



Title	Estimation of the number of feeding arteries of spinal arteriovenous malformations by using three-dimensional digital subtraction angiography
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1 Title:

2 Estimation of the number of feeding arteries of spinal arteriovenous malformations by using three-dimensional
3 digital subtraction angiography

4
5 Abstract

6 Purpose: Spinal angiography is the gold standard for evaluation or diagnosis of spinal arteriovenous
7 malformations (AVMs). However, some feeding arteries might be overlooked when multiple feeders exist. This
8 study aimed to retrospectively review cases of spinal intra-dural AVMs, which were identified by three-
9 dimensional digital subtraction angiography (3D-DSA), and attempted to estimate the number of feeding arteries.

10 Methods: We retrospectively reviewed patients with spinal intra-dural AVMs who underwent 3D-DSA at
11 Hokkaido University Hospital from January 2005 to December 2016. We selected 9 patients in whom we could
12 obtain data of multi-planar reconstruction of 3D-DSA. We measured the computed tomography (CT) values of
13 feeding arteries and draining veins. The CT values represented the averages of maximum CT values of 5
14 continuous axial slices. The ratio of the CT value of feeders to that of drainers (F/D ratio) was calculated. The
15 correlation between the F/D ratio and the number of feeders was examined with Pearson's correlation
16 coefficient.

17 Results: The average number of feeders was 2.3 (1-4) and the number of feeders was significantly positively
18 correlated with the F/D ratio ($r = 0.855$, $P = .003$).

19 Conclusions: We conclude that the number of feeding arteries of spinal intra-dural AVMs can be estimated by
20 using the F/D ratio obtained from 3D-DSA.

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22 Key words: spinal arteriovenous malformations, 3D-DSA, F/D ratio, estimation, perimedullary AVF,
23 intramedullary AVM

Introduction

Spinal arteriovenous malformations (AVMs) are abnormal connections between arteries and veins of the spine which do not go through the capillary arteries. They can cause various neurological disabilities, and it is important to diagnose them accurately. Spinal angiography is the gold standard for evaluation or diagnosis of spinal AVMs. However, some feeding arteries might be overlooked when multiple feeders exist. This is because spinal angiography requires selective angiography and cannulating a catheter into some segmental arteries is sometimes difficult. Three-dimensional computed tomography angiography (3D-CTA) can identify multiple segmental arteries simultaneously. However, distinguishing feeding arteries from draining veins and identifying tiny feeding arteries using 3D-CTA is not easy. In recent years, three-dimensional digital subtraction angiography (3D-DSA) has become available and it is an improvement in radiological examinations. However, there have been few reports on evaluation of spinal AVMs by 3D-DSA.

Therefore, we retrospectively reviewed cases of spinal intra-dural AVMs, which had been identified by 3D-DSA, and attempted to estimate the number of feeding arteries.

Methods

Patients and the protocol of 3D-DSA

The study was approved by the Institutional Review Board of Hokkaido University and all patients provided written informed consent. We retrospectively reviewed a cohort of patients with spinal intra-dural AVMs who underwent 3D-DSA at Hokkaido University Hospital from January 2005 to December 2016. 20 patients with spinal intra-dural AVMs were performed 3D-DSA, and we selected 9 patients in whom we could obtain data of multi-planar reconstruction (MPR) of 3D-DSA. None of them had renal failure before and after examination. The AXIOM Artis dBA (Siemens, Forchheim, Germany) was used for all procedures. All of the patients underwent selective spinal angiography with a 1240×960 pixel matrix system. The C arm rotated by 188° (from right anterior oblique 89° to left anterior oblique 99°), and 126 images were taken for 5 seconds in each of the mask images and contrast images. The start delay for rotational acquisition was 1-2 seconds. The contrast medium was non-ionic

and its concentration was 300 mg/ml. All images were transferred to the Syngo X Workplace (Siemens) and reconstructed to slice data.

Sampling data

We measured the computed tomography (CT) values of feeding arteries and draining veins. Theoretically, when a lesion has a single feeder, contrast medium that is injected from the feeder is not diluted, and the CT value of the feeder will be equal to that of the drainer. However, when the lesion has multiple feeders, contrast medium that is injected from one of the feeders is diluted by blood from the other feeders. Therefore, the CT value of the feeder will be greater than that of the drainer (Fig. 1). On the other hand, no matter how many drainers there are, each of the CT values of the drainers are equal, because contrast medium is not diluted any more in a distal of AVMs.

