Comparison of the efficacy of two different treatments for venous malformation with rapid drainage

SHIWEI YANG, PING LIU, LONG SUN, CHUNFANG HU and YINGXUE HAO

Department of Vascular Surgery, First Affiliated Hospital of Third Military Medical University (Army Medical University), Chongqing 400038, P.R. China

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Abstract. Venous malformation with rapid drainage is a common venous system disease, which is mainly manifested by the rapid return of blood to the lungs and heart with less oxygen. The present study aimed to examine the effects of digital subtraction angiography (DSA)-assisted interventional therapy and radiofrequency therapy assisted by ultrasound on venous malformation and to provide clinical evidence of the treatment efficacy for the selection of the optimal strategy. From September, 2018 to July, 2019, 41 patients with types II, III and IV venous malformations at the department of vascular surgery at the authors' institution were enrolled in the present retrospective study. Two different treatments were used: Coil embolization with sclerosing agent under DSA, and radiofrequency ablation with sclerosing agent under ultrasound guidance. The follow-up of the patients was conducted according to an established plan. The duration of the surgery, the duration of hospitalization, treatment cost, treatment efficacy and other clinical indicators were recorded in detail and comparatively analyzed. In the comparison of background characteristics and surgical information of the 2 groups of patients, significant differences were observed in the duration of surgery (P<0.001), post-operative hospital duration (P<0.001), treatment costs (P<0.001) and treatment efficacy between the 2 treatment methods (P=0.033) (all P-values were <0.05). On the whole, the present study demonstrates that DSA contrast-enhanced coil packing and sclerotherapy are associated with a longer duration of surgery, a more extended duration of hospitalization and a higher treatment cost compared with ultrasound-guided radiofrequency therapy; however, the treatment efficacy of DSA contrast-enhanced coil packing and sclerotherapy may be more advanced than that of ultrasound-guided radiofrequency ablation.

Correspondence to: Dr Yingxue Hao, Department of Vascular Surgery, First Affiliated Hospital of Third Military Medical University (Army Medical University), 30 Yanzheng Street, Gaotan, Shapingba, Chongqing 400038, P.R. China
E-mail: haoyingxue@hotmail.com

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Introduction

Venous malformations are common vascular malformations observed in clinical practice, mostly congenital venous dysplasia, with an incidence of approximately 1% in the population, of which approximately 7% of cases are adolescents. Superficial vascular malformations are mostly characterized by skin discolorations, with cyan-purple-colored lesions appearing on the skin. However, some venous malformations occur deeper into the muscle layer, and patients often exhibit symptoms of swelling and tenderness. As the boundary of the venous malformation is not clear, the curative effects of surgical resection are limited, and relapse is relatively common. Thus, the effective treatment of venous malformations has posed a significant issue in the field of vascular surgery (1,2).

According to Puig's classification (3), venous malformations are classified into the following 4 types: Type I, no obvious venous reflux; type II, normal venous reflux; type III, thickening of the venous reflux; type IV, vascularization and thickening of the malformation cavity. Simple sclerotherapy for type I malformations can achieve good therapeutic outcomes. However, as some type II, III and IV malformations exhibit rapid venous reflux, good therapeutic outcomes cannot be achieved with sclerosing agent alone. Increasing the dose of the sclerosing agent also increases the risk of complications. However, traditional surgical resection is gradually retiring from the first-line treatment, since it is easy to cause skin flap edema post-operatively, as well as necrosis and a high recurrence rate (4,5). For the treatment of such venous malformations, in recent years, percutaneous coil packing + anhydrous ethanol treatment has been gradually used in clinical practice, which has a definite effect and is widely accepted by experts. However, the surgery involves interventional procedures, and has absolute contraindications for patients allergic to contrast agents (6). With the application of certain novel medical devices, the application of radiofrequency (RF) ablation in the treatment of venous malformations has been frequently reported. This method is minimally invasive and is currently favored clinically. Note that when the lesion is adjacent to the nerve area, radiofrequency surgery is associated with a risk of direct thermal injury to the nerve and post-operative neuroedema (7).

