

# Clinical Characteristics of Dural Arteriovenous Shunts in 446 Patients of Three Different Ethnicities

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## Summary

Dural arteriovenous shunts (DAVSs) developing in either the ventral, dorsal or lateral epidural spaces (VE, DE and LE-shunts) predictably drain in either cranio/spino-fugal or –petal directions. Associated conditions like venous outflow restrictions (VOR) may be responsible for changes in this drainage pattern. The goal of this study was to compare demographic, angiographic and clinical characteristics of different types of DAVS in Europe, South America, and Asia to find out whether the same clinical profile is present in different ethnicities.

Charts and angiographic films of 446 patients with DAVS from three hospitals in Europe, Asia and South America were retrospectively evaluated. Clinical symptoms were separated into benign and aggressive and the presence or absence of cortical venous reflux (CVR) and VOR was noted.

LE-shunts were present in elderly men and were always associated with CVR resulting in aggressive symptoms. VE-shunts were present in females and almost always had benign symptoms. There were no differences among the three populations for these shunts. DE-shunts in the Asian population were more aggressive secondary to a higher rate of VOR with associated CVR.

VE-shunts rarely lead to CVR even in the presence of VOR, whereas LE-shunts invariably lead to CVR, irrespective of the population investigated. CVR in DE-shunts is not related to the primary disease (i.e. the shunt itself) but to associated factors that led to VOR. Since the occurrence of these varied between different ethnicities, DE-shunts were aggressive in the Asian population and benign in the European and South American populations.

## Introduction

We have recently introduced a new classification system of dural arteriovenous shunts (DAVS) based on the craniospinal epidural venous characteristics and by which the specific reflux patterns of these lesions can be explained<sup>1</sup>. This classification enables anticipation of the natural history of both spinal and cranial dural arteriovenous fistulae by grouping them into three different types according to the relationship of the epidural venous spaces with the afferent veins from the bone, and central nervous system<sup>2,3</sup>.

The ventral epidural (VE) DAVS are shunts that drain into those veins whose primary function is the drainage of bony structures<sup>4,5</sup>. Since these veins normally drain outside the bony limits, there is no subarachnoid (spinal or corti-

cal) venous reflux (CVR) unless there are outflow restrictions that will lead to secondary reflux towards the brain. The following locations are encountered in this group: “vertebral body”, basi-occipital, sigmoid sinus, petrous pyramid, basi-sphenoid, adjacent sphenoid wings and related dural structures.

The dorsal epidural (DE) DAVS are shunts that open into those veins resulting from the confluence in the epidural space of two different systems – the osseous system draining the spinous processes and cranial vault and the leptomeningeal system of the brain<sup>6</sup>. These venous channels coalesce to become the dural sinuses cranially. Since the venous pressure within the dural sinuses is usually low, antegrade, craniofugal flow of these dural AV shunts is normally observed<sup>7</sup>. CVR may occur following associated venous outflow restriction, or with high flow shunts. In this group, the medial occipital sinus, torcular, transverse and accessory epidural sinuses, and the superior sagittal sinus lesions are found.

The lateral epidural (LE) DAVS open directly into veins draining the central nervous system, therefore retrograde cortical or spinal venous reflux is always present. In this group, the lateral marginal sinus, falco-tentorial sinus, petrosal and basal-tentorial sinuses, intraorbital shunts and lamina cribiformis shunts are found as well as the spinal dural AV shunts draining into the perimedullary veins<sup>8</sup>.

This new classification has the ability to predict the drainage of the shunts based on the craniospinal venous anatomy and the presence of venous outflow restrictions and therefore their natural history.

The goal of this study was to compare dural arteriovenous shunts in different geographic locations (i.e. Europe, Asia, South America) to find out whether the classification can be applied to different populations and, if so, whether the disease distribution and symptoms are the same in different geographic groups.

