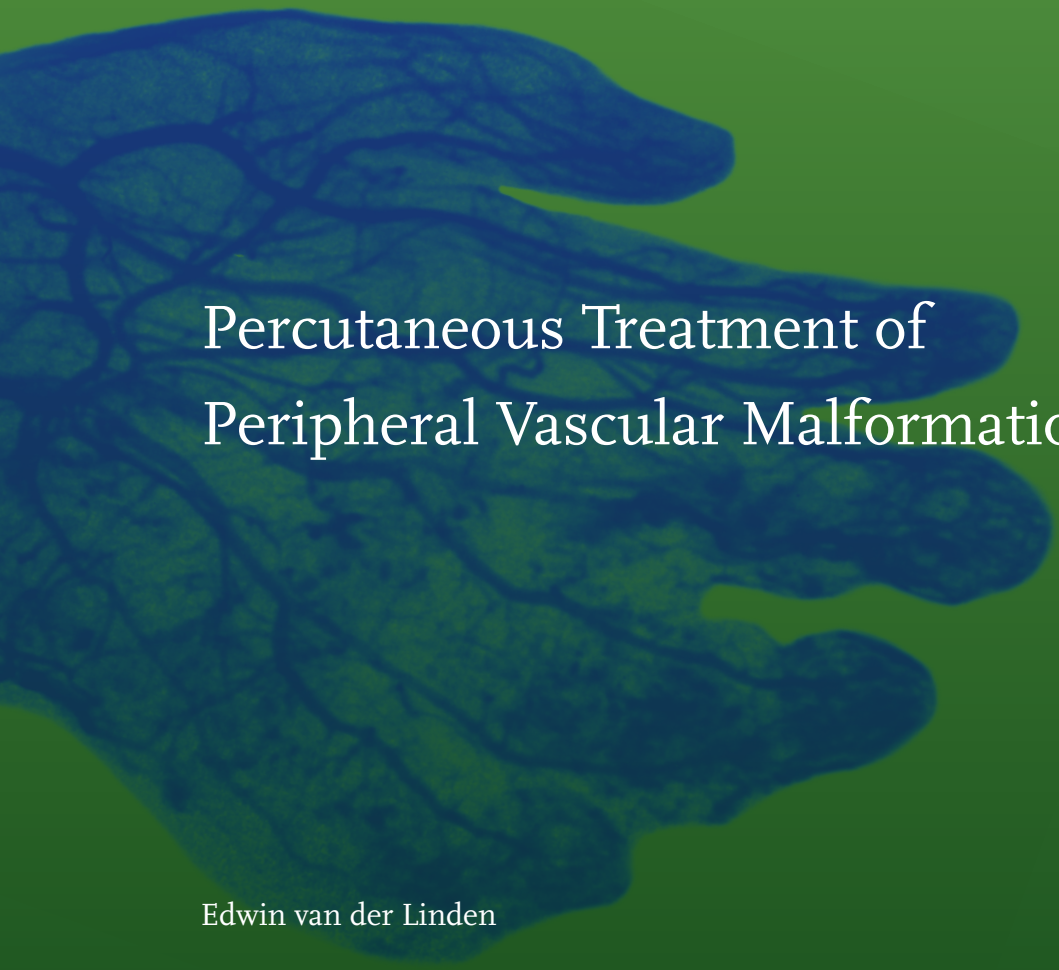

Percutaneous Treatment of Peripheral Vascular Malformations

Edwin van der Linden

Percutaneous Treatment of Peripheral Vascular Malformations

Percutaneous Treatment of Peripheral Vascular Malformations

Percutane behandeling van perifere vasculaire malformaties

Proefschrift

ter verkrijging van de graad van doctor aan de
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Contents

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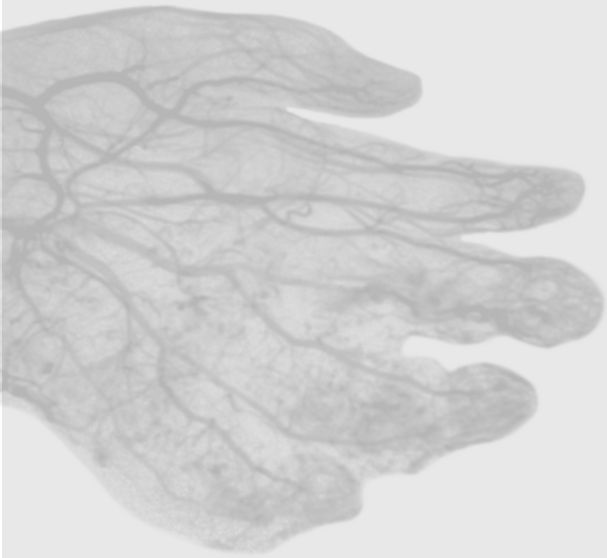
Chapter I

Introduction



Current Concepts in the Classification, Histological Findings, Pathogenesis, Genetics, and Treatment of Vascular Malformations

Vascular malformations arise from errors in the morphological processes that shape the embryonic vascular system during fetal development. These developmental errors result in abnormal clusters of blood vessels. Although these lesions are present at birth, they might not become visible until weeks or even years after birth. Typically, the lesions grow in proportion to the growth of the child. A vascular malformation will not disappear without treatment. Vascular malformations occur in 1.5% of the population and the male to female ratio is 1:1[1]. The symptoms can vary, and they include cosmetic complaints, tissue ulceration, pain, swelling, and functional limitations. In some patients the symptoms are mild, in which case conservative measures might be sufficient. In contrast, patients with severe symptoms might require more invasive treatment. Surgery, interventional radiology, laser therapy or a combination of techniques are used in the treatment of vascular malformations.

However, as a result of their rarity, the correct diagnosis and treatment of vascular malformations is difficult, because most physicians do not see these problems often enough to become knowledgeable about their management.

For the purpose of this review we performed a literature search to outline the classification, pathogenesis and histological findings, clinical presentation, and treatment of peripheral vascular malformations.

We used the PubMed and MeSH databases for the literature search. The following MeSH terms were used: vascular malformations, haemangioma, and arteriovenous malformations, with the subheadings: classification, aetiology, genetics, surgery, and therapy. A specific time interval, 1960 to 2010, was used. In addition, we included in the search the names of groups of investigators who are known to be associated with the different topics and reference lists from other review articles on the same topics. We limited our search to only peripheral vascular malformations and excluded supratentorial and spinal vascular malformations, as well as those of the abdominal and thoracic organs. We focused on publications that described the classification, pathogenesis and genetics of the condition, and non-interventional radiology treatments. This identified a total of 110 publications. The use of an additional database did not reveal any other publications.

Classification of vascular anomalies

A large variety of classifications has been used, and they are based primarily on the anatomy, histology, physical appearance or development of the malformation.

Biological classification

The International Workshop for the Study of Vascular Anomalies, later renamed the International Society for the Study of Vascular Anomalies (ISSVA), was founded by Mulliken and Young to improve the accuracy of the classification, diagnosis, and management of all vascular anomalies. In 1982, Mulliken and Glowacki proposed a classification that was based on the biological and pathological differences among lesions[2]. This classification became the foundation of the modern classification system for vascular anomalies. Vascular anomalies were divided into two categories: haemangiomas and vascular malformations (Table 1). Haemangiomas were described as those lesions that exhibit rapid neonatal growth and hypercellularity during a phase of proliferation, followed by a phase of involution characterized by diminished cellularity and fibrosis. Vascular malformations were described as those lesions that are present at birth, increase in

size in proportion to the growth of the child, and do not regress spontaneously. Vascular malformations are composed of normal flat endothelial-lined vascular spaces with normal rates of cell turnover. They were subdivided further by these authors into: fistulae; arterial (arteriovenous) malformations (AVM); capillary malformations; venous malformations (VM); and lymphatic malformations (LM).

In 1983, Burrows and coworkers incorporated angiographic differentiation and flow characteristics into the classification[3]. They also incorporated the level of embryological defect that was responsible for each type of anomaly and subdivided each of these categories of anomaly into two distinct anatomical–pathological subtypes: truncular and extratruncular. The truncular form, which is often more severe than the extratruncular form, arises as a consequence of a relatively late embryonic error of maturation within a differentiated vascular trunk and leads to the development of regional vascular aplasia, obstruction or dilatation. The extratruncular form is caused by a relatively early embryonal dysplasia within the primitive undifferentiated capillary network and presents in either a diffuse–infiltrating or limited–localized pattern. In 1988, at the 7th Meeting of the ISSVA in Hamburg, this was incorporated into the "Hamburg Classification" of vascular defects (Table 2).

In 1992, at the ISSVA meeting in Colorado, a consensus clarified the term "vascular anomaly" to describe all vascular tumours and malformations. This consensus is still used and the suffix ''-oma'' is now used only to refer to lesions that demonstrate cellular hyperplasia[4]. The final modern classification of vascular anomalies, after Mulliken, which is based on histology, clinical behaviour, and flow characteristics was adopted at the ISSVA in Rome in 1996[4]. The most recent and complete version appeared in 2007 (Table 3)[5].

Table 1

Classification of vascular lesions in infants and children

Haemangiomas	Malformations
Proliferating phase	Venous
Involuting phase	Capillary
	Arterial
	Lymphatic
	Fistulae

Data from Mulliken JB, Glowacki J. Hemangiomas and vascular malformations in infants and children: a classification based on endothelial characteristics. Plast Reconstr Surg 1982;69:412–20.

Table 2

Anatomopathological classification of vascular defects (Hamburg classification)

Type	Forms	
	Truncular	Extratruncular
Predominantly arterial defects	Aplasia or obstructive	Infiltrating
	Dilatation	Limited
Predominantly venous defects	Aplasia or obstructive	Infiltrating
	Dilatation	Limited
Predominantly lymphatic defects	Aplasia or obstructive	Infiltrating
	Dilatation	Limited
Predominantly AV shunting defects	Deep	Infiltrating
	Superficial	Limited
Combined/mixed vascular defects	Arterial and venous	Infiltrating haemolymphatic
	Haemolymphatic	Limited haemolymphatic

Based on the 7th Meeting of the International Workshop on Vascular Malformations, Hamburg, Germany, 1988.
Abbreviation: AV, arteriovenous.

Table 3

International society for the study of vascular anomalies classification of vascular anomalies

Tumours	Vascular malformations	
	Simple	Combined
Infantile haemangioma	Capillary (C)	Arteriovenous fistula
Congenital haemangioma	Lymphatic (L)	Arteriovenous malformation (AVM)
Tufted angioma	Venous (V)	CVM
Kaposiform haemangioendothelioma		CLVM
Haemangiopericytoma		LVM
Pyogenic granuloma		CAVM
Spindle-cell haemangioendothelioma		CLAVM

Based on Scientific Committee of the 11th Meeting of the International Society for the Study of Vascular Anomalies, Rome, Italy, 1996. Data from Enjolras O. Classification and management of the various superficial vascular anomalies: hemangioma and vascular malformation. J Dermatol 1997;24:701–10; and Garzon MC, Huang JT, Enjolras O, et al. Vascular malformations: Part I. J Am Acad Dermatol 2007;56:353–70 [quiz: 371–4].

Classification on the basis of anatomical and haemodynamic features

In 1993, Jackson and coworkers[6] simplified the classification of Burrows and coworkers to give two different flow patterns within vascular malformations: low flow (which corresponded to VMs) and high flow (which corresponded to AVMs); they retained separate categories for LMs and haemangiomas. Their purpose was to create a "system directly related to investigation and treatment" (Table 4). LMs have been subdivided into macrocystic, microcystic and mixed varieties on the basis of the size of the lesion cavity. For simplicity, many now consider LMs to be in the low-flow category.

In 2006, Chow et al[7] proposed a modified angiographic classification for peripheral high-flow AVMs. Peripheral AVMs were categorized into four types according to the angiographic morphology of the nidus:

type I (arteriovenous fistulae), type II (arteriolovenous fistulae), type IIIa (arteriolovenulous fistulae with nondilated fistula), and type IIIb (arteriolovenulous fistulae with dilated fistula). The purpose was to determine the value of this classification in the assessment of therapeutic outcomes and approaches to the ethanol embolization of AVMs in the body and extremities. This classification can be regarded as a modification of the earlier classification proposed by Houdart et al[8], who classified intracranial AVMs into three types on the basis of the morphology of the nidus: arteriovenous, arteriolovenulous, and arteriolovenulous fistulae.

A new classification system that focused on low-flow malformations, and specifically VMs, was proposed by Puig et al in 2003[9]. This system includes four types of VM (Table 5). It can be used to plan therapy and suggests a higher risk of complications during percutanenous sclerotherapy for type III and type IV lesions, when compared with type I and type II lesions.

Table 4

Classification of vascular anomalies by vascular dynamics

I.	Haemangioma
II.	Vascular malformations a. Low-flow (VM) b. High-flow (AVM)
III.	LM

Table 5

Classification of venous malformations based on anatomical and haemodynamic features of the lesion and adjacent veins[7]

Type	Description
Type I	(Almost) isolated malformation without peripheral drainage
Type II	Malformation that drains into normal veins
Type III	Malformation that drains into dysplastic veins
Type IV	Venous ectasia

Clinical classification

A clinical staging system for high-flow malformations (the Schobinger classification) was introduced at the 1990 meeting of the ISSVA in Amsterdam. Kohout et al[10] modified the Schobinger classification to increase simplicity (Table 6). This clinical classification can be used to plan therapy. Stage I lesions remain stable for long periods. Expansion (stage II) is usually followed by pain, bleeding, and ulceration (stage III). Once present, these symptoms and signs progress inevitably until the malformation is treated.

In general, we use the classification of Jackson and coworkers[6] to describe vascular malformations with respect to the different diagnostic modalities. To plan the treatment of low-flow VMs with percutaneous sclerotherapy, we use the classification system of Puig et al[9], and to plan embolization therapy for high-flow AVMs, we use the classification of Chow et al[7].

Histological findings

By conventional microscopy, vascular malformations show irregular, variably dilated or thickened dysplastic-appearing vascular channels that are lined with flat mature endothelial cells without valves[2,11]. These vascular spaces are usually filled with erythrocytes that are surrounded with collagenous tissue, which is sometimes accompanied by fat. The wall of the vascular malformation shows an absence of the internal elastic lamina and a relative paucity or intermittent absence of smooth muscle[11]. Occasionally, locules of disorganized smooth muscle are seen that emanate from the vascular wall into the surrounding stroma[11]. Localized intravascular coagulopathy is frequently present within venous malformations[12]. These luminal thrombi can develop further, and become calcified to form phleboliths. Intraluminal clotting with subsequent ingrowth of capillaries is common. If this process is particularly exuberant, it is called Masson's papillary endothelial hyperplasia[11,13,14]. This process can lead to further vascular restriction. In addition, this phenomenon can evolve into a mass-like lesion within the malformation that contains cores of hyalinized tissue lined by endothelial tissue in a sinusoidal or papillary pattern.

Capillary malformations are characterized by abnormal ectatic channels, the size of capillaries to venules, within both the papillary and the upper reticular dermis[15]. The walls of the vessel are thin and lined with flat endothelium that is mature in appearance. There is normal development of the vascular channels, which show dilatation of the cutaneous vascular plexus with no increase in vessel number.

AVMs typically show "arterialization" of the venous outflow, and the media is thickened by increased muscle fibres, fibrosis, and the accumulation of glycosaminoglycan. The internal elastic membrane is relatively preserved. The increased flow through the afferent arterial system causes degenerative changes in the artery, which displays thickening of the media, dilatation, and tortuosity[16].

Lymphatic malformations can be differentiated from venous malformations by the fact that lymphatic malformations are filled predominantly with lymphatic fluid, with lymphoid aggregates in the adjacent stroma.

Table 6.

Clinical staging system for documenting the presentation and evolution of an AVM (Schobinger classification)

Stage	Clinical signs
Stage I (quiescence)	Pink–blue stain, warmth, and arteriovenous shunting by Doppler study
Stage II (expansion)	Same as stage I plus enlargement, pulsations, thrill, bruit, and tense and tortuous veins
Stage III (destruction)	Same as stage II plus dystrophic skin changes, ulceration, tissue necrosis, bleeding, or persistent pain
Stage IV (decompensation)	Same as stage III plus cardiac failure

Pathogenesis and genetics

The normal vascular system arises during embryogenesis via two processes: vasculogenesis and angiogenesis. Vasculogenesis refers to the development of vascular channels as a result of the differentiation of mesenchymal cells into endothelial cells, which leads to the formation of a primary capillary plexus. Angiogenesis refers to the development of new vessels that is caused by the remodelling and sprouting of the primary capillary plexus. This process is accompanied by the migration of smooth muscle cell precursors from mesenchymal and neural crest cells towards the endothelial tubes to become the smooth muscle cell layers of the blood vessel walls. After further changes in size and mural structure, this process leads to the formation of arteries, capillaries, veins, and lymphatic vessels[17].

Vascular malformations are caused by errors in the complex processes of normal vasculogenesis and angiogenesis during embryonic development. Studies in transgenic mice have demonstrated a crucial role for vascular endothelial growth factor (VEGF), transforming growth factor-β (TGF-β), angiopoietin-1 (Ang-1) and -2 (Ang-2), and ephrin B2, and their receptors. These signalling molecules and their receptors have also been implicated in human vascular anomalies that are believed to be caused by localized errors in vascular morphogenesis[18].

Normal communications exist between arteries and veins that bypass the capillary bed. These communications are needed for temperature regulation and to adapt the distribution of flow to different organs. The autonomic nervous system and local hormones regulate this capacity. It is thought that there is a lack of regulation in AVMs, which results in the progressive dilatation of these existing channels. An AVM enlarges or extends by the progressive dilatation of the fistels and by the opening of collateral channels.

Vascular malformations are almost all sporadic, nonfamilial developmental errors. Some vascular malformations develop after traumatic formation of arteriovenous fistulae, and these can mimic developmental errors.

There are a few inherited forms of vascular malformation that are associated with various syndromes.

Capillary malformations were once referred to as port-wine stains; this term is now outdated. Genetic studies have mapped a locus for capillary malformations to chromosome 5q14-21, and this locus corresponds to a defect in the RASA1 gene[19]. The RASA1 gene encodes the p120 Ras GTPase-activating protein. When mutated, p120 Ras GTPase-activating protein binds to Krev-1/rap1a, an integrin β1–mediated cell adhesion and angiogenesis protein. The pathogenesis of capillary malformations is not understood. The lack of sympathetic innervation regulating blood flow in vessels with capillary malformation is believed to produce progressive ectasia of the capillaries and medium-sized venules, with the development of thin walls and flat endothelial cells. Approximately 30% of affected individuals have high-flow AVMs that are located more deeply, in addition to the capillary malformation (CM-AVMs)[20]. Approximately one-third of patients who have CM-AVMs have Parkes–Weber syndrome[20].

Venous malformations occur sporadically in approximately 95% of cases. The aetiopathogenesis of sporadic VMs and syndromes that are associated with venous anomalies, which include blue rubber bleb nevus syndrome, Maffucci syndrome, and Klippel–Trenaunay syndrome, is unknown. Small, multifocal VMs that are located on the skin and mucosae are sometimes inherited in an autosomal dominant fashion. These lesions are called cutaneomucosal venous malformations, and they are caused by mutations in the TEK gene, which encodes the tyrosine kinase receptor TIE2[21,22].

High-flow AVMs can occur in association with other vascular anormalies, for example CM-AVM and Parkes–Weber syndrome as mentioned above, and these syndromes are discussed with capillary malformations. Rendu–Weber–Osler syndrome (hereditary haemorrhagic telangiectasia) is an autosomal dominant disorder that is characterized by cutaneomucosal telangiectasias, epistaxis, and often AVMs in the lung, liver, gastrointestinal tract, and central nervous system[23,24]. At least four genetic loci have been associated with Rendu–Weber–Osler syndrome, with mutations identified in the genes that encode endoglin and activin receptor-like kinase[25,26].

Although many syndromes have a known genetic basis, the genetic contributions to most syndromes that are associated with vascular malformations are not understood fully. Identification of a lesion or syndrome that suggests a genetic cause can lead to a more accurate diagnosis and improved management and treatment of the disease.

Clinical presentation

The diagnosis of vascular malformations can usually be made from the clinical history and physical examination. All vascular malformations are present at birth, but usually they are identified later in childhood or young adulthood because the period of greatest enlargement of the lesion occurs from infancy to puberty. Continued growth within the malformation can also result in clinical manifestations later in life. Accelerated growth in adults has been reported as a result of trauma, haemorrhage, partial resection, or the hormonal influences of pregnancy[27,28]. Low-flow VMs are typically soft, compressible, variably blue-tinged masses that can enlarge with dependent positioning and the Valsalva manoeuvre. High-flow AVMs show hyperaemia, increased temperature, pulsatility or a palpable local thrill[29]. Vascular malformations often invade the surrounding fascial planes and can infiltrate subcutaneous tissue, muscle, bone, joints, neurovascular structures, and even viscera.

Patients commonly experience symptoms as a result of five related mechanisms:

1 Venous engorgement secondary to dependent positioning, exercise, and after prolonged stasis, for example when awakening in the morning, frequently results in significant swelling and pain[27,28].
2 The mass effect may cause local compression or distension of local nerves, fascia, or capsular structures, leading to pain.
3 Local infiltration or the mass effect may cause muscular contracture or a restricted range of motion of an adjacent joint.
4 Local haemorrhage, or even haemarthrosis, can cause significant pain and impairment.
5 Local stasis on a background of a chronic low-grade localized intravascular coagulopathy and thrombophilic state within the lesion results frequently in local thrombosis and thrombophlebitis[12,30].

Treatment

The decision to intervene, rather than treat a patient with a vascular malformation conservatively, depends on the symptoms. These symptoms are often temporally inconstant and highly variable. Often, in a patient with only mild symptoms, the most significant complaint is that of anxiety regarding the diagnosis, prognosis, and natural history of the disease. This can be resolved successfully by reassuring the patient of the indolent, non-neoplastic nature of the lesion and that intervention can be considered whenever the symptoms warrant.

Patients whose symptoms do not meet the threshold for intervention or those do not wish to have an intervention can be managed with elevation of the involved area during sleep and avoidance of those activities that maximize the symptoms. Some lesions might be sensitive to hormones, therefore cessation of the use of oral contraceptives might provide relief[31,32]. Most patients with venous malformations (88%) have localized intravascular coagulopathy with low fibrinogen levels and a low platelet count, and elevated levels of fibrin degradation products[12,33]. This chronic low-grade localized coagulopathy leads to thrombosis and pain, which can be managed successfully with aspirin therapy[14,28]. Pressure garments or stockings can reduce the symptoms successfully and should be implemented early and continuously during the course of the disease[14,28,33]. Elastic garments slow the progression of venous distension, deformity, ulceration and pain, and reduce the occurrence of chronic localized intravascular coagulopathy[33].

