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EVALUATION OF THE LOWER LIMB VASCULATURE BEFORE FREE FIBULA FLAP TRANSFER. A PROSPECTIVE BLINDED COMPARISON BETWEEN MAGNETIC RESONANCE ANGIOGRAPHY AND DIGITAL SUBTRACTION ANGIOGRAPHY

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Introduction The aim of this study was to compare magnetic resonance angiography (MRA) with digital subtraction angiography (DSA) in the preoperative assessment of crural arteries and their skin perforators prior to free fibular transfer. *Patients and methods* Fifteen consecutive patients, scheduled for free vascularized fibular flap transfer, were subjected to DSA as well as MRA of the crural arteries of both legs ($n = 30$). All DSA and MRA images were assessed randomly, blindly, and independently by two radiologists. Each of the assessors scored the degree of stenosis of various segments on a 5 point scale from 0 (occlusive) to 4 (no stenosis). The Cohen's Kappa coefficient was used to assess the agreement between DSA and MRA scores. In addition, the number of cutaneous perforators were scored and the assessors were asked if they would advise against fibula harvest and transplantation based on the images. *Results* A Cohen's Kappa of 0.64, indicating "substantial agreement of stenosis severity scores" was found between the two imaging techniques. The sensitivity of MRA to detect a stenosis compared with DSA was 79% (CI95%:60–91), and a specificity of 98% (CI95%: 97–99). In 53 out of 60 assessments, advice on suitability for transfer were equal between DSA and MRA. The median number of cutaneous perforators that perfuse the skin overlying the fibula per leg was one for DSA as well as MRA ($P = 0.142$).*Conclusions* A substantial agreement in the assessment of stenosis severity was found between DSA and MRA. The results suggest that MRA is a good alternative to DSA in the preoperative planning of free fibula flap transplantation. © 2013 Wiley Periodicals, Inc. Microsurgery 33:539–544, 2013.

The fibula free flap has become the microsurgeon's workhorse for the reconstruction of osseus or osteocutaneous defects of the head and neck region,[1,2] trunk,[3,4] and extremities.[3–6] Peripheral arterial occlusive disease or congenital anomalies of any of the crural vessels may hamper its use because of potential insufficiency of the flap's peroneal vascular pedicle or impairment of the remaining anterior and posterior tibial vascular supply after harvest of these peroneal vessels.[7–9] To prevent these type of complications, preoperative assessment of the crural vascular supply is essential in free fibula flap candidates.[10,11] Among the various methods available to assess the vascular supply, conventional selective digital subtraction angiography is the generally accepted standard.[9,12–14] Some surgeons still rely on physical examination and the ankle-arm index, previous research has however shown that both are not accurate enough to detect legs or arteries with subclinical peripheral arterial occlusive disease or vascular variation.[11] Although angiography does have this ability, it is an expensive and invasive procedure featuring a morbidity rate of 0.5–3.9%, a complication rate of 3–5%, and a mortality rate of 0.03%.[7,15,16] Hence, a safer, and at least equally accurate alternative for routine preoperative angiographic assessment would be favorable.

Magnetic resonance angiography (MRA) is increasingly being applied in the assessment of crural arterial disease over the last few years.[17] Improvements of technology and protocols have allowed MRA to provide high levels of reliability in the detection of such arterial disease, as compared with digital subtraction angiography (DSA).[17] Still, this reliability has, to date, predominantly been assessed in patients with vascular disease. MRA has been proposed by some reconstructive surgeons as a method of vascular assessment prior to free fibular transfer in non-symptomatic patients,[18–20] but these series lacked a comparison to DSA. To date, we could only find two studies comparing DSA and MRA in free fibular transfer.[21,22] In these studies MRA was, however, made after the harvest of the fibular flap. Moreover, until now there has not been one study concerning the possibility to visualize skin perforators with DSA. There have been four studies trying to answer this question for MRA, however without comparing this method to other imaging technique available.[20,23–25]

The aim of this study was to compare MRA with DSA in the preoperative assessment of the crural arteries and its skin perforators prior to free fibular transfer.