### Material and Methods

This is a retrospective review of 446 consecutive patients presenting with dural arteriovenous shunts (DAVS) from three large referral centers for neurovascular diseases in three different continents: 150 consecutive cases were selected from Southeast Asia (Ramathibodi Hospital, Bangkok, Thailand during June 2000-Dec 2006), 150 consecutive patients were from Europe (Bicêtre Hospital, Paris, France during Sept 1992-Dec 2006) and 146 consecutive patients came from South America (Hospital Beneficencia Portuguesa, Sao Paulo, Brazil April 2001-Dec 2006). All participating hospitals are tertiary referral centers for neurovascular diseases and the ethnicities of the patients were confirmed to be from each continent. Patient demographics, clinical symptoms, shunt localization, classification group as outlined in the introduction. Presence of cortical and spinal perimedullary venous reflux (CVR) and outflow modifications (stenosis/occlusion) were reviewed by evaluating both the patients' charts and reviewing their films.

Clinical symptoms were separated into two groups – benign and aggressive<sup>9-11</sup>. The aggressive symptoms include seizures, intracranial hemorrhage, motor or sensory deficits, visual field

Table 1 Characteristics of each group.

	VE	DE	LE
Age (years)	51.6 (1-87 +/- 16)	34.5 (0-82 +/- 25)*	56 (26-77 +/- 10)
F/M	137/70*	38/61	18/96*
Clinical symptoms (Benign/Aggressive)	191/16*	46/53	24/90*
CVR	26%*	57%	100%
VOR	61%	71%*	9%*
(Exclude CS/Spinal)	(122/1)	(0/0)	(0/39)

\* Statistically significant ( $p < 0.001$ , 99% CI) - N.B. 26 patients with mixed types were excluded.

defects, aphasia, global neurological defects (dementia, delayed psychomotor development, macrocrania) and other nonhemorrhagic neurological deficits such as incontinence<sup>12,13</sup>. Other symptoms were defined as being of the benign type (incidental diagnosis, nonspecific headaches, cranial nerve deficits, chemosis/proptosis, bruit)<sup>14,15</sup>.

Shunt localization was divided into the three groups of the classification described above into ventral epidural (VE), dorsal epidural (DE) and lateral epidural (LE) groups depending on the localization of the shunt. The mixed groups of shunts were excluded from the statistical analysis. Comparisons between the three centers were made for demographics (age and gender), angiographic results (presence of cortical or spinal venous reflux, associated outflow restrictions) and clinical findings (benign versus aggressive symptoms)<sup>16-19</sup>. The cavernous sinus lesions (CS) and spinal lesions were excluded from evaluation of the venous outflow restriction (VOR) because nonvisualization of the outflow pathways could be due to thrombosis (i.e. true outflow restriction) or compartmentalization of the cavernous sinus (without outflow restriction) and thrombosis or fibrosis of the pial emissary bridging veins of the cord occurs with normal aging and therefore cannot be determined by angiography. Statistical significance was calculated using Chi-square and one way ANOVA tests.

## Results

### General Information

There were a total of 446 patients, 207 females (46%) and 239 males with an average age of 49 years (0-87 years). 275 patients (61.7%) had benign symptoms, the remainder had aggressive symptoms. CVR was present in 54.7%. 46% of the patients had evidence of VOR.

The characteristics of each group are summarized in Table 1. These results confirm our previous studies in that there is a female predominance for VE shunts, a male predominance for LE shunts, and DE shunts being present in younger patients. Since all LE shunts are associated with CVR, clinical symptoms are more aggressive, while VE lesions without CVR or VOR are benign lesions. The three types of DAVS have the same clinical characteristics in the different geographic localiza-

Table 2 Comparison of the patient characteristics within and among the three hospitals.

	Hospital		
	Asia	Europe	South America
Classification group			
– VE	109*	35	63
– DE	18	48	33
– LE	11	59	44
Mixed types	12	8	6
Age (years)	50.4	41.5	52.9
F/M	91/59*	61/89	55/91*
Clinical symptoms (Benign/Aggressive)	109/41*	83/67	99/47*
CVR**	49%	65%*	50%
VOR (Exclude CS/spinal)**	83%*	64%*	24%*
CS lesions** / Spinal	(83/7)	(11/28)	(35/5)
<p>* Statistically significant (<math>p &lt; 0.001</math>, 99% CI) comparing within the same hospital.  ** Statistically significant (<math>p &lt; 0.001</math>, 99% CI) comparing the 3 hospitals.</p>			

tions testifying for the validity of the classification system.

