VER
Vascular & Endovascular Review

A comparison between Percutaneous Bleomycin and Polidocanol in management of peripheral venous malformations

Ahmed Emad Mahdy Mohamed, Mohamed El-Ghareeb Abo El Maaty, Haitham Nasser, Mina Emil Edward

Radiodiagnosis Department, Faculty of Medicine, Ain Shams University

Corresponding Author
Ahmed Emad Mahdy Mohamed
E-mail: abdullahmawkili4@gmail.com

ABSTRACT

Background: Venous malformations (VMs) are congenital slow-flow vascular anomalies that can cause pain, swelling, functional impairment, and cosmetic concerns. Sclerotherapy has become a primary, minimally invasive treatment option, with Bleomycin (an antineoplastic antibiotic) and Polidocanol (a detergent sclerosant) being commonly used agents. Both have demonstrated efficacy in reducing lesion size and symptoms, yet direct comparisons of their safety profiles, complication rates, and patient outcomes remain limited.

Objective: To compare between Bleomycin and polidocanol injection in the treatment of peripheral venous malformations as regard the reduction in size/session, number of sessions used, postprocedural pain, cost and complications.

Patients and Methods: This randomized clinical trial was conducted on 24 patients with peripheral low flow vascular malformation who randomly classified into 2 groups: group A: 12 patients subjected to Polidocanol injection, group B; 12 patients subjected to Bleomycin percutaneous injection, at 'Interventional radiology unit' at the Radiology Department "Ain Shams University hospitals, Cairo, Egypt, to compare between Bleomycin and polidocanol injection in the treatment of peripheral venous malformations as regard the reduction in size/session, number of sessions used, postprocedural pain and complications.

Results: In this study of 24 patients (58.3% male, median age 10 years) with venous malformations, the upper limb was most affected (46.2%). Pain (70.8%) and swelling/disfigurement (91.7%) were common. Sclerotherapy with Bleomycin or Polidocanol (50% each) resulted in reduced lesion sizes (median 9 cm^3 to 4 cm^3 at 1 month, further declining by 6 months) and pain scores (median 8 to 0). By 6 months, 54.2% achieved complete response, 41.7% partial, and 4.2% stable. Complications (62.5%) included pain (50%) and swelling (45.8%). Polidocanol showed higher local complications (83.3% vs. 41.7%, p=0.035) but no significant differences in efficacy between agents.

Conclusion: In this randomized clinical trial, both Bleomycin and Polidocanol demonstrated comparable efficacy in reducing lesion size and alleviating pain over a six-month period. By one month, all patients in both groups exhibited partial responses. At six months, the Polidocanol group had a higher rate of complete response (66.7% vs. 41.7%), although this difference was not statistically significant (P = 0.351). While Polidocanol showed a trend toward more complete responses, it was associated with a significantly higher incidence of complications (83.3% vs. 41.7%, P = 0.035), particularly pain (75% vs. 25%, P = 0.014) and swelling (66.7% vs. 25%, P = 0.041). In contrast, Bleomycin had fewer overall complications, but still yielded effective clinical outcomes.

KEYWORDS: Percutaneous Bleomycin, Polidocanol, Peripheral Venous Malformations.

How to Cite: Ahmed Emad Mahdy Mohamed, Mohamed El-Ghareeb Abo El Maaty, Haitham Nasser, Mina Emil Edward, (2025) A comparison between Percutaneous Bleomycin and Polidocanol in management of peripheral venous malformations, Vascular and Endovascular Review, Vol.8, No.2, 58-71. **DOI**: *https://doi.org/10.15420/ver.2025.08.02.58-71*

INTRODUCTION

Venous malformations (VMs) are the most common congenital vascular malformation formed by ectatic venous channels lined by a single endothelial layer, affecting 1%–4% of the population. These gradually expanding venous channels infiltrating normal tissue lead to cosmetic complaints, pain, swelling, organ dislocation, and functional limitations, depending on the mass location and extent of involvement as well as the expansion rate. Typically, percutaneous sclerotherapy is the gold standard treatment to reduce the volume of the malformation. The sclerosants most commonly used for treating VMs including ethanol, bleomycin, and foam (such as polidocanol) cause damage to the endothelium lining the VMs with subsequent inflammation and fibrosis to obliterate the ectatic venous channels and reduce the size of the lesion ***(Van Der Vleuten et al., 2014)***.

