensatz zu den thorakolumbalen Fisteln, wo die Fistelzone fast ausschließlich auf der dorsalen Seite der Nervenwurzel lokalisiert ist, häufig im vorderen Bereich einer Nervenwurzel befindet. Alle diese anatomischen, bisher nicht beschriebenen Besonderheiten sollten sowohl während der spinalen diagnostischen Angiographie als auch der operativen Behandlung berücksichtigt werden.

Ein weiterer Bestandteil dieser kumulativen Habilitation waren die bisher in der Literatur selten beschriebenen seAVF. Die Fistelzone befindet sich bei den seAVF im epiduralen Raum und durch bisher ungeklärten Prozesse kommt es im Lauf der Zeit zu einer Arterialisierung der intraduralen Venen über die retrograde Füllung einer Radikularvene. In unserer Datenbank konnten wir eine komplexe und oftmals variable Angiomorphologie dieser Fisteln feststellen. Der Aufbau des AV-Shunts variiert hier von einer umschriebenen epiduralen Fistelzone bis hin zu einem komplexen über mehrere Segmente ausgedehnten arterialisierten Gefäßkonvolut. Des Weiteren konnten wir

nachweisen, dass die arterielle Versorgung dieses arterialisierten epiduralen Gefäßkonvoluts über mehrere Segmentarterien erfolgen kann. Unsere Analyse zeigte zudem, dass die Drainagevene bei diesen Fisteln in einer Distanz von mehreren Segmenten von der eigentlichen epiduralen Fistelzone lokalisiert werden kann. Diese Erkenntnisse beeinflussen die Therapieentscheidung fundamental.

Basierend auf unseren anatomischen Beobachtungen in diesem Patientengut ist eine operative Versorgung dieser Fisteln zu bevorzugen. Eine endovaskuläre Versorgung ist aufgrund der angiomorphologischen Komplexität dieser Fisteln mit einem deutlich erhöhten Risiko eines Rezidivs verbunden, sodass wir aufgrund unserer Analyse von einer primären Embolisation der Läsion abraten.

Des Weiteren wurden im Rahmen der Habilitation mehrere Analysen hinsichtlich des postoperativen Langzeitverlaufs durchgeführt. In erster Linie wurde der Einfluss der frühen postoperativen Heparinisierung auf den Langzeitverlauf erstmalig in der Literatur analysiert. Unsere Daten zeigten zwar keinen signifikanten Einfluss der Heparinisierung, wir konnten jedoch eine deutliche Erholung bei Patienten registrieren, die eine frühe postoperative Verschlechterung der Symptome erlitten hatten.

Das Phänomen der postoperativen Verschlechterung trotz suffizienter Okklusion einer sdAVF wurde in der Literatur nur selten beschrieben. Wir vermuten, dass es in Folge der operativen Ausschaltung einer sdAVF und des daraus resultierenden abrupten Stopps des arteriellen Blutflusses in die perimedullären Venen zur Bildung von Mikrothromben in diesem Venensystem kommt. Diese Mikrothromben können wiederum weitere Gefäßverschlüsse verursachen und die venöse Drainage des Rückenmarks negativ beeinflussen. Durch die von uns registrierte Besserung der Symptome nach einem Ansetzen der Heparinisierung bei diesen Patienten kann diese Hypothese bekräftigt werden.

Basierend auf diesen Ergebnissen ist eine routinemäßige Heparinisierung nach der Ausschaltung einer sdAVF nicht sinnvoll. Sollte es jedoch postoperativ zu einer akuten Verschlechterung der Symptome kommen, ist eine Heparinisierung der betroffenen Patienten indiziert, bis sich die neu aufgetretenen Symptome gebessert haben.

Des Weiteren wurden im Rahmen dieser Habilitation die Langzeitergebnisse sowie der Einfluss unterschiedlicher klinischer und bildmorphologischer Parameter auf den gesamten postoperativen Langzeitverlauf untersucht. Unsere Analyse zeigte, dass eine längere Symptomdauer mit einem deutlich schlechteren funktionellen Status zum Zeitpunkt der Analyse assoziiert ist. Bedauerlicherweise konnten wir auch feststellen, dass sich die Symptomdauer bei Patienten mit sdAVF über die letzten drei Jahrzehnte trotz der enormen Entwicklung der diagnostischen Verfahren in demselben Zeitraum nicht verkürzt hat. Diese Beobachtung spiegelt möglicherweise einen weiterhin bestehenden Mangel an Kenntnissen über diese Pathologien in den behandelnden Disziplinen wider.

Es ist grundsätzlich zu beachten, dass mittels einer MRT-Untersuchung im Rahmen der Abklärung einer Gangataxie mit ungeklärter Ursache die gesamte spinale Achse abgebildet werden muss, um alle möglichen strukturellen Veränderungen zu erfassen. Typische kernspintomographische Veränderungen bei einer vaskulären Pathologie der spinalen Achse sind erweiterte intradurale Gefäße sowie ein medulläres Ödem mit oder ohne Kontrastmittelaufnahme. Bei solchen Veränderungen sollte unbedingt eine erweiterte Gefäßdarstellung der spinalen Achse veranlasst werden.

In dieser Hinsicht liefern modernste Techniken wie die spinale zeitaufgelöste dynamische Kernspinangiographie (z. B. TWIST-MR-Angiographie) oder weitere spezielle bildgebende Verfahren im Rahmen der spinalen DSA (z. B. Dyna-CT) zudem exzellente diagnostische Ergebnisse.

Durch eine frühzeitige Diagnosestellung und adäquate Therapie kann die chronisch progressive Schädigung des Rückenmarks bei den betroffenen Patienten verhindert oder zumindest reduziert werden. Bei der Therapieplanung ist die Erfahrung der beteiligten neuroradiologischen und neurochirurgischen Fachdisziplinen in der Behandlung dieser Art von Gefäßmalformationen ausschlaggebend.

Das Ziel weiterer wissenschaftlicher Arbeiten sollte unter anderem darin bestehen, die bisher wenig studierte venöse Drainage des Rückenmarks genauer zu untersuchen. Des Weiteren sollten die aus einer pathologischen AV-Kurzschlussbildung resultierenden pathophysiologischen Prozesse sowohl histopathologisch als auch bildmorphologisch intensiver erforscht werden.

Dies alles könnte die bisher lange Symptomdauer bis zur korrekten Diagnosestellung einer sdAVF wesentlich verkürzen, die Therapieplanung deutlich verbessern und somit das Risiko einer irreversiblen Schädigung des Rückenmarks reduzieren, wodurch in erster Linie das Leiden der betroffenen Patienten gelindert werden könnte.

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Anlagen
08.01. Anlage 1

ORIGINAL ARTICLE

Arterial Hypertension Is Associated with Symptomatic Spinal Dural Arteriovenous Fistulas

Fidaa Jablawi, Omid Nikoubashman, Michael Mull

OBJECTIVE: **To determine possible systemic factors that may induce or be associated with the pathogenesis and pathologic course of spinal dural arteriovenous fistulas (SDAVFs), the most common type of arteriovenous disorder of the spinal cord and its meninges.**

METHODS: **We assessed the role of possible systemic (vascular) risk factors (arterial hypertension, diabetes mellitus, fat metabolism disorders, and nicotine dependence) by comparing the prevalence of these risk factors in an SDAVF cohort of 59 patients with the prevalence in the general population.**

RESULTS: **Age-corrected prevalence of arterial hypertension in the SDAVF cohort was significantly higher than in the general population ($P < 0.001$). Prevalence of diabetes mellitus ($P = 0.150$.), nicotine dependence ($P = 0.561$), adiposity ($P = 0.217$), and fat metabolism disorders ($P = 0.125$) did not differ from prevalence of comparable cohorts in the general population.**

CONCLUSIONS: **Our results and data from the literature suggest that arterial hypertension may play an important role in the development of SDAVF-related symptoms or the development of SDAVFs in the presence of other predisposing factors.**

INTRODUCTION

Spinal dural arteriovenous fistulas (SDAVFs) are the most common type of arteriovenous (AV) disorder involving the spinal cord and its meninges and account for 70% of all spinal AV shunts.[1,2] Clinical and radiologic characteristics of SDAVFs and treatment strategies have been the subject of various studies in the last 2 decades.[1,3] Nonetheless, the pathophysiology, in particular, the etiology, of SDAVFs is not yet fully understood.[4-10] It is currently assumed that SDAVFs are acquired lesions.[3] However, clinical factors that may induce or be associated with SDAVFs are currently unknown. The purpose of our study is to determine possible systemic factors that may induce or be associated with the pathogenesis and the pathologic course of SDAVFs.

MATERIALS AND METHODS

After obtaining permission from the local ethics board, we retrospectively searched our medical database for all patients who underwent spinal digital subtraction angiography in our institution between 2006 and 2016 and identified 59 consecutive patients with angiographically verified SDAVFs. The initial diagnosis of SDAVF was based on clinical and radiologic criteria that comprised 1) clinical sequelae of myelopathy resulting in motor or sensory disturbances with or without vegetative bladder/bowel dysfunctions and 2) magnetic resonance imaging findings of congestive myelopathy of the spinal cord and/or visibly engorged perimedullary veins. All suspected cases of SDAVF were verified by digital subtraction angiography. All clinical data, including demographics, clinical and neurologic presentation, comorbidities, and premedication, and radiologic data were assessed by the primary treating physicians and reevaluated for this study. To assess the role of possible systemic (vascular) risk factors, we compared the prevalence of cardiovascular diseases, including arterial hypertension, diabetes mellitus, fat metabolism disorders, and nicotine dependence, in our SDAVF cohort with the comparable prevalence in the general population in Germany. The investigated risk factors were defined according to respective societies.[11,12]

Key words
- Arterial hypertension
- Congestive myelopathy
- Risk factors
- Spinal arteriovenous malformation

Abbreviations and Acronyms
AV: Arteriovenous
SDAVF: Spinal dural arteriovenous fistula

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Table 1. Vascular Risk Factors of Patients with Spinal Dural Arteriovenous Fistula

Risk Factor	Cohort	Age Group (Years) 50–59		60–69		70–79		>80	
Hypertension	General population	20%	$P < 0.001$*	25%	$P < 0.001$*	31%	$P < 0.001$*	32%	$P = 0.003$*
	SDAVF	64%		80%		76%		86%	
Diabetes mellitus	General population	7%	$P = 0.96$	14%	$P = 0.627$	19%		21%	$P = 0.173$
	SDAVF	7%		10%		6%		0%	
Adiposity	General population	18%	$P = 0.325$	21%	$P = 0.114$	20%	$P = 0.797$	16%	$P = 0.869$
	SDAVF	27%		35%		22%		14%	
Nicotine dependence	General population	24%	$P = 0.672$	14%	$P = 0.481$	7%	$P = 0.416$	3%	$P = 0.621$
	SDAVF	27%		20%		11%		0%	
Fat metabolism disorders	General population	35%	$P = 0.291$	48%	$P = 0.038$*	53%	$P = 0.141$	38%	$P = 0.012$*
	SDAVF	27%		25%		39%		86%	

Age-corrected prevalence of clinical (vascular) risk factors (50–59 years, $n = 14$; 60–69 years, $n = 20$; 70–79 years, $n = 17$; >80 years, $n = 7$). One 36-year-old patient with adiposity was excluded from this analysis to ensure comparability with the literature. *P* values were calculated with the original data provided by the Robert Koch Institute Department of Epidemiology and Health Monitoring.[11,12]

SDAVF, spinal dural arteriovenous fistula.

*Significant *P* value.

Statistical Analysis

We compared the prevalence of possible risk factors in our cohort and the general population using the Pearson χ^2 and Fisher exact tests depending on data distribution. *P* values ≤ 0.05 were defined as significant. All statistical analyses were performed with IBM SPSS Statistics for Windows Version 23 (IBM Corp., Armonk, New York, USA).

RESULTS

Mean age of all patients ($N = 59$) was 66.86 years ± 10.38 (median, 68 years; range, 36–85 years). There were 45 male patients (77%). All patients presented with various combinations of progressive neurologic deficits. There were 43 (69%) patients with paraparesis, 28 (47%) patients with ataxia, 26 (44%) patients with sensory disturbance, and 12 (20%) patients with bladder/bowel dysfunction. The average symptom duration before diagnosis was 20 months ± 23 (median, 12 months; range, 1–120 months). Fistula locations ranged from Co to S3. Most SDAVFs were located in the thoracolumbar region ($n = 31$).

Vascular risk factors in our cohort and the general population are compared in Table 1. The age-corrected prevalence of arterial hypertension in our cohort was consistently significantly higher than in the general population ($P < 0.001$).[12] The prevalence of diabetes mellitus ($P \geq 0.173$), nicotine dependence ($P \geq 0.416$), and adiposity ($P > 0.114$) did not differ from the prevalence of comparable cohorts in the general population, whereas the prevalence of fat metabolism disorders correlated inconsistently with prevalence in the general population ($P = 0.012$–0.291).[11,12]

DISCUSSION

The first studies dealing with SDAVFs were published by Kendall and Logue in 1977 and Merland et al. in 1980.[13] Although SDAVFs are the most common type of AV disorders of the spinal cord and its meninges, little is known about their etiology.[1,13] In contrast to SDAVFs, various theories about the natural history of intracranial dural AV fistulas have been established.[14-16] The presence of microscopic dural communications between arteries and veins at the proximity of cranial venous sinuses has been previously described in the literature.[17,18] It was hypothesized that venous sinus thrombosis with associated intravenous hypertension and venous outflow obstruction might initiate the opening of these channels and form AV shunts into the venous sinuses.[14,19] An additional angiogenesis, as a part of the inflammatory process that organizes and recanalizes the thrombosed sinuses, was considered to influence the progression of these fistulas.[19] Concerning SDAVFs, Merland et al.[20] assumed that an insufficient venous outlet of the spinal cord induced the development of these fistulas and their clinical symptoms.

It has been hypothesized that once a fistula is present, the progressive fibrosis or thrombosis of radicular venous outlets could reinforce the medullar venous hypertension due to a decreased venous drainage.[20,21] However, the relationship between an AV fistula of the spinal dura and meningeal venous thrombosis has never been proven.[13,14] In the past, the pathophysiologic focus in most publications dealing with SDAVFs has been on local changes.[5,6,22] It is generally assumed that anatomic predispositions and local hemodynamic changes favor the development of SDAVFs.[8] Accordingly, we hypothesized that systemic diseases that affect the vascular system may be associated with

the development of SDAVFs. In our study, the most common finding in patients with SDAVFs was a co-occurrence of arterial hypertension. The age-corrected prevalence of arterial hypertension in our cohort was consistently significantly higher than in the general population (Table 1), supporting the hypothesis that systemic diseases may be associated with SDAVFs.[11,12] The simplest conceivable pathophysiologic correlation between arterial hypertension and SDAVFs would be that chronic arterial hypertension, in the presence of other predisposing factors, opens or maintains preexisting AV dural shunts. Supporting this hypothesis, in an intraoperative study of 9 patients with SDAVFs, Hassler et al.[5] registered a markedly increased circumscribed venous pressure (60%–87.5% of the mean systemic arterial blood pressure) in arterialized draining veins. The mean venous pressure in the dural AV fistulas was increased to 74% of the systemic arterial pressure, and it increased concomitantly with the elevated arterial pressure. According to the authors, this concomitant increase of venous pressure with arterial pressure may explain the typical clinical deterioration that patients experience during physical activity.

According to the same rationale, it may be possible that asymptomatic preexisting SDAVFs become symptomatic in the presence of arterial hypertension. Asymptomatic SDAVFs have been rarely reported in the literature. In our series, we found one 52-year-old patient with an incidental SDAVF in the upper thoracic region. Sato et al.[21] reported 2 patients with asymptomatic SDAVFs. In contrast to symptomatic SDAVFs, in all 3 asymptomatic fistulas, there was no medullary edema on magnetic resonance imaging despite the existence of dilated perimedullary veins. The average age of these 3 asymptomatic patients was approximately 10 years younger than the age of symptomatic patients in the respective series. Although the sample size is too small to draw definite conclusions, these findings may imply that SDAVFs may be asymptomatic initially and that progressive venous hypertension and subsequent medullary congestion induce clinical symptoms over time.

Data in the literature also support a more complex hypothesis concerning the relationship between arterial hypertension and SDAVFs. It could be possible that chronic arterial hypertension favors the development of SDAVFs. In a cadaveric study that did not address SDAVFs, Tadie et al.[4] observed glomus-like elements at the passage point of the radicular vein through the dura mater. Tadie et al.[4] considered these glomus-like elements as initial stages of AV fistulas and hypothesized that these elements could become manifest fistulas in the presence of chronic venous hypertension. In another cadaveric study whose focus was not SDAVFs, Thron et al.[8] distinguished between a narrow slit type and spongy-like nodular type of the transdural course of radicular veins. This theory is supported by cadaveric studies reported by other authors, which showed that physiologic vessel walls of intradural veins were thinned and replaced by a layer of arachnoid and dural tissue.[8,13,23,24] Although hypothetical, it is conceivable that the combination of 1) spongy-like nodular radicular veins, 2) thinned transdural vessel walls, and 3) arterial hypertension might favor the development of AV shunts. An associated venous outflow disorder could reinforce this pathophysiologic condition.

Given that most patients who have arterial hypertension do not develop an SDAVF, it is unlikely that arterial hypertension is the only cause of SDAVFs. Rather, it is conceivable that arterial hypertension is a cofactor that might aggravate SDAVF-related symptoms or that favors the development of SDAVFs in the presence of other predisposing factors. In the end, one must bear in mind that the discussion of the etiology of SDAVFs is highly speculative, as hypotheses concerning the etiology of SDAVF are usually based on physiologic studies, especially considering that histopathologic studies of SDAVFs are still lacking. Nevertheless, our results and data from the literature suggest that arterial hypertension may influence SDAVF-related symptoms or favor the development of SDAVFs in the presence of other predisposing factors.

Limitations

Two major limitations of our study are the relatively small sample size without an adequate control cohort and the retrospective approach, both of which provoke speculative interpretation of our data to some extent. Nevertheless, our comparison with the general population may serve as a first cornerstone for future histologic studies, particularly considering there are very few data concerning this topic in the literature.

CONCLUSIONS

Our results and data from the literature suggest that arterial hypertension may contribute to the development of SDAVF and/or its related symptoms in the presence of other predisposing factors. We hypothesize that a combination of 1) spongy-like nodular radicular veins, 2) thinned transdural vessel walls, and 3) arterial hypertension might favor the development of AV shunts. Further anatomic and histologic studies are required to prove or disprove this hypothesis.

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ORIGINAL RESEARCH
SPINE

Clinical and Radiologic Characteristics of Deep Lumbosacral Dural Arteriovenous Fistulas

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ABSTRACT

BACKGROUND AND PURPOSE: Spinal dural arteriovenous fistulas located in the deep lumbosacral region are rare and the most difficult to diagnose among spinal dural arteriovenous fistulas located elsewhere in the spinal dura. Specific clinical and radiologic features of these fistulas are still inadequately reported and are the subject of this study.

MATERIALS AND METHODS: We retrospectively evaluated all data of patients with spinal dural arteriovenous fistulas treated and/or diagnosed in our institution between 1990 and 2017. Twenty patients with deep lumbosacral spinal dural arteriovenous fistulas were included in this study.

RESULTS: The most common neurologic findings at the time of admission were paraparesis (85%), sphincter dysfunction (70%), and sensory disturbances (20%). Medullary T2 hyperintensity and contrast enhancement were present in most cases. The filum vein and/or lumbar veins were dilated in 19/20 (95%) patients. Time-resolved contrast-enhanced dynamic MRA indicated a spinal dural arteriovenous fistula at or below the L5 vertebral level in 7/8 (88%) patients who received time-resolved contrast-enhanced dynamic MRA before DSA. A bilateral arterial supply of the fistula was detected via DSA in 5 (25%) patients.

CONCLUSIONS: Clinical symptoms caused by deep lumbosacral spinal dural arteriovenous fistulas are comparable with those of spinal dural arteriovenous fistulas at other locations. Medullary congestion in association with an enlargement of the filum vein or other lumbar radicular veins is a characteristic finding in these patients. Spinal time-resolved contrast-enhanced dynamic MRA facilitates the detection of the drainage vein and helps to localize deep lumbosacral-located fistulas with a high sensitivity before DSA. Definite detection of these fistulas remains challenging and requires sufficient visualization of the fistula-supplying arteries and draining veins by conventional spinal angiography.

ABBREVIATIONS: AV = arteriovenous; CE-MRA = time-resolved contrast-enhanced dynamic MRA; FV = filum terminale vein; lsSDAVF = deep lumbosacral spinal dural arteriovenous fistula; SDAVF = spinal dural arteriovenous fistula

Despite being the most common spinal vascular malformation, spinal dural arteriovenous fistulas (SDAVFs) are rare and still underdiagnosed entities.[1,2] The incidence of SDAVF in the general population is 5–10/million/year.[3-5]

A recent meta-analysis of all case series that included >5 patients concluded that men were affected 5 times more often than women and that the mean age at the time of diagnosis was 55–60 years.[6] If not treated properly, SDAVFs are associated with a considerable morbidity with progressive spinal cord symptoms.[1,7,8] The clinical presentation of an SDAVF can be ascribed to venous congestion due to pathologic arteriovenous (AV) shunts in most cases.[9] Initial symptoms are often nonspecific.[3] They include gait difficulties, symmetric or asymmetric sensory symptoms such as paraesthesia in 1 or both feet, diffuse or patchy sensory loss, and radicular pain.[6] More than 80% of all SDAVFs are located between T6 and L2, but SDAVFs can occur anywhere along the dura of the spinal canal.[7] According to various reports, fistulas in the sacral region occur in approximately 4% of patients with SDAVFs.[6,10] However, larger series dealing with SDAVFs located in the deep lumbosacral region (lsSDVAF) are still lacking in the literature. The purpose of our study was to evaluate the clinical and radiologic data of 20 patients with lsSDAVFs presenting to our center between 1990 and 2017.