There were statistically significantly more VE shunts in Asia with a female predominance, more benign clinical symptoms, a higher rate of VOR and more CS lesions. Europe had a statistically significant lower mean age compared with the other two hospitals, presumably due to a referral bias, slightly more patients with aggressive symptoms, a higher rate of CVR, slightly more cases with VOR and more spinal lesions. There were statistically significantly more male patients in South America, more benign clinical symptoms and a lower rate of VOR (Tables 2 and 3).

### Age and Sex

Being a referral center for pediatric neurovascular patients, Europe had a significantly lower average age of the patients in the DE group compared with the remaining two hospitals. No statistical difference was found in the remaining groups. In addition, there was no significant difference in the female-to-male ratio within each classification group between the three hospitals. A female predominance was

Table 3 Comparison of the different type of shunts between the three hospitals.

	VE			DE			LE		
	Asia	Europe	South America	Asia	Europe	South America	Asia	Europe	South America
Age (Years)	50.0	52.1	54.1	50.9	19.7*	47	57.2	56.2	55.5
F/M	77/32	21/14	39/24	5/13	24/24	9/24	0/11	13/46	5/39
Clinical symptoms (Benign/Aggressive)	101/8	32/3	58/5	1/17*	23/25	22/11*	1/10	8/51	15/29
CVR	31%	23%	19%	94%*	52%	42%	100%	100%	100%
VOR (Exclude CS/Spinal)	80%	75%	32%	94%	88%	3%*	20%	16%	3%

\* Statistically significant ( $p < 0.001$ , 99% CI)

observed for VE-shunts while the LE group had a male predominance.

#### Clinical Symptoms: Benign vs. Aggressive

There was no statistical difference in the benign to aggressive symptoms ratio among the three hospitals in the VE and LE groups, with more benign symptoms for the VE shunts and more aggressive for the LE group. In the DE group, there were many more patients with aggressive clinical symptoms in Asia (17:1), the reason for this being a higher rate of cortical venous reflux and venous outflow restriction in this particular AV shunt type and ethnic group (see next paragraph). South America (22:11) had the highest ratio of benign clinical symptoms, with the lowest rate of cortical venous reflux and venous outflow restriction in this particular AV shunt type and ethnic group (see next paragraph).

#### Angiographic Details: Cortical or Spinal Venous Reflux and Venous Outflow Restrictions

Most of the patients in the VE group in all three hospitals did not have cortical or spinal venous reflux while all of the patients in the LE group had CVR. There were no significant differences in these two groups among the three hospitals. Statistically significant differences among the three hospitals were found in the DE group: In Asia nearly all patients had CVR (94%), whereas only half of the patients in Europe and South America (52% and 42%, respectively) had CVR. Venous outflow restrictions were present in most cases in

the VE and DE groups from Asia and Europe, whereas most of the cases in South America did not have any venous outflow modifications (Table 3).

To sum these results up, while there were no differences in age or sex within the different groups among the three institutions, there was a strikingly higher occurrence of CVR and VOR in the DE group in Asia, compared to both South America and Europe, with a concomitantly higher number of aggressive clinical symptoms. DE AV shunts seem to be more aggressive in Asia because of the associated comorbidities (i.e. venous outflow restrictions) than in South America. In comparison, VE shunts with their benign symptoms and LE shunts with their aggressive symptoms behave the same throughout the different populations. However, the occurrence of cortical venous reflux and venous outflow modifications in the benign VE lesions was also higher in Asia than in Europe or South America.

## Discussion

### Pertinence of the Three Groups of Classification

The general data concerning the three groups – the VE, DE and LE DAVS confirm those of our previous studies<sup>1,20</sup>, although the three populations from each hospital represent different population groups, i.e. South-East Asia, Europe and South America. Being tertiary referral centers for neurovascular diseases, it is likely that the referral patterns are similar and that therefore, the results truly reflect the results of dif-

ferent ethnic populations and not only the results of different referrals, although this bias cannot be completely excluded. The VE shunts had a female predominance with a low rate of CVR and, thus, a benign course. The DE shunts had a lower average age and CVR may occur even without the presence of venous outflow restriction, for example in high-flow conditions of the shunt. The LE shunts had a male predominance and CVR was always present. The clinical onset was at a later age, with no patients presenting before the age of 26 years.

