Value of Time Resolved Imaging of Contrast KineticS (TRICKS) and high resolution T2 volumetric MR sequence at 3T in evaluation of spinal vascular malformations

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CERTIFICATE

This is to certify that the work incorporated in this thesis titled ***"Value of Time Resolved Imaging of Contrast KineticS (TRICKS) and high resolution T2 volumetric MR sequence at 3T in evaluation of spinal vascular malformations"*** *for the degree for DM "(Neuroimaging and Interventional Neuroradiology)" has been carried out by Dr. Satyanarayana Mandalapu under our supervision and guidance. The work done in connection with this thesis has been carried out by the candidate himself and is genuine.*

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I hereby declare that this thesis titled ***"Value of Time Resolved Imaging of Contrast KineticS (TRICKS) and high resolution T2 volumetric MR sequence at 3T in evaluation of spinal vascular malformations"*** *has been prepared by me under the supervision and guidance of Dr.Santhosh K (Associate Professor), Dr Kesavadas (Professor), and Dr.Kapilamoorthy TR (Professor & HOD), Department of Imaging Sciences and Interventional Radiology, Sree Chitra Institute for Medical Sciences and Technology, Trivandrum.*

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Dr. Satyanarayana Mandalapu

ABBREVIATIONS

4D TRAK	-	*4D Time Resolved Angiography using Keyhole*
ASA	-	*Anterior spinal artery.*
AVF	-	*Arteriovenous fistula.*
AVM	-	*Arteriovenous malformations.*
CE MRA	-	*Contrast enhanced magnetic resonance angiography.*
CT	-	*Computed tomography.*
DSA	-	*Digital subtraction angiography.*
DAVF	-	*Dural arteriovenous fistula.*
ETL	-	*Echo train length.*
EVOH	-	*Ethylene vinyl alcohol.*
FOV	-	*Field of view.*
IIA	-	*Internal iliac artery.*
MRI	-	*Magnetic resonance imaging.*
NBCA	-	*N-Butyl Cyanoacrylate.*
NPV	-	*Negative predictive value.*
PPV	-	*Positive predictive value.*
PM AVF	-	*Perimedullary arteriovenous fistula.*
PSA	-	*Posterior spinal artery.*
PVA	-	*Poly Vinyl Alcohol*
SCVM	-	*Spinal cord vascular malformations.*
SPACE	-	*Sampling Perfection with Application Optimized Contrasts using different flip angle Evolution.*
TE / TR	-	*Time to echo / Time to repeat.*
TOF	-	*Time of flight.*
TRICKS	-	*Time Resolved Imaging of Contrast KineticS.*
TWIST	-	*Time resolved angiography With Stochastic Trajectories.*

INDEX

Introduction

Introduction

Spinal vascular malformations are rare diseases and include arterio-venous malformations and arteriovenous fistulas at various locations in the spine and its coverings. They can be acquired (spinal DAVF) or congenital (spinal AVM). Depending on the type of vascular malformation and level and pathophysiology, their presentation can be acute, subacute or chronic. Spinal arteriovenous malformations mostly present with hematomyelia, which may lead to its diagnosis at an early stage. Diagnosis of spinal DAVF and perimeduallry AVF is delayed and can result in significant cord damage due to venous hypertension and ischemia that may be irreversible(1)(2).

MRI is the initial investigation method of choice, which depicts cord hyperintensity on T2 sequences, multiple flow voids in the subarachnoid space and a nidus within the cord in case of AVM. Other findings like hematomyelia, aneurysms, venous sacs and contrast enhancement can also be depicted(3)(4)(5)(6). Digital subtraction angiography (DSA) is the gold standard investigation of choice. Disadvantages of DSA include increased radiation exposure, large volume of contrast and a smaller risk of spinal cord infarction(7)(8)(9).

Developments in MRI like higher magnet strengths, faster imaging techniques, and robust data-sampling methods have improved the diagnostic performance of MRI. CT and MR angiography have shown to be useful in localizing the level of fistula in DAVF and angioarchitecture in spinal AVM in multiple studies (10)(11)(12)(4)(13)(14)(15). Dynamic MR contrast studies like TRICKS are useful in localizing the level of fistula in DAVF and Perimedullary fistula(16)(17)(18). High resolution T2 MR sequences like SPACE have excellent contrast between cord and CSF with supressed CSF flow artefacts and can be reconstructed in different planes(19)(20). High spatial resolution is necessary to localise the arteries supplying the cord and vascular malformation, small

size of the shunt in the DAVF and PM AVF; and angioarchitecture of AVM. The shunt in the AVM and high flow perimedullary AVF are high and requires high temporal resolution to identify the arteries and veins and the degree of shunting. Even with significant developments in MRI, there has been a compromise between spatial and temporal resolution as the MRI sequences are dependent on time. 3D Fast spin echo sequences like CUBE provides high spatial resolution between the adjacent structures and images can be reconstructed in different planes, so are helpful in evaluating the spinal vascular malformations. The disadvantage is that, there is no temporal resolution. In contrast to CUBE sequence, TRICKS sequences has good temporal resolution but poor spatial resolution. Advantages of both the sequences can be used in evaluating the spinal vascular malformations.

Our centre is a major tertiary referral centre for management of all neurovascular disorders. Our department of IS & IR has been actively involved in the management of various neurovascular lesions. In this study, we evaluate the role of CUBE and TRICKS MRI in evaluation of spinal vascular malformation in comparison to the gold standard DSA.

Aims and objectives

Aims and objectives

1. To analyse the accuracy of dynamic contrast MR angiography (TRICKS) at 3T in depicting type of vascular malformation in comparison to digital subtraction angiography (DSA).
2. To analyse the accuracy of high resolution T2 volumetric MR sequence (CUBE) at 3T in depicting type of vascular malformation in comparison to digital subtraction angiography.
3. To analyse the accuracy of identifying the spinal vascular malformation level in comparison to DSA.
4. To analyse the accuracy of identifying the feeders and nidal characteristics comparison to DSA.

Review of literature

Review of literature

Brief History

History of spinal vascular malformations points out how understanding angioarchitecture and pathophysiology led to the development of present treatment modalities.

In brief, the history can be divided into:

1) Early observations (1860s-1912): Lesions recognized only at autopsy.

2) Middle ages (1912-1960): Sporadic surgical intervention with bad results.

3) Modern era (beginning in the 1960s): Advances in radiology and microsurgical instrumentation.

In 1885, Hebold described spinal vascular malformation as venous aneurysm at autopsy. In 1889 Gaupp, described a 45-year-old female with progressive leg weakness, who was found to have venous varix compressing the cord and described it as "Haemorrhoids of the pia mater spinalis". In 1900, Brasch, described the pathology of SCAVM. Cobb reported several cases of SCAVM and their variable presentations. He also noted the relationship between SCAVM and skin lesions. In 1926, Foix and Alajouanine, reported subacute necrotising myelopathy with vascular malformation in the cord and attributed this to be a consequence of toxic or infectious agents. Later, Lhermitte and Wyburn-Mason reported similar findings. In 1928, Michon reported spinal subarachnoid haemorrhage due to ruptured spinal AVM. In 1943, Roger Wyburn Mason reported progression and natural history of 96 patients and classified them as arteriovenous angiomas (32%) and venous angiomas (68%). He classified them initially as angioma racemosum arteriosum and angioma racemosum venosum. He later classified into five subtypes: 1. angioma racemosum venosum, 2. Arteriovenous anomalies, 3. Arterial anomalies, 4. Syphilitic aneurysm, and 5. telangiectasias.

In 1958, Hook and Lidvall, reported cervical AVM on vertebral artery injection. In 1962, First spinal angiography was done by Rene Djindjian at Lariboisiere Hospital. In 1965, Doppman and Dichiro demonstrated the use of subtraction angiography and Dichiro pioneered selective spinal angiography. The modern classification was first proposed by DiChiro, Doppman, and Ommaya in 1971 and spinal vascular malformations were classified into single coiled vessel lesions (present Type I or Spinal DAVF), intramedullary glomus type of AVM (type II), and juvenile type (Type III). In 1977, Rene Djindjian described intradural perimedullary AVF. Later, Hero's classified the same as type IV malformation. Merland et al sub classified type IV into IVA, IVB and IVC. Pathophysiology, natural history and the site of shunt in DAVF was described by Logue, Aminoff, and Kendall between 1960-1970. They also described venous hypertension and vascular steal as the pathophysiology in manifestations of vascular malformations. Fahrendorf et al, first reported visualisation of spinal AVM using MRI.

Blood supply of cord(21)(22)(23)(24)

Arterial supply

In first few weeks of life, the embryo divides in to 31 somites (metameres) from rostral to caudal direction, each receiving a pair of segmental arteries from dorsal aorta. The structures that arise from each somite such as bone, skin muscles, nerve, neural tissue and its coverings are supplied by the same segmental artery. Any anomaly at this stage results in metameric syndromes like Cobb syndrome. These arteries grow and form anastomosis both in axial and longitudinal axis. Between sixth week to four months, the axially organised structures disappear and longitudinal system evolves. Of the 62 pairs (31 dorsal and 3 ventral), only 4-8 ventral radicular and 10-20 dorsal radicular arteries remains.

Segmental arteries in cervical regions arise from ascending cervical artery, deep cervical artery, vertebral artery, ascending pharyngeal artery and occipital arteries; in thoracic region from supreme intercostal, superior intercostal and posterior intercostal arteries, in lumbosacral regions from lumbar, median sacral and lateral sacral arteries. On catheter angiogram, segmental arteries are identified based on the hemi vertebral blush and bony land marks.

Segmental branches from aorta travel along the vertebral bodies, supplying the latter with small branches and then dividing into three branches:1. Ventral or lateral branch (posterior intercostal or lumbar artery proper); 2. Dorsal or middle branch supplying dorsal muscular and cutaneous areas; 3. Spinal or medial branch.

The spinal branch enters intervertebral foramen and divides into three branches: 1. anterior (Retrocorporeal) and 2. posterior (Prelaminar) spinal canal arteries, supplying vertebral bodies, ligamentous structures and dura. 3. Radicular artery coursing along the spinal nerve and divides into anterior and posterior branches, that travel along the anterior and posterior nerve roots respectively. There are radicular arteries at every segmental level.

Depending on the supply to dura, or pial surface or ASA, the nomenclature differs.

- Radicular arteries or radiculomeningeal arteries – they are present at every segmental level. They disappear in the roots before reaching the pial surface. Do not supply the cord.
- Radiculopial arteries: As the name indicates supply the pial surface and give contribution to the posterior spinal artery and the pial plexus. Vary in number between 10-12 and are smaller in calibre than anterior radiculomedullary artery.
- Radiculomedullary arteries: Supply the anterior part of spinal cord and feeds the anterior spinal artery. Average number ranges from 2-14. Calibre is larger than posterior radiculopial arteries and the luminal calibre changes in the longitudinal axis (smaller in

thoracic and larger in lumbar region). In the lumbar region, a large radiculomedullary artery supplies the ASA and is called artery of lumbar enlargement or arteria radicula magna of Adamkiewicz. It generally arises from T9-T12 levels in 75% of population and on the left side in 80%. Artery of cervical enlargement is seen in between C4-C8 levels, mostly arising from deep cervical artery.

The arterial supply of spinal cord can be divided into longitudinal and axial systems. Longitudinal system comprises of ASA in anterior median sulcus and posterior paramedian PSAs. Both these are reinforced by multiple radiculopial and radiculomedullary arteries from various levels. Multiple communications exist between ASA and PSA around the conus medullaris and it is termed as vasa corona.

Transverse system or intrinsic system comprises of pial perforators supplying the cord peripherally, predominantly into white matter (centripetal system) and from sulcal and sulcocommisural arteries from ASA to the grey matter (centrifugal system).

Venous drainage

Venous drainage differs from arterial system in that, veins does not follow the course of arteries and the drainage of spinal cord is predominantly dorsal. Intrinsic venous system can be divided in central or sulcal veins and peripheral or radial veins. Sulcal veins drains the ipsilateral hemicord around the central sulcus and pial veins drain the periphery of the cord.

Both the sulcal and radial veins drain into major collectors in the pia, one anteriorly along the ASA called anterior median spinal vein and three posterior veins namely, posterior median vein and posterolateral veins.

These anterior and posterior pial veins drains into radiculomedullary veins (8-14 anterior radiculomedullary veins and nearly 20 posterior radiculomedullary veins). These

radiculomedullary veins pierce the dura along the anterior or posterior nerve roots and drain into paravertebral and intervertebral plexuses. The oblique and zig-zag course of radiculomedullary vein in the dura possibly act as functional valve, preventing retrograde reflux.

Classifications of spinal vascular malformations

Various classifications have been proposed based on genetics, pathophysiology, anatomy and on surgical observations.

The modern and frequently followed Anson and Spletzer classification for spinal vascular malformations, was first proposed by DiChiro, Doppman, and Ommaya in 1971 and were classified into single coiled vessel lesions (Present Type I or Spinal DAVF; Anson Spletzer classified into type Ia and Ib based on number of feeders), intramedullary glomus type of AVM (type II), and juvenile type (Type III). In 1977, Rene Djindjian described intradural perimedullary AVF. Later, Hero's classified the same as type IV malformation. Merland et al subcalssified type IV into IVA, IVB and IVC.

Anson and Spletzer classification:

Type I: Spinal dural arteriovenous fistula.

Type II: Glomus type of intramedullary AVM.

Type III: Juvenile type of intramedullary AVM.

Type IV: Perimedullary arteriovenous fistula.

IV A: Micro fistula with single arterial feeder.

IV B: Fistula with multiple feeders.

IV C: Macrofistula with multiple feeders and venous sacs.

Spletzer et al Proposed a classification based on pathophysiology, neuroimaging, intraoperative findings, and anatomy. It encompasses the surgically treated vascular malformations of the cord, mainly based on location and pathophysiology (25). He classified into:

1. Neoplastic vascular lesions: Hemangioblastoma, Cavernous malformation
2. Spinal aneurysms
3. Arteriovenous fistulas: extradural, intradural, ventral and dorsal
4. Arteriovenous malformation: Extradural–intradural, Intradural, Intramedullary (Compact, Diffuse, Conus medullaris)

Rodesch et al, classified spinal cord AV malformations based on genetics into three groups:

1) Genetic hereditary lesions caused by a genetic disorder affecting vascular germinal cells. Example: hereditary haemorrhagic telangiectasia(HHT).

2) Genetic non-hereditary, lesions due to somatic mutations sharing metameric links.

They present with multiple shunts in the spinal cord, nerve root, bone, paraspinal, subcutaneous, and skin tissues. Examples: Cobb syndrome (Myelomere). Klippel-Trenaunay and Parkes-Weber syndromes also belong to this group.

3) Single lesions due to incomplete expression. Lesions involving spinal cord, nerve root and filum terminale lesions.

He also divided vascular malformations into AVM and AVF. He classified AVF into micro and macro fistulas (26).

Krings et al classified spinal vascular malformations based on anatomy of feeding artery, angioarchitecture of shunt and shunt volume. He first differentiated shunting from non-shunting lesions like cavernomas of cord. If a shunt is present, based on the feeding artery, vascular malformations are subdivided into DAVF, fed by a radiculomeningeal artery and the pial AV

shunts supplied by radiculopial and radiculomedullary arteries. Pial AV shunts are further subdivided based on nidus architecture in fistulous and glomerular shunts. Finally, fistulous shunts are subcalssified according to shunting volume into Micro and Macro fistulae. (27).

In 2008, Geibprasert S, Lasjaunias P and colleagues reported new classification for cranio-spinal arteriovenous shunts and divided into 3 groups; ventral epidural, dorsal epidural, and lateral epidural groups, on the basis of the embryologic development of the venous drainage of the surrounding structures (28). Based on this classification, spinal DAVF will be fall into the category of lateral epidural group.

Rangel-Castilla et al classified Extradural spinal AVM or AVF based on venous drainage (29).

Type A: Venous drainage into perimedullary venous plexus.

Type B: Venous drainage into batson plexus.

B1: Venous sac compressing the cord.

B2: No compression on the cord.

Topographically, Spinal vascular malformations can be classified in to AVM and AVF(30).

A) AVM

1) Intramedullary (also known as Type II or glomus-type AVM)

2) Pial

3) Epidural

4) Intra- and extramedullary (Type III, intradural-extradural, juvenile AVM, or metameric AVM)

B) AVF

1) Pial AVF (Type IV, spinal cord AVF, ventral intradural AVF, or perimedullary AVF)

a) Small

b) Large

c) Giant

2) Dural AVF (Type I or dorsal intradural AVF)

3) Epidural AVF (also known as extradural AVF).