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MATERIALS AND METHODS

After obtaining permission from our local ethics board, we retrospectively evaluated the medical and radiologic reports of the RWTH Aachen University Hospital for patients diagnosed with SDAVF between January 1990 and March 2017. SDAVFs located above the L5 vertebral level and arteriovenous malformations of the filum terminale were excluded from our analysis.

Two experienced physicians analyzed the radiologic data blinded to all clinical data. A reference standard for statistical analysis was established in a consensus reading.

The extension of the T2 signal hyperintensity and the medullary contrast enhancement were qualified by the number of vertebral levels shown to be affected on T1 and T2 MR images. The appearance of the perimedullary veins was rated subjectively as absent, mild, or prominent due to their tortuous and dilated appearance on the T1 and T2 images.

The neurologic status was assessed according to the Aminoff-Logue disability score (AL-score). We re-evaluated the documented neurologic status at the time of admission (AL-score), the duration of symptoms from onset until diagnosis, as well as previous misdiagnosis and treatment.

Diagnostic Tools

MR Imaging/MRA. Before admission to our center, all 20 patients underwent extensive spinal DSA and/or MR imaging (0.5T and/or 1.5T). Two experienced physicians analyzed the radiologic data blinded to all clinical data. A reference standard for statistical analysis was established in a consensus reading.

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Moreover, 8/19 patients who were admitted after time-resolved contrast-enhanced MR angiography (CE-MRA) in our institution underwent additional spinal CE-MRA (1.5T) before DSA. MRA was performed on a clinical 1.5T MR imaging system with a phased array spine coil. The MR imaging protocol included 3 different pulse sequences: First, T2-weighted survey images were acquired to depict the course of the spinal cord as an anatomic reference. Second, MR fluoroscopy, performed with administration of a 2-mL test bolus of gadolinium-based contrast agent (gadopentetate dimeglumine; vial concentration, 0.5 mol/L), was used to determine the optimal scan delay between contrast injection and the start of the MRA acquisition. Finally, we performed a dynamic 2-phase 3D fast-spoiled gradient-echo pulse sequence with 45 mL of contrast agent. These 2 phases served to distinguish relatively early contrast enhancement, which mainly involves (normal and/or pathologic) arteries and arterialized veins, from later enhancement in which arteries and arterialized veins but also normal veins are visualized together. The number of sections was individually adjusted (range, 75–85 mm; 45–51 mm) to include the vertebral column, usually from T3 to S5. The precise evaluation was then achieved by MPR and maximum intensity projection. If initial CE-MRA findings were suspicious for a fistula zone, we performed additional coronal and axial contrast-enhanced T1-weighted images focused on the suspected fistula region. Further details about our spinal CE-MRA technique have been previously described.[1,11]

DSA. After re-evaluation of all previous spinal angiographic examinations performed elsewhere before admission to our center, we finally focused our further DSA examinations on the lumbosacral region.

DSA was performed with a femoral approach in a dedicated biplanar neuroangiographic suite. Standardized angiography included selective manual injections of 4–5 mL of 300 mg/mL of iodinated nonionic contrast medium into the lumbar and intercostal arteries. Furthermore, injections into both vertebral arteries, the costocervical arteries, the thyrocervical trunks, and the arterial feeders of the sacral region were added. Imaging was in the anteroposterior direction with 2 frames per second. Oblique and lateral views were added to elucidate the morphology of the AV shunt as well as the intradural course of the draining veins. Film sequences of at least 5–20 seconds were obtained. In 2 patients, in whom lsSDAVF was previously diagnosed elsewhere before referral to our center, our DSA examinations included solely the deep lumbosacral region.

Statistics

Pearson χ^2 tests and Fisher exact tests were used when applicable. Student *t* tests and Mann-Whitney *U* tests were used when applicable after testing for data distribution with a Shapiro-Wilk test. *P* values with an α level of $\leq$.05 were significant. All statistical analyses were performed with SPSS 23 software (IBM, Armonk, New York).

RESULTS

We identified 194 patients with SDAVFs located anywhere along the spine. Twenty (10.3%) of these patients had lsSDAVFs and were included in our study.

Clinical Features

Table 1 provides an overview of clinical findings in all 20 patients included in this study. Seventeen of 20 (85%) patients were men. The mean age was 63 ± 5 years (median, 63.5 years; range, 53–78 years). Overall, 16 (80%) patients experienced a gradual onset and progressive deterioration of neurologic function. The remaining 4 (20%) patients had a rapid deterioration of their motor function in the lower extremities within a mean period of 2.5 months (range, 1–4 months) and presented with a severe motor disability at time of admission.

However, the most common neurologic finding at time of admission at our institution was subjective and objective gait disturbances of the lower extremities. Paresis in the lower extremities was present in 17 (85%) patients. The remaining 3 patients (15%) had a slowly progressive ataxia and hypesthesia without manifest motor deficits. Sensory symptoms in various severities were documented in 18 (90%) patients and comprised diffuse loss of sensation and/or paresthesia in the lower extremities. One (case 15) of these 18 patients had dysesthesia from the T12 level downward. Fourteen (70%) patients presented with a sphincter dysfunction at time of admission to our institution.

The mean time between clinical onset and diagnosis in all 20 patients was 15 ± 12 months (median, 15 months; range, 1–36

Table 1: Clinical presentation of patients with deep lumbosacral spinal dural arteriovenous fistulas

Case No.	Age (yr)/Sex	Duration of Symptoms (mo)	Symptoms at Time of Diagnosis	AL-Score	Previous Diagnosis and Treatment
1	66, M	24	Paraparesis 3/5[a], sensory transverse lesion L5, sphincter dysfunction	3	Lumbar disc prolapse: discectomy L4–5
2	56, M	36	Paraparesis 3/5, sensory transverse lesion L2	3	
3	63, M	24	Paraparesis 2–3/5, sensory transverse lesion L1, sphincter dysfunction	4	
4	60, M	30	Paraparesis 4/5, sensory transverse lesion L4, sphincter dysfunction	3	Lumbar disc prolapse: discectomy L3–4, L4–5
5	71, M	14	Distal accentuated paraparesis 3/5, mild hypesthesia of the right leg	3	
6	66, M	18	Paraparesis 3/5, sensory transverse lesion L5, sphincter dysfunction	4	Lumbar spinal stenosis: dorsal decompression L1–2
7	55, M	2	Paraplegia and anesthesia below T8, sphincter dysfunction	5	
8	67, M	26	Paraparesis 4/5, sensory transverse lesion T12, sphincter dysfunction	2	Intramedullary tumor: biopsy
9	73, M	9	Paraparesis 3/5, sensory transverse lesion T5, sphincter dysfunction	4	Intramedullary tumor: biopsy
10	70, M	3	Paraparesis 3/5, sensory transverse lesion S1, sphincter dysfunction	4	
11	69, M	6	Paraparesis 1–2/5, sensory transverse lesion L4, sphincter dysfunction	5	
12	67, F	12	No paresis, hypesthesia below T11, ataxia	1	
13	63, M	1	Paraparesis 3/5, sphincter dysfunction	3	
14	61, M	11	Distal accentuated paraparesis 3/5, hypesthesia of the right leg, ataxia, sphincter dysfunction	3	Lumbar spinal stenosis: dorsal decompression and discectomies L4–5, L5–S1
15	67, F	9	Paraparesis 4/5, dysesthesia below T12, paresthesia on the dorsum of the left foot	2	Lumbar disc prolapse: discectomy L5–S1
16	63, M	ND	No paresis, sensory transverse lesion L1, ataxia, sphincter dysfunction	1	Repeat insufficient embolizations of lsSDAVF
17	55, M	10	Monoparesis left foot	1	Lumbar stenosis: dorsal decompression
18	78, M	4	Spastic paraparesis 3/5, paresthesia in both feet, sphincter dysfunction	4	
19	74, M	24	Paresis of the left leg 4/5, diffuse paresthesia of the lower extremities	2	
20	53, F	6	No paresis, diffuse paresthesia of the lower extremities, mild ataxia, mild sphincter dysfunction	1	

Note:—AL-Score indicates Aminoff-Logue disability score; ND, no data.
[a] Muscle strength grade.

Table 2: Radiologic features of deep lumbosacral spinal dural arteriovenous fistulas

	MRI/MRA						DSA	
Case No.	Shunt Location	T2/T1 Hyperintensity (Extension)	Contrast Enhancement (Extension)	Perimedullary Vein Enlargement (Extension)	Prominent FV	Prominent Lumbar Vein	DSA until Diagnosis	Arterial Feeder
1	S1 R	T7-conus	T9–T10	Mild, T7–T8	No	No	4	Iliolumbar artery R
2	L5 R	T9–T11	T5–T11	Mild, T5–T11	No	Yes	4	Iliolumbar artery R
3	S1 L	T8-conus	Absent	Absent	Yes	No	4	Middle sacral artery L
4	S1 R	T9-conus	Absent	Mild, T10–T12	Yes	No	3	Iliolumbar artery R
5	S1 R	T3-conus	ND	ND	Yes	No	3	Iliolumbar artery R
6	L5 L	T8-conus	T9-conus	Mild, T10–T12	No	Yes	2	L5 L
7	S1 R	T6-conus	T8–T12	Mild, T7–T11	No	Yes	2	Lateral sacral artery L
8	S2 R	T10–T12	T11–T12	Mild, T11–T12	Yes	No	3	Lateral sacral artery R
9	L5 L	T4-conus	T9–T12	Absent	No	Yes	3	L4 L
10	S1 R	T4-conus	Absent	Severe, T6-conus	Yes	No	2	Lateral sacral artery R
11	S1 R	T6-conus	T12–L1	Mild, T6-conus	No	Yes	5	Iliolumbar artery bilateral
12	S3 R	T10-conus	T12	Severe, T7-conus	Yes	No	3	Lateral sacral artery bilateral
13	S1 R	T2-conus	T12-conus	Mild, T8-conus	Yes	No	4	Iliolumbar artery R
14	S2 L	T5-conus	T7-conus	Mild, T8–L3	Yes	No	4	Iliolumbar artery bilateral
15	S1 L	T5-conus	Absent	Severe, T7-conus	Yes	No	2	Lateral sacral artery L
16	S2 L	Absent	T10–11	Absent	Yes	No	2	Iliolumbar artery L
17	S1 L	T5-conus	T4–L1	Mild, T3–T4	Yes	No	2	Iliolumbar artery bilateral
18	S2 L	T8–T12	T8–T11	Mild, T9–T12	Yes	No	5	Iliolumbar artery bilateral
19	L5 R	T8-conus	T8-conus	Severe, T6–T12	No	Yes	2	Iliolumbar artery R
20	S2 R	T12-conus	T9-conus	Mild, T7–T11	No	Yes	1	Lateral sacral artery

Note:—R indicates right; L, left; ND, no data.

months). The mean Aminoff-Logue disability score at time of admission was 3 ± 1.5 (median, 3; range, 1–5).

Overall, 9 of 20 (45%) patients had undergone other treatments before admission to our institution. Six of these 9 patients underwent microsurgical lumbar dorsal decompression and/or discectomy due to the assumption of a spinal degenerative disease. Two other patients underwent a biopsy with the assumption of an intramedullary tumor. The remaining patient was admitted to our center due to recurrence of the lsSDAVF after repeat endovascular treatment performed elsewhere.

Radiologic Findings

Table 2 provides an overview of radiologic findings in all 20 patients.

On preoperative MR imaging, there was a medullary T2-weighted hyperintense signal in all except 1 patient (95%) (mean, 7 vertebral levels; range, 0–13 vertebral levels). The signal alteration involved the conus medullaris in 16 (80%) patients. There was intramedullary contrast enhancement in 15 (75%) patients (mean, 3 vertebral levels; range, 1–10 vertebral levels). Another 16 (85%) patients presented with an enlargement of the perimedul-

lary veins in the upper thoracic and/or thoracolumbar region in various extensions (mean, 4 vertebral levels; range, 0–7 vertebral levels). The filum terminale vein (FV) was dilated in 12 (60%) patients; in another 7 (35%) patients, other dilated lumbar veins were detected. In the remaining patient, no pathologic changes of the FV or the lumbar radicular veins were obvious in the presence of dilated perimedullary veins.

All 20 patients underwent repeat spinal DSA until a definite diagnosis was established (mean, 3 DSAs; range, 2–5 DSAs).

Overall, 8 (40%) patients received preoperative spinal CE-MRA, which revealed no evidence of an SDAVF in the upper thoracic or thoracolumbar region. However, in 7 of these 8 (88%) patients, CE-MRA demonstrated a prominent FV or lumbar radicular vein in the MIP, and MPR images suggested fistula localization in the deep lumbosacral region.

In 4 (20%) patients, the dilated perimedullary veins in the thoracolumbar region were microsurgically exposed and the direction of flow was assessed via Doppler sonography. The subsequent DSA was focused on the lumbosacral region, and a lsSDAVF could be identified in all 4 patients.

DSA revealed, in 17 (85%) patients, an arterial supply via the arches of the internal iliac arteries, namely the iliolumbar ($n = 11$) and the lateral sacral arteries ($n = 6$). The remaining 3 patients presented with an arterial supply via the middle sacral artery and the L4 and L5 segmental arteries, respectively.

In 5 (25%) of these 20 patients, DSA demonstrated a bilateral arterial supply via both the iliolumbar arteries ($n = 4$) and lateral sacral arteries ($n = 1$). There were no major complications related to angiography.

DISCUSSION

Because most studies that deal with lsSDAVFs are case reports and smaller case series, more comprehensive studies are lacking.[12] Thus, it was our aim to describe the clinical and radiologic features of lsSDAVFs in a series of 20 consecutive patients who presented to our institution. In the literature, the sacral region was considered a rare location for SDAVFs (4%).[10,13] However, the incidence of lsSDAVF in our recent series accounts for up to 10.3% of patients with SDAVF. This higher rate of lsSDAVFs in our series is explained by the large number of patients with suspected SDAVFs who were referred to our institution as a tertiary referral center for spinal vascular diseases. Moreover, our current study also included SDAVFs localized at the L5 vertebral level ($n = 4$).

Nonetheless, to the best of our knowledge, our study represents, at the time of this writing, the largest single-center series dealing with clinical and radiologic features of lsSDAVF.

Clinical Features

The clinical presentations of SDAVFs of various locations are often nonspecific and may mimic a variety of conditions.[14-16] Initial symptoms reported in the literature range from low back pain to complete spastic paraplegia.[4,15,17] Comparing our recent findings with a previous analysis of SDAVFs presented to our center between 1989 and 2002, we observed no essential differentiations between clinical symptoms caused by lsDAVFs and those caused by SDAVFs in other locations.[18] Similar to patients with SDAVFs in other locations, most patients in our recent study had a slightly progressive paraparesis, sensory abnormalities, and sphincter dysfunctions at time of admission.[18]

Moreover, the relatively high rate of misdiagnosis in patients with lsSDAVFs (40%) demonstrates the difficulties in detecting the suspected fistula and the broad spectrum of probable differential diagnoses.

These difficulties, in turn, may lead to clinically relevant delays until the correct diagnosis is established. It has been hypothesized that clinical symptoms become more severe the longer the correct diagnosis and treatment are delayed and the venous congestion persists.[4,10,19] We could not identify a significant correlation between symptom duration and the severity of morbidity for all 20 patients ($P = .41$). Nevertheless, intraindividual progressive deterioration of symptoms was present in all our patients.

Radiologic Findings

Consistent with findings of fistulas in other locations, typical MR imaging findings in our series were a combination of intramedullary edema and dilated perimedullary vessels.[9,20] In most cases, the spinal cord demonstrated contrast enhancement reflecting a disturbance of the blood-cord barrier in the presence of venous congestion.[1,21,22]

Nevertheless, the enlargement of the perimedullary veins was absent and mild in 14 (70%) patients and prominent in only 4 (20%) patients. Additionally, dilated FV or radicular veins in the deep lumbosacral region were the hallmark of lsSDAVFs in our MR images and were present in 95% of patients.

In all 7 of 8 (88%) patients who underwent CE-MRA, the arterialized FV and lumbar veins appeared even more prominent than the enlarged perimedullary veins in the respective cases. Moreover, the multiplanar reconstruction of CE-MRA images in our series allowed a sufficient differentiation between FV and other lumbar veins. At least 3-mm sagittal sections in T1/T2 MR images are necessary to identify these veins.

The prominent appearance of the FV in patients with lsSDAVF has been previously discussed in a few reposts.[20,23] However, our recent findings demonstrate that the deep lumbosacral course of either a prominent arterialized FV or other lumbar radicular veins combined with typical medullary congestion should always evoke the differential diagnosis of an AV shunt in this region, even in the absence of prominent perimedullary veins (Figure).

One of the milestones in the diagnostic evaluation of spinal vascular malformations was the development of time-resolved contrast-enhanced MR angiography.[1,11] In a series reported by Mull et al,[1] the MRA-derived level of the feeding artery in SDAVFs agreed with DSA findings in 14 of 19 cases, including 2 patients with lsSDAVF at the S1–2 level. In the remaining 5 cases, a mismatch of only 1 vertebral level (not side) was noted for the feeding artery.

CE-MRA facilitates localizing the AV shunt by focusing the DSA on the assumed fistula region, resulting in a shorter intervention time, less contrast agent application, and a lower exposure dose.[1,11]

In fact, the need for microsurgical exploration to identify the blood flow in the arterialized veins in the thoracolumbar region

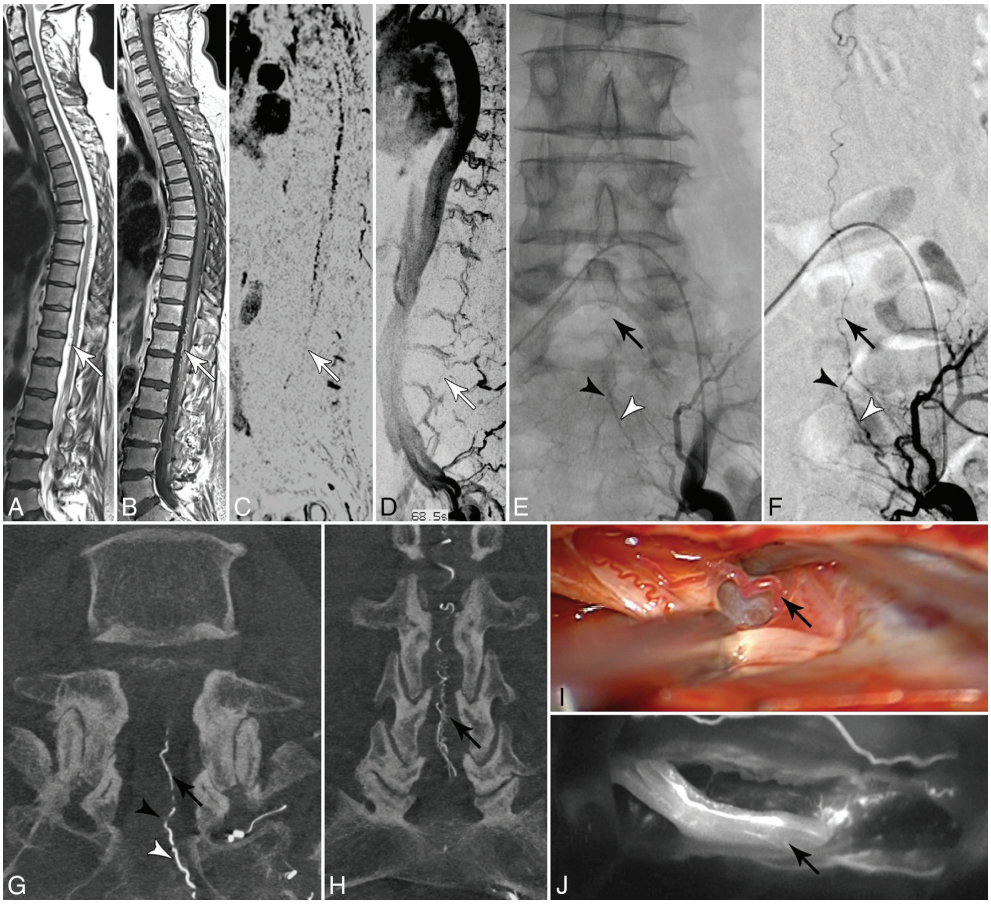

FIGURE. *A* and *B*, Sagittal T2- and contrast-enhanced T1-weighted images reveal congestive myelopathy and dilated perimedullary veins (*white arrows*). *C* and *D*, Spinal CE-MRA shows dilated radicular veins in the lumbar region suspicious for an SDAVF in the lumbosacral region (*white arrows*). *E–H*, DSA examinations identify the fistula in the dural sleeve of the left S2 root (*black arrowhead*) supplied via the lateral sacral artery (*white arrowhead*). Note the upward draining sacral radicular vein (*black arrow*). *I* and *J*, Intraoperative indocyanine green angiography confirms the intradural course of the arterialized draining vein (*black arrow*) embedded at the ventral side of the S2 nerve root.

decreased in our series after establishment of the CE-MRA technique in our center.

Due to our recent experience, we found that more advanced 4D-MRA techniques with better time resolution may provide additional information about the flow direction in the intradural arterialized veins.