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PATIENTS AND METHODS

Demographics

Over a period of three years 15 consecutive patients scheduled for free fibular transfer participated in thisstudy after they had provided oral and written consent. The population consisted of 12 men and 3 women with a median age of 49 year (range, 22–66 year). In all but one patient, fibula free flap transplantation was planned for mandibula reconstruction. In the remaining patient, the flap was planned for reconstruction of a defect in the humerus after resection of osteosarcoma ($n = 1$). In theincluded patients a DSA as well as a MRA was made of the crural arteries of both legs.

The study protocol was approved by the medical ethical committees of the Academic Medical Center and the Netherlands Cancer Institute-Antoni van Leeuwenhoek Hospital, Amsterdam (MEC 02/239 #03.17.0112).

Digital Subtraction Angiography

Following application of local anesthesia at the groin using 10 ml of mepiracain 2% without adrenaline (Scandicain; Astra Zeneca, Sodertalje, Sweden) puncture of the femoral artery was performed through either the ipsilateral or contralateral femoral artery approach. Via a 5-F introducer sheath (Terumo, Tokyo, Japan), a 5-F catheter (Berenstein; William A. Cook, Queensland, Australia) was placed at the level of the proximal popliteal artery. Selective DSA images were obtained from the distal thigh to the foot with use of a standard angiographic unit (Integris V-5000; Philips, Hamburg, Germany), and a 17- to 38-cm field-of-view image intensifier and a 1024 x 1024 display matrix or a comparable angiographic unit (Axiom Artis; Siemens, Erlangen, Germany). For these selective arteriograms, 15–30 ml of contrast agent (Accupaque 300; Bracco, Milano/Italy) was injected at a rate of 5–7 ml/second. The typical total volume of injected contrast material ranged between 28 and 40 ml. Anteroposterior and lateral views were chosen to best depict the arteries at the discretion of the interventional radiologist by using a field of view of 28–38 cm.

All angiographies were performed at the Department of Interventional Radiology of the Academic Medical Center in Amsterdam by the same investigator (KvL) to prevent bias.

Magnetic Resonance Angiography

The MRA's were made using a 1.5 T MR-scanner (Signa echospeed, General Electric Medical Systems, Milwaukee WI) using a phased array spine coil and the 9.0 software-release. The patients were positioned feet first in a supine position with the feet positioned in slight plantar flexion. Pillows and straps were used to prevent motion-artifacts. The legs were positioned in such a way that the field of view contained the entire lower leg from the joint space of the knee to the phalanges of the foot. This positioning took 10 min on average.

A 3D-Time-of-Flight (TOF) fast spoiled gradient sequence was used in a sagittal plane, featuring the parameters FA 35, TE 1.5 ms., TR 6 ms, FOV 46, slab thickness 3 mm,1.5 mm spacing, matrix 256 x 192, nex 1, rec FOV 0.8, zip 512. First, a nonenhanced basic series needed for the subtractions was obtained. Subsequently, 0.25 ml/kg of gadopentetate dimeglumine (Magnevist, Schering, Berlin, Germany) was administered by a power injector into the medial cubital vein with a flow-rate of 3 ml/s (maximum of 25 ml gadopentetate dimeglumine). Hereafter the cubital vein was flushed using 30 ml of saline 0.9% administered at the same flow-rate. Six identical consecutive series were made of the same field-of-view. With this technique no popliteal bolus timing is needed and the series with the most optimal arterial enhancement, without venous overprojection, can be chosen for evaluation. The actual scan time, including localizers, measured 6–8 min.

Subtractions were made of the six phases that each showed a different vascular filling dependent on the flow velocity and the extent of the proximal stenosis or occlusion. Multiplanar reconstruction (MPR) and maximum intensity projection (MIP)-reconstructions were made in anteroposterior, anterolateral, and posterolateral directions at the work station (General Electric Medical Systems, Milwaukee WI).