Epidemiology

Spinal Dural Arteriovenous fistula

These are the most common vascular malformation of the spine and accounts for approximately 60-80% of all vascular malformations. Mostly these are underdiagnosed entity. The reported rate in German hospital is approximately 5–10/million/year (31). These are diagnosed in middle to old age. In a meta-analysis that included the reported series of more than 5 patients, there were about 1178 patients of which 968 were male and 210 were female (almost 5:1 ratio). At the time of diagnosis, the mean age was 55-60yrs. Of 1178 patients, only 14 (1%) patients had age less than 30 years and youngest patient was 22 years. Most of the DAVF are located in thoracolumbar spine, 80% located between T6-L2 level. In the same above series, only 23 patients (2%) had cervical DAVF and 47 patients (4%) had sacral DAVF. Most of the DAVF are single; multiple DAVFs are extremely uncommon with approximately 0.5% (6 patients) in the above meta-analysis (32).

Spinal cord arteriovenous malformations

Incidence of spinal AVM in comparison to brain AVM is varied with reports ranging from 1:4 to 1:8. When compared to the volume of brain and spine, the incidence of spinal AVM and brain AVM appears same.

Spinal AVM presents within first three decades of life and account for approximately 25% of all spinal vascular malformations. Most of them are distributed along the spinal axis, with most common location being cervicothoracic spine. Rosenblum et al evaluated 81 patients with spinal vascular malformations and found DAVF in 27 patients (33%) and AVM in 54 patients (67%). The intradural AVM were sub classified into intramedullary AVM's in 43 patients (53.1%) (Glomus type in 14 patients (17.3%) and Juvenile in 29 patients (35.8%)) and direct AV fistulas in 11 patients (13.5%). Male predominance was noted. Spinal AVM was detected at a younger age from 4 to 58 years (Mean 27 +/- 12.1 years) with 65% of patients being younger than 25 years. Nidus is seen within the spinal cord in 80%, on dorsal surface in 9%, and on ventral surface in 11%. Multiple feeding arteries ranging from 2 to 6 are identified in 72% of AVM patients. Associated vascular malformation were described in 10 patients with AVM, mostly an additional AVM (3 patients) and extra spinal arterial hypoplasia (3 patients) (33). Rodesch et al evaluated 155 patients with spinal cord AVF, of which 81% are single lesions and 19% are multiple. He reported spinal AVF associations in ten cases of Cobb syndrome, three cases of Klippel-Trenaunay syndrome, and two cases of Parkes-Weber syndrome. Of the macrofistulae in the cord, 83% were associated with HHT (34).

Perimedullry arteriovenous fistula

These are usually seen in middle aged population with a wide range of age at presentation, from as early as 3 weeks to 55 years of age. Both male and females are affected equally. Yung Jung Lee et al reported 44 cases of SCAVM of which 18 were peri medullary fistulas. The mean age of presentation was 43 years, and male to female ratio of 1.6:1. Most of them were located in lower thoracic cord and filum terminale (83%) and the rest were seen in cervical spine (13%). Multiple arterial feeders were seen in 11 of 18 patients (61%). In a series of 19 patients reported by Cho et

al, the mean age was 28 years and 17 of 19 lesions were located in conus medullaris. In their series, 9 patients were of type IVA, 6 of IVB and remaining type IV C. Gueguen, *et al.* reported 11 cases of Type IV spinal cord AVM's, of which six were females and five were males, and age at onset of symptoms ranged between 14 and 42 years. Three of the presented with SAH and others with progressive symptoms.

Angioarchitecture and Pathology (35)

Dural arteriovenous fistula

These are slow flow fistulas. Arterial supply is seen from radicuomeningeal artery, that might be normal or dilated. Multiple tiny fistulous communications are seen in the meninges of dorsal root sleeve and the adjacent dura matter, that drains into a medullary vein. The draining vein shows hyalinisation with areas of thrombosis, recanalization and endothelisation. Grossly, dilated veins will be seen running in cranio-caudal direction on the surface of the cord.

Histological examination of venous congestive myelopathy shows distorted architecture of parenchyma with gliosis and thick hyalinized vessels seen in 100% of patients, variable myelin loss in 71%, mild glial atypia in 57%, hemosiderin deposition in 71%, increased Rosenthal fibres in 43%, vascular thrombosis and necrosis in 29% (36). These changes particularly involve lateral corticospinal tract and then spreads to adjacent portion of white matter of lateral funiculus. Later, advanced changes involve anterior grey matter and posterior white matter with consistent sparing of anterior median segments.

Arteriovenous malformation

These are high flow fistulas. Grossly, tortuous vascular mass occurs on the surface of the cord, predominantly in posterior region with minority in anterior region. These vessels are seen in

leptomeninges and are opaque due to fibrous thickening, iron pigment deposition and due to old haemorrhages. Arteries are either normal or dilated and mostly supplied by radiculopial arteries and in minority by radiculomedullary arteries. Histologically, there is disorganisation in the structure of the vessel with duplication, interruption, distortion of internal elastic lamina, variable thickening of media, aneurysmal thinning and dilatation of the vessels, or focal thickening and hyperplasia of the lumen. These arteries lead into cluster of vessels lined with endothelium called nidus. The nidus drains into a single or multiple vein, that are enlarged and form a vascular mass. Veins are dilated and thin-walled or may have considerably thickened wall due to mural connective tissue proliferation, and severe fibrous or hyaline transformation, In glomus AVM, the nidus is compact with no intervening spinal cord parenchyma. In juvenile AVM, the nidus extends over few vertebral segments with intervening cord parenchyma. The cord appears shrunken with some cystic changes (35).

Perimedullary arteriovenous fistula

These are also either low or high flow fistulas and are divided into type A, B and C. High flow fistulas are seen in first to second decade of life and type A fistulas present in fifth decade of life. These fistulas are seen on the surface of the cord in the pia matter with a fistulous communication between radiculopial or radiculomedullary artery to veins of coronal plexus. Venous sacs are seen predominantly in high flow fistulas. The transition between the artery and the vein is not clearly demarcated. The veins are arterialised and show vascular remodelling. Venous congestive myelopathic changes similar to DAVF are seen in the cord on histology (36).

Pathophysiology (1)(32)(2)

Patients with spinal vascular malformation present in acute, subacute and chronic states with episodes of worsening due to physical activity. These variations are due to different pathophysiological features.

The main pathophysiology behind the manifestations of spinal vascular malformations include

1. Venous hypertension – Progressing to myelopathy.
2. High flow and steal – Ischemia, aneurysmal formation and venous dilatations and further leading to haemorrhage.
3. Mass effect on the cord due to arterial aneurysms and venous sacs.

Venous hypertension:

Venous hypertension is the most common pathophysiological basis in spinal DAVF, PM AVF and in delayed presentations of SCAVM. Because of the AVF or AVM, the pressure inside the draining veins increase as high as 74% of mean arterial pressure. This leads to reduced arteriovenous gradient and further causing decrease in perfusion pressure to the cord, to as low as 30%, leading to chronic ischemia. Due to vasodilatation and vasoregulatory failure, pressure is transmitted into capillaries, leading to cord oedema and disruption of blood brain barrier. Neovascularisation occurs as a result of chronic hypoxia. During exertion and exercise, the venous pressure increases, which further reduces the perfusion pressure, leading to worsening. Due to less number of venous outflow channels in thoracic cord and differential pressure effects in relation to heart and gravity effects, the conus medullaris is the most dependent part and is possibly the most common site to be affected first.

Arterial steal

This pathophysiology is mainly seen in AVM and perimedullary AVF due to large AV gradients. Steal phenomenon causes decrease supply to the cord in perinidal regions. Arterial steal is less likely considered the mechanism in pathophysiology.

High flow

High flow causes vortex flow and lead to formation of arterial aneurysms and venous ectasia. These aneurysms can bleed, causing hematomyelia and spinal SAH. Very high flow fistulas and large AVM can cause cardiac overload and congestive cardiac failure.

Mass effect

The arterial aneurysms and venous sacs can cause mass effect on adjacent cord parenchyma and cause myelopathic changes.

Natural history and clinical symptoms (24)(22)

Dural arteriovenous fistula

Age; Mean age is above 50 years and range from 25 to 78 years.

Sex: More common in males (5:1).

Location: most common is lower thoracic and upper lumbar regions, followed by upper thoracic spine, followed by sacral regions. DAVF in cervical regions are very rare with an incidence of approximately 2.5%. Venous drainage is seen into intracranial in 60% and along with venous sacs has propensity for spinal SAH. Van dijk et al reported that the frequent location is in mid thoracic region and is seen on left side.

Manifestations:

Slowly progressive with an interval of 10.5 months between initial symptoms and diagnosis. No evidence of haemorrhage noted.

Van dijk et al showed that initial manifestations are spastic gait in 55%; sensory symptoms (paraesthesia) in 47% and backpain in 33%.

At presentation, 96% of patients have weakness, paraesthesia's in 90%, bowel and bladder symptoms (65 and 82%), and pain in 55%. Sexual dysfunction is not well reported in studies.

Aggravating factors include manoeuvres that increase intraabdominal and thoracic pressures (Exercises and passing stools); change in posture.

Arteriovenous malformation

Mean age of presentation mid 20's. In about 20% of cases, it is diagnosed under 16 years of age. In 50% of cases, symptoms are present before 16yrs.

Sex distribution: In paediatric patients, Male dominance is noted (80%), In adults, no sex predominance noted.

Manifestations:

Most common spinal haemorrhage followed by non-haemorrhagic manifestations.

Spinal haemorrhage: Most common is hematomyelia and spinal SAH. Devastating presentation. Subdural hematoma and epidural hematomas are seen rarely and may indicate the presence of metameric lesions. Clinical features include back pain that radiates along the spine, headache and neck rigidity, if lesions are in cervical spine. Neurological presentation depends on the tracts involved. Postulated causes include rupture of arterial aneurysm, false aneurysm, spinal cord veins, nidus and haemorrhagic venous infarct.

Seen in 50-70% 0f SCAVM patients. Most common in cervical lesions (57-78%) than thoracolumbar (20-37%).

At presentation,75% had bleed. Approximately, 70% have some improvement after the event and 80% will have some form of disability. Rebleeds are seen in approximately 25% of patients. Mortality after first haemorrhage is approximately 6% and after second haemorrhage is 18% with overall mortality ranging from 20.5 – 30%.

In correlation of angioarchitecture with bleed rates, children, cervical cord lesions and presence of false intranidal aneurysms have more propensity to bleed. Arterial aneurysms, arteriovenous fistula in nidus and venous ectasia does not correlate with bleed rate.

Non haemorrhagic manifestations

Initial symptom of root pain is seen in 15-20%. Weakness in 33% at presentation and eventually developed in 90% patients. Sensory symptoms are seen in 70% and impotence in 50%. In all patient's bowel and bladder is involved. Bruit is seen in 8% and indicated a high flow lesion. Other manifestations include kyphosis, scoliosis, recurrent UTI, decubitus ulcer.

Prognosis:

40% have step wise deterioration. 80% has relapses. Most of them die at around 41-51 years of age, mostly as a complication of neurologic disorder.

Aggravating factors include manoeuvres that increase intraabdominal and thoracic pressures (Exercises and passing stools); change in posture, pregnancy and menstruation.

Perimedullary Arteriovenous fistula

Also called as type IV spinal cord AVM, intradural ventral AVF, intradural direct AVF, and spinal cord AVF. These are abnormal fistulas between medullary arteries and pial veins with an intervening nidus. Classified in to A (Micro AVF), B (multiple feeders without venous sacs), C (with multiple feeders and giant venous sacs). In children, Type IV C is associated with HHT.

Approximately 13-20% of spinal AVM.

Mean age of presentation second to fourth decade, ranging from new born to 53 years. In about 75%, they present before 25 years and in about 25%, before 15 years.

Sex distribution: No sex predominance noted.

Location: Most common location is in the conus followed by lower thoracic spine.

Untreated, complete transection symptoms appear in about seven to nine years.

Pathophysiology is similar to spinal DAVF, venous congestion, most common. Other factors in types IV B and C are arterial steal and mass effect, due to venous sacs.

Most common presentation is slowly progressive symptoms like paraparesis, sensory symptoms, bowel and bladder involvement and impotence, as seen in 75% of patients. One third cases present with spinal haemorrhage, mostly seen in children and type IV C lesions. Haemorrhage is seen from venous side of the lesion.

Mourier and co-workers evaluated 35 patients with PM AVF with age ranging from 2 to 42 years (mean 25 years). Thirty-two patients presented with slowly progressive dysfunction of the conus medullaris and cauda equina, and four patients were suspected to have SAH.

Diagnostic imaging of spinal vascular malformations

Clinical presentations and features of spinal vascular malformations are similar to demyelination, infection and neoplasms, and hence imaging plays a significant role in its diagnosis. Gold standard imaging of choice of spinal vascular malformations is DSA, as images can be acquired with superior spatial and temporal resolution. However, drawbacks of spinal vascular malformations include selective catheterisation of multiple segmental arteries resulting in long procedure times, long radiation exposure, large volumes of contrast administration that is nephrotoxic and risk of

spinal cord infarction(7)(8)(9). Due to advancements in CT and MRI, these malformations can be diagnosed at an early stage and may even help in treatment planning.

Computed tomography

Myelography

On CT myelography DAVF is seen as serpiginous blood vessels along the cord extending for long segments along with beading appearance of the cord.

CT Angiography

It can be used in diagnosis of spinal vascular malformations and to localise the fistula and arterial feeders(14). Advantages include high spatial resolution, differentiate type of fistula and bone from vessels. Disadvantage include use of ionising radiation, contrast administration, no temporal resolution and could not differentiate arteries from veins.(37)

Lai et al using 16 slice CT could identify engorged vessels in perimedullary regions in eight DAVF patients and could localise level of fistula in all patients, in comparison to DSA(10).

Li et al differentiated type I SDAVF from type IVA DAVF using 16 detector row helical scanner by identifying artery of Adamkiewicz in type IVA PM AVF and short radiculomeningel feeder in type I DAVF(38).

Gaosi Ja et al used 64 slice CT in evaluating 17 patients with spinal vascular malformations and compared with the gold standard DSA. He could differentiate the type of malformation in all patients and could identify 16 of 20 feeding vessels on CTA. Four feeding vessels could not be identified and 2 turned out to be false positives. (14)

Magnetic resonance imaging

MRI findings of spinal DAVF include cord swelling, increased T2 signal within the cord, hypo intensity on T1WI, peripheral T2 hypo intensity in the cord, flow voids anterior and posterior to

cord and parenchymal enhancement. Most of the flow voids are posterior to the cord (39). In the largest published study, Gilbertson et al evaluated MRI findings in 66 patients with SDAVF and reported T2 hyperintense signal in the cord in 100%, contrast enhancement in 88%, cord enlargement in 45%, and flow voids on surface of cord (35% onT1WI and 45% on T2WI (39). Hurst et al reported MRI findings in 11 patients with DAVF and reported cord enlargement in six (55%); T2 hyperintensity in 10 (100%) of 10; flow voids in 10 (91%) of 11 on T2WI and seven (70%) of 10 on contrast-enhanced images; and parenchymal cord enhancement in nine (90%) of 10 and peripheral T2 hypointensity around hyperintensity in all the patients(40).

Toossi et al evaluated the utility of MRI in spinal AVF in 34 patients and found sensitivity of spinal cord T2 hyperintensity or flow voids was 100% and the specificity of T2 hyperintensity and flow voids was 97% and concluded that in patients with myelopathy, spinal angiography is mandatory, in the presence of both T2 hyperintensity and flow voids but may be not required if both of these findings are absent (41). Presence of flow voids without myelopathy has poor predictive value for suspecting spinal DAVF (42).

Sequences employed:

T1: To identify haemorrhage. Flow voids can be identified. Hypointensity in cord edema.

T2: Hyperintensity in cord edema with peripheral hypointensity, flow voids around the cord, nidus within the cord, venous sacs and aneurysms.

GRE: Identifies haemorrhage.

CE MRA: To identify the type of malformation, location of fistula and arterial feeders.

Post contrast T1: Location of fistula, cord enhancement and enhancing vessels.

Nonspecific findings like cord edema is also seen in spinal cord infarction, myelitis and neoplasm. Flow voids can be seen in severe spinal stenosis (extends for only 1-2 vertebrae and seen proximal

to the stenosis); extradural AVF (flow voids can be seen extending outside the spinal canal and can be identified on contrast administration); artefacts due to CSF pulsations (discontinuous, bulkier and often seen in thoracic cord).

3D sequences:

CUBE is 3D fast spin echo with non-selective refocusing pulses with variable flip angels. Different vendors have different names namely, CUBE (GE), SPACE (Siemens), VISTA (Philips). Reduced flip angle reduces SAR. When refocusing flip angles are less than 180°, natural equilibrium exists between longitudinal and transverse magnetization. Initially, very low flip angles are applied, followed by larger flip angles, so that decaying longitudinal magnetization is converted back to transverse magnetization, so as to provide signal for over a longer time (20). Advantages of CUBE sequence include, good image contrast (vertebral disc/CSF and Body/ CSF), better visibility of nerve rootlets, fewer CSF flow artifacts, less motion artifacts and can be reconstructed in different planes. Fellner et al first reported the application of 3D SPACE sequence in localizing the fistula level and arterial feeder in a 56-year-old male patient with SDAVF, following which, both the angiogram and embolisation was completed in single sitting (43).

