Diagnostic Methods, Treatment Modalities, and Follow-up of Extracranial Arteriovenous Malformations

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***Key Words**: congenital vascular malformations; arteriovenous malformations; diagnosis; treatment; transarterial lung perfusion scintigraphy.*

***Summary.** Objective. Arteriovenous malformations (AVMs) are an uncommon vascular pathology that remains challenging to accurately diagnose and successfully treat. This study introduces a novel way to evaluate AVM treatment outcomes using transarterial lung perfusion scintigraphy (TLPS) and reports our treatment results.*

Material and Methods. The patients treated for extracranial AVMs were studied retrospectively. Diagnosis and outcomes were based on clinical data, ultrasonography, magnetic resonance imaging, computed tomography, angiography, and TLPS studies. The influence of gender; location, form, and stage of AVMs; first attempt at treatment; and treatment modalities was analyzed. Outcomes were defined as positive (cure, improvement, and remission) or negative (no remission and aggravation).

Results. Of the 324 patients with congenital vascular malformations, 129 (39.8%) presented with AVMs, and the data of 56 treated patients with AVMs were analyzed. Of the 29 patients in the endovascularly treated group, 15 in the surgically treated group, and 12 in the combined treatment group, 24 (82.8%), 14 (93.3%), and 10 patients (83.3%), respectively, had positive outcomes ($P>0.05$). All outcomes were positive in surgically treated patients with extratruncular limited AVMs, and these patients were more likely to be cured as compared with those who had other forms of AVMs (OR, 5.8; 95% CI, 1.1–29; $P=0.02$). The patients with more advanced AVMs (stages III and IV) and with AVMs in the gluteal and pelvic region were more likely to have the worst outcomes than those with stage II AVMs (OR, 8.2; 95% CI, 1–72; $P=0.03$) and with AVMS in other locations (OR, 5.8; 95% CI, 1.1–29; $P=0.02$), respectively. Gender and age did not significantly influence treatment results ($P>0.05$). The TLPS data of 17 patients showed AV shunting ranging from 0% to 92%, which combined with other results helped identify 9 patients who needed further interventions, 6 who were treated successfully, and 2 who had insignificant shunting.

Conclusions. The best outcomes were achieved in surgically treated patients with localized lesions and less advanced AVMs. For the first time in Lithuania, a modified TLPS method has been introduced that enhances a hemodynamic assessment of AV shunting and provides with a more accurate evaluation of AVMs to better serve in planning future treatments.

Introduction

Congenital vascular malformations (CVMs), including arteriovenous malformations (AVMs), are a less common pathology that remains one of the most diagnostically and therapeutically challenging diseases to treat (1–5). In contrast to hemangiomas that are benign vascular endothelium tumors, CVMs are developmental abnormalities of the vascular system (6–8). Clinical presentations range from asymptomatic birthmarks to extensive high-flow arteriovenous (AV) shunts that can be life threatening (3, 4, 7–9). While present at birth, CVMs can be clinically latent, only manifest later in life, and do not undergo spontaneous involution, as their growth is usually commensurate with the body's growth (6–8). Hemodynamic features, such as AV shunting, venous stasis, ischemia, as well as iatrogenic factors of trauma, biopsies, inappropriate interventions, and hormonal changes, can accelerate progression of CVMs and morbidity (7–9).

Based on the Hamburg classification system introduced in 1988, CVMs are grouped by predominant vessel type and include arterial, venous, arteriovenous, lymphatic, and combined vascular defects

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Table 1. The Modified 1988 Hamburg Classification of Vascular Malformations (11)

Type	Anatomic Form	
	Truncular	Extratruncular
Predominantly arterial defects	Aplasia or obstruction Dilatation	Infiltrating Limited
Predominantly venous defects	Aplasia or obstruction Dilatation	Infiltrating Limited
Predominantly arteriovenous shunting defects	Deep arteriovenous fistulae Superficial arteriovenous fistulae	Infiltrating Limited
Predominantly lymphatic defects	Aplasia or obstruction Dilatation	Infiltrating Limited
Combined vascular defects	Arterial and venous without shunt Hemolymphatic with or without shunt	Infiltrating hemolymphatic Limited hemolymphatic

that are further subdivided into truncular and extratruncular forms (Table 1) (1, 3, 9–13). Another classification system suggested by Mulliken and Glowacki and adopted by the International Society for the Study of Vascular Anomalies in 1996 takes into account vascular flow characteristics. It defines CVMs as slow-flow (capillary, lymphatic, venous) or fast-flow (arterial, arteriovenous fistulas, arteriovenous malformations) lesions, as well as complex combined syndromes of CVMs (2, 3, 11, 13).

AVMs including fast-flow arteriovenous malformations and arteriovenous fistulas are congenital vascular lesions that form between the fourth and sixth weeks of gestation as the developmental errors of the vascular system (14). AVMs are characterized by direct blood flow from an artery to a vein; therefore, they lack a normal capillary bed (15–18). A central core or nidus of abnormal connections between tortuous enlarged feeding arteries and draining veins is found in the majority of AVMs (15–17). Initially AVMs can compress surrounding tissues and cause cosmetic defects, but as they progress to invade vital structures, patients often experience significant pain and functional impairment (3, 15, 19, 20). Eventually abnormal hemodynamics can lead to a "steal phenomenon" and venous hypertension with ischemic ulcers, venous stasis dermatitis and can progress to gangrene, life-threatening hemorrhages, and even high-output cardiac failure (3, 15, 19, 20).

