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Efficacy and safety of embolo-sclerotherapy of arteriovenous malformations with foam sodium tetradecyl sulphate

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Abstract

BACKGROUND:

To evaluate the efficacy and safety of embolo-sclerotherapy (EST) particularly with foamed sclerotherapy in the treatment of arteriovenous malformations (AVMs).

METHODS:

All patients with AVM who underwent interventional therapy i.e. EST from January 1st, 2015 – December 31st, 2019 were identified through a prospective database. Types of AVM were classified according to Schobinger's classification. The outcome measures assessed efficacy and complications. The former was divided into four groups: no response, mild response, moderate response, and complete response.. Complications were defined as any tissue or functional damage, distal embolization or tissue reaction. Continuous variables were compared using analysis of variance (ANOVA) F test and discrete variables were analysed using Chi-squared tests. $P < 0.05$ was considered significant.

RESULTS:

A total of 65 patients were included. There was no statistical difference amongst the volume of foam STS 3% or alcohol used across all types of AVM. Overall, majority of patients (86.2%) reported some degree of improvement following interventional therapy. Six (9.2%) patients experienced complications including necrosis and amputation. The proportions of complication were significantly different across the categories ($p=0.009$). Patients with type III AVM seemed to report more complications than others.

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CONCLUSIONS:

Foam sclerotherapy was clinically effective and safe for patients with AVM. This study showed that foam sclerotherapy with STS 3% provided a safe and efficacious alternative sclerosant to ethanol despite it was not often reported to be used to treat AVM. However, a combination of embolic agents is likely required to treat type IV AVMs.

Keywords

Interventional therapy, embolo-sclerotherapy, arteriovenous malformation, foam sclerotherapy

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Introduction

Congenital vascular malformations have a worldwide prevalence of 0.3-1.5% (1) These lesions occur during early vascular development, resulting in dysplastic abnormally formed vessels that consist of arteries, veins, capillaries or lymphatics or a combination of these (1–3). Arteriovenous malformations (AVMs) are lesions with an arterial component, hence high flow, and constitute approximately 10% of congenital vascular malformations (1).

Recently, embolo-sclerotherapy (EST) with the aim of complete occlusion of the nidus is increasingly considered as the mainstay intervention for AVM (4). Commonly used EST agents for AVM include metallic coils, ethanol, and n-butyl cyanoacrylate (5,6). Ethanol, the main liquid sclerosant used to treat AVMs, has been shown to be effective with acceptable risks when used by experienced operators (7–11). Meanwhile, the literature on the efficacy and safety of the use of surfactant sclerosants such as sodium tetradecyl sulphate (STS) and polidocanol on AVMs is scarce. The surfactant sclerosants which induce thrombosis, intimal necrosis and fibrosis are often used to treat venous and lymphatic vascular malformations instead. They are often converted to foam because of its increased viscosity leads to greater “dwell-time”, endothelial contact, and higher effectiveness per unit dose (12). Therefore, the aim of this study was to evaluate the efficacy and safety of EST as the mainstay interventional treatment for AVMs, with a particular focus on foamed STS 3% as the sclerosant of choice based on the experience of a single specialist vascular anomalies centre.

Methods

This is a retrospective audit study of a prospectively collected departmental database, with no patient identifiable data used, that was approved by the local clinical audit and governance committee.

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Embolo-sclerotherapy

All patients referred to our centre with non-central nervous system AVM underwent evaluation by a multi-disciplinary team consisting vascular surgeons, interventional radiologists, and a clinical nurse specialist who subsequently directed decisions on intervention. All ESTs were carried out by consultant interventional radiologists and/or consultant vascular surgeons with subspecialty interest and training in treating vascular anomalies. EST was our favoured treatment for patients with rapidly growing and/or symptomatic AVM, which included pain, disfigurement, pressure effect, ulceration, bleeding, ischemia, and cardiac failure. Patients with asymptomatic or minimally symptomatic lesions, which were stable in size, were managed conservatively. Pre-procedural cross-sectional imaging i.e. computed tomography (CT) and/or magnetic resonance (MR), with or without duplex ultrasonography were performed on all patients to aid planning. All ESTs during the study period were performed under general anaesthesia to limit patient movement and anxiety. All ESTs of AVM were performed under selective catheter angiography and direct injection. All ESTs during this study were carried out with fluoroscopic guidance with digital subtraction angiography performed to confirm accurate position of the catheter and/or needles, and to assess the flow; either in a vascular hybrid theatre with a floor mounted C-arm or standard operating theatre with a mobile C-arm. Ultrasound was also used in some cases. ESTs were performed either with foam sclerosants (sodium tetradecyl sulphate (STS) 3%; mixed with air in a 1:4 ratio), ethanol, embolization coils, other substances such as Onyx™ Embolic System (Medtronic) and Gelfoam® (Pfizer), or a combination of them, and the choice of agents used was at the operator's discretion. However, our preferred sclerotherapy agent was foam STS 3% and this was purely from our own experience as there were not much literature published on this. STS works by producing maximum endothelial damage with minimal thrombus formation thereby resulting in fibrosis of the lesion and subsequent

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shrinkage. Ethanol and coils were occasionally used, often in combinations, for lesions that were perceived to be more aggressive by the operator. ESTs were also performed at times prior to or as stage for open surgery to reduce the risk of bleeding. The majority of the ESTs were carried out as day cases and followed up in the out-patient clinic at around six to twelve weeks post-operatively.