Kannath et al, retrospectively evaluated 16 patients with DAVF using 3D SPACE sequence and found accurate level of fistula in 13 out of 16 (81.5%) by observer one and 14 out of 16 (87.5%) patients by observer two and within one vertebral level in 14/16 (87.5%) and 15/16 (93.7%) patients by observer one and two respectively with good inter-rater agreement. The side was accurately identified in 14/16 and 15/16 patients respectively with good inter-rater agreement(19). He also demonstrated that preoperative localization of feeder level by 3D SPACE helped in lesser cannulation of the arteries and decreased procedure times, that reached statistical significance in comparison to historical cohort (44).

In comparing 2D T2W sequences and 3D images there was better identification of flow voids on 3D sequences whereas cord signal intensity is better depicted on T2WI sequences (45).

3D CISS is a fully refocused steady-state gradient-echo MRI sequence. 3D CISS and FIESTA sequences also have high spatial resolution between and CSF, cord and vertebral bodies. It has been used in brain parenchyma to evaluate cranial nerves, cisternal spaces, ventricles and cavernous sinuses (46). Signal intensity of the cord cannot be appreciated. Flow voids can be traced upto neural foramen similar to CUBE sequence. The whole spine has to be acquired in three stations and the time is a little longer than CUBE sequence. Rizvi et al demonstrated the usefulness of 3D CISS in diagnosing spinal vascular malformation using 3D CISS, when the flow voids are not visualised on T2 WI (47). Morris et al used 3D CISS and FIESTA images in three cases to diagnose and localise the arterial feeder level in complex cases of DAVF. Using information from the 3D MR myelography sequences selective angiography and surgery were planned (48).

Contrast enhanced MRI:

Vascular sequences:

Previous MR techniques like 3D TOF MRA and PC MRA have not been demonstrated to be useful in depicting spinal arteries and veins due to its poor spatial resolution and less flow in the spinal arteries (11). Mascalchi et al used phase contrast angiography (PCA) for detecting the SDAVFs and identifying the arterial feeders of SAVM in 12 of 15 of patients. However, localisation of draining veins, fistula and normal arteries were limited or not possible in some cases because of low flow and small size. (49). Binkert et al first realized fast CE MRA with acquisition times of 24 seconds was able to identify feeding artery to SDAVF or SAVM(12). Contrast enhanced 3D MR angiography could visualise the artery of Adamkiewicz(50). CE 3D MRA is a T1 weighted fast GRE sequence with short TR (fast acquisition), short TE (decrease flow related artefacts) and

small flip angels. Synchronisation of peak contrast in arteries and centre k-space sampling can be achieved with best guess, test bolus, automatic triggering and MR fluoroscopy techniques. By combining auto-triggered elliptical 3D CE MRA and rapid bolus contrast injection and robust timing, Binkert et al identified 2 of 3 DAVF and Farb et al identified 8 of 9 cases. Advantages of CE MRA include high SNR, CNR and spatial resolution(12) (51). Contrast of image depends on timing of the acquisition of centre K space filling during peak concentration of contrast within the arteries. Only a single image is acquired and no information is available on passage of contrast. Two commonly used techniques include a strong bolus technique (high concentration of contrast is injected temporarily) and long and slow contrast injection, both exploiting the first passage of contrast. In the former technique, arteries and veins can be differentiated but with the latter, it is difficult. (11). Nijenhuis et al identified artery of Adamkiewicz artery in patients undergoing thoracoabdominal repair using a two-phase acquisition technique spaced at 40seconds intervals (first phase imaging arteries and second phase imaging arteries and veins) by injecting 45 ml of gadolinium contrast. He identified artery of Adamkiewicz in all 9 patients and could visualise posterior spinal arteries in some, that changed the surgical approach in three patients(50). Luetmer et al evaluated 31 patients suspected with SDAVF using the two phase CR MRA technique and identified SDAVF in 20 of 22 patients, level of fistula in 14 patients and side in 13 patients(15). Mull et al used similar technique and evaluated 34 patients with spinal vascular malformation and correlated with DSA. He could exactly locate site of fistula in 14 of 19 patients with DAVF and in other 5 patients with in one vertebral level. He identified 10 of 11 AVM and their arterial feeders, but could not differentiate glomus from fistulous type in 4 patients (13).

TRICKS: With improvement in gradients and faster imaging techniques, temporal profile of contrast kineties can be studied. To shorten a scan time in 3D image different techniques such as

short TR, rectangular FOV, partial Fourier transform, reduced spatial resolution, parallel imaging, radial K-space sampling and change in k-space data acquisition could be employed. Concept of TRICKS is based on variable rate of K-Space sampling, where central low frequency is more frequently sampled than peripheral high frequency data. Temporal interpolation of previously acquired and zero filling can be done in slice dimension. Advantages of TRICKS sequence include high SNR, provides temporal resolution, can be acquired in any orientation, preserves signal in complex regions, minimised motion artefacts, insensitive to timing of contrast, test bolus is not required and decreased gadolinium dosage.

Time resolved MRA by different vendors:

- Multi-Centric Keyhole (TRICKS – GE):

4 regions (3 central + 1 peripheral). Central > intermediate > peripheral k-spaces sampled with decremental frequency. Temporal resolution might be poor with improvement in spatial resolution.

- Centric Keyhole (4D TRAK - Philips):

2 regions only sampled, Oval central & peripheries. Centric version of classic keyhole imaging.

- Semi randomized Centric Keyhole (TWIST – Siemens):

2 regions only sampled. Central k-space sampled alternatively with incomplete peripheral k-space. Peripheral k-space is acquired over many cycles.

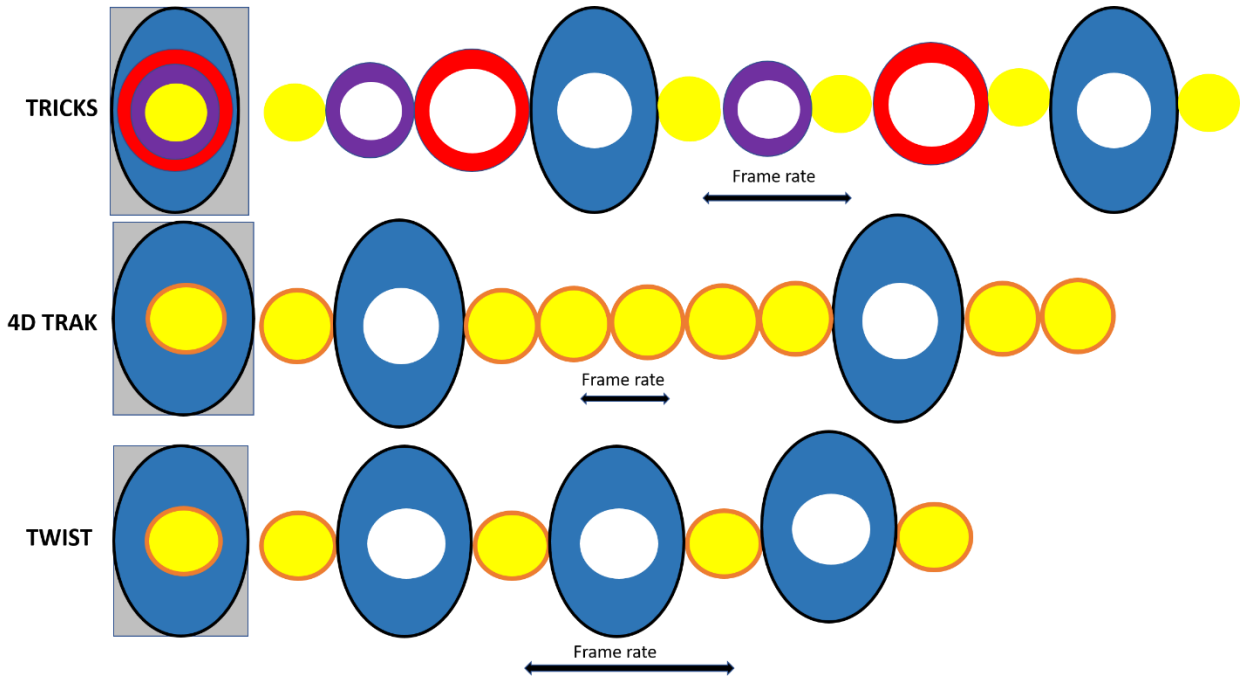


Figure 1. Pattern of filling in k-space by different vendors. a,GE. b, Philips. c, Siemens.

These sequences are increasingly used in evaluation of vasculature in extremities, brain and spine. Ali et al evaluated spinal vascular malformations (AVM and DAVF) using time resolve spinal MRA using 1.5 T Siemens machine achieving a frame rate of 2.32 to 6.75 sec. Of 11 patients undergoing TRSMRA, location of the arterial feeders were identified in all 6 patients with in one vertebral level and in other 5 negative findings, DSA also did not reveal any vascular malformation.(17)

Amarouche et al retrospectively evaluated role of TRICKS with temporal resolution of 1.8 seconds and craniocaudal axis coverage of 34cms and compared with the gold standard criterion DSA in 45 patients with 47 spinal vascular lesions. Of 33 DAVF, arterial feeder could be located within one vertebral level in 27 patients and within 2 vertebral levels in 30 patients. Side of the arterial feeder was located in 22 patients. Perimedullary AVF were erroneously diagnosed as DAVF. Identification of arterial feeder in SCAVM and PM AVF was poor. (16)

Saindane et al retrospectively evaluated 18 patients with suspected DAVF using TRICKS sequence at 1.5T MRI with temporal resolution of 7 seconds and FOV coverage of 35cms. Of 8 patients with DAVF on DSA, TRICKS sequence could identify arterial feeder level within one vertebral level in 6 patients(18).

Digital subtraction angiography

2D-DSA is the gold standard investigation of choice in diagnosing spinal vascular malformations due to its high spatial and temporal resolution. Spinal cord extends from lower margin of foramen of magnum up to L1-2 level and spinal arteries can arise any level cranially from vertebral artery till internal iliac arteries caudally. All arteries need to be catheterised to complete the spinal angiogram and identify the arterial supply to the cord and vascular malformations. On DSA, venous hypertension can be indirectly ascertained by delayed visualisation of artery of Adamkiewicz in the venous phase(30). Drawbacks of DSA include high radiation dose, large volume of contrast administration, longer duration of procedure, need for breath holding, requirement of general anaesthesia, and small risk of neurological deficit (7). DSA becomes more difficult if the aorta is atherosclerotic and tortuous.

3D rotational DSA can supplement the conventional DSA and provide better information on the type and angioarchitecture of complex vascular malformations. It can be used for planning treatment, however it has drawbacks such high radiation, and technical difficulties in obese patients and in evaluating lesions at shoulder level(52)(53).

Therapeutic management

In 1912, Feodor Krause identified spinal cord AVM at surgery and attempted ligation with bad outcome. In1914, Charles Elsberg first ligated the vessel (in DAVF) and removed the nerve root

from where the vein was arising, and the patient improved after surgery. Many attempts were made until 1960's with poor results. In 1960, Yasargil and Krayenbhul published experience with microsurgical instrumentation for treating spinal AVM. Ommaya showed that simple ligation of vessel improves outcome. After the pathophysiological description by Kendall and Louge, approach to treatment changed from stripping of entire vein to simple ligation as demonstrated by doppman and oldfield. Symon et al demonstrated the outcome of surgery to preoperative disability. In1960, era of endovascular has begun and Luessenhop and Spence performed first embolization of intracerebral AVM. In1968, first reports of spinal AVM were published. Due to advancements in catheters and embolization devices, embolization of spinal vascular malformations has become the treatment of choice or as a presurgical technique.

Spinal vascular malformations are treated by surgical and endovascular methods with varying success rates and complications. Due to introduction of operating microscope, outcome of spinal vascular malformations has improved. Due to introduction of newer microcatheters and embolization materials (Particles like PVA and embospheres; Liquid embolic agents like NBCA and EVOH), embolization has become the first modality of treatment. In cases of failed intervention, surgery is being considered.

Dural arteriovenous fistulas:

In early twentieth century, the whole vein was stripped during surgery, which resulted in bad outcome. After the pathophysiology described by Kendall and Louge, approach to treatment changed from stripping of entire vein to simple ligation, as demonstrated by Doppman and Oldfield (54). SDAVF can be treated by both surgical and endovascular methods. Initially, they were treated with particle embolization, which resulted in early good results. As the particle embolization is not permanent, it resulted in high recanalization approaching 90% as demonstrated by Morgan and

Marsh(55). Outcome after embolization with NBCA was more durable and resulted in adequate angiographic occlusion(56). Various rates of recanalization and good outcome were described, ranging from 25% to 90%. New EVOH based liquid embolic agent is an alternative to NBCA, although long term results are not known(57).

Even in cases with common origin of ASA and the feeding artery of the DAVF, embolization can be done safely in 75% of patients(58). Embolization is not possible in all patient's due to common origin of ASA and the feeding artery; and technical difficulties. Surgical ligation of the initial few centimetres of the draining vein can be in cases of failed embolization patients. In the meta-analysis of Steinmetz et al, success rates of surgery were 98% as compared to 48% for embolisation(59).

Arteriovenous malformation

Treatment for spinal AVM depends on various factors like the clinical condition, medical comorbidities, location of lesion and angioarchitecture. Both surgical and endovascular treatments are associated with significant risk of neurological deficits, as the arteries supplying the AVM can also supply the normal cord parenchyma(60). However, treatment may prevent the progression of disease. Various treatment modalities include complete excision or obliteration, partial treatment or conservative management. Primary goal in management of SCAVM is to preserve neurological function but not complete cure. Targeted treatment can obliterate aneurysms (arterial or intranidal pseudoaneurysms), decrease size and flow across the nidus, reducing the venous hypertension and can modify the natural history(61). Embolization can be performed with particles (PVA particles) or liquid embolic agents (NBCA and EVOH) with varied success rates and complications(62)(63)(64).

Perimedullary arteriovenous fistula

Complete obliteration of the fistula is ideal, even though partial occlusion can improve the patient symptoms. Surgical or endovascular management depends on location and angioarchitecture of PMF. Type A are microfistulas and are not amenable to treatment by endovascular means in most cases due to location and size of the feeder and the surgical correction is the treatment of choice. Endovascular treatment may be feasible in some patients(65). Type B and C lesions, endovascular method is the treatment of choice and surgical excision is indicated where endovascular methods are not possible. Surgical treatment involves interruption of the arterial supply followed by disconnection of the draining vein close to the fistula. Angiographic occlusion and clinical outcomes are varied in various studies(66). Surgical excision results in more favoured outcome than treatment by endovascular means(67).

Materials and methods

Materials and methods

This study is a prospective observational study. All patients with clinically suspected or diagnosed spinal vascular malformations underwent MRI of whole spine 3T (Discovery 750W GE MR) with sequences including CUBE and TRICKS and were later evaluated by spinal angiography (Innova 3131 GE machine).

Inclusion and exclusion criteria

(i) Inclusion Criteria:

1. All patients with clinically suspected or diagnosed spinal vascular malformations who present to OPD between May 2015 to August 30, 2017 were included in study.
2. All patients who were evaluated with both MRI including advanced sequences such as TRICKS OR CUBE and DSA were included

(ii) Exclusion Criteria:

1. Contraindications to MRI like cardiac pacemakers, metal prosthesis and gadolinium administration.
2. Contraindication to DSA like contrast allergy, renal failure.
3. Patient not evaluated with advanced MRI sequences or having incomplete DSA.

Magnetic resonance imaging technique

CUBE

CUBE is a 3D fast spin echo sequence with long echo train lengths and variable flip angels. Parameters used are TE - 60 - 115ms, TR - 2500ms, ETL – 90, FOV - 30 cms, Slice thickness - 1.6mm, Matrix – 288x288. Whole spine is acquired in 2 to 3 stations depending on the vascular malformations and time of acquisition for each station is 6 minutes and 8 seconds. Images are

acquired in sagittal space and are reconstructed in different planes (Axial, sagittal, coronal and obliques) and analysed in PACS (picture archiving and communication system)
(AGFA Healthcare NV) and VOXAR 3D software installed in the PACS.

1)Identifying level of feeders on CUBE sequence

On sagittal image, identify flow voids of greatest concentration and scroll the sagittal images in left and right parasagittal images. Flow voids that course the parasagittal regions are followed in cranial and caudal directions. The flow void that courses into the neural foramen without interruption is identified. Additional orthogonal planes or oblique sections are evaluated to confirm the location of the fistula and the feeder is presumed from the intersegmental artery that supplies the foramen.