Table 7.

Criteria for intervention in vascular malformations

Author	Absolute indications	Relative indications
Lee[34]	Haemorrhage	Disabling pain or discomfort of a progressive nature
	Secondary complications of venous hypertension	Functional disability or impairment that affects daily activity and the quality of life
	Lesion located in a life- or limb-threatening region (e.g. proximity to the airway)	Cosmetically severe deformity accompanying physical or psychological disability and negative impact on the quality of life
	Lesions that threaten vital functions (e.g. seeing, hearing, eating or breathing)	Vascular-bone syndrome with rapid progress of long bone growth discrepancy accompanied by significant pelvic tilt or compensatory scoliosis
		Lesions located at a region with a high risk of complication (e.g. haemarthrosis, deep vein thrombosis)
		Lesions with recurrent infection or sepsis
Tan[35]	Haemorrhage	Nonsevere cosmetic deformity
	Disabling pain that necessitates the use of oral analgesia	
	Functional impairment secondary to swelling or pain	
	Tissue loss or ulceration	
	Severe cosmetic deformity	

With respect to the decision to intervene, it is important to take into consideration the level of patient morbidity and the expected level of risk related to the treatment. The most important indications for nonconservative treatment of a vascular malformation are if the lesion causes pain, functional impairment or cosmetic problems[28]. Given that these signs and symptoms are difficult to quantify objectively, various criteria have been provided to direct therapy (Table 7)[34,35]. Surgery, interventional radiology, laser therapy or a combination of techniques are used in the treatment of vascular malformations. The type of therapy used depends highly on the type and extent of the malformation. Therefore, it is very important to classify the lesion correctly and to determine the extent of the vascular malformation using MRI before therapy is planned.

Laser therapy is usually effective for superficial skin lesions such as capillary malformations or port-wine stains. Laser therapy uses the principle of selective photothermolysis, which can destroy specific targets within the skin selectively at a depth of up to 2 mm. Current generation lasers use epidermal cooling devices that minimize damage to the surrounding structures and lessen the discomfort associated with treatment. The response to treatment is variable, but some investigators have reported a good response in as many as 80% of patients treated[36]. Most patients need multiple treatments to obtain cosmetically acceptable results, and complete disappearance of the lesion is unlikely.

Surgical resection of the vascular malformation is a good option in patients who have a focal well-defined VM that is confined to a single or specialized muscle group, or that is causing a neurological or compression syndrome, and in patients where there is a good possibility of anatomical and functional restoration[14]. However, many lesions are infiltrative, and involve multiple muscle groups or fascial planes. In these cases, surgical excision results in an unacceptably high functional and cosmetic deficit[37]. Increasingly, sclerotherapy has been described as either an indispensable adjunct to surgery or as the minimally invasive stand-alone therapy of choice for most VMs[5,28,34,38]. In particular, localized VMs are treated predominantly

by sclerotherapy. Diffuse infiltrating VMs are treated best with sclerotherapy with or without adjunctive surgery. Laser therapy with an Nd:YAG laser might be helpful for small localized or mucosal lesions where there are concerns about the possibility of superficial scarring following sclerotherapy[39].

Of all vascular malformations, AVMs are the most difficult to treat. Radical resection is often difficult and dangerous and fails frequently, which results in a high incidence of recurrence. Historically, surgical ligation of arteries was employed as palliative therapy for high-flow AVMs, but was largely unsuccessful. When the arterial blood supply to an AVM is ligated proximally, the lesion will continue to grow and more collateral vessels will develop. This makes access for the purpose of embolization therapy impossible[40]. "Vascular casting" of the central portion (nidus) of high-flow AVMs with the use of transcatheter embolotherapy techniques was postulated to be a superior method for the management of high-flow AVMs than surgical or radiological ligation of the supplying arteries[41]. Treatment of stage I lesions (using the Schobinger classification) has been shown to have a higher success rate, which suggests that early intervention might preclude the possible complications that are feared in the resection of stage II or III lesions[10]. Multimodal treatment, which includes preoperative embolization and complete surgical resection, is usually necessary for the management of AVMs. Preoperative embolization reduces intraoperative blood loss, allows more complete surgical resection, and therefore decreases postsurgical morbidity and mortality[10,42]. Cyanoacrylate embolotherapy alone, or in combination with surgical resection of the AVM, has been shown to provide excellent palliation in patients with high-flow AVMs[43]. However, many of the patients in the aforementioned study had a poor long-term clinical outcome and eventually required amputation of the affected limb.

Purpose and outline of the Thesis

The main purpose of this thesis was to evaluate the mid- and long-term effects of the percutaneous treatment of low-flow venous malformations and high-flow arterial venous malformations. We also evaluated two special treatment options that can be used if other treatments are not possible.

Chapter Two discusses the use of conventional and dynamic contrast-enhanced MR parameters to categorize vascular malformations by means of the vascular dynamics, in accordance with the classification of Jackson and others[6]. **Chapter Three** describes the long-term clinical outcome, patient satisfaction, and complication rate in a large series of 66 patients who were treated percutaneously for symptomatic vascular malformation. In **Chapter Four** the long-term clinical outcome and complication rate after percutaneous treatment of vascular malformations in a group of 23 children are discussed. RF ablation as an alternative treatment option for symptomatic peripheral vascular malformations when other treatments have failed or are not possible is addressed in **Chapter Five**. In **Chapter Six**, we discuss the option of retrograde transvenous alcohol embolization during venous outflow occlusion and flow arrest as a method of treatment for type II high-flow AVMs whenever a transarterial or direct puncture treatment approach does not seem to be feasible or has proven to be unsuccessful. Finally, the treatment of a venous malformation in the suprapatellar recessus of a 14-year-old female rugby player is presented in **Chapter Seven.** A general discussion is provided in **Chapter Eight.**

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Chapter 2

Value of Dynamic Contrast-Enhanced MR Imaging in Diagnosing and Classifying Peripheral Vascular Malformations

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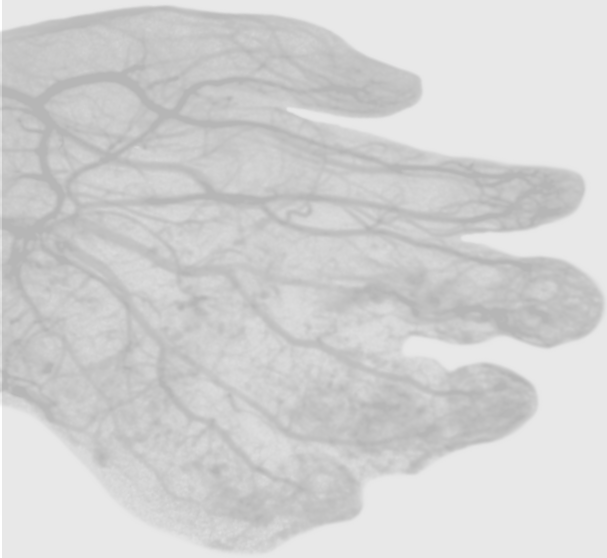


AJR 2002; 178:1181-1187

Abstract

Objective: Our purpose was to evaluate prospectively whether MR imaging, including dynamic contrast-enhanced MR imaging, could be used to categorize peripheral vascular malformations and especially to identify venous malformations that do not need angiography for treatment.

Subjects and methods: In this blinded prospective study, two observers independently correlated MR imaging findings of 27 patients having peripheral vascular malformations with those of diagnostic angiography and additional venography. MR diagnosis of the category, based on a combination of conventional and dynamic contrast-enhanced MR parameters, was compared with the angiographic diagnosis using gamma statistics. Sensitivity and specificity of conventional MR imaging and dynamic contrast-enhanced MR imaging in differentiating venous from nonvenous malformations were determined.

Results: Excellent agreement between the two observers in determining MR categories ($\gamma = 0.99$) existed. Agreement between MR categories and angiographic categories was high for both observers ($\gamma = 0.97$ and 0.92). Sensitivity of conventional MR imaging in differentiating venous and nonvenous malformations was 100%, whereas specificity was 24-33%. Specificity increased to 95% by adding dynamic contrast-enhanced MR imaging, but sensitivity decreased to 83%.

Conclusion: Conventional and dynamic contrast-enhanced MR parameters can be used in combination to categorize vascular malformations. Dynamic contrast-enhanced MR imaging allows diagnosis of venous malformations with high specificity.

Introduction

Although the nomenclature of vascular lesions of soft tissues remains complicated, the classification of Mulliken and Glowacki[1] is most often used. This classification divides soft-tissue vascular lesions into hemangiomas and vascular malformations. Hemangiomas appear in early infancy, grow rapidly, and undergo involution. However, vascular malformations, presumably, are present at birth, increase in proportion to the growth of the child, and do not regress spontaneously[2-5].

Peripheral vascular malformations can be divided into various categories depending on the predominant anomalous channels: lymphatic, venous, capillary, and arterial malformations. Combinations of vascular malformations also commonly occur, such as capillary-venous and arteriovenous malformations[1,2]. Alternatively, malformations can be categorized as either high- or low-flow on the basis of hemodynamic flow characteristics. Malformations with arterial components are considered high-flow (arterial malformations containing macrofistulas and arteriovenous malformations containing microfistulas through a vascular nidus), and those without arterial components are considered low-flow lesions (venous, capillary, and lymphatic malformations)[6].

Peripheral vascular malformations often require treatment because they tend to enlarge, cause pain, ulceration, severe deformity, and decreased function of the affected extremity[1]. Appropriate treatment of peripheral vascular malformations, which often consists of multiple treatment sessions, depends on accurate characterization of the type of vascular malformation and its hemodynamic characteristics. Transarterial embolization appears to be the most effective treatment in high-flow arterial and arteriovenous malformations, with occasional subsequent surgical resection[6,7]. Direct percutaneous puncture with embolic materials (sclerotherapy) is described as a successful treatment in venous lesions[1,8,9].

The aim of this study was to assess whether MR imaging, including dynamic contrast-enhanced MR imaging, can be used to categorize vascular malformations and to identify patients with venous malformations that do not need angiography for treatment.

Subjects and Methods

Patients

Between April 1996 and May 2000, 27 consecutive patients scheduled for angiography because of a clinically suspected high-flow peripheral vascular malformation (11 male and 16 female; age range, 2-86 years; median, 27 years) were prospectively included. All patients were examined with our standard MR protocol, consisting of dynamic contrast-enhanced MR imaging and diagnostic angiography. Additional closed-system venography was performed in 15 of 27 patients, including all six patients showing no abnormalities on venous phase angiography. Selection criteria for closed-system venography were absence of abnormalities on venous phase angiography or incompletely visualized venous morphology by angiography alone. Our study group consisted of 13 capillary-venous, six venous, four arteriovenous, and four arterial malformations, on the basis of the combined findings of angiography and venography[10,11] (Table 1). In all patients, MR imaging preceded angiography and venography. The range of time between MR imaging and diagnostic angiography was 0-56 weeks (median interval, 5 weeks). Patients did not receive treatment in this time period. Lesions were located in the lower extremity ($n = 16$), upper extremity ($n = 5$), pelvis ($n = 3$), face ($n = 2$), and chest wall ($n = 1$). Malformations located in the central nervous system were not included.

The institutional review board approved the study protocol, and informed consent was obtained from all patients.

Angiography and Venography

Selective and superselective angiography, with digital subtraction techniques, was performed in all patients using an Integris Cesar angiographic unit (Philips Medical Systems, Shelton, CT). Closed-system venography was performed by direct percutaneous contrast injection into the lesion with a fine needle to show the extent of the anomaly and its ramifications and connections. All angiograms and venograms were interpreted by one interventional radiologist who was unaware of the MR findings. The results of venography were integrated with the angiographic findings to optimize the gold standard for categorizing peripheral vascular malformations. Criteria for diagnosis are listed in Table 1[11].

MR Imaging

MR imaging was performed on a 0.5- or 1.5-T MR system (T5-11 or NT 15 Gyroscan; Philips Medical Systems) using a surface coil when possible. We used the body coil in two patients with large lesions. The imaging protocol consisted of T1-weighted fast spin-echo sequences (TR range/TE range, 530-600/12-25; echo-train length, 3) and T2-weighted fast spin-echo sequences (2209-5492/60-150; echo-train length, 5-12; slice thickness, 6-12 mm) with frequency-selective fat saturation. Saturation slabs cranial to the lesion were used in all patients. These sequences were followed by a dynamic contrast-enhanced study. For dynamic contrast-enhanced MR imaging, a magnetization prepared T1-weighted three-dimensional gradient-echo sequence (9.5-15/3-6.9; flip angle, 30°; nonselective inversion preparatory pulse; preparatory-pulse delay time, 165 msec to obtain T1 tissue contrast without signal from vessels; number of excitations, 1; matrix size, 128 × 256; field of view, 250-400 mm; section thickness, 7-10 mm) was used after an IV bolus injection of gadopentetate dimeglumine (Magnevist; Schering, Berlin, Germany) of 0.1 mmol/kg of body weight. Bolus injection was begun 5 sec after the start of data acquisition. The injection rate using a power injector was 2 mL/sec, immediately followed by a saline flush of 20 mL at the same injection rate. Depending on the size of the lesion, we obtained from two to eight sections at each time interval. The time interval, or temporal resolution, was 3 sec for at least 84 sec. Temporal resolution was 5 sec for the period between 85 and 119 sec, 10 sec for the period between 120 and 189 sec, and 15 sec for the period between 190 and 300 sec. The first unenhanced image was subtracted from the contrast-enhanced dynamic images using standard commercially available software.

Two radiologists without knowledge of the clinical and angiographic findings independently evaluated all MR examinations. In addition, a consensus interpretation was made for each patient. The consensus interpretation was used to describe the MR features. Individual scores was used to describe discordance between individual MR features, to determine agreement between categorization based on MR criteria and angiographic diagnosis for both observers, and to determine the interobserver agreement of the MR classification. In each patient, the conventional MR images were evaluated first; subsequently, the contrast-enhanced MR images were added for evaluation.

On conventional MR images, we evaluated signal characteristics related to adjacent normal fat and normal muscle and the presence or absence of flow voids and dilated venous spaces. Flow voids were defined as low signal intensities in blood vessels visible on T2-weighted fast spin-echo images. Dilated venous spaces were defined as ectatic dilated vascular structures. We analyzed by visual inspection on the dynamic contrast-enhanced subtraction images the time interval between start of arterial enhancement and onset

of lesion enhancement. The start of arterial enhancement was evaluated in an artery that was not part of the lesion. Early enhancement was defined as lesion enhancement within 6 sec after the start of arterial enhancement, whereas late enhancement was defined as lesion enhancement later than 6 sec after arterial enhancement. On the basis of the results with the first pass of gadopentetate dimeglumine after injection of 2 mL/sec in extremity musculoskeletal tumors, an arbitrary threshold of 6 sec (interval arterial and lesion enhancement) was chosen[12-15].

Our hypothesis was that late lesion enhancement (>6 sec after arterial enhancement) represents venous malformations, and conversely, early lesion enhancement (≤6 sec after arterial enhancement) represents malformations with any arterial or capillary component, such as arterial, arteriovenous, and capillary – venous malformations. Moreover, the presence of dilated venous spaces was used as a criterion to diagnose venous or capillary – venous malformations. The presence of flow voids was considered indicative of the presence of micro- or macrofistulas in arteriovenous or arterial malformations, respectively (Table 2).

Statistical Analysis

Each MR feature was analyzed separately for its association with the categories of vascular malformations using the chi-square test. Features with a *p* value of less than 0.05 were considered significant.

Gamma statistic (γ) was used to assess statistically the concordance between MR imaging and angiographic diagnosis because both these variables are ordinal[16]. The gamma statistic can range between -1.0 and +1.0. With higher levels of concordance between MR imaging and angiographic diagnosis, the gamma tends toward +1.0, and in the contingency table, the frequencies concentrate along the diagonal. Interobserver variability was determined to evaluate whether both observers agreed about the category of each patient.

The differentiation between venous and nonvenous malformations by conventional MR imaging and dynamic contrast-enhanced MR imaging, separately, was compared with regard to sensitivity and specificity.

Table 1

Diagnoses based on angiography and venography

Diagnosis of malformation	Criteria
Venous	Normal afferent arteries, normal capillary bed, contrast pooling in dilated stagnant venous spaces in late venous phase or
	No abnormalities on late venous phase angiography, but ectatic venous spaces on closed-system venography
Capillary-venous	Abnormal capillaries in arterial phase, contrast pooling in dilated stagnant venous spaces in late venous phase
Arteriovenous	Direct arteriovenous communications (microfistulas) through vascular nidus. Afferent arteries and efferent veins are frequently hypertrophied and tortuous
Arterial	Dilatation and lengthening of afferent arteries, early opacification of enlarged efferent veins by macrofistulas

Note. Data taken from[11].

Table 2

Classification of vascular malformations based on MR feature

Malformation	Early enhancement	Late enhancement	Dilated venous spaces	Flow voids
Venous		Present	Present	
Capillary-venous	Present		Present	
Arteriovenous	Present			Present
Arterial	Present			Present

Results

MR Features

For each observer, the scores describing individual MR features correlated significantly (p = 0.001-0.009) with the angiographic diagnosis (Table 3). The observers disagreed only on the presence or absence of dilated venous spaces in four capillary-venous and one arterial malformation and on the presence or absence of flow voids in two capillary-venous malformations.

Consensus interpretation of the two observers was used to describe the MR features. All lesions displayed predominantly low signal intensity compared with muscle, with small areas of signal intensity slightly higher than that of skeletal muscle but less than that of fat on T1-weighted images. In all lesions, signal intensity was high on T2-weighted images. Dilated venous spaces were seen in 22 of 27 malformations. Flow voids were recorded in all four arterial malformations, in two of four arteriovenous, and in one of 13 capillary-venous malformations. Flow voids were not observed in the six venous malformations (Table 4). Five of six venous malformations enhanced late (>6 sec after arterial enhancement). Twelve of 13 capillary-venous malformations enhanced early (≤6 sec). All four arteriovenous and all four arterial malformations displayed early enhancement (Table 4). The largest lesion diameter ranged from 2.0 to 24.5 cm (median, 7.0 cm)

Table 3

MR features (individual review) of peripheral vascular malformations (n = 27) and their association with categories of vascular malformations

MR features	Angiographic diagnosis				p^a
	Venous (n = 6)	Capillary-venous (n = 13)	Arteriovenous (n = 4)	Arterial (n = 4)	
Observer 1					
Start of enhancement					
> 6 sec	5	1	0	0	0.001
≤ 6 sec	1	12	4	4	0.001
Dilated venous space					
Present	6	12	2	1	0.009
Absent	0	1	2	3	0.009
Flow voids					
Absent	6	12	2	0	0.001
Present	0	1	2	4	0.001
Observer 2					
Start of enhancement					
> 6 sec	5	1	0	0	0.001
≤ 6 sec	1	12	4	4	0.001
Dilated venous spaces					
Present	6	10	2	0	0.007
Absent	0	3	2	4	0.007
Flow voids					
Absent	6	10	2	0	0.007
Present	0	3	2	4	0.007

[a] Chi-square test.

Table 4

MR features (consensus review) of peripheral vascular malformations (n = 27)

MR features	Angiographic diagnosis			
	Venous (n = 6)	Capillary-Venous (n = 13)	Arteriovenous (n = 4)	Arterial (n = 4)
Start of enhancement				
> 6 sec	5	1	0	0
≤ 6 sec	1	12	4	4
Dilatated venous spaces				
Present	6	13	2	1
Absent	0	0	2	3
Flow voids				
Absent	6	12	2	0
Present	0	1	2	4

Table 5

MR diagnosis versus angiographic diagnosis of vascular malformations

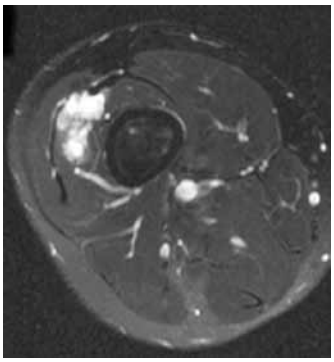
MR diagnosis	Angiographic diagnosis				γ[a]
	Venous (*n* = 6)	Capillary-Venous (*n* = 13)	Arteriovenous (*n* = 4)	Arterial (*n* = 4)	
Observer 1					
Venous	5	1	0	0	
Capillary-venous	1	11	2	0	0.97
Arterial or arteriovenous	0	1	2	4	
Observer 2					
Venous	5	1	0	0	
Capillary-venous	1	9	2	0	0.92
Arterial or arteriovenous	0	3	2	4	

[a] Gamma statistic (γ) was used to assess statistically the concordance between MR imaging and angiographic diagnosis because both these variables are ordinal[16]

Diagnosis of Categories

Interobserver agreement of the MR classification of the four categories of vascular malformations found in our population was high (γ = 0.99). Agreement between diagnosis of categories based on MR criteria and angiographic diagnosis was high for both observers (γ = 0.97 and 0.92) (Table 5, Figs. 1-3). Both observers correctly classified all four arterial and two of four arteriovenous malformations. The two incorrectly classified arteriovenous malformations were classified by both observers as capillary-venous malformations. One venous malformation showing early enhancement was incorrectly classified as capillary-venous malformation by both observers. Two (15%) of 13 and four (31%) of 13 capillary-venous malformations were incorrectly classified by observers 1 and 2, respectively (Table 5).

The sensitivity of conventional MR imaging for differentiating venous and nonvenous malformations was 100% (6/6), with a specificity of 24-33% (5/21 for dilated venous spaces and 7/21 for flow voids) (Table 4). For the combination of conventional and dynamic contrast-enhanced MR imaging, sensitivity was 83% (5/6) and specificity, 95% (20/21).



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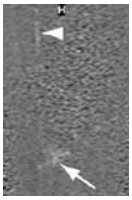

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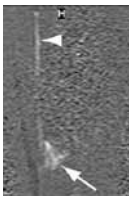

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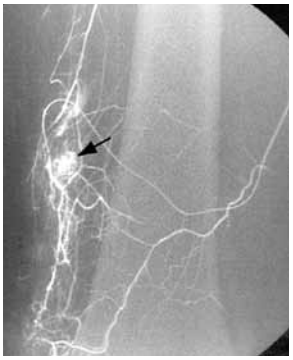

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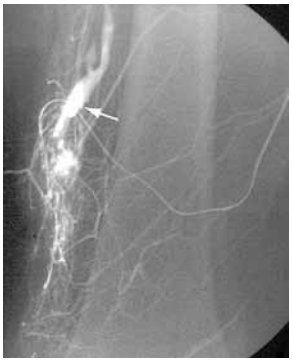

E

Fig. 1. 18-year-old man with peripheral vascular malformation in vastus intermedius muscle of upper leg. Diagnostic angiography confirmed MR categorization of capillary-venous malformation.