Based on previous cases of venous malformations treated by ultrasound-guided RF in the department of vascular surgery at the authors' institution, the present study compared the clinical data of patients who underwent coil packing and sclerosing agent injection guided by conventional digital subtraction angiography (DSA) in the same period, aiming to explore the therapeutic effects of the 2 different methods in type II, III and IV venous malformations.

Patients and methods

Study subjects. From September, 2018 to July, 2019, 53 patients with type II, III and IV venous malformations were admitted to the Department of Vascular Surgery, Southwest Hospital of Army Medical University. According to the inclusion and exclusion criteria (Table I), 41 patients were finally enrolled in the present study, including 16 males and 25 females, aged between 6-45 years, with an average age of 26.40±6.35 years. The procedures and the complete treatment process were explained in detail to the patients and their family members, including the complications and associated costs; the surgical method used for each patient was selected by the patients themselves. Both treatment methods were explained in detail to the patients and each patient voluntarily selected the treatment option. All surgeries were performed by physicians with intermediate professional titles or above at the department of vascular surgery who had been engaged in vascular surgery or related specialties for >5 years. After obtaining informed consent for participating and publishing the images with their features from all patients, the study protocol was approved by the Ethics Committee of Southwest Hospital of Third Military Medical University.

Treatment strategies

i) Percutaneous or arterial coil packing + anhydrous ethanol treatment. The surgery was performed in the DSA room, and patient was placed in a supine position. In the case of a dorsal malformation, the patient was placed in prone position during the surgery. Following general anesthesia, routine disinfection and draping were performed. Iodixanol contrast agent (Visipaque, GE Healthcare) was used. In total, 17 patients underwent routine catheterization angiography from the femoral artery and trans-arterial angiography. A total of 12 patients exhibited no obvious femoral artery pulsation touched on the body surface. As there may be individual differences in the morphology of femoral artery in anatomy, ultrasound is needed to locate the femoral artery. According to the size of the malformation nest and the diameter of the drainage vein, the diameter and quantity of the coils (Visipaque, GE Healthcare) placed were determined for tamponade. The total volume of anhydrous ethanol was controlled at 0.5 ml/kg body weight (some small veins were injected with 1% polidocanol). Anhydrous ethanol emulsifier (anhydrous ethanol:iodized oil, 5:1 v/v) was injected into the malformation cavity under DSA fluoroscopy, and the injection was terminated after the malformation cavity was filled with contrast agent under fluoroscopy (8). Using anhydrous ethanol with lipiodol was instrumental in thrombus formation by local anesthesia injection, facilitating the surgical process.

ii) Radiofrequency ablation + sclerotherapy. All patients who underwent RF were first localized in the ultrasound department to draw a brief diagram. Detailed information, such as drainage vessel and the diameter of the vessel, were indicated on the body surface. The surgery was performed during the day in an operating room. The patient was placed in a supine position. The surgical site was routinely disinfected and draped. Local anesthesia was performed at the radiofrequency site. The drainage vein was examined by ultrasound, and a radiofrequency needle was inserted after confirmation. The tip of the needle was approximately 1 cm away from the normal vein for radiofrequency ablation. After the drainage vein was closed by ultrasound, the other drainage veins were again closed by ablation. In the post-operative ultrasonography, sclerosing agent was percutaneously injected (lauromacrogol or 3% polidocanol) if venules with blood flow signals were found (9).