Patients and data collection

All patients with AVM who underwent EST in our centre from January 1st, 2015 – December 31st, 2019 were identified through a prospectively collected database. Patient demography, types and anatomical features of the AVM, presenting symptoms, procedural information, treatment outcome, complications and follow-up data were collected and reviewed retrospectively. Types of AVM were classified according to Schobinger's classification (13) which encompasses four stages: type-I is quiescent, type-II is expansive phase, type-III is destruction and type-IV is decompensation. The outcome measures assessed efficacy and complication. These were assessed in the out-patient clinic at six to twelve weeks to allow resolution of swelling and changes directly related to EST. Both lesion size and patient symptoms were assessed clinically. Efficacy outcome were divided into four groups: no response, mild response (symptoms still persist that are affecting quality of life without complete resolution of lesion), moderate response (alleviation of symptoms without complete resolution of lesion), and complete response (lesion completely resolved clinically).

Complications were defined as any tissue or functional damage, distal embolization or tissue reaction and were determined by our multi-disciplinary team prospectively.

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Statistical analysis

All statistical analysis was performed using SPSS version 25 statistical software package (SPSS, Armonk, NY: IBM Corporation). There was only one patient with type I AVM and was therefore, not considered for statistical analysis but included in the descriptive statistics. Continuous variables like age or number of procedures for different types were compared using analysis of variance (ANOVA) F test while other discrete variables were compared across the categories using chi-squared tests. $P < 0.05$ was considered significant.

Results

Patient demography and clinical characteristics

A total of 65 patients with AVM and had EST during the study period were included. Their mean age was 36 years (range 1 – 74 years). Three patients had syndromic AVM; Parkes Weber syndrome (n=2) and Maffucci syndrome (n=1). Table 1 summarizes the demography, presenting symptoms, and previous interventions of all the patients included in the study based on the Schobinger's classification. Meanwhile, table 2 summarizes the anatomical location, tissue involvement, and syndromic association of the AVM of all the patients included in the study based on the Schobinger's classification. Most patients presented with swelling (92.3%) and pain (89.2%). Majority of the AVM were located in the upper limbs followed by head and neck, lower limbs, pelvis and genitals, and chest and abdomen. Over 90% and 70% of the AVM involved the subcutaneous and skin respectively. Only head and neck showed significantly higher proportion amongst type III AVM than other anatomical locations ($p=0.024$). Presenting symptoms (bleeding, ulceration/blisters, and cardiac involvement) are significantly different. Swelling was significantly more common in type II AVM ($p=0.015$) while bleeding and ulceration/blisters only present in type II AVM ($p < 0.001$).

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Interventional therapy

Table 3 summarizes the first EST received by all the patients included in the study while supplementary table 1 shows the subsequent procedures, during the trial period of 5 years based on the Schobinger's classification. In all the procedures, there was no statistical difference amongst the volume of foam STS 3% or alcohol used across all types of AVM. From the second procedure onwards, only a few patients received interventional therapy and most of them were carried out in type II and III patients. Hence, it was not meaningful to determine the statistical significance. During patient's first procedure 44 patients (67.7%) received foam STS 3% only, but from the third procedure onwards the majority of patients received a combination of treatment.

Outcomes and follow-up

Table 4 summarizes the adjuvant therapy received by all the patients recruited in the study based on Schobinger's classification. Meanwhile, table 5 summarizes the outcomes and follow-up of all the patients included in the study based on Schobinger's classification. The efficacy outcome categories were not significant across all types of AVM. Overall, majority of patients (86.2%) shown an improvement in symptoms and lesion size following interventional therapy. Patients with type II AVM seemed to report "complete response" more than the other types. This is likely because the majority of our study population were type II lesions and are often well localised therefore amendable to a favourable treatment outcome. A moderate/complete response was reported in 70% and 68% of type II and III lesions respectively. In both type I and IV lesions only mild response was reported. Six (9.2%) patients experienced complications including upper lip necrosis, left forequarter amputation, finger amputation, mass effect (external compression to bladder), left sided partial facial weakness and post thrombotic syndrome. Of these patients four were treated

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with foam STS 3%, one did not receive any treatment and one was treated with a combination of foam STS 3%, ethanol and coils. It is important to point out the patient who needed the forequarter amputation was mostly secondary to progression of the aggressive AVM involving the chest and whole of upper limb causing significant “stealing” of the blood supply from his arm despite embolo-sclerotherapy leading to ischemia and necrosis necessitating the surgery. Despite not caused by EST, this is included as an outcome complication. The proportions of complication were significantly different across the categories ($p=0.009$); Patients with type III AVM seemed to report more complications than others. This could be because type III lesions are associated with destructive tissue changes such as non-healing skin ulcerations and tissue necrosis which accounted for the majority of complications in our study. Table 6 and 7 summarizes the efficacy outcomes for different categories of intervention, and anatomical locations respectively. The efficacy outcome categorizes were significant with STS 3% foam ($p=0.020$) but no significance across different anatomical locations.