While an accurate history and physical examination are important diagnostic tools, a precise diagnosis of AVMs can be difficult and crucial for proper treatment (13, 16). Doppler ultrasound can be helpful in differentiating between fast- and low-flow vascular anomalies (21–23). Magnetic resonance imaging (MRI) is essential in determining a lesion extent and its relationship to the adjacent anatomical structures (16, 22–25). Computed tomography (CT) helps visualize bony involvement (15, 16, 23). Angiography remains the current gold standard for a definitive diagnosis and provides with structural information about AV shunts that is indispensable in planning endovascular or surgical interventions (8, 12, 16, 22, 25–35). Whole body blood pool scintigraphy (WBBPS) and transarterial lung perfusion scintigraphy (TLPS) are nuclear imaging techniques that have been more recently introduced to evaluate CVMs. WBBPS allows localizing high- or low-flow lesions (3, 12, 31, 34). TLPS provides with additional quantitative information on blood volume shunting through the AVM (3, 12, 31, 34).

Current treatment options consist of surgical resection, endovascular embolization, and combination of these modalities. To date, there is no pharmacotherapy available (16, 36). Despite recent advancements, AVMs are still rarely cured and might need lifelong multisessional therapy. As such, an accurate diagnosis is important in order to determine the need for intervention, appropriate modalities and timing. Therefore, the evaluation of interim outcomes is extremely important, as it allows tailoring subsequent treatment strategies (5, 15, 16, 22, 31–44).

The goals of our study were to retrospectively evaluate AVM diagnostic possibilities and to assess the influence of gender; location, form and stage of lesions; first attempt at treatment; and treatment modalities on outcomes. We also review our follow-up assessment abilities and correlate them to further treatment plans. This study reports the first cases of modified TLPS that has been used to evaluate and follow up AVMs.

Material and Methods

Among 324 patients with extracranial CVMs, 129 (39.8%) presented with AVMs. A total of 66 patients (51.2%) were treated; 10 were excluded from this study, as they were lost to follow-up. The data of 56 patients were included in the retrospective analysis that was conducted from 2000 to 2012 with a mean follow-up of 3.9±1.2 years.

Gender, anatomic location, age at the onset of symptoms, clinical manifestations, first attempt at treatment, lesion stage, and treatment modalities were documented and analyzed in association with treatment results. AVMs were divided into 5 groups according to the location: head and neck, upper extremities, trunk, gluteal and pelvic region, and lower extremities. Age categories were defined as childhood (birth to 7 years), adolescence (7 to 21 years), and adulthood (more than 21 years). The presenting pathology was categorized using the Hamburg classification and the Schobinger staging for symptom severity (Table 2).

AVMs were first diagnosed based on clinical manifestations (Fig. 1) and Doppler ultrasound (US) data. Clinical assessment was also used to follow-up treated lesions and included a subjective and objective improvement of clinical signs and symptoms, such as reduction of swelling or pain, improved range of motion, ulcer healing, bleeding cessation, improvement of cosmetic deformity, quality of life, and change in the Schobinger stage.

Table 2. The Schobinger Staging of Arteriovenous Malformations for Symptom Severity (14, 16, 44)

Stage	Clinical Finding
I (quiescence)	Warmth, pink-bluish stains, shunting on Doppler. Arteriovenous malformation can mimic capillary malformation or involuting hemangioma
II (expansion)	Enlargement, pulsation, thrill, bruit, tortuous tense veins
III (destruction)	Dystrophic skin changes, ulceration, bleeding, pain or tissue necrosis. Bony lytic lesion can occur
IV (decompensation)	Cardiac failure

MRI was used to verify the diagnosis and to assess outcomes based on anatomical changes after treatment (Fig. 2). MRI was performed on a 1.5-T scanner (Avanto, Siemens Medical Solutions, Erlangen, Germany) using dedicated coils. A comprehensive routine imaging protocol was based on isotropic T2 and T1-VIBE sequences (both with and without fat suppression). Conventional time-of-flight MR angiography and phase-contrast MR angiography were used in some cases, but limited by motion artifacts and the need to demonstrate the long segments of arteries in a short imaging time. For contrast-enhanced images, time-resolved high-spatial-resolution multiphase 3D MR angiography with subsequent image subtractions was performed (flash-3D sequence, 0.15–0.2 mmol/kg gadolinium-based contrast medium at an injection rate of 1.2–2.0 mL/s using an automated injection system by Spectris, Medrad, Pittsburgh, PA).

Standard angiography demonstrated the areas of AV shunting with superselective catheterization used to visualize directly involved feeding arteries and further guide therapeutic interventions (Fig. 3). After the treatment, angiography reflected changes in the qualitative hemodynamic activity at the nidus.

TLPS was used for an initial diagnosis and follow-up of lesions. For this procedure, macroaggregated albumin radiolabeled with technetium-99m was injected through an intra-arterial catheter, placed in the afferent artery proximal to the AVM nidus, which was left after an intra-arterial diagnostic or treatment

Fig. 1. Clinical manifestations of congenital vascular malformations in different anatomic regions

A and D, head and neck; B and C, upper extremities; E, F, H, and J lower extremities; G, gluteal and pelvic region; I, truncal region.