Assessment Protocol

All DSA and MRA images were assessed randomly, blindly and independently by two interventional radiologists with at least 6 years of experience with vascular imaging techniques. Each of the assessors scored the degree of diameter stenosis of the various segments of all three crural arteries as: 0 occlusion/aplasia; 1- severe stenosis (>50%); 2- moderate stenosis (25–50%); 3- light stenosis (<25%), 4- no stenosis; or 5- "not informative," e.g., because of movement, artifacts, or insufficient supply of contrast.

For this assessment, 11 segments of the crural arteries were distinguished: (1) the popliteal artery; (2) the tibioperoneal trunk; (3–11) the proximal, middle, and distal parts of each of the three crural arteries. The number of skin perforators of the peroneal artery was also scored.

In addition to the segmental scoring and the number of skin perforators, the assessors were asked to indicate for each leg and each angiography, be it the DSA or MRA, whether or not they advised against transplantation of a fibula free flap based on their assessment of the angiography. Criteria to advice against transplantation were a stenosis or occlusion of the anterior and posterior tibial artery or of the peroneal artery. Furthermore congenital anomalies at the trifurcation of the vessels were a reason to advice against transplantation.

Table 1. Overview of the DSA and MRA Scores, as well as the Scores Per Segment

		Stenosis severity					
		Occlusion/ aplasia (0)	Severe stenosis (1)	Moderate stenosis (2)	Light stenosis (3)	No stenosis (4)	Not-informative (5)
	Proximal	0	0	1	7	288	4
DSA	Middle	0	0	3	5	165	7
	Distal	0	1	3	10	117	49
	Total	0	1	7	22	570	60
	Proximal	0	0	0	14	286	00
MRA	Middle	0	0	1	11	168	0
	Distal	1	1	2	12	158	6
	Total	1	1	3	37	612	6

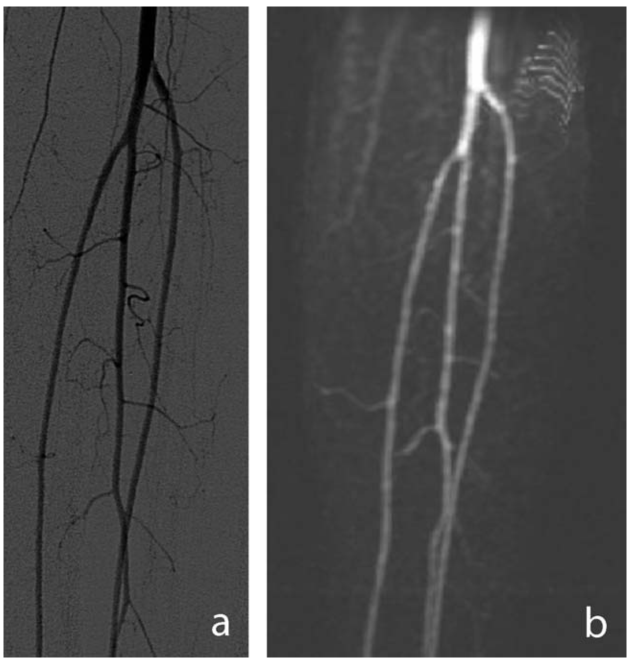

*Figure 1. DSA (**a**) and MRA (**b**) image of the same leg. Both images were scored as "no stenosis" for the shown segments, "no septocutaneous perforators," and "suitable for transfer."*

A total of 330 segments (30 legs x 11 segments) was scored by each assessor. One hundred and fifty out of those 330 segments were in the proximal section, 90 in the middle section, and 90 in the distal section. Given the two assessors, we compared a total of 660 scores per imaging method.