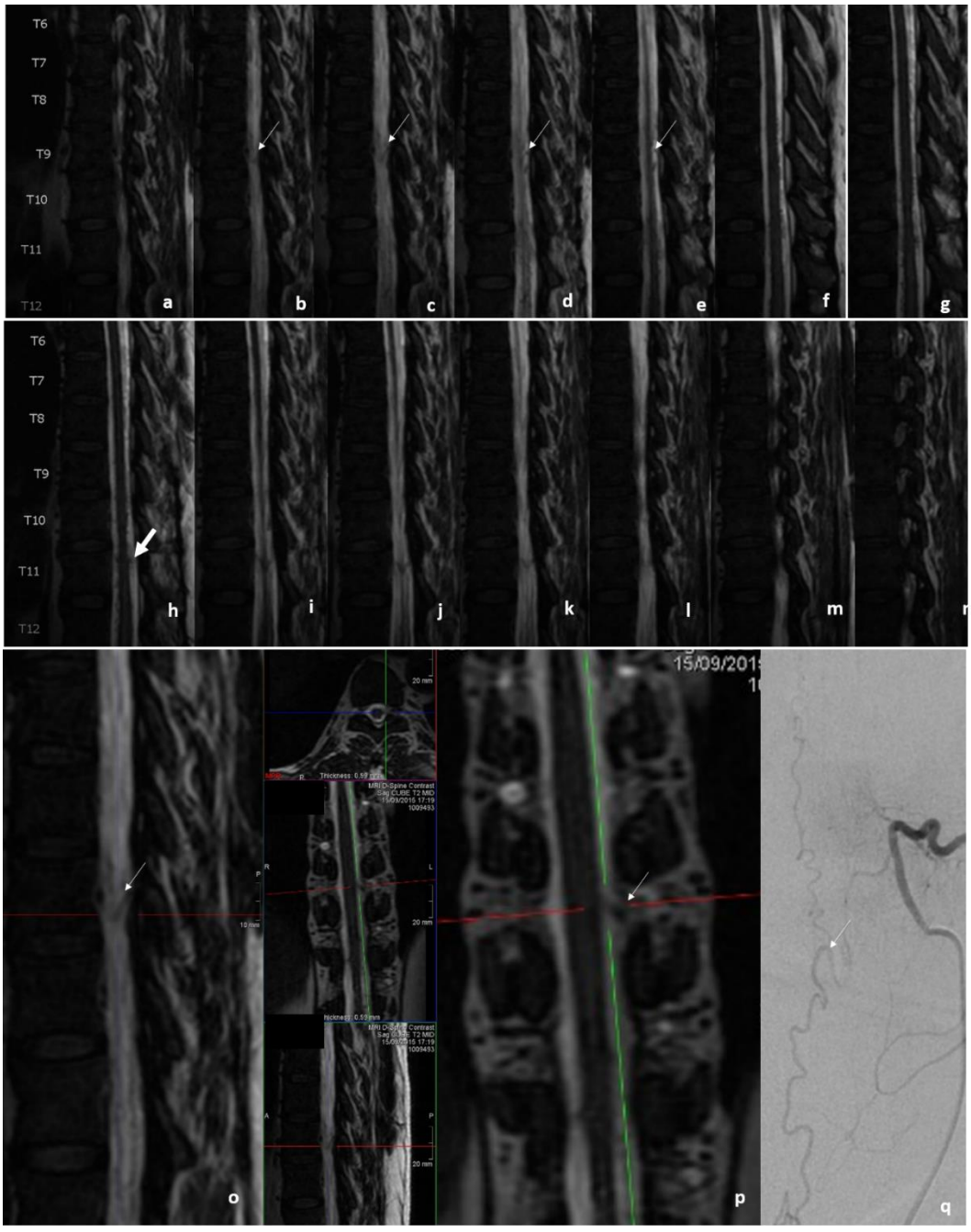


Figure 2: Illustrative case - Identification of arterial feeder using CUBE sequence.

On sagittal images, identify the arteries of greatest concentration. a-o, Sagittal images are scrolled from left to right side, identifies the flow void in left parasagittal region (thin white arrows). On reconstruction and correlating on different planes, fistulous level is identified and is correlated to the level of arterial feeder.

Time Resolved Imaging of Contrast KineticS (TRICKS)

Tricks sequence is type of K space filling in which central lower frequency is sampled frequently than the peripheral K space, giving a higher contrast than resolution. By lowering the number of k space filling, temporal resolution is increased at the cost of spatial resolution. In TRICKS sequence in GE Machine, K space is segmented into four concentric areas and the central space is more frequently sampled. The FOV of TRICKS is 46 cms in cranio-caudal direction. So, TRICKS FOV is positioned after evaluating standard MR sequences and 3D sequences. Centre of FOV is positioned depending on the maximum concentration of flow voids. In AVM, centre of FOV is the nidus and if there is no nidus, centre is positioned at the level of maximum concentration of flow voids.

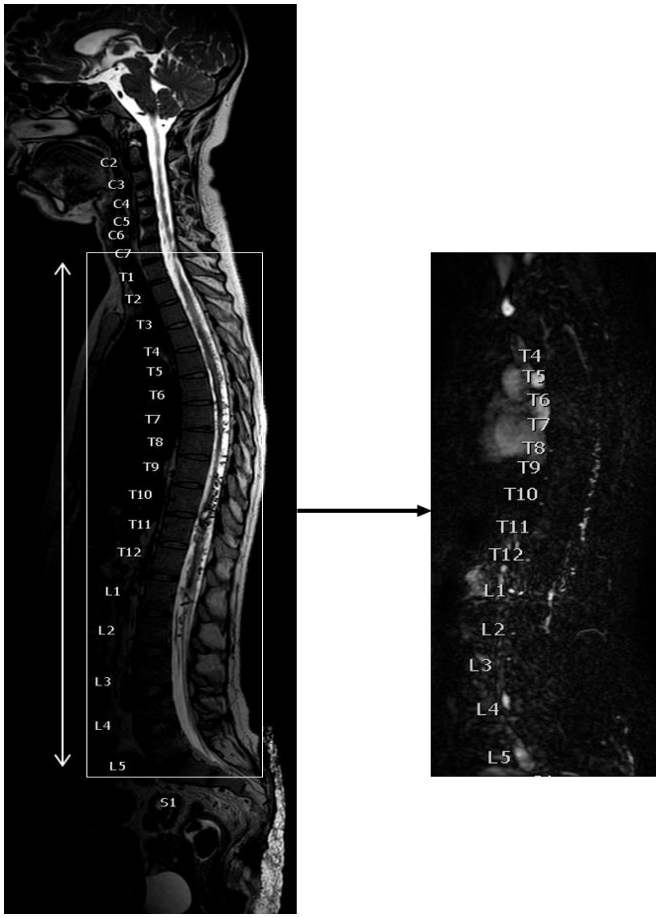


Figure 3: TRICKS FOV is positioned according to the greatest concentration of flow voids. FOV is 46 cms in the present study.

Contrast Dose: 0.2mmol/kg body weight (15-18ml) of gadolinium contrast (Gadodiamide – Omniscan) is injected at a rate of 3.5ml /sec followed by 20ml of saline chase at the same rate.

Parameters for TRICKS sequence: Two tricks sequences were done.

In the initial 7 cases, the following parameters with a temporal resolution of 4.2 sec and scan duration of 1minute and 43 seconds: TR – 4ms, TE – 1.4 -11ms, FOV – 46cms in CC, Slice thickness – 2, NEX – 1, Matrix – 512x256, FA – 30, Phases – 20.

In the remaining patients following parameters with a temporal resolution of 3.1sec and scan duration of 1minute and 15seconds: TR – 3.7ms, TE – 1.4 -11ms, FOV – 46cms in CC, Slice thickness – 2, NEX – 0.75, Matrix – 512x256, FA – 20, Phases – 20.

Images are acquired in sagittal planes and are reconstructed in different planes (coronal, axial, obliques) and analysed in PACS (picture archiving and communication system)

(AGFA Healthcare NV) and VOXAR 3D software installed in the PACS. Images are processed into MIP images and fusion of CUBE and TRICKS sequences are done and reviewed by two independent investigators.

Identification of feeder on TRICKS sequence

Earliest appearance of contrast at the vertebral level is identified and the artery / vein is then followed to the neural foramen. If the vein is followed to the neural foramen, then the side and level of fistula is noted. If the vessel could not be traced to the neural foramen, earliest appearance of the contrast is taken as the level of feeder. Direction of flow is noted by evaluating the different phases of TRICKS sequence.

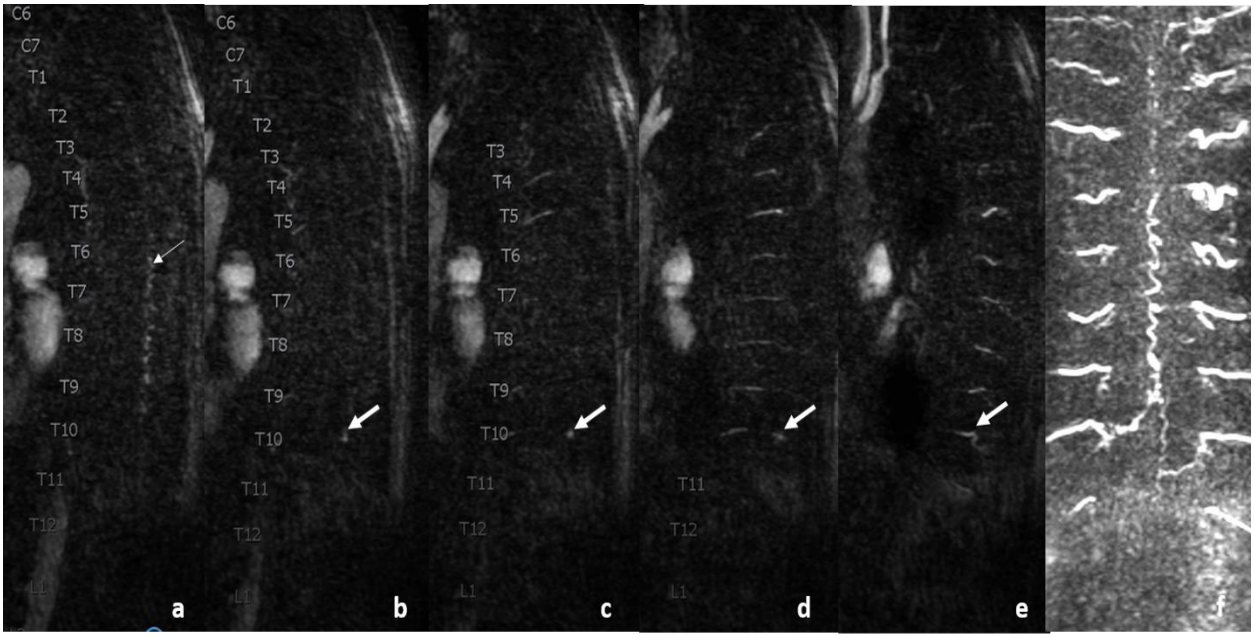


Figure 4: Illustrative case - Identification of arterial feeder level on TRICKS sequence. a, Presence of flow voids in the spinal canal. b–e, the arterial feeder is tracked from the flow voids in central canal to the intercostal artery, identifying the feeder level. f, Coronal MIP image shows the arterial feeder level from right T10 intercostal artery.

Dural arteriovenous fistula:

CUBE: Identifying the vein and correlating it to the site of DAVF and the feeder level.

TRICKS: Identify the earliest appearance of vein and the correlating to the site of the fistula and feeder.

CUBE and TRICKS: Identify the earliest appearance of contrast and the evaluate the CUBE sequence for the fistulous site and feeder level.

Arteriovenous malformation

CUBE: Identifying the flow void near the nidus and then trace the flow void to artery. There might be a confusion between artery and the draining vein because of lack of temporal resolution.

TRICKS: Identifying arteries in early phases and then tracing up to the nidus.

CUBE and TRICKS: Overlapping of CUBE and TRICKS sequence can be done and the feeding arteries can be traced.

Perimedullary arteriovenous fistula

CUBE: Tracing the vessels is similar to DAVF, but in contrary to DAVF, here we trace the arteries.

TRICKS: Earliest appearance of contrast and tracing the vessel upto neural foramen.

CUBE and TRICKS: Fusion of CUBE and TRICKS imaging can be done and the arteries are traced.

Digital subtraction angiography

All patients underwent spinal angiogram after MRI with in a span of 1- 4 weeks. DSA was done on GE Innova 3131 biplane flat plane system.

Procedure:

Under strict aseptic conditions and local anaesthesia, right common femoral artery was punctured and 6F arterial sheath was secured. Heparin loading dose of 2500 IU was administered and 1000 IU of heparin was administered every hour thereafter. Using 5F vertebral Glidecath (Terumo, Tokyo, Japan), angiograms of bilateral common carotid, internal carotid, vertebral arteries and subclavian arteries were performed. Using 5F/4F left coronary catheter (Cordis, Miami, USA), selective catheterisation of intercostal and lumbar arteries was done and angiograms were obtained. Other catheters like right coronary (Cordis, Miami, USA), Cobra (Terumo, Tokyo, Japan) and Simmonds catheter (Cordis, Miami, USA), were used as required depending on the anatomy. Angiogram images are acquired at 2.5 to 4 frames per second and 3D rotational

angiogram was obtained when required. Type and location of vascular malformation, arterial feeders level, number of feeders and angioarchitecture were evaluated.

Data collection and analysis

Data was collected as per the proforma elucidating clinical features and imaging features. MRI data of patients ie CUBE and TRICKS was separately analyzed by two independent neuroradiologists (first observer with 7 years' experience and second observer with two years' experience) blinded to the case particulars. The combined data of CUBE and TRICKS were analyzed after 4 weeks of initial analysis. The DSA data was analyzed by a single neuroradiologists who was also blinded to the MRI observations. Magnetic Resonance Imaging details (MRI) were analyzed for following aspects of spinal vascular malformations: CUBE and TRICKS images of each patient were independently analyzed for presence of vascular malformation, site and type (SDAVF or SAVM), level, feeding arteries (number and their level), nidus characteristics (size, site and intranidal aneurysm).

Statistical analysis of the data was performed by calculating sensitivity, specificity, positive and negative predictable values in identifying the type and location of vascular malformation. The accuracy of the modalities and kappa coefficient of inter modality and interobserver variability were also calculated. Kappa value of less than 0.20 indicated poor agreement, 0.20 to 0.40 indicated fair agreement, 0.40 to 0.60 indicated moderate agreement, 0.60 to 0.80 and 0.80 to 1 indicated good and very good agreement respectively.

Results

Results

Total of 31 patients met the inclusion criteria. Three patients were excluded due to uninterpretable images secondary to patient motion artifacts (one AVM and DAVF each) and refusal of consent (one patient).

In two patients with recurrent DAVF and one patient with residual AVM, no feeder level could be identified on DSA and were also excluded. Remaining 25 patients were available for final analysis. (Figure 1)

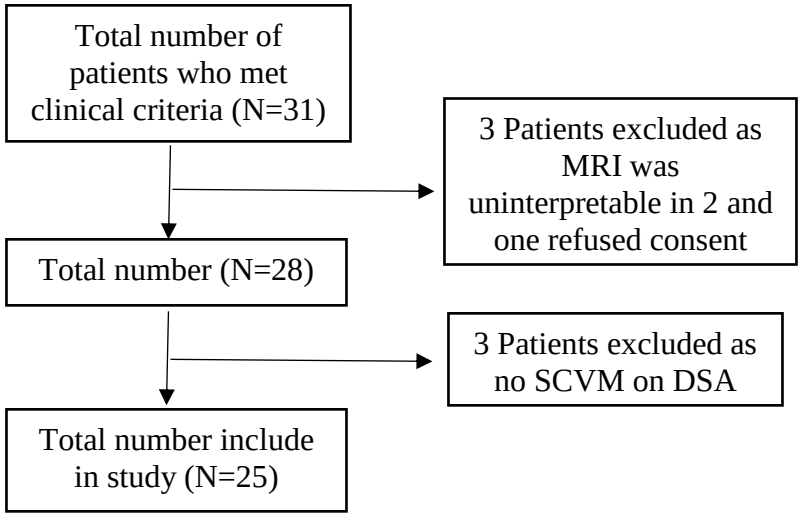


Figure 5. Number of patients in the study.

Patient characteristics

Dural arteriovenous fistula

Out of 10 patients, 9 were male and one was female (M: F= (9:1). Age ranged from 49- 67 years and the patients had comorbidities like diabetes 40% (4 patients) and hypertension in 20%(2 patients). All patients presented insidiously with sudden worsening in 3 patients related to motor activity or exertion. Initial symptoms were varied and symptoms progressed over time to involve other modalities over a mean time of 11.4 months, ranged from 4 to 24 months. Most of the patients

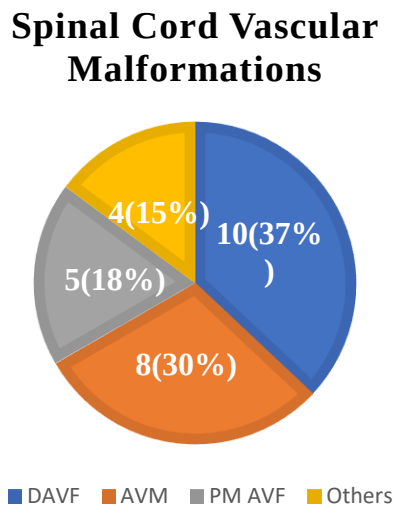
required single support for daily activities with variable involvement of bladder and bowel symptoms. Aminoff logue scale for disability for various functions were Gait - median 3, ranged from one to four; Micturition - median 1, ranged from zero to three; Bowel median - 1, ranged from zero to three.