Evaluation of treatment efficacy. The duration of the surgery, treatment costs, blood loss, duration of hospitalization and other routine clinical indices were recorded in detail. Patients were requested to revisit the hospital for re-examination at 2 weeks, 1 month, 36 months and six months post-operatively. The follow-up period was completed in January, 2020. Symptoms, pain degree, and the number and diameter of the malformation cavity were recorded in detail. The criteria for the evaluation of the efficacy of the treatments were as follows: i) Effective: The malformation cavity continued to shrink, symptoms were alleviated, 6 months after the re-examination of ultrasound or contrast it was found that the malformed blood vessels had disappeared, and the patient reported that the symptoms had improved. If patients with recurrence were found at the re-examination, and the above curative effects were achieved after retreatment, treatment was regarded as effective; ii) Ineffective: Malformed blood vessel malformation existed, symptoms were slightly alleviated or not obvious. Malformed blood vessels could still be observed at re-examination by ultrasound or magnetic resonance. Changes in symptom reported by the patients were not significant. The effective rate was calculated as follows: Effective rate=effective cases/total no. of patients, as previously described (10).

Statistical analysis. Measurement data are expressed as the means ± standard deviation, and comparative analysis was performed using an independent samples t-test or Mann-Whitney U test. Enumeration data are expressed as a percentage (%) and the Chi-squared (χ^2) test was used for comparative analysis. All data were analyzed and processed using SPSS 19.0 software. $P<0.05$ considered to indicate a statistically significant difference.

Results

A total of 41 cases were included in the present study, of which 12 were treated with radiofrequency ablation of the drainage vein and sclerotherapy, and 29 were treated with DSA-assisted coil packing and sclerotherapy. All patients were safely discharged without any severe post-operative complications.

Comparison of clinical data in general. Under the guidance of DSA, the average duration of surgery was 96.34±19.68 min,

Table I. Inclusion and exclusion criteria used in the present study for patient selection.

Inclusion criteria	Exclusion criteria
1. Patients who fully understand the purpose of the study, and actively cooperated with the therapist 2. Complete relevant clinical data 3. Post-operative regular reexamination and complete related data	1. Patients with other severe diseases and contraindications related to ultrasound or angiography (4 patients) 2. Incomplete relevant clinical data (5 patients) 3. Those who refused to cooperate with this study (1 patient) 4. Loss to follow-up (2 patients)

Table II. Statistical data of the clinical cases (n=41).

Information parameter	Radiofrequency group (n=12)	Spring coil group group (n=29)	P-value
Age (years)	27.33±7.86	26.19±5.62	0.896
Course of disease (months)	28.96±8.24	30.13±8.75	
Sex			0.99
Male	5 (12.2%)	11 (26.8%)	
Female	7 (17.1%)	18 (44.0%)	
Site of malformation			0.497
Head and neck	4 (9.7%)	13 (31.7%)	
Trunk and limbs	8 (19.5%)	16 (39.0%)	
Puig's type			0.234
II	6 (14.6%)	9 (21.9%)	
III	6 (14.6%)	15 (36.6%)	
IV	0 (0%)	5 (12.2%)	
Duration of surgery (min)	40.08±7.15	96.34±19.68	<0.001
Blood loss (ml)	7.5±3.1	10.1±2.9	0.121
Duration of hospitalization (days)	1.0±0.0	4.4±1.3	<0.001
Cost of treatment (USD)	1,424±136	2,803±364	<0.001
Post-operative pain	6 (50.0%)	13 (44.8%)	0.763
Dose (ml)	9.0±1.5 (stiffening agent)	7.0±3.5 (anhydrous ethanol)	0.319

the bleeding volume was 10.1±2.9 ml, the treatment cost was 2,803±364 USD, the average number of coils was 7.3 and anhydrous ethanol use was 7.0±3.5 ml. In total, 13 patients complained of pain post-operatively, and the pain was relieved following the injection of painkillers, and the average duration of hospitalization was 4.4±1.3 days. At 3 months post-operatively, 4 patients were still found to have malformed blood vessels upon re-examination. Ultrasound examination revealed blood flow signals in the malformation cavity.