A. Transverse T2-weighted fat-saturated fast spin-echo MR image (TR/TE, 2956/80) exhibits mass consisting of multiple high-signalintensity dilated venous spaces.

B. Sagittal dynamic contrast-enhanced subtraction MR image shows start of arterial enhancement (*arrowhead*) with immediate lesion enhancement (*arrow*).

C. Sagittal dynamic contrast-enhanced subtraction MR image, obtained at same level as B but 6 sec later, shows arterial enhancement (*arrowhead*) and more intense lesion enhancement (*arrow*). On basis of MR criteria of early lesion enhancement (6 sec after arterial enhancement), presence of dilated venous spaces, and absence of flow voids, we categorized this lesion as capillary-venous malformation.

D. Arterial phase of superselective angiogram (not wedged) of small branch of superficial femoral artery shows dilated capillaries or small venules (*arrow*).

E. Venous phase of angiogram shows contrast pooling in dilated veins (*arrow*).

Discussion

The goal of imaging peripheral vascular malformations, besides defining the anatomic extent of the lesion, is to classify the malformations into the different categories – for example, arterial, capillary, venous, and lymphatic malformations and combinations of these. The identification of venous malformations is of clinical importance because currently direct percutaneous sclerosis is considered the treatment of choice for venous malformations[6,7,9,17-20]. Direct percutaneous puncture of the dilated stagnant venous spaces is usually performed using sonographic guidance. Hence, correct diagnosis of venous malformations with MR imaging would obviate excluding arterial components on angiography. Although the combined venous (capillary-venous) malformations may also be treated by direct percutaneous sclerosis, additional diagnostic arterial angiography is necessary before treatment to visualize the extent of the capillary component. In all other categories of peripheral vascular malformations, diagnostic arterial angiography is necessary to determine the arterial contribution and, especially, to rule out arterio-venous shunting defects.

Conventional MR imaging is reported to be successful in categorizing vascular malformations and in defining the anatomic extent of vascular malformations[21-23]. These reports have focused on using the presence or absence of flow voids in characterizing these malformations. Rak et al.[22] described the presence of flow voids in all untreated arterial and arteriovenous malformations. This finding is partly supported by our results. In our population, all arterial malformations exhibited flow voids; however, only two of four arteriovenous malformations showed flow voids. The absence of flow voids and the presence of dilated venous spaces was shown in all venous and capillary-venous malformations (Table 3). Hence, these two conventional MR features can be used to identify arterial malformations and some of the arteriovenous malformations, but these features cannot be used to differentiate venous and capillary-venous malformations (both low-flow malformations).

By combining dynamic contrast-enhanced MR characteristics with morphologic findings, we could differentiate, to some extent, the various peripheral vascular malformations (Table 3): late enhancement, absence of flow voids, and the presence of dilated venous spaces are indicative of venous malformations; early enhancement, the absence of flow voids, and the presence of dilated venous spaces are indicative of capillary-venous malformations; early enhancement and the presence of flow voids are indicative of arterial or arteriovenous malformations.

Discordance between MR and angiographic findings occurred in two of four arteriovenous malformations. Both observers misclassified these two arteriovenous malformations as capillary-venous malformations because of the absence of flow voids. A second type of discordance occurred in one patient with a capillary-venous malformation that was misclassified as a venous malformation by both observers. We did not appreciate early enhancement because the small capillary component was outside the dynamic scan volume (Table 4). The third type of discordance occurred in a capillary-venous malformation and can be explained by the presence of calcifications seen on radiographs that were not made available at the time of MR interpretation. Both observers thought these small signal voids represented rapid flow in micro- or macrofistulas of a high-flow arterial or arteriovenous malformation rather than calcifications. The least experienced observer misdiagnosed another two capillary-venous malformations as arterial or arterio-venous malformations. We believe that the level of experience can explain these two mistakes. Finally, one venous malformation showing early enhancement was misclassified as a capillary-venous malformation by both observers.

We performed dynamic contrast-enhanced MR imaging in an attempt to better differentiate the various

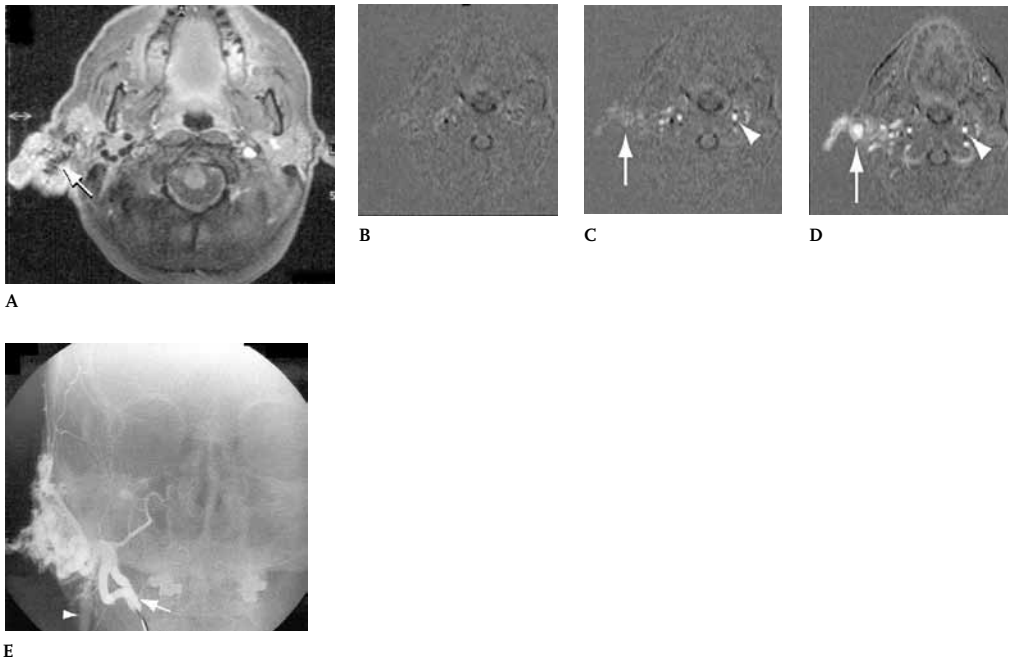

Fig. 2. 50-year-old woman with peripheral vascular malformation of right ear.

A. Enhanced transverse T1-weighted MR image shows enhancement of vascular malformation with serpiginous signal voids (arrow). A = anteriroir, L = left.

B. Dynamic contrast-enhanced subtraction MR image was obtained before arrival of IV bolus of gadopentetate dimeglumine.

C. Dynamic contrast-enhanced subtraction MR image, obtained at same level as B but 3 sec later, shows start of arterial enhancement (arrowhead) with immediate lesion enhancement (arrow).

D. Dynamic contrast-enhanced subtraction MR image, obtained at same level as A and B 3 sec later than C, shows arterial enhancement (arrowhead) and more intense lesion enhancement (arrow). This lesion was categorized on MR imaging as arterial or arteriovenous malformation on basis of early lesion enhancement and presence of flow voids.

E. Selective angiogram of right external carotid artery shows characteristics of arterial malformation. Note dilatation and lengthening of afferent arteries (*arrow*) followed by early enhancement of enlarged efferent veins (*arrowhead*) by macrofistulas.

categories and, especially, to try to identify the purely venous malformations. Using conventional MR imaging, we could differentiate venous and nonvenous malformations with high sensitivity (100%) but with low specificity (24-33%). By adding dynamic contrast-enhanced MR imaging, specificity increased to 95%, with acceptable sensitivity remaining at 83%. Hence, the absence of early enhancement can be used to identify pure venous malformations. However, dynamic enhancement cannot be used as a feature to differentiate high- and low-flow malformations because all arterial and arteriovenous (high-flow) malformations, as well as all except one capillary-venous (low-flow) malformation, displayed early enhancement.

A disadvantage of our study was the inclusion of only clinically suspected high-flow malformations. We did not have capillary malformations (port-wine stains) and lymphatic malformations in our study group, and subsequently, the number of patients with venous vascular malformations was relatively small. Although port-wine stains can be easily diagnosed because of the typical skin discoloration[5], they can be the clinically visible portion of a combined low-flow vascular malformation. Most lymphatic malformations

present early in childhood and are typically located in the neck and axilla[24,25]. The cystic nature, with high signal intensity on T2-weighted images and rim enhancement on contrast-enhanced MR images, is displayed on MR images[26]. Another disadvantage of our study is the limitation of dynamic scan volume and the lack of correlation with findings on color Doppler sonography, which is, especially in children with vascular anomalies, a frequently used, widely available, noninvasive imaging modality. However, MR imaging is superior to color Doppler sonography in exhibiting the anatomic extent of the vascular lesion and allows a more exact diagnosis of low-flow malformations when the sonographic findings are nonspecific[27-29].

In conclusion, the combination of conventional and dynamic contrast-enhanced MR features can be used to categorize vascular malformations. Late enhancement (>6 sec after arterial enhancement) is indicative of the presence of pure venous malformations. Therefore, the additional value of dynamic contrast-enhanced MR imaging is to allow a more specific diagnosis of venous malformations relative to capillary-venous malformations and high-flow vascular malformations. In our opinion, all venous vascular malformations diagnosed with these MR criteria can be treated by direct percutaneous embolization without diagnostic arterial angiography.

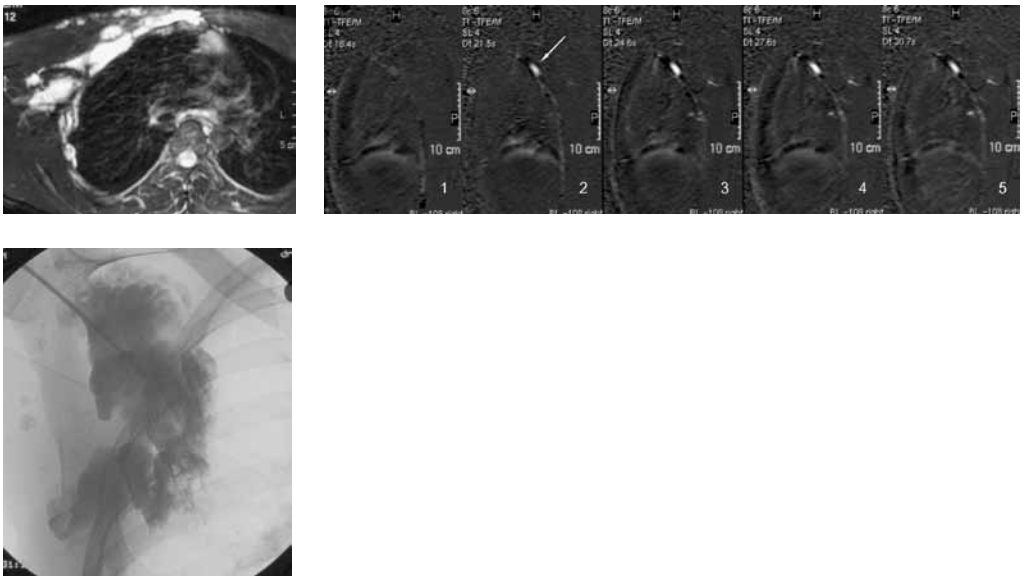

Fig. 3. 20-year-old man with peripheral vascular malformation of chest wall.

A. Transverse T2-weighted fat-saturated MR image (TR/TE, 2947/80) shows lesion consisting of multiple dilated venous spaces. L = left.

B. Sagittal oblique dynamic contrast-enhanced subtraction MR image, obtained 9 sec after start of arterial enhancement (5), contains largest part of vascular malformation. No abnormal early lesion enhancement (within 6 sec after arterial enhancement) is exhibited. On basis of MR criteria of late enhancement, presence of dilated venous spaces, and absence of flow voids, we categorized this lesion as venous malformation.

C. Venogram shows percutaneously placed needle and filling of abnormal venous spaces. Superselective angiography showed normal afferent arteries and normal capillary bed (not shown).

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Chapter 3

Long-term Patient Satisfaction after Percutaneous Treatment of Peripheral Vascular Malformations

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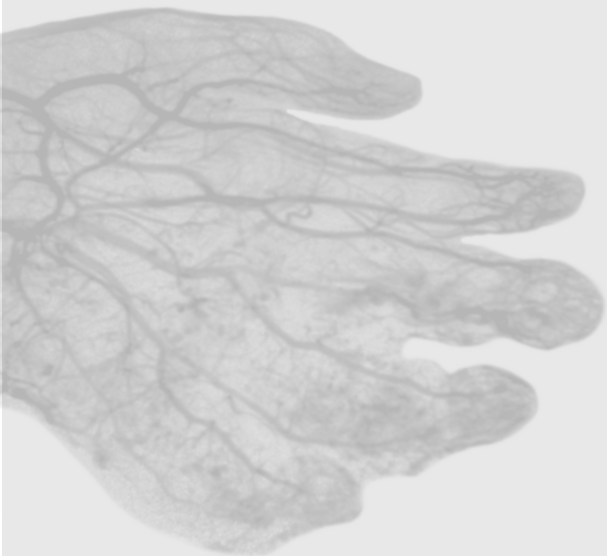

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Abstract

Purpose: To determine long-term patient satisfaction for percutaneous treatment by using sclerosing agents (sclerotherapy) and/or arterial embolization for peripherally located vascular malformations (VMs). This treatment has been described as successful; however, there is a relative paucity of published long-term results.

Materials and Methods: This retrospective study was institutional review board approved; 107 patients treated for symptomatic VM were evaluated. After informed consent was obtained, 66 patients were sent a questionnaire regarding treatment effectiveness and patient satisfaction. Patient files and imaging data were retrieved to obtain information regarding the VMs and VM treatment. Kaplan-Meier survival curves were constructed to analyze clinical success rates over time.

Results: The most frequent reasons for patients to seek treatment were pain (89%, $n = 59$) and swelling (91%, $n = 60$). The majority of VMs were the low-flow venous type (83%, $n = 55$). Three months after treatment, clinical success was reported for 58% ($n = 38$) of patients and clinical failure was reported for 42% ($n = 28$). At 1-, 2-, 3-, 4-, and 5-year follow-up, clinical success was 49%, 49%, 42%, 42%, and 42%, respectively. Twenty-seven (40%) patients experienced complications, 12 of which required additional treatment. In all, 35 (53%) patients reported being satisfied with their treatment. Patient satisfaction was closely correlated with clinically successful long-term outcome of treatment.

Conclusion: Initial partial or complete relief of VM complaints after percutaneous treatment is expected in 58% of patients, irrespective of VM size or classification. These results were durable over a 5-year follow-up period.

Introduction

Peripheral vascular malformations (VMs) are structural vascular abnormalities that can be divided into various categories, depending on their morphologic or hemodynamic characteristics[1–4]. Symptoms may vary and include cosmetic complaints, tissue ulceration, pain, swelling, and functional limitations. In some patients, symptoms are mild, in which case conservative measures may be sufficient. Patients with severe symptoms may require more invasive treatment.

Percutaneous treatment by using transarterial embolization is generally considered as the first line of treatment for high-flow arterial VMs[5–7] . For low-flow venous lesions, direct percutaneous puncture with injection of sclerosing agents (sclerotherapy) has been described as a successful therapy[6,8,9]. Both treatments target the central nidus to alleviate the symptoms of the malformation.

Researchers in most studies have focused on the technical and short-term results of treatment, which have generally indicated that VMs are difficult to treat and that most patients require multiple therapeutic sessions before clinical effect is reached[8,10,11]. However, there is a lack of articles documenting the mid- and long-term clinical outcome of percutaneous treatment of VMs. Only a few long-term clinical results after percutaneous treatment of high-flow malformations in the pelvis and extremities have been described[6,12].

Information regarding mid- and long-term results after percutaneous treatment of peripheral low-flow VMs and high-flow arterial VMs is desirable to counsel patients about realistic expectations regarding the outcome of therapy. To provide such data, it is of interest to include information regarding patient satisfaction as a major outcome parameter as an indicator of patient experience of treatment results. Accordingly, the purpose of this study was to assess the mid- and long-term effects after percutaneous treatment of low-flow VMs and high-flow arterial VMs, taking into account patient satisfaction regarding VM treatment in relation to VM characteristics.

Materials and methods

Patients

The analysis in this study was performed on the treatment of 66 patients. Patients gave written informed consent for treatment and study inclusion, and institutional review board approval was obtained. Medical files for 107 consecutive patients who had undergone percutaneous treatment for peripheral VMs between September 1995 and July 2006 were retrieved. This study was undertaken in 2007; the July 2006 deadline was chosen to ensure adequate follow-up in all patients. Exclusion criteria were patients under 18 years of age and patients who had died. Potential study candidates were contacted by telephone and sent a questionnaire if they agreed to participate. Key questions included whether the treatment had been effective in relieving the signs and symptoms of the VM, and whether the patient was satisfied with the treatment. A sample question was as follows: "With hindsight, would you have taken this treatment again?"

Patient Files and Imaging Studies

Data were retrieved from the clinical patient records regarding the presenting signs, symptoms, and complaints that had prompted the patient to seek medical treatment. The pretreatment imaging studies were retrieved from the radiologic archives.

VM location and size were determined at pretreatment T2-weighted fast spin-echo magnetic resonance (MR) imaging (repetition time msec/echo time msec, 2209–5492/60–150; echo train length, 5-12; and section thickness, 6–12 mm) that were obtained with frequency-selective fat saturation and contrast material–enhanced T1-weighted fast spin-echo sequences (530–600/12–25; echo train length, three; and section thickness, 6–12 mm) by using a 1.5-T MR imaging system (NT 15 Gyroscan; Philips Medical Systems, Best, the Netherlands), all of which are part of our standard diagnostic VM work-up. We calculated the volume of the VM, assuming the lesion to be an ellipsoid with a specific length, width, and height. The lesion volume was therefore estimated by using the following formula: $(4/3\pi) \times \text{radius } 1 \times \text{radius } 2 \times \text{radius } 3$, or $0.7 \times \text{height} \times \text{length} \times \text{width}$ (all measurements were obtained in milliliters).

VM extension was defined by examining muscle infiltration, bone involvement, and location in subcutaneous tissue. We used a combination of imaging techniques (MR imaging, dynamic MR imaging, and angiography or phlebography) to classify VMs (according to the classification of Mulliken and Glowacki[2]) in high-flow arterial VMs or low-flow venous or venous-capillary VMs[1,2,4,13]. VMs with arterial components are considered as high-flow lesions (arterial malformations containing macrofistulas and arteriovenous malformations containing microfistulas through a vascular nidus), and those without arterial components are considered as low-flow lesions (venous, capillary, and lymphatic malformations).

Treatment Protocol

For the purpose of this analysis, treatment refers to the total number of therapy sessions per patient. Treatment for peripheral VMs is typically tailored to each lesion and to each patient; therefore, it is not possible to cite a standard treatment protocol.

The general approach to treatment of high-flow arterial VMs was the use of arterial embolization with enbulcrilate (Histoacryl; Braun Aesculap, Tuttlingen, Germany) and iodized poppy-seed oil (Lipiodol; Guerbet, Roissy, France), typically in a 1:2 ratio, where the nidus of the lesion was superselectively catheterized by using a coaxial catheter system (Turbo Tracker 18 Microcatheter; Boston Scientific, Natick, Mass). In selected cases in which the nidus could not be completely embolized transarterially, the procedure was combined with direct percutaneous injection of the venous outflow to embolize the nidus retrograde. Treatment of low-flow VMs was generally performed by using direct percutaneous injection of either the sclerosing agent ethanol (96% solution), or 10 mg/mL polidocanol (Aethoxysklerol 1%; Kreussler, Wiesbaden, Germany), often by using ultrasonographic guidance for needle placement. In all patients, the injected volume of sclerosant was calculated by using a test injection of contrast material under fluoroscopy prior to treatment. Polidocanol was typically mixed with absorbable gelatin compressed sponge (Gelfoam; Pfizer, Puurs, Belgium) to create a foam that would reduce washout and increase contact time with the VM endothelium. Whenever the test injection of contrast material showed direct or fast filling of the deep (normal) draining veins, adjunct measures to reduce the blood flow through the VM during treatment were taken liberally by using pressure tourniquets, venous compression bands, or venous embolization coils to occlude the draining veins. Tourniquets proximal to the VM were sometimes applied at a pressure of 300 mm Hg to control arterial inflow[10,14,15]. A limited number of patients with low-flow VMs were treated with radiofrequency ablation after unsuccessful initial attempts with direct percutaneous puncture[16].

Procedures were generally performed on patients given a general anesthetic followed by an overnight stay, with the exception of direct punctures of low-flow VMs with polidocanol, which were performed in our hospitals as outpatient procedures either with or without local anesthetic.

Questionnaire

A single questionnaire was sent to the patients in 2007. In the questionnaire, we asked about specific symptoms before and after treatment and about the occurrence of any complications (Appendix E1). Patients were asked for specific symptoms (pain, swelling, and functional and cosmetic complaints). It was also possible to fill in additional symptoms. The clinical effect of treatment for the different symptoms was assigned a grade on a four-point scale: score 1, worsening of symptoms; score 2, no change in symptoms; score 3, partial improvement of symptoms; and score 4, complete relief of symptoms. It was asked whether there was any initial clinical success after treatment, whether symptoms had recurred, and if so, for how long after treatment. It was also asked whether patients had sought additional treatment in another hospital. Finally, it was asked whether patients were satisfied with their treatment. All unclear responses were resolved by using additional telephone interviews. The questionnaires were evaluated for all patients together, and separately for low-flow VMs and high-flow arterial VMs. Complete clinical success was defined as disappearance of all complaints. Partial clinical success was defined as partial improvement of the complaints. Clinical failure was defined as no change in symptoms or worsening of symptoms after treatment.

Statistical Analysis

Comparison of rates of patient satisfaction and initial clinical outcome between groups was performed by using the χ^2 test. The clinical success rates of treatment over time were evaluated by using the Kaplan-Meier analysis. Multivariable analysis of various factors regarding initial clinical outcome after treatment and patient satisfaction rate was performed by using logistic regression. A two-sided p value of 0.05 was considered significant for all analyses. Data were analyzed by using software (SPSS, version 11.0; SPSS, Chicago, Ill).

Results

From September 1995 until July 2006, we treated 107 consecutive patients with peripheral VM. Of these 107 patients, 41 were excluded, leaving 66 for analysis.

We excluded from analysis 13 patients who were less than 18 years old, 14 who could not be traced, two who had died, and 12 who were unwilling to participate. After informed consent was obtained, a questionnaire was sent out to the remaining 66 patients (28 men, 38 women; median age, 32 years; range, 18–66 years). All questionnaires were returned and used for analysis. Mean follow-up time was 39 months (median, 30 months; range, 6–147 months).