Data Analysis

When a segment was scored as "not informative" by an observer in either DSA, MRA or both groups, this segment was excluded from further analysis. Technique agreement and inter-observer agreement was assessed with Cohen's Kappa coefficient for the remaining scores. This coefficient can be interpreted as follow: 0–0.2 as little to no match, 0.2–0.4 as a fair match, 0.4–0.6 as a moderate match, 0.6–0.8 as a substantial match, and 0.8–1.0 as an almost perfect match.[26]

The scores were divided into two groups for calculation of the sensitivity and specificity of detecting a stenosis. The first group included the no stenosis scores (score 4). The second group included the occlusion/aplasia, severe, moderate and light stenosis scores (scores 0, 1, 2, and 3). For this calculation the DSA group was used as the gold standard.

The popliteal artery, the tibioperoneal trunk and the proximal thirds of the three crural arteries were referred to as "proximal segments". The middle thirds of the peroneal artery and the anterior and posterior tibial artery were referred to as "mid segments," and likewise the distal thirds of these three crural vessels as "distal segments".

The Wilcoxon signed-rank test was used to compare the number of skin perforators scored per leg. A P-value <0.05 was considered to be statistically significant. Statistical analyses were performed using IBM SPSS statistics version 19 (IBM Corporation, Armonk, NY)

RESULTS

DSA vs. MRA

With the use of DSA, 570 segments were scored as no stenosis, 22 as light stenosis, seven as moderate stenosis, one as severe stenosis. No segments were scored as being occluded. Sixty segments were judged as not-informative. In the MRA group 612 segments were scored as no stenosis, 37 as light stenosis, three as moderate stenosis. Severe stenosis and occlusion were both scored once, six segments were judged as not-informative. Cohen's Kappa for agreement was found to be 0.64 between DSA and MRA implying a substantial agreement of stenosis severity scores. A Cohen's Kappa for agreement between the two radiologist was found to be 0.55 implying a moderate match.

Total counts of stenosis severity scores per segment are shown in Table 1 for DSA and MRA. The counts are categorized by location (proximal, mid, and distal). An example of a DSA and a MRA of the same patient is depicted in Figure 1.

The sensitivity of MRA to detect a stenosis compared with DSA is 79% (CI95%:60–91). The specificity was found to be 98% (CI95%: 97–99).

Judgment of Suitability for Fibula Transfer

In 53 out of the 60 assessments, the opinions for suitability for fibula transfer were equal between DSA and MRA. Six legs were rated as suitable on MRA while unsuitable on DSA. One leg was rated unsuitable on MRA while suitable on DSA. In all legs that were rated as unsuitable for transfer on either DSA or MRA or both, fortunately the contra lateral leg was scored suitable for transfer on both DSA and MRA and was therefore used.

Skin Perforators from Peroneal Artery

The median number of skin perforators from the peroneal artery per leg was 1 for both DSA (range 0–3, mean 0.84 and of SD 0.96) and MRA (range 0–2, mean of 0.67 and SD of 0.61) ($P = 0.142$). The number of scored perforators per imaging technique is depicted in Figure 2.