As regards the drainage venous radiofrequency ablation + sclerotherapy group, the average duration of surgery was 40.08+7.15 min, the bleeding volume was 7.5±3.1 ml, the treatment cost was 1,424±136 USD, the average puncture point was 4.4 and polyethylene glycol (foam) use was 9±1.5 ml. In total, 6 patients complained of pain post-operatively, and 8 patients exhibited ecchymosis or pigmentation on their skin. The day ward model was adopted. The patients remained in hospital for 1 h post-operatively, and were discharged without any adverse reactions. In the post-operative reexamination, thrombus formation was observed in 4 cases, and the pain of pressing was relieved slightly after a wet compress of 50% magnesium sulfate solution was used, and blood flow signal was found in 9 cases. The detailed results of the 2 treatments are presented in Table II.

Comparison of the efficacy of the 2 treatments. The effect of DSA-guided coil packing on the treatment of venous malformations is definite. In particular, in the treatment of more complex venous malformations, the drainage speed of the vein is reduced to the greatest extent through the filling of the spring coil. Only a small amount of deformed blood vessels cannot be placed with the spring coil; thus, the injection of anhydrous ethanol or polidocanol is necessary (Fig. 1). In the present study, there was only one case of dorsal vascular malformation. After placing multiple coils through multiple approaches, the abnormal vessels were still observed in the angiography. It was not excluded that the coils were not accurately placed in the malformation nest due to some intraoperative causes (Fig. 2). The statistical data indicated that the overall treatment efficacy was 96.5% (28/29, Table III).

Ultrasound-guided radiofrequency ablation has a positive effect in the malformation nest with clear drainage vein and

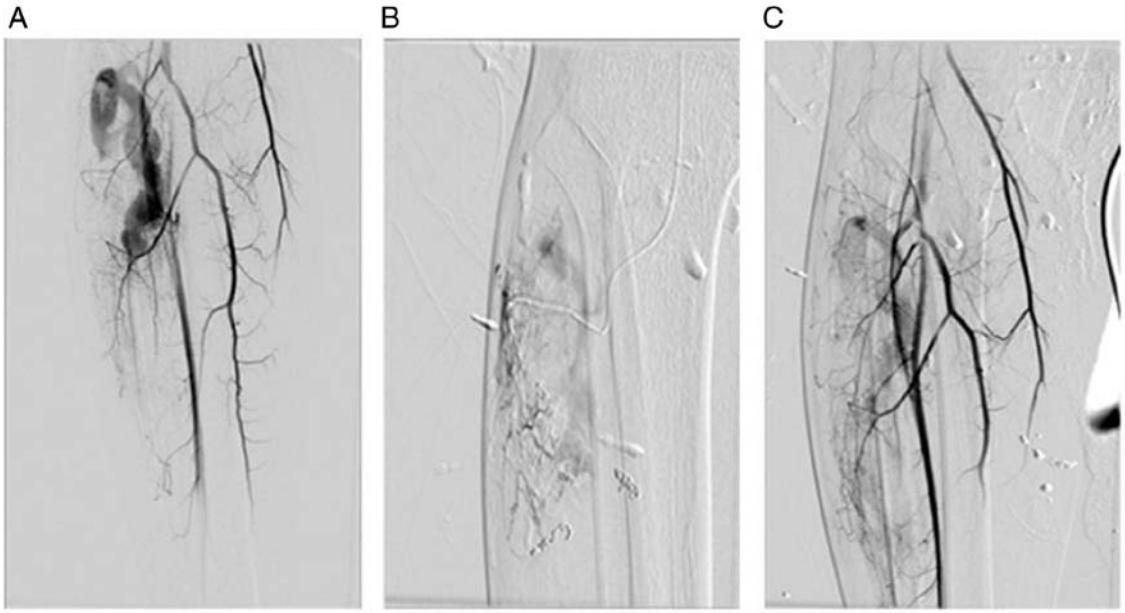

Figure 1. Interventional treatment of venous malformations in the lower extremities. (A) Large draining veins could be observed in the pre-operative period. (B) Coil packing + a small amount of anhydrous ethanol injection. (C) Post-operative angiography revealed that the drainage vein had disappeared.