#### *Characteristics of DAVS Referral in Each Center*

In Asia, there were significantly more female patients with VE shunts, which correlates with the previously reported large series concerning cavernous DAVS, which came from Asian countries. Both in VE and in DE lesions cortical or spinal venous reflux and venous outflow restrictions were encountered statistically significantly more often, indicating that associated comorbidities may be present in this ethnic group leading to a modification of the natural history of these shunts. This effect was most pronounced for the DE lesions that tended to be aggressive lesions with more CVR and VOR.

In Europe, there were slightly more male patients present. Most shunts were in the DE and LE group with aggressive clinical symptoms. The lower average age in DE lesions can be attributed to more pediatric cases that are due to a referral bias of this center. Although there were less CVR and VOR compared to Asia it occurred more often compared to Brazil.

Relatively more male patients were observed in South America. The patients had more benign clinical symptoms and there was a low rate of associated venous outflow restriction and a low number of patients with cortical venous reflux.

#### *Characteristics of Each Type of DAVS in the Various Population Groups*

Ventral epidural DAVS can be considered benign since cortical venous reflux is unlikely to be present and –owing to embryologic considerations – can only occur when severe associated outflow restrictions are present. Even though outflow restrictions are present (which, as pointed out above happened more often in Asia and least often in South America), cortical venous reflux and concomitant aggressive

symptoms are rare findings. These shunts can therefore be considered benign lesions at presentation since even under the presence of outflow restrictions, aggressive symptoms due to cortical venous reflux rarely occur.

Within the dorsal epidural DAVS the described venous outflow restrictions led to the most pronounced differences among the three different hospitals. Since in Asia, a high rate of associated venous outflow restriction together with CVR, which was mainly due to thrombosis, was present, these lesions acted aggressively in this population<sup>21</sup>. The South American population had a significantly higher number of patients without either associated venous outflow restriction or CVR compared with the two other countries leading to a benign symptomatology of this type of shunt. In addition, there were significantly more male patients in Asia and South America and there was a lower average age in Hospital 2 (Europe), the latter being presumably due to a referral bias.

Since the primary disease in the lateral epidural DAVS (i.e. the LE dural arteriovenous shunt) invariably leads to CVR and therefore a more aggressive course, there were no comorbidities to interfere with the clinical course. It is therefore not surprising that this group was very homogeneous among the three different ethnicities and there was no statistical difference among the countries: neither the clinical findings nor the angiographic findings nor the male dominance and older age of presentation were different in this group, indicating that symptomatology within these types of shunts are due to the disease itself (i.e. invariable CVR with concomitant aggressive symptoms) and are not dependant on associated comorbidities that may alter the clinical course of the lesions.

#### **Conclusions**

Age, sex, primary angiographic and clinical pattern of the three different DAVS types do not vary depending upon the three populations reviewed. This is a strong indicator for the validity of the classification in three distinct pathological entities. These primary diseases (i.e. VE; DE and LE arteriovenous dural shunts) seem to behave similarly throughout the three populations investigated. However, they can be modified by associated comorbidities such as venous outflow restrictions follow-

ing stenosis, thrombosis or occlusion of the normal drainage pattern. The comorbidities are not the same in different populations leading to different secondary manifestations of the primary disease. Clinical manifestations may be linked to the primary shunt (in LE shunts) or to the comorbidity (secondary venous outflow restrictions leading to cortical or spinal venous reflux)<sup>13,22</sup>. VE lesions are benign and only rarely lead to cortical venous reflux even in the presence of venous outflow restrictions, whereas LE lesions invariably lead to cortical venous reflux owing to embryological considerations. The profound differences in the aggressiveness of DE shunts among the three populations were not related to the primary disease (i.e. the shunt itself) but rather to associated comorbidities that led to cortical venous reflux following outflow restrictions. Since the occurrence of

these comorbidities varied among different populations, DE lesions were aggressive in the Asian population and benign in the European and South American populations.

Possible unknown genetic or hormonal factors may predispose the shunts to develop in the three described locations and specific environmental factors will bring some of the shunts from a relatively benign course to an aggressive one. Further studies of these factors and comorbidities are still needed as they may have an important role in further prevention of this disease.

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