DSA remains the criterion standard for the definite diagnosis of SDAVF.[1,3,14,21] Whenever a spinal AV shunt is suspected, an angiography of all thoracic and lumbar segmental arteries is required. In nonconclusive cases, further examination of cervical and pelvic arterial feeders is required.[20]

However, despite technologic advances, DSA of the pelvic region remains technically challenging. A trivial-but-common problem that resulted in an impaired DSA image quality was bowel dysfunction, present in most patients in our series. We could overcome these difficulties by the prophylactic administration of spasmolytic medication 1 day before or during the DSA.

Moreover, due to the low-flow character of these fistulas and the long drainage up to the conus medullaris, lsSDAVFs could be easily missed by inexperienced readers during DSA. Thus, prolonged DSA series with additional oblique and lateral projections are recommended in these patients.

The fistula locations in our series ranged from L5 to S3 level. Sixteen of 20 (85%) demonstrated an arterial supply via arches of the internal iliac arteries. The arterial supply of the remaining 3 fistulas was unusual: Case 3 presented with an lsSDAVF localized at the S1 level, with an arterial supply via the middle sacral artery; cases 6 and 9 presented with a fistula localized at the L5 level with an arterial supply via an atypical L5 segmental artery arising from the abdominal aorta and a descending L4 segmental artery, re-

spectively. Most interesting, fistulas localized at the L5 level (n = 4) presented with a broad variety of arterial feeders comprising the iliolumbar arteries and L4 and L5 segmental arteries.

Moreover, 5 (25%) of 20 patients in our series presented with a bilateral arterial supply via the arches of both internal iliac arteries (On-line Figure).

The detection of a bilateral arterial supply of an lsSDAVF was significantly higher in patients who were diagnosed after establishment of CE-MRA in 2003 in our center ($P < .05$). This finding reflects growth in our own experience in diagnosing theses fistulas and the development of multimodal diagnostic tools.

The complex angioarchitecture in the deep lumbosacral region with a variant and frequently bilateral arterial supply may contribute to difficulties in identifying the fistula. Thus, an optimal DSA examination for the sacral region requires selective and long visualization of all lumbar segmental arteries, the middle sacral artery, and both internal iliac arteries and their arches. If these examinations remain nonconclusive, super selective catheterization of potential feeding arteries in the pelvic and lumbar region may be indicated. Moreover, the bilateral arterial supply in these patients could be sufficiently visualized in series with superselective distal microcatheter injection, resulting in a better opacification of the feeding arteries.

Whenever the AV shunt is identified, the ipsilateral and contralateral feeding arteries above and below the fistula should be examined to exclude the possibility of multiple arterial feeders to the fistula zone from the adjacent arteries.[1,24]

Nonetheless, once an AV shunt in the deep lumbosacral region is suspected, the most probable differential diagnosis for an SDAVF is an arteriovenous malformation of the filum terminale. In both cases, namely SDAVF and filum terminale–AVM, symptoms are caused by medullary venous congestion resulting in comparable myelopathic disorders and a progressive clinical course. In contrast to lsSDAVFs, the filum terminale artery arising from the anterior spinal artery predominantly feeds a filum terminale–AVM.

Even though the filum terminale–AVM is an extremely rare disease, one should be aware of this differential diagnosis in every suspected AV shunt located in the deep lumbosacral region.

In inconclusive repeat DSAs, the search for the exact fistula localization should not be discontinued in patients with a high probability of an SDAVF.[25] In certain cases, a surgical exploration of the arterialized perimedullary veins might be helpful; to facilitate the detection of the fistula localization in subsequent DSA in 4 patients with repeat nonconclusive DSA examinations, we microsurgically exposed the arterialized perimedullary veins in the thoracolumbar region at the level with the greatest vein enlargement. We then assessed the direction of blood flow in these veins via intraoperative Doppler sonography. In all 4 cases, a caudocranial blood flow was detected. Thus, subsequent DSA examinations were focused on the thus assumed deep lumbosacral origin of the fistula. This strategy was successful in all 4 cases.

In summary, we note that lsSDAVFs remain diagnostically challenging, even in experienced hands. Spinal CE-MRA provides, in most the cases, a sufficient visualization of the perimedullary and lumbar draining veins and facilitates the subsequent DSA examinations. However, for a precise fistula localization, DSA remains the criterion standard diagnostic tool. The low-flow characteristics of these fistulas with a frequently variant arterial supply and problems of optimal visualization may cause serious difficulties in localizing the fistula via DSA. Thus, optimized DSA examinations require a sufficient visualization of all potential feeding arteries and draining veins in the pelvic and lumbar regions.

In practice, prolonged series as well as additional oblique and special lateral projections help visualize the intradural course of the draining vein up to the conus.

CONCLUSIONS

Clinical symptoms caused by lsSDAVFs are often nonspecific and may mimic a variety of conditions. The presence of a dilated FV and/or lumbar radicular vein on MR imaging/CE-MRA combined with typical congestive medullary changes should always evoke the differential diagnosis of an arteriovenous shunt in the deep lumbosacral region, even in the absence of perimedullary dilated veins. However, identifying lsSDAVF via DSA remains challenging due to the complex and variant spinal arterial supply in this region and the difficulties in the optimal visualization of the lumbosacral region.

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Treatment strategy and long-term outcome in patients with deep lumbosacral arteriovenous fistulas. A single center analysis in nineteen patients

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ABSTRACT

Objective: Deep lumbosacral dural arteriovenous fistulas (lsDAVF) are rare and present serious diagnostic and treatment difficulties. In our current analysis we present our treatment strategy and the long-term clinical outcome of nineteen patients with lsDAVF.

Patients and methods: We retrospectively analyzed our radiological and medical records for patients presenting with SDAVF between 1990 and 2018 at the University Hospital Aachen. We identified twenty patients with a lsDAVF. All patients were treated surgically. One patient died of pulmonary embolism three months after treatment and was excluded from our outcome analysis. Clinical data at time of admission, discharge, one year after discharge and at the last follow-up were evaluated according to modified Aminoff-Logue disability score (AL-score) for this analysis.

Results: Mean age was 65 ± 7 years (median, 67; range, 53–78), sixteen patients (84 %) were male. After surgery, four patients developed a recurrent fistula in the same shunt zone and were re-treated microsurgically. Follow-up data one year after treatment was available in 15 patients. No relevant changes in AL-score were observed within this period. For the long-term follow-up analysis, data of 13 patients were available; 38.5 % of patients developed late functional deterioration.

Conclusion: In our cohort, patients with deep lumbosacral dural arteriovenous fistula had a higher risk of early recurrence compared to patients with thoracolumbar SDAVF, with a considerable percentage of late functional deterioration. Thus strict clinical and radiologic long-term follow-up examinations are recommended in those patients.

1. Introduction

The vast majority of spinal dural arteriovenous fistulas (SDAVF) reported in the literature are located in the thoracolumbar area. In a previous report from our institution, only 10.3 % of all patients with SDAVF presented with a deep lumbosacral location. [1] In these fistulae, diagnostic and treatment strategies pose particular challenges due to the location as well as the complex angiomorphology of the arteriovenous (av) shunt.

However, since the majority of studies that deal with the treatment of lsDAVF consist of case reports and smaller case series, there is still no specific data about the long-term outcome of these patients. Therefore, we aim in our current analysis to present the clinical long-term outcome after surgical treatment of patients with this rare and difficult to diagnose subgroup of SDAVF.

Abbreviations: lsDAVF, deep lumbosacral dural arteriovenous fistula; SDAVF, spinal dural arteriovenous fistula; av, arteriovenous; AL-score, modified Aminoff-Logue disability score

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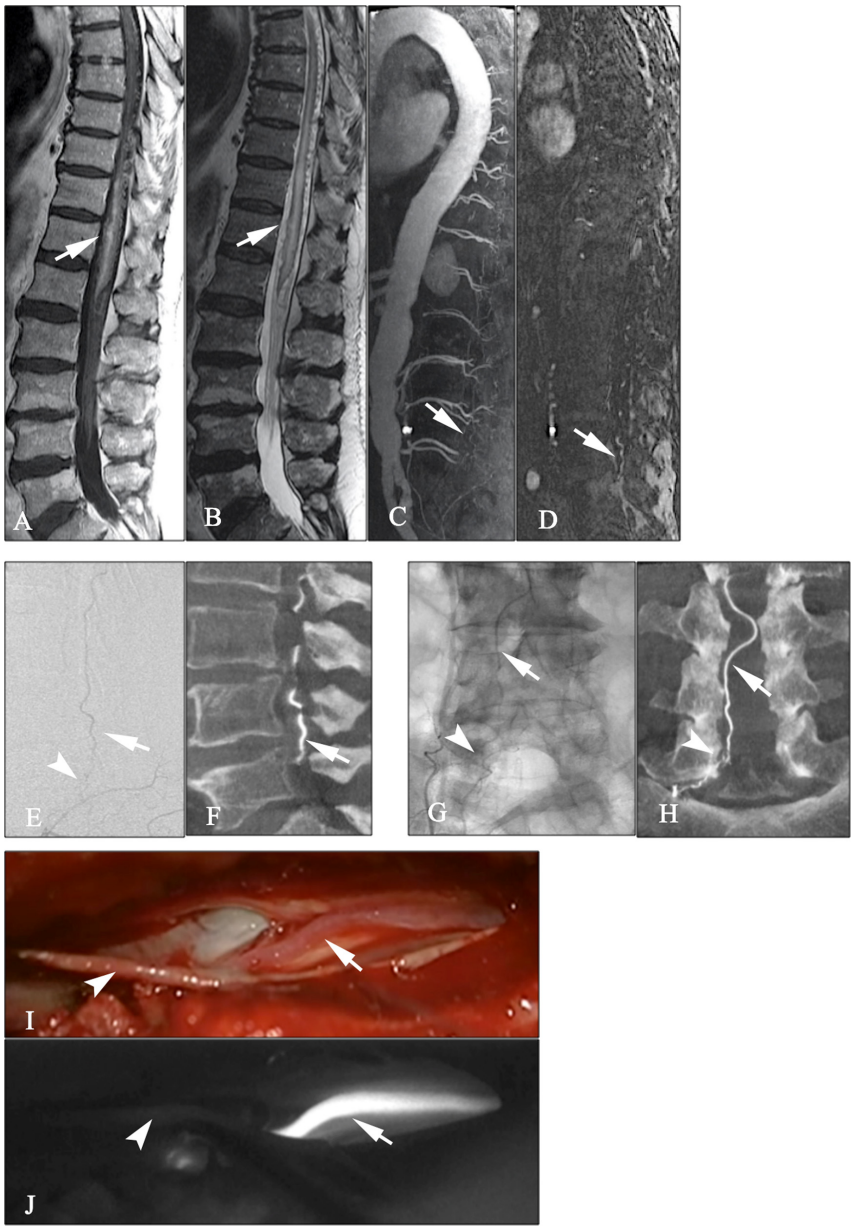

Fig. 1. A and **B:** Sagittal T2- and contrast-enhanced T1-weighted images show congestive myelopathy and dilated perimedullary veins (white arrows). **C** and **D:** Spinal CE-MRA identifies a pathologically arterialized radicular vein in the deep lumbosacral region suspecting an arterivenous shunt in this region. **E–H:** DSA and Dyna-CT examinations in lateral and p. a. projections precisely localize the fistula point in the dural sleeve of the right L5 root (white arrowheads) draining via the L5 radicular vein (white arrows). **I–J**: Intraoperative findings and ICG videoangiography confirms the intradural (dura: white arrowheads) course of the arterialized draining radicular vein (white arrows). (ICG: Indocynine green).

2. Patients and methods

2.1. Patients

We retrospectively analyzed our radiological and medical records for patients presenting with SDAVF between 1990 and 2018 at the RWTH University Hospital Aachen. We identified twenty patients with a SDAVF localized in the deep lumbosacral region below L4 vertebral level (lsDAVF). Spinal epidural arteriovenous fistulas in this region were excluded from the current analysis and reported elsewhere [20]. The diagnosis of in these patients was based on clinical and radiological criteria comprising myelopathic symptoms, congestive myelopathy on MR images and angiographic verification of the fistula location.

All but one patient received a microsurgical interruption of their fistula. This patient underwent endovascular treatment and died of unrelated pulmonary embolism three months after treatment, and was therefore excluded from our long-term outcome analysis. Fig. 1 demonstrates neuroradiologic and intraoperative findings of a patient with deep lumbosacral fistula.

2.2. Surgical treatment

Microsurgical treatment was performed under general anesthesia in the prone position. We verified the radiological level of the fistula with intraoperative fluoroscopic controls. A partial or total hemilaminectomy with partial medial facettectomy was performed at the marked level to explore the nerve roots and the dura on the side of the fistula. A paramedian dural incision was made. The arterialized draining vein was identified under microscope and the intravenous arterial blood flow was confirmed via intraoperative Doppler ultrasound (n = 17) and indocyaningreen angiography in the latter two patients. The arterialized vein was coagulated and divided. If there was hypervascularization of the radicular and/or periradicular dura, we gently coagulated the respective area. There was no need for dura resection in any of the cases. We closed the dura in watertight fashion without using dural graft in all cases.

2.3. Outcome and follow-up

After treatment, all patients received neurological examinations on a daily basis during their stay in our department. Postoperative magnetic resonance imaging (MRI) examinations were acquired routinely within one week after surgery in all patients. Early postoperative DSA was performed in 6/19 patients during hospitalization to evaluate the surgical results.

We used the Aminoff-Logue disability score (AL-score) (Table 1) to evaluate the documented functional condition at time of admission in our institution, at time of discharge, and on follow-up exams [2] (Table 2).

All patients received neurological and radiological (MRI) follow-up exam within 6–12 weeks after discharge, as well as annual clinical and MRI examinations for a minimum of three years after treatment.

Table 1
Modified Aminoff-Logue disability score.

Grade	Characteristics
Gait disturbances	
0	Normal
1	Leg weakness, abnormal walk or stance, but no restriction of activity
2	Restricted activity
3	Requiring 1 stick for walking
4	Requiring 2 sticks, crutches or walker
5	Confined to wheelchair
Micturition	
0	Normal
1	Hesitancy, frequency, urgency
2	Occasional urinary incontinence or retention
3	Total urinary incontinence or retention

3. Results

Sixteen of nineteen (84 %) patients were male. Mean age was 65 ± 7 years (median, 67; range, 53–78). Radiologic characteristics and clinical presentations of all nineteen patients have been previously described by our group elsewhere [1].

All nineteen patients received microsurgical interruption of the lsDAVF. One case with delayed cerebrospinal fluid leakage was treated successfully with lumbar drainage. No other operative or perioperative complications related to surgical treatment were documented in the remaining patients.

Early postoperative DSA examinations were obtained in 6/19 (31.6 %) patients due to surgeons preference to evaluate the surgical result; no residual fistula was detected in any of these cases. All patients received clinical and MR follow-up exams in our center three months after discharge. Further annual clinical and MR follow-up examinations were recommended in all patients. In case of ongoing medullar venous congestion, persisting symptoms or functional deterioration after postoperative improvement of the functional condition early CE-MRA and DSA were indicated.

3.1. Clinical outcome

The most common neurological findings at time of admission in our institution were subjective and objective gait disturbances of the lower extremities, which were seen in all cases. Sensory symptoms of variable severity were seen in eighteen (90 %) patients and comprised diffuse loss of sensation and/or paresthesia in the lower extremities. One patient suffered dysesthesia from the T12 level on downwards. Thirteen (68.4 %) patients presented with a bladder dysfunction at time of admission. Mean time between clinical onset and diagnosis was 15 ± 1 months (median, 12; range, 1–36). The mean AL-score for gait at time of admission was 3 ± 1.4 (median: 3, range; 1–5) and for micturition was 1.8 ± 1.35 (median: 2, range; 1–3)

Long-term outcome was not available in four patients at the one-year follow-up who were lost during follow-up and additional two other patients at the last follow-up who die of causes not related to their SDAVF during follow-up.

At time of discharge (n = 19), the mean AL-score for gait was 3 ± 1.35 (median: 3, range; 1–5). The AL-score for gait had improved in three (16 %) and was unchanged in sixteen (84 %) patients. The micturition was unchanged in all nineteen patients.

At the one-year follow-up (n = 15), the mean AL-score for gait was 2.8 ± 1.5 (median: 3, range; 0–5). The AL-score for gait was improved in six (31.6 %) patients, unchanged in eight (42.1 %) patients, and worsened in one (5.3 %) patient. The mean AL-score for micturition was 1.7 ± 1.43 (median: 3, range; 0–3). Micturition was improved in one (5.3 %) and unchanged in eighteen patients (94.7 %). During the one-year-follow-up, three patients were re-admitted to our center due to progressive neurological deterioration (n = 1) or persisting motor disabilities and medullar edema (n = 2). The fistula occlusion was previously confirmed in two of these three patients via early postoperative DSA. All three cases presented a dural av shunt in the same previous fistula zone and were treated microsurgically. No further surgery related complications were reported in any of the cases.

Follow-up data exceeding one year was available in 13/19 (68.4 %). Table 2 provides an overview of follow-up results. Mean long-term follow-up was 85.7 ± 71.6 months (median, 69.5; range, 10–231 months). One of these thirteen patient was re-admitted to our center 21 months after surgery due to a persistence of medullar edema in the follow-up MR-exams despite of fistula occlusion was confirmed via early postoperative DSA. Angiographic follow-up examinations showed a recurrent lsDAVF in the same previous fistula zone and microsurgical

Table 2
Baseline characteristics and long-term outcome analysis of patients with deep lumbosacral SDAVF. Neurological outcome was determined according to the Aminoff-Logue score (AL-scores) for gait (G) and micturition (M). (n.d.: no data).

Case No.	Age & sex	Fistula location	Duration of symptoms (months)	AL-score				Fistula Recurrences
				Pre-treatment	At discharge	Follow-up (one year)	Last follow-up	
1	66/M	S1r	24	G3, M2	G3, M2	n.d.	n.d.	No
2	67/M	L5 re	18	G2,M0	G2,M0	n.d.	n.d.	No
3	63/M	S2 l	24	G2, M0	G1, M0	n.d.	n.d.	No
4	67/M	S2r	26	G2, M2	G2, M2	n.d.	n.d.	No
5	73/M	L5 l	9	G5, M3	G5,M3	G4,M3	n.d.	No
6	55/M	S1 r	2	G5, M3	G5, M3	G5, M3	n.d.	Yes (10mon)
7	71/M	S1 l	11	G4, M3	G4,M3	G4,M3	G4,M3	Yes (7mon)
8	63/M	S1 l	24	G4, M3	G4,M3	G4,M3	G4,M3	No
9	63/M	S1 l	1	G4, M3	G4, M3	G5, M3	G5,M3	No
10	55/M	S1 l	10	G1, M0	G1, M0	G1, M0	G1,M0	No
11	56/M	L5 r	36	G3, M0	G3, M0	G3,M0	G4,M0	No
12	74/M	L5 r	24	G3, M0	G3, M0	G1,M0	G1,M0	No
13	60/ M	S1 r	30	G3, M3	G3, M3	G3, M3	G4, M3	Yes (1mon)
14	71/M	S1 r	14	G4, M0	G4, M3	G3, M3	G5, M3	Yes (21mon)
15	70/ M	S1 r	3	G5, M3	G4, M3	G3, M3	G4, M3	No
16	67/ F	S3	12	G1, M0	G1, M0	G0,M0	G0,M0	No
17	78/ M	S1 r	4	G4 (5), M3	G4, M3	G3, M2	G3, M2	No
18	53/F	S2 l	7	G1, M0	G1,M0	G1,M0	G1,M0	No
19	67/ F	S1 l	9	G2, M1	G2, M1	G2, M1	G3, M1	No

re-treatment was performed successfully without further complications.

At long-term follow-up, the mean AL-score was 3 ± 1.68 (median: 4, range; 0–5). Compared with the one-year follow-up AL-score for gait at last follow-up had worsened in five (38.5 %) patients and was unchanged in the other eight (61.5 %). Micturition was unchanged in all thirteen patients.

4. Discussion

Our aim was to systematically investigate the clinical long-term outcome and evaluate our treatment strategy in patients with lsDAVF.

We found that outcome within one year after surgery is similar to that of SDAVF of other locations [1,3]. Clinical symptoms of the majority of patients in our study were stable within the first year after definitive treatment. In our long-term follow-up analysis within a mean period of 85.7 ± 71.6 months (range, 10–231 months), however, there was late deterioration of gait in 5/13 (38.5 %) patients.

To the best of our knowledge, there is only one study in the literature that deals with long-term outcome of patients with lsDAVF including data of eleven patients reported recently by Gioppo el al. [4]. In their long-term analysis within a mean period of 31 months (range 6–57 months) the gait was improved in 8/11 (73 %) patients and stable in 3/11 (27 %). Micturition improved in 4/11 (36 %) patients and remained stable in 7/11 (64 %) patients. No functional deterioration was reported in any of these patients [4].

Late functional deterioration in patients with SDAVF, in general, is a well-known but still understudied phenomenon [5,6]. The higher rate of late deterioration in our current cohort compared with the recently reported series by Gioppo et al. about thirteen cases with sacral SDAVF might be explained by the markedly longer follow-up period in our analysis [4].

In general, it has been hypothesized that late functional deterioration after treatment of patients with SDAVF might be caused by not fully understood long-term changes of spinal cord hemodynamics [6,7]. Nonetheless, our data do not allow determining the definite cause of this late functional deterioration in these patients. Our results provide also no sufficient explanation for the markedly higher rate of late deterioration in lsDAVF compared with that of an unpublished series of other 40 patients with SDAVF (20 %) in higher levels, who were treated in our center between 2006 and 2016.