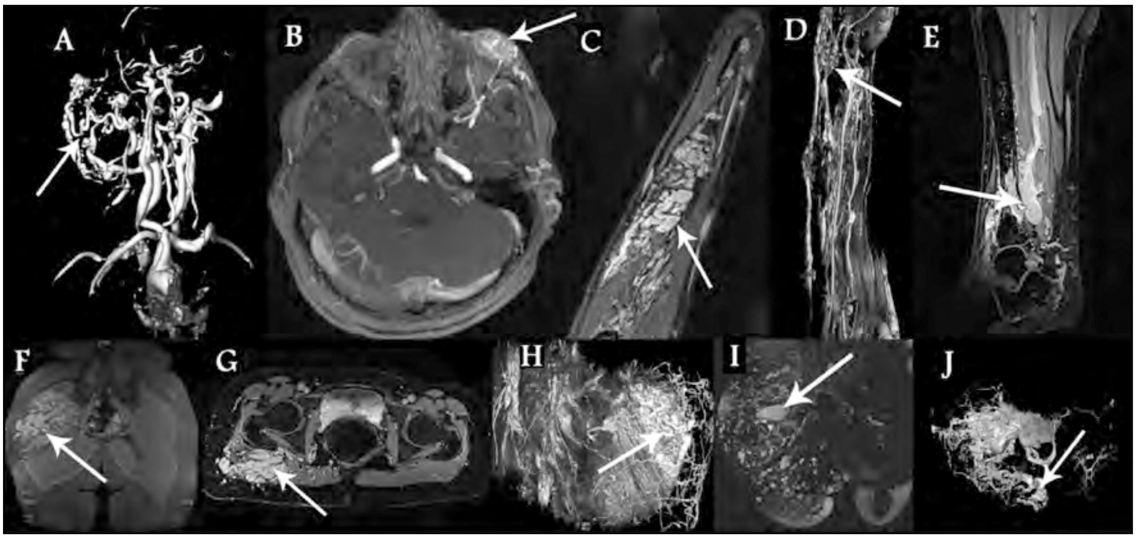

Fig. 2. Presentation of arteriovenous malformations with foci of abnormal vasculature on magnetic resonance imaging studies
A and B, head and neck; C and D, upper extremities; E, lower extremity; F–J, gluteal and pelvic regions

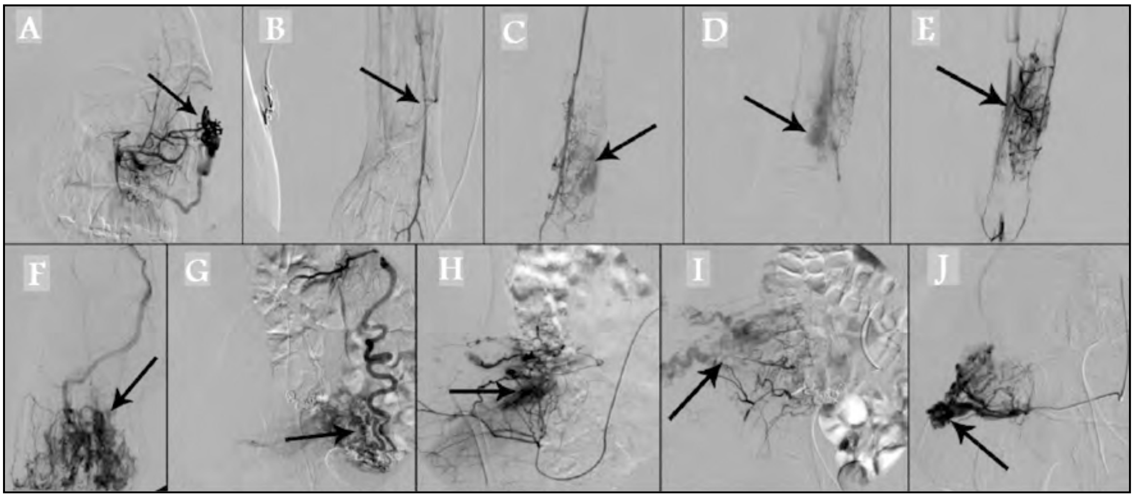

Fig. 3. Presentation of arteriovenous malformations on angiography
A, head; B, upper extremity; C–E, lower extremity; F, foot; G, pelvic region; and H–J, gluteal region AVMs with contrast in the feeding arteries and the nidus, and filling of the draining veins.

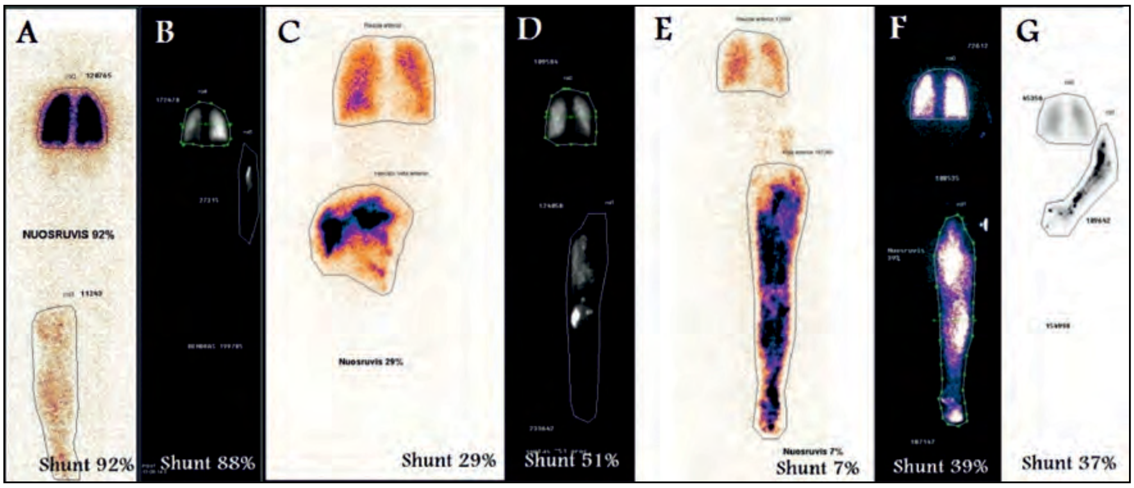

Fig. 4. Presentation of arteriovenous malformations on transarterial lung perfusion scintigraphy
A, D, E, and F show AV shunting of various degrees in the lower extremities; B and G, in the upper extremities; and C, in the gluteal region.