To begin with, we identified feeders and drainers with conventional DSA. The region of interest (ROI) was set to cover only one vessel in axial images of MPR (Fig. 2), but not to cover several vessels or only part of a vessel. The maximum CT value was computed in the ROI, and then the average of 5 consecutive axial slices was calculated as a representative value. The ratio of the average CT value of feeders ($\overline{F\text{ Max}}$) to that of drainers ($\overline{D\text{ Max}}$) (F/D ratio) was calculated.

In some cases, most of which are cervical lesions, a catheter is placed in the vertebral artery, which feeds a multiple segmental artery. This situation would lead to underestimation of the F/D ratio. This is because when several feeding arteries are branched from the distal of the catheter, the contrast medium will enter all of the branched feeding arteries. In this case, the contrast medium is not diluted with blood in the periphery of the blood vessel in which the catheter is placed. On the other hand, when a catheter is put in a single feeding artery at the periphery, and a contrast medium is injected, blood flow from other blood vessels dilutes the contrast medium (Fig. 3). For example, when several feeding arteries are branching from a vertebral artery, it can be corrected by multiplying the CT value of the feeder by the number (n) of feeders diverging from the vertebral artery.

The number of feeders were determined by verifying conventional DSA carefully. If DSA was performed repeatedly, each data was verified and all of them were integrated.

Statistical analysis

The correlation between the corrected F/D ratio and the number of feeders was examined with Pearson's correlation coefficient. Analyses were performed with JMP Pro 13.1.0 software (SAS, Cary, NC, USA).

Results

The clinical characteristics of 9 patients are summarized in Table 1. Of the 9 patients, 4 were males and 5 were females. The mean age of the patients was 26.2 years (range, 4-65 years). Three (cases 3, 5, 7) of the patients were categorized as perimedullary AVF, 2 of them (cases 2, 9) as intramedullary AVM, and the others (cases 1, 4, 6, 8) as both perimedullary AVF and intramedullary AVM. The lesions were located in the cervical and thoracic spinal cord; 5 were cervical, 3 were thoracic, and 1 was a cervicothoracic lesion. Most of them had pain associated the lesions, and they underwent various treatments: surgery, embolization, radiation, or combination of them.

The details of feeders and data associated with CT values are shown in Table 2. The average number of feeders was 2.3 (range, 1-4). In some cases, not all of the feeders were revealed in the first spinal angiography, but they were all observed in the second spinal angiography. The number of feeders described in Table 2 includes all of the feeders, not only the feeders that were revealed in the first spinal angiography. In cases 1 and 7, the right vertebral arteries were catheterized when we performed 3D-DSA, and we then observed 3 and 2 feeders from the arteries, respectively. Therefore, "n" in cases 1 and 7 was 3 and 2, respectively (n = 1 in the other cases). $\overline{F\text{ Max}}$, $\overline{D\text{ Max}}$, the F/D ratio, and the corrected F/D ratio were calculated in each case.

Fig. 4 shows the correlation between the number of feeders and the corrected F/D ratio. The number of feeders was significantly positively correlated with the corrected F/D ratio ($r = 0.855$, $P = .003$). The number of feeders could be predicted by the following formula: number of feeders = $0.4410 - 0.8812 \times [\text{corrected F/D ratio}]$.

Illustrative case

Now I show an example. Patient 3 (Table 1), 4-year-old boy visited our hospital with headache. He was diagnosed

with spinal perimedullary arteriovenous fistula (AVF) by spinal angiography. Conventional spinal angiography revealed the feeding arteries of the AVF were the right C5 segmental artery, the right thylocervical artery and the right Th6 intercostal artery (Fig. 5A-C). Then, 3D-DSA with injection of the right thylocervical artery was performed (Fig. 5D). After that, the axial and coronal projection of the 3D-reconstructed images were created (Fig. 6), and F/D ratio was calculated as described above.

Discussion

This study showed that the number of feeders was significantly correlated with the F/D ratio. Using the formula described above, once we identify a feeder of spinal AVMs and perform 3D-DSA of the feeder, we are able to predict the number of remaining feeders. To the best of our knowledge, there have been no reports on predicting the number of feeders of spinal AVMs or other diseases. Therefore, our method is novel.