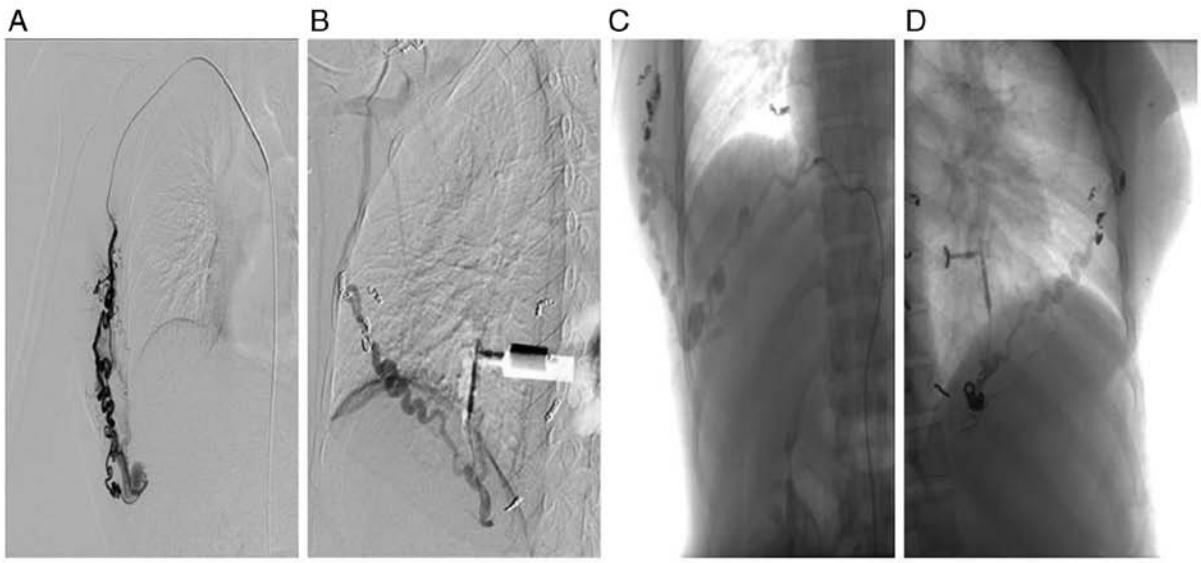

Figure 2. Interventional treatment of dorsal vascular malformations. (A) Pre-operative angiography revealed obvious malformed vessels. (B) Intraoperative coil packing via the subclavian artery. (C) The malformed blood vessels were still visible in the intraoperative transcostal arteriography. (D) Spring coils and anhydrous ethanol injection were performed again following percutaneous puncture.

is easy to identify by ultrasound. The specific cycles of the ablation process are determined by the sensitivity of venous malformation to ablation. In the present study, the surgery was conducted in 12 patients. In a case of venous malformation on the right side of the face, ultrasound revealed that several malformation nests connected with the external jugular vein through a drainage vein. Under guidance, the malformation cavity was closed by radiofrequency and treated with a small amount of sclerosing agent, achieving good results (Fig. 3). However, it was less effective on more complex venous malformations. For example, in a case of venous malformation in the buttock, given the large consumption of coils and increased costs, radiofrequency ablation was used; however, the surgery aggravated the ulcer. The patient complained of buttock pain, and the abnormal blood vessels did not evidently disappear in the post-operative angiography (Fig. 4). In addition, there were 3 patients with recurrent deformities at only 1 week post-operatively, which required radiofrequency again. The statistical data indicated that the overall treatment efficacy was 66.7% (8/12, Table III).

Discussion

Type II, III and IV venous malformations exhibit rapid blood reflux speed. During treatment, it is necessary to block the drainage vein first, attenuate the flow rate and then inject

Table III. Comparative analysis of the treatment efficacy of the 2 methods used.