Table 1

Peripheral VM location and size

Location	No. of VMs	Mean size (mL)*	No. of high-flow arterial VMs
Face	1	41 (1)	0
Scalp	2	113 (2)	2
Cheek	5	53 (5)	1
Nose	1	1 (1)	1
Ear	1	143 (1)	1
Lip	1	4 (1)	0
Yaw	1	8 (1)	0
Neck	3	464 (3)	0
Chest wall	1	191 (1)	0
Arm	8	792 (4)	2
Hand	8	10 (8)	0
Buttock / Pelvis	3	420 (3)	1
Labia	2	30 (2)	1
Penis	1	17 (1)	0
Leg	21	81 (18)	1
Feet	7	32 (7)	1
Total	66	145 (59)	11

* Number of patients from which mean size was calculated is in parentheses.

Lesion Characteristics

A description of VM location, size, and lesion type for evaluated patients is provided in Table 1. The majority of VMs (44 of 66) were located in the extremities. MR imaging helped define the extension of the VMs in 65 patients. Infiltration of a single muscle was present in 23 patients; infiltration of multiple muscles, in 25. Bone involvement was present in 11 patients. Seventeen patients had no muscle infiltration or bone involvement. VMs were located in the subcutaneous tissue in 48 patients. The size of the VMs was measured in 59 patients. The mean volume was 145 mL (median, 21.7 mL; range, 1–3000 mL). In seven patients, the lesion size could not be measured; the VM showed diffuse extension throughout an extremity, which precluded measuring VM volume in six patients, and pretreatment MR imaging could not be traced in one patient. The majority of VMs (83% [55 of 66]) were of the low-flow type; 48 were venous VMs and seven were venous-capillary VMs. Eleven (17%) lesions were high-flow arterial VMs.

Table 2

Mean number of therapy sessions performed with the percutaneous treatment options

Embolization material	No. of patients	Mean no. of therapy sessions*
Ethanol	34	1.2 (1, 1-5)
Ethanol in combination with enbulcrilate	5	1.4 (1,5, 1-2)
Ethanol in combination with polidocanol	2	2.0 (2, 2)
Enbulcrilate	6	1.7 (1, 1-3)
Polidocanol	12	3.1 (3, 1-8)
Radiofrequency ablation	7	1.0 (1, 1)

* Numbers in parentheses are the median, followed by the range.

The number of therapy sessions and the materials used for treatment are listed in Table 2. The number of therapy sessions ranged from one to eight (mean, 1.6) for all 66 patients treated. The median number of sessions needed for 59 patients who received endovascular treatment was one, (mean, 1.9). Ethanol was used as therapeutic agent in a majority (41 of 66) of patients, which is partially a result of the fact that polidocanol has been introduced as a sclerosant only in recent years. These results demonstrate the extreme heterogeneity of the study population.

Clinical Success

Complete or partial clinical improvement at 3 months after treatment was reported by eight (12%) and 30 (45%) of 66 patients, respectively; clinical failure within 3 months after treatment was reported by 28 (42%). Table 3 shows clinical results of treatment according to type of VM (high vs low flow). Complete or partial 3-month clinical success was reported in seven (64%) of 11 high-flow VMs and 31 (56%) of 55 low-flow VMs treated ($p = 0.98$). Complete clinical success was reported in two (18%) of 11 high-flow arterial VMs and six (11%) of 55 low-flow VMs ($p = 0.87$).

Kaplan-Meier analysis showed that clinical success remained relatively stable over time (Figure). At 1, 2, 3, 4, and 5 years after treatment, the clinical success rates (partial and complete) of all 66 patients were reported to be 49%, 49%, 42%, 42%, and 42%, respectively. There was no significant difference ($p = 0.43$) between sustained clinical success at 5 years after treatment between high-flow arterial VMs (55%) and low-flow VMs (39%). All recurrences of complaints after initial success were reported in the patient group with initial partial clinical success; no recurrences were seen in the patients with initial complete clinical success. Thus, the majority of patients (58% [38 of 66]) experienced initial (3-month) clinical improvement. However, long-term (5-year) complete relief of symptoms was only reported in eight (12%) of 66 patients. One patient reported being treated in another hospital for a small low-flow VM in the leg with a resection.

Table 3

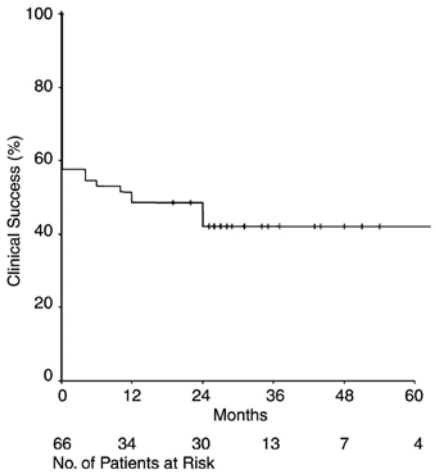
Clinical results

Outcome	High-flow VMs (%)	Low-flow VMs (%)	Total VMs (%)
Clinical failure within 3 months after treatment	36 (4/11)	44 (24/55)	42 (28/66)
Complete clinical success 3 months after treatment	18 (2/11)	11 (6/55)	12 (8/66)
Partial clinical success 3 months after treatment	46 (5/11)	45 (25/55)	46 (30/66)
Clinical success 5 years after treatment*	55	39	42
Satisfied with treatment	64 (7/11)	51 (28/55)	53 (35/66)

Note.–Data in parentheses are raw numbers used to calculate percentages.

* Kaplan-Meier estimate ($p = 0.53$ for high-flow versus low-flow VMs).

Figure 1.



Kaplan-Meier graph shows clinical success after treatment. Marks on line represent durations of follow-up of patients who had no relapse of symptoms. Initial lowering of curve represents 28 (42%) patients in whom treatment was not successful.

Complications

Complications of treatment were classified according to the Society of Interventional Radiology reporting standards (17) and listed in Table 4. Twenty-seven (40%) of 66 patients reported complications after treatment. Three patients reported two complications each. In 12 (18%) patients, complications were listed as major because they needed additional treatment for these complications, or disturbances were permanent. Three patients required surgery for postinterventional tissue necrosis; in one patient, this manifested as local baldness on the head. Two patients had neurologic disturbances (type E) and one had a deep wound infection (type D), all of which resulted from radiofrequency ablation treatment. The other complications ($n = 23$) resulted from the use of ethanol as the sclerosant (three patients were treated with ethanol and enbulcrilate). None of the complications resulted from the use of polidocanol as sclerosant. No mortality (F-type complication) resulted from to the procedure.

Table 4

Complications from embolization

Outcome	Type of complication						Embolization*			
	A	B	C	D	E	F	Ethanol	Polidocanol	Enbulcrilate	Rf ablation
Impaired and/or delayed wound healing (n = 11)	-	5	-	1	2	-	10	-	3	1
Limitations in motion (n = 4)	-	2	-	1	1	-	3	-	-	1
Pain (persisting) (n = 3)	1	2	-	-	-	-	2	1	-	-
Inflammation and/or infection (n = 4)	1	2	-	1	-	-	3	-	-	1
Sensibility disturbances (n = 3)	-	-	-	-	3	-	1	-	-	2
Swelling (n = 3)	3	-	-	-	-	-	3	-	-	-
Hematoma (n = 1)	1	-	-	-	-	-	-	1	-	-
Pulmonary edema (requiring hospitalization) (n = 1)	-	-	-	1	-	-	1	-	-	-

Note. Complications were defined by using the Society of Interventional Radiology guidelines: Type A are minor, require no therapy, and have no consequence; type B are minor, require nominal therapy (including overnight admission for observation only), and have no consequence; type C are major and require therapy that includes minor hospitalization (<48 h); type D are major and require major therapy (causing an unplanned increase in level of care) and include prolonged hospitalization (>48 h); type E are major and result in permanent adverse sequelae; and type F result in death of patient.

* Three patients had complications after using ethanol in combination with histoacryl.

Patient Satisfaction and Subgroup Analysis

Thirty-five (53%) of 66 patients reported being satisfied with the treatment and would opt to undergo treatment again if faced with the choice. Good clinical success and patient satisfaction were closely related: Three (11%) of 28 patients without clinical success and 32 (84%) of 38 patients with clinical success reported being satisfied with their treatment ($p < 0.001$). Fifty-four patients received general anesthetic for treatment and 12 patients received local anesthetic for treatment. There was no significant difference in outcome between these groups. No significant difference regarding patient satisfaction was found between the groups with partial and complete clinical success ($p = 0.309$). Univariate and multivariate analysis (logistic regression) of volume, type of VM, and treatment protocol did not show a significant difference for the percentage of patients who reported being satisfied with the treatment. The same applied to the success rate. Analysis by using location was not feasible given the small numbers. We did not find significant differences among the treatment methods (ethanol, polidocanol, etc) with regard to patient satisfaction.

Signs and symptoms before and after percutaneous VM treatment are listed in Table 5. Before VM treatment, the majority of patients complained of pain (89% [59 of 66]) and swelling of the lesion (91% [60 of 66]). Patients reported complete or partial pain relief (59% [35 of 59]) and decrease of swelling (57% [34 of 60]). An increase of complaints also occurred. There was an increase in pain in eight (14%) of 59 patients, swelling in six (10%) of 66 patients, functional complaints in 10 (23%) of 44 patients, and cosmetic complaints in five (17%) of 29 patients. Thus, pain and swelling are the symptoms that were best controlled with percutaneous therapy. By contrast, functional and cosmetic complaints were less well controlled with percutaneous treatment.

Table 5

Symptoms before and after percutaneous VM treatment

Symptom	Before treatment (%)	After treatment (%)			
		Complete relief	Partial relief	No relief	Worsening
Pain	89 (59/66)	25 (15/59)	34 (20/59)	27 (16/59)	14 (8/59)
Swelling	91 (60/66)	20 (12/60)	38 (23/60)	32 (19/60)	10 (6/60)
Functional impairment	67 (44/66)	23 (10/44)	18 (8/44)	36 (16/44)	23 (10/44)
Cosmetic complaint	44 (29/66)	4 (1/29)	31 (9/29)	48 (14/29)	17 (5/29)

Note. Numbers in parentheses are raw data used to calculate percentages.

Discussion

In this study, we evaluated the results after percutaneous treatment of low-flow VMs and high-flow arterial VMs, with special interest in patient experience regarding clinical effect and overall patient satisfaction with the therapy. Major findings were that clinical success, measured by partial or complete relief of symptoms, was reported by 38 (58%) of 66 patients with durable long-term results in most patients, and that clinical success, as reported by the patient, was strongly related to patient satisfaction. A rather large group of 28 (42%) patients had no clinical success 3 months after treatment. VM size, classification, or percutaneous treatment method chosen had no effect on clinical success.

Our clinical results are consistent with earlier reports regarding follow-up clinical results after percutaneous treatment on studies that included 4–87 patients[10-12,18-20]. The more current and larger of these studies also illustrate the large heterogeneity in presentation of these lesions[11,19,20]. Clinical improvement was reported as 68%–100%, with a mean follow-up of 17–84 months[10-12,18-21]. Our study differs from earlier studies because it focused on whether the patient was satisfied with treatment. We think that patient satisfaction is the most relevant outcome for this benign disorder, especially when considering the frequent complications of treatment, which often involve multiple treatment sessions.

It has been well recognized that VMs are difficult to treat. Our study results agree with results of two studies that showed improvement in 64% and 78% of patients after treatment for high-flow arterial VMs[14,18]. In our series, we did not find a difference in recurrence rate between low-flow VMs and high-flow arterial VMs. Yet, high-flow arterial VMs have been reported to have high recurrence rates, particularly in the extremities, when the lesions are extensive and involve multiple-limb arteries[6]. A tentative explanation for the relatively low recurrence rate in our series is that all high-flow lesions involved only single arteries.

In our study, as in previous patient series, we encountered a high complication rate, attesting to the fact that the decision to offer treatment in these patients should not be taken lightly. Our complication rate was 40% (27 of 66) but complications were fortunately minor for the majority of patients with spontaneous cure. Twelve (18%) patients needed additional treatment for major complications, which is consistent with earlier reports [9,11,19,21]. Major complications, such as tissue necrosis, have been reported in 10%–30% of patients and have been related to the VM site, the tissue type being embolized, the material used for embolization, and experience with the procedure[5]. All major complications (13 complications in 12 patients) in our study resulted from the use of ethanol as the sclerosant (n = 10) or radiofrequency

ablation (n = 3). Radiofrequency ablation was performed when other percutaneous treatment options failed. The introduction of newer sclerosant materials, such as polidocanol, seems to reduce major complication rates. Overall, substantial clinical failures experienced by 28 (42%) of 66 patients and resulted in worsening of any symptoms in 29 (15%) of 192.

This study had limitations. The study regarded an inventory of patient satisfaction as a study outcome. No clinical physical parameters, such as change in VM volume, were used to determine the treatment effect. Patient satisfaction experience may differ from the actual clinical physical outcome after treatment.

Because of the difficulty in managing VMs; the large interindividual variation in size, shape, and type; and the variation in percutaneous treatment options, it is difficult to inform patients about the realistic expectations for percutaneous treatment of their VMs. Given our results, we are now able to inform patients that: Initial partial or complete relief of VM complaints after percutaneous treatment is expected in 58% (38 of 66) of patients, irrespective of VM size or classification. There is a considerable chance of complications occurring during treatment in 40% (27 of 66) of patients, most of which are mild and temporary, whereas major complications occurred in 18% (12 of 66) of patients. In our experience, the major complications were associated with ethanol or radiofrequency ablation. Radiofrequency ablation was used in highly selective cases after technically unsuccessful initial therapy. In cases with therapy failure, patients may experience worsening of symptoms.

Advances in knowledge

Percutaneous treatment of vascular malformation improves clinical symptoms in 58% of patients after 3 months and the results are durable at long-term 5-year follow-up in 42%.

Fifty-three percent of patients were satisfied with the treatment after long-term 5-year follow-up.

Implication for patient care

The study results may be used to provide VM patients with realistic expectations regarding percutaneous vascular malformation treatment.

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Appendix E1

Questionnaire

I participated in this research and answered the questions below. Yes / No

1. Where is the vascular malformation located in your body?

_____

2. Did you have one or more of the following symptoms before treatment?

Complaints before the treatment	No	Yes
Pain	❑	❑
Swelling	❑	❑
Function restriction (move, bend, etc)	❑	❑
Cosmetic complaints	❑	❑
Other complaints where you had charge of:		
1	❑	❑
2	❑	❑
3	❑	❑

3. If your answer for one or more symptoms was "yes," what happened with this symptom after treatment?

Complaints after the treatment	Complete relief	Partial improvement	No change
Pain	❑	❑	❑
Swelling	❑	❑	❑
Function restriction (move, bend, etc)	❑	❑	❑
Cosmetic complaints	❑	❑	❑
Other complaints where you had charge of			
1	❑	❑	❑
2	❑	❑	❑
3	❑	❑	❑

4. If relapse occurred, indicate how long after treatment the symptoms returned?

_____ months

5. Were you generally satisfied with the effects of the treatment? Yes / No

Explanation (if needed):

_____

6. Were you treated in another hospital for the same symptoms after treatment in our institution? Yes / No

If yes, how many treatments?

_____

7. Have side effects and/or complications occurred after treatment? Yes / No

If yes, indicate complication and whether you underwent treatment for this complication.

Chapter 4

Percutaneous Treatment of Peripheral Vascular Malformations in Children: Long Term Clinical Outcome

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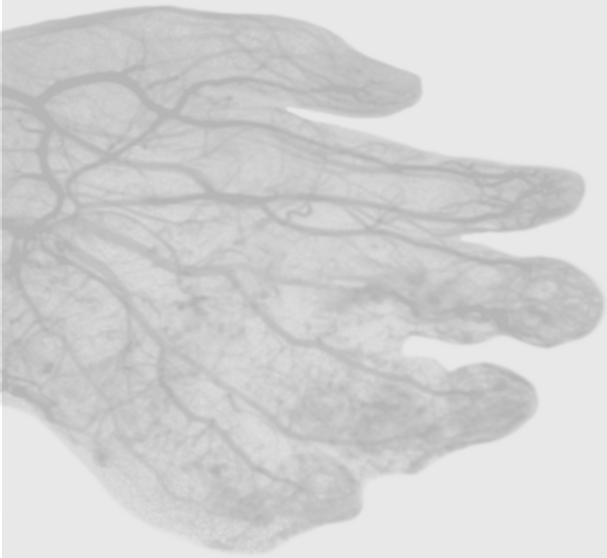
Addendum: manuscript is submitted on behalf of the Working Group Vascular malformations Rotterdam (WEVAR); Prof.dr A.P. Oranje, G. Madern, P.de Laat and Prof. P.T.M. Patynamma



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Abstract

Purpose: This study was designed to assess the rate of complications and clinical failure at 3 and 12 months after percutaneous treatment of vascular malformations in children. Furthermore, we describe patient satisfaction of treatment results during up to 5 years of follow-up.
Materials and methods: In a retrospective cohort study, we evaluated 26 patients younger than aged 19 years who were treated for symptomatic vascular malformations. Data on treatment outcomes and patient satisfactions were obtained with a precoded structured questionnaire. Patient files and imaging data were retrieved to obtain information regarding the vascular malformations and treatment. Clinical success was defined as disappearance or as partial improvement of the complaints. Patient satisfaction was declared whenever patients answered in the questionnaire that they were satisfied with the treatment results.
Results: Of 26 eligible patients, we included 23 (88%). The mean follow-up was 36 (range 15-127) months. Posttreatment, 87% (20/23, 95% confidance interval (CI) (66-97%) of patients reported clinical success at 3 months. At 1, 2, 3, 4 and 5 years of follow-up this percentage was 74%, 59%, 59%, 59% and 59%, respectively. Eleven (48%, 95% CI 27-69%) patients had experienced complications and 22% (95% CI 7-44%) major complications, of which 5 had required additional treatment. In all, 83% (19/23) of the patients reported to be satisfied with the treatment.
Conclusion: Percutaneous treatment of vascular malformations improved clinical symptoms in 87% of the patients at 3 months and were sustainable for half of all patients during a 5-years follow-up period. However, major complications were seen in 22%.

Introduction

Peripheral vascular malformations are structural vascular abnormalities that can be divided into various categories, depending on the morphology or on the basis of hemodynamic characteristics[1-4]. Symptoms may vary and include cosmetic complaints, tissue ulceration, pain, swelling and functional limitations. Symptoms are often mild, in which case conservative measures may be sufficient.

Children with severe symptoms may require more invasive treatment. Symptomatic low–flow venous malformations (VMs) are the most common vascular malformation in infants. Approximately 50% appear in childhood or adulthood[5]. For low-flow VMs, direct percutaneous puncture with injection of sclerosing agents (sclerotherapy) has been described as a successful therapy in children[6]. Percutaneous treatment by transarterial embolization is generally considered the first-line treatment for high-flow arterial venous malformations (AVMs)[7-9]. Both treatments are designed to treating the central nidus to cure the symptoms of the malformation.

Most studies have focused on the technical and short-term results of treatment, which generally indicate that vascular malformations are difficult to treat and that most patients require multiple therapeutic sessions before clinical effect is reached[6,10-12].

In a previous analysis we found that percutaneous treatment of vascular malformations improved clinical symptoms in 58% of the adult patients after 3 months and that these results were durable at 5-year follow-up in 42%. After 5 years, 53% of patients were satisfied with the treatment[13].

In children, though, long-term clinical outcomes of vascular malformation treatment and patients' satisfaction are unknown. This information, however, is needed to counsel parents about realistic expectations regarding the outcome of therapy. Accordingly, the purpose of this study was to assess the mid- and long-term outcomes and complication rate after percutaneous treatment of low- and high-flow vascular malformations in children taking into account patient satisfaction regarding the treatment of vascular malformations in relation with the vascular malformation characteristics.

Material and Methodes

Patients

In this retrospective cohort study we included consecutive patients who were treated for peripheral vascular malformations at the Erasmus University Medical Center and who were younger than 19 years at time of percutaneous treatment between May 1996 and July 2008.

The analysis in this study was based on treatment in 26 consecutive patients. Medical files of all patients were retrieved. Patients were followed until March 2010.

Exclusion criteria were patients of 19 years or older at the first treatment. Potential study candidates were sent an information letter and if they agreed to participate, they were sent a questionnaire. If the patient was younger than aged 12 years at time of follow-up, the information letter was sent to the parents. This information letter was sent to the patients themselves who were older than 12 years. In case that the children were younger than 12 years, the questionnaire was filled in together with the parents. The precoded and structured questionnaire contained questions on whether the treatment had been effective in relieving the signs and symptoms of the vascular malformation and whether patients were satisfied with the treatment. Patients gave written, informed consent and the Institutional Review Boards of our hospital approved the study.

Patient files and imaging studies

Data were obtained from the clinical patient records regarding the presenting signs and symptoms that had prompted the patients to seek medical treatment. The pretreatment imaging studies were obtained from the radiological archives.

Location and size of the vascular malformations were determined on pretreatment T2-weighted and contrast enhanced T1-weighted MRI, which is part of our standard diagnostic workup of vascular malformations. Lesion volume (in mL) was estimated by using the formula: length (cm) × width (cm) × height (cm) × 0.7. Extension of vascular malformations was defined considering muscle infiltration, bone involvement and location in subcutaneous tissue. Vascular malformations were classified according to the classification of Mulliken and Glowacki by using a combination of MRI, dynamic MRI, and angiography or phlebography, as high-flow AVMs or low-flow VMs[1,2,4]. Malformations with arterial components are considered high-flow lesions (arterial malformations containing macrofistulas and arteriovenous malformations containing microfistulas through a vascular nidus), and those without arterial components are considered low-flow lesions (venous, venous capillary, and lymphatic malformations). Differentiation between high-flow and low-flow vascular malformations was either on digital subtraction angiography or dynamic contrast-enhanced MRI and by using criteria as previously described[1]

Treatment protocol

Treatment for peripheral vascular malformations is typically tailored to the specific lesion and specific patient characteristics and it is therefore not possible to cite a standard treatment protocol. For the purpose of this analysis, "treatment" refers to the total number of consecutive therapy sessions in a patient. The general approach to treat high-flow AVMs was by using arterial embolization with enbulcrilate (Histoacryl, Braun Aesculap AG & CO, Tuttlingen, Germany) and iodinated poppy-seed oil (Lipiodol, Guerbet, Roissy CdG Cedex, France) typically in a 1:2 mixture, whereby the nidus of the lesion was superselectively catheterised using a coaxial catheter system. Treatment of low-flow VMs was generally done by direct percutaneous injection of either the sclerosing agent ethanol 96%, or polidocanol (10, 30 mg/mL, Aethoxysklerol 1% or 3%, Kreussler & Co. Wiesbaden, Germany), often using ultrasound guidance for needle placement. Polidocanol was typically mixed with gel foam or air to create a foam to reduce washout and increase contact time with the VM endothelium. In selected cases, transarterial embolization was combined with direct percutaneous injection. Adjunct measures to reduce the blood flow through the VM during treatment were taken liberally, by using pressure tourniquets, venous compression bands or venous embolization coils to occlude draining veins. Pressure tourniquets proximal to the malformation tightened with a pressure of 300 mmHg were sometimes applied to control arterial inflow[11,14,15]. Procedures were generally performed under general anaesthesia followed by an overnight stay, with the exception of direct punctures of low-flow VMs with polidocanol of the older children, which in our hospitals were performed as outpatient treatment with or without local anesthesia. Treatment protocol did not change in the 12-year inclusion period.