Arteriovenous malformation

Eight patients were diagnosed with AVM on DSA. Patients age ranged from 15-53 years, most of the patients were in third decade. 5 were males and 3 were females (1.66:1). Most of them presented (6 patients,75%) acutely with low backache, sensory and motor symptoms with variable involvement bowel and bladder. One patient presented with only backache and was diagnosed as AVM on imaging. Of the patients who presented acutely, there was improvement in motor power and paresthesia in 5 patients. One patient had acute presentation in childhood at 14 years of age with backache, followed by sensorimotor, bowel and bladder involvement. She was imaged 15 years after her symptoms and was diagnosed as AVM. Aminoff logue scale for disability for various functions were Gait - median 2, ranged from one to six; Micturition - median 1, ranged from zero to three; Bowel median - 1, ranged from zero to three.

Perimedullary arteriovenous fistula

All patients were males and aged between 27 to 78 years. Symptoms and presentation were similar to DAVF. Aminoff logue scale for disability for various functions are Gait - median 3, ranged from two to four; Micturition - median 1, ranged from one to two; Bowel median - 1, ranged from one to two.



Type of spinal vascular malformation	Patient number (DSA)
Type I **A** **B**	10 8 2
II & III	8 (6&2)
IV **A** **B** **C**	5 3 2 0
Extraspinal AVM	2
Total	25

Figure 6. Distribution of cases on DSA

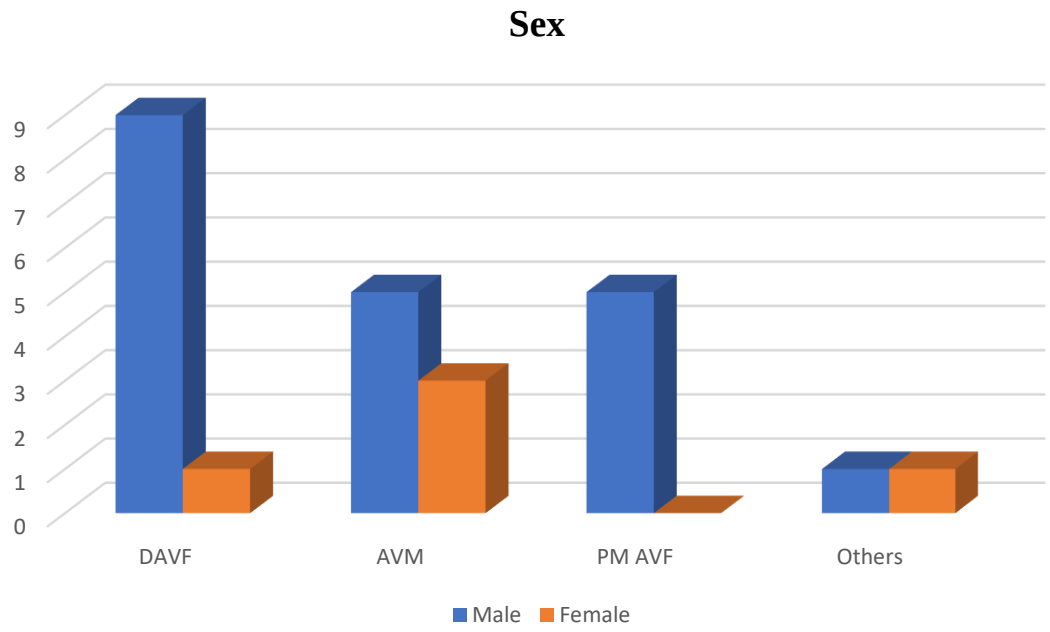


Figure 7. Male to female ratio in different vascular malformations.

	DAVF	AVM	PM AVF
Mean Age in years (Range)	57.7 (49-67)	29 (15-53)	52 (27-78)
Sex			
Males	9	5	5
Females	1	3	0
Comorbidities			
Diabetes	4	1	2
Hypertension	2	0	1
Presentation			
Acute/subacute	0	6	1
Chronic	10	2	4
Clinical features			
Initial symptoms			
Low backache	3	5	3
Sensory symptoms	3	5	2
Motor weakness	4	7	0
Symptoms at diagnosis			
All (M/S/Bla/Bow)	8	7	5
Some symptoms	2	3	0
Time to diagnosis (months)	11.4 (4-24)	0-15 years	13.4 (1-24)

Table 1. Clinical characteristics of patients in the study.

Distribution of patients based on findings of DSA

Out of 25 patients, 10 were diagnosed as DAVF, 8 as AVM, 5 as Perimedullary AVF and 2 are extraspinal AVF.

Location of SCVM	DAVF (10)	PMF (5)
Cervical	0	0
Upper thoracic (T1-6)	2	0
Lower thoracic (T7-12)	4	0
Lumbar	2	5
Sacral	2	0

SC AVM (8)	
Cervical	1
Cervicothoracic	1
Thoracic	3
Thoracolumbar	2
Filum terminale	1

Table 2. Distribution of spinal vascular malformations at different levels of spinal cord.

DAVF: Most DAVF were located in lower thoracic spine (4 patients), and the distribution at upper thoracic, lumbar and sacral levels were equal (2 patients each). No DAVF was identified in cervical region.

AVM: AVMs were distributed all over the cord from cervical to lumbosacral level and most of them were located in thoracic spine (4).

PM AVF: All perimedullary AVF were located in lumbar level. Two were of type IVB and others were type IVA. No Type IVC lesions were identified.

Conventional MRI (T2, T1, GRE) Findings:

Dural arteriovenous fistula

Flow voids are seen both anterior and posterior to cord on T2WI and extended for a variable length from foramen magnum to sacral levels. T2 hyperintensity is seen with in the cord in all the patients and extended for >3 vertebral segments in all patients except for one patient who had hyperintensity involving conus and extended up to 2 segments. In 6 patients hyperintensity was seen from T6 to conus level and in 3 patients it extended above T6 vertebral level. Peripheral hypointensity surrounding hyperintensity was seen in all patients. There was no evidence of flow voids with in the cord. Thickening of the spinal cord was seen in 4 patients, while in the other patients, cord was of normal size or mild atrophy seen.

Arteriovenous malformation

Flow voids were seen with in the cord at the level of nidus with expansion of the cord. T2 hyperintensity extended for short segment <3 in 3 patients and in the remaining patients it extended for more than 3 vertebral segments. In 5 patients, GRE images showed evidence of blooming, indicating bleed.

Perimedullary arteriovenous fistula

Flow voids were seen anterior to and posterior to cord with no flow voids inside the cord. T2 hyperintensity extended for >3 segments in all patients

Identifying the type of vascular malformation by CUBE and TRICKS sequences

In diagnosing the presence of spinal vascular malformation, the sensitivity, specificity, PPV and NPV are 100%, 33%, 92.6% and 100% respectively. Low specificity is due to the less number of true negative cases.

Number of patients 25				
Type of lesion	DSA	CUBE	TRICKS	CUBE & TRICKS
I A **I B**	8 2	13	12 1	11 1
II & III	8 (6 &2)	8	7	8
IV (A, B & C)	5	3	4	4
Others **Type V DAVF** **Vertebral AVF**	 1 1	1 1 -	1 1 -	1 1 -

Table 3. Categorization of patients by the type of vascular malformation by different modalities.

Dural arteriovenous fistula

In diagnosing DAVF, CUBE and TRICKS sequence had sensitivity, specificity, PPV and NPV of 100%, 80%, 77% and 100% respectively. CUBE sequence misdiagnosed two cases of PM AVF and one case of vertebral AVF as DAVF. TRICKS sequence misdiagnosed one case of AVM, PM AVF and vertebral AVF as DAVF. By combining both the sequences, sensitivity, specificity, PPV and NPV are 100%, 92%, 83% and 100% respectively.

Arteriovenous malformation

CUBE sequence had sensitivity, specificity, PPV and NPV of 100%. TRICKS had sensitivity, specificity, PPV and NPV of 87.5%, 100%, 100% and 94.4% respectively. In one patient with extradural AVM and spinal cord AVM, TRICKS sequence misdiagnosed AVM as spinal DAVF.

Perimedullary arteriovenous fistula

CUBE sequence had sensitivity, specificity, PPV and NPV of 60%, 100%, 100% and 91% respectively. TRICKS had sensitivity, specificity, PPV and NPV of 80%, 100%, 100% and 95% respectively.

	Sensitivity	**Specificity**	**PPV**	**NPV**
Presence of spinal vascular malformation				
CUBE	100%	33%	92.6%	100%
TRICKS	100%	33%	92.6%	100%
Combined	100%	33%	92.6%	100%
DAVF				
CUBE	100%	80%	77%	100%
TRICKS	100%	80%	77%	100%
Combined	100%	80%	77%	100%
AVM				
CUBE	100%	100%	100%	100%
TRICKS	87.5%	100%	100%	94.4%
Combined	100%	100%	100%	100%
PM AVF				
CUBE	60%	100%	100%	91%
TRICKS	80%	100%	100%	95%
Combined	80%	100%	100%	95%

Table 4. Sensitivity, specificity, PPV and NPV of CUBE and TRICKS sequences in diagnosing and identifying the type of spinal vascular malformation.

Location of vascular malformation by CUBE and TRICKS

In localizing spinal vascular malformation, CUBE sequence correctly localized fistula with in one vertebral level in 9 of 10 DAVF patients (90%), all patients of AVM (100%), 2 of 5 PMAVF patients (40%).

In localizing spinal vascular malformation, TRICKS sequence correctly localized fistula within one vertebral level in 6 of 10 DAVF patients (60%), 7 of 8 AVM patients (87.5%), 2 of 5 PM AVF patients (40%) and in patient with type V intracranial DAVF. Other vertebral AVF was not localised. Both the observers had similar findings.

	CUBE		**TRICKS**	
	Correctly located	**Not localized**	**Correctly located**	**Not localized**
DAVF	9 (90%)	1 (10%)	6 (60%)	4 (40%)
AVM	8 (100%)	0	7(87.5%)	1 (12.5%)
PM AVF	2 (40%)	3 (60%)	2 (40%)	3 (60%)

Table 5. Localization of fistula and AVM level by CUBE and TRICKS sequences.

Identifying feeder level with CUBE and TRICKS sequences

Dural arteriovenous fistula

Exact level:

CUBE identified accurately in 60% (6 out of 10) by observer 1 and 50% (5 out of 10) by observer 2. TRICKS sequence identified accurately in 50% of patients by both the observers.

Within one vertebral level:

The level of the feeder within one vertebral level could be accurately identified on the CUBE sequence in 90% (9 of 10) of patients by observer 1 and in 80% (8 out of 10) by observer 2 with good inter-rater agreement (Kappa-0.667).

Correspondingly, using TRICKS sequence, feeder level could be correctly identified within one vertebral level in 60% of patients by observer 1 and 70% of patients by observer 2 with good interrater agreement (Kappa-0.692).

OBSERVER 1									
Case no.	Age (Y) / sex	CUBE		TRICKS		CUBE&TRICKS		DSA	
		Level	Side	Level	Side	Level	Side	Level	Side
3	65/M	-	-	T12	-	T12	-	L2	Right
5	49/M	T9	Left	T11	Right	T9	Left	T8	Left
6	54/M	T5	Right	T 6	Left	T5	Right	T5-6	Right
7	54/M	T6	Right	T7	Right	T6	Right	T5-6	Both
8	50/M	L2	Left	T12	Left	L2	Left	L3	left
14	67/M	T10	Right	T10	Right	T10	Right	T10	Right
15	63/M	S2	Right	S2	Right	S2	Right	S2	Right
21	49/M	T9	Left	T8	-	T9	Left	T9	Left
22	60/F	T11	Right	T10	-	T11	Right	T10	Right
27	66/M	S2	Left	S2	Left	S2	Left	S2	left

OBSERVER 2									
Case no.	Age (Y) / sex	CUBE		TRICKS		CUBE&TRICKS		DSA	
		Level	Side	Level	Side	Level	Side	Level	Side
3	65/M	-	-	T12	-	T12	-	L2	Right
5	49/M	T9	Left	T11	Left	T9	Left	T8	Left
6	54/M	T5	Right	T 5	Right	T5	Right	T5-6	Right
7	54/M	T6	Right	T7	Right	T6	Right	T5-6	Both
8	50/M	L2	Left	T12	-	L2	Left	L3	left
14	67/M	T10	Right	T10	Right	T10	Right	T10	Right
15	63/M	S2	Right	S2	Right	S2	Right	S2	Right
21	49/M	T9	Left	T8	-	T9	Left	T9	Left
22	60/F	T11	Left	T10	-	T11	Right	T10	Right
27	66/M	-	-	S2	Left	S2	Left	S2	left

Table 6. Localization of level and side of arterial feeder by CUBE, TRICKS and, combined CUBE and TRICKS in comparison to DSA as read by both observers in patients with DAVF.

Inter modality agreement (kappa) for feeder level with in one vertebral level for both readers		
	Observer 1	Observer 2
CUBE and DSA	0.881	0.762
TRICKS and DSA	0.659	0.659
Combined CUBE & TRICKS Vs. DSA	0.881	0.881
CUBE and TRICKS	0.451	0.355

Table 7. Kappa value for localization of feeder level with in one vertebral level for both readers in DAVF.

When compared to the gold standard of invasive conventional DSA, CUBE showed a very good to good agreement by both readers. TRICKS also showed good agreement with DSA between both readers. However, when TRICKS and CUBE were combined, they showed an improvement over the individual agreement scores to consistently very good for both observers.

The laterality of the arterial feeder was misinterpreted in one case but otherwise showed good inter-rater agreement for identification of side of the feeder (Kappa - 0.667).

When multiple feeders were present (in 2 patients), CUBE and TRICKS were able to delineate only one feeder (1 of 3 and 1 of 2). In all these cases, DSA showed that these feeders arose within one adjacent vertebral level from the site of fistula.

Arteriovenous malformation

Dominant feeder was found in 6 out of 8 patients on CUBE and TRICKS by both the observers.

When identifying the dominant feeder, there was an improved kappa of fair to moderate agreement between all the modalities (CUBE versus DSA; TRICKS versus DSA and CUBE and TRICKS combined versus DSA) for both observers. In the other 2 patients, where arterial feeder was not detected, there was only one arterial feeder supplying the AVM on DSA. There was only fair to good agreement between the CUBE and TRICKS sequence in identifying the dominant feeder.

Inter modality agreement for dominant feeder for both the observers		
	Observer 1	Observer 2
CUBE and DSA	0.564	0.564
TRICKS and DSA	0.564	0.564
Combined CUBE & TRICKS vs DSA	0.564	0.564
CUBE and TRICKS	0.671	0.503

Table 8. Kappa value for localization of dominant feeder for both readers in AVM.

With regards to identifying all feeders to a cord AVM, there was only poor to fair agreement between the modalities (CUBE versus DSA; TRICKS versus DSA and CUBE and TRICKS combined versus DSA) for both the observers. Of 21 feeders on DSA, by CUBE sequence, observer 1 and 2 identified 6 (28.5%) and 7 (33.3%) arterial feeders respectively. By TRICKS sequence and combined CUBE and TRICKS sequences, observer I and 2 identified 10 (47.6%) and 13 (61.9%) feeders respectively. On TRICKS sequence, two false positives were identified by both the observers.

Inter modality agreement for all feeder levels for both the observers		
	Observer 1	Observer 2
CUBE and DSA	0.302	0.249
TRICKS and DSA	0.394	0.469
Combined CUBE & TRICKS vs DSA	0.484	0.469

Table 9. Kappa value for localization of all the feeders supplying AVM for both readers.

Arteriovenous malformation with Multiple arterial feeders

Five out of 8 patients with SCAVMs had multiple arterial feeders. CUBE and TRICKS were able to delineate more than one feeder in 4 of these patients while it failed to detect multiplicity in 1 patient. In all these cases, DSA showed that these feeders arose within one adjacent vertebral level from the site of AVM. Intranidal aneurysms were identified in 3 patients (75%) and was missed in patient by both the observers.