Discussion

EST with or without surgery is often the treatment of choice for AVM, usually with multiple sessions required to achieve satisfactory results (14–16). Our preference for foam STS 3% as the main sclerosant was found to be efficacious and safe in this study. Of the 65 patients who had interventional therapy, only three (4.7%) reported no improvement in symptoms, and six (9.2%) did not attend follow-up, presumably due to poor outcome. Of these patients, two were treated with foam STS 3%, one was treated with thalidomide, one was treated with coils only, two were treated with a combination of foam STS 3% and ethanol and two had a diagnostic angiogram only. Meanwhile, 87.5% of patients treated with EST reported at least some degree of symptoms improvement. Studies (8–10,14,16–19) have reported in the range

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of 40-80% of improvement in symptoms after successful EST. However, this was one of the very few studies, if any, to demonstrate that foam sclerotherapy with STS 3% was efficacious and safe to treat AVM, and therefore, could be used as an alternative to other sclerosants including ethanol. Studies have also shown that multiple sessions of EST were required for AVM control and adequate treatment response (20,21). This was evident in our study where patients received approximately two EST sessions (mean 2.48, range 1-12). Our study does not entirely demonstrate that patients only received foam sclerotherapy with STS 3%. However, within the patient's first procedure 68% of patients only received foam STS 3% with subsequent procedures requiring a combination of embolic agents. This symbolises the reality of clinical practice where often a combination of agents is required and highlights the challenges in the management of AVMs.

Amongst the various embolic agents available, liquid agents are considered most appropriate in the treatment of AVM because of their ability to achieve penetration of the nidus or target vessel and occlude feeders (22). Ethanol is a commonly used embolic agent and often considered the most effective in the treatment of AVM (8,10,23). However, there were serious complications associated with this agent such as nerve injury, skin ulceration and acute pulmonary hypertension with cardiopulmonary collapse (8,10,24–26). The complication rate reported in our study, within the entire group, was low (9.2%), with only two cases that were irreversible and resulted in amputations; with one was due to disease progression rather than the EST. The reported complication rates varied greatly in the literature and were dependent on factors such as the anatomical location, extent of AVM and embolic agent used (27–30). Complications as high as 65% have been reported with ethanol (24,31). The low complication rate, in our centre, was likely attributed to the highly experienced clinicians who performed these procedures and reinforces the fact that AVM

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should be managed in a multi-disciplinary approach within a high-volume specialist centre.

Our study demonstrated that when comparing different treatment modalities that STS 3% foam was associated with a better efficacy outcome. A comparison of anatomical locations and outcome success did not show any significance suggesting that there is no particular region in the body that has better outcomes. However, it should be noted that the chest and abdomen, upper limb and head and neck had no response rates of 1 (20.0%), 2 (8.3%) and 1 (6.3%) respectively. This highlights the challenges in the treatment of AVMs, in particular locating the nidus, where incomplete embolization can result in hypoxia which stimulates a cascade of events leading to post-embolization angiogenesis (32).

There are several limitations of the study. Firstly, the prospective data collection and subsequent analysis could have introduced biases. Secondly, the sample size was relatively small although the number of patients included in our study compared favourably with most previous reports. Thirdly, the outcome measures were subjective, and the clinicians assessing them were not blinded. Finally, the time frame of this study would have impacted the results as the experience from the clinicians from a diagnostic and treatment perspective was rapidly evolving.. However, our major finding from this study is that sclerotherapy with foam STS 3%, as the mainstay interventional therapy with or without surgery for symptomatic AVMs, is safe and effective as an alternative to ethanol when treating AVMs.

Conclusion

EST as the mainstay intervention for patients with symptomatic AVMs, with foam STS 3% as the favoured sclerosing agent, is clinically effective and safe. This study showed that foam STS 3% provided a safe and efficacious alternative to ethanol and other EST agents.

However, a combination of embolic agents is likely required to treat type IV AVMs.

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Our complication rates also compared favourably to the literature. Further work will be required with a large sample population to assess other variables which may influence the effectiveness of EST foam in the treatment of AVM.

Conflicts of Interest

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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Authors contribution

CP: Conception and design, analysis and interpretation, data collection, writing manuscript, critical revision, approval of the manuscript, statistical analysis

DRBA: Conception and design, analysis and interpretation, data collection, critical revision, approval of the manuscript

NE: data collection, critical revision, approval of the manuscript

AP: data collection, critical revision, approval of the manuscript

MK: data collection, critical revision, approval of the manuscript,

JT: data collection, critical revision, approval of the manuscript,

GH: data collection, critical revision, approval of the manuscript,

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CSL: Conception and design, analysis and interpretation, data collection, writing manuscript,
critical revision, approval of the manuscript

JB: data collection, critical revision, approval of the manuscript, statistical analysis

All authors read and approved the final version of the manuscript

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Table 1. Demography, presenting symptoms, and previous interventions of all the patients included in the study based on the Schobinger's types of arteriovenous malformations. Mean (SD) are reported for continuous variables and number (percent) are reported for the categorical variables. EST: Emboloscclerotherapy; STS: sodium tetradecyl sulphate.