Questionnaire

A single questionnaire (see Appendix 1) was sent to the patients in December 2009. Complete clinical success was defined as disappearance of all complaints, according to the patient and/or his parents. Partial clinical success was defined as partial improvement of the complaints, according to the patient and/or his parents. Clinical failure was defined as no change or worsening of one of the symptoms after

treatment, as assessed after treatment. Partial clinical failure was defined if not all symptoms relapsed after treatment.

Statistical analysis

Data were entered in Excel without patients name and analyzed using SPSS (version 17.0; SPSS Inc., Chicago, IL). Follow-up time was calculated as time from treatment completion to March 2010. Survival time was calculated from date of treatment completion to date of recurrence of symptoms. Survival curves were constructed using the Kaplan-Meier method. To assess differences at the 5% significance level, two-sided Fisher's exact test or Chi-square tests were used. Complications of treatment were classified according to the Society of Interventional Radiology (SIR) reporting standards[16].

Results

From May 1996 until July 2008, we treated 26 consecutive patients younger than aged 19 years with peripheral vascular malformations and patient files and imaging data were available for all 26 patients. Excluded were two patients who could not be traced, and one patient who was unwilling to participate. All remaining 23 (88%) patients returned the questionnaire. Median age at treatment was 15 years (range, 0-18), and seven were male. Only one patient was treated twice for the same location but was sent a questionnaire for only the last treatment. Median follow-up time was 25 (range, 15-127) months. Treatment course for each patient are summarized in Table 1.

Table 1

Treatment course in 26 patients with peripheral vascular malformations

Patient Sex Age	Type of vascular malformation	Location of vascular malformation	Prior treatments (> 1 years before final treatment)	Type treatments (session)	Type sclerosant	Volume of sclerotant (mL)	Time between sessions (Months)	Complications*	Ultimate response	Relapse of complaints (Months after treatment)
1/M/14	VM	Foot	D (2)	D (1)	Ethanol	5	-	None	CR	Partial relapse (9)
2/M/0	AVM	Elbow		A (1)	PVA	-	-	None	PR	
3/F/15	AVM	Buttock		A (1)	Ethanol	19	-	Necrosis, scar	PR	
4/F/17	VM	Foot		D (1)	Polidocanol	4	-	None	PR	Partial relapse (9)
5/F/10	VM	Face		D (1) D (2)	Polidocanol Polidocanol	10 4	- 4	Necrosis, pain, swelling	F	
6/F/12	VM	Foot		D (1) D (2)	Polidocanol Polidocanol	2 2	- 3	None	PR	
7/F/17	AVM	Labia		A/D (1) A/D (2)	Histoacryl/Ethanol Histoacryl/Ethanol	1.5/10 0.5/8	- 8	Necrosis	PR	
8/F/10	AVM	Face		A (1) R (2) R (3)	Histoacryl Ethanol Ethanol	3.5 25 25	- 3 2	Necrosis, scar, pain, swelling	PR	
9/F/17	VM	Calve		D (1) D (2) D (3) D (4)	Polidocanol Polidocanol Polidocanol Polidocanol	20 10 24 22	- 2 1 2	None	PR	
10/M/6	VM	Face		D (1)	Polidocanol	5	-	None	PR	
11/M/15	VM	Cheek		D (1) D (2)	Polidocanol Polidocanol	16 22	- 1	Pain, swelling	CR	
12/M/17	VM	Scrotal		D (1) D (2) D (3)	Polidocanol Polidocanol Polidocanol	6 15 20	- 2 3	Pain, swelling	PR	
13/M/17	VM	Cheek		D (1)	Polidocanol	15	-	None	PR	Partial relapse (18)
14/F/17	VM	Hand		D (1) D (2)	Polidocanol Polidocanol/Ethanol	15 4/0.5	- 3	None	F	
15/F/12	AVM	Lip		A/D (1)	Histoacryl/Ethanol	1/12	-	Necrosis, scar	PR	
16/F/15	VM	Foot		D (1) D (2)	Polidocanol Polidocanol	8 12	- 2	None	PR	Partial relapse (18)
17/F/15	VM	Elbow		D (1)	Polidocanol	6	-	None	PR	
18/F/17	VM	Hand		D (1)	Ethanol	6	-	Limitation in movement	F	
19/F/15	VM	Buttock		D (1) D (2) D (3)	Polidocanol Polidocanol Polidocanol	20 35 20	- 1 1	None	PR	

Table 1

Treatment course in 26 patients with peripheral vascular malformations

Patient Sex Age	Type of vascular malformation	Location of vascular malformation	Prior treatments (> 1 years before final treatment)	Type treatments (session)	Type sclerosant	Volume of sclerotant (mL)	Time between sessions (Months)	Complications*	Ultimate response	Relapse of complaints (Months after treatment)
20/F/13	VM	Cheek		D (1)	Ethanol	15	-	None	CR	
21/F/15	VM	Hand		D (1)	Polidocanol	16	-	Pain, swelling	PR	Complete relapse (24)
22/M/5	VM	Cheek		D (1) D (2)	Polidocanol Polidocanol	17 15	- 2	Pain, swelling	PR	Partial relapse (12)
23/F/7	VM	Labia		D (1)	Ethanol	30	-	Necrosis, scar	PR	
24/F/14	VM	Shoulder	D (2)	D (1)	Polidocanol	2	-	-	-	-
25/F/15	AVM	Eyelid		A (1)	PVA	-	-	-	-	-
26/F/18	VM	Cheek		D (1) D (2) D (3)	Polidocanol Polidocanol Polidocanol	2 4 3	- 2 2	-	-	-

The first 23 patients responded to the questionnaire.

M = Male, F = Female

VM = Venous Malformation, AVM = Arterio Venous Malformation.

D = Direct puncture, A = Arterial catheterization, R = Retrograde transvenous catheterization

CR= Complete Response, PR = Partial Response, F = Failure

* Complications mentioned in the questionnaire.

Table 2.

Location, size, lesion-type and extension in 26 young patients with peripheral vascular malformation

	n	Median (25-75p) size (ml)	Extension of the vascular malformations on MRI		
Location			**Subcutis**	**Muscle infiltration**	**Bone involvement**
Head / Neck	10	10.5 (3.6 – 89.7)	9	4	1
Arm / Hand	6	10.8 (6.2 – 75.8)	6	5	0
Buttock / Pelvis	3	60.4 (48.7 -)	2	2	0
Labia	2	17.5 (4.5 -)	2	0	0
Leg / Feet	5	3.5 (1.2 – 5.9)	5	5	0
Total	26	13.9 (6.4 – 62.3)	24	16	1

Location, size lesion-type and extension of vascular malformations.
Number of patients from which the median size with 25th – 75th percentile was calculated is given between parentheses.
n = number of patients. Median size = median VM size in ml.

Table 3.

Clinical results after treatment in children with peripheral vascular malformations

Outcome	**High flow AVMs** *n* **(%)**	**Low flow VMs** *n* **(%)**	**Total vascular malformations** *n* **(%, 95%CI)**
Total	5	18	23
Clinical failure within 3 months after treatment	0 (0%)	3 (17%)	3 (13%, 95%CI 3-34%)
Partial clinical success 3 months after treatment	5 (100%)	12 (66%)	17 (74%, 95%CI 52-90%)
Complete clinical success 3 months after treatment	0 (0%)	3 (17%)	3 (13%, 95%CI 3-34%)
Satisfied with treatment	5 (100%)	14 (78%)	19 (83%, 95%CI 61-95%)

Table 4.

Signs and symptoms before and after treatment in children with peripheral vascular malformations

Symptom	**Before treatment**	**After treatment**			
		Complete relief *n* **(%)**	**Partial relief** *n* **(%)**	**No relief** *n* **(%)**	**Worsening** *n* **(%, 95%CI)**
Total (*n*)	23				
Pain	16 (70%)	8 (50%)	6 (38%)	1 (6%)	1 (6%, 1-30%)
Swelling	22 (96%)	5 (23%)	11 (50%)	4 (18%)	2 (13%, 1-29%)
Functional impairment	13 (57%)	4 (31%)	5 (38%)	3 (23%)	1 (8%, 0.2-36%)
Cosmetic complaints	14 (61%)	3 (21%)	5 (36%)	3 (23%)	2 (14%, 2-43%)
Other	6 (26%)	4 (67%)	1 (17%)	1 (17%)	0 (0%, 0-46%)

Lesion characteristics

Vascular malformations were located in the extremities in 42% (11/26) of patients (Table 2). In 88% (23/26) of patients the lesion involved the subcutaneous tissue. The majority of lesions, 77% (20/26) were low-flow VMs.

The median number of consecutive therapy sessions was 1.5 per patient (range, 1-4). Clinical response after last therapy session was initially successful for two patients, but symptoms relapsed after more than one year without therapy sessions. These patients were treated again.

Therapeutic agents included Polidocanol (Aethoxysklerol 3%) in 32 of 48 sessions, and Ethanol in 13. In two small, high flow AVMs, we used polyvinyl alcohol particles (Contour 150/250 (Boston Scientific, Natick, US)) to embolize the fistulas. Histoacryl or combination of histoacryl with ethanol 96% was used in three high-flow AVMs. General anesthesia was used in 45% (22/48) and local anesthesia was used in 55% (26/48).

Clinical success

Three months after treatment of 23 patients, 3 (13%) reported complete and 17 (74%) partial clinical improvement (Table 3). Complete or partial clinical success was reported in all (5/5) of the high-flow AVMs and 66% (12/18) of the low-flow VMs treated. Complete clinical success was reported in none (0/5) of the high-flow AVMs and 17% (3/18) of the low-flow VMs.

At 1, 2, 3, 4 and 5 years, the clinical success rate (partial plus complete) was 74%, 59%, 59%, 59% and 59%, respectively. Two patients were available at 5 years follow-up. Long-term (5-year) complete relief of symptoms after 5 years was reported in 2 (9%).

Complications

Forty-eight percent (11/23, 95% confidence interval (CI) 27-69%) of the patients reported complications after treatment (Table 1). A total of 19 different complications were reported: 10 minor complications require no therapy and have no consequence (A-type complications), and 4 minor complications required nominal therapy, includes overnight admission for observation only and have no consequence (B-type complications). Five major complications resulting in permanent adverse sequelae (E-type complications), of these 4 patients had impaired/delayed wound healing and one patient had limitation in motion. Two patients required an operation for postinterventional tissue necrosis. Five of the six patients with tissue necrosis were related to use of ethanol as sclerotant (three combination of ethanol with Histoacryl). None of the major complications were related to use of polidocanol as sclerosant. No mortality (F-type complication) was related to the procedure. Nineteen of 23 (83%) patients were satisfied with treatment.

Before treatment of the vascular malformations, 96% of patients complained of swelling of the lesion and 70% of pain (Table 4). Patients reported complete or partial pain relief in 88% (14/16) and decrease of swelling in 73% (16/22). Increases of complaints per symptom are listed in Table 4. Relapse of symptom occurred in 9 of 23 patients (39%), of whom 4 had all symptoms mentioned before the treatment.

Discussion

In children with peripheral vascular malformations, clinical success by partial or complete relief of symptoms was obtained in 87% (20/23) of the patients with durable long-term results in 59% of the patients. Satisfaction with the treatment of children was high (83%). Complication rate was high (48%) with 22% major complications.

Our results are consistent with earlier reports regarding follow-up results after percutaneous treatment in children, which included 8-59 patients[6,17,18]. These studies investigated outcome based on technical success, and clinical patient records data were used to determine their status after therapy. Clinical improvement was reported in 59-75% with mean follow up of 3-24 months in these studies. However, technical success and patient record data as reported by the treating physician may overestimate patient experience regarding clinical success and satisfaction. Berenguer et al. reported an overall degree of satisfaction with the treatment of craniofacial venous malformations in children and adults of 78% (29/37 patients)[5]. In our previous study, we reported a lower satisfaction rate of 53% (35/66) in adults, which may be related to the age and larger diversity of vascular malformations of that patient group[13].
Major complication rate (22%) was consistent with earlier reports[6,13,17]. Major complications such as tissue necrosis, have been reported in 10-30% of patients and have been related to the VM site, the tissue type being embolized, the material used for embolization, and experience with the procedure[7].
A study limitation is that the treatment effect was not assessed by a clinical physical parameter, such as change in volume of vascular malformation, but by an inventory of patient satisfaction as study outcome. Patient satisfaction experience may under- or overestimate the actual physical outcome results after treatment. Study limitations include recall bias, where patients may have forgotten minor complications especially in case of occurrence of major complication. This may have resulted in an overestimation of clinical success. Another limitations are the small sample size, resulting in wide confidence intervals. Due to small numbers it was not feasible to assess risk factors for incomplete success of treatment. In all, the complication rate may have been even higher than our data suggest.
The results need replication is a larger study where the influence of disease characteristics on long-term outcomes can be investigated. Because vascular malformations are rare, it needs to be assessed in a prospective multicenter study.

Conclusion

Our study gives clinical physicians treatment results and complication rates of vascular malformations in children. Given our results we are now able to inform patients that initial partial or complete relief of vascular malformation complaints after percutaneous treatment is expected in 87% of children who need treatment because of complaints, irrespective of vascular malformation size or classification, and that there is a considerable chance of major complications (22%) during treatment.

Advances in knowledge:
Based on this study, percutaneous treatment of vascular malformations in pediatric patients provides complete or partial improvement of clinical symptoms in 87% of the patients after three months, and the results can be durable at long-term (5-years) follow-up in 59%. This is at the cost of a 22% incidence of major complications.

Implications for patient care:
The study results may provide patients and their parents with peripheral vascular malformations realistic expectations regarding percutaneous vascular malformation treatment in children.

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Appendix 1

The questions mentioned below are filled in with my parents? Yes / No

1. Where is the vascular malformation located in your body?

_____

2. Did you have charge of one or more of the following complaints before the treatment?

Complaints before the treatment	No	Yes
Pain	❑	❑
Swelling	❑	❑
Function restriction (move, bend, etc)	❑	❑
Cosmetic complaints	❑	❑
Other complaints where you had charge of:		
1	❑	❑
2	❑	❑
3	❑	❑

3. If at one or more complaints the answer was "yes": What has happened with this complaint after the treatment?

Complaints after the treatment	Complete relief	Partial improvement	No change	Worsening
Pain	❑	❑	❑	❑
Swelling	❑	❑	❑	❑
Function restriction (move, bend, etc)	❑	❑	❑	❑
Cosmetic complaints	❑	❑	❑	❑
Other complaints where you had charge of				
1	❑	❑	❑	❑
2	❑	❑	❑	❑
3	❑	❑	❑	❑

4. If any relapse. Can you indicate how long after the treatment the complains returned? Can you also indicate if the complains are worse than before treatment?

Complaints after the treatment	Relapse	Worsening	Months after treatment	
Pain	❑	❑	_____	months
Swelling	❑	❑	_____	months
Function restriction (move, bend, etc)	❑	❑	_____	months
Cosmetic complaints	❑	❑	_____	months
Other complaints where you had charge of				
1	❑	❑	_____	months
2	❑	❑	_____	months
3	❑	❑	_____	months

5. Are you generally satisfied concerning the impact of the treatment? ❑ Yes / ❑ No
Explanation (if needed)

_____

6. Have side effects and/or complications appeared after the treatment? ❑ Yes / ❑ No
If yes, which complication and did you have had treatment for this complication?

_____

Side effect / complication:	Treatment	
1. Pain	❑ Yes	❑ No
2. Swelling	❑ Yes	❑ No
3. Function restriction (move, bend, etc)	❑ Yes	❑ No
4. Hematoma	❑ Yes	❑ No
5. Nerve damage	❑ Yes	❑ No
6. Scar / Cosmetic complaints	❑ Yes	❑ No
_____	❑ Yes	❑ No

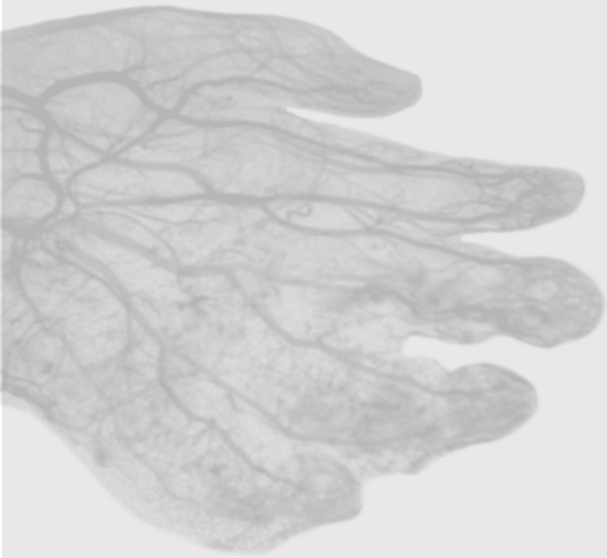
Explanation (if needed)

_____

Chapter 5

Radiofrequency Ablation for Treatment of Symptomatic Low-flow Vascular Malformations after Previous Unsuccessful Therapy.

Edwin van der Linden,
Jelle Overbosch,
Lucia J.M. Kroft.



J Vasc Interv Radiol 2005; 16:747–750

Abstract

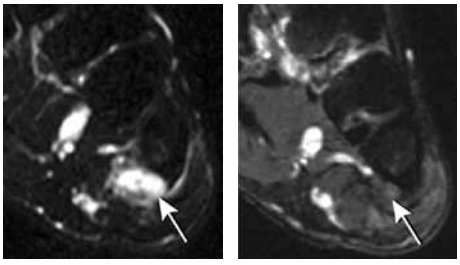
Three patients with low-flow soft-tissue vascular malformations were treated with radiofrequency (RF) ablation. Other treatment options had proven unsuccessful. After RF ablation treatment, two patients were free of symptoms and one reported decreased symptoms followed by a return of symptoms within 1 year. No procedure-related complications occurred. It is suggested that RF ablation may be offered as an alternative treatment option for symptomatic vascular malformations when others have failed or are not possible.

Introduction

Soft-tissue vascular anomalies are common abnormalities usually seen at birth or in early childhood. These anomalies can be divided into hemangiomas and vascular malformations according to the classification of Mulliken and Glowacki[1]. Distinction is important because of their different clinical approaches and prognoses. Vascular malformations do not regress spontaneously, unlike most hemangiomas, and often require treatment when they grow in size and symptoms occur, particularly pain and functional impairment[2-4]. Treatment depends on the subtype of the vascular malformation. High-flow malformations, which have an arterial component, are treated by transarterial embolization, sometimes followed by surgical resection[1-4]. Low-flow malformations such as capillary, venous, or combined malformations are usually treated by percutaneous embolization with or without surgery[2-5]. Although percutaneous embolization of low-flow vascular malformations is usually successful[6-8], lesions are inaccessible for percutaneous embolization in 8% of cases[8]. For these patients, radiofrequency (RF) ablation may be an alternative treatment option. RF ablation is a safe and minimally invasive technique used mainly for local treatment of solid tumors in radiologic practice[9,10]. In this article, we report three patients in whom RF ablation was used as a treatment for low-flow vascular malformations for which other treatment options had failed or were not possible to perform.

Case reports

Three patients with low-flow vascular malformations were treated with RF ablation during 2003 and 2004. RF ablation is a regular treatment method in our hospital for various benign and malignant tumors in cases in which surgery is not an option. Our institution does not require approval for retrospective reports. Informed consent was obtained from all three patients.



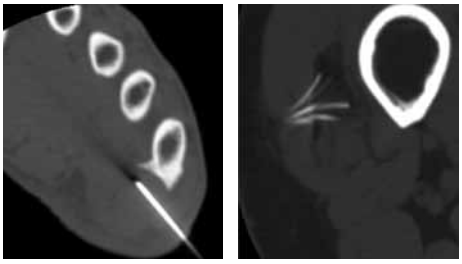
A **B**

Figure 1.

Coronal MR imaging of the left forefoot at the level of the metatarsal bones before RF ablation treatment of a capillary–venous malformation (arrow, A) in patient B. Follow-up MR imaging showed no residual mass (arrow, B). MR imaging technique was a T2-weighted spin-echo sequence with fat suppression. Repetition times were 3711 msec (A) and 2,520 msec (B); echo times were 80 msec (A) and 50 msec (B).

Patient A (female, 33 years of age) had a history of vascular malformations in the calf with recurrence after surgical treatment. She presented with new symptoms localized to the ventral side of the left ankle, where a soft, nonpulsatile mass was palpable. Magnetic resonance (MR) imaging showed a 1-cm-diameter lesion

located between the tendons of the extensor digitorum longus and extensor hallucis longus muscles with characteristics compatible with a capillary–venous vascular malformation. Because of the small vessel size, percutaneous embolization was not considered to be an option. RF ablation was offered as an alternative treatment option. Under general anesthesia and with use of ultrasound (US) guidance, a 1-mm-diameter RF ablation probe (Radionics, Burlington, MA) was introduced into the malformation. A 1-cm-volume ablation was performed in two adjacent locations at 90°C (194°F) for 4 minutes for each position, resulting in an ablation area of 1 cm × 1 cm × 2 cm. The patient was discharged within hours after the procedure. Seven months later, she reported that she had been virtually without symptoms for 5 months after the RF ablation procedure, but symptoms had recurred during the past 2 months. The symptoms were the same as before the RF ablation treatment, most notable at night. Follow-up MR imaging was unchanged compared with that before RF ablation treatment, compatible with residual lesion and/or recurrence. At present, she is treated conservatively with antithromboembolic stockings with moderate success. No further procedure is planned.

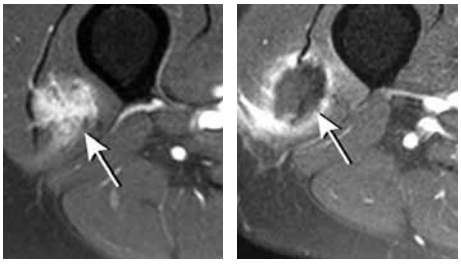


A **B**

Figure 2.