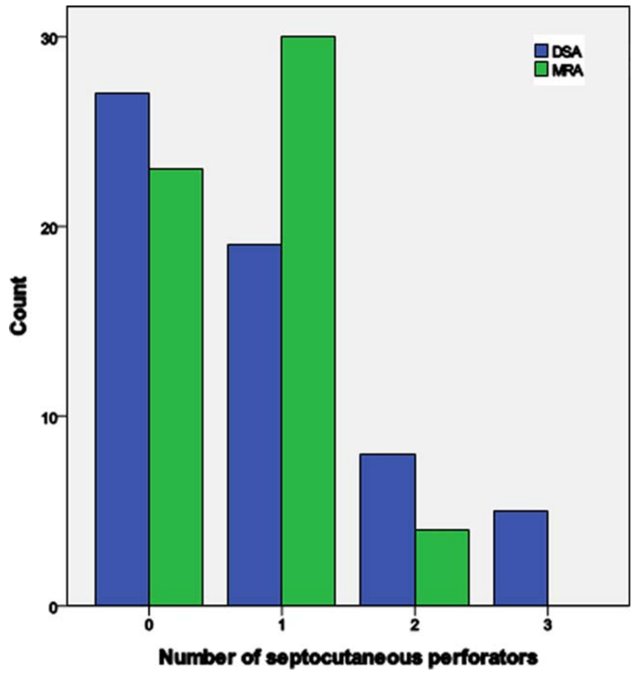

Figure 2. Number of perforators per leg for DSA and MRA. The horizontal axis shows the number of septocutaneous perforators scored per leg per imaging technique. On the vertical axis the number of times this was scored by the observers. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

DISCUSSION

The aim of this study was to compare MRA with DSA in the preoperative assessment of the crural arteries and its skin perforators prior to free fibular transfer. For this purpose we prospectively compared the MRA and DSA images of 15 patients. We found a substantial agreement (Cohen's Kappa 0.64) between DSA and MRA concerning the ability to detect and assess arterial stenosis and its degree. A sensitivity of 79% (CI95%:60–91) and a specificity of 98% (CI95%: 97–99) was found for MRA, relative to the gold standard DSA. In most cases there was an agreement for suitability for fibula transfer between DSA and MRA and the number of septocutaneous perforators scored was found not to differ significantly between DSA and MRA. No congenital anatomical vascular anomalies were observed by the two assessors in this series of nonsymptomatic patients. At the same time, the assessors felt that the imageof the crural vascular tree (poplitial, peroneal and anterior and posterior tibial arteries) on MRA was of such a good quality, that an abnormal branching pattern of the arteries would definitively have been detected by MRA. Compared wit DSA, no technical drawbacks were encountered with the use of MRA.

Ideally the sensitivity score should have been higher to safely conclude that MRA could replace DSA in the work-up of free fibula flap transfer. It should be noted that the majority of the assessed segments in our study had little or no stenosis, hence the rather wide range of the confidence interval for sensitivity 79% (CI95%:60–91). Higher sensitivities of over 95% for MRA have been reported in studies comparing MRA to DSA for peripheral arterial occlusive disease.[27,28] Moreover, the MRI, type of contrast, and software package used might have been of influence in the detection of stenosis.

The reasons for imaging prior to free fibular flap harvesting are to rule out (congenital) vascular anomalies and peripheral arterial occlusive disease, which can both jeopardize the viability of the harvested flap or the donor limb. Apart from DSA and MRA, other techniques such as colour duplex sonography (CDS)[29] and computed tomographic angiography (CTA)[30–33] have also been described for this purpose. CDS has been reported to be able to accurately map the crural vessels and cutaneous perforators. The advantages it offers are its low costs, no morbidity and detailed information about the flow in vessels.[29] Disadvantages are however that it is less reproducible because of its real life dynamics and that it does not lead to a 2D or 3D image like the other vascular imaging techniques.[34] CTA has been reported to accurately predicted the course and location of the peroneal artery and perforators as well. Like MRA the advantage of CTA is that it provides an accurate 3D image of the artery, its perforators and the surrounding anatomy. Compared to MRA, CTA is able to visualize vessels with a smaller diameter of up to 0.3 mm. A major disadvantage of CTA however is its use of radiation and the necessity to use iodinate contrast medium.[30–33] Especially the vasospastic action of the contrast medium is a serious drawback, because it can make the accurate assessment of small-calibre vessels difficult.[35]

A number of authors have reported their findings with the use of solely MRA prior to free fibula flap transfer.[18,20,23,24] Most were positive about the possibilities that MRA offers although there is discussion about the ability of MRA to detect skin perforators. In their prospective study Fukaya et al.[20] preoperatively investigated among others the number of skin perforators found on MRA. Among the seven patients included (seven legs), a total of 13 perforators were detected on the MRA, of which 12 were confirmed during surgery. Based on these findings they encourage the use of MRA prior to free fibula flap transfer. In their retrospective report Miller et al.[24] were less positive about the ability of MRA to detect septocutaneous perforators. They reviewed the radiological findings of 123 patients who underwent preoperative MRA as part of surgical planning for fibula free flap tissue transfer and compared these to intraoperative finings. Two patients were found to have a single perforator originating from the posterior tibial artery during surgery, while MRA suggested the perforators to arise from the peroneal artery. Analysis of the entire cohort demonstrated that agreement between the number of perforators documented on MRA and the number found intraoperatively approached zero (unweighted $\kappa = -0.088$, $P = 0.04$).