We hypothesize that, hemodynamic changes as well as progressive myelopathy might be probable causes of late functional deterioration in SDAVF patients despite sufficient interruption of av shunts and complete regression of venous congestion.

Notably, the rate of relatively early recurrences in 4/ 15 (27 %) cases in the current cohort of patients with lsDAVF was also higher than the 1 % in a cohort of 59 patients with thoracolumbar SDAVF treated in our center between 2006 and 2016 [8].

The main goal of SDAVF treatment should be a complete disconnection of the av shunt and consecutive reduction of the venous congestion in the spinal cord [5,6]. Generally, optimal treatment by means of endovascular embolization and/or surgical interruption of SDAVF is still a controversial subject in the literature [9–13]. In line with various other referral centers, microsurgical occlusion has been the treatment of choice in the vast majority of patients with SDAVF in our center, including those in the deep lumbosacral region [9,10,14,15].

To the best of our knowledge, specific investigations about the efficacy of endovascular treatment of lsDAVF in a comparable large sample series are still lacking in the literature.

However, the understanding of the specific morphology of the arterial supply and the venous drainage in the deep lumbosacral region is essential for an effective treatment management of SDAVF localized in this area. In a previous report by our group we found that lsDAVF are characterized by: 1) a frequent low-flow av shunt with subsequent small drainage veins ascending to the conus medullaris, 2) a bilateral arterial supply, 3) a frequently anterolaterally localized shunt zone (in contrast to SDAVF in the thoracolumbar region where the shunt zone is typically localized dorsolaterally in the respective nerve root sleeve) [8,16]. All of which could make both angiographic as well as intraoperative identification of the shunt zone and its respective arterialized drainage veins challenging resulting in a higher rate of recurrent or residual fistula (27 %).

Three of four patients with recurrent lsDAVF have received an early postoperative DSA within the same inpatients stay with no evidence for a residual fistula. Consecutive DSA studies showed a recurrent fistula in the same previous shunt zone. Given these pitfalls, it is possible that there was either actual delayed recurrence due to revascularization via collateral microvascular channels of the shunt zone due to complex arterial supply, or that the actual shunt zone and drainage vein could have been partially or completely missed out in DSA exams and/or during the microsurgical inspection due to the low-flow character of these fistulas.

To overcome the diagnostic difficulties of this subgroup of SDAVF,

various considerations should be made during MRI and DSA exams [1,17,18]. Moreover, if surgical treatment is performed, intraoperative doppler sonography and indocyanine green angiography (ICG) images might facilitate the intraoperative identification of the fistula zone and the draining vein, which is frequently located ventrolaterally to the respective nerve root [19].

In summary, the complex vascular morphology of the deep lumbosacral region makes the treatment of SDAVF in this region challenging. Even in experienced hands, lsDAVF are characterized by a relatively high rate of recurrent and/or residual shunts after surgical treatment. Specific data about endovascular treatment of lsDAVF are still lacking in the literature.

Furthermore, these patients present a higher rate of late deterioration in long-term follow-up in comparison with patients of higher located SDAVF and the impaired functional status of the vast majority of patients with lsDAVF remains unchanged after treatment. Thus, clinical and MR follow-up examinations including spinal MRA, should be carried out strictly within at least the first three years after treatment in order to rule out residual or recurrent fistulas. Particularly in patients with persisting or deterioration of clinical symptoms and/ or radiologic findings evident for congestive myelopathy spinal MRA and DSA should be performed in order to rule out residual or recurrent fistulas.

5. Limitations

A major limitation of our study is the small sample size and the retrospective approach with the lack of systematic follow-up exams, both of which provoke speculative interpretation of our data to some extent. As lsDAVFs are a rare but relevant entity, our results may nevertheless serve as helpful reference to optimize the diagnostic, therapeutic and follow-up strategies of this subgroup of SDAVF.

6. Conclusions

In our cohort, patients with deep lumbosacral dural arteriovenous fistula had a higher risk of early recurrence (27 %) compared to patients with thoracolumbar SDAVF, with a considerable percentage of late functional deterioration. Thus, we recommend strict follow-up examinations via MRI/ MRA for these patients at least within a period of three years after treatment to rule out recurrent and/or residual av shunts.

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Original Article

Double spinal dural arteriovenous fistulas

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ABSTRACT

Background. – Spinal dural arteriovenous fistulas (SDAVF) are usually solitary lesions. Synchronous and/or metachronous double SDAVF have rarely been reported in the literature. We report on three patients with double SDAVF and present our single center experience in the diagnostic and treatment management in these patients.
Material and methods. – We retrospectively revised our medical database for all patients who were diagnosed and treated in our center due to a SDAVF between 1990 and 2017. All data including demographics, clinical presentations, as well as radiological data were re-evaluated for this study.
Results. – Three (1.4%) of 209 consecutive patients with SDAVF presented double SDAVF with different arterial feeders and venous drainage patterns. All three patients were men. The mean age at time of diagnosis was 67.9 ± 10 years (median; 68, range: 53–82). Myelopathic symptoms were reported in all three cases. All three fistulas were located in the thoracolumbar region between T7 and L2. MRI/CE-MRA showed medullar T2-hyperintensity, intramedullary contrast-enhancement and dilatation of perimedullar veins in various extensions.
Conclusion. – Double SDAVF are extremely rare and were found in 1.4% of patients in our series. The vast majority of the reported double SDAVF in the literature has been detected synchronously within an area of equal or less than three vertebral levels. Thus, whenever the SDAVF is identified, further injections of the fistula-zone neighbored segmental arteries might be recommended. However, due to the extremely low incidence of double SDAVF a complete spinal DSA is not indicated.

Introduction

SDAVF is the most frequent vascular disease of the spinal cord and its meninges and accounts for about 70% of all spinal arteriovenous (av) pathologies of the spinal cord and its meninges. The disease becomes symptomatic predominantly in elderly men between 40 and 60 years [1,2].

SDAVF are usually solitary lesions and are commonly localized in the thoracolumbar region, They may be encountered from the sacral region, supplied via spinal branches of the iliolumbal arteries or the middle sacral artery, to the level of the foramen magnum supplied via cervical feeders including both vertebral arteries, the thyreocervical and costocervical trunk and the ascending cervical artery [3–5]. The venous drainage in all these spinal arteriovenous shunts occur typically transdurally into the coronal venous plexus producing medullar venous hypertension that leads to swelling and edema within the spinal cord and accompanies the characteristic symptoms of a slowly progressive paraparesis, bowel and bladder dysfunction and sensory disturbances [6].

The fistula-zone itself is predominantly located at or in the nerve root sleeve, supplied by meningoradicular branches of a segmental artery and draining transdurally into the coronar venous plexus [7].

However, multiple SDAVFs have rarely been reported in the literature. (Table 1) In this study we report on the clinical and radiologic features of three patients with double SDAVF and present our single center experience in the diagnostic and treatment management in this patients series.

Material and methods

After obtaining permission from our local ethics board, we retrospectively revised our medical database for all patients who were diagnosed and treated in our center due to a SDAVF between 1990 and 2017.

The initial diagnosis of SDAVF was based on clinical and radiological criteria that comprised:

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Table 1
Overview of all twenty-eight cases of double spinal dural arteriovenous fistulas reported in the literature (including present cases). n.d.: no data.

Author	Age and sex	Timing of diagnosis	Location			Treatment
			Lesion 1	Lesion 1	Lesion 3	
Thiebot et al. [31], 1986	24, F	synchronous	T4 r	T12 l	L4, L5 r	n.d.
Merland et al. [32], 1985	n.d.(4 cases)	n.d.	n.d.	n.d.		n.d.
Barnwell et al. [33], 1991	69, F	metachronous	C1-C2 r	C5-C6 r		surgery
Pierot et al.	47, M	synchronous	T6l	T8r		combined
[14], 1993	64, M	synchronous	T8 r	T9 l		surgery
Chaloupka et al. [34], 1995	48, M	synchronous	L1 l	T9 l		combined
Dam-Hieu et al. [35], 2001	49, M	synchronous	T6 r	L1r		surgery
van Dijk et al. [36], 2002	62, M	metachronous	T5 (n.d.)	T9 (n.d.)		(n.d.)
El-Serwi et al. [37], 2006	47, M	synchronous	T7 r	T5 r		embolization
Sugawara et al. [38], 2005	72, M	metachronous	T6	L1		surgery
Rizvi et al. [39], 2006	50, M	metachronous	T9	L-1		combined/surgery
Shankar et al. [40], 2011	61, M	synchronous	C1,C2 l	C6 l	C3, C6 r	embolization
Ge et al. [41],	30, M	synchronous	T12 l	L1 l		surgery
2013	62, M	synchronous	T6 l	T3 r		embolization
Oshita et al. [42], 2011	74, M	synchronous	C1	C1		surgery
Cenzato et al. [43], 2007	45, M	synchronous	T5 r	T6 l		surgery
Dagar et al. [44], 2010	58, M	metachronous	T12 l	L1 r		surgery
Hanakita et al. [45], 2012	57, M	synchronous	T7r	T12 l		surgery
Hetts et al. [46], 2013	40, M	synchronous	C5-C6 l	C5-C6 r		surgery
Avecillas-Chasín	72, M	metachronous	T7 r	T12 r		embolization/surgery
et al. [47], 2015	51, M	metachronous	C1 r	C1 l		surgery
Kaku et al. [48], 2017	56, M	metachronous	C1 r	S2 r		surgery
Present cases						
1 [26]	63, M	metachronous	L1 r	L2 l		surgery
2	65, M	synchronous	T8 l	T9 r		surgery
3	51, M	synchronous	T7 l	T7 r		surgery

- clinical squeal of myelopathy resulting in motor or sensory disturbances with or without vegetative bladder-bowel dysfunctions and;
- MR imaging findings of congestive myelopathy of the spinal cord and/or visibly engorged perimedullary veins.

All suspected cases of SDAVF were verified by DSA. All clinical data including demographics, clinical and neurological presentation, as well as radiological data were assessed by the primary treating physicians and re-evaluated for this study.

Results

We identified 209 consecutive patients with angiographically verified SDAVF. Three (1.4%) of these 209 patients presented double SDAVF and were included in the recent study. (Table 1)

All three patients were men. The mean age at time of diagnosis was 67.9 ± 10 years (median; 68, range: 53–82). All three patients presented with paresis, gait ataxia, and sensory deficits in the lower extremities in various severities. Sphincter dysfunction was present in one of these three patients at time of admission in our center.

All SDAVF were located in the thoracolumbar region between T7 and L2. T2w-hyperintense signal and elongation and/or dilatation of perimedullar veins were present in all three patients. There was intramedullary contrast enhancement in two of these three patients. All three patients underwent a microsurgical interruption of their fistulas. One patient showed postoperatively a space occupying epidural hemorrhage in the post-operative MRA. The hematoma was surgically evacuated without further procedural complications.

Illustrative case

This 51-year-old man complained of a one-year history of weakness and ataxia in the lower extremities, accompanied by cramping pain in both thighs. During the year he had also developed paraesthesia in the dorsal and medial site of the both thighs and feet. Slowly progressive urinary and bowel incontinence followed. At time of admission neurological examination revealed proximal accentuated spastic paraparesis grade 3/5 with gait ataxia and brisk tendon reflexes in the lower extremities. All sensory modalities were reduced in the dorsal site of the both thighs. Magnetic resonance imaging (Fig. 1) revealed a medullar edema of the thoracic spinal cord from T 6 to the conus at L1 vertebral level with centromedullary hyperintensity in T2-weighted images. No medullar contrast enhancement was shown. Enlarged and tortuous perimedullar veins became apparent by flow voids and contrast enhancement, extending from the craniocervical region to T6 vertebral level dorsally to the spinal cord. CE-MRA revealed a pathologic early arterialization of the enlarged perimedullar veins suggesting a SDAVF at the level of T6/T7 intervertebral foramen. Spinal angiography showed a dural arteriovenous shunt at the level of the intervertebral foramen T6/T7 supplied by meningeal branches of the left T7 segmental artery as assumed in the CE-MRA. Further examinations of the ipsilateral and contralateral segmental arteries showed a bi-segmental arterial supply of the left av shunt at T7 via a dural branch from the right T6 segmental artery. The venous drainage of this fistula was ascending to cranicervical region continuing into the left sigmoid sinus. Interestingly, we identified an additional SDAVF localized at the level of the right T6/T7 intervertebral foramen and supplied by the right T7 segmental artery showing a different and less prominent ascending venous drainage pattern. Both fistulae were occluded microsurgically in the same session via laminectomy of T7.

Discussion

Though SDAVFs are considered to be an acquired disease, their precise etiology is still unknown [7]. In the presence of an av shunt in the spinal dura, venous hypertension in the coronal venous plexus causes usually a chronic reduction of the intramedullary av pressure gradient [8]. These hemodynamic changes were considered in the literature to be the most pathophysiological contributing factor of congestive myelopathy [9–11]. Nevertheless, for successful treatment management a sufficient opacification and

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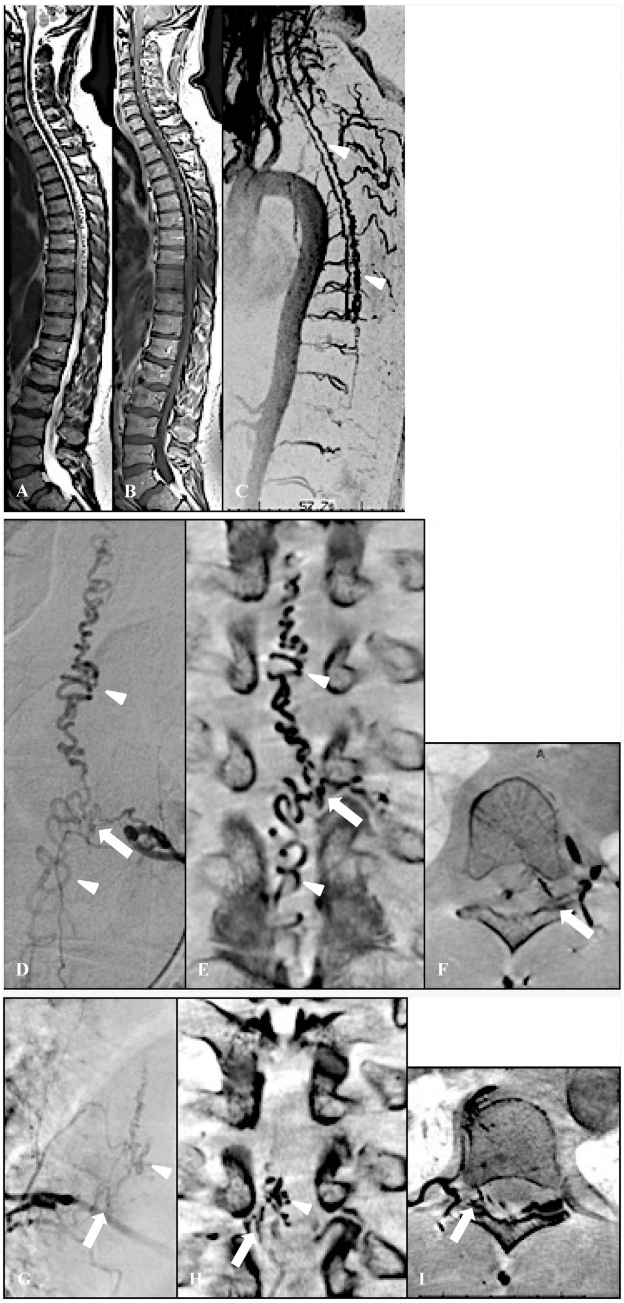

Fig. 1. A–B. Sagittal T2- and contrast-enhanced T1-weighted images show medullar edema in the thoracic region and extensive dilated perimedullar veins. C. Spinal CE-MRA (MIP) reveals abnormal arterialized perimedullar veins in the thoracic and cervical region (white arrowhead). D–I. DSA examinations in pa projection as well as axial and coronar MPR of Dyna-CT of the left T 7 segmental artery. D–F. Identify primarily a SDAVF (white arrow) with ascending and descending perimedullar draining veins (white arrowhead). Further DSA examinations. G–I. Of the fistula zone neighbored segmental arteries reveal a second fistula (white arrow) supplied via the right T7 segmental artery and presenting a different and less prominent venous drainage pattern (white arrowhead).

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profound understanding of the angiomorphology of the fistula via spinal MRI/CE-MRA and DSA are mandatory [12].

Among 209 SDAVF patients who were treated in our institution between 1990 and 2017, only three (1.4%) cases presented a double SDAVF with different arterial feeders, distant fistula zones and various venous drainage patterns.

Multiple SDAVFs have been mentioned in the literature only incidentally in case reports or in few larger case series without further specific descriptions. Table 1 provides an overview about all reported double SDAVF in the literature. An analysis of Merland et al. about 57 patients included four cases with double SDAVFs, estimating an incidence for double SDAVF of 7% in the respective series [13]. However, the authors did not specifically describe the location of neither the fistula zones nor the venous drainage pattern in these four patients. In another series of 50 patients, Pierot et al. reported on two (4%) patients with double SDAVF [14].

Nonetheless, sufficient data about the true incidence of double SDAVF is still missing in the literature. Various factors might hinder the precise estimation of the incidence of double SDAVF. On the one hand, classic SDAVFs are generally a rare entity; Thron et al. assumed an annual incidence for SDAVF of 5–10 cases per million [7]. Due to this low incidence of SDAVF and to the diagnostic difficulties, patients with suspected SDAVF are mainly referred to specialized centers with high expertise in diagnosing and treating this kind of spinal vascular diseases [15]. This might induce, in turn, a referral selection bias in statistical analysis of these patients. On the other hand, the variability of diagnostic, treatment and follow-up strategies in the various referral centers might result also in a discrepancy in the estimated rate of double fistula [16–19].

All three patients in our recent series have been referred to our center due to chronic progressive myelopathic symptoms and radiological findings evident of a SDAVF. Paraparesis and gait ataxia were present in all three patients at time of diagnosis. Case 2 suffered additionally bowel dysfunction at time of admission in our center. MR images in all three cases demonstrated medullar edema and pathologically enlarged perimedullar vessels in various extensions along the thoracolumbar region. Two of these three patients presented centromedullary contrast enhancement in various extensions.

Even though the very small sample size of our recent series does not allow a statistical analysis, we observed no major differences between the clinical presentations and MR findings of this series and those of patients with solitary SDAVF diagnosed in our center [1]. Nonetheless, the typical but non-specific neurological and radiological findings in SDAVF patients contribute, generally, to often misdiagnosing and subsequent delay of the correct diagnosis and treatment [20].

In the last two decades advanced diagnostic tools have been developed to facilitate the diagnosis of spinal vascular malformations [12,21]. Since 2004/2005, we perform initially spinal CE-MRA in SDAVF patients whenever it is possible [12,22]. CE-MRA may serve to detect, localize, and characterize, various types of spinal AV shunts with a high sensitivity [12]. In a previously reported series by our group, CE-MRA could correctly predict the level of the fistula within one vertebral level in nineteen patients with SDAVF [12]. Hence, we usually focus our DSA examinations primarily on the suspected region shown in the prior CE-MRA [12]. All three patients underwent a spinal selective DSA examination in our center for definite diagnosis.

Including the present cases, sufficient data about the timing of the diagnosis was available for twenty-five of all twenty- eight double SDAVF cases. In sixteen (64%) of these twenty-five patients the second fistula was localized in a distance of equal or less than three vertebral levels from the first identified one. Furthermore, in eleven (69%) of these sixteen cases the double SDAVF have been diagnosed synchronously during the same DSA examination.

This frequently close spatial relationship between double SDAVF might be based on common etiological factors. SDAVF were considered to occur secondary to thrombosis and/or outlet disorder of spinal venous system resulting in a so-called medullar venous congestion. Thus it is conceivable that, the presence of a single SDAVF could promote the development of a second fistula due to the subsequently increased medullar venous pressure and the concomitant venous stagnation and thrombosis in the adjacent veins.

Based on our own experience, once a SDAVF is identified further injections of all neighbored ipsi- and contralateral segmental arteries above and below the fistula-zone might be necessary for sufficient visualization of the angiomorphology. Nonetheless due to the:

- extremely rare incidence of double SDAVF and;
- due to the fact that the vast majority of reported double SDAVF were localized in a circumscribed area of the spinal dura and have been often synchronously identified, a routine complete DSA examination of all spinal cords feeding segmental arteries might not be indicated.

It might be otherwise recommended only in cases of discrepancy between CE-MRA findings and the verified fistula location on DSA, such like various suspected arterial feeder and/or different venous drainage patterns.

All three patients in our recent study underwent microsurgical interruption of their SDAVF. Data about treatment strategy of double SDAVF are available for twenty-one of all reported twenty-eight cases. Thirteen (62%) of these twenty-one cases underwent surgical treatment, other five (24%) cases received endovascular and surgical treatment, and the remaining three (14%) patients received solely endovascular embolization.

The main goal of treatment is to disconnect the av shunt and to reduce the venous congestion of the spinal cord by endovascular embolization and/or surgical interruption [16,23–25].

Surgical interruption was the first-line therapy for all SDAVF in our center [17,26]. Our treatment strategy is in line with various large representative series [19,27]. It is a safe, effective and relatively simple intervention with the exception of sacral fistulae [17]. In a large meta-analysis dealing with sixteen studies that provided information on surgical success rates Steinmetz et al. reported a success rate of 97.9% for surgical treatment regardless of SDAVF localization [19]. In contrast, the success rate of endovascular treatment reported in various studies ranged between 69.2% and 89.5% [28–30].