	<i>Type I</i>	<i>Type II</i>	<i>Type III</i>	<i>Type IV</i>	<i>Total</i>	<i>P-value</i>
No of patients	1	43	19	2	65	
Age	8.00 (-)	35.02 (16.54)	35.74 (19.41)	73.0 (2.83)	35.98 (18.48)	0.014
Sex						0.888
Male	0 (0.0%)	16 (37.2%)	8 (42.1%)	1 (50.0%)	25 (38.5%)	
Female	1 (100.0%)	27 (62.8%)	11 (57.9%)	1 (50.0%)	40 (61.5%)	
Presenting symptoms						
Pain	0 (0.0%)	41 (95.3%)	16 (84.2%)	1 (50.0%)	58 (89.2%)	0.051
Swelling	1 (100.0%)	42 (97.7%)	16 (84.2%)	1 (50.0%)	60 (92.3%)	0.015
Bleeding	0 (0.0%)	0 (0.0%)	9 (47.4%)	0 (0.0%)	9 (13.8%)	<0.001
Ulceration/Blisters	0 (0.0%)	0 (0.0%)	6 (31.6%)	0 (0.0%)	6 (9.2%)	<0.001
Dystrophic skin change	0 (0.0%)	1 (2.3%)	2 (10.5%)	0 (0.0%)	3 (4.6%)	0.353
Cardiac impairment	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (100.0%)	2 (3.1%)	<0.001
Tinnitus	0 (0.0%)	0 (0.0%)	1 (5.3%)	1 (1.5%)	1 (1.5%)	0.300
Previous intervention						
None	1 (100.0%)	25 (58.1%)	10 (52.6%)	1 (50.0%)	37 (56.9%)	0.907
EST with foam STS 3%	0 (0.0%)	14 (32.6%)	6 (31.6%)	1 (50.0%)	21 (32.3%)	0.868
EST with alcohol	0 (0.0%)	2 (1.8%)	1 (5.3%)	0 (0.0%)	3 (4.6%)	0.945
Surgery	0 (0.0%)	3 (7.0%)	6 (31.6%)	1 (50.0%)	10 (15.4%)	0.019
Coil embolization	0 (0.0%)	3 (7.0%)	1 (5.3%)	0 (0.0%)	4 (6.2%)	0.903

Table 2. Anatomical location, tissue involvement, and syndromic association of the congenital vascular malformation of all the patients included in the study based on the Schobinger's types of arteriovenous malformation. Mean (SD) are reported for continuous variables and number (percent) are reported for the categorical variables.

	<i>Type I</i>	<i>Type II</i>	<i>Type III</i>	<i>Type IV</i>	<i>Total</i>	<i>P-value</i>
Anatomical location						
Chest and Abdomen	0 (0.0%)	3 (7.0%)	2 (10.5%)	0 (0.0%)	5 (7.7%)	0.816
Upper Limb	0 (0.0%)	18 (41.9%)	5 (26.3%)	1 (50.0%)	24 (36.9%)	0.473
Lower Limb	0 (0.0%)	12 (27.9%)	4 (21.1%)	0 (0.0%)	16 (24.6%)	0.601
Head and Neck	1 (100.0%)	7 (16.3%)	9 (47.4%)	0 (0.0%)	17 (26.2%)	0.024
Pelvis and Genitals	0 (0.0%)	4 (9.3%)	1 (5.3%)	1 (50.0%)	6 (9.2%)	0.119
Tissue involvement						
Skin	1 (100.0%)	35 (81.4%)	14 (73.7%)	1 (50.0%)	51 (78.5%)	0.493
Subcutaneous tissue	1 (100.0%)	43 (100.0%)	18 (94.7%)	1 (50.0%)	63 (96.9%)	<0.001
Intramuscular	0 (0.0%)	13 (30.2%)	3 (15.8%)	2 (100.0%)	18 (27.7%)	0.036
Intraosseous	0 (0.0%)	1 (2.3%)	2 (10.5%)	0 (0.0%)	3 (4.6%)	0.353
Syndromic associations	0 (0.0%)	0 (0.0%)	3 (15.8%)	0 (0.0%)	3 (4.6%)	0.024

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Table 3. Interventional therapy (1st procedure) received by all the patients included in the study during the trial period of 5 years based on the Schobinger's types of arteriovenous malformations. STS: sodium tetradecyl sulphate. *The volume stated refers to the volume of liquid STS 3% before converted to foam (mixed with air in 1:4 ratio).