procedure. The GE Infinia, a dual-head gamma camera, fitted with low-energy high-resolution collimators was used to acquire whole body (anterior and posterior) images. A quantitative assessment of blood shunting through the AVM nidus to the lungs was done on a GE Xeleris workstation. TLPS provided with a quantitative hemodynamic percentage of AV shunting volume through the nidus in the extremities and the gluteal, pelvic and truncal regions using the following formula to calculate a shunting percentage:

$$\text{Shunting (\%)} = \text{counts of limb with AVM shunt} / (\text{counts of lung} + \text{counts of limb with AVM shunt}) \times 100\%.$$

The data of clinical assessment, US, MRI, CT, and angiography were combined with the findings of TLPS to classify the patients based on a shunting percentage into the following groups: 1) insignificant AV shunting, 0%–10%; 2) hypodynamic 10%–20%; 3) moderate, 21%–50%; 4) hyperdynamic, 51%–90%; and 5) extremely hyperdynamic, 90%–100%.

The patients were selected for treatment based on the symptoms and current and future risk of complications. The indications for treatment were divided into absolute and relative and are described in Table 3 (3).

Treatment involved embolization, surgical resection, and a combined approach that included embolization and surgical resection. Outcomes were based on clinical assessment and data from the abovementioned imaging studies. Cure was defined as a complete resolution of clinical symptom/signs with no evidence of AVMs on MRI, dissolution of AVMs on angiography, and insignificant shunting through the nidus on TLPS. Improvement was defined as a noticeable improvement of clinical signs/symptoms, with a residual but distinct reduction of the lesion on MRI, near complete cessation at the nidus with some suspicion along the feeding artery and draining veins seen on angiography, and insignificant or hypodynamic shunting on TLPS. Remission was defined as a partial improvement or stabilization seen in clinical signs/symptoms and on MRI, a partial reduction or stabilization of residual nidus activity on angiography, and a reduction of shunting on TLPS by more than 10% as compared before and after treatment. No remission was defined as no changes in clinical presentation, MRI and angiography images, and less than 10% change in AV shunting on TLPS. Aggravation was defined as a progression of clinical presentation and expansion of AVMs on MRI and angiography studies with more than 10% increase in AV shunting on TLPS. Treatment outcomes were categorized as good (cure or improvement), positive (cure, improvement, or remission), and negative (no remission or aggravation).

Statistical analysis was performed by SPSS program, version 17. The relationships between 2 categorical variables in 2×2 contingency tables were assessed by the chi-square or the Fisher exact test. For tables with large samples, the chi-square test was used. For small samples when the expected frequencies in any of contingency table cells were below 5, the Fisher exact test was applied. The level of significance was set as $P<0.05$; odds ratio (OR) and 95% confidence interval (CI) were calculated. Quantitative data were described using descriptive statistics: mean and standard error of the mean.

Table 3. Indications for Arteriovenous Malformation Treatment in 56 Patients

Indication	n (%)*
Absolute indication	
Hemorrhage	8 (14.3)
Ischemia (arterial insufficiency, ulceration, gangrene)	10 (17.9)
Chronic venous insufficiency with venous hypertension	37 (66.1)
High-output cardiac failure	2 (3.6)
Lesions located in life-threatening area	9 (16.1)
Relative indication	
Various signs and symptoms affectingquality of life	56 (100)
Disabling or intractable pain	55 (98.2)
Functional impairment	46 (82.1)
Cosmetic deformity (with or without functional disability)	49 (87.5)
Vascular-bone syndrome with limb length discrepancy	26 (46.4)
Lesion with potentially high risk of complications (hemarthrosis, fracture or limb threatening location)	4 (7.1)
Bone involvement (intraosseal lesion or bone destruction)	5 (8.9)

*All patients had more than one indication for treatment.

Results

In this study, enrolling 56 patients aged from 2 to 61 years (mean, 20.3±1.4 years), the male-to-female ratio was 1:1.5. The majority (80.4%) of the lesions were located in the extremities and the gluteal and pelvic regions. Less than three-fourths (71.4%) of AVMs were of extratruncular infiltrating and 19.6% were of limited type (Table 4).

Forty-five AVMs (80.4%) were first detected during childhood, 8 (14.3%) during adolescence, and 3 (5.4%) in adulthood. The first attempt at treatment during childhood occurred in 7 patients (12.5%), during adolescence in 27 (48.2%), and during adulthood in 22 (39.3%). All treated patients were symptomatic as summarized Table 5 and had AVMs of the following Schobinger stages: stage II, expansion (n=27, 48.2%); stage III, destruction (n=27, 48.2%), and stage IV, decompensation (n=2, 3.6%). Schobinger stage I AVMs were not treated.