Spinal AVMs often have multiple feeders. Singh et al. reviewed 74 patients who were diagnosed with spinal AVMs [1]. In their review, 47.1% of the patients with perimedullary AVF had multiple feeders and 45.5% with intramedullary AVM had multiple feeders. In our cohort of spinal AVMs, 45.8% of the patients with perimedullary AVF, 20.0% of the patients with intramedullary AVM, and 100% of the patients with a combination of intramedullary AVM and perimedullary AVF had multiple feeders. The result of our cohort are consistent with the ones of Singh et al. In summary, approximately half of the cases of spinal intra-dural AVMs had multiple feeders. Therefore, these feeders should not be overlooked. However, we may overlook some feeders using the current imaging modalities for spinal AVMs because of the following disadvantages. The method of 3D-CTA cannot detect tiny feeders because of its spatial resolution [2]. Because the voxel size is $0.5 \times 0.5 \times 1.0$ mm in general, feeders of a diameter less than 0.5 mm can be missed. Moreover, selective angiography cannot be performed in 3D-CTA, which may also lead to missing the presence of feeders because of low contrast resolution. Some feeders are also sometimes overlooked in conventional DSA because of technical difficulties. Arteriosclerotic changes or certain anomalies of segmental arteries sometimes prevent a catheter from cannulating and make performing selective angiography difficult. Actually, some feeders were

overlooked in the first spinal angiography in 2 cases in our study. Therefore, we consider that predicting the number of feeders is important, and focused on the ratio between the CT value of feeders and drainers. For clinical application, residual feeders should be carefully sought if the formula suggests that there should be more feeders. However, this search does not need to be extensive to prevent overlook if the formula suggests that no more feeders than those already detected should be present.

The radiation dose associated with spinal angiography should be taken into consideration when discussing the usefulness of 3D-DSA because a high radiation dose may cause radiation-induced injuries. Some reports that compared the radiation dose associated with 3D-DSA and 2D-DSA have suggested that the former is lower than the latter (36%-63% lower in cumulative dose) [3-5]. Based on these previous results, our method for estimating the number of feeders with 3D-DSA is able to be used from the perspective of the radiation dose.

This study has some limitations as follows. First, we assumed that blood flow from each feeder would be equal, although this is unlikely. Second, blood flow velocity and the injection rate of contrast medium were not fixed. Blood flow velocity changes with various factors, such as cardiac output and vessel diameter. The injection rate of contrast medium might be fixed with the injector, but the catheter sometimes moves back because of the powerful injection. Therefore, we usually injected contrast medium manually in spinal angiography. Third, we only estimated segmental arteries as feeders and did not take minor arteries into account. We should also note that our study only included a small series of patients. Further studies are required to more accurately estimate the number of feeders of spinal AVMs.

In conclusion, our study shows that the number of feeders of spinal AVMs is significantly positively correlated with the F/D ratio obtained from 3D-DSA. By using the F/D ratio, the number of feeding arteries of spinal intradural AVMs can be estimated.

Compliance with ethical standards

Conflict of interest: None of the authors has any potential conflict of interest.

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Figure legends

Fig. 1: Schema of the AVM with multiple feeders in an angiogram.

When the lesion has multiple feeders, contrast medium (white arrow) that is injected from one of the feeders (feeder 1) is diluted by blood without contrast medium (black arrow) from the other feeders (feeder 2). As a result, diluted contrast medium flows in drainer (double arrows). Therefore, theoretically, the CT value of the feeder (a) will be greater than that of the drainer (b).

Fig. 2: The method of setting the ROI.

The ROI was placed in an axial image of MPR of 3D-DSA. The ROI was set to cover only one vessel, but not to cover several vessels or only part of a vessel.

Fig. 3: Schema of difference between an angiogram from an artery before diverging some feeding arteries and from a single feeding artery after being diverged

In an angiogram from an artery before diverging some segmental arteries, contrast medium sometimes shows multiple feeders. This situation leads to underestimation of the F/D ratio. This is because when several feeding arteries are branched from the distal of the catheter, the contrast medium will enter all of the branched feeding arteries (white arrow). In this case, the contrast medium is not diluted with blood in the periphery of the blood vessel in which the catheter is placed (A). On the other hand, when a catheter is put in a single feeding artery at the periphery, and a contrast medium is injected (white arrow), blood flow from other blood vessels (black arrows) dilutes the contrast medium (double arrows) (B).

Fig. 4: Correlation between the number of feeders and the corrected F/D ratio.

The number of feeders shows a significant positive correlation with the F/D ratio ($r = 0.855$, $P = .003$).

Fig. 5: Conventional spinal angiography and 3D-DSA of patient 3 (Table 1).

The feeding arteries of the AVF were the right C5 segmental artery (A: angiogram of right vertebral artery), the

1 right thylocervical artery (B: that of thylocervical artery) and the right Th6 intercostal artery (C: that of right Th6
2 intercostal artery).

3

4 Fig. 6: 3D-reconstruction of right thylocervical artery.

5 The coronal image of the 3D-reconstructed images showed the feeding artery and the draining vein. 5 consecutive
6 axial images of the feeding artery and the draining vein were extracted while checking the coronal image.

7