OBSERVER 1									
Case no.	Age (Y) / sex	CUBE		TRICKS		CUBE&TRICKS		DSA	
		DF	OF	DF	OF	DF	OF	DF	OF
1	30/M	Lt T9	-	RtT9	-	Rt T9	-	Rt T9	B/l T10
4	15/F	Rt T3	-	Lt T3	Rt T5	Rt T3	Lt T3, Rt C6	Rt T3	Lt T3, Rt C6, Lt T4
10	29/F	Rt L1	-	Rt L1	-	Rt L1	-	Rt L1	-
11	41/M	-	-	Rt T10		Rt T10	-	Lt T9	-
16	18/F	Rt C3	-	Rt C3	-	Rt C3	-	Rt C3	Lt C3, B/l C5, Rt C6
17	53/M	Lt L5	-	Lt L5	-	Lt L5	-	Lt L4	B/l L5
24	25/M	Lt L2	-	T10	-	T10	-	Lt T8	-
25	29/M	Lt T9	Rt T9, Lt T11, Lt L2	Lt T9	Rt T9, Lt T11, Lt L2	Lt T9	Rt T9, Lt T11, Lt L2	Lt T9	Rt T9, Lt T11, Lt L2

OBSERVER 2									
Case no.	Age (Y) / sex	CUBE		TRICKS		CUBE&TRICKS		DSA	
		DF	OF	DF	OF	DF	OF	DF	OF
1	30/M	Rt T9	-	Rt T9	Lt T10	Rt T9	Lt T10	Rt T9	B/l T10
4	15/F	Rt T3	Rt C6	Rt T3	Rt C6, Lt T3	Rt T3	Rt C6, Lt T3	Rt T3	Lt T3, Rt C6, Lt T4
10	29/F	Rt L1	-	Rt L1	-	Rt L1	-	Rt L1	-
11	41/M	-	-	T11	-	T11	-	Lt T9	-
16	18/F	Rt C3	-	Rt C3	Lt C3	Rt C3	Lt C3	Rt C3	Lt C3, B/l C5, Rt C6
17	53/M	-	-	Lt L5	-	Lt L5	-	Lt L4	Rt L5, Lt L5
24	25/M	Rt T12	-	T10	-	T10	-	Lt T8	-
25	29/M	Lt T9	-	Lt T9	Lt T11, L2	Lt T9	Lt T11, L2	Lt T9	Rt T9, Lt T11, Lt L2

Table 10. Localization of dominant arterial feeder (DF) other feeders (OF) by CUBE, TRICKS and combined imaging of CUBE and TRICKS in comparison to DSA as read by both observers in patients with AVM.

Perimedullary arteriovenous fistula

Dominant feeder or single feeder could be identified on CUBE in 4 out of 5 (80%) patients by observer 1 and 3 out of 5 (60%) patients by observer 2. Similarly, TRICKS sequence could identify feeder in 4 of 5 (80%) patients by both the observers.

Of 7 feeders on DSA, by CUBE sequence, observer 1 and 2 identified 4 (57.1%) and 3 (42.8%) arterial feeders respectively. By TRICKS sequence and combined CUBE and TRICKS sequences, observer I and 2 identified 4 (57.1%) and 5 (71.4%) feeders respectively. On TRICKS sequence, one false positive was identified by observer one and two false positives were identified by the observer 2.

Two out of 5 patients had multiple feeders. Cube could identify only single feeder level in 2 patients by both the observers. However, TRICKS could identify both the feeders in one patient by observer 2 and only one feeder was identified by observer 1.

Inter modality agreement (kappa) for feeder level with in one vertebral level for both readers		
	Observer 1	Observer 2
CUBE versus DSA	0.523	0.391
TRICKS versus DSA	0.523	0.674
CUBE & TRICKS versus DSA	0.523	0.674
CUBE and TRICKS	0.816	0.378

Table 11. Kappa value for localization of all the feeders supplying PM AVF for both readers.

OBSERVER 1									
Case no.	Age (Y) / sex	CUBE		TRICKS		CUBE&TRICKS		DSA	
		DF	OF	DF	OF	DF	OF	DF	OF
2	35/M	Lt T10	-	Lt T10	-	Lt T10	-	Lt T10	Rt L4
12	59/M	-	-	Lt T11	-	Lt T11	-	Lt T8	-
20	45/M	Lt L1	-	Rt L1	-	Lt L1	-	Lt L1	Lt IIA
26	53/M	Lt T9	-	Lt T9	-	Lt T9	-	Lt T9	-
28	78/M	Lt T11	-	Lt T11	-	Lt T11	-	Lt T11	-

OBSERVER 2									
Case no.	Age (Y) / sex	CUBE		TRICKS		CUBE&TRICKS		DSA	
		DF	OF	DF	OF	DF	OF	DF	OF
2	35/M	Lt T10	-	Lt T10	Rt L4	Lt T10	Rt L4	Lt T10	Rt L 4
12	59/M	-	-	T 11	-	T11	-	Lt T8	-
20	45/M	Lt L1	-	Lt L1	Rt L1	Lt L1	-	Lt L1	Rt S2
26	53/M	-	-	Lt T9	-	Lt T9	-	Lt T9	-
28	78/M	Lt T11	-	Lt T11	-	Lt T11	-	Lt T11	-

Table 12. Localization of level and side of arterial feeder by CUBE, TRICKS and combined CUBE and TRICKS in comparison to DSA as read by both observers in patients with PM AVF.

In perimedullary AVFs when compared to the gold standard of DSA, both TRICKS and CUBE both individually and combined showed a moderate to good agreement by both readers. Observer 1 has good agreement with CUBE and TRICKS equally while observer 2 found most feeders with TRICKS sequence.

Treatment

Dural arteriovenous fistula

Nine out of 10 patients underwent embolisation by NBCA. One patient didn't consent for procedure after DSA evaluation. Three of nine patients developed worsening of neurological status after embolisation and two among these patients improved after 2 weeks, but the neurological

status of the other patient remained static. On follow up there was improvement in disability scores, mostly for gait by scores of one to two.

Arteriovenous malformation

Five out of 8 patients underwent partial embolisation using PVA particles. In two patients embolisation was not possible due to arterial access related problems and in other patients embolisation was deferred because, there were no deficits and except for backache. No patient worsened after embolisation.

Perimedullary arteriovenous fistula

One patient was embolized with NBCA and he worsened after embolisation with increased weakness in bilateral lower limbs, urinary retention and incontinence. In two other patients, embolisation was attempted, due to access related problems, it was abandoned. The two other patients refused further treatment.

Representative cases

Representative cases

Dural arteriovenous fistula

Case 1

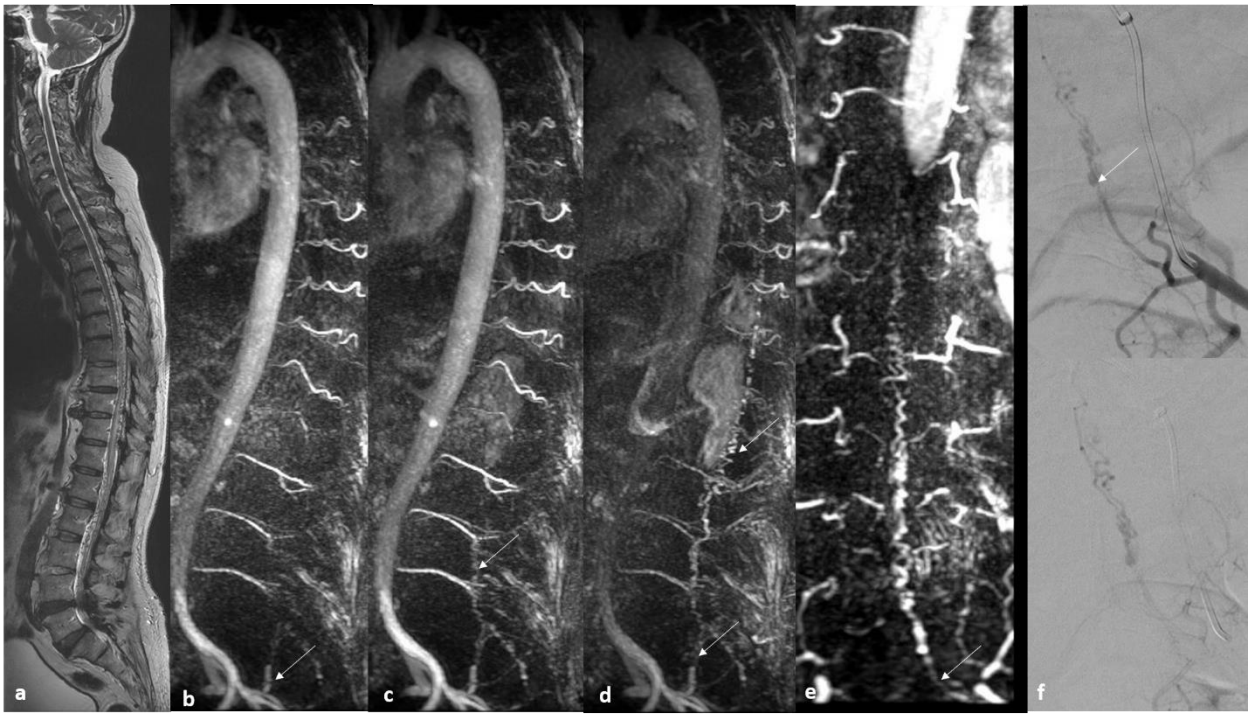


Figure 8. A 66-year-old male presented with complaints of weakness in bilateral lower limbs since one and half years, sensory disturbance for 6 months, constipation for four weeks with no bladder symptoms. a, CUBE image showed flow voids in the CSF spaces with no evidence of nidus within the cord and feeder from left S2 level. b, c, d. Sequential MIP images shows flow of contrast from S2 level and extending superiorly. e, Coronal MIP image demonstrates the feeder level from left internal iliac artery. f, DSA images confirming the feeder level from lateral sacral artery of left internal iliac artery.

Case 2

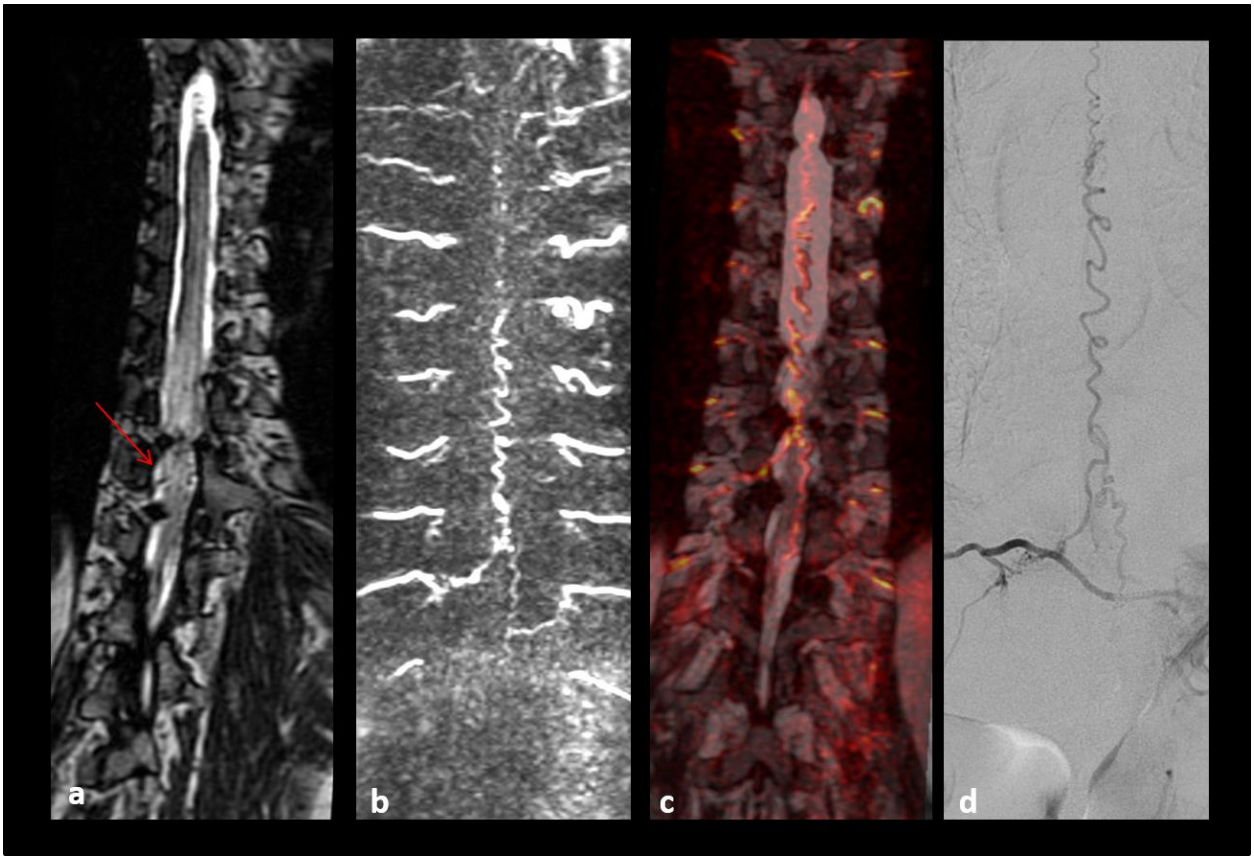


Figure 9. A 67-year-old hypertensive male presented with weakness of bilateral lower limbs, followed by sensory disturbances, with bladder disturbances for four months. a. Vein was traced to the intervertebral foramen at right T10 level on CUBE sequence. b. Phase 4 of TRICKS sequence showing arterial feeder level at right T10 level. c. Fusion imaging showed excellent spatial resolution. d. DSA image showing feeder level at right T10 level.

Arteriovenous malformation

Case 3

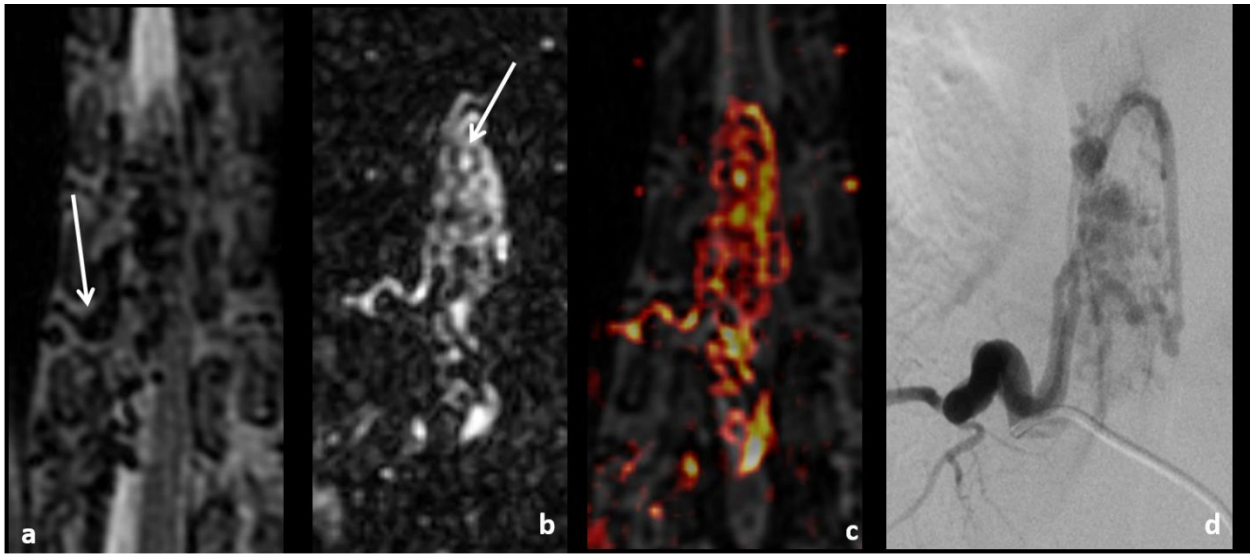


Figure 10. A 30-years-old male presented with weakness in right lower limb for 15 years with worsening for one month. a, CUBE image showing flow voids traversing the neural foramen (arrow). b, Phase 4 of TRICKS sequence shows arterial feeder from the intercostal artery with intranidal aneurysm (arrow). c, Fusion imaging of CUBE and TRICKS shows excellent spatial resolution. d, DSA image confirming the arterial feeder level from right T9 intercostal artery.