	<i>Type I</i>	<i>Type II</i>	<i>Type III</i>	<i>Type IV</i>	<i>Total</i>	<i>P-value</i>
1st Procedure						
No of patients	1	43	19	2	65	
Sclerotherapy						
Foam STS 3%*	1 (100.0%)	38 (88.4%)	16 (84.2%)	1 (50.0%)	56 (86.2%)	0.442
<1 ml	0 (0.0%)	6 (14.0%)	3 (15.8%)	0 (0.0%)	9 (13.8%)	
1-5 ml	1 (100.0%)	22 (51.2%)	8 (42.1%)	0 (0.0%)	31 (47.7%)	
6-10 ml	0 (0.0%)	10 (23.2%)	4 (21.1%)	1 (50.0%)	15 (23.1%)	
11-15 ml	0 (0.0%)	0 (0.0%)	1 (5.3%)	0 (0.0%)	1 (1.5%)	
16-20 ml	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	
>20ml	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	
Alcohol	0 (0.0%)	11 (25.6%)	7 (36.8%)	1 (50.0%)	19 (29.2%)	0.137
<1 ml	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	
1-5 ml	0 (0.0%)	2 (4.7%)	5 (26.3%)	0 (0.0%)	7 (10.8%)	
6-10 ml	0 (0.0%)	3 (7.0%)	2 (10.5%)	1 (50.0%)	6 (9.2%)	
11-15 ml	0 (0.0%)	6 (14.0%)	0 (0.0%)	0 (0.0%)	6 (9.2%)	
Others						0.957
Coil embolization	0 (0.0%)	2 (4.7%)	0 (0.0%)	0 (0.0%)	2 (3.1%)	
Gelfoam	0 (0.0%)	1 (2.3%)	0 (0.0%)	0 (0.0%)	1 (1.6%)	

Table 4. Adjuvant therapy received by all the patients recruited in the study based on Schobinger's types of arteriovenous malformation. Mean (SD) are reported for continuous variables and number (percent) are reported for the categorical variables.

	<i>Type I</i>	<i>Type II</i>	<i>Type III</i>	<i>Type IV</i>	<i>Total</i>	<i>P-value</i>
Targeted medication						0.741
None	1 (100.0%)	37 (86.0%)	14 (73.7%)	2 (100.0%)	54 (83.1%)	
Propranolol	0 (0.0%)	0 (0.0%)	1 (5.3%)	0 (0.0%)	1 (1.5%)	
Sirolimus	0 (0.0%)	2 (4.7%)	1 (5.3%)	0 (0.0%)	3 (4.6%)	
Thalidomide	0 (0.0%)	4 (9.3%)	3 (15.8%)	0 (0.0%)	7 (10.8%)	

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Table 5. Outcomes and follow-up of all the patients included in the study based on Schobinger's types of arteriovenous malformation. Mean (SD) are reported for continuous variables and number (percent) are reported for the categorical variables.

	<i>Type I</i>	<i>Type II</i>	<i>Type III</i>	<i>Type IV</i>	<i>Total</i>	<i>P-value</i>
Efficacy outcome						0.401
No response	0 (0.0%)	2 (4.7%)	1 (5.3%)	0 (0.0%)	3 (4.7%)	
Mild response	1 (100.0%)	8 (18.6%)	4 (21.1%)	2 (100.0%)	15 (23.4%)	
Moderate response	0 (0.0%)	13 (30.2%)	3 (15.8%)	0 (0.0%)	16 (25.0%)	
Complete response	0 (0.0%)	17 (39.5%)	8 (42.1%)	0 (0.0%)	25 (38.5%)	
Failed to follow-up	0 (0.0%)	3 (7.0%)	3 (15.8%)	0 (0.0%)	6 (9.2%)	
Complications	0 (0.0%)	1 (2.3%)	4 (21.1%)	1 (50.0%)	6 (9.2%)	0.009
Mean no. of procedures	1.0 (-)	2.28 (1.98)	3.16 (2.81)	1.0 (0.0)	2.48 (2.25)	0.238
Follow-up duration (days)	104.0 (-)	748.17 (536.33)	1093.22 (664.48)	915.5 (908.63)	841.84 (598.21)	0.119

Table 6: Distribution of Outcomes for different categories of intervention for high-flow AVMs.

	<i>STS 3% Foam</i>	<i>Coils</i>	<i>Alcohol</i>	<i>Gelfoam</i>	<i>Surgery</i>	<i>Medication</i>
No Response	1 (1.9%)	1 (16.7%)	1 (5.0%)	0 (0.0%)	1 (25.0%)	1 (9.1%)
Mild Response	12 (22.2%)	1 (16.7%)	6 (30.0%)	0 (0.0%)	0 (0.0%)	5 (45.5%)
Moderate Response	16 (29.6%)	2 (33.3%)	7 (35.0%)	1 (50.0%)	1 (25.0%)	2 (18.2%)
Complete Response	22 (40.7%)	1 (16.7%)	5 (25.0%)	1 (50.0%)	2 (50.0%)	3 (27.3%)
Failed to follow-up	3 (5.6%)	1 (16.7%)	1 (5.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
P-value	0.020	0.426	0.482	0.858	0.266	0.282

Table 7: Distribution of Outcomes for anatomical locations for high-flow AVMs.