All included patients in our recent series received a neurological examination in a daily basis and a MRI examination within one week after surgery. We usually recommend, in all SDAVF patients, further clinical and MR follow-up examinations three, six months, and twelve months after discharge. Extensive clinical and neuroradiological examinations should be, however, performed in case of progressive deterioration after treatment, persistence of symptomatology and/or pathological MRI findings six months after treatment, or in case of late neurological deterioration after initial improvement with no evidence of other possible contributing pathologies [12]. In those cases, CE-MRA and DSA re-examinations should comprise all spinal cord feedings arteries to exclude local recurrence, second SDAVF, or possible other spinal vascular pathologies.

Limitations

Major limitations of our study are the small sample size and the retrospective approach, both of which might provoke speculative interpretation of our data to some extent.

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However, our recent observations may provide an overview of specific diagnostic and treatment strategies of this rare disease, in particular since the incidence of double SDAVF is extremely low and there are very few data concerning this fistuals in the literature.

Conclusion

Double SDAVF are extremely rare and have been yet reported in overall twenty-eight patients in the literature (including the present cases). The rate of double SDAVF in our series accounts for 1.4% of all SDAVF in our own series. The vast majority of the reported cases has been detected synchronously and the multiple fistulas were localized within an area of equal or less than three vertebral levels. Due to these observations, the routine opacification of the SDAVF neighbored ipsi- and contralateral segmental arteries might be recommended in all SDAVF patients, but a complete spinal DSA is not indicated once the dural av shunt is identified. However, if clinical and/or neuroradiological follow-up examinations revealed an evidence of a persisting av shunt, spinal CE-MRA and complete DSA are mandatory.

Disclosure of interest

The authors declare that they have no competing interest.

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ORIGINAL RESEARCH
INTERVENTIONAL

Spinal Epidural Arteriovenous Fistula with Perimedullary Venous Reflux: Clinical and Neuroradiologic Features of an Underestimated Vascular Disorder

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ABSTRACT

BACKGROUND AND PURPOSE: The purpose of this study was to discuss the clinical and radiologic characteristics of spinal epidural arteriovenous fistulas (SEAVF) and demonstrate their specific angiomorphology in a single-center series.

MATERIALS AND METHODS: Thirteen consecutive patients were diagnosed with SEAVF at RWTH Aachen University Hospital between 2006 and 2018 and were included in this study. All patients had MR imaging and DSA before treatment; 10 of these 13 patients received contrast-enhanced MRA (CE-MRA).

RESULTS: The mean patient age was 72 ± 8 years. Paraparesis was present in 12 (92%) patients. Sphincter dysfunction and sensory symptoms were observed in 7 (54%) and 6 (46%) patients, respectively. The mean duration of symptoms was 6 ± 8 months. Congestive myelopathy on MR imaging was present in all patients. Prominent arterialized perimedullary veins were demonstrated in only 3 cases. CE-MRA revealed arterialized perimedullary veins and an arterialized epidural pouch in 9/10 (90%) patients, mostly located ventrolaterally. DSA demonstrated a multisegmental extension of the arterialized ventrolateral epidural pouch in 6 (46%) cases. An intradural radicular drainage vein was localized distant from the original fistula point in 3 (23%) patients.

CONCLUSIONS: Congestive myelopathy with an acute/subacute clinical course was the dominant finding in spinal epidural arteriovenous fistulas. CE-MRA is a powerful diagnostic tool for identifying arterialized perimedullary veins as well as an arterialized epidural pouch. While arterialized perimedullary veins frequently present with only mild enlargement and elongation in spinal epidural arteriovenous fistulas, the arterialized epidural pouch is frequently located ventrolaterally and may extend over several vertebral levels. DSA remains the criterion standard to precisely visualize a spinal epidural arteriovenous fistula and its intradural radicular drainage vein, which may be located distant from the fistulous point.

ABBREVIATIONS: AV = arteriovenous; CE-MRA = contrast-enhanced MRA; SDAVF = spinal dural arteriovenous fistula; SEAVF = spinal epidural arteriovenous fistula

Various classifications have been established for spinal vascular malformations and fistulas based on their vascular supply, venous drainage pattern, and nidus location and morphology. The most common classification of spinal vascular diseases was developed by Oldfield and Doppman in 1988.[1] They classified these lesions into 4 types comprising classic spinal dural arteriovenous fistulas (SDAVFs), glomus arteriovenous malformations, congenital juvenile arteriovenous malformations, and perimedullary arteriovenous fistulas. The much rarer spinal epidural arteriovenous fistulas (SEAVFs) were not included in this classification.

In contrast to the SDAVF, the arteriovenous (AV) shunt in the SEAVF is located in the epidural space. The venous drainage of these AV shunts varies from pure epidural fistulas with extradural venous drainage to combined epidural and intradural venous reflux.[2]

A SEAVF with perimedullary venous reflux has been thought to present with nonspecific myelopathic symptoms comparable with those of a typical SDAVF.[3,4] However, their precise angiographic and clinical presentations have not yet been investigated in a large number of patients and might still be unfamiliar to most neurologic and radiologic physicians.

A clear recommendation for treatment technique and strategy

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is also still lacking in the literature. The goal of treatment is, however, the interruption of the intradural radicular drainage vein to stop the arterialization of perimedullary veins and additionally the obliteration of the arterialized epidural pouch to decrease the risk of residual or recurrent fistula. These goals can be achieved either surgically or endovascularly.

To further characterize this extremely rare subgroup of fistulas, we identified 13 patients presenting with an SEAVF with perimedullary venous reflux to demonstrate their anatomic features and clinical and radiologic presentation.

MATERIALS AND METHODS

After obtaining permission from our local ethics board, we retrospectively evaluated the medical and radiologic reports of patients with an SEAVF diagnosed between January 2006 and February 2018 in RWTH Aachen University Hospital. All clinical data, including demographics and clinical presentation, were assessed by the treating physicians and re-evaluated for this study. In particular, we re-evaluated the neurologic status at time of admission to our institution, the duration of symptoms from onset until diagnosis, as well as previous misdiagnoses and treatment. The documented functional condition at time of discharge was rated as worse, stable, or improved.

All patients underwent spinal MR imaging ($n = 13$) and/or contrast-enhanced MRA (CE-MRA) ($n = 10$) before spinal angiography. Five (39%) of these 13 patients underwent repetitive DSA for a definite diagnosis. As a rather new technique, C-arm flat panel CT was performed in the last 5 patients of this cohort.

Radiologic data were analyzed blinded to all clinical data by both the first and last author. The first author is an interventional neuroradiologist with >30 years' experience in spinal angiography and spinal vascular diseases; the last author is a consultant neurosurgeon with a many years' experience in clinical, radiologic, and surgical aspects of spinal vascular diseases. A reference standard for statistical analysis was established in a consensus reading. We retrospectively evaluated the arterial supply, venous drainage patterns, and location and extension of the arterialized epidural pouch in our DSA findings of all included patients.

MR/CE-MRA Imaging

MR imaging was performed in 7 patients at 1.5T (Intera, Release 10:3; Philips Healthcare, Best, the Netherlands) and in 6 patients at 3T (Prisma; Siemens, Erlangen, Germany) ($n = 6$) as part of the routine clinical work-up. Sagittal T2- and pre- and postcontrast T1-weighted images were obtained as well as axial T2- and contrast-enhanced T1 images of the thoracolumbar region. In 1 patient, examination was limited to the lumbar and deep thoracic regions only. The craniocaudal extension of the T2 signal hyperintensity and the medullary contrast enhancement were qualified by the number of vertebral levels shown to be affected on T1 and T2 MR images. The appearance of the perimedullary veins was rated subjectively as mild, moderate, or prominent due to their tortuous and dilated appearance in the T1 and T2 images.

Contrast-enhanced MR angiography was performed on a clinical 1.5T MR imaging system with a phased array spine coil in 4 patients. To emphasize the arterial phase of the bolus enhancement relative to the venous enhancement, we sampled the *k*-space using elliptic centric ordering, which allowed separation into arterial and mixed arterial-venous enhancement. Further details about this CE-MRA technique have been previously described by our group elsewhere.[5,6]

In 6 patients, time-resolved angiography with stochastic trajectories was performed on a clinical 3T MR imaging system. This CE-MRA also divides *k*-space into 2 regions but samples them alternately using a semi-randomized method. It allows a rapid acquisition of multiple images during the passage of the contrast bolus.

DSA

Selective spinal DSA was performed via a femoral approach in a dedicated biplanar neuroangiographic suite (Artis zee biplane; Siemens). Standardized angiography included selective manual injections of 4–5 mL of 300 mg/mL of iodinated nonionic contrast medium into the lumbar and intercostal arteries. If the preceding MRA examination suggested the level of a SEAVF, DSA protocol included at least injection of the segmental arteries, on both sides, 1 level above and below the suggested level. Imaging was in the anteroposterior direction with 2 frames per second. Oblique and lateral views were added to depict the morphology of the AV shunt as well as the intradural course of the draining vein. Film sequences of at least 5–20 seconds were obtained. Furthermore, 3D C-arm conebeam CT acquisitions (so-called Dyna-CT; Siemens) were performed in the last 5 patients in this cohort with a total acquisition time of 8 seconds. The arterial injection for the conebeam CT angiogram allowed both early and late opacification throughout the acquisition. MPRs were performed using an external postprocessing workstation.

The extension of the epidural pouch, the arterialized perimedullary veins, and the location of the perimedullary veins (dorsal, ventral) were analyzed on the basis of CE-MRA and DSA.

RESULTS

Clinical Presentations

Ten (77%) of 13 patients were men. The mean age was 72 ± 8 years (median, 77 years; range, 59–83 years). Overall, 10 (77%) patients presented with a relatively short clinical course (<6 months) with progressive motor weakness in the lower extremities. The remaining 3 (23%) patients experienced a gradual onset and progressive deterioration of neurologic function. The mean interval between symptom onset and diagnosis was 6 ± 8 months (median, 3 months; range, 1–24 months) when excluding 1 statistical outliner in this series with a symptom duration of 60 months (Table 1).

The most common neurologic findings at admission in our institution were gait disturbances due to paraparesis in 12 (92%) patients. The remaining 1 (8%) patient had neurogenic claudication without manifest motor deficits. Eight (62%) patients reported sphincter dysfunction at admission to our institution. Sensory symptoms in various severities were documented in 7 (54%) patients and comprised diffuse loss of sensation and/or paresthesia in the lower extremities.

All 13 patients underwent microsurgical interruption at our center. Microsurgical dorsal lumbar decompressions and discectomies due to assumption of a spinal degenerative disease were

Table 1: Clinical presentation of patients with spinal epidural arteriovenous fistula

Patient No.	Age (yr)/Sex	Duration of Symptoms (mo)	Symptoms at Diagnosis	Status at Discharge
1	78, M	6	Paraparesis, sphincter dysfunction	Improved
2	63, M	1	Paraparesis, sphincter dysfunction hypesthesia below T10	Stable
3	77, M	1.5	Paraparesis, hypesthesia L4, ataxia, sphincter dysfunction	Stable
4	60, F	1.5	Paraplegia, hypesthesia disturbances below T10	Improved
5	68, F	24	Neurogenic claudication <100 m	Improved
6	77, M	1.5	Paraplegia, hypesthesia below L1, sphincter dysfunction	Stable
7	64, F	1	Paraparesis, sphincter dysfunction	Improved
8	83, M	60	Paraparesis , hypesthesia, sphincter dysfunction	Stable
9	72, M	0	Paraparesis, hypesthesia, sphincter dysfunction	Stable
10	80, M	12	Paraparesis, sphincter dysfunction	Stable
11	77, M	2	Paresis of left foot, ataxia	Stable
12	78, M	3	Paraparesis, hypesthesia	Stable
13	59, M	5	Ataxia	Stable

Table 2: Angiomorphologic characteristics of spinal epidural arteriovenous fistulas

Patient No.	Arterial Feeder[a]	Origin of Intradural Radicular Drainage Vein[a]	Extension of Epidural Pouch[b]	Extension of Arterialized Perimedullary Veins[b]	Location of Arterialized Perimedullary Veins[b]	No. of DSAs until Diagnosis
1	L3 R	L3 L	L3–L4	T8–T12	D = V	2
2	L3 bilateral, L4 L	L3 L	L2–L4	T3–T12	D = V	2
3	L1 R	L1 R	L1	ND	D < V	1
4	L3 bilateral	L3 R	L3	T9–L1	D > V	1
5	Left iliolumbar artery	S1	S1	T7–T12	D > V	3
6	T10 L and T11 L	L2 L	T 10–L3	T6–L1	D = V	3
7	L1 L	L2 L	L1–L2	T3–T12	D = V	1
8	T12 L	T12 L	T12 L	T11	D > V	3
9	L3 L	L3 L	L3 L	T6–T12	D < V	1
10	L4 R	L4 R	L2–L4	T3–T10	D = V	1
11	L3 L	S1 bilateral	L3–S1	T10–L1	D > V	1
12	L3 R	L3 R	L3 R	T9–T12	D < V	1
13	L1 R	L1 R	L1 R	T10–L1	D > V	1

Note:—D indicates dorsal to spinal cord; V, ventral to spinal cord; L, left; R, right; ND, no data.
[a] DSA.
[b] MRA/DSA.

performed elsewhere before a definite diagnosis in 3 (23%) of these 13 patients.

Radiologic Findings

Data of preoperative MR images were available in all 13 patients (Table 2). There was a centromedullary multisegmental T2WI hyperintense signal with involvement of the conus medullaris in all patients (mean, 7 vertebral levels; range, 1–13 vertebral levels). Intramedullary contrast enhancement was present in 10/12 (83%) patients (mean, 3 vertebral levels; range, 1–10 vertebral levels).

Enlargement and elongation of arterialized perimedullary veins in the thoracic and/or thoracolumbar region were detected in various manifestations in all patients, mild in 6 (50%), moderate in 3 (25%), and prominent in the remaining 3 (25%) patients. The arterialized perimedullary veins were localized predominately dorsal to the spinal cord in 5 (42%) and ventrally in 3 (25%). In the other 5 patients, arterialized perimedullary veins were observed dorsal and ventral to the spinal cord. In 9 (90%) of 10 patients who underwent CE-MRA before DSA at our center, the arterialized ventrolateral epidural pouch was additionally detected, triggering the diagnosis of an SEAVF.

In 5 patients, >2 DSA examinations were necessary to establish the diagnosis of SEAVF (Table 2).

Angiographically, 10 (77%) of the 13 fistulas were in the lumbar region, and 2, (15%) in the lower thoracic region below T10, respectively. The remaining (8%) fistula was located in the sacral region. The arterialized ventrolateral epidural pouch in 6 (46%) of 13 patients extended over several vertebral levels (mean, 2 vertebral levels; range, 1–3 vertebral levels). Multiple arterial feeders were detected in 3 (23%) patients.

Furthermore, the intradural radicular drainage vein originated in 3 (23%) patients distant from the level of the fistula-feeding segmental artery, ipsilaterally in 2, patients 6 and 7, and bilaterally in patient 11 (range, 1–3 vertebral levels) (Table 2).

DISCUSSION

Definition and Pathogenic Aspects of SEAVF

Arteriovenous disorders of the epidural venous plexus have been rarely reported in the literature.[2,7,8] Paraspinal AV shunts were first clearly described by Cognard et al[9] in 2 patients with retrograde filling of intradural veins. The first SEAVF in our institution was diagnosed in 2006 and reported elsewhere.[10] Since then, SEAVFs have been more frequently diagnosed in our center. The finding might reflect a better understanding of this particular vascular disorder as well as the growing diagnostic impact of spinal MR angiography.

The angioarchitecture, namely the feeding arteries, the venous

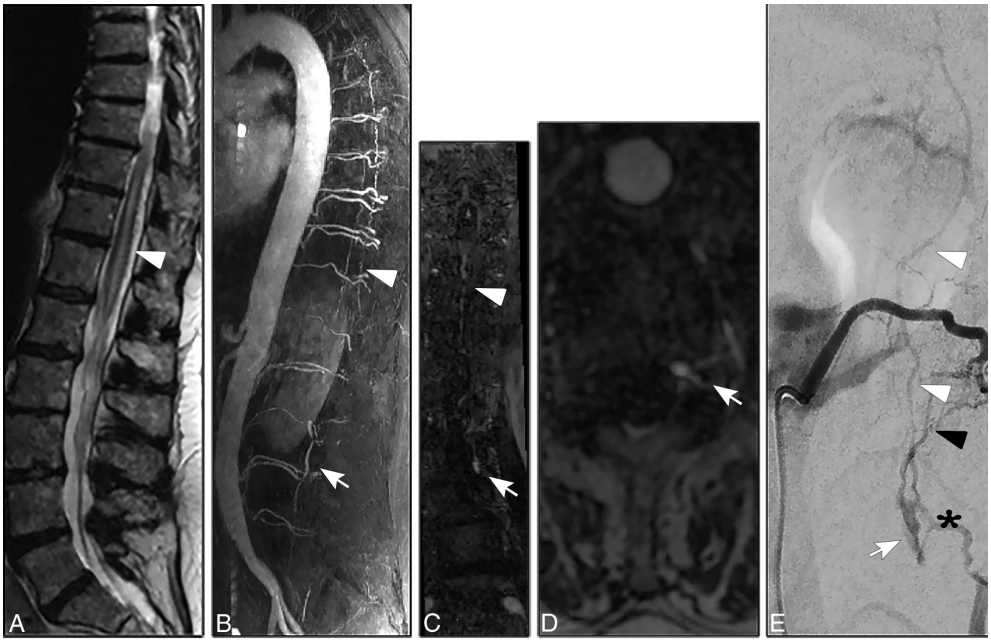

FIG 1. *A*, Sagittal T2- weighted images (3T; T2-TSE; slice thickness, 3 mm) reveal extensive congestive myelopathy (*white arrowhead*). *B–D*, Spinal CE-MRA (3T; time-resolved imaging with strochastic trajectories (TWIST); sagittal MIP; coronal and axial MPR) shows arterialized pouch in the lumbar ventrolateral epidural space (*white arrows*) in association with arterialized perimedullary veins in the thoracic region (*white arrowheads*) suspicious for a SEAVF in the lumbar region. *E*, DSA in lateral projection shows a SEAVF (*white arrow*) supplied via branches of the left L2 segmental artery (*black arrowhead*) and drained via the respective intradural radicular vein (*white arrowheads*). Note the extraspinal venous outlet (*asterisk*).

drainage pattern, and the location of the AV shunt itself, differentiate these SEAVFs from the more frequent SDAVF.[8]

Concerning the angioarchitecture in SEAVF, the blood supply of the epidural arterial arcade is usually derived from numerous osseous and epidural branches of the segmental arteries with multisegmental and/or collateral anastomoses running along the spinal epidural space.[7,11] In contrast, SDAVFs are usually supplied via radiculomeningeal branches of the radicular arteries, which run within the dural sleeve of the respective nerve roots.[12]

The venous drainage in SEAVF can occur epidurally and transdurally via an intradural radicular drainage vein into the perimedullary venous plexus, in contrast to the venous drainage in classic SDAVF, which occurs exclusively transdurally into the perimedullary venous plexus.[2]

Concerning the location of the AV shunt, the fistulous zone in all our patients was in the ventral and ventrolateral epidural spaces with variable craniocaudal extension of the arterialized epidural pouch along several vertebral levels (Fig 1).

In 1 patient, the epidural shunt was even more complex, crossing the midline; multiple compartments of the epidural plexus were filled ventrally as well as the contralateral intradural radicular vein on the same vertebral level (Fig 2).