Table 4. Distribution of 56 Treated Arteriovenous Malformations Based on Anatomic Areas and Lesion Forms as Defined by the Hamburg Classification

Localization	n (%)	Lesion Form			
		Truncular		Extratruncular	
		Deep	Superficial	Infiltrating	Limited
Head and neck	9 (16.1)	0	2	5	2
Upper extremity	8 (14.3)	0	1	6	1
Trunk	2 (3.6)	0	0	1	1
Gluteal and pelvic region	11 (19.6)	0	2	9	0
Lower extremity	26 (46.4)	0	0	19	7
Total	56 (100)		5 (8.9)	40 (71.4)	11 (19.6)

Table 5. Distribution and Frequency of Different Symptoms and Signs in 56 Treated Patients With Arteriovenous Malformations Arranged From the Most to Least Frequent Presentation

Sign and Symptom	n (%)
Pain	55 (98.2)
Cosmetic deformity	49 (87.5)
Functional impairment	46 (82.1)
Cutaneous blush (port vine stain)	44 (78.6)
Local tumor or soft tissue hypertrophy	34 (60.7)
Phlebectasia and venous hypertension	33 (58.9)
Limb length discrepancy (>1 cm)	26 (46.4)
Thrill	18 (32.1)
Pulsation	12 (21.4)
Lesion with potentially high risk of complications	10 (17.9)
Lesions located in life-threatening area	9 (16.1)
Bleeding	8 (14.3)
Tissue necrosis	6 (10.7)
Bone involvement/destruction	5 (8.9)
Gangrene	3 (5.4)
Cardiac overload	2 (3.6)

Endovascular treatment was applied in 29 patients (51.8%), surgical in 15 (26.8%), and combined in 12 (21.4%).

Embolization procedures were performed in the following anatomical regions: the head and the neck (n=7, 24.1%), the upper extremities (n=3, 10.3%), the gluteal and pelvic region (n=8, 27.6%), and the lower extremities (n=11, 37.9%). Embolotherapy was applied in 5 cases (17.2%) of truncular and 24 cases (82.8%) of extratruncular superficial lesions. Based on the Schobinger staging, 15 stage II (51.7%), 12 stage III (41.4%), and 2 stage IV (6.9%) AVMs were treated with an endovascular approach. Eighteen patients (62.1%) required more than one session.

Surgical resections were performed in the following anatomical regions: the head and the neck (n=2, 13.3%), the upper extremities (n=5, 33.3%), and the lower extremities (n=8, 53.3%). In this treatment category, 8 patients (53.3%) had extratruncular superficial and 7 (46.7%) extratruncular limited AVMs. According to the Schobinger staging, 7 surgically treated patients (46.7%) had stage II and 8 (53.3%) stage III lesions. Six patients (40.0%) required more than one operation.

Combined surgical/endovascular treatment was performed in the following regions: truncal (n=2, 16.7%), gluteal and pelvic (n=3, 25.0%), and lower extremities (n=7, 58.3%). Extratruncular superficial AVMs made up 66.7% (n=8) and limited 33.3% (n=4) of all lesions. According to the Schobinger staging, 5 (41.7%) were stage II and 7 (58.3%) were stage III lesions. Eight patients (66.7%) required more than one combined intervention.

Based on gender, outcomes in men and women were good in 11 (50.0%) and 21 (61.8%), positive in 17 (77.3%) and 31 (91.2%), and negative in 5 (22.7%) and 3 patients (8.8%), respectively (all $P>0.05$).

Among 9 patients with AVMs in the head and neck, outcomes were good in 5 patients (55.6%) and remission was achieved in 4 (44.4%), with overall positive outcomes in all patients. Among 8 patients with lesions in the upper extremities, good outcome was recorded in 5 patients (62.5%) and remission was achieved in 3 patients (37.5%) with overall positive outcomes in all cases. Remission was documented in 2 patients (100%) with AVMs in the truncal region. In 11 patients with AVMs in the gluteal and pelvic regions, good outcomes were achieved in 6 (54.5%), remission in 1 (9.1%), and negative outcomes in 4 patients (36.4%) with an overall positive outcome in 7 patients (63.6%). In 26 patients with AVMs in the lower extremities, good outcomes was seen in 14 (53.8%), remission in 8 (30.8%), and negative outcomes in 4 patients (15.4%) with overall positive outcomes in 22 patients (84.6%). Patients with AVMs in the gluteal and pelvic regions were more likely to have the worst outcomes as compared with those with AVMs in other locations (OR, 5.8; 95% CI, 1.1–29; $P=0.02$). The best outcomes were achieved in patients having AVMs in the upper extremities and the head and neck ($P=0.04$).

In 5 patients with truncular AVMs, remission was achieved in 3 patients (60.0%), and 2 patients (40.0%) had a negative outcome. Among patients with extratruncular infiltrating AVMs, good outcomes were documented in 21 (52.5%), remission in 13 (32.5%), and negative outcomes in 6 patients (15.0%). Positive outcomes were achieved in all patients (100%) with extratruncular limited AVMs. However, there were no significant differences due to a small sample size, but the patients with extratruncular limited AVMs were more likely to be cured than those with other forms of AVMs (OR, 5.8; 95% CI, 1.1–29; P=0.02).