	<i>Chest and abdomen</i>	<i>Upper Limb</i>	<i>Lower Limb</i>	<i>Head and Neck</i>	<i>Pelvis and Genitals</i>
No Response	1 (20.0%)	2 (8.3%)	0 (0.0%)	1 (6.3%)	0 (0.0%)
Mild Response	2 (40.0%)	6 (25.0%)	2 (12.5%)	4 (25.0%)	1 (16.7%)
Moderate Response	2 (40.0%)	4 (16.7%)	7 (43.8%)	3 (18.8%)	2 (33.3%)
Complete Response	0 (0.0%)	10 (41.7%)	4 (25.0%)	8 (50.0%)	3 (50.0%)
Failed to follow-up	0 (0.0%)	2 (8.3%)	3 (18.8%)	0 (0.0%)	0 (0.0%)
P-value	0.173	0.685	0.051	0.594	0.854

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Supplementary Table 1. Interventional therapy (2nd procedure onwards) received by all the patients included in the study during the trial period of 5 years based on the Schobinger's types of arteriovenous malformations.. STS: sodium tetradecyl sulphate. *The volume stated refers to the volume of liquid STS 3% before converted to foam (mixed with air in 1:4 ratio).

	<i>Type I</i>	<i>Type II</i>	<i>Type III</i>	<i>Type IV</i>	<i>Total</i>	<i>P-value</i>
2nd Procedure						
No of patients	0 (0.0%)	21 (48.8%)	11 (57.9%)	0 (0.0%)	32 (49.2%)	
Sclerotherapy	0 (0.0%)	21 (48.8%)	11 (57.9%)	0 (0.0%)	32 (49.2%)	0.988
Foam STS 3%*						
<1 ml	0 (0.0%)	4 (9.3%)	2 (10.5%)	0 (0.0%)	6 (9.2%)	
1-5 ml	0 (0.0%)	10 (23.3%)	7 (36.8%)	0 (0.0%)	17 (26.2%)	
6-10 ml	0 (0.0%)	5 (11.6%)	2 (10.5%)	0 (0.0%)	7 (10.8%)	
11-15 ml	0 (0.0%)	1 (2.3%)	0 (0.0%)	0 (0.0%)	1 (1.5%)	
16-20 ml	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	
>20 ml	0 (0.0%)	1 (2.3%)	0 (0.0%)	0 (0.0%)	1 (1.5%)	
Alcohol	0 (0.0%)	14 (32.6%)	8 (42.1%)	0 (0.0%)	22 (33.8%)	0.949
<1 ml	0 (0.0%)	5 (11.6%)	0 (0.0%)	0 (0.0%)	5 (7.7%)	
1-5 ml	0 (0.0%)	2 (4.7%)	3 (16.7%)	0 (0.0%)	5 (7.7%)	
6-10 ml	0 (0.0%)	2 (4.7%)	1 (5.6%)	0 (0.0%)	3 (4.6%)	
11-15ml	0 (0.0%)	1 (2.3%)	1 (5.6%)	0 (0.0%)	2 (3.1%)	
16-20 ml	0 (0.0%)	0 (0.0%)	1 (5.6%)	0 (0.0%)	1 (1.5%)	
>20ml	0 (0.0%)	4 (9.3%)	2 (10.5%)	0 (0.0%)	6 (9.2%)	
Others						0.590
Coil embolization	0 (0.0%)	3 (7.0%)	0 (0.0%)	0 (0.0%)	3 (4.6%)	
3rd Procedure						
No of patients	0 (0.0%)	13 (30.2%)	8 (42.1%)	0 (0.0%)	21 (32.3%)	
Sclerotherapy	0 (0.0%)	13 (30.2%)	8 (42.1%)	0 (0.0%)	21 (31.2%)	0.949
Foam STS 3%*						
<1 ml	0 (0.0%)	4 (9.3%)	0 (0.0%)	0 (0.0%)	4 (6.2%)	
1-5 ml	0 (0.0%)	7 (16.3%)	5 (26.3%)	0 (0.0%)	12 (18.5%)	
6-10 ml	0 (0.0%)	1 (2.3%)	3 (15.8%)	0 (0.0%)	4 (6.2%)	
11-15 ml	0 (0.0%)	1 (2.3%)	0 (0.0%)	0 (0.0%)	1 (1.5%)	
16-20 ml	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	
>20 ml	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	
Alcohol	0 (0.0%)	13 (30.2%)	8 (42.1%)	0 (0.0%)	21 (32.3%)	0.871
<1ml	0 (0.0%)	8 (18.6%)	7 (36.8%)	0 (0.0%)	15 (23.1%)	
1-5 ml	0 (0.0%)	2 (4.7%)	0 (0.0%)	0 (0.0%)	2 (3.1%)	
6-10 ml	0 (0.0%)	3 (7.0%)	0 (0.0%)	0 (0.0%)	3 (4.6%)	
11-15 ml	0 (0.0%)	0 (0.0%)	1 (5.3%)	0 (0.0%)	1 (1.5%)	
16-20 ml	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	
>20 ml	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	
Others						0.942
Coil embolization	0 (0.0%)	3 (7.0%)	1 (5.3%)	0 (0.0%)	4 (6.2%)	
Open surgery	0 (0.0%)	2 (4.7%)	0 (0.0%)	0 (0.0%)	2 (3.1%)	
4th Procedure						
No. of patients	0 (0.0%)	6 (14.0%)	6 (31.6%)	0 (0.0%)	12 (18.5%)	
Sclerotherapy	0 (0.0%)	6 (14.0%)	6 (31.6%)	0 (0.0%)	12 (18.5%)	0.960
Foam STS 3%*						
<1 ml	0 (0.0%)	1 (2.3%)	2 (10.5%)	0 (0.0%)	3 (4.6%)	
1-5 ml	0 (0.0%)	3 (7.0%)	4 (21.1%)	0 (0.0%)	7 (10.8%)	
6-10 ml	0 (0.0%)	1 (2.3%)	0 (0.0%)	0 (0.0%)	1 (1.5%)	
11-15 ml	0 (0.0%)	1 (2.3%)	0 (0.0%)	0 (0.0%)	1 (1.5%)	
16-20 ml	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	
>20 ml	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	