The frequent ventral/ventrolateral location of the arterialized ventrolateral epidural pouch in an SEAVF could be explained by the rich venous anastomoses of the relatively wide ventral epidural space in the thoracic and lumbar regions.[13] The posterior venous plexus is not well-appreciated angiographically and is not regularly involved in any pathologic process.[3,14] In contrast to the SEAVF, the AV shunt in a classic SDAVF is usually located within the dural sleeve of the nerve root dorsolaterally in the thoracolumbar region and mainly ventrolaterally in the deep lumbosacral region.[5,15]

Nonetheless, the precise pathomechanism of the transdural venous drainage in both SDAVFs and SEAVFs is still unclear.[15,16] An anti-reflux-impeding mechanism between both the epidural and perimedullary venous systems has been a matter of dispute in various anatomic studies.[12,17-21] Tadié et al[17] reported an anti-backflow system within the transdural course of the radicular veins, resulting from narrowing and zigzagging of the vein walls while crossing the dura. Thron et al[12] differentiated 2 types of transdural venous courses: a slit-like and a zigzag bulgy type. Both types of transdural venous courses might act as a valve protecting against reflux from the epidural into the coronal venous plexus.[10,12] Nonetheless, due to the valveless venous walls of the epidural plexus, it is also conceivable that this anti-reflux mechanism might decompensate under high-pressure conditions and the venous blood could flow in either direction.[18,19,21-23] A retrograde filling of radicular veins from the epidural venous plexus has also been observed in a few anatomic studies.[10,12,17,19,24,25] Moreover, during spinal DSAs and epidural phlebography, epidural shunts without reflux into the perimedullary veins have been occasionally visualized.[15]

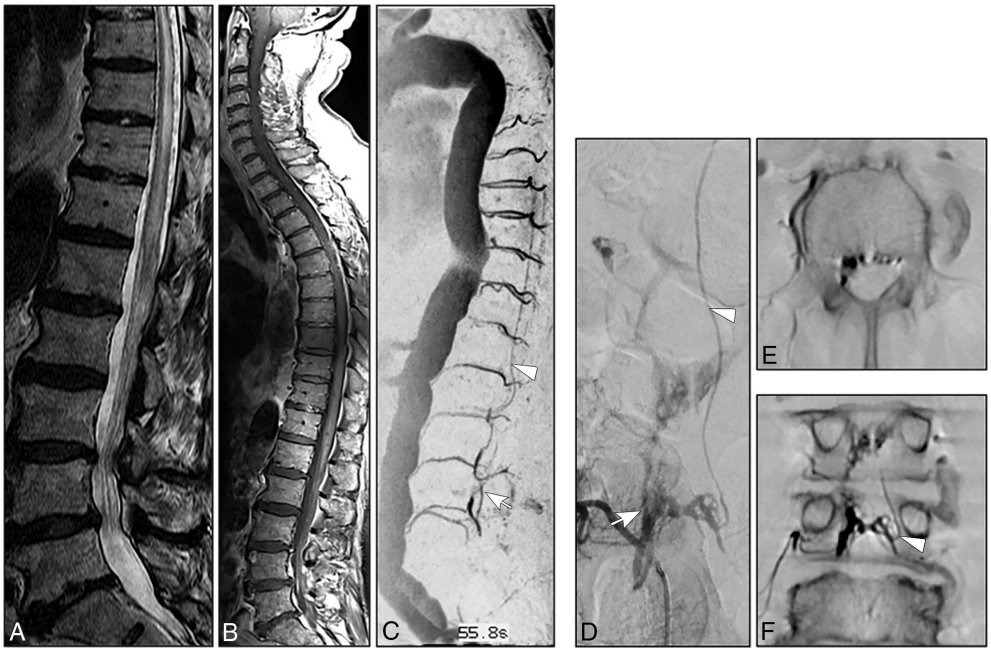

FIG 2. *A–B*, Sagittal T2- and contrast-enhanced T1-weighted images (3T; T2-TSE; T1-TSE; slice thickness, 3 mm) show extensive congestive thoracic myelopathy. *C*, Spinal CE-MRA (sagittal MIP) reveals an abnormal arterialized epidural pouch in the lumbar region (*white arrow*) in addition to thoracic arterialized perimedullary veins (*white arrowhead*). *D*, DSA (posteroanterior projection) exams identify the fistula in the epidural space on the vertebral level of L4 (*white arrow*), supplied via the right L4 segmental artery and drained by the contralateral L4 intradural radicular vein (*white arrowhead*). *E* and *F*, Axial and coronal MPR of DynaCT, 2 mm, 8 seconds rotation: Note the multisegmental and bilateral extension of the arterialized epidural pouch and the left sided origin of the intradural radicular drainage vein crossing the dura at the contralateral neural foramen (*white arrowhead*).

On the basis of these observations, one could assume that epidural shunts might occur more frequently than previously thought, but they often remain asymptomatic as long as the transdural anti-reflux mechanism remains intact.[10,12]

An intravenous stasis and/or acute hydrostatic disturbances within these arterialized elongated epidural compartments might reinforce the development of venous thrombosis. This may, in turn, induce acute disruption of the dural anti-reflux mechanisms causing transdural venous drainage and subsequent congestive myelopathy.[26] Supporting this hypothesis, the origin of the arterialized radicular vein in 3 (23%) patients in our series was caudal to the epidural AV shunt (Fig 3).

Clinical Presentation

Due to the extremely low incidence of SEAVFs, clinical presentations of these lesions have been rarely reported systematically in larger sample series.[14,27] Most patients in our study presented with motor weakness of the lower extremities, sphincter dysfunction, and sensory disturbances (Table 1) at admission. After treatment, clinical symptoms of most patients in our study stabilized or were mildly improved at discharge.[14,27] This result is in accordance with those in case series reported by Kiyosue et al[14] and Nasr et al.[27]

Due to the arterialization of the perimedullary venous plexus, several progressive pathophysiologic changes can occur in the spinal cord and its vessels, such as hyalinization, vascular calcification, necrosis, and gliosis, all potential contributors to irreversible functional deterioration of the spinal cord.[28-30]

One major finding in our current analysis was the relatively rapid clinical course of SEAVFs compared with classic SDAVFs. This might be triggered by acute hemodynamic changes of the venous outflow of the spinal cord caused by thrombosis and/or hydrostatic changes in the epidural and perimedullary venous plexus.[7]

Radiologic Findings

The hallmarks of SEAVFs on MR imaging in our current cohort were the following: 1) congestive thoracolumbar myelopathy with a high rate of conus medullaris involvement, 2) a predominantly nonprominent appearance of the pathologically arterialized perimedullary veins in most cases (75%), and 3) the presence of ventrally/ventrolaterally located arterialized epidural venous pouches detected in 9 of 10 patients with CE-MRA preceding DSA.

The value of CE-MRA in diagnosing an SDAVF has been previously reported by our group.[6] In a series of 19 patients with SDAVFs, the correct localization could be achieved in 14 (74%) patients. In the remaining 5 patients, a mismatch of only 1 vertebral level was noted.[6] Our current findings are supported by

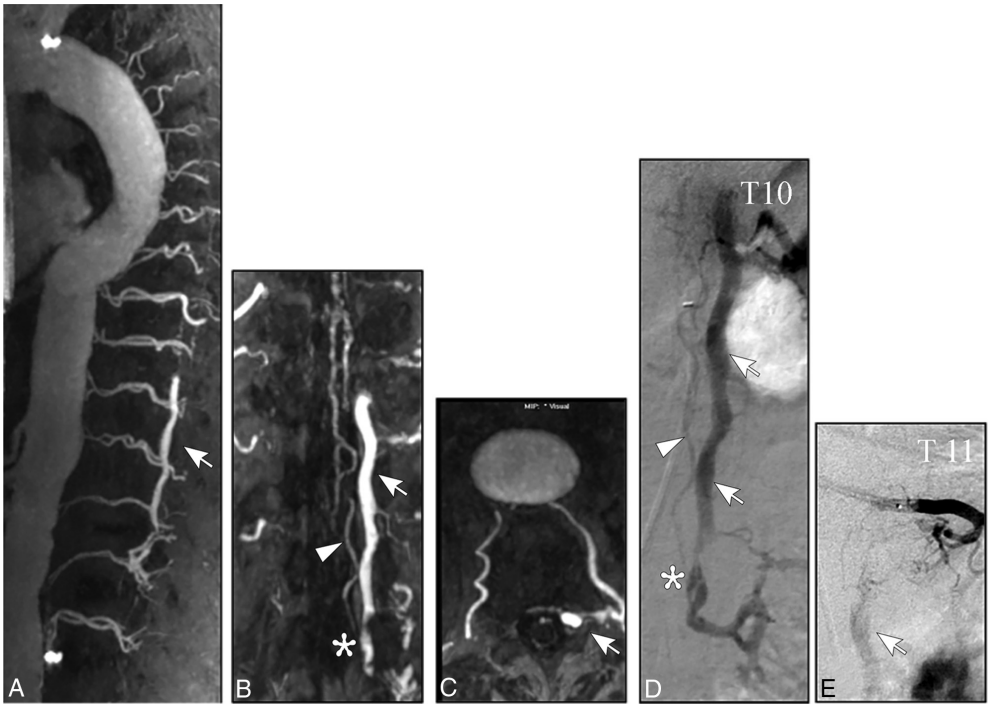

FIG 3. *A*, Spinal CE-MRA (1.5 T, sagittal MIP) reveals an extensive pathological arterialization of a ventrolateral epidural venous pouch extending over four vertebral levels (*white arrow*). *B–C*, Further reconstructions of the source MRA images (coronal and axial MPR) demonstrate precisely the epidural pouch (*white arrow*) and show the filling of the intradural radicular drainage vein (*white arrowhead*). *D–E*, DSA exams (posteroanterior projections) identify the multisegmental ventrolateral epidural pouch of the SEAVF (*white arrow*) with multiple left-sided arterial feeders supplied by the thoracic segmental arteries T 10 and T 11. Note the distant origin of the intradural radicular drainage vein (*asterisk*).

Mathur et al,[31] who recently observed, in a series of 7 patients with SEAVFs, a high accuracy and reliability of CE-MRA for identification and localization of these lesions.

DSA is, however, still regarded as a basic diagnostic tool for the angiomorphologic, pretherapeutic evaluation in spinal AV fistulas and malformations.[6,32-34] In 5 (38%) of 13 patients, even repetitive spinal DSA remained inconclusive and did not sufficiently depict the suspected AV shunt before referral to our center.

Based on our experience, reasons for this failure rate were insufficient opacification of the respective segmental artery based on atherosclerosis and anatomic obstacles and a too-short DSA series, resulting in missing the intradural radicular and/or perimedullary veins. Moreover, 4 of these 5 patients did not undergo spinal CE- MRA initially, which may have facilitated the diagnosis via subsequent DSA.

Spinal angiography offers a dynamic visualization of the angioarchitecture of vascular malformations, including the arterial feeders, the morphology of AV shunts/venous pouches, and the draining veins.[32]

Overall, 12 (92%) fistulas were located in the thoracolumbar region and were supplied by segmental arteries. The remaining (8%) fistula was located in the sacral region and was supplied by branches of the left iliolumbar artery. Also, multisegmental or collateral arterial feeders of the arterialized ventrolateral epidural pouch were present in 3 (23%) of our patients. In contrast, of 196 patients with SDAVFs treated at our center between 1990 and 2017, only 9 (4.6%) fistulas presented with a multisegmental or bilateral arterial supply.[5,35]

The predominant thoracolumbar location of SEAVFs and the higher rate of multiple arterial feeders of SEAVFs compared with classic SDAVFs could also be explained by the wide epidural space and the rich epidural anastomotic arterial network in this region.[3,7,13]

The arterialized epidural pouch extended over several vertebral levels in 6 (46%) patients. The intradural radicular drainage vein in 3 of these 6 patients was distant from the epidural fistulous point. This multisegmental distance between the fistulous feeding artery and the origin of the intradural radicular drainage vein has never been previously observed in any classic SDAVF at our center.[15,35]

Because the main goal of treatment of SEAVF is the disconnection of the intradural radicular drainage vein as well as the complete interruption of arterialized epidural compartments, the precise localization of the intradural radicular drainage vein in SEAVF is essential to reduce the risk of residual or recurrent fistulas irrespective of the treatment technique and strategy.

Limitations

A major limitation of our study is the small sample size and the retrospective approach. Because spinal epidural arteriovenous fistulas are a very rare but clinically relevant entity, our results may, nevertheless, serve as an orientation for future studies, in particular because there are scarce data concerning this topic in large cohorts in the literature.

CONCLUSIONS

Congestive myelopathy with an acute or subacute clinical course is a dominant finding in SEAVFs. The presence of myelopathic symptoms combined with medullary venous congestion with or without contrast enhancement on MR imaging should require CE-MRA, even in cases of nonprominent perimedullary veins. In SEAVFs, CE-MRA is a powerful noninvasive diagnostic tool to identify the epidural AV shunt itself and detect arterialized perimedullary veins. DSA remains obligatory for the angiomorphologic analysis of the epidural AV shunt, which frequently extends ventrolaterally over several vertebral levels. DSA is mandatory for identifying the origin of the intradural radicular drainage vein that may be located distant from the epidural fistulous point.

Disclosures: Ahmed Othman—*UNRELATED*: *Grants/Grants Pending*: Bayer Healthcare, unrestricted grant*; *Payment for Lectures Including Service on Speakers Bureaus*: GE Healthcare, speakers bureaus. Gerrit Alexander Schubert—*UNRELATED*: *Payment for Lectures Including Service on Speakers Bureaus*: Braun Aesculap. *Money paid to the institution.

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ORIGINAL ARTICLE

Anticoagulation Therapy After Surgical Treatment of Spinal Dural Arteriovenous Fistula. Effectiveness and Long-Term Outcome Analysis

Fidaa Jablawi[1,2], Gerrit Alexander Schubert[3], Franz-Josef Hans[3,4], Michael Mull[1]

■ OBJECTIVE: **Effectiveness and safety of anticoagulation therapy (AC) after treatment of spinal dural arteriovenous fistula (sdAVF) are still inadequately discussed in the literature and are addressed in this study.**

■ METHODS: **We retrospectively analyzed our medical database for patients with sdAVF treated in our institution between 2006 and 2016. Neurologic status at time of admission, discharge, and last follow-up was assessed via Aminoff-Logue disability score.**

Patient cohorts were dichotomized as group A (postoperative therapeutic heparinization) and group B (routine thromboembolic prophylaxis with low-dose heparin).

■ RESULTS: **Fifty-three patients were included in this analysis. In group A ($n = 11$), no acute deterioration was reported. In group B ($n = 42$), 4 patients developed acute postoperative deterioration; therapeutic AC was initiated in all 4 patients resulting in complete neurologic recovery within the inpatient stay. However, the incidence of postoperative deterioration did not reach statistical significance between treatment groups ($P = 0.57$).**

Data of 40 patients were available for long-term analysis (mean, 53.4 ± 36 months). Neurologic status did not differ significantly between both groups at time of admission ($P = 0.093$), discharge ($P = 0.723$), and last follow-up ($P = 0.222$).

■ CONCLUSIONS: **Acute postoperative deterioration in patients with sdAVF is a clinically relevant complication and was present in 7.5% of patients in our series. Although routine therapeutic AC did not decrease the rate of acute deterioration significantly, our findings imply that therapeutic AC in cases of acute postoperative deterioration might be a safe and efficient treatment option.**

INTRODUCTION

Initial symptoms of sdAVF usually comprise sensorimotor disturbances, gait difficulties, sphincter dysfunction, and less frequently, radicular pain.[1,2] Because of the nonspecific nature of their signs and symptoms, sdAVFs are often misdiagnosed as spinal degenerative disease, peripheral neuropathy, transverse myelitis, or medullar neoplasm.[3-5]

Since the first description of sdAVF by Aminoff and Logue in 1974, several explanations for the underlying cause have been provided.[4,6-9] However, medullar venous congestion was considered to be the most important pathophysiologic mechanism inducing myelopathic symptoms.[10] In the presence of an arteriovenous (AV) shunt, various pathologic changes have been observed in the draining veins and the coronal venous plexus, including progressive fibrosis and thrombosis.[7,11,12] Also,

Key words
- Heparinization
- Long-term outcome
- Spinal arteriovenous malformation
- Surgical treatment

Abbreviations and Acronyms
AC: Anticoagulation therapy
AL: Aminoff-Logue
AV: Arteriovenous
DSA: Digital subtraction angiography
LMWH: Low-molecular-weight heparin
MRI: Magnetic resonance imaging
PTT: Partial thrombin time
sdAVF: Spinal dural arteriovenous fistula
UFH: Unfractionated heparin

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microvascular thrombosis has been detected frequently in the spinal cord parenchyma of patients with sdAVF.[13]

The complete interruption of the respective draining vein should be the main goal of treatment.[3,14] Nonetheless, acute postoperative deterioration is a rare and thus understudied phenomenon in these patients.[10,15] The rapid development of microthrombosis in the coronal venous plexus immediately after disconnection of the fistula was considered to induce acute functional deterioration.[15] Based on this hypothesis, various studies recommended the use of anticoagulation (AC) after treatment of sdAVF.[15,16] However, the role of postoperative AC is still insufficiently studied. It is the purpose of this study to present our single-center experience and evaluate the effectiveness and safety of immediate postoperative AC therapy in microsurgically treated patients with sdAVF as a treatment approach for possible acute deterioration and/or acceleration of neurologic recovery.

METHODS

Patients

After obtaining permission from our local ethics board, we retrospectively analyzed our prospectively maintained medical database for all patients treated in our institution for angiographically verified sdAVF between June 2010 and February 2016. The diagnosis of sdAVF in these patients is based on clinical and radiologic criteria comprising 1) myelopathic symptoms including motor and/or sensory disturbances with or without vegetative bladder-bowel dysfunctions, 2) magnetic resonance imaging (MRI) findings of medullar edema, medullar contrast enhancement, and/or engorged perimedullary veins, and 3) angiographic verification of sdAVF. All clinical data including demographics, clinical and neurologic presentation, and surgery reports as well as clinical and radiologic follow-up data were assessed by the treating physicians and re-evaluated for this study.

We dichotomized our cohort regarding the administration of AC as follows:

1) therapeutic treatment group (A): routine postoperative therapeutic AC.
2) prophylactic group (B): routine thromboembolic prophylaxis only.

The therapeutic AC was performed empirically and based on the individual surgeon's preference. In general, that was considered standard operating procedure at the time, but was changed later, resulting in the 2 cohorts described in our current study.

Surgical Treatment

The microsurgical procedure was performed under general anesthesia in the prone position. The level of the fistula was verified with intraoperative fluoroscopy. A partial or total hemilaminectomy at the marked level was performed to explore the dura and the respective nerve root at the site of the fistula. A paramedian dural incision was then made, followed by microscopic verification of the arterialized draining vein and confirmation of arterialization via intraoperative Doppler sonography and indocyanine green angiography. The arterialized vein was then coagulated and disconnected from the dura, followed by watertight dural closure. In cases of extradural hypervascularization of the radicular and/or periradicular dura, the respective fistular area was also coagulated extradurally.

AC Therapy

In the therapeutic treatment group (A), patients received therapeutic AC with parenteral unfractionated heparin (UFH) aimed at a partial thrombin time (PTT) of 40–50 seconds or high-dose weight-adjusted low-molecular-weight heparin (LMWH) (1 mg/kg body weight twice a day) initiated within 3 hours after surgery. We controlled PTT 12 hours after initiating the therapeutic AC and then on a daily basis and adapted according to the goal PTT.

In the prophylactic group (B), all patients received routine postoperative antithrombotic prophylaxis via low-dose LMWH (40 mg/0.4 mL) only, initiated on the first postoperative day. In cases of acute postoperative deterioration, patients received secondary therapeutic AC via UFH (goal PTT of 40–50 seconds).

Outcome and Follow-Up

After surgery, all patients received neurologic examinations on a daily basis. All patients underwent postoperative MRI routinely within 1 week after surgery. Early postoperative digital subtraction angiography (DSA) was performed only if intraoperative findings did not confirm complete fistula interruption. Additional follow-up analysis was performed via telephone survey with an overall

Table 1. Demographic and Clinical Findings of Both Therapeutic and Prophylactic Treatment Groups

Patients	All Patients (n = 53)	Therapeutic Group (A, n = 11)	Prophylactic Group (B, n = 42)	Statistical Significance (*P* Value)
Age (years)	67.1 ± 11	67.45 ± 10	67 ± 11	0.637
Sex (female/male)	15:38	3:8	12:30	0.932
Duration of symptoms (months)	19.8 ± 23	15.45 ± 19.58	20.97 ± 24.63	0.385
AL score at time of diagnosis	2.83 ± 1.5	3.1 ± 1.4	2.73 ± 1.5	0.093
Acute postoperative deterioration	4 (7.5%)	No patients	4 patients	0.57
AL score at time of discharge	2.34 ± 1.2	2.28 ± 1.5	2.36 ± 14	0.723
AL score at time of follow-up	2.42 ± 1.8 (n = 40)	2.7 ± 1 (n = 7)	2.36 ± 2 (n = 33)	0.222

AL, Aminoff-Logue.

Table 2. Clinical Findings of Patients with Acute Postoperative Deterioration After Surgical Treatment of Spinal Dural Arteriovenous Fistula

Case Number	Clinical Presentations		Anticoagulation Therapy, Duration (Days)	Outcome at Time of Discharge
	At Time of Admission	Early Postoperative		
1	Mild ataxia	Paraparesis 4/5, dysesthesia, mild ataxia, mild bladder dysfunction	UFH, 6	Unchanged to pretreatment
2	Distal accentuated paraparesis 3/5, ataxia, bladder dysfunction	Paraparesis 1/5, transverse sensory disturbance T10, bladder dysfunction	UFH, 8	Unchanged to pretreatment
3	Distal accentuated paraparesis 4/5, ataxia	Proximal accentuated paraparesis 2/5	1) UFH, 7 2) UFH, 8	Unchanged to pretreatment
4	Paraparesis 3/5, hypesthesia	Paraparesis 2/5, dysesthesia	UFH, 7	Unchanged to pretreatment

UFH, unfractionated heparin.

mean follow-up period of 52.7 ± 36.8 months (median, 53.5; range, 3–156 months).

The Aminoff-Logue (AL) disability score was used to evaluate the functional condition at the time of admission (pretreatment), at the time of discharge, and at the time of our telephone survey. In cases of otherwise unrelated death, functional status before death was determined by discussions with family members.

Statistics

Pearson's χ^2 test and Fisher exact tests were used as applicable. Student t test and Mann-Whitney U test were used depending on modality of data distribution as tested for by Shapiro-Wilk test. P values with an α level $\leq$0.05 were defined as significant. All statistical analyses were performed with SPSS version23 software (IBM Corp., Armonk, New York, USA).

RESULTS

Of 59 patients with sdAVF diagnosed and treated in our institution within the specified time period, 6 were excluded from this analysis because of incomplete medical records.

The occlusion rate based on postoperative MRI/magnetic resonance angiography follow-up examinations after initial surgical interruption of sdAVF was 98% in our cohort. Only 1 patient was found to have a residual fistula on early postoperative DSA, which was occluded surgically 2 days after the initial operation. Procedure-related complications were observed in 3 patients (6%). Two patients developed wound infection and 1 patient was treated for postoperative cerebrospinal fluid leakage.