Historically, VMs have been treated surgically; however, in recent years, percutaneous sclerotherapy has been used, either as a preoperative support to reduce lesion size, as a postoperative complement, or as a single approach ***(Legiehn & Heran, 2008)*** A variety of sclerosing agents is described in the literature, including alcohol, detergents, and hyperosmotic solutions. Although each sclerosant has a different mechanism of action, they all result in damage or destruction of the dysmorphic endothelium lining the VM. This leads to a decrease in the size of the lesion and/or a change in its physiologic characteristics, resulting in symptom

alleviation.

More recently, the use of **bleomycin**, a cytotoxic antitumor agent, has been favoured because it has been shown to have clinical efficacy combined with a low side-effect profile ***(Spence et al., 2011).***

Bleomycin liquid as a sclerosant for VMs can lead to fewer complications and side effects and have good tolerance, better prognosis, and a lower cost ***(Sun et al., 2020).*** However, it has low sclerosing efficiency because of its fluidity and easy dilution by blood, and a lifetime dose limit exists to reduce the risk of pulmonary fibrosis (less than 400 mg or 5 mg/kg), limiting its use for large VMs.
Polidocanol: Polidocanol is a local anesthetic also used as a sclerosant for VMs with fewer side effects than absolute ethanol ***(Müller et al., 2018)***. There is some evidence that polidocanol foam, made by mixing polidocanol with sterile air (Tessari technique ***(Tessari et al., 2001)***), has a higher rate of obliteration compared to the application of liquid polidocanol ***(Yamaki et al., 2008)***.

AIM OF THE WORK

To compare between Bleomycin and polidocanol injection in the treatment of peripheral venous malformations as regard the reduction in size/session, number of sessions used, postprocedural pain, cost and complications.

PATIENTS AND METHODS

Study Setting: Interventional Radiology Unit, Radiology department, Ain Shams University Hospitals
Study Period: 12 months of data collection, injection of the agent and follow up of response and complications (1-12/ 2024)
Study Population: ***Inclusion Criteria:*** Patients with peripheral low flow vascular malformation, no age predilection, informed consent to participate in the study, poor surgical candidate and refusing to undergo surgery. ***Exclusion Criteria:*** patients with head and neck malformations, abnormal coagulation profile, allergy to injected medication and refusal of the procedure done.

Sampling Method: Convenience sampling
Sample Size: 24 patients with peripheral low flow vascular malformation divided randomly into 2 groups (12 patients in each group).

Ethical Considerations: An informed oral consent explaining the procedure details will be obtained from all patients prior to the study. The study will be conducted according to the stipulation of ASU ethical and scientific committee and after their approval. The privacy of participants and confidentiality of data will be guaranteed during the various phases of the study
Study Tools: Full history taking: with attention to symptoms of high flow cardiac failure, clinical examination: inspection, and palpation, ultrasound: Volume of the lesion before treatment, doppler examination to determine whether its low or high flow and MRI to confirm of low flow malformation.

Study Procedures: **Patient preparation:** Detailed explanation of the procedure including benefits and risks, laboratory tests usually include CBC, a blood coagulation profile, preprocedural measurement of the lesion by US and obtaining a signed informed consent. **Procedure duration:** The procedure takes about 20-40 minutes. **Machine used:** The study will be done at Ain shams university using hospitals on Mindray Ultrasound machine and Philips monoplane machine. **Follow up of the patients:** Patients underwent intervention will be followed up clinically and sonographic ally after 1 and 6 months of injection and the need for additional sessions will be determined upon sonographic size of the lesion.

Procedure details: Patients are classified into two groups

Group A: Patients that are to be submitted to **Polidocanol** injection, the Injection site is selected by palpation and corresponded to the area where venous dilation is largest. The injection technique consists of percutaneous puncture of the lesion with a 21-gauge butterfly needle introduced perpendicularly to the skin surface and into the anomalous venous space. Blood reflux to confirm proper needle positioning. Iodinated contrast media is then slowly and gradually injected into the lesion under fluoroscopic guidance, and opacification of the anomalous space monitored. Percutaneous injection of 5ml Polidocanol (foam (3%) will be generated by mixing the sclerosing liquid with air in a ratio of 1 to 2 using Tessari technique). The maximum will not exceed 2 mg/kg. A slightly compressive dressing will be applied. Patients remain under observation for approximately 30 minutes before discharge.