Seven patients treated in childhood had the following outcomes: good (n=4, 57.1%) and remission (n=3, 42.9%) with an overall positive outcome in all 7 patients. Of the 27 patients treated during adolescence, 23 (85.2%) had overall positive outcomes: good outcomes were documented in 17 patients (63.0%) and remission was achieved in 6 patients (22.2%), while 4 patients had negative outcomes (14.8%). Among 22 patients treated in adulthood, good results were achieved in 11 (50.0%) and negative in 4 (18.2%) with overall positive outcomes in 18 patients (81.8%). The differences in outcomes between these age groups were not statistically significant (P>0.05).

The outcomes of treatment by various lesion stages were as follows: good (n=21, 77.8%), remission (n=5, 18.5%), and negative (n=1, 3.7%) for stage II lesions; good (n=11, 40.7%), remission (n=10, 37.0%), and negative (n=6, 22.2%) for stage III lesions; and remission (n=1, 50.0%) and negative (n=1, 50.0%) for stage IV lesions. The patients with stage III and IV lesions were more likely to have worse outcomes than those with stage II lesions (OR, 8.2; 95% CI, 1–72; P=0.03).

The detailed results of endovascular, surgical, and combined treatment are shown in Table 6. A complete cure of AVMs was rarely achieved in all treatment modalities. However, good outcomes were achieved in 13 patients (44.8%) treated with embolization, 11 (73.3%) with resection, and 8 (66.7%) with combined treatment, with overall positive results in 24 patients (82.8%) treated with embolization, 14 (93.3%) with surgical resection, and 10 (83.3%) with combined treatment. Among 27 surgically treated patients with or without embolization, good results were obtained in 19 (70.4%) and positive outcomes in 24 cases (88.9%), but there was no significant difference (P>0.05).

In general, cure was documented in 8 (14.3%), improvement in 24 (42.9%), remission in 16 (28.6%), no remission in 4 (7.1%), and aggravation in 4 patients (7.1%). Good results were achieved in 32 (57.1%), positive in 48 (85.7%), and negative in 8 patients (14.3%). In summary, 85.7% of treated patients had a positive outcome.

A modified TLPS method was used to evaluate AV shunting not only in the extremities, as previously described, but also in the truncal, gluteal, and pelvic regions (Fig. 4) (3, 12, 33, 34). A total of 17 patients underwent TLPS (upper extremities, 3; lower extremities, 9; trunk, 1; gluteal and pelvic region, 4), and AV shunting ranging from 0% to 92% was documented, with the highest degree of shunting seen in the upper and lower extremities, as well as in the gluteal and pelvic region. Of these 17 patients, 10 underwent TLPS after endovascular treatment, 2 after surgical resection, and 3 after combined treatment; 2 patients underwent this method during a diagnostic stage. The data of TLPS combined with the findings of US, MRI, and angiography studies helped identify 3, 4, and 2 patients who would need further endovascular, surgical, and combined treatment, respectively, and 6 patients who would need no additional intervention. Two patients were found to have no significant AV shunting with predominantly venous malformations.

Discussion

Congenital vascular anomalies occur in about 1%–2.6% of neonates (6). Already back in 1964–1965, Malan and Puglionisi accurately recognized AVMs as fast-flow vascular anomalies (36, 45, 46). However, despite new achievements in AVM treatment, results are often unsatisfactory (3, 12, 15, 47).

Although AVMs are rare, they exhibit more aggressive, unpredictable, and dangerous clinical behavior than venous malformations or other forms of CVMs. The fast turbulent flow created between high-pressure arterial and low-pressure, low-resistance venous system is responsible for a destructive hemodynamic effect that determines clinical symptoms, challenging treatment, frequent expansion, and high recurrence rates (3, 12, 15, 18, 31–33). In our study, AVMs made up 39.8% of all CVMs.

AVM lesions can be located in various anatomic areas and sometimes occur simultaneously in several regions (15, 48). In our study, only extracranial AVMs were analyzed, 80.4% of which were located in the extremities and the gluteal region. Previous studies emphasize the importance of an individualized treatment approach based on lesion location

Table 6. Treatment Outcomes in 56 Patients With Arteriovenous Malformations According to the Various Treatment Modalities: Endovascular, Surgical, and Combined (Embolization With Surgical Resection)

Treatment Modality	n	Outcome					
		Cure	Improvement	Remission	No Remission	Aggravation	Positive Results*
Endovascular	29	2 (6.9)	11 (37.9)	11 (37.9)	2 (6.9)	3 (10.3)	24 (82.8)
Surgical	15	4 (26.7)	7 (46.7)	3 (20)	1 (6.7)	0 (0)	14 (93.3)
Combined	12	2 (16.7)	6 (50)	2 (16.7)	1 (8.3)	1 (8.3)	10 (83.3)
Total	56	8 (14.3)	24 (42.9)	16 (28.6)	4 (7.1)	4 (7.1)	48 (85.7)

Values are number (percentage).
*Positive results include cure, improvement, and remission.

and size, and potential risks associated with an intervention (3, 14, 15). In functionally and cosmetically insignificant areas, such as the extremities or the trunk, surgical and earlier aggressive therapy might be applied. In functionally or cosmetically important areas, such as the face, joints, or visceral organs, endovascular, conservative, and delayed therapy, if it is possible, should be selected (3, 14, 15). The majority of AVMs (77.8%) in the head and neck region were treated with an endovascular approach; in the lower extremities, endovascular (42.3%), surgical (30.8%), and combined (26.9%) treatment was applied. In the gluteal and pelvic region, AVMs were mostly (72.7%) treated with endovascular interventions. Outcomes depended on lesion location, with the worst results seen in the gluteal/pelvic and best in the upper extremity, head and neck regions. However, all gluteal and pelvic AVMs were of more complex pathology (only truncular and extratruncular infiltrating forms) and advanced stage (stages III and IV, 72.7%).