Acute postoperative deterioration of the pretreatment neurologic status was observed in 4 patients (7.5%) in our series. No complications associated with AC were observed.

The data of 40 patients were available for long-term outcome analysis, with 13 patients lost to follow-up as a result of unregistered changes of address or telephone number (Table 1).

Therapeutic Treatment Group (A)

Eleven patients had therapeutic AC (mean duration, 7.2 ± 0.8 days; range, 6–8 days). No AC-related complications were reported during the inpatient stay.

Early outcome analysis showed improvement of AL score for gait in 4 (36%) and unchanged AL score in 7 patients (63.6%) at

Table 3. Initial Neuroradiologic Findings of Patients with Acute Postoperative Deterioration After Surgical Treatment of Spinal Dural Arteriovenous Fistula

Case Number	Sex/Age (Years)	Preoperative Finding				
		Fistula Location	Adamkiwiecz Artery	Medullar Contrast Enhancement	Medullar Edema	Enlargement of Perimedullar Veins
1	M, 66	T11 L	L1 R	T10-L1	T6-L1	T11-L1
2	M, 67	T11 R	Not identified*	T8-L1	T3-L1	T3-L1
3	M, 69	L2 L	L1 L	No contrast enhancement	No edema	T5-L1
4	M, 81	T12 L	T12 L	T8-L1	T5-L1	T11-T 12

M, male; L, left; R, right.
*Adamkiewicz artery was not identified in the thoracolumbar region from T7 to L1.

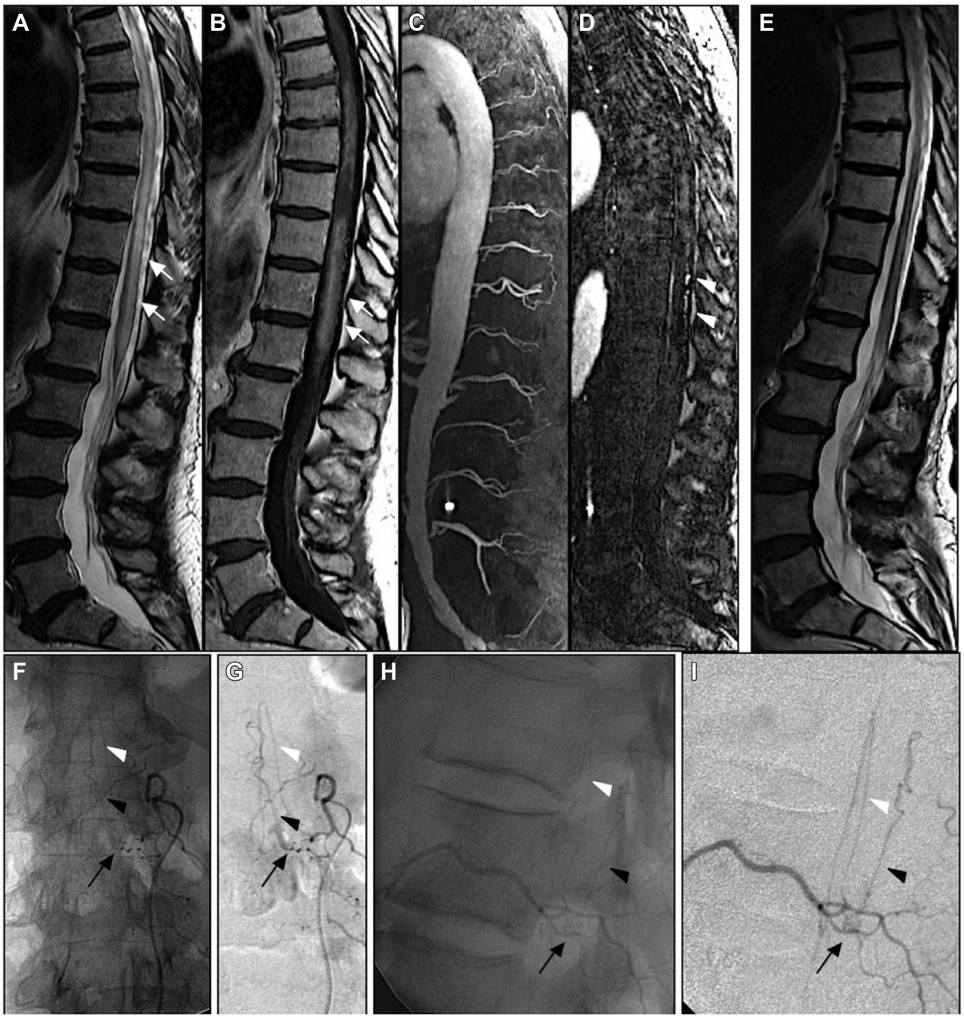

Figure 1. Preoperative magnetic resonance imaging (**A**, **B**) shows congestive myelopathy (T2) and medullar contrast enhancement (T1) at the level of the thoracolumbar junction (*narrow white arrows*). (**C**, **D**) Contrast-enhganced magnetic resonance angiography shows an arterilized perimedullar vein at vertebral level T10 to T12 (source images; **D**, *white arrowheads*). (**E**) Follow-up T2-weighted magnetic resonance imaging shows significant reduction of myelopathy. (**F**–**I**) Pretreatment spinal digital subtraction angiography identifies the fistula point (*black arrows*) at the level of the left T12 nerve root with the respective drainage vein (*black arrowheads*). The Adamkiewicz artery arises at the same level and side of the identified fistula (*white arrowheads*).

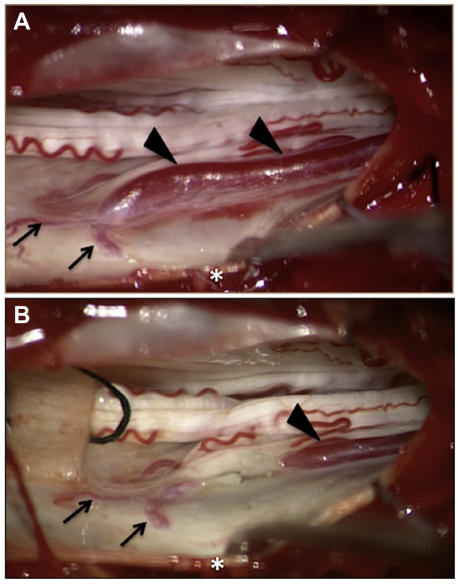

Figure 2. Intraoperative images show the draining radicular vein of a spinal dural arteriovenous fistula (*black arrowheads*) localized dorsolaterally to the left T11 nerve root before (**A**) and after (**B**) microsurgical interruption. The arteriovenous shunt is supplied via radiculomeningeal branches (*black arrows*, dura, *asterisk*) of the left T11 segmental artery. Note the decreased diameter of the proximal segment of the draining vein after microsurgical disconnection. (**B**, *black arrowhead*).

the time of discharge, compared with the pretreatment status. None of the patients developed acute postoperative deterioration.

For long-term analysis, data of 7 patients (64%) were available in this group. Mean long-term follow-up was 73.9 ± 16 months (median, 76; range, 53–97 months). At the time of last follow-up, 3 patients (43%) reported further gait improvement, 2 patients (29%) were unchanged, and another 2 patients (29%) reported late functional deterioration of gait.

Prophylactic Group (B)

A total of 42 patients were included in this group. Four of these 42 patients developed acute deterioration within the first 2 postoperative days (mean, 0.75, range; 0–2 days) (Table 2), but the difference between group A and B did not reach statistical significance ($P = 0.57$) (Table 1). Secondary therapeutic AC (UFH, PTT of 40–50 seconds) was initiated in all 4 patients with acute deterioration, immediately after exclusion of hemorrhage via emergency MRI. Neurologic deterioration resolved completely within a few days after therapeutic AC (mean, 6.8 ± 1.2 days; range, 5–8 days). One patient (case 3) developed secondary aggravation of his paraparesis 3 days after termination of secondary therapeutic AC, which in turn resolved completely after restarting AC. At the time of discharge, all 4 patients presented an unchanged neurologic status compared with the pretreatment status.

At the time of discharge ($n = 42$), the gait had improved in 19 patients (45%) and was unchanged in 23 patients (55%). At long-term follow-up ($n = 33$; mean, 48.2 ± 39.4 months; median, 34 months; range, 3–156 months), 17 patients (51.5%) reported gait improvement, 11 patients (33.3%) were unchanged, and 5 patients (15%) reported late deterioration of their gait disturbances.

Neurologic status did not differ significantly between group A and B at the time of admission ($P = 0.093$), discharge ($P = 0.723$), and last follow-up ($P = 0.222$) (Table 2).

DISCUSSION

The aim of treatment of sdAVF is the reduction of medullar venous congestion via disconnection of the AV shunt, by surgical interruption and/or endovascular embolization.[14,16,17]

The occlusion rate in our recent series was 98% after initial surgery. Our results were comparable to those provided in the literature: Saladino et al.[18] reported complete surgical obliteration in 146 of 154 patients with sdAVF (94.8%). In a large meta-analysis of 16 studies, Steinmetz et al.[19] reported a success rate of 97.9% for surgical treatment. Thus, in our center, surgical interruption is the fist-line treatment for sdAVF, with reported endovascular occlusion rates in the literature ranging from 46% to 89.5% and a higher rate of recurrences.[16,19-22] Regardless of the treatment strategy, the posttreatment clinical course is usually variable.[18,20,23] Supplementary therapy with beneficial influence on the clinical course in these patients has not yet been identified. The administration of steroids postoperatively has been discussed previously in several studies, but various investigators have observed a higher incidence of acute posttreatment deterioration with administration of steroid therapy in these patients.[24-26]

Postoperative low-dose heparinization via UFH as well as weight-adjusted LWMH administration have been regarded to be effective and safe for prophylaxis and/or treatment of venous thromboembolism after neurosurgical procedures without an excessive bleeding risk.[27,28] However, the use of AC therapy after fistula occlusion in particular is a well-known practice and a plausible treatment approach given the risk of rapid thrombosis of all affected vasculature.[15,16] However, this particular treatment issue is still insufficiently studied.

Therapeutic AC was performed in our center empirically and based on the individual surgeon's preference after surgical treatment of patients with sdAVF.

In our series, we observed no acute postoperative deterioration or AC-related complications in patients receiving therapeutic AC (group A). In group B, 4 of 42 patients developed an acute postoperative deterioration within the first 2 postoperative days, but the difference was not statistically significant. Therapeutic AC was initiated in all patients with acute postoperative deterioration, resulting in a resolution of neurologic symptoms within a few days after AC.

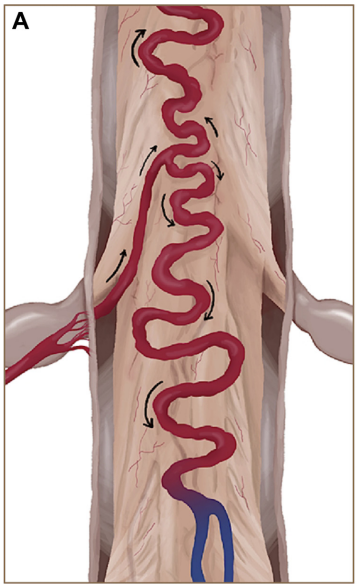

Figure 3. Graphic representation of a spinal dural arteriovenous fistula in the thoracolumbar region, (**A**) before interruption of the arterialized draining vein with a blood flow in cranial and caudal direction in the perimedullar veins (*black curved arrows*), (**B**) after coagulation of the proximal segment of the draining vein (*black arrow*) with possible thrombosis and/or stasis in this segment and additional hemodynamic changes of the venous blood flow in the perimedullar veins.

The pathomechanisms of acute deterioration after fistula interruption have been discussed in a few reports.[16,22,29,30] Criscuolo et al.[10] hypothesized that in the prone position, a transmission of the increased intra-abdominal and intrathoracic pressure to the spinal venous system could increase the medullar venous congestion and subsequently the risk of additional cord injury during surgery. Even more complex anatomic predispositions and local hemodynamic changes could also contribute to the acute postoperative deterioration. In 1 patient with acute postoperative deterioration in our series (Table 3, case 4), the origin of the Adamkievicz artery was located on the same side of the fistula-supplying radicular artery (Figure 1). In case 3, the Adamkiewicz artery was identified 1 vertebral level below the fistula zone. Thus, it is conceivable in these cases that vasospasm of the Adamkiewicz artery might have been induced through surgical manipulation and/or coagulation, resulting in additional acute disturbance of the arterial blood supply of the spinal cord.

In case 1, the Adamkiewicz artery was localized on the contralateral side and 2 vertebral segments above the verified sdAVF. In case 2, selective angiography of the segmental arteries from T7 to L1 showed no evidence for the Adamkiewicz artery in the respective levels (Table 3), making local vessel constriction a potential but not the sole contributor to neurologic worsening.

In 3 of these 4 patients, an extensive medullar congestion and edema (75%) with a mean extension of 9.3 ± 1.5 vertebral levels (range, 8–11 vertebral levels) (Table 3, cases 1, 2, and 4) was observed in the pretreatment MRI.

Because the spinal cord drains mainly through small-caliber radiculospinal veins, venous drainage may become sensitive to acute hemodynamic alterations in the coronal venous plexus.[31]

Hassler et al.[15,32] observed in an intraoperative study that even although no blood flow was detectable in the large draining veins after fistula occlusion, these veins did not collapse completely and a residual intravenous pressure remained measurable (Figure 2). Thus, it is conceivable that this hemodynamic situation could, in turn, predispose the dilated valveless perimedullar veins to stasis and/or microthrombosis provoking a secondary increase of the medullar venous pressure (Figure 3). Supporting this theory, case 3 in our series redeteriorated 3 days after terminating the postoperative AC and recovered completely after AC was initiated again. Furthermore, few case reports have shown the occurrence of acute deterioration after endovascular embolization of sdAVF.[22,29,30] All these cases were treated successfully with AC,

based on the assumption of a postinterventional thrombosis in the venous system of the spinal cord.[30]

Based on these observations, we assume that in surgically treated patients 1) the prone position during surgery, associated with an elevated systemic venous pressure, could increase the preexisting medullar venous hypertension; and 2) the subsequent disconnection of the AV shunt could, in addition, lead to acute changes of the microcirculation and/or to development of microthrombosis in the dilated and engorged perimedullar veins. Moreover, patients with preexisting extensive venous congestion might be more sensitive to such acute hemodynamic changes.

Thus, AC therapy in these patients might sustain venous outflow of the spinal cord and reduce thereby the risk of additional acute medullary compromise. In addition, shortening of operating time may reduce the risk of probable additional medullar injury as a result of increased systemic venous pressure in prone position. This factor should be considered particularly in patients with extensive medullar venous congestion.

Our study provides a comparison of long-term outcome of patients with and without therapeutic AC after microsurgical interruption of sdAVF. Routine therapeutic AC did not result in a significant improvement of functional outcome during hospitalization or during long-term follow-up, and neurologic results overall were in accordance with other reports.[19,33]

The rate of gait improvement reported in various microsurgical studies with follow-up times <100 months ranged between 38% and 67%.[14,16,33,34] It was also presumed that long-term outcome of patients with sdAVF is predicted by the age of the patients at time of diagnosis, the duration of symptoms before diagnosis, and the severity of pretreatment neurologic disabilities.[22,33,35] Moreover, the long-term deterioration after treatment of sdAVF is a described phenomenon in the literature and has been observed in 7 of 40 patients (18%) who were eligible for long-term follow-up in our recent series.[20,23] In their long-term analysis with >100 months of follow-up, Tacconi et al. reported a late deterioration in 65% of patients, whereas only 10% improved and 25% were unchanged. These investigators suggested generalized hemodynamic abnormalities of the spinal cord vessels together with the effects of age on a previously compromised cord.[20,23]

Microsurgical treatment of sdAVF is an effective and safe treatment modality.[16] Although the sample size is too small to draw a definite conclusion, our findings imply that the use of AC therapy might be safe and effective in treating patients with acute postoperative deterioration after fistula occlusion. However, routine postoperative AC does not influence functional improvement at time of discharge or at time of long-term follow-up.

Limitations

A major limitation of our study is the small sample size and the retrospective approach with an inherent interpretational bias. Because sdAVF is a rare but clinically relevant entity, our results may nevertheless serve as an orientation for future supplementary treatment options and algorithms.

CONCLUSIONS

Acute postoperative deterioration of patients with sdAVF is a clinically relevant complication after surgical treatment and was present in 7.5% of patients in our series. Routine therapeutic AC might not reduce the risk of acute postoperative deterioration significantly or influence the long-term outcome. However, our findings imply that AC might be a safe and effective treatment option in reversing acute postoperative deterioration, possibly by sustaining venous microcirculation and outflow of the spinal cord.

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ORIGINAL RESEARCH
SPINE

Long-Term Outcome of Patients with Spinal Dural Arteriovenous Fistula: The Dilemma of Delayed Diagnosis

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ABSTRACT

BACKGROUND AND PURPOSE: The impact of various radiologic and clinical features on the long-term outcome in spinal dural arteriovenous fistulas is still unclear; thus, they are the purpose of this study.

MATERIALS AND METHODS: We retrospectively analyzed our medical data base for all patients treated for spinal dural arteriovenous fistula in our institution between 2006 and 2016. Patient age, neurologic status at the time of diagnosis, the duration of symptoms from onset to diagnosis, and follow-up information were evaluated. The extent of medullary T2WI hyperintensity, intramedullary contrast enhancement, and elongation of perimedullary veins on MR imaging at the time of diagnosis were additionally analyzed.

RESULTS: Data for long-term outcome analysis were available in 40 patients with a mean follow-up of 52 months (median, 50.5 months; range, 3–159 months). The mean age at the time of diagnosis was 69.27 ± 9 years (median, 71 years; range, 53–84 years) with a male predominance ($n = 32$; 80%). The mean duration of symptoms was 20.2 months (median, 10 months; range, 1–120 months). Shorter duration of symptoms at the time of diagnosis was significantly correlated with better outcome of symptoms ($P < .05$).

CONCLUSIONS: Spinal dural arteriovenous fistulas are characterized by interindividually variable clinical presentations, which make a determination of specific predictors for long-term outcome more difficult. Fast and sufficient diagnosis might result in a better outcome after treatment. The diagnosis of spinal dural arteriovenous fistula remains markedly delayed, reflecting an ongoing lack of knowledge and awareness among treating physicians of this rare-but-serious disease.

ABBREVIATIONS: AL-score = Aminoff-Logue disability score; CE-MRA = contrast-enhanced MRA; sdAVF = spinal dural arteriovenous fistula

Spinal dural arteriovenous fistulas (sdAVFs) usually become symptomatic in elderly men, who are affected 5 times more often than women.[1] Symptoms caused by sdAVF comprise gait disturbances with or without paresis, sensory disturbances in the lower extremities, pain, and sphincter and erectile dysfunctions.[2] An estimation based on a series assessed previously in RWTH Aachen University Hospital revealed an incidence rate for sdAVF of up to 5–10 million per year in the general population.[3]

The predictive value of several radiologic and clinical factors in patients with sdAVF has been controversially discussed in the past.[4,5] The existence of a plethora of case series implies a lack of universal consensus on possible predictors for long-term outcome.[5]

Because sdAVF is a particularly rare disease and is frequently misdiagnosed for several months to years, gathering a sufficient number of patients for a meaningful analysis is an inherent challenge. At the same time, gathering long-term outcome data of a predominantly elderly and comorbid patient population is associated with several logistic difficulties. Moreover, a comparative analysis of various studies to dramatically increase sample size is hampered by relevant variations in diagnostic and therapeutic strategies in different referral centers.[3,5] Thus, our current study aims to fill this gap by providing clinical and radiologic features as well as follow-up information of a considerable cohort of microsurgically treated sdAVFs.

MATERIALS AND METHODS

We retrospectively analyzed our medical data base for all patients treated for sdAVF at RWTH Aachen University Hospital between 2006 and 2016.

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Aminoff-Logue disability score for gait

Grade of Gait Disturbances	Characteristics
0	Normal
1	Leg weakness, abnormal walk or stance, but no restriction of activity
2	Restricted activity
3	Requiring 1 cane for walking
4	Requiring 2 canes, crutches, or walker
5	Confined to wheelchair

The diagnosis of sdAVF was performed on the basis of the following criteria: 1) myelopathic symptoms, including gait disturbances with or without vegetative urinary dysfunctions; 2) findings of congestive myelopathy with or without engorged perimedullary veins on MR images; and 3) angiographic confirmation of an sdAVF.

Clinical data including patient age, neurologic status at diagnosis, and duration of symptoms from onset to diagnosis were assessed by the treating physicians and re-evaluated for this study. Radiologic data were electronically available and reviewed accordingly. Clinical data were obtained by chart review and/or telephone survey.

We routinely aim to perform an early postoperative MR imaging during the inpatient stay, 3–6 months after discharge, and annually in the first three years after treatment for all patients with sDAVFs. In case of persistence or deterioration of clinical symptoms and/or radiologic findings indicative of congestive myelopathy, we additionally perform spinal MRA and DSA to rule out residual or recurrent fistulas.

Neurologic status at time of diagnosis and at last follow-up was assessed using the Aminoff-Logue disability score for gait (AL-score) (Table).[6] The long-term outcome was assessed on the basis of changes of the AL-score across time and was rated as improved, stable, or aggravated. To analyze the significance of the duration of symptoms on long-term outcome, we categorized the time from onset to diagnosis as follows: 1) ≤6 months, 2) 7–18 months, and 3) > 18 months. The extent of medullary edema, intramedullary contrast enhancement, and engorgement of perimedullary veins on MR imaging at diagnosis was recorded and rated according to the number of affected vertebral levels. The location of the sdAVF verified by spinal DSA was categorized as follows: 1) thoracic: T3–T9; 2) thoracolumbar: T10–L4; and 3) deep lumbosacral: below L4.[7]

Statistics

Data were expressed as means ± SD and median and range. Correlation analysis and group comparisons were performed with nonparametric statistics. Data analysis was performed with SPSS Statistics for Windows, Version 25.0 (IBM, Released 2017, Armonk, New York.)