Therapeutic method	Therapeutic outcome		P-value
	Effective	Ineffective	
Radiofrequency group	8	4	0.033
Spring coil group	28	1	

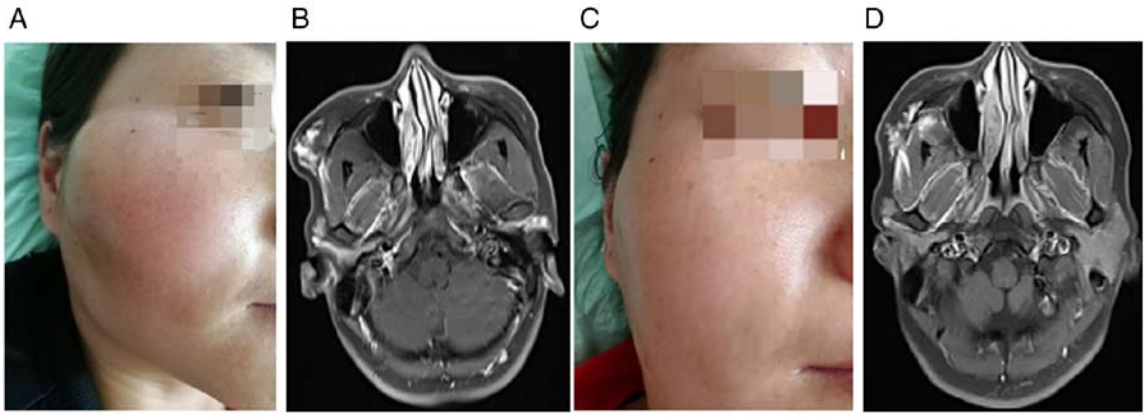

Figure 3. Radiofrequency + sclerotherapy for facial vascular malformations. (A) Facial mass was observed preoperatively. (B) Magnetic resonance revealed venous malformations. (C) The mass disappeared at 3 months post-operatively. (D) Magnetic resonance revealed that the mass had disappeared 3 months post-operatively.