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1Alcohol	0 (0.0%)	6 (14.0%)	6 (31.6%)	0 (0.0%)	12 (18.5%)	0.974
<1 ml	0 (0.0%)	4 (9.3%)	3 (15.8%)	0 (0.0%)	7 (10.8%)	
1-5 ml	0 (0.0%)	1 (2.3%)	2 (10.5%)	0 (0.0%)	3 (4.6%)	
6-10 ml	0 (0.0%)	1 (2.3%)	1 (5.3%)	0 (0.0%)	2 (3.1%)	
11-15 ml	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	
16-20 ml	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	
>20 ml	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	
Others						0.870
Coil embolization	0 (0.0%)	0 (0.0%)	1 (5.3%)	0 (0.0%)	1 (1.5%)	
Open surgery	0 (0.0%)	0 (0.0%)	1 (5.3%)	0 (0.0%)	1 (1.5%)	
5th Procedure						
No of patients	0 (0.0%)	3 (7.0%)	3 (15.8%)	0 (0.0%)	6 (9.2%)	0.774
Sclerotherapy	0 (0.0%)	3 (7.0%)	3 (15.8%)	0 (0.0%)	6 (9.2%)	
Foam STS 3%*						
<1 ml	0 (0.0%)	0 (0.0%)	1 (5.3%)	0 (0.0%)	1 (1.5%)	
1-5 ml	0 (0.0%)	1 (2.3%)	2 (10.5%)	0 (0.0%)	3 (4.6%)	
6-10 ml	0 (0.0%)	2 (4.7%)	0 (0.0%)	0 (0.0%)	2 (3.1%)	
11-15 ml	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	
16-20 ml	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	
>20 ml	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	
Alcohol	0 (0.0%)	3 (7.0%)	3 (15.8%)	0 (0.0%)	6 (9.2%)	
<1 ml	0 (0.0%)	3 (7.0%)	2 (10.5%)	0 (0.0%)	5 (7.7%)	0.806
1-5 ml	0 (0.0%)	0 (0.0%)	1 (5.3%)	0 (0.0%)	1 (1.5%)	
6-10 ml	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	
11-15 ml	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	
16-20 ml	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	
>20 ml	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	
Others						
Coil embolization	0 (0.0%)	0 (0.0%)	1 (5.3%)	0 (0.0%)	1 (1.5%)	
6th Procedure						
No of patients	0 (0.0%)	2 (4.7%)	3 (15.8%)	0 (0.0%)	5 (7.7%)	0.486
Sclerotherapy	0 (0.0%)	2 (4.7%)	3 (15.8%)	0 (0.0%)	5 (7.7%)	
Foam STS 3%*						
<1 ml	0 (0.0%)	0 (0.0%)	1 (5.3%)	0 (0.0%)	1 (1.5%)	
1-5 ml	0 (0.0%)	0 (0.0%)	2 (10.5%)	0 (0.0%)	2 (3.1%)	
6-10 ml	0 (0.0%)	2 (4.7%)	0 (0.0%)	0 (0.0%)	2 (3.1%)	
11-15 ml	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	
16-20 ml	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	
>20 ml	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	
Alcohol	0 (0.0%)	2 (4.7%)	3 (15.8%)	0 (0.0%)	5 (7.7%)	
<1 ml	0 (0.0%)	2 (4.7%)	2 (10.5%)	0 (0.0%)	4 (6.2%)	0.737
1-5 ml	0 (0.0%)	0 (0.0%)	1 (5.3%)	0 (0.0%)	1 (1.5%)	
6-10 ml	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	
11-15 ml	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	
16-20 ml	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	
>20 ml	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	
Others						
Coil embolization	0 (0.0%)	0 (0.0%)	1 (5.3%)	0 (0.0%)	1 (1.5%)	
7th Procedure						
No of patients	0 (0.0%)	1 (2.3%)	2 (10.5%)	0 (0.0%)	3 (4.6%)	0.539
Sclerotherapy	0 (0.0%)	1 (2.3%)	2 (10.5%)	0 (0.0%)	3 (4.6%)	
Foam STS 3%*						
<1 ml	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	
1-5 ml	0 (0.0%)	1 (2.3%)	2 (10.5%)	0 (0.0%)	3 (4.6%)	
6-10 ml	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	
11-15 ml	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	
16-20 ml	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	
>20 ml	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	