Case 4

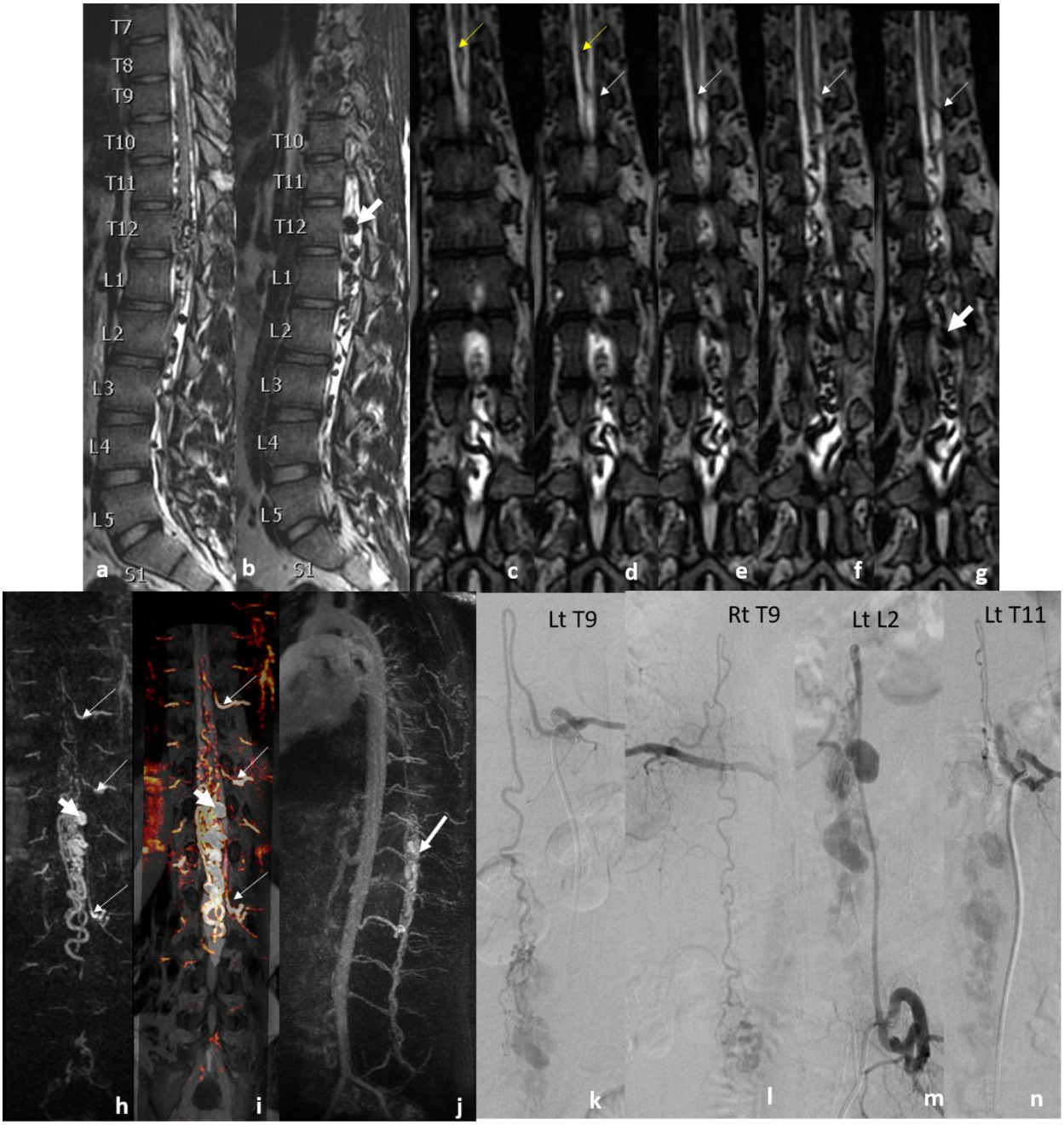


Figure 11. A 29-year-old male presented with complains of low backache for one month. a & b, Sagittal image of CUBE sequence showed flow voids within the cord and CSF spaces and a dilated flow void, possible intranidal aneurysm (Thick arrow). c to g, Coronal CUBE images showing dilated ASA (yellow and white arrows), nidus and intranidal aneurysm. h, Phase 4 of TRICKS sequence showed arterial feeders from left T9, T11 and L2 levels (arrows). i, Fusion imaging showed good spatial resolution and the arterial feeder levels and intranidal aneurysm. j, MIP

imaging showed the nidus. k to n, DSA confirmed the arterial feeders as described. TRICKS image could not identify the right T9 arterial feeder.

Case 5

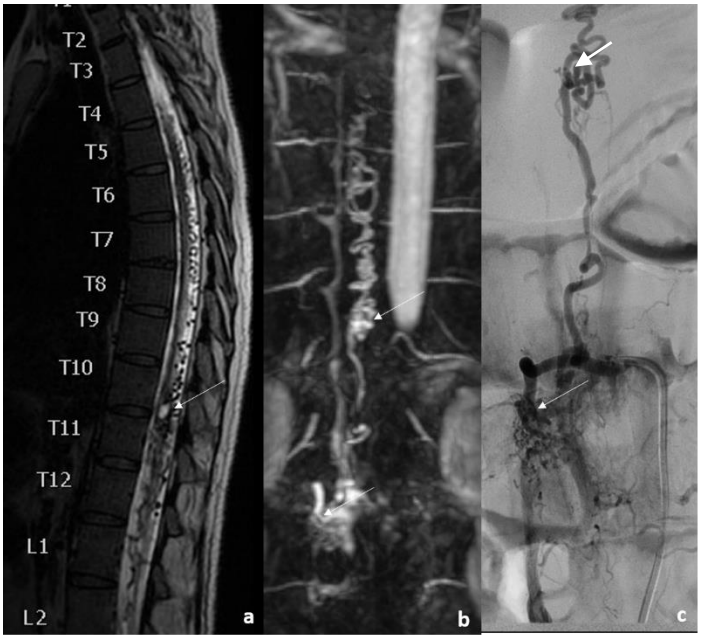


Figure 12. A 29-year-old female patient presented with paresthesia's in bilateral lower limbs followed by urinary incontinence and sudden onset of weakness and constipation for six years. a, Sagittal CUBE image showed nidus at T10-11 levels and multiple flow voids and cord hyperintensity. b, TRICKS sequence showed extradural AVM that was falsely as DAVF and the nidus was assumed to be the engorged veins. c, DSA identifying the arterial feeder, nidus and intranidal aneurysm.

Case 6

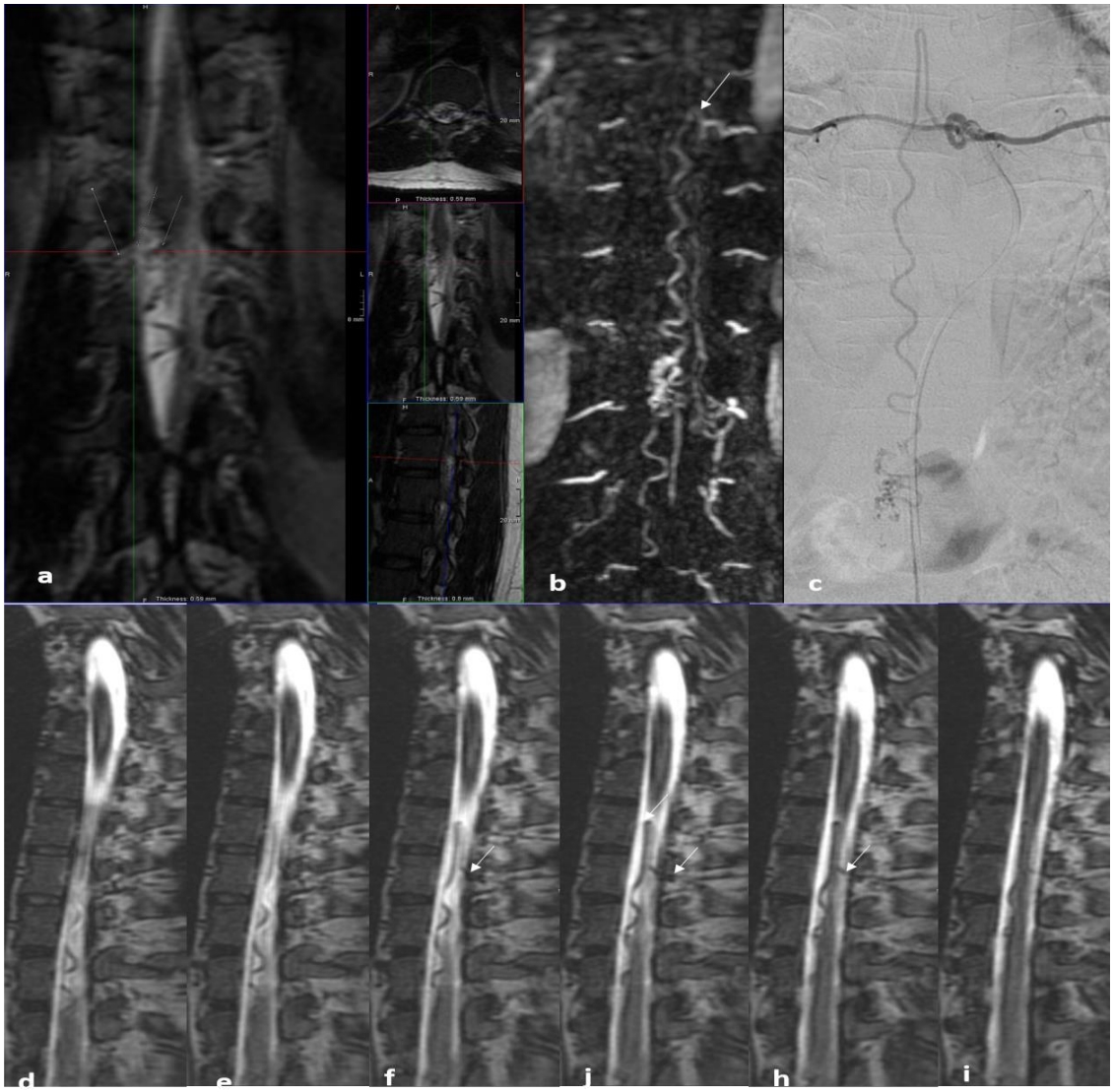


Figure 13. A 25-year-old male patient presented with complaints of paresthesia's and weakness in lower limbs for 3 months. a, CUBE image falsely identified the arterial feeder level from right T12 level. b, TRICKS sequence showed the arterial feeder level from left T8 level, although hairpin bend of ASA was not visualized. c, DSA confirmed the feeder level from left T8 intercostal artery. d to i, retrospectively on evaluation of CUBE in oblique sagittal views, the arterial feeder is clearly identified.

Perimedullary arteriovenous fistula

Case 7

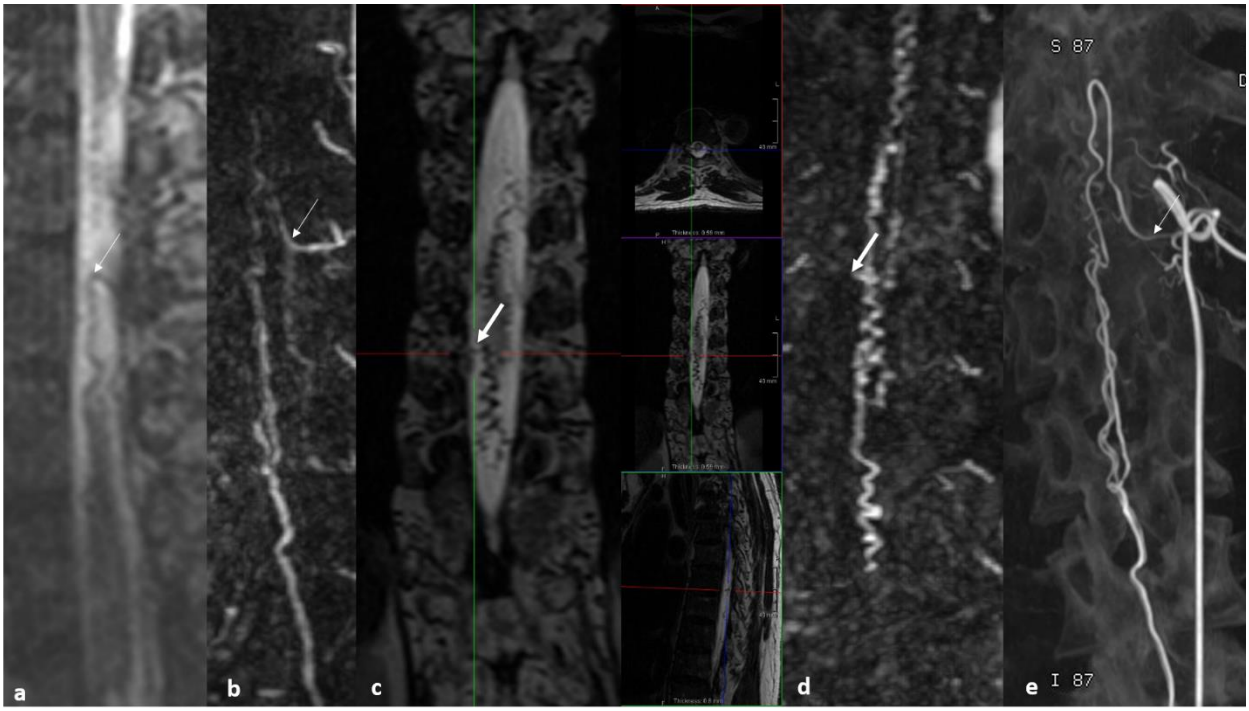


Figure 14. A 78-year-old male presented with complaints of low backache for 2 years, paresthesia's and weakness in bilateral lower limbs since one and half years, and urinary incontinence for six months. a, CUBE image showed dilated ASA from left T11 intercostal artery. b, Phase 4 of TRICKS sequence showed ASA arising from left T11 intercostal artery. c, Cube images showed another flow void is seen tracking towards neural foramen at right T6 level. d, TRICKS sequence showed the flow void at right T6 neural foramen is a continuation of vein rather than arterial feeder. e, DSA confirmed the feeder level from left T11 intercostal artery.

Case 8

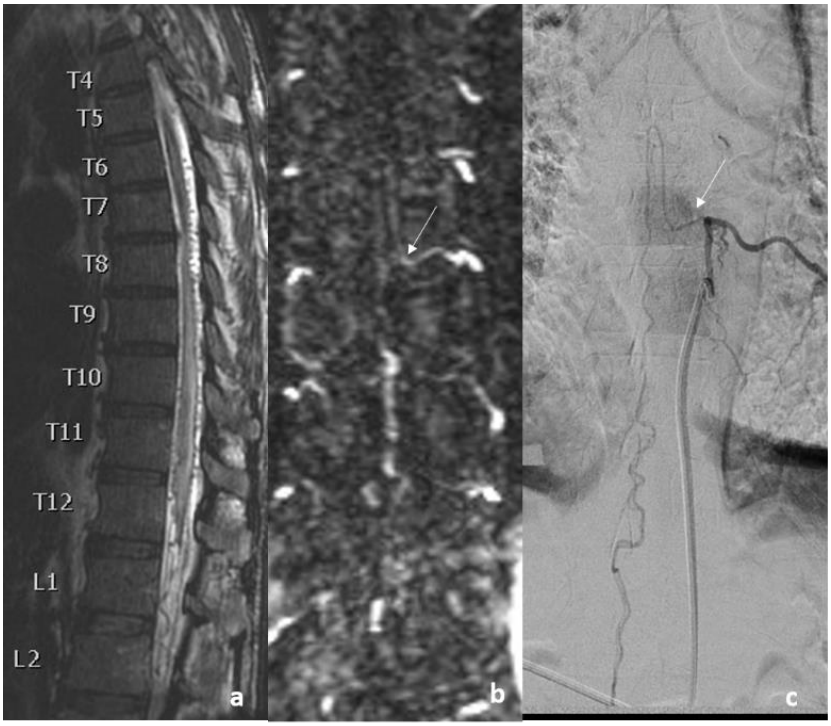


Figure 15. A 53-year-old male presented with complaints of paresthesia's, weakness in bilateral lower limbs since one and half years, constipation for one year and urinary incontinence for one month. a, CUBE image showed multiple flow voids with in the CSF spaces. b, Phase 5 of TRICKS sequence showed ASA arising from left T9 intercostal artery. c, DSA confirmed the feeder level from left T9 intercostal artery.

Case 9

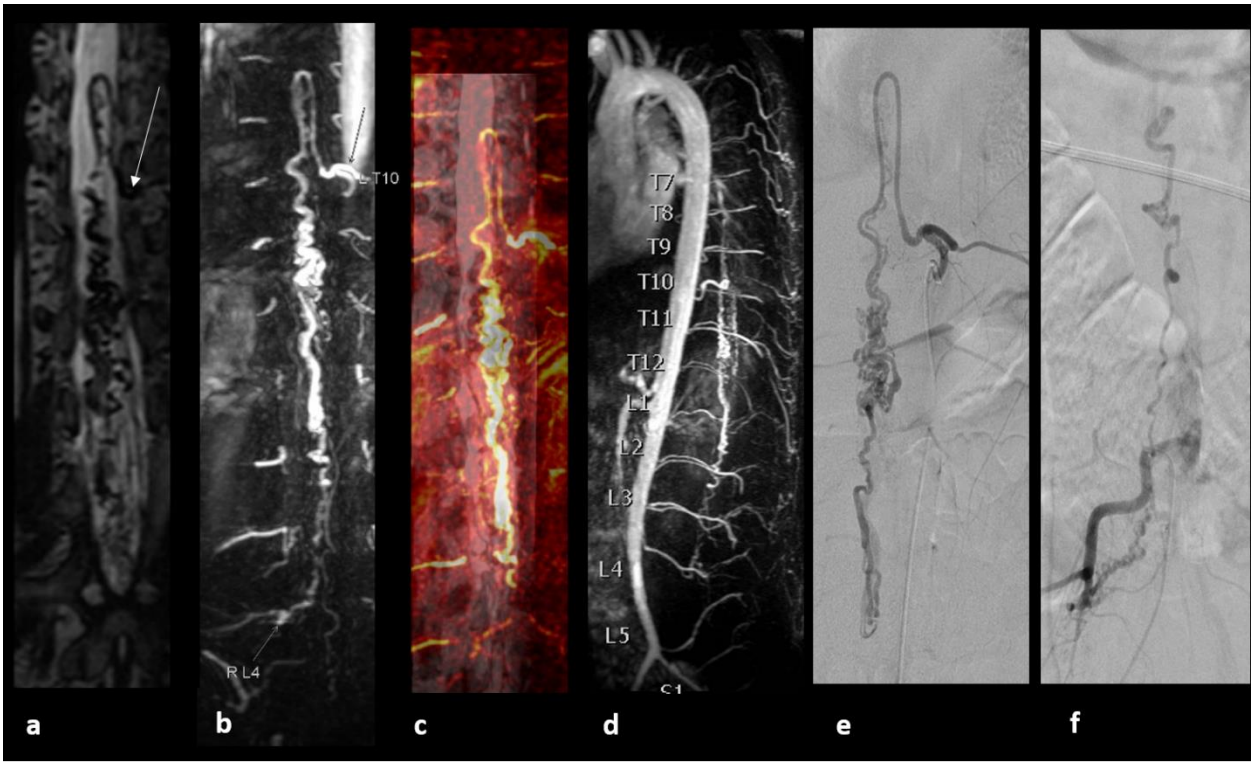


Figure 16. A 30-year-old male, known case of perimedullary AVF, presented with back pain, weakness and urinary incontinence for one month. a, Coronal CUBE image showed the feeder from left T10 intercostal artery. b, TRICKS sequence showed arterial feeders from left T10 level and right L4 level (white arrows). c, Fusion imaging showed excellent spatial resolution. d, MIP image showed both the arterial feeders. e & f, DSA demonstrated both the arterial feeders.