Group B: Patients are to be submitted to **Bleomycin** percutaneous injection. Injection site was selected by palpation and corresponded to the area where venous dilation was largest. The injection technique consisted of percutaneous puncture of the lesion with a 21-gauge butterfly needle introduced perpendicularly to the skin surface and into the anomalous venous space. Blood reflux confirmed proper needle positioning. Iodinated contrast media was then slowly and gradually injected into the lesion under fluoroscopic guidance, and opacification of the anomalous space monitored. Following description of VM characteristics and quantification of the volume drained into the venous system, The powder of bleomycin A5, 8 mg in dose, was dissolved by solution containing dexamethasone (5 mg, 1 mL; and lidocaine 2% (4 mL). If the size of malformations was less than 10 × 15 mm by ultrasonography, dexamethasone and lidocaine were reduced to half dose, while the injected bleomycin A5 dose remained 8 mg each time. However, there is a potential risk of pulmonary fibrosis after bleomycin admission. Therefore, bleomycin must be used in a very small dose with no more than 1 mg/kg body weight per session. A slightly compressive dressing will be applied. Patients remained under observation for approximately 30 minutes before discharge.

Interpretation of Results: The primary endpoint is short-term pain relief, which will be determined as the difference in the numeric rating scale (NRS) scores before and 1 and 6 months after the therapy.

Statistical Analysis: Data were collected, revised, coded and entered to the Statistical Package for Social Science (IBM SPSS) version 27. The quantitative data were presented as mean, standard deviations and ranges when parametric and median, inter-quartile range (IQR) when data found non-parametric. Also qualitative variables were presented as number and percentages. The one-sample Kolmogorov-Smirnov test can be used to test that a variable is normally distributed.

The comparison between groups regarding qualitative data was done by using ***Chi-square test*** and/or ***Fisher exact test*** when the expected count in any cell found less than 5.

The comparison between two independent groups with quantitative data and non-parametric distribution were done by using

Mann-Whitney test.

The confidence interval was set to 95% and the margin of error accepted was set to 5%. So, the p-value was considered significant as the following: P-value > 0.05: Non-significant (NS). P-value < 0.05: Significant (S). P-value < 0.01: Highly significant (HS).

RESULTS

The median age of the studied patients was 10 (IQR: 6.5–15) years ranged from 3 to 45 years. There were 14 males (58.3%) and 10 females (41.7%) **(Tab. 1)**

Table (1): Demographic data and characteristics of the studied patients

		Total no.= 24
Age	**Median (IQR)**	10 (6.5 - 15)
	Range	3 – 45
Sex	**Female**	10 (41.7%)
	Male	14 (58.3%)
Site of VMs	**Lower limb**	4 (30.8%)
	Upper Limb	6 (46.2%)
	Trunk	3 (23.1%)
Pain	**No**	7 (29.2%)
	Yes	17 (70.8%)
Swelling/Disfigurement	**No**	2 (8.3%)
	Yes	22 (91.7%)
Limb Dysfunction	**No**	20 (83.3%)
	Yes	4 (16.7%)
Sclerosant agent	**Bleomycin**	12 (50%)
	Polidocaonol	12 (50%)
Number of sessions	**Median (IQR)**	2 (1 - 2)
	Range	1 – 5

As regard clinical characteristic, the most commonly affected site was the upper limb (46.2%), followed by the lower limb (30.8%) and trunk (23.1%) Notably, pain was reported in the majority of cases (70.8%), and swelling or disfigurement was present in an overwhelming 91.7% of patients. Limb dysfunction affected 4 patients (16.7%). Regarding treatment, sclerotherapy was equally divided between Bleomycin and Polidocanol, with each being used in 50% of cases. The median number of treatment sessions was 2 (IQR: 1–2), though some patients required up to five sessions. **(Tab. 1)**

Table (2): Size of lesion at different times among the studied patients

Size of the lesion		**Total no.= 24**
Pretreatment	Median (IQR)	9 (5.5 - 13.5)
	Range	4 – 20
1 month post treatment in cm3	Median (IQR)	4 (3 - 8)
	Range	2 – 15
6 month post treatment in cm3	Median (IQR)	0 (0 - 3)
	Range	0 – 8

Table (2) illustrated reduction in lesion size among the studied patients over time. Prior to treatment, the median lesion size was 9 cm^3 with an interquartile range (IQR) of 5.5–13.5 cm^3, and the lesion sizes ranged from 4 to 20 cm^3. One month after treatment, there was a notable decrease, with the median lesion size reducing to 4 cm^3 (IQR: 3–8 cm^3) and a range of 2–15 cm^3.