(A) Coronal CT image of the left forefoot at the level of the metatarsal bones during the RF ablation procedure in patient B shows positioning of the 1-mm-diameter RF ablation probe inside the vascular malformation. (B) Axial CT image of the right upper leg during the RF ablation procedure in patient C shows positioning of the multitip RF ablation probe inside the vascular malformation.

Patient B (male, 38 years of age) had a venous vascular malformation located adjacent to the left fifth metatarsal bone. After surgical removal, his symptoms were unchanged. On MR imaging, a residual 1-cm-diameter lesion was shown (Fig 1a), with rapid enhancement after gadolinium dimeglumine administration, which was diagnosed as a capillary–venous vascular malformation. Because of the small vessel size, percutaneous embolization was not considered to be an option and RF ablation was offered as an alternative treatment. Under general anesthesia and with use of computed tomographic (CT) guidance, a 1-mm-diameter RF ablation probe (Radionics) was introduced in the lesion (Fig 2a). Four minutes of coagulation at 90°C (194°F) was performed and repeated twice more after electrode repositioning to treat the whole lesion. The patient was discharged within hours after the procedure. MR imaging 7 months after RF ablation treatment showed no residual mass (Fig 1b). Fourteen months after the procedure, the patient reports that he is still free of symptoms.



A **B**

Figure 3.

Axial MR imaging of the right upper leg of patient C before (A) and after (B) RF ablation treatment. MR imaging sequence was T1-weighted spin-echo with fat suppression after administration of gadolinium dimeglumine (repetition time/echo time, 550/8 msec). A heterogeneous enhancing lesion is shown in the vastus intermedius muscle (A, arrow). There was rapid enhancement after gadolinium dimeglumine administration (not shown), findings typical for a capillary-venous malformation. After RF ablation treatment, a central area of low signal intensity is shown, surrounded by an enhancing ring, representing central necrosis with surrounding enhancing edema (B, arrow).

Patient C (female, 22 years of age) presented with a vascular malformation localized in the lateral side of the right upper leg. On MR imaging, a lesion 7 cm × 2 cm × 2 cm in size was confirmed at the dorsal aspect of the vastus intermedius muscle (Fig 3a), with characteristics diagnostic for a capillary–venous malformation. Initially, percutaneous embolization was performed with use of 98% ethanol, but the procedure was technically difficult as a result of the small vessel size. There was only a minimal decrease in symptoms reported 9 months after embolization. Follow-up MR imaging findings were unchanged compared with the preembolization study. Because the percutaneous embolization treatment had been technically difficult to perform, RF ablation was offered as an alternative treatment option. Under general anesthesia and with use of CT guidance, a multitip StarBurst XL probe (Rita Medical Systems, Mountain View, CA) was introduced into the lesion (Fig 2b). After deploying of the needle to 2 cm, the probe was heated to 80°C (176°F). This was followed by deployment to 3 cm and heating to 105°C (221°F) and finally to 3 cm with a final temperature of 110°C (230°F). This last temperature was maintained for 5 minutes.

The procedure was repeated after repositioning to cover the entire lesion, resulting in a total ablation volume of 4 cm × 4 cm × 5 cm. The patient was discharged the day after the RF ablation procedure. Follow-up MR imaging showed no evidence of residual mass (Fig 3b). Eight months later, she reports that she is still free of symptoms.

Discussion

Low-flow vascular malformations are lesions consisting of anomalous channels lined with normal endothelium, without arterial involvement[1]. The diagnosis is usually made by physical examination and can be confirmed by a combination of static and dynamic MR imaging[3-6]. Surgical resection, medical therapy, and transarterial and percutaneous treatments have all shown limited success in treating low-flow vascular malformations, for which direct-puncture percutaneous sclerotherapy is considered the best treatment option[4,6,7].

Percutaneous treatment of low-flow vascular malformations is usually successful, but these lesions can be difficult to treat as a result of inaccessibility of lesions or because of frequent recurrences[5,6,8]. Recently, we treated two patients with lesions that were inaccessible because the small vessel size hampered percutaneous sclerotherapy treatment, and in one patient with an earlier unsuccessful percutaneous sclerotherapy treatment session, a repeat session was not an option. In these patients, RF ablation treatment was offered as a treatment option. All three patients tolerated the RF ablation treatment well and no complications were recorded.

RF ablation is a minimally invasive, safe procedure. In radiologic practice, it is used widely for the treatment of several benign and malignant tumors. The complication rate is low, largely comprising nonspecific problems caused by the placement of the electrode or the actual thermal treatment itself, as well as complications from tissue-specific treatment[9,10]. In low-flow soft-tissue vascular malformations in the extremities, care should be taken to avoid nerves and major vascular structures during RF ablation treatment. In addition, we suggest that RF ablation treatment of low-flow vascular malformations should be reserved for patients in whom more conventional treatment options such as percutaneous embolization, attempted by an experienced interventional radiologist, have shown no success. No complications occurred in the three patients we treated with RF ablation.

Of the three patients treated with RF ablation as reported herein, two are symptom-free after 14 and 8 months of follow-up, respectively. One patient (patient A) reported a return of symptoms within 1 year after RF ablation, after a symptom-free period, and the symptoms were as severe as before RF ablation treatment. During her RF ablation session, the probe was positioned under US guidance and the location of the needle was verified before heating. Follow-up MR imaging showed no scars near the persisting malformation, confirming accurate positioning of the probe in the malformation during RF ablation treatment. The RF ablation procedure may have resulted in thrombosis of the lesion, followed by reorganization and dissolving of thrombus in the following months. This may explain the temporary relief of symptoms. All three patients remain under care of their vascular surgeons.

In three patients, RF ablation treatment was offered when percutaneous sclerotherapy or resection was not possible to perform. Two patients became free of symptoms and the third had temporary relief of symptoms. We suggest that RF ablation may be used for the treatment of symptomatic soft-tissue low-flow vascular malformations when other treatment options have failed.

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Chapter 6

Retrograde Transvenous Ethanol Embolization of High-Flow Peripheral Arteriovenous Malformations

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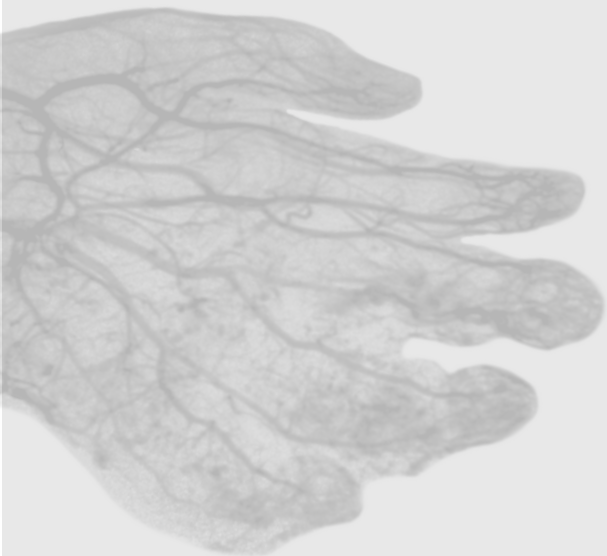
Peter M.T. Pattynama.



CVIR Resubmitted June 2011

Abstract

Retrograde transvenous ethanol embolization of high-flow AVMs is a technique that can be used to treat complex AVMs whenever conventional interventional procedures have proved insufficient. This is a retrospective study of the clinical effectiveness and complications of retrograde embolization in five patients who had previously undergone multiple arterial embolization procedures without clinical success. Clinical outcomes were good in all patients, but were achieved at the cost of serious although transient complications in three patients. Retrograde transvenous ethanol embolization is a highly effective therapy for high-flow AVMs. However, due to the high complication rate, it should be reserved as a last resort when conventional treatment options have failed.

Introduction

High-flow arteriovenous malformations (AVMs) are characterized by direct, low-resistance fistulas in the nidus between arteries and veins. High-flow AVMs can be categorized according to the angiographic morphology of the nidus: type I (arteriovenous fistulae), type II (arteriolovenous fistulae), type IIIa (arteriolovenulous fistulae with nondilated fistula), and type IIIb (arteriolovenulous fistulae with dilated fistula)[1]. AVMs with arteriolovenous fistulae have been referred to as AVMs with a dominant outflow vein (DOV). Percutaneous treatment of peripheral AVMs (i.e., AVMs that are located outside the central nervous system) is aimed at obliteration of the nidus. The two first-line treatment methods to achieve this purpose are transarterial embolization of the high-flow fistula[2,3,4] and, alternatively, direct percutaneous puncture and the injection of sclerosing agents into the nidus. However, in some patients, neither treatment option might be technically feasible, or both might be unsuccessful. Transarterial embolization might fail because of the inability to achieve a suitable superselective catheter position that is sufficiently close to the nidus, or because the nidus is comprised of too many individual arterial feeders and/or multiple arteriovenous fistulas, especially in patients who have undergone prior surgery or proximal embolization with coils. In addition, AVMs might be inaccessible to direct percutaneous puncture.
For these rare instances, the technique of retrograde embolization has been proposed, in which the draining veins of the AVMs are occluded temporarily but completely. During this period of flow arrest, the nidus of the AVM and adjacent feeding arteries can be filled by slow continuous retrograde injection of a liquid embolic agent such as ethanol. Exposure of the nidus and the abnormal feeding arteries to ethanol should lead to destruction of the nidus. High-flow AVMs with a single dominant draining vein and multiple small tortuous feeding arterioles, as seen with type II arteriolovenous fistulae, are most suitable for this retrograde approach to AVM embolization[1,5,6,7]. Herein, we report our experience with transvenous retrograde ethanol embolization of complex high-flow peripheral AVMs in five consecutive patients.

Material and methods

Between 2001 and 2008, we treated five patients with high-flow AVMs (three male, two female; age range, 10–80 years) by the use of retrograde transvenous ethanol embolization in the setting of a tertiary referral center. Table 1 lists the characteristics and the location of the AVMs, clinical signs and symptoms, and the duration of follow up. Our Institutional Review Board does not require approval for retrospective case reports.

Technique of retrograde transvenous embolization

In all the patients, conventional arterial embolization treatment with n-butyl-2-cyanoacrylate (Histoacryl, Braun Aesculap AG & CO, Tuttlingen, Germany) glue mixed with iodinated poppy-seed oil (Lipiodol, Guerbet, Roissy, France) had been attempted previously, but had yielded unsatisfactory results. Attempts at arterial embolization of the AVM in one patient (patient 5) failed because it proved impossible to reach the nidus with the microcatheter. In all five patients, we had noticed on the angiogram that the AVMs drained directly into a single dilated vein (Figure 1). As a consequence, we considered these patients to be suitable candidates for retrograde transvenous embolization. This procedure was always done under general anesthesia. During the procedure, 3000 IU of heparin were administered to minimize the risk of thrombosis at the access site.

For retrograde embolization, the draining vein was blocked using an occlusion balloon (patients 1, 2, and 5), a pressure tourniquet (patient 3) or manual compression (patient 4). For balloon occlusion, we used a low-pressure low-profile occlusion balloon (PTS sizing balloon, 20–40 mm diameter; NuMed, Inc, Hopkinton, NY, USA). This balloon is compatible with ethanol. Access to the occluded draining vein was via the guidewire channel of the occlusion balloon or through an introducer sheath placed in addition. Upon occlusion of the draining vein, we performed venography to confirm stasis of flow in the draining vein. Contrast injections were performed to quantify the volume of ethanol needed to immerse the nidus fully. Care was taken to avoid overt retrograde filling of the arterial feeding vessels, because we were concerned that this might result in spillage of the embolic material into the arterial side of the circulation. Next, 96% ethanol was instilled through the inflated balloon catheter (or through the additionally placed introducer sheath), which was left in place for 5–10 minutes. After the appropriate dwell time for the alcohol, while flow arrest was still induced by balloon or manual occlusion, as much alcohol as possible was aspirated before the balloon was deflated. A control angiogram was performed through a selective catheter in the feeding arteries of the AVM, and if we encountered residual fistulae the entire procedure was repeated.

Results

Diagnostic work-up revealed a type II AVM in four patients. The remaining patient (patient 3) had a mixed type II and IIIb AVM, but the treated region in his hand was mainly a type II AVM. A total of seven retrograde ethanol embolization procedures were performed in these five patients. The procedure was repeated in two patients because the symptoms increased in severity (patient 1 after 13 months, patient 2 after 14 months). The characteristics of the patients and the outcome of the treatment are summarized in Table 1.

Long-term benefit and improvement was achieved in four of the five patients who were treated with retrograde ethanol embolization. The average symptom-free interval was 3.3 years (median, 1.5 years; range, 1–7.5 years). In patient 3, therapy was successful without further episodes of arterial bleeding, and healing of the ulceration on the thenar side of the hand was noted. However, after 18 months of follow up, the forearm was amputated because of further worsening of hand function due to swelling and intolerable pain that was refractory to pain medication.

In most cases, approximately 50% of the ethanol injected could be withdrawn after embolization. In one case (patient 4) none of the ethanol could be withdrawn as a result of incomplete venous blockage.

Table 1

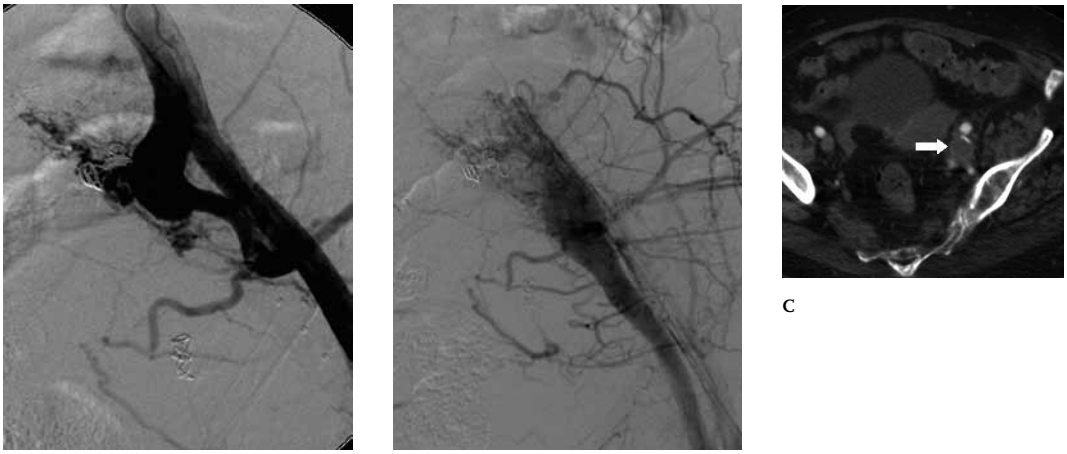
Patient characteristics

Patient/ sex/ Age (y)	Site	Previous therapy* (*n*)	Complaints before treatment	Date of retrograde treatments	Amount of ethanol used	Longest period of response	Outcome after treatment	Complications
1/F/72 (Figure 1)	Pelvis	A (4)	Pain, functional impairment, edema of left leg	1-3-2001 4-4-2002	10 ml 16 ml	7.5 y	Free of symptoms	None
2/F/10 (Figure 2)	Head / neck	A (2)	Swelling of neck and tongue, disturbing buzzing noise in both ears	21-11-2006 30-1-2008	25 ml 25 ml	1.5 y	Free of symptoms	Necrosis of the lower lip
3/M/51	Hand	A (2)	Pain, swelling, arterial bleeding	18-6-2001	10 ml	1 y	Arterial bleeding disappeared. Worsening of hand function and increase of pain, therefore hand was amputated.	None
4/M/37	Skull	A (1) D (1)	Bleeding, swelling	3-11-2004	35 ml	5 y	Free of symptoms	Cardiovascular collapse; local skin necrosis
5/M/80	Pelvis	None	Pain, functional impairment, edema of left leg	20-12-2007	15 ml	1.5 y	Free of symptoms	None (pneumonia might have been related to the treatment)

* *n* = number of previous treatments, A = arterial embolization treatment with n-butyl-2-cyanoacrylate, D = direct puncture embolization of the nidus with n-butyl-2-cyanoacrylate

Complications

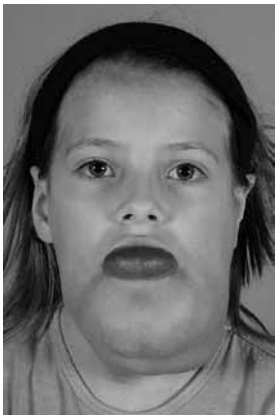
Three patients developed four transient complications after the retrograde ethanol embolization procedure. In the days following the treatment, patient 2 developed severe necrosis of the lower lip, which healed completely over the course of several weeks with conservative treatment only and with only minor scarring (Figure 2). The treatment of patient 4 was complicated by cardiovascular collapse, which required a 2-day stay in the intensive care unit and assisted ventilation. After the procedure, this patient also developed local necrosis of the skin, together with focal baldness of the skull. During recovery, patient 5 developed pneumonia, which resulted in a prolonged (2-week) hospital stay; this complication was attributed to the embolization procedure. The patient made an otherwise uneventful recovery.



A B C

Figure 1, Patient 1

Diagnostic work-up revealed a type II AVM in the pelvis with multiple feeders that originated from the left and right internal iliac arteries and drained into the left external iliac vein. Once the left common iliac vein had been ligated, the venous outflow of the AVM was blocked, with resultant high venous pressure and decreased perfusion of the left leg. Over the course of 6 months, we performed four sessions of selective arterial embolization of the multiple arterial feeders of the AVM with n-butyl-2-cyanoacrylate/Lipiodol and coils, which resulted in acceptable initial relief of the pain in the leg. However, the last embolization was complicated by ischemia of the right sciatic nerve, presumably because of inadvertent embolization of branches of the right internal iliac artery that supplyed the sciatic plexus. The patient needed intensive rehabilitation and pain management for this complication. After 6 months the sciatic pain in the right leg had subsided but there was progression of the venous swelling and pain in the left leg. Angiography showed newly formed diffuse fistulae in the AVM that arose from the left iliac artery (1A and 1B). We decided to perform retrograde transvenous embolization with ethanol under balloon occlusion of the left external iliac vein. A total of 10 mL of 96% ethanol was used. Control angiography showed substantial but incomplete reduction of the fistulae, which we decided to accept. After treatment, the symptoms subsided. One year later, we performed a second retrograde venous embolization because the severity of the symptoms had increased. Following this second treatment, the fistulae had disappeared and the complaints in the left leg were cured. The patient remains free of symptoms due to the AVM. CT-angiography performed 7 years after the last treatment for a chronic diabetic ulcer of the right foot still shows permanent occlusion of the AVM (1C, Arrow).



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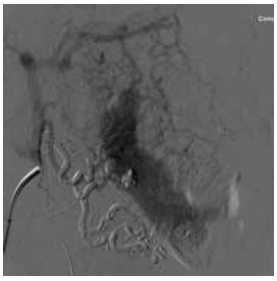

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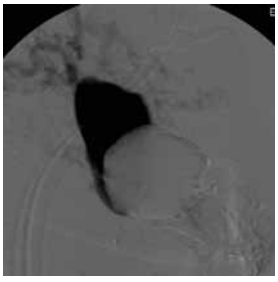

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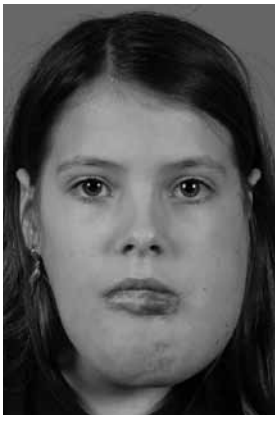

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Figure 2, Patient 2

A 10-year-old girl presented with a type II AVM of the chin and neck region. She had disfiguring swelling of the neck, chin, and lower lip with secondary hypertrophy of the mandible (2A, date of photograph 20-11-2006; one day before first retrograde treatment), and she complained of an annoying continuous buzzing noise in her left ear that often kept her awake during the night; this noise was produced by the high-flow arteriovenous fistula. Angiography showed the presence of multiple arteriovenous fistulae that arose from the left and right external carotid arteries and drained into a massively enlarged single left-sided draining vein. Two treatment sessions of superselective arterial embolization were performed with n-butyl-2-cyanoacrylate/Lipiodol. However, diffuse arteriovenous fistulae remained (2B). It was also apparent that the symptoms returned quickly after the treatment sessions. It was felt that we could not control the arteriovenous fistulae completely with arterial embolization, and we decided to apply retrograde transvenous embolization. The draining vein was occluded with a balloon (2C), and the nidus was filled in a retrograde direction with 25 mL of 96% ethanol. In the days after treatment, the patient developed severe necrosis of the lower lip, which healed completely over the course of several weeks with conservative treatment only and with only minor scarring (2D, date of photograph 27-2-2008; 15 months after first retrograde treatment). The treatment was successful in decreasing the swelling of the chin and neck, and the buzzing sound had disappeared together with the fistulae. After one year of follow up, the patient returned with some progressive swelling of the region. We decided to do a second retrograde embolization. Angiography showed fistulae arising from the right but not the left external carotid artery. Retrograde transvenous embolization with a further 25 mL of ethanol was successful and complete and the patient and her parents were very satisfied with the final result. Seventeen months after the treatment, the patient is still free of symptoms.

Discussion

This small series shows that retrograde transvenous ethanol embolization is an effective therapy for complex high-flow peripheral AVMs with a DOV that are refractory to transcatheter arterial embolization as the first-line therapy. Retrograde embolization was very effective, with complete and durable results. However, these results were achieved at the cost of a high rate of serious complications, which proved to be transient in all three cases.

Selective embolization of the nidus via the arterial side is the first-line treatment for AVMs in our institution because it is effective in 64% of patients[8]. In general, arterial embolization is performed using a mixture of n-butyl-2-cyanoacrylate and iodinated poppy-seed oil (Lipiodol), whereby the nidus of the lesion is catheterized superselectively using a coaxial catheter system. The aim of this technique is to treat the central nidus, and embolization must be performed as near as possible to, or across, the arteriovenous communications. Occlusion that is too far proximally, as in our patient 4, invariably results in recurrence of the AVM in all cases.

Type II and Type IIIb AVMs can also be treated via direct percutaneous puncture. However, the transarterial approach is preferred because normal arteries around the AVM are easier to detect and adverse embolization of these arteries is less likely to occur with this approach than with direct puncture. In addition, with direct puncture, ethanol can leak into adjacent soft tissues, which results in necrosis[6].