The selection of treatment modalities depends on the form of lesions. Truncular and extratruncular infiltrating as well as limited AVMs usually need different therapy, as their course differs. Extratruncular infiltrating lesions arise in early stage of embryonic development and originate from mesenchymal cells (3, 12, 31). Therefore, they grow rapidly and exhibit diffuse infiltration (3, 12, 31). These factors determine a challenging multistage treatment with high recurrence rates. Such lesions constitute the majority of vascular malformations, as seen in our study (71.4%), and are preferably treated with endovascular or combined approaches (3, 12, 31). Truncular forms develop in latter stages of embryonic life, exhibit very high flow, and as a result are extremely challenging or even impossible to treat (3, 12, 31). Best outcomes are achieved with endovascular or combined treatments (3, 12, 31). In our study, more than half of extratruncular infiltrating lesions (60%) and all truncular lesions were treated using an endovascular approach. The results were suboptimal in the truncular AVM group, with a remission rate of only 60% and negative outcome rate of 40%, while in the extratruncular infiltrating AVM group, 85.0% of patients had positive outcomes. Extratruncular limited forms are localized AVMs that are amenable to surgical treatment alone (3, 12, 31). All our patients with these lesions were treated surgically and had uniformly good outcomes. The patients with extratruncular limited AVMs were also more likely to be cured as compared with those with other forms of AVMs.

Treatment outcomes often depend on when these lesions are first treated. As compared with other CVMs, AVMs are a pathology more difficult to treat that generally must be addressed earlier in life. Some authors suggest that the treatment of symptomatic lesions should begin at the age of 2 years, but can be delayed if lesions are quiescent or less bothersome (12, 33). Better outcomes are usually achieved if treatment is initiated in childhood or early adolescence (12, 15, 33). However, the management of AVMs rarely starts during childhood. In our study, 80.4% of AVMs were detected at birth or during infancy, but 87.5% of patients were first treated in adolescence or adulthood, and only 7 patients (12.5%) received treatment in childhood. These data suggest that many patients might be misdiagnosed and receive a proper treatment later in life. Our results might also suggest that superior outcomes can be achieved with an earlier initiation of treatment, as 100% of patients had positive results in childhood, 85.2% in adolescence, and 81.8% in adulthood. However, positive outcomes in childhood were not statistically significant ($P>0.05$) due to a small sample size (7 of the 56 treated patients).

The Schobinger staging is important in choosing a proper treatment, and most authors recommended that treatment should be offered for stages II, III, and IV lesions (3, 14–16, 36, 43, 49). Some studies suggest intervening in the case of stage I lesions due to higher success rates and lower progression; however, other authors report that 17.4% of childhood AVMs remain asymptomatic and unchanged until adulthood (3, 14–16, 36, 43, 49). Therefore, not all early AVMs might require an immediate intervention. In our study, only symptomatic patients with stage II, III, and IV lesions were treated. Less favorable outcomes were achieved in more advanced AVMs, as 96.3% of patients with stage II and 77.8% of patients with stage III AVMs had positive outcomes and only 1 of the 2 patients with stage IV lesions had remission. Comparison between stages showed a significant difference and indicated that intervention at an earlier stage was more likely to succeed.

The selection of treatment depends on the form, location, and extent of the lesion, as well as specific treatment risks. In general, the goal is to control symptoms, preserve function, and improve anatomical deformities (15, 16, 31). While surgical resection offers the best chance for long-term disease control, a complete extirpation of the nidus is challenging given the diffuse nature of this pathology that often involves several tissue planes and vital structures (15, 16, 22, 35, 37–39). Superselective embolization can be used to reach the nidus through transarterial, transvenous, or direct puncture approaches (5, 15, 16, 22, 26–29). In our study, the majority of the lesions (80.4%) were truncular or extratruncular infiltrating, and radical surgical excision could not be achieved if attempted. Therefore, endovascular and combined intervention is a more suitable treatment of this pathology (3, 14–16, 22, 26–29, 36, 43, 49). Embolization aims at eradicating the nidus, without disturbing the feeding arteries, as embolization of the feeding arteries is contraindicated and equivalent to arterial ligation (3, 14–16, 22, 26–29, 36, 43, 49). However, an endovascular approach is frequently not the best curative treatment, as 98% of AVMs recur within 5 years after embolization (3, 14–16, 36, 43, 49). In our group, 29 patients were treated with only endovascular intervention, and positive results were achieved in 24 cases (82.8%). However, 18 (62.1%) of these patients needed a multisession treatment ranging from 2 to 10 sessions, and 5 patients (17.2%) were found to have an untreatable nidus. The results of endovascular treatment were somewhat worse as compared with surgical or combined treatment, but these differences were not statistically significant.