Table (3): Pain according to NRS score at different times among the studied patients

Pain according to NRS score		**Total no.= 24**
Pretreatment	**Median (IQR)**	8 (6 – 9)
	Range	5 – 10

1 month post treatment	**Median (IQR)**	5 (4 – 6)
	Range	3 – 8
6 month post treatment	**Median (IQR)**	0 (0 – 3)
	Range	0 – 6

There was a significant reduction in pain levels among the studied patients over time, as measured by the Numerical Rating Scale (NRS). Before treatment, the median pain score was 8, with an interquartile range (IQR) of 6–9 and a range of 5–10. One month after treatment, the median pain score decreased to 5 (IQR: 4–6), with a range of 3–8, indicating an early improvement in pain relief. By six months post-treatment, the median pain score further declined to 0 (IQR: 0–3), with a range of 0–6. **(Tab.3)**

Table (4): Satisfaction at 1 month and 6 months post treatment among the studied patients

What's your satisfaction about the lesion appearance/ disfigurement		**Total no.= 24**
1 month post treatment	Partial response	24 (100%)
6 month post treatment	Partial response	10 (41.7%)
	Complete response	13 (54.2%)
	Stable	1 (4.2%)

As regard patient satisfaction, at one month post-treatment, all 24 patients (100%) reported a partial response. By six months post-treatment, patient satisfaction improved significantly, with 13 patients (54.2%) achieving a complete response. Meanwhile, 10 patients (41.7%) still reported a partial response. Only 1 patient (4.2%) had a stable condition, showing no further improvement. **(Tab. 4)**

Table (5): Complications post treatment among the studied patients.

		Total no.= 24
Complications	No	9 (37.5%)
	Yes	15 (62.5%)
	Pain	*12 (50.0%)*
	Swelling	*11 (45.8%)*
	Abnormal skin Color	*2 (8.3%)*
	Bleeding	*1 (4.2%)*

A total of 15 patients (62.5%) reported complications, while 9 patients (37.5%) did not experience any. Among the reported complications, pain was the most common, affecting 12 patients (50%), followed closely by swelling in 11 patients (45.8%). Less frequently observed complications included abnormal skin color in 2 patients (8.3%) and bleeding in 1 patient (4.2%). **(Tab.5)**

Table (6): Comparison between sclerosant agent groups regarding demographic data and characteristics of the studied patients

		Sclerosant agent		**Test value**	**P-value**	**Sig.**
		Bleomycin	**Polidocaonol**			
		No.= 12	**No.= 12**			
Age	Median (IQR)	11 (8.5 - 15)	8.5 (5 - 15.5)	-0.724≠	0.469	NS
	Range	3 – 45	3 – 42			
Sex	Female	5 (41.7%)	5 (41.7%)	0.000*	1.000	NS
	Male	7 (58.3%)	7 (58.3%)			
Site of VMs	Lower limb	4 (50%)	0 (0%)	4.550*	0.103	NS
	Upper Limb	2 (25%)	4 (80%)			
	Trunk	2 (25%)	1 (20%)			
Pain	No	3 (25%)	4 (33.3%)	0.202*	0.653	NS
	Yes	9 (75%)	8 (66.7%)			
Swelling/Disfigurement	No	2 (16.7%)	0 (0%)	2.182*	0.140	NS
	Yes	10 (83.3%)	12 (100%)			
Limb Dysfunction	No	10 (83.3%)	10 (83.3%)	0.000*	1.000	NS
	Yes	2 (16.7%)	2 (16.7%)			
Number of sessions	Median (IQR)	2 (1.5 - 3)	2 (1 - 2)	-0.971≠	0.332	NS
	Range	1 – 4	1 – 5			

P-value > 0.05: Non significant; P-value < 0.05: Significant; P-value < 0.01: Highly significant
*: Chi-square test; ≠: Mann-Whitney test

Comparison between sclerosant agents: In comparison between sclerosant agents, there was no significant difference in age distribution between the two groups, with a median age of 11 years (IQR: 8.5–15) in the Bleomycin group and 8.5 years (IQR: 5–15.5) in the Polidocanol group (P = 0.469, NS). The gender distribution was also comparable, with an equal proportion of females (41.7%) and males (58.3%) in both groups (P = 1.000, NS). **(Tab. 6)**

Regarding lesion sites, the lower limb was affected in 50% of patients in the Bleomycin group but not in the Polidocanol group,

whereas upper limb involvement was more common in the Polidocanol group (80% vs. 25%). However, this difference was not statistically significant (P = 0.103, NS). The presence of pain and swelling/disfigurement did not differ significantly between the two groups (P = 0.653 and P = 0.140, respectively). Limb dysfunction was observed in 16.7% of patients in both groups, with no statistical difference (P = 1.000, NS). **(Tab. 6)**