RESULTS

A total of 59 patients with sdAVFs were identified. Data for long-term outcome analysis were available in 40 patients, with the remaining 19 patients being lost to follow-up due to unknown changes of address ($n = 11$) or incomplete clinical and radiologic data ($n = 8$). Twenty-eight (70%) of these 40 patients were referred to our center from elsewhere due to clinically and radiologically suspected spinal arteriovenous pathology with nonconclusive MR imaging and/or DSA examinations. All 28 patients underwent at least 1 spinal MR imaging, and 17 of them underwent at least 1 spinal DSA before admission to our institution.

After angiographic visualization of the sdAVF in our center, all 40 patients were treated via microsurgical disconnection of the intradural drainage vein. Only 1 patient was found to have a residual fistula on early postoperative DSA, which was occluded surgically 2 days after the initial operation. Procedure-related complications were observed in 2 (5%) patients. One patient developed a wound infection, and 1 patient was treated for postoperative CSF leakage.

Clinical Features

The mean age at diagnosis ($n = 40$) was 69.27 ± 9 years (median, 71 years; range, 53–84 years) with a male predominance ($n = 32$, 80%). The mean duration of symptoms from onset to diagnosis was 20.2 months (median, 10 months; range, 1–120 months). Gait disturbances were present in all 40 patients. Paraparesis was observed in various manifestations in 29/40 (73%) patients. Another 11/40 (27%) patients had ataxia or neurogenic claudication without overt paresis in the lower extremities. The mean AL-score for gait at diagnosis was 3 ± 1.6 (median, 3; range, 0–5).

Radiologic Findings

Preoperative MR imaging ($n = 40$) and additional spinal contrast-enhanced MRA (CE-MRA) ($n = 34$) examinations were available for this analysis. Medullary edema was detected in 35/40 (88%), extending, on average, over 5.5 ± 3 vertebral levels (median, 6 vertebral levels; range, 1–12 vertebral levels). Intramedullary contrast enhancement was observed in 30/40 (75%), on average extending over 4 ± 2.4 vertebral levels (median, 4 vertebral levels; range, 1–8 vertebral levels). Engorged perimedullary veins in the thoracic and/or thoracolumbar region were observed in all 40 patients, with a mean extension of 7.5 ± 4.6 vertebral levels (median, 7 vertebral levels; range, 1–18 vertebral levels). On DSA, 17 sdAVFs were located in the thoracic, and 19, in the thoracolumbar region. Four fistulas were located in the deep lumbosacral region.

Long-Term Outcome

After a mean follow-up of 52 ± 37 months (median, 50.5 months; range, 3–159 months), the mean AL-score was 2.5 ± 1.8 (median, 3; range, 0–5). Clinical follow-up outcome was improved in 21/40 (53%), stable in 11/40 (28%), and aggravated in 8/40 (20%) patients. Chances for good long-term outcome were not influenced by patient age ($P = .152$) or by the neurologic status at diagnosis ($P = .324$) (Fig 1). A longer duration of symptoms from onset to diagnosis was significantly associated with worse long-term outcome ($P = .008$). Patients with a shorter clinical course (≤6 months) had an improvement of their gait disturbances up to 1 grade on the AL-score (Fig 1). No significant correlation was observed

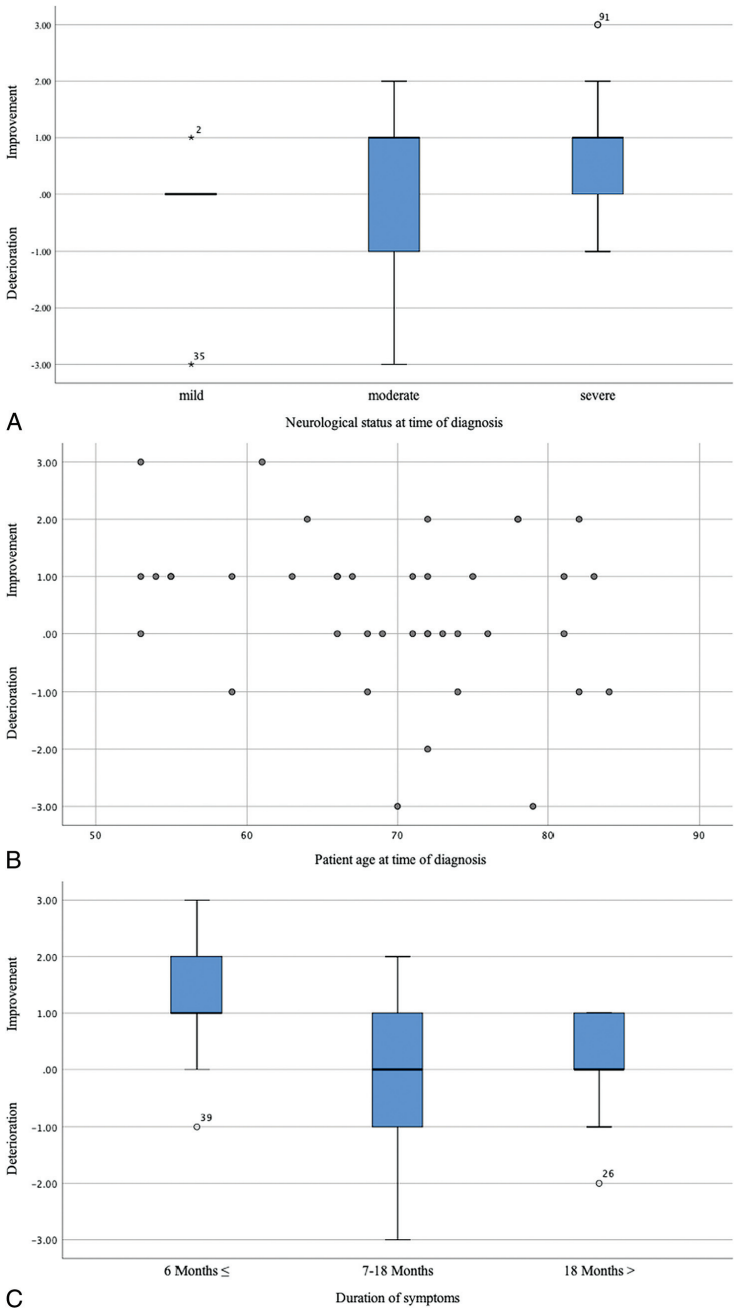

FIG 1. *A*, Boxplot demonstrates the correlation between long-term outcome and neurologic status at diagnosis evaluated by the AL-score and dichotomized into mild: AL-score 0–1; moderate: AL-score 2–3; and severe: AL-score: 4–5. *B*, Scatterplot demonstrates the relationship between long-term outcome and patient age at diagnosis. *C*, Boxplot demonstrates the correlation between long-term outcome and the duration of symptoms at diagnosis. The x-axis indicates the initial and follow-up AL-scores.

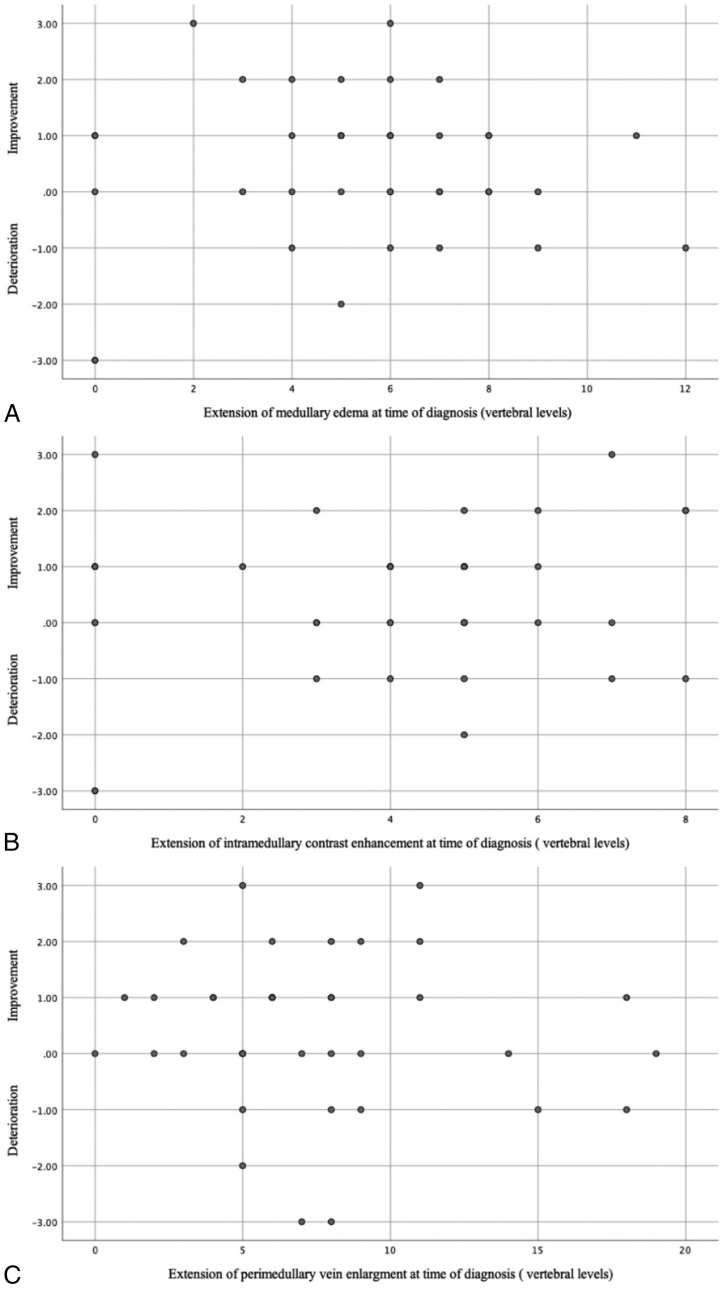

FIG 2. Scatterplot demonstrates the relationship between long-term outcome and extension of medullary edema (*A*), intramedullary contrast enhancement (*B*), and perimedullary vein enlargement at diagnosis (*C*). The x-axis indicates the initial and follow-up AL-scores.

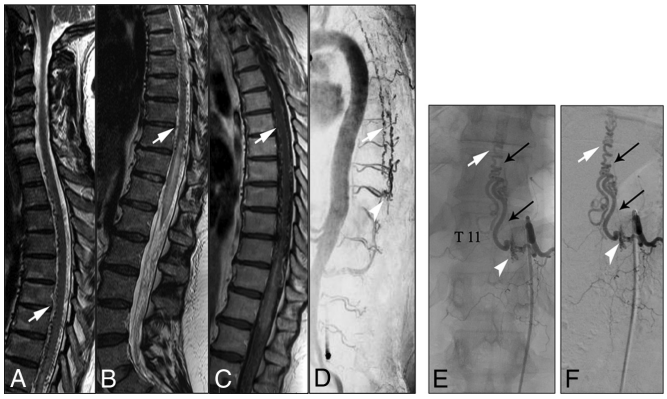

FIG 3. *A–C*, T2- and T1-weighted MR images demonstrate elongated perimedullary veins (*white arrows*) associated with medullary edema and centro-medullary contrast enhancement in the lower thoracic region. *D*, CE-MRA image shows the arterialized perimedullary veins in the thoracic region (*white arrow*) and depicts the shunt zone at the T11 vertebral level (*white arrowhead*). *E* and *F*, Spinal DSA examination (posterior-anterior projection) of the left T11 segmental artery shows the hypervascularized fistula zone (*white arrowhead*) with a dilated and elongated intradural drainage vein. Note the origin of the Adamkiewicz artery from the same fistula side (*small black arrows*).

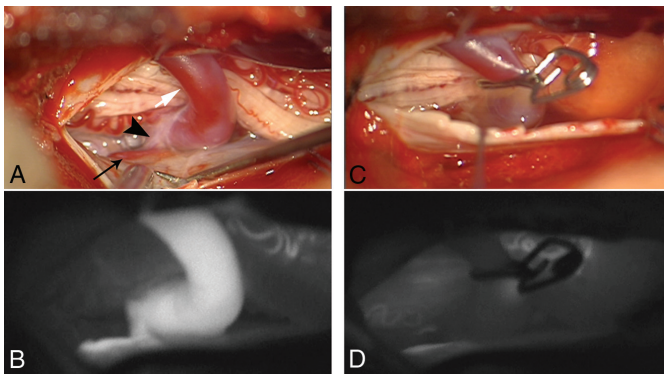

FIG 4. *A*, Intraoperative images show the fistula zone (*black arrowhead*), a narrow arterial feeder (*small black arrow*), and the elongated radicular drainage vein (*white arrow*). *B*, Indocyanine green images confirm the pathologic arterialization of the elongated radicular vein. *C* and *D*, The radicular drainage vein is disconnected via clip ligation, and indocyanine green videoangiography confirms the interruption of the pathologic arterialization.

between long-term outcome and the extent of medullary edema ($P = .638$), intramedullary contrast enhancement ($P = .425$), and engorgement of the perimedullary veins ($P = .672$) (Fig 2). There was also no relationship between the fistula location and the long-term outcome in our cohort.

Long-term follow-up MR imaging examinations were available for 21 patients with a mean follow-up of 14.5 ± 11.6 months (median, 12 months; range, 1–44 months). All 21 patients demonstrated a regression of the medullary venous congestion, reflecting a sufficient interruption of the arteriovenous shunt. The clinical and/or radiologic follow-up examinations were performed by their local physicians in the remaining 19 patients. No clinical/radiologic findings suggesting a recurrent sdAVF were re-ported in any of these patients.

Illustrative Case

A 56-year-old woman presented with progressive gait disturbances during the past 4 months. Neurologic examinations at the time of admission showed spinal ataxia, proximal accentuated paraparesis, and hypoesthesia below T10. In the initial CE-MRA in our center, T2WI and T1WI showed centro-medullary edema and contrast enhancement extending from the T10 vertebral level to the conus medullaris (Fig 1). Arterialized perimedullary veins were de-tected in the thoracic region dorsally as well as ventral to the myelon. Further MRA sequences suggested an arteriovenous shunt at the level of the T11 segmental artery. The subsequent DSA was primarily focused on this region. A sdAVF could be identified at the level of the left T11 nerve root receiving arterial supply via radiculomeningeal branches of the left T11 segmental artery. The venous drainage into the perimedullary venous plexus occurred via the elongated left T11 radicular vein (Fig 3). After left-sided hemilaminectomy at the T11 vertebral level, the hypervascularized fistula zone and the elongated radicular drainage vein were identified. The drainage vein was disconnected via clip ligation (Fig 4). In the annual follow-up examinations after treatment, gait disturbances and paraparesis had improved markedly. MR images showed a complete regression of medullary congestion (Fig 5).

DISCUSSION

Clinical Features

Among all analyzed clinical factors in our current cohort, only a shorter duration of symptoms before treatment (≤6 months) was associated with a better long-term outcome. Patient age and the neurologic status at diagnosis had no influence on the long-term outcome.

Most surprising, the most stunning finding among patients in our current cohort was the long duration of symptoms of almost 2 years from onset to definite diagnosis. This was unchanged

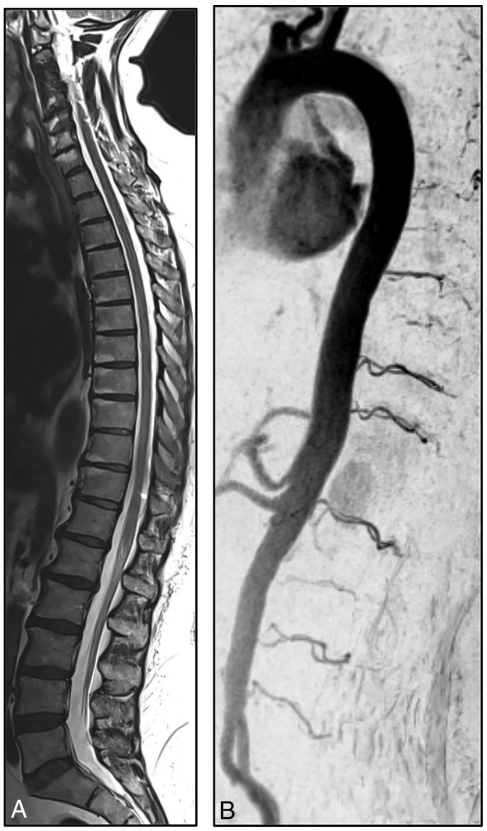

FIG 5. Follow-up T2-weighted MR image and CE-MRA 3 years after treatment show a complete regression of medullary edema and alteration of perimedullary veins.

compared with an older cohort from our group (91 patients diagnosed between 1988 and 2002, mean duration of symptoms of 20 ± 19 months; $P = .533$).[8] Moreover, to the best of our knowledge, a mean duration of symptoms of <1 year has never been reported in any of the large representative series in the literature.[4,5,9]

Because high-quality MR imaging/MRA and DSA are more readily available currently than in the past, we assume that our actual observation is reflecting an ongoing lack of awareness and experience in dealing with this rare disease of nonspecific clinical and radiologic presentations. This may also explain the relatively high rate of patients who were referred to our center with nonconclusive clinical and radiologic findings (28/40), despite repetitive MR imaging and/or DSA examinations performed in their local hospitals.

In the early phase of the disease, the diffuse symptoms of sdAVF are commonly confused with more frequent disease entities such as spinal degenerative diseases or polyneuropathy. In cases with the above-mentioned, nonspecific symptoms but a lack of typical findings of degeneration or polyneuropathy, we recommend imaging the whole spine with T2WI. Whenever a medullary congestion with or without elongated perimedullary vessels is present, further spinal MRA and/or DSA examinations should be considered.

Radiologic Findings

There is a universal consensus in the literature that medullary venous hypertension is the basic pathomechanism behind the symptomatology of sdAVF. If the fistula is left untreated, induced congestive myelopathy usually progresses to medullary ischemia, leading to disturbances of the spinal cord–blood barrier.[10] These pathophysiologic changes induce typical-but-nonspecific medullary edema and contrast enhancement with or without engorgement of perimedullary veins on MR images.[1,11]

Regardless of the treatment technique, the prognostic impact of initial neuroradiologic findings on long-term outcome in patients with sdAVFs is still a matter of dispute.[12,13] Hetts et al[14] demonstrated in a series of 31 patients, a positive correlation between early functional recovery after treatment and the extent of elongated perimedullary veins at diagnosis. In a cohort of 65 patients treated either microsurgically or endovascularly with a mean follow-up of 6 months reported by Cenzato et al,[15] sdAVFs in the lower thoracic segments (T9–T12) were associated with more severe symptoms but tended to improve more after treatment. Midthoracic (above T9) and lumbar (below T12) fistulas in their series were associated with a lower incidence of improvement.[15] In contrast, Dhandapani et al[16] reported a higher improvement rate in patients with sdAVFs below the T9 level in 22 microsurgically treated patients within a mean follow-up of 7 months.

Compared with the rather short follow-up periods in these studies, our current analysis had a mean follow-up of 52 ± 37 months and showed no correlation between the extensions of medullary edema, centro-medullary contrast enhancement, or elongation of perimedullary veins, and the long-term outcome. Also, the fistula location showed no influence on the long-term outcome in our analysis.

We assume that the chronic pathologic arterialization of the spinal venous system could induce irreversible changes of medullary venous outflow that may significantly affect the functional recovery, even after sufficient interruption of the arteriovenous shunt.[2,17]

In a previous analysis by our group, we found that the elongation of perimedullary veins on MR images is more dominant in the earlier phase of this disease.[2] These dilated veins may maintain the medullary venous outflow, reflecting a better compensation of the medullary venous hypertension and result in a better outcome if the sdAVF was sufficiently diagnosed and treated in this phase of the disease. A sufficient visualization of the spinal venous system is, however, still associated with major diagnostic difficulties. It could clarify several unclear aspects of this disease and should be the subject of further studies.

Limitations

Our study has several limitations. First, because our institution is a tertiary referral center for spinal vascular diseases, there is a

high risk of referral bias in our current analysis, resulting in a longer duration from symptom onset to diagnosis. Another risk of bias is the retrospective approach of this study, which may provoke speculative interpretation of our data to some extent. Another limitation is that we retrospectively determined the Aminoff-Logue disability scale through chart review. The AL-score itself has a limited value in the interpretation of neurologic status.

CONCLUSIONS

Spinal dural arteriovenous fistulas are characterized by interindividually variable clinical presentations that make a determination of specific predictive factors for the long-term outcome more difficult. Our current analysis implies the importance of early diagnosis for a better neurologic outcome. However, despite major developments in neuroradiologic noninvasive diagnostic tools in the past decades, the diagnosis of sdAVF remains markedly delayed. Our current study may raise the awareness of neurologists of this rare disease and emphasize the importance of early diagnosis in these patients.

Disclosures: Gerrit Alexander Schubert—*UNRELATED: Consultancy*: Carl Zeiss Meditec AG, Jena, Germany. Manuel Dafotakis—*UNRELATED: Board Membership*: Merz Pharma, *Comments*: dystonia and spasticity; *Payment for Lectures Including Service on Speakers Bureaus:* Merz Pharma, Ipsen, Allergan, *Comments*: botulinum toxin therapy.

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