The report of Holzle et al.[22] in 2011 also compared DSA and MRA in the evaluation of the vessels of the lower leg in 15 patients scheduled for microsurgical fibular transfer. While in our study MRA and DSA was performed prior to surgery, in their study DSA was performed preoperatively and MRA postoperatively. Both techniques were used to compare vessel size at the trifurcation; hypoplastic or missing vessels; appreciable stenosis, vascular occlusions, and atherosclerotic malformations; and overall vascular anatomy of both limbs. With regards to vessel size, the results showed that for the operated lower leg the anterior and posterior tibial arteries were judged larger on the postoperative MRA than on the preoperative DSA ($P = 0.045$). In the nonoperated leg there was no difference. The findings with regards to the other variables were alike in their study. They concluded that high resolution MRA enabled a reliable judgment of the lower leg vessels equal to DSA. A drawback of the study of Holzle et al.[22] is however that the MRA was performed post-operatively; therefore, comparison of the DSA and MRA images of the operated legs is impossible.

In some studies the findings of MRA were compared with the intraoperative findings. We chose not to do this, since we only harvested the fibula from one side. Furthermore intraoperative findings are limited as well. Intraoperative findings do not give detailed information about all the involved arteries, the percentage of stenosis and potential variations in their course. They only give information about the site surgically assessed and is therefore, in our vision, not complete enough to use as reference.

More legs were scored unsuitable for transfers using DSA compared to MRA, two versus seven respectively. This could not be explained by the difference in scores of stenosis and occlusion/aplasia (scores 0, 1, 2, and 3 combined) between DSA and MRA as they were about equal, 29 versus 32, respectively. This difference was most likely caused by the higher number of segments scored as "not informative" in the DSA group, 60 versus 6, respectively. We choose to exclude these scores as they were often the result of technical difficulties or errors, for example by movement of the patient during the imaging. As we wanted to compare the outcome of both techniques and not the technical difficulties and errors we decided to exclude these scores from further analysis. However because of the fact that the score "not informative" was given ten times more often in the DSA group, this could be an argument to prefer MRA over DSA.

Strong points of our study were that prospective design as well as the random and blind assessment of all images, decreasing the chance on bias. Furthermore, DSA as well as MRA investigations were performed prior to surgery, in contrary to some of the study described above.[22] There are however also limitations. First of all the outcome of DSA and MRA were not compared to the "real" golden standard; the anatomy of each scanned individual. Because of obvious reason it is not possible to dissect the involved legs after performing the scans. As DSA has been the standard for years in the work-up of free fibula flap transfers, we chose to use DSA as the standard in our study and compare MRA to DSA instead of the other way around. It is however important to realize that in the comparison of two methods with one of them defined as the "golden standard" the other method can only score as good as, and definitely not better than the golden standard.

CONCLUSIONS

We found a substantial agreement between DSA and MRA concerning the ability to detect and assess the degree of arterial stenosis. In the majority of the cases there was an agreement for suitability for fibula transfer between DSA and MRA. The number of skin perforators scored did not differ significantly between DSA and MRA.

On the basis of the results of this study we believe that MRA is a good alternative to DSA in the preoperative work-up of free fibula flap transfers. It is less invasive, does not use nefrotoxic contrast mediums, and patients are not exposed to ionizing radiation. Although the sensitivity found in this study for the MRA should have ideally been higher, we believe that with current developments with regards to MRA this will only improve over the years.

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