Cho et al. reported that coil embolization of the DOV of type II AVMs before the injection of ethanol was preferred. Thereafter, either the direct puncture or transvenous approach was used primarily for ethanol embolization of this type of AVM (17 of 19 AVMs). Coil embolization was not performed for superficial lesions because very superficial coils can erode through the overlying skin and cause ulceration. For such patients, the authors used other techniques to occlude flow, such as external pneumatic pressure cuffs or an intravascular occlusion balloon catheter. In the study by Cho et al., the AVMs were cured in thirteen patients (68%) and six patients achieved improvement[7].

When this approach or the first alternative approach, namely direct percutaneous puncture of the nidus, fails, the retrograde transvenous approach should be considered whenever it is feasible to occlude a single draining venous compartment close to the nidus, and when this venous compartment can be accessed with a catheter through which to instill the sclerosing agent. With respect to retrograde transvenous embolization procedures, we only have experience with 96% ethanol, but one can assume that other embolic agents, such as polidocanol (10 mg/mL, Aethoxysklerol, Kreussler & Co. Wiesbaden, Germany) as a liquid or as a foam, might also be effective.

Retrograde embolization is required only rarely; hence we believe that the technique is relatively unknown and underutilized. There have only been isolated case reports that describe this technique[1,5,7,9,10]. However, we think that retrograde embolization is useful in certain cases.

Limitations

The procedure is only possible in patients with type II AVM with a DOV.

A cause of concern is the high rate of complications of the retrograde transvenous embolization procedure. Complications occurred in three of our five patients. In the two patients with tissue necrosis, we think that this was caused by the instillation of too much ethanol, which filled the arterial feeding vessels in a retrograde direction and was then flushed into the arterioles that vascularized the skin. One procedure was

complicated by cardiovascular collapse that presented as pulseless sinus tachycardia with elevated pressures of the pulmonary artery and right ventricle, which necessitated resuscitation. We hypothesize that this complication occurred because of venous leakage of ethanol into the vasculature of the lung after incomplete venous occlusion by manual compression. (The alternative cause of pulmonary embolization as a result of ethanol-induced thrombosis seemed to be excluded by a normal CT-angiography of the pulmonary artery after the procedure). These complications underscore the importance of performing test injections of contrast medium before the instillation of the liquid embolic agents, to ensure adequate venous occlusion and provide an accurate estimate of the required volume of sclerosing agent. It is probably better to err on the side of safety and to repeat the procedure in the same session if necessary when postprocedural angiography shows incomplete transvenous embolization.

We believe that retrograde transvenous ethanol embolization during venous outflow occlusion and flow arrest represents a method to treat type II high-flow AVMs whenever a transarterial approach or direct puncture treatment does not seem to be feasible or has proven to be unsuccessful.

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Chapter 7

Venous Malformation in the Suprapatellar Recessus of a 14 Year Old Female Rugby Player.

F.A.R. Jansen,
E. van der Linden,
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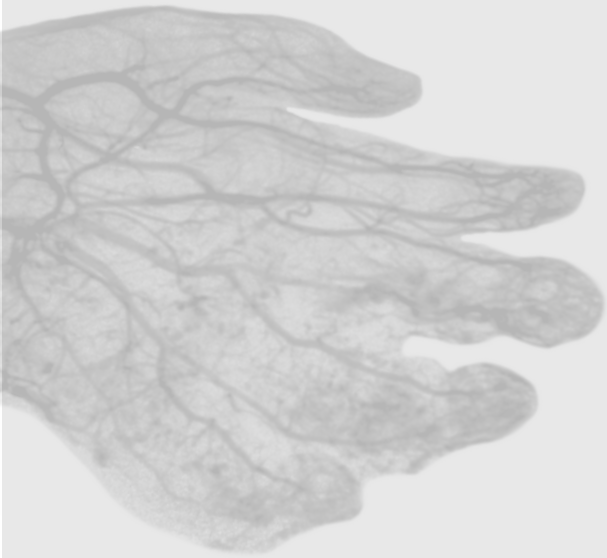
C. de Winter.



Sport & Geneeskunde Mei 2011

Abstract (English)

Venous malformations are a rare cause of exercise related pain. These benign congenital lesions can cause invalidating complaints in the sporting population. Other symptoms can be (recurrent) swelling, restricted range of motion, cosmetic complaints or skin lesions. The clinical presentation is often atypical and frequently the diagnosis is made after a long delay. Clinically the diagnosis can be missed or confused with other (vascular) disorders. Further investigation consists of ultrasonography and intravenous contrast-enhanced MRI. The preferred treatment of this benign disorder consists of sclerotherapy, which has a relatively high complication rate and risk of recurrence.
In this article we present a case of venous malformation and discuss the clinical presentation, further investigations and therapeutic possibilities.

Abstract (Nederlands)

Veneuze malformaties zijn een zeldzame oorzaak zijn van inspanningsgerelateerde pijnklachten. Het zijn benigne aangeboren afwijkingen, maar kunnen voor sporters invaliderende klachten geven. Naast pijn bestaan die uit (recidiverende) zwelling, bewegingsbeperking, cosmetische klachten of huidafwijkingen. Vaak is het klinisch beeld atypisch en is er sprake van een lange vertraging voor de diagnose gesteld wordt. Het beeld wordt klinisch frequent gemist of verward met andere (vasculaire) afwijkingen. Aanvullend onderzoek bestaat uit echografie en MRI met intraveneus contrast. De voorkeursbehandeling van deze benigne afwijking bestaat uit sclerotherapie, een behandeling met een relatief hoog complicatierisico waarbij de kans op recidieven aanwezig blijft.
In dit artikel worden het klinisch beeld, aanvullend onderzoek en therapeutische mogelijkheden besproken aan de hand van een casus.

Inleiding

Vasculaire afwijkingen (hemangiomen en vasculaire malformaties) zijn met name bekend om hun dermale presentaties, zoals het juveniele (aardbei)hemangioom en de wijnvlek. Het zijn aandoeningen die vaak voorkomen, maar zelden significante morbiditeit geven[1]. Diverse syndromen zijn bekend waarbij de patiënt op meerdere plaatsen vaatafwijkingen heeft, zoals het Sturge-Weber syndroom (capillaire malformaties), het Klippel-Trénaunay syndroom (oppervlakkige veneuze malformaties), het Parkes Weber syndroom (arterioveneuze malformaties) en het Beckwith-Wiedemann syndroom (capillaire malformaties in het gelaat)[2].

Volgens de indeling van Mulliken (Tabel 1) dient onderscheid gemaakt te worden tussen vaattumoren (hemangiomen) en vaatmalformaties, hetgeen beide aangeboren afwijkingen van het vaatendotheel zijn. Hemangiomen zijn aangeboren vaattumoren die in de neonatale periode een karakteristieke hypercellulaire hyperproliferatieve fase hebben, gevolgd door een involutiefase met verminderde cellulariteit en fibrose. Vaatmalformaties zijn tevens aanwezig vanaf de geboorte, maar hebben een groeipatroon proportioneel aan de groei van de rest van het lichaam en gaan niet spontaan in regressie. Zij bestaan uit vasculaire ruimtes met normaal gedifferentieerd endotheel weefsel[3], en kunnen onderverdeeld worden in malformaties met lage flow (bijvoorbeeld veneuze malformaties) en malformaties met hoge flow (bijvoorbeeld arterioveneuze malformaties). Daarnaast zijn er aparte categorieën voor lymfatische malformaties en gecombineerde vormen, die soms tot de low flow afwijkingen gerekend worden omdat de behandeling overeenkomt.

Naslag in de literatuur toont dat de naamgeving lange tijd bron van misvatting is geweest. Met name de term hemangioom wordt regelmatig op onjuiste wijze gebruikt, als daadwerkelijk gerefereerd wordt aan een veneuze malformatie[4,5], hetgeen het zoeken naar bruikbare literatuur bemoeilijkt.

Deze casusbespreking heeft als doel het herkennen van één van de low flow malformaties (de veneuze malformatie), en de therapeutische opties te bespreken in een review van de literatuur.

Tabel 1

Vasculaire afwijkingen volgens de ISSVA/Mulliken classificatie 1996. Vasculaire malformaties geordend op vasculaire dynamiek en flow.

Vascular tumors	Vascular malformations	
	Low flow	High flow
Infantile hemangioma	Capillary malformations	Arteriovenous malformations
Congenital hemangioma	(port-wine stains, telangiectases)	Combined
Tufted angioma	Venous malformations	(CAVM, CLAVM)
Kaposiform hemangioendothelioma	Glomuvenous malformations	
Hemangiopericytoma	Lymphatic malformations	
Pyogenic granuloma	(macrocystic, microcystic, combined)	
Spindle-cell hemangioendothelioma	Combined	
	(CLM, CLVM, CVM, CMTC)	

Afkortingen: ISSVA, International Society for the Study of Vascular Anomalies; CLM, capillary-lymphatic malformation; CLVM, capillary-lymphatic venous malformation; CVM, capillary VM; CMTC, cutis marmorata; CAVM, capillary arteriovenous malformation; CLAVM, capillary-lymphatic AVM.

Casus

Een 14-jarige rugbyspeelster presenteerde zich met een bij inspanning (hardlopen) recidiverende pijn en zwelling in het rechter bovenbeen vlak boven de knie. De klachten waren 6 jaar geleden begonnen, na een stomp trauma op de vastus medialis van de m. quadriceps femoris. Destijds werden de klachten geduid als groeipijn, maar zij zijn continu sluimerend aanwezig gebleven en waren de laatste tijd langzaam progressief. De klachten waren het meest manifest tijdens hurken en gelokaliseerd mediaal boven de knie; patiënte moest de training steeds vaker staken hierdoor. Zij klaagde tevens over giving way en crepiteren van de knie. Er was geen sprake van bewegingsbeperking. Fysiotherapeutische behandeling waarbij getraind werd buiten het klachtengebied had onvoldoende resultaat geleverd. In verband met toelating op een speciale school met ruimte voor topsport (LOOT-school) werd verzocht een sportarts te raadplegen in verband met de lange klachten duur.

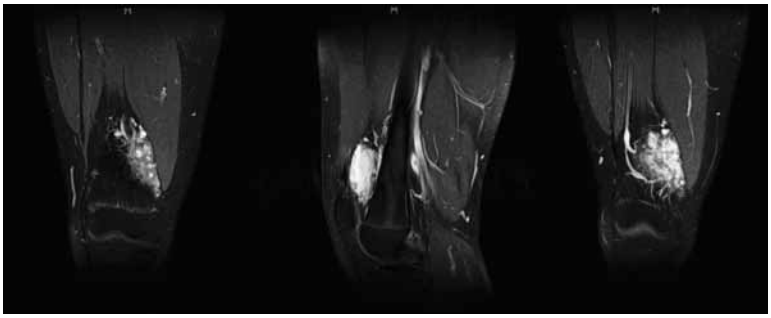
Bij lichamelijk onderzoek werd een knie zonder hydrops gezien met een volledige range of motion. Aan de huid werden geen opvallende afwijkingen gezien. Er was geen sprake van instabiliteit en de meniscusprovocatietesten waren negatief. Weerstandstesten van de m. quadriceps femoris waren negatief. Pas bij het tweede bezoek aan de sportarts (direct na inspanning) werd een palpabele weke delen zwelling gevonden in het gebied van de vastus medialus obliquus, die tevens pijnlijk was.

Differentiaal diagnostisch werd gedacht aan myositis ossificans, exostosen van de distale femur, ingekapseld hematoom of andere posttraumatische musculaire pathologie. In verband met de langdurige klachten werd een weke delen of botmaligniteit minder waarschijnlijk geacht.

Röntgenopnames van de knie toonden geen afwijkingen en bij verdere progressie van de klachten en het ontstaan van een lichte extensiebeperking werd patiënte verwezen voor echografisch onderzoek na belasting, waarbij ter plaatse van de zwelling mogelijk een spoor vocht gezien werd.

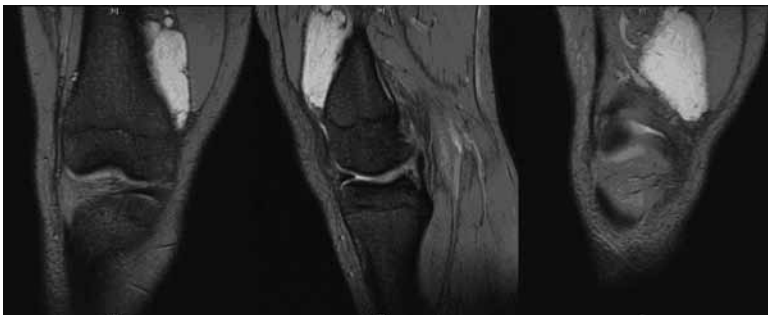
Voor verdere analyse werd een MRI verricht. Hierop werd een gelobde vochtcollectie van 5,5 cm gezien, ventromediaal gelegen tussen de distale metafyse van het femur en de vastus medialis (Figuur 1). Een hierop volgende MRI met contrast toonde een veneuze malformatie dorsaal van de recessus suprapatellaris, zonder relatie met het synovium van de knie (Figuur 2). Patiënte werd aangeboden aan de interventieradioloog ter embolisatie, die na direct aanprikken van de laesie een afgepaste hoeveelheid polidocanol (een lokaal vaatsclerosans) injecteerde (Figuur 3). Daags na het scleroseren had de patiënte nog een stijf gevoel in het bovenbeen, maar de zwelling en de pijnklachten waren verdwenen.

Vier weken later toonde echografische controle een volledige occlusie van de malformatie. Omdat de klachten tevens verdwenen waren was een vervolg flebografie of behandeling niet nodig. Vijf maanden na de behandeling is patiënte nog steeds klachtenvrij en sport weer als voorheen.



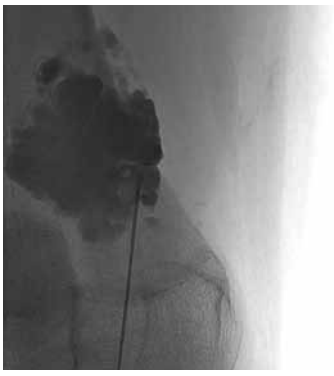
Figuur 1

Conventionele MRI van de knie (T2-gewogen) toonde een opvallende, gelobde vochtcollectie ventromediaal tussen distale metafyse van het femur en de m. quadriceps vastus medialis gelegen.



Figuur 2

MRI met gadolinium contrast (T1 gewogen) toonde in de weke delen dorsaal van de recessus suprapattellaris een massa van 43 x 35 x 16 mm, met sedimentatiespiegels en afvoerende vaten.



Figuur 3

Röntgenopname van de procedure. Percutaan werd met lumbaal naald het caudale gedeelte van de veneuze malformatie aangeprikt. Eerst werd flebografie verricht waarop vulling van de gehele malformatie zichtbaar was met afvloed in het normaal veneuze systeem. Vervolgens werd gekeken met hoeveel milliliter contrastvloeistof er net géén vulling was van het afvoerende veneuze systeem (zichtbaar in deze figuur: vulling van 2/3e deel van de malformatie, nauwelijks veneuze afvloed). Vervolgens werd eenzelfde hoeveelheid (10ml) polidacanol ingespoten.

Discussie

Veneuze malformaties (VMs), zoals in deze casus besproken, hebben een incidentie van 1-2 per 10.000 en een prevalentie van 1%[4]. Veertig procent betreft de huid of het slijmvlies van de hoofd-hals regio, in 40% van de gevallen is een extremiteit aangedaan en bij de overige 20% de romp. De laesies kunnen zowel oppervlakkig voorkomen als dieper gelegen zijn in subcutaan weefsel, spieren, botten of organen. Een persoon kan tevens op meerdere lokaties aangedaan zijn. Onderzoek met transgene muizen heeft aangetoond dat bepaalde groeifactoren en receptoren betrokken zijn in de afwijkende vasculoneogenese in de embryonale fase[6]. De morfologie van de vaatkluwen bij een VM is afwijkend van normaal veneweefsel. Het weefsel is zwakker, met een dunne vaatwand en gladde spierlaag. Hierdoor neemt de elasticiteit af en kan de bloedstroom stagneren bij drukverhogende momenten zoals staan en sporten. Tevens is er vaak een afwijkende afvoer met als gevolg stasis. Als gevolg dilateren de vaten verder en kunnen stolsels in de vaten vormen, die kunnen calcificeren tot flebolieten en in zeldzame gevallen emboli verliezen[7]. In principe is de aandoening benigne en in milde gevallen zijn de klachten gering.
Hoewel overlap bestaat tussen de klinische presentaties van verschillende vasculaire afwijkingen, kan de diagnose veneuze malformatie vaak gesteld worden op basis van anamnese en lichamelijk onderzoek alleen. De klassieke presentatie is die van (1) een recidiverende zwelling bij lang staan of inspanning, (2) pijn -als gevolg van lokale compressie- en (3) bewegingsbeperking -als gevolg van ingroei in een gewricht of peri-articulair massa effect. Deze typische klachten tonen progressie in de groeispurt van de puberteit. Toename wordt echter ook beschreven in de zwangerschap, na een (stomp)trauma of na een partiële resectie. Tevens kan de huid lokaal blauw doorschemeren en klagen patiënten soms over varicositas (soms in combinatie met vage pijnklachten de enige klacht). Lokaal of in een aanliggend gewricht kunnen bloedingen ontstaan. Soms treden coagulopathieën als gevolg van stasis op[5]. Het beeld is lang niet altijd eenduidig en enkele case-reports beschrijven zeer afwijkende presentaties, zoals die lijkend op meniscuslijden of een partiële peesruptuur[8,9].
Anders dan bij arterioveneuze malformaties is er bij VMs vaak géén sprake van lokale roodheid en warmte, noch een palpabele thrill of pulsaties. Daarnaast zijn arterioveneuze malformaties vaak al bij de geboorte direct evident, VMs spelen typisch pas later op[5]. De presentaties van andere low flow laesies kunnen echter sterk lijken op die van een VM. Een voorbeeld hiervan is lymfatische malformaties, die typisch reactief in omvang toenemen bij systemische virale infecties of ontsteking van de malformaties zelf. Daarnaast kan er sprake zijn van een -zeer zeldzame -glomuveneuze malformatie, die zich oppervlakkiger presenteert als blauw-paarse nodules en minder vaak progressief is. Daarnaast kunnen gecombineerde vormen voorkomen. Vanwege de overlappende klinische presentaties, de relatieve zeldzaamheid en de verwarring met het concept hemangioom, worden veneuze malformaties vaak gemisdiagnosticeerd, leidend tot lange doctor's delay en ineffectieve en/of overinvasieve therapieën[4]. In de sportgeneeskundige praktijk is het derhalve belangrijk om de diagnose te overwegen bij iedere (jonge) sporter die hulp zoekt voor onverklaarde inspanningsgerelateerde pijnklachten en/of lokale zwelling.
Aanvullend onderzoek heeft als doel de diagnose vaatmalformatie te stellen en het onderscheid te maken tussen low en high flow. Dit onderscheid is essentieel voor de keuze van behandeling. In principe is de eerste stap bij verdenking vaatmalformatie het verrichten van echografie. Hiermee kan de diagnose echter niet altijd bevestigd worden, aangezien andere vasculaire aandoeningen dezelfde echografische presentatie kunnen hebben. Eventueel kan met echo-doppler technieken het onderscheid tussen high en low flow gemaakt worden[4]. In deze casus werd de laesie niet gevonden of over het hoofd gezien bij echografie. Derhalve moet laagdrempelig verder radiologisch onderzoek ingezet worden in de vorm van MR diagnostiek.

Conventionele MRI biedt, zoals ook gedemonstreerd in onze casus, beperkte mogelijkheden om te differentiëren tussen de verschillende typen vaatmalformaties. Toevoeging van (al dan niet dynamische) contrast- enhancement (DCE-MRI) komt de waarde van het onderzoek echter zeer ten goede[10]. Met de komst van deze MR mogelijkheden met hoge sensitiviteit en specificiteit werden diagnostische angiografieën overbodig, en het is dan ook niet geïndiceerd dit invasieve onderzoek in te zetten.
CT heeft geen aanvullende waarde. Het nemen van een diagnostisch biopt is bij een vastgestelde vaatmalformatie niet nodig, tenzij de bevindingen bij echografie of MRI atypisch zijn. Soms worden in een vroeg analyse stadium conventionele röntgenopnamen gemaakt. Hierop kunnen dystrofische calcificatie van de spier, flebolieten in de vaten of aangrenzende botafwijkingen gezien worden. Röntgenopnamen hebben echter geen diagnostische waarde.
De behandeling van een vastgestelde veneuze malformatie bestaat uit (een combinatie van) conservatieve, radiologische of chirurgische interventies. Laesies die tot weinig klachten leiden kunnen conservatief behandeld worden met nachtelijke elevatie van het aangedane ledemaat, vermijden van activiteiten die tot klachten leiden en lokale compressie met een steunkous of elastische bandage. Het effect van deze interventies bij sporters die klachten hebben tijdens inspanning is niet onderzocht. Afhankelijk van de wens van de patiënt en de mate van klachten bij inspanning kan direct gekozen worden voor invasievere behandeling. Volledige resectie is de enige ingreep die recidief onmogelijk maakt. Chirurgisch ingrijpen leidt echter in veel gevallen tot onacceptabel grote defecten aangezien de laesies vaak invasief groeien en diverse spierloges of lichaamscompartimenten beslaan. Derhalve is sclerotherapie de laatste jaren steeds verder ontwikkeld als de eerste keus behandeling, ook voor diep gelegen laesies. Hierbij wordt een toxisch middel zoals polidocanol (aethoxysclerol 3%) of alcohol 98% direct in de malformatie gespoten, waardoor de laesie fibroseert. Sclerotherapie behandelt alleen de vaten die ingespoten worden, en neemt de onderliggende oorzaak niet weg, daardoor blijven recidieven (op lange termijn) mogelijk. Radiofrequente ablatie kan bij veneuze malformaties als alternatieve percutane behandeling gebruikt worden als sclerotherapie niet mogelijk is[12].
De frequentie van complicaties bij de sclerotherapeutische behandeling (Tabel 2) varieert in de geraadpleegde literatuur van 12 tot 40%, en is voornamelijk hoog bij het gebruik van ethanol[7,11]. De meeste complicaties komen voort uit de lekkage van sclerotans lokaal, in de systemische circulatie of in het longweefsel. Diverse alternatieve, minder agressieve sclerotiserende middelen en methoden met lager complicatierisico zijn bekend, zoals het gebruik van polidocanol.[7]

Tabel 2

Complicaties van percutane sclerosering

Lokaal	Systemisch
Weefselnecrose	Coagulopathie
Blaarvorming	Longembolie
Littekenvorming	Hemolyse
Vertraagde wondgenezing	Cardiovasculaire shock
Perifeer zenuwletsel	Longoedeem
Zwelling (compartimentsyndroom)	Hyperthermie
Infectie	Aritmieën
Pijn	

Om klinisch resultaat te krijgen zijn er vaak meerdere behandelsessies nodig. Afname van klachten binnen enkele weken na sclerosering wordt beschreven in 58-75% van de patiënten[7,11]. Het succes op lange termijn lijkt afhankelijk van het initiële succes, waarbij recidief voornamelijk optreedt bij patiënten die in eerste instantie niet volledig van hun klachten af waren[11]. Zorgvuldige informatievoorziening is essentieel bij deze behandeling met relatief hoog complicatierisico; aangezien de aandoening benigne is dient de patiënt op basis van goede counseling zijn/ haar keuze te maken.
De gevonden literatuur op het gebied van behandeling van veneuze malformaties betreft uitgebreide case series, maar geen case-control of cohortstudies. De tevredenheid van de patiënt op lange termijn is de belangrijkste uitkomst, echter dit is nog weinig onderzocht[11]. Grote gecontroleerde trials betreffende de beste techniek zijn niet voorhanden, mede omdat de gebruikte methoden afhankelijk zijn van het type malformatie. Behandeling dient dan ook te gebeuren in een centrum met ervaring en expertise op het gebied van deze interventieradiologie.