A complete surgical eradication of the nidus is often only possible in limited extratruncular AVMs that are small and well-localized (1, 3, 15, 16, 37–39). Due to potential hemorrhage, large residual deformities, injuries to adjacent structures and high recurrence rates, a wide extirpation of large extratruncular infiltrating AVMs is dangerous and not recommended (1, 3, 15, 16, 37–39). However, AVMs that are not accessible by embolization techniques may be approached with surgical resection (16). Surgical treatment can be combined with embolization before or after operative excision, and compared to embolization alone, it has been shown to offer superior long-term control, especially in lower stage lesions (14–18, 37–41, 50). Embolization done before surgical excision reduces blood loss and the size of the lesions and may improve operative results after excision (14–16, 40, 41). However, despite a complete eradication of the nidus, AVMs recur within 5 years in estimated 81%–86.6% of patients (14–18, 50). In our series, 27 patients (48.2%) were treated surgically or with a combined approach, and positive results were seen in 24 cases (88.9%). Nine patients (33.3%) required more than one treatment session. Better results were seen in the surgical or combined groups in comparison with the endovascular group only, but this difference was not statistically significant (P>0.05). Overall, the best results were seen in the surgical group; however, most of these patients presented with extratruncular limited forms that generally have a less complicated pathology and the best treatment outcomes. In extratruncular limited AVMs treated with surgical resection alone, cure was significantly more likely (P<0.05). Our results suggest that if feasible, surgical treatment should be offered in order to achieve the best outcomes. In summary, 85.7% of patients had positive results, suggesting that it is possible to control AVM lesions, achieve remission, and often prevent further progression of clinical symptoms. In some cases, it is even possible to attain a complete cure.

Paradoxically, AVM treatment is a traumatic event that generates local hypoxia and can stimulate a lesion to enlarge. Inadequate treatment can cause more problems than a natural disease progression. Therefore, the accurate diagnosis of hemodynamic activity extent is critical in therapy planning and follow-up (3, 12, 31, 34). For this purpose, we focused our attention on early description of TLPS method described by Lee et al. (3, 12, 31, 34). As various noninvasive and invasive tests were developed, this method was somewhat abandoned (34, 51). While US, MRI, and angiographic studies offer adequate information on other forms of CVMs, the same does not apply to AVMs. These studies can evaluate AVM anatomy and provide with a limited visual assessment of hemodynamic shunting activity that is very important in AVM presentation. TLPS is the only method that can document quantitative information about AV shunting volume (3, 12, 31, 34). AVMs can be present in the different localizations and can be of different extension with sometimes unclear AV shunting extent due to small hidden shunts. Therefore, an accurate measurement of AV shunting in all nidi is very important for the assessment of tissue circulation and can predict future complications (3, 12, 31, 34). Further treatment course depends of this information, as some patients need an immediate treatment, while others can wait longer or do not need any intervention at all as aggressive treatment may only provoke dormant AVMs to progress rapidly. For example, in 6 patients with insignificant or hypodynamic shunting of 0%–20%, treatment was found to be unnecessary and it could be dangerous. In 4 patients with moderate shunting of 20%–50%, the decision was taken that surgical or combined treatment might be necessary, but can also be delayed. In 4 patients that had hemodynamically significant shunting of 50%–90%, immediate treatment was recommended. In 1 patient with life-threatening shunting of >90%, the decision was taken that despite the best treatment efforts, eradication of the nidus would not be possible. The accurate volume of shunting can also guide treatment strategies. When significant shunting is seen, surgical excision is more likely to result in excessive bleeding; therefore, endovascular treatment might be more appropriate (3 cases). After the shunting volume has been reduced by embolization, a safer and more comprehensive surgical excision can be done (4 cases). The percentage of AV shunting influenced the choice and timing of treatment administration, as patients with a higher degree of shunting were more likely to undergo an endovascular or combined intervention sooner. A change in shunting quantity allows assessing interim results, guiding further steps, and observing patients during follow-up. In addition, TLPS can reveal hidden micro AV shunts and discover arteriovenous shunting in combined hemolymphatic vascular defects. In making treatment and follow-up decisions, TLPS data are always combined with clinical signs/symptoms and findings from other diagnostic methods (3, 12, 31, 34).

Here we report our first experience with the TLPS method in Lithuania for evaluating AV shunting in AVMs. We improved our ability to assess AV shunting by performing this study not only in the extremities, but also in the gluteal, pelvic, and truncal regions. However, the applicability of TLPS is limited if AVMs are located in the head and neck, thoracic region, or visceral organs. When performed in the head and neck or the viscera, TLPS can be dangerous due to possible microembolisation in the brain and visceral organs, respectively. In the thorax, it is challenging to quantify AVM shunting due to the superimposition of AVMs with the lungs.

The main limitation of this study is a small sample size; therefore, statistical significance was not always achieved. Clinical cases are highly individual with diagnostic and treatment approaches tailored to each patient; therefore, the comparison between treatment strategies was challenging. As AVM progression is unpredictable, only retrospective data collection and analysis are possible.

Conclusions

Arteriovenous malformations present a difficult pathology that is clinically challenging to treat. In our study, 3 different treatment modalities were applied, and 85.7% of the outcomes achieved were positive. The best results were achieved by surgical resection of arteriovenous malformations, especially in extratruncular limited forms and with respect to cure. Outcomes were more favorable in the case of lower stage lesions. Gender and timing of the first attempt at treatment did not significantly influence treatment results. The worst outcomes were seen in the case of arteriovenous malformations in the gluteal and pelvic region compared with other locations, and the best outcomes in the head, neck, and upper extremities.

A modified TLPS method allowed more accurate assessment of quantitative shunting status not only in the extremities, but also in the gluteal, pelvic, and truncal regions. It offers an improved diagnosis, especially in difficult cases of arteriovenous malformations, aids in choosing proper treatment methods and timing, as well as helps avoid unnecessary treatment and provides more accurate follow-up.

Statement of Conflict of Interest

The authors state no conflict of interests.

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Received 25 April 2012, accepted 13 August 2012