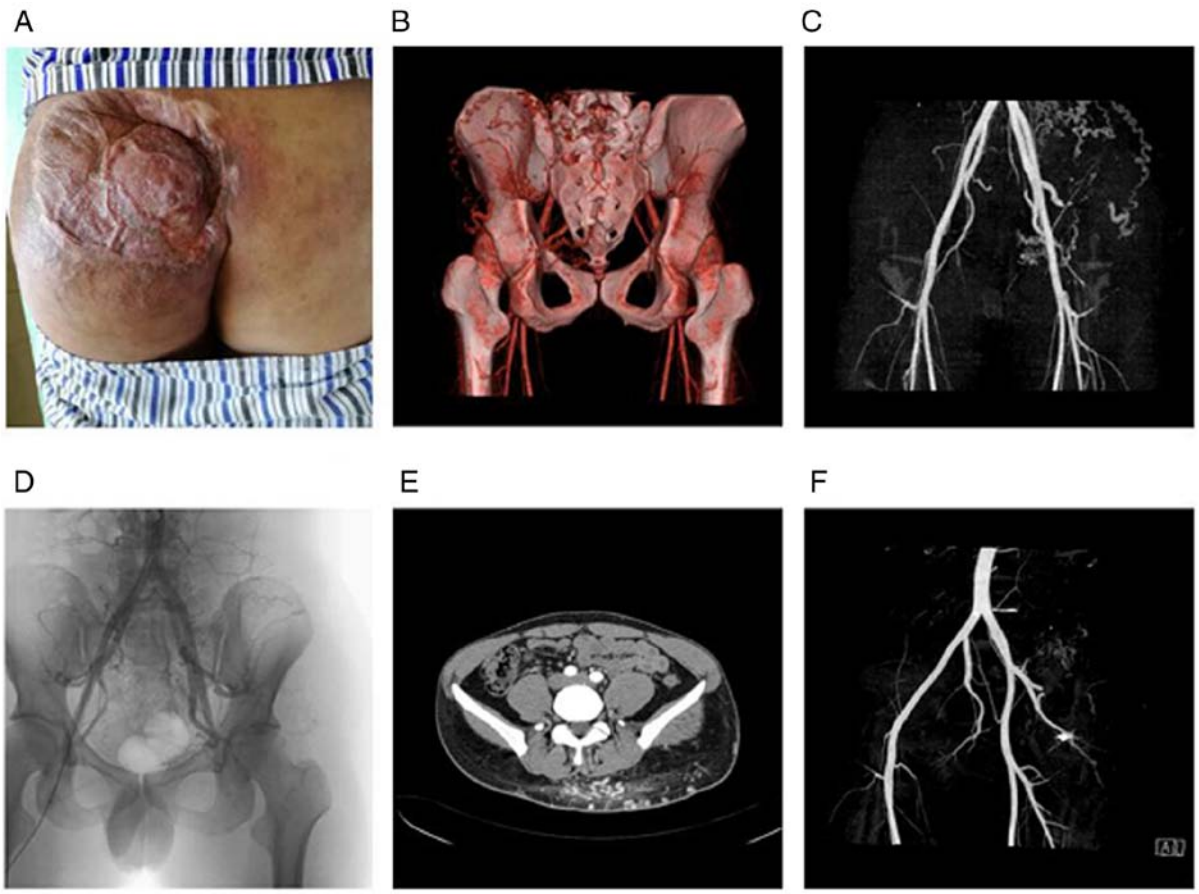

Figure 4. Buttock vascular malformations with radiofrequency and sclerotherapy. (A) Large area ulcer in the buttock could be observed pre-operatively. (B) Pre-operative CTA and 3D imaging. (C) Pre-operative CT examination. (D) Imaging at 6 months post-operatively. (E) CT examination at 6 months post-operatively. (F) CT examination at 6 months post-operatively.

sclerosing agent to achieve an opitmal effect. The current schemes of sealing drainage vein include surgical incision and ligation, endoluminal spring coil embolization, percutaneous puncture and spring coil packing, as well as ultrasound-guided radiofrequency ablation of drainage vein (11). The authors used this procedure to treat some patients in the early stages and did not obtain good feedback on the effect. However, it remains controversial whether all cases are suitable for coil embolization. The aim of the present study was to explore the curative effects of these 2 types of surgery for venous malformations by comparing cases undergoing ultrasound and with those of radiofrequency in the same time period, which provided reference for the clinical treatment of the disease.

In the present study, the general clinical data were mainly compared, such as the duration of surgery, treatment costs and the duration of hospitalization. Through the comparison it was found that regardless of the treatment cost or duration of surgery, the duration of hospitalization of ultrasound-guided radiofrequency was much lower than that of DSA, as the radiofrequency could be completed under local anesthesia, and the trauma was small. However, DSA surgery requires the puncture of the femoral artery; thus, the surgical risk is relatively high. This is also the advantage of ultrasound-guided radiofrequency therapy. As the majority of the enrolled patients were cured after the first treatment, the frequency of second surgery was low and it was slightly difficult to perform a comparison. In the present study, it was considered that both treatment methods were suitable for almost all the venous system diseases if no surgical contraindications are identified.

Treatment efficiency is the core index for the evaluation of a treatment. In the present study, the efficacy of 2 groups of cases was evaluated, referring the criteria for treatment efficacy in the treatment guidelines for vascular malformations (12). The overall treatment efficacy of DSA-guided venous malformation treatment was much higher than that of radiofrequency. Under DSA, each drainage vein is clearly displayed, including key information, such as drainage blood speed, drainage vein diameter, etc. In the treatment process, the spring coil can also be placed at the critical site accurately. After the blood flow speed is reduced, the injection of a sclerosing agent and effective compression can achieve a good treatment effect. The reference vein diameter is used to select the sclerosing agent. For the malformation nest with a diameter >5 mm, anhydrous ethanol is generally used. For a small one, foam sclerotherapy is used, which has also been widely accepted by experts (7). The key point of the procedure is to place the spring coil in the correct position. Whether through direct percutaneous puncture to the malformation nest or through the femoral vein approach, the key is to fill the malformation nest with a suitable diameter and a sufficient number of coils. Spring coil tamponade under DSA angiography is a reliable method for the treatment of vascular malformations at present. Although the relevant reports may differ in the selection of approach, auxiliary sclerosing agent, embolic material, the surgical method and treatment principle are consistent (13).