Discussion

Discussion

In diagnosing the presence of spinal vascular malformation, CUBE, TRICKS and combined evaluation of CUBE and TRICKS had the sensitivity, specificity, PPV and NPV of 100%, 33%, 92.6% and 100% respectively. The sensitivity, NPV and PPV were high and specificity is low in comparison to Amarouche et al who reported 98% sensitivity, 63% specificity, 93% PPV, and 83% NPV. This increased sensitivity, PPV and NPV is because two sequences are used in evaluating spinal vascular malformations, with high spatial and temporal resolution. However, low specificity in the study might be related to the less number of true negative cases, due to referral bias.

Evaluation of DAVF:

Diagnosis*:*

In diagnosing as DAVF, CUBE sequence had sensitivity and specificity of 100% and 80% respectively. Our results were better than the previously reported by Saindane et al, though number of true negatives were less. Flow voids within the spinal subarachnoid space with no evidence of nidus were falsely diagnosed as DAVF as seen in two cases of perimedullary AVF and one case of extraspinal AVM. TRICKS sequence had sensitivity and specificity of 100% and 80% respectively. False positives occurred due to small size of the nidus in one AVM (Case 5 in figures), which was misinterpreted as draining vein, in one perimedullary AVF where ASA was not visualized and the other in extraspinal AVM, where nidus could not be visualized clearly. By combined evaluation of both the sequences, specificity had improved to 92%, because AVM was correctly interpreted on CUBE and one PMAVF was correctly identified on TRICKS sequence.

Localization of arterial feeder level:

CUBE sequence identified level of arterial feeders exactly in 50-60% of patients and within one vertebral level in 80-90% of patients with good interrater agreement. The side was predicted in all cases except one. High localization of arterial feeder by CUBE sequence is related to high spatial resolution with excellent separation of cord parenchyma, CSF, flow voids and bone. Our results are comparable to the study by Kannath et al (Kannath, et al. 2016), in which arterial feeders and side were identified within one vertebral level in 94% of patients (15 of 16 patients) using SPACE sequence on 1.5T MRI machine. TRICKS sequence identified level of arterial feeders exactly in 50-60% and within one vertebral level in 60-70% of patients with good interrater agreement.

In the present study, identification of feeder level within one vertebral level on TRICKS was seen in 70% of subjects, which was slightly lesser than 81.8% (27 of 33 patients) reported by Amarouche et al(16). Saindane et al reported feeder localization with in one vertebral level in 85.7% (6 of 7 patients) (18) and Ali et al reported100% detection in a small study of six patients. (17). However, the side prediction was similar to other studies(16)(18). By combined evaluation of CUBE and TRICKS sequence, arterial feeder with in one vertebral level is identified in 90% of patients by both the readers, though there is some interrater discrepancy in evaluating either sequences alone. In one case of DAVF, arterial feeder was not located on initial evaluation by one observer, but was clearly identified when both the sequences are combined. When the arterial feeder level is not identified in first attempt by CUBE sequence, TRICKS can locate the segment of the spine to be looked, for identifying the arterial feeder. In presence of multiple feeders, all the feeders are seen within one vertebral level. So, identification of one arterial feeder will be helpful in planning for DSA.

Evaluation of AVM

Diagnosis

CUBE sequence had 100% sensitivity and specificity, due to depiction of focal altered signal intensity and presence of flow voids with in the cord parenchyma. TRICKS sequence had sensitivity of 87.5% and specificity of 100%, and this was because of small AVM in one case was misinterpreted as DAVF. Combined evaluation by both the sequences also has sensitivity and specificity of 100% mainly because of high spatial resolution of CUBE sequence.

Localization of arterial feeders:

CUBE sequence could identify dominant feeder in 75% (6 out of 8) patients and nearly 30% of all feeders in AVM patients. Our study is the first study in depicting the arterial feeders to AVM by CUBE sequence, though the arterial feeder detection rate is low. This is because differentiation of arteries and veins are not possible as the sequence has no temporal resolution. TRICKS sequence could identify dominant feeder in 75% (6 out of 8) patients and 50-60% of all feeders supplying the AVM. This improved identification on TRICKS, sequence was due to separation of arterial and venous phases in TRICKS sequence as compared to no temporal resolution on CUBE sequence. Intranidal aneurysms were identified in 75% of patients (3 of 4 patients) by both the sequences. Evaluating AVM by both the sequence offset the disadvantages of both the sequences. CUBE sequence, due to its high spatial resolution, helps in identifying AVM while arterial feeders are better identified on TRICKS sequence, due to its good temporal resolution. Amarouche et al(16) evaluated the utility of TRICKS sequence in evaluating spinal vascular malformations and found low correlation with DSA in identifying all the arterial feeders, though only 3 of 50 patients are diagnosed with AVM. Our results are better in identifying all the feeders, dominant feeder and

side of the arterial feeders. This might be because of higher spatial resolution due to increased matrix size in the present study, though temporal resolution is slightly lesser of 3.1 and 4.2 seconds as compared to 1.8 seconds.

Evaluation of perimedullary fistula

Diagnosis

CUBE sequence had sensitivity of 60% and specificity of 100%. Two cases of PM AVF are falsely diagnosed as DAVF, as both disease entities have flow voids in subarachnoid space, but with different arterial supply. TRICKS sequence had sensitivity and specificity of 80 and 100% respectively. This improved resolution is due to improved identification of dilated ASA on TRICKS sequence. Combined evaluation has similar sensitivity and specificity of TRICKS. Location of the fistula was identified exactly in only 2 of 5 patients by both the sequences in type IVB cases. In cases of type IV A, location of fistula could not be identified because transition of artery to vein could not be identified on both the sequences.

Localization of arterial feeders:

Dominant feeder or single feeder could be identified in 80% of patients (4 out of 5 patients) by both the sequences. CUBE and TRICKS sequence could identify 57% and 71% of all the feeders respectively. Identification of dilated ASA with multiple flow voids in subarachnoid space can differentiate PM AVF from DAVF, because normal ASA is too small to be detected by CUBE and TRICKS. Our findings are in contrast to Amarouche et al(16) study where arterial feeder was identified in only two out of 10 patients. This discrepancy might be due to improved visualization of ASA in the present study, which may be inturn attributed to higher spatial resolution due to increased matrix size.

Utility of combined of CUBE and TRICKS sequences in evaluating spinal vascular malformations:

In the present study CUBE sequence was more accurate than TRICKS sequence in identifying the type of vascular malformation, differentiating DAVF from AVM and identifying arterial feeder level in DAVF. Small size of the fistula and proximal vein may lead false localization on TRICKS sequence due to faint opacification and background noise. TRICKS sequence is better than CUBE sequence in identifying the arterial feeder in SCAVM and PM AVF. This might be due to the temporal resolution of TRICKS which helps in identifying the feeding arteries such as ASA or PSA and also in differentiating arteries from veins.

There was moderate agreement between the CUBE and TRICKS in diagnosing the type of vascular malformation and identifying the arterial feeder levels, but when both these modalities are combined there was improved agreement. This might be because, advantages of these two sequences are combined, while offsetting the disadvantages. CUBE sequence has very good spatial resolution in differentiating the cord parenchyma, flow voids, CSF and adjacent bones but no temporal resolution. TRICKS sequence has good temporal resolution but moderate spatial resolution, due to suppression of back ground tissue.

While combining the two sequences for evaluation, time of acquisition is slightly prolonged. However due to the obvious advantages such as accurate differentiation of spinal vascular malformation and delineating the arterial feeders, use of CUBE and TRICKS will not only help in the diagnosis, but also in the preoperative assessment of spinal vascular malformation. Such information will help in tailoring the spinal DSA study and enable the operator to plan intervention in single sitting. This approach will have the advantage of reduction in procedural time and risks of spinal DSA, radiation exposure, contrast load and overall reduced hospital stay(44).

Our study has several strengths. Study design was prospective, blinded and done on 3T MRI machine. Spinal vascular malformations were evaluated with two different sequences which characterizes the anatomical and physiological aspects of the pathology. Two raters blinded to the diagnosis evaluated the study in order to assess the reproducibility of observation in real world scenario. TRICKS FOV was positioned after evaluating conventional MRI sequences, to avoid non-inclusion of the spinal segment, supplying the spinal malformation. Present study is the first study to evaluate AVM and PM AVF using 3D CUBE sequence.

There are few limitations to the study. Due to the rarity of the disease, the number of patients in the study was less. Two different parameters with different temporal resolution were used for TRICKS sequence while optimizing the MR sequence in the initial phase of the study. However, we believe that it may not have any influence in the diagnostic capability of the sequence, as there was no significant change in temporal resolution achieved as a result.

Conclusion

Conclusion

- CUBE and TRICKS sequences are helpful in evaluating the spinal vascular malformations. CUBE sequence is more helpful in identifying the type of spinal vascular malformation; level of fistula and arterial feeder in DAVF. TRICKS sequence is more helpful in localizing the level of dominant arterial feeders in AVM and perimedullary AVF.
- Combined evaluation of CUBE and TRICKS sequences increase the sensitivity and specificity in identifying and classifying spinal vascular malformation. Both the sequences are complimentary to each other with different advantages and improve the confidence level of the readers in identifying the level of arterial feeders.
- Though DSA is not replaceable in evaluating spinal vascular malformations, both CUBE and TRICKS sequences helps in planning DSA and intervention, thus reducing the risks associated with-it.

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Annexures

PROFORMA

Sree Chitra Tirunal Institute for Medical Sciences & Technology

Proforma For Spinal Vascular Malformations Study

A. General Information

1.1 Name

1.2 Age

1.3 Sex

1.4 Hospital No

1.5 Address

1.6 Phone number

1.7 Mobile

1.8 Email id

1.9 Date of admission

1.11 Date of discharge/death

. B. Clinical Details

Chief complaints/duration of symptoms:

History of presenting complaints: Onset/duration/progression.

Past history/treatment history:

Examination:

General

Systemic:

CNS

/CVS/RS/PA

Aminoff & Logue's scale of disability

Gait

Micturition

Bowel

C. Investigations

If any USG

CT/CT ANGIO

MRI/MRA(previous)

D. MRI and DSA

		MRI (TRICKS)	MRI (CUBE)	DSA
Vascular malformation	Present /Absent			
Site	At what vertebral body level			
Type	SDAVF/SAVM			
	SDAVF Number of feeders and their vertebral levels			
	SAVM Feeding arteries - Number and levels. Nidus – site, size and intranidal aneurysms. Fistula – site and number. Venous sac – size and level.			
Duration of angiogram procedure				

E. Complications

Post MRI :

Neurological deficit (post DSA) : Transient (<24hrs)/ permanent.

F. Treatment :

Complications :

G. Follow Up :

CONSENT FORM

TITLE OF THE STUDY: - VALUE OF TIME RESOLVED IMAGING OF CONTRAST KINETICS (TRICKS) AND HIGH RESOLUTION T2 VOLUMETRIC MR SEQUENCE AT 3T IN EVALUATION OF SPINAL VASCULAR MALFORMATIONS.

You ……..……. have been informed that you have abnormal connections between blood vessels (arteries and veins) in and around the spinal cord. If the condition is left untreated it may cause progressive weakness of both lower limbs, unable to walk and bed ridden, moderate to severe back pain, altered sensation, retention of urine, constipation and death if not treated. You are required to undergo a CE MRI and DSA to know the site and extent of the lesion and the various blood vessels that supply for definitive treatment of the lesion. You are being requested to participate in a study which will evaluate the Value of DCE-MR angiography and high resolution T2 volumetric MR sequence at 3T in evaluation of spinal vascular malformations (same disease as yours). For this purpose, the data of your clinical records, investigations, previous endovascular treatment procedures and follow up investigations will be accessed and analyzed.

You will have to undergo MRI imaging, where you are put in a magnetic field of high strength and images of cord are acquired with and without injecting intravenous gadolinium based contrast, which is a part of imaging before the angiographic procedure. The side effects of gadolinium contrast can be mild (nausea, vomiting) to severe and rare side effects like nephrogenic systemic fibrosis, which is more common in long standing renal failure.

After imaging, you have to undergo, angiography which is the gold standard for imaging of spinal vascular malformations. In conventional angiography, a long tube is inserted into the blood vessels from your groin and the arteries supplying the vascular malformations are accessed by watching in television and contrast is injected through the long tube and images are acquired. Though the above method has been oversimplified, it is complicated and is associated with certain risks. In the groin, there may be bleeding, hematoma formation and the blood vessel may be obstructed due to clot formation requiring minor operation to save the leg. There may be chances of weakness in bilateral lower limbs, speech problems and loss of vision. Rarely a state of unconsciousness (coma) or even death may occur. Best of efforts will be exercised towards treatment while avoiding such complications. We attempt to make you aware that this is a very special procedure carrying very small but significant risks and it is performed only because this is the only pre-operative measure. If you like any more detailed information, we will be glad to discuss further with you.

Does this study pose any side effects to the participant?

NO. We will be accessing the MRI images and angiographic details of conventional spinal angiography and assess the Value of DCE-MR angiography and high resolution T2 volumetric MR sequence at 3T in evaluation of spinal vascular malformations.

If you take part what will you have to do?

If you agree to participate in this study, you will be required to undergo contrast enhanced MRI and conventional angiography. All other treatments that you are already on will be continued and your regular treatment will not be changed during this study. No additional procedures or blood tests will be conducted routinely for this study. If at any time you experience any problems, you will be expected to report this to the doctor.

Can you withdraw from this study after it starts?

Your participation in this study is entirely voluntary and you are also free to decide to withdraw permission to participate in this study. If you do so, this will not affect your usual treatment at this hospital in any way.

What will happen if you develop any study related injury?

There are **NO** additional study related injuries as we are only collecting and analyzing the data from your medical records.

What happens after the study is over?
You may or may not benefit from the study, after the study we will be able to assess the Value of DCE-MR angiography and high resolution T2 volumetric MR sequence at 3T in evaluation of spinal vascular malformations, the results of which may be used for your follow up and for other patients like you.
Will your personal details be kept confidential?
The results of this study will be published in a medical journal but you will not be identified by name in any publication or presentation of results. However, your medical notes may be reviewed by people associated with the study, without your additional permission, should you decide to participate in this study.

If you have any further questions you can contact me in interventional Radiology OPD or in the telephone number 04712524518, 9447961100 or email: satyanarayana@sctimst.ac.in.

Signature (or Thumb impression) of the Subject/Legally Acceptable

Representative: _____ Date: _____/_____/_____

Signatory's Name: _____

Signature of the Investigator: _____Date: _____/_____/_____

Study Investigator's Name: _____

Signature of the witness (if needed) _____Date: _____/_____/_____

Name of the Witness (if needed): _____

Participant's name: Date of Birth / Age (in years):

I_____,

Son/daughter of _____

(Please tick boxes)

- Declare that I have read the above information provide to me regarding the study: Value of DCE-MR angiography and high resolution T2 volumetric MR sequence at 3T in evaluation of spinal vascular malformations and have clarified any doubts that I had. [ ]

- I also understand that my participation in this study is entirely voluntary and that I am free to withdraw permission to continue to participate at any time without affecting my usual treatment or my legal rights. [ ]
- I understand that the study staff and institutional ethics committee members will not need my permission to look at my health records even if I withdraw from the trial. I agree to this access. [ ]
- I understand that my identity will not be revealed in any information released to third parties or published. [ ]
- I voluntarily agree to take part in this study. [ ]
- I received a copy of this signed consent form. [ ]

Name:

Signature:

Date:

Name of witness:

Relation to participant:

Date:

(Person Obtaining Consent): I attest that the requirements for informed consent for the medical research project described in this form have been satisfied. I have discussed the research project with the participant and explained to him or her in nontechnical terms all of the information contained in this informed consent form. I further certify that I encouraged the participant to ask questions and that all questions asked were answered.

_____

Name and Signature of Person Obtaining Consent

Principal Investigator.

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