Finally, the median number of treatment sessions was 2 (IQR: 1.5–3) for Bleomycin and 2 (IQR: 1–2) for Polidocanol, with a range of 1–4 sessions for Bleomycin and 1–5 for Polidocanol, showing no significant difference between the two treatments (P = 0.332, NS). **(Tab. 6)**

Table (7): Comparison between sclerosant agent groups regarding size of lesion pretreatment, 1 month and 6 months post treatment of the studied patients

		Sclerosant agent		Test value	P-value	Sig.
		Bleomycin	Polidocaonol			
		No.= 12	No.= 12			
Size of the lesion pretreatment ?	Median (IQR)	9 (5 - 16)	9 (5.5 - 12.5)	-0.203≠	0.839	NS
	Range	4 – 20	4 – 18			
Size of the lesion 1 month post treatment in cm3	Median (IQR)	4 (3 - 9)	4 (3 - 7)	-0.147≠	0.883	NS
	Range	2 – 15	2 – 14			
Size of the lesion 6 month post treatment in cm3	Median (IQR)	2.5 (0 - 3.5)	0 (0 - 2)	-1.356≠	0.175	NS
	Range	0 – 8	0 – 5			

P-value > 0.05: Non significant; P-value < 0.05: Significant; P-value < 0.01: Highly significant
≠: Mann-Whitney test

Table (7) showed a comparison of lesion size between Bleomycin and Polidocanol at different time points. Both groups had a median lesion size of 9 cm^3 pretreatment, with no significant difference (P = 0.839). At 1 month, the median size reduced to 4 cm^3 in both groups (P = 0.883). By 6 months, further reduction was observed (2 cm^3 for Bleomycin, 0 cm^3 for Polidocanol), but the difference remained non-significant (P = 0.175).

Table (8): Comparison between sclerosant agent groups regarding pain score according to NRS pretreatment, 1 month and 6 months post treatment of the studied patients.

		Sclerosant agent		Test value	P-value	Sig.
		Bleomycin	Polidocaonol			
		No.= 12	No.= 12			
According to NRS From 1 to 10 rate your pain pretreatment	Median (IQR)	7 (6 - 8)	8 (7.5 - 10)	-1.807≠	0.071	NS
	Range	5 – 10	6 – 10			
According to NRS From 1 to 10 rate your pain 1 month post treatment	Median (IQR)	5 (4 - 6)	5.5 (4 - 6)	-0.517≠	0.605	NS
	Range	3 – 6	4 – 8			
According to NRS From 1 to 10 rate your pain 6 months post treatment?	Median (IQR)	2 (0 - 3.5)	0 (0 - 2.5)	-1.200≠	0.230	NS
	Range	0 – 6	0 – 4			

P-value > 0.05: Non significant; P-value < 0.05: Significant; P-value < 0.01: Highly significant
≠: Mann-Whitney test

Comparison between sclerosant agent groups regarding pain score, pretreatment, the median pain scores were 7 (Bleomycin) and 8 (Polidocanol), with no significant difference

(P = 0.071). At 1 month, pain levels decreased in both groups (5 vs. 5.5), remaining statistically non-significant (P = 0.605). By 6 months, pain scores further dropped (2 vs. 0), but again, no significant difference was found (P = 0.230). These results suggest both agents effectively reduce pain over time, with comparable outcomes.

Table (9): Comparison between sclerosant agent groups regarding satisfaction about the lesion appearance/disfigurement at 1 month and 6 months post treatment of the studied patients

What's your satisfaction about the lesion appearance/ disfigurement		Sclerosant agent		Test value	P-value	Sig.
		Bleomycin	Polidocaonol			
		No.= 12	No.= 12			
1 month post treatment	Partial response	12 (100%)	12 (100%)	-	-	-
6 month post treatment	Partial response	6 (50%)	4 (33.3%)	2.092*	0.351	NS
	Complete response	5 (41.7%)	8 (66.7%)			
	Stable	1 (8.3%)	0 (0%)			

P-value > 0.05: Non significant; P-value < 0.05: Significant; P-value < 0.01: Highly significant
*: Chi-square test

At 1 month, all patients in both groups (100%) showed a partial response. By 6 months, more patients in the Polidocanol group achieved complete response (66.7% vs. 41.7%), while partial responses were higher in the Bleomycin group (50% vs. 33.3%). Only one patient in the Bleomycin group showed a stable lesion. However, the difference was not statistically significant (P = 0.351). **(Tab. 9)**

Table (10): Comparison between sclerosant agent groups regarding post treatment complications of the studied patients.

		Sclerosant agent		Test value	P-value	Sig.
		Bleomycin	Polidocaonol			
		No.= 12	No.= 12			
Complications	No	7 (58