With the popularization of radiofrequency, some medical institutions have carried out ultrasound-assisted radiofrequency ablation for the treatment of venous malformations; however, the efficacy and indications remain unclear (9). The authors' department has carried out radiofrequency in 12 cases of vein malformations; however, the overall effect was worse than DSA. Ultrasonography has great limitations; thus, it cannot clearly reveal the specific information of each malformed blood vessel, and cannot accurately guide the direction and depth of the radiofrequency needle. Due to the high heat production of the needle, it causes edema of the surrounding tissues and compresses other malformed blood vessels. After the swelling disappears, revascularization occurs, which is consistent with the reports from other institutions in China (14). In the present study, in this group, 3 patients experienced recurrence and the reappearance of malformation at 1 week post-operatively, indicating that radiofrequency has great limitations in the treatment of venous malformations. It may however, be effective for venous malformations with a small number of malformations and clear layers. However, it had a limited effect for more complex venous malformations, and the recurrence rate was higher than that of coils under DSA angiography.

In the application of radiofrequency in the treatment of venous malformations, some scholars consider that for complex venous malformations, spring coil combined with radiofrequency can achieve a better curative effect. Given the complexity of venous malformations, available studies to date do not provide clear indication criteria (15,16). However, some scholars consider that multiple radiofrequency treatments can achieve good results. Generally, the interval between each treatment is approximately 2 weeks. Through ultrasound, radiofrequency is applied immediately after identifying the draining vein. In the present study, this method was also used to treat 1 patient, achieving good results. At present, scholars in China in related fields still have different opinions on the indication of radiofrequency for venous malformations; thus, further clinical research is warranted on this matter to clarify all the related issues (17).

The present study still has some limitations: Firstly, the sample size included was small, and thus the statistical analysis results may be biased, limiting the credibility of the findings. Secondly, the present study was designed and carried out in a single center and thus, heterogeneity was inevitable. The accuracy of the evaluation of surgical efficacy under the guidance of the same standard at the same department may be lower than that in a multi-center study. Thirdly, the present study was a non-randomized controlled retrospective study, and the evidence of the reliability of evidence-based medicine was relatively weak. It should be noted that in the collection of previous data, a small number of patients were not enrolled in the study due to incomplete clinical data. It is worth considering whether these data would have provided different results if they were included in the statistical analysis (18,19).

In conclusion, the present study suggests that coil packing under DSA angiography has obvious advantages in the treatment of venous malformations, particularly for complex type III and IV venous malformations. For type II venous malformations with obvious relative malformed vessels, radiofrequency ablation can be used.

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Availability of data and materials

All data generated or analyzed during this study are included in this published article or are available from the corresponding author on reasonable request.

Authors' contributions

SY was involved in the study design, data acquisition, data analysis and interpretation, statistical analysis, manuscript writing and drafting, manuscript editing and manuscript reviewing. PL was involved in the study design, data acquisition, and manuscript writing and drafting. LS was involved in data acquisition, data analysis and interpretation, statistical analysis and in revising the manuscript. CH was involved in data analysis and interpretation, statistical analysis, and in the writing and editing of the manuscript. YH was involved in the study design, manuscript writing and drafting, manuscript editing, manuscript revising and manuscript reviewing. All authors read and approved the final manuscript.

Ethics approval and consent to participate

The study protocol was approved by the Ethics Committee of Southwest Hospital of Third Military Medical University. Written informed consent was obtained from all patients.

Patient consent for publication

Written informed consent was obtained from the patients for participating and publishing the images with their features.

Competing interests

The authors declare that they have no competing interests.

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