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Alcohol	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	
<1ml	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	
1-5 ml	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	
6-10 ml	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	
11-15 ml	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	
16-20 ml	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	
>20 ml	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	
8th Procedure						
No of patients	0 (0.0%)	1 (2.3%)	1 (5.3%)	0 (0.0%)	2 (3.1%)	
Sclerotherapy	0 (0.0%)	1 (2.3%)	1 (5.3%)	0 (0.0%)	2 (3.1%)	0.793
Foam STS 3% *						
<1 ml	0 (0.0%)	1 (2.3%)	0 (0.0%)	0 (0.0%)	1 (1.5%)	
1-5 ml	0 (0.0%)	0 (0.0%)	1 (5.3%)	0 (0.0%)	1 (1.5%)	
6-10 ml	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	
11-15 ml	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	
16-20 ml	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	
>20 ml	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	
Alcohol	0 (0.0%)	1 (2.3%)	1 (5.3%)	0 (0.0%)	2 (3.1%)	0.793
<1 ml	0 (0.0%)	0 (0.0%)	1 (5.3%)	0 (0.0%)	1 (1.5%)	
1-5 ml	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	
6-10 ml	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	
11-15 ml	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	
16-20 ml	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	
>20 ml	0 (0.0%)	1 (2.3%)	0 (0.0%)	0 (0.0%)	1 (1.5%)	
9th Procedure						
No of patients	0 (0.0%)	1 (2.3%)	2 (10.5%)	0 (0.0%)	3 (4.6%)	
Sclerotherapy	0 (0.0%)	1 (2.3%)	2 (10.5%)	0 (0.0%)	3 (3.6%)	0.810
Foam STS 3% *						
<1 ml	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	
1-5 ml	0 (0.0%)	1 (2.3%)	1 (5.3%)	0 (0.0%)	2 (3.1%)	
6-10 ml	0 (0.0%)	0 (0.0%)	1 (5.3%)	0 (0.0%)	1 (1.5%)	
11-15 ml	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	
16-20 ml	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	
>20 ml	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	
Alcohol	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	
<1 ml	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	
1-5 ml	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	
6-10 ml	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	
11-15 ml	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	
16-20 ml	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	
>20 ml	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	
Others						0.487
Coil embolization	0 (0.0%)	1 (2.3%)	0 (0.0%)	0 (0.0%)	1 (1.5%)	
10th Procedure						
No of patients	0 (0.0%)	1 (2.3%)	1 (5.3%)	0 (0.0%)	2 (3.1%)	
Sclerotherapy	0 (0.0%)	1 (2.3%)	1 (5.3%)	0 (0.0%)	2 (3.1%)	0.923
Foam STS 3% *						
<1 ml	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	
1-5 ml	0 (0.0%)	1 (2.3%)	1 (5.3%)	0 (0.0%)	2 (3.1%)	
6-10 ml	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	
11-15 ml	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	
16-20 ml	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	
>20 ml	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	
Alcohol	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	
<1 ml	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	
1-5 ml	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	
6-10 ml	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	
11-15 ml	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	
16-20 ml	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	

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>20 ml	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	
11th Procedure						
No of patients	0 (0.0%)	1 (2.3%)	0 (0.0%)	0 (0.0%)	1 (1.5%)	
Sclerotherapy	0 (0.0%)	1 (2.3%)	0 (0.0%)	0 (0.0%)	1 (1.5%)	0.815
Foam STS 3% *						
<1 ml	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	
1-5 ml	0 (0.0%)	1 (2.3%)	0 (0.0%)	0 (0.0%)	1 (1.5%)	
6-10 ml	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	
11-15 ml	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	
16-20 ml	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	
>20 ml	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	
Alcohol	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	
<1 ml	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	
1-5 ml	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	
6-10 ml	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	
11-15 ml	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	
16-20 ml	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	
>20 ml	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	
Others						0.815
Coil embolization	0 (0.0%)	1 (2.3%)	0 (0.0%)	0 (0.0%)	1 (1.5%)	
12th Procedure						
No of patients	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	
Sclerotherapy	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	
Foam STS 3%						
<1 ml	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	
1-5 ml	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	
6-10 ml	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	
11-15 ml	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	
16-20 ml	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	
>20 ml	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	
Alcohol	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	
<1 ml	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	
1-5 ml	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	
6-10 ml	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	
11-15 ml	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	
16-20 ml	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	
>20 ml	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	
Others						0.915
Open Surgery	0 (0.0%)	1 (2.3%)	0 (0.0%)	0 (0.0%)	1 (1.5%)	

Short title: Foam sclerotherapy with STS in arteriovenous malformations

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