Conclusie

Veneuze malformaties zijn veelvoorkomende aandoeningen die in zeldzame gevallen bij sporters klachten geven. Het is echter een reële verklaring voor pijnklachten en lokale zwelling gerelateerd aan inspanning. Differentiaal diagnostisch moet gedacht worden aan myositis ossificans, ossale exostose, ingekapseld hematoom of andere (posttraumatische) musculaire pathologie en een weke delen of botmaligniteit. Lokale ingroei in bot of gewricht kan misleidende klachten geven, mede hierdoor kan er sprake zijn van een lange delay voor de diagnose wordt gesteld. De tijd tot sporthervatting kan door snelle analyse en therapie geminimaliseerd worden. De behandeling bestaat uit sclerotherapie, hierbij is het complicatierisico echter hoog. Adequate informatieverschaffing is van essentieel belang, en behandeling dient plaats te vinden in een centrum met de aanwezige expertise.

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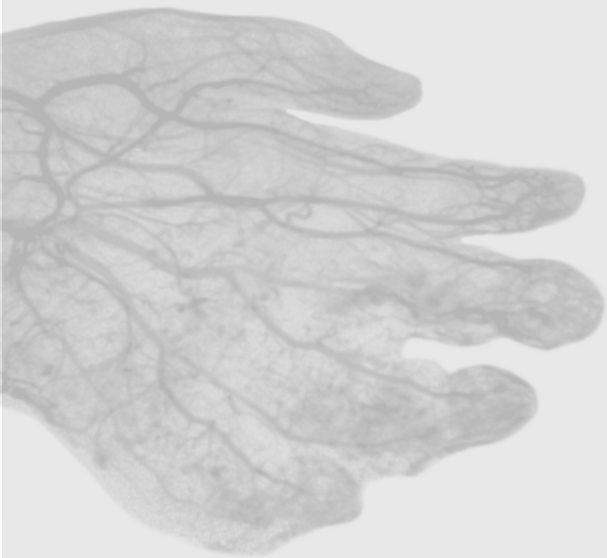
Chapter 8

Summary and Conclusions



Chapter 1 provides a general introduction to the thesis. This chapter reviews the classification, pathogenesis and histological findings, clinical presentation, and treatment of peripheral vascular malformations. Vascular malformations are developmental errors of the vascular system. Peripheral vascular malformations often require treatment because they tend to enlarge, which can cause pain, ulceration, severe deformity, and decreased function of the affected extremity. Surgery, interventional radiology, laser therapy or a combination of techniques are used in the treatment of vascular malformations. The planning of therapy depends on the subtype of the vascular malformation. Appropriate treatment of peripheral vascular malformations is only possible with adequate diagnosis and classification. With respect to the decision to intervene, it is important to take into consideration the level of patient morbidity and the expected level of risk related to the treatment.
This thesis reports the clinical effects of the percutaneous treatment of symptomatic peripheral vascular malformations and its complication rate. In addition, two special treatment options are evaluated for use in cases where other treatments are not possible.

In **Chapter 2**, conventional and dynamic contrast-enhanced MRI are evaluated to categorize vascular malformations by means of vascular dynamics. In this blinded prospective study, two observers independently correlated MRI findings for 27 patients with peripheral vascular malformations with the findings of diagnostic angiography and additional venography. The sensitivity and specificity of conventional MRI and dynamic contrast-enhanced MRI in terms of differentiating venous from nonvenous vascular malformations were determined. There was an excellent agreement between the two observers with respect to the determination of the MRI categories ($\gamma = 0.99$). The sensitivity of conventional MRI in differentiating venous and nonvenous malformations was 100%, whereas the specificity was 24–33%. The specificity was increased to 95% by the addition of dynamic contrast-enhanced MRI, but the sensitivity decreased to 83%.
Conventional and dynamic contrast-enhanced MR parameters could be used in combination to categorize vascular malformations. Dynamic contrast-enhanced MRI allowed the diagnosis of venous malformations with high specificity.

In **Chapter 3**, the clinical results of percutaneous treatment using sclerosing agents (sclerotherapy) and/or arterial embolization for peripheral vascular malformations (VMs) in 66 adult patients are presented. In this retrospective study, the patients were sent a questionnaire that assessed treatment effectiveness and patient satisfaction. Patient files and imaging data were retrieved to obtain information regarding the VMs and their treatment. The most frequent reasons that patients sought treatment were pain (89%, $n = 59$) and swelling (91%, $n = 60$). The majority of vascular malformations were of the low-flow venous type (83%, $n = 55$). Three months after treatment, clinical success was reported for 58% of the patients ($n = 38$) and clinical failure was reported for 42% ($n = 28$). At follow-up examinations at 1, 2, 3, 4, and 5 years, the rate of clinical success was 49%, 49%, 42%, 42% and 42%, respectively. Twenty-seven patients (40%) experienced complications, 12 of which required additional treatment. In all, 35 patients (53%) reported being satisfied with their treatment. Patient satisfaction was closely correlated with a successful long-term clinical outcome.
Percutaneous treatment of vascular malformations improved clinical symptoms in 58% of patients after 3 months and the results were durable at long-term follow-up (5 years) in 42%.

In **Chapter 4**, the clinical outcome of 23 patients younger than 19 years old who were treated for symptomatic vascular malformations was evaluated. In this retrospective cohort study, data on treatment outcomes and patient satisfaction were obtained using a precoded structured questionnaire. Patient files and imaging data were retrieved to obtain information regarding the vascular malformations and their treatment. The mean follow-up after the last treatment was 36 months (range 15–127 months). Following treatment, 87% (20/23; 95% CI 66–97%) of patients reported clinical success at 3 months. At follow-up examinations at 1, 2, 3, 4, and 5 years, this percentage was 74%, 59%, 59%, 59% and 59%, respectively. Eleven (48%; 95% CI 27–69%) patients had experienced complications and 22% (95% CI 7–44%) had major complications, for which five had required additional treatment. In all, 83% (19/23) of the patients reported that they were satisfied with the treatment.
Percutaneous treatment of vascular malformations improved clinical symptoms in 87% of patients after 3 months and the results were durable at long-term follow-up (5 years) in 59%. This was at the cost of a 22% incidence of major complications.

In **Chapter 5**, radiofrequency (RF) ablation is proposed as an alternative treatment option for patients with low-flow peripheral vascular malformations. Three patients with low-flow soft-tissue vascular malformations were treated with RF ablation after other treatment options had proven unsuccessful. After RF ablation treatment, two patients were free of symptoms and one reported decreased symptoms followed by a return of symptoms within 1 year. No procedure-related complications occurred.
It is suggested that RF ablation might be offered as an alternative treatment option for symptomatic vascular malformations when other types of treatment have failed or are not possible.

In **Chapter 6**, we describe retrograde transvenous ethanol embolization of high-flow AVMs as a technique to treat type II AVMs whenever conventional interventional procedures have proved inadequate. The clinical effectiveness of retrograde transvenous ethanol embolization and resulting complications were evaluated in five patients in this retrospective study. The clinical outcomes were good in all patients, but came at the cost of serious although transient complications in three patients.
Retrograde transvenous ethanol embolization is a highly effective therapy for type II high-flow AVMs, but because of the high complication rate it should be reserved for use as a last resort when conventional treatment options have failed.

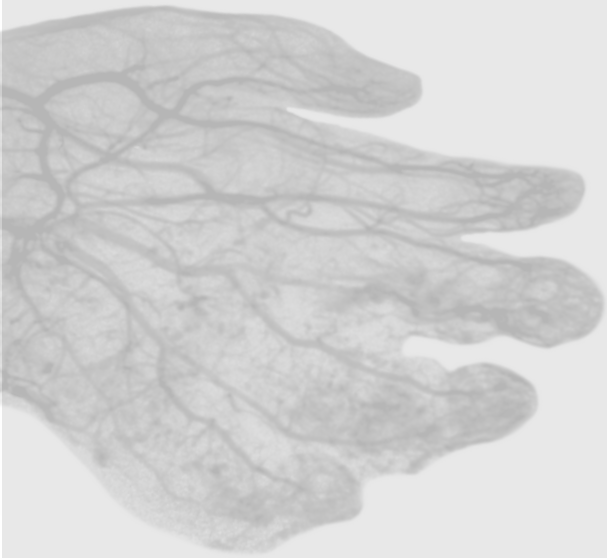
In **Chapter 7**, we present a case report of a talented female rugby player in whom a symptomatic venous malformation in the suprapatellar recess of the knee was treated with sclerotherapy. Vascular malformations can cause invalidating complaints in the sporting population; the clinical presentation is often atypical and frequently the diagnosis is made after a long delay.
The purpose of this case report was to show that after sclerotherapy the perspective of the patient with regard to her sporting career did not need to change.

Conclusion

Conventional MRI in combination with dynamic contrast-enhanced MRI is preferred in the diagnostic work-up of patients with vascular malformations. In combination, these techniques can be used to differentiate low-flow from high-flow vascular malformations, which is crucial for the planning of treatment.
Percutaneous treatment of vascular malformations improved clinical symptoms in 58% of adult patients and the results were durable at long-term follow-up (5 years) in 42% of patients. Patient satisfaction was related closely to clinical success. There is a considerable likelihood of complications occurring during treatment in 40% of adult patients; although most complications were mild and temporary, major complications occurred in 18% of patients.
The results of percutaneous treatment of vascular malformations in children were comparable with those in adults. In children, percutaneous treatment improved clinical symptoms in 87% of patients and these effects were sustainable for half of all patients over a 5-year follow-up period. Major complications were seen in 22% of patients.
RF ablation therapy can be used to treat symptomatic soft-tissue low-flow vascular malformations when other treatment options have failed.
Retrograde transvenous ethanol embolization is a highly effective therapy for type II high-flow AVMs, but because of the high complication rate it should be reserved for use as a last resort when conventional treatment options have failed.

Chapter 9

Samenvatting en Conclusies



Samenvatting

Hoofdstuk 1 is een algemene inleiding op het proefschrift. In dit hoofdstuk worden de classificatie, pathogenese, histologische bevindingen, klinische presentatie en behandeling van perifere vasculaire malformaties besproken. Het betreft een literatuur onderzoek waarbij we ons met name gericht hebben op de classificatie, genetische achtergronden en niet interventie radiologische behandelingen van vasculaire malformaties.
Vasculaire malformaties ontstaan door fouten in de ontwikkeling van het vasculaire systeem. De meeste vasculaire malformaties blijven subklinisch en geven geen klachten. Pas bij het ontstaan van klachten is een behandeling te overwegen. De belangrijkste klachten waarmee de patiënten zich presenteren zijn progressieve zwelling, pijn, ulceratie, cosmetische klachten, en bewegingsbeperking. Chirurgische, interventie radiologische, lasertherapie of gecombineerde technieken worden gebruikt bij de behandeling van vasculaire malformaties. De planning van de therapie bij een patiënt met een vasculaire malformatie is sterk afhankelijk van het subtype. Passende behandeling van perifere vasculaire malformaties is alleen mogelijk bij een adequate diagnose en classificatie. Bij het besluit om te behandelen is het belangrijk om rekening te houden met het niveau van morbiditeit en de verwachte omvang van het risico van de behandeling.
In dit proefschrift wordt de effectiviteit van de percutane behandeling van symptomatische perifere vasculaire malformaties geanalyseerd, met bijzondere aandacht voor de kans op complicaties van de behandeling. Verder bespreken we een tweetal alternatieve percutane behandelingsmethoden bij patiënten waar de reguliere behandeling niet mogelijk is.

In **hoofdstuk 2** wordt conventionele en dynamische MRI onderzocht ter karakterisering van vasculaire malformaties met betrekking tot hun vasculaire dynamiek. Dit werd prospectieve geanalyseerd in een groep van 27 patiënten met perifere vasculaire malformaties. MRI bevindingen werden door twee waarnemers onafhankelijk van elkaar bekeken en gecorreleerd van met de diagnostische angiografie. Aanvullende informatie werd gebruikt met een eventuele beschikbare flebografie van de vasculaire malformaties. Ter onderscheiding van veneuze en niet veneuze vasculaire malformaties werd de sensitiviteit en specificiteit van conventionele MR en dynamische MRI na toediening van gadolineum bepaald. We vonden een uitstekende overeenkomst tussen de twee waarnemers bij het classificeren van vasculaire malformaties in de verschillende subtypes met behulp van MRI ($\gamma = 0{,}99$). Sensitiviteit van de conventionele MRI in het onderscheiden veneuze en niet veneuze vasculaire malformaties was 100%, terwijl de specificiteit 24-33% betrof. Specificiteit werd verhoogd tot 95% door de toevoeging van dynamische MRI, maar dit ging ten koste van de sensitiviteit die dan daalt naar 83%.
De combinatie van conventionele en dynamische MR kunnen gebruikt worden om de verschillende subtypes van vasculaire malformaties te categoriseren. Met behulp van dynamisch MRI kan de diagnose van veneuze malformaties met een hoge specificiteit gesteld worden.

In **hoofdstuk 3** worden de klinische resultaten beschreven van percutane behandeling met behulp van scleroserende agentia (sclerotherapie) en/of arteriële embolisatie van perifeer gelegen vasculaire malformaties van 66 volwassen patiënten. Dit werd retrospectieve geanalyseerd waarbij patiënten een vragenlijst toegestuurd kregen met vragen over de behandeling, effectiviteit en tevredenheid. Informatie over de vasculaire malformaties en behandeling werden verkregen uit de patiëntendossiers en radiodiagnostische gegevens. De meest voorkomende indicaties voor het behandelen van de vasculaire

malformatie waren pijn (89%, *n* = 59) en zwelling (91%, *n* = 60). De meerderheid van de vasculaire malformaties betrof het lage flow, veneuze type (83%, *n* = 55). Drie maanden na de behandeling was de behandeling klinisch succesvol in 58% (*n* = 38) van de patiënten en niet succesvol voor 42% (*n* = 28) van de 66 patiënten. Na 1 -, 2 -, 3 -, 4 - en 5-jaar follow-up, was het klinisch succes respectievelijk 49%, 49%, 42%, 42% en 42%. Zevenentwintig (40%) patiënten melden complicaties van de behandeling, waarbij 12 patiënten aanvullende behandeling ten gevolge van de complicatie behoefde. Vijfendertig patiënten (53%) meldde tevreden zijn met hun behandeling. Tevredenheid over het resultaat van de behandeling was nauw gecorreleerd met klinisch succesvolle lange termijn resultaat van de behandeling.
Percutane behandeling van vasculaire malformaties verbetert 3 maanden na de behandeling de klinische symptomen in 58% van de patiënten en de resultaten zijn in 42% van de patiënten duurzaam op lange termijn (5-jaars follow-up).

In **hoofdstuk 4** worden de klinische resultaten van de behandeling van symptomatische vasculaire malformaties bij 23 patiënten jonger dan 19 jaar geëvalueerd. In deze retrospectieve studie werden de gegevens over de behandelingsresultaten en tevredenheid met behulp van een vragenlijst verkregen. Informatie over de vasculaire malformaties en behandeling werden verkregen uit de patiëntendossiers en radiodiagnostische gegevens. De gemiddelde follow-up na de laatste behandeling was 36 maanden (bereik 15-127 maanden). Drie maanden na de behandeling meld 87% (20/23, 95% CI 66-97%) van de patiënten klinisch succes. Na 1-, 2-, 3-, 4- en 5- jaar follow-up was dit percentage klinisch succes respectievelijk 74%, 59%, 59%, 59% en 59%. Bij 11 patiënten (48%, 95% CI 27-69%) traden complicaties op tengevolge de behandeling, waarvan 22% (95% CI 7-44%) ernstige complicaties. Vijf patiënten behoefde aanvullende behandeling ten gevolge van de complicatie. In totaal meldde 83% (19/23) van de patiënten tevreden te zijn met de behandeling.
Percutane behandeling van vasculaire malformaties geeft na drie maanden in 87% van de patiënten verbetering van de klinische symptomen en de resultaten zijn in 59% van de patiënten duurzaam op de lange termijn (5-jaar follow-up) Dit gaat echter ten koste van ernstige complicaties in 22% van patiënten.

In **hoofdstuk 5** wordt radiofrequente ablatie (RFA) voorgesteld als een alternatieve behandelingsoptie voor patiënten met perifere "low-flow" vasculaire malformaties. Drie patiënten met perifere vasculaire malformaties werden behandeld met RFA. Bij deze patiënten hadden andere behandeling niet geholpen of waren niet mogelijk. Na de RFA behandeling waren twee patiënten vrij van klachten. Een patiënt melde vermindering van symptomen gevolgd door terugkeer van de symptomen binnen 1 jaar. Er traden geen behandeling gerelateerde complicaties op.
RFA kan als een alternatieve behandelingsoptie worden aangeboden bij symptomatische vasculaire malformaties als andere therapieën hebben gefaald of niet mogelijk zijn.

In **hoofdstuk 6** beschrijven we retrograde transveneuze ethanol embolisatie van "high-flow" arterioveneuze malformaties (AVM's) als een techniek om type II AVM's te behandelen bij patiënten waar conventionele behandelingen onvoldoende hielpen. In deze retrospectieve studie werd de klinische effectiviteit en complicaties van de 5 patiënten behandeld met retrograde transveneuze ethanol embolisatie geëvalueerd. De klinische uitkomsten was bij alle patiënten succesvol. Echter bij 3 patiënten traden ernstige complicaties op. Retrograde transveneuze ethanol embolisatie is zeer effectieve therapie voor type II high-flow AVM, die vanwege de hoge percentage complicaties moet worden gebruikt, wanneer de meer conventionele behandeling opties hebben gefaald.

In **hoofdstuk 7** presenteren we een casus van een talentvolle vrouwelijke rugby speler die werd behandeld met sclerotherapie voor een symptomatische veneuze malformatie in de resessus suprapatellaris van de knie. Veneuze malformaties zijn aandoeningen die in zeldzame gevallen bij sporters klachten geven. De klinische presentatie is vaak atypisch mede hierdoor kan er sprake zijn van een lange vertraging voor de diagnose.
Het doel van deze casusbespreking was te laten zien dat bij deze patiënt na sclerotherapie van de vasculaire malformatie de toekomst verwachting niet hoefde te veranderen met betrekking tot haar sportloopbaan.

Conclusie
Conventionele MRI in combinatie met de dynamische MRI heeft de voorkeur in de diagnostische work-up van patiënten met vasculaire malformaties. In combinatie kunnen ze worden gebruikt om low-flow van high-flow vasculaire malformatie te onderscheiden. Dit onderscheid is cruciaal voor de therapie planning van vasculaire malformaties.
Percutane behandeling van vasculaire malformaties verbetert de klinische symptomen in 58% van de volwassen patiënten en de resultaten zijn in 42% van de patiënten duurzaam op lange termijn (5-jaars follow-up).
Tevredenheid over het resultaat van de behandeling was nauw gecorreleerd met het klinisch succes van de behandeling. Er is een aanzienlijke kans dat er complicaties optreden tijdens de behandeling. De kans op complicaties is 40% van de behandelde patiënten, waarvan de meeste mild en tijdelijk zijn. Ernstige complicaties treden bij 18% van de patiënten op.
De resultaten van de percutane behandeling van vasculaire malformaties bij kinderen zijn vergelijkbaar met de volwassen groep. Bij kinderen verbeteren de klinische symptomen na percutane behandeling in 87% van de patiënten. Deze verbetering was duurzaam voor de helft van alle patiënten over een 5-jaar follow-up periode. Ernstige complicaties werden gezien bij 22% van de behandelde patiënten.
Behandeling van vasculaire malformaties met RFA kan worden gebruikt bij patiënten waarbij andere behandeling opties gefaald hebben.
Retrograde transveneuze ethanol embolisatie is een zeer effectieve therapie voor type II high-flow AVM, die vanwege de hoge percentage complicaties moet worden gereserveerd als een laatste redmiddel, wanneer andere behandelingen niet helpen.

Curriculum Vitae

Edwin van der Linden is geboren in Leiden op 4 juli 1964. Hij behaalde het atheneum B diploma in 1984, aan de Louise de Coligny s.g. in Leiden. In datzelfde jaar begon hij met zijn studie geneeskunde aan de Rijksuniversiteit Leiden. Van april t/m juli 1990 doorliep hij zijn keuze coassistentschap op de afdeling radiologie van het LUMC, waar hij onderzoek deed naar het optimaliseren van het afbeelden van kraakbeen met behulp van MRI. Ook verbleef na zijn artsexamen in 1992 op dezelfde afdeling om mee te werken aan een zevental hoofdstukken van het text-atlas "MRI and CT of the musculoskeletal system" van J.L. Bloem en D.J. Sartoris. In april 1993 startte hij zijn opleiding tot radiologie in het LUMC te Leiden (Prof. Dr. A.E. van Voorthuisen en Prof. Dr. J.L. Bloem). Vlak na het beëindigen van de opleiding in april 1998 heeft hij een fellowship interventieradiologie voor een periode van drie maanden St Anthonius Ziekenhuis in Nieuwegein gevolgd. Direct na zijn opleiding trad hij toe tot de stafradiologie van het LUMC, aanvankelijk als interventieradioloog, later als hoofd van de sectie interventieradiologie. Van juli 2006 t/m juli 2008 heeft hij als interventie radioloog gewerkt in het Erasmus MC in Rotterdam (Prof.dr. G.P. Krestin). In deze periode heeft hij het meeste werk voor zijn promotie onderzoek verricht. In oktober 2008 trad hij toe tot de maatschap radiologie van het Medisch Centrum Haaglanden. Edwin van der Linden is getrouwd en heeft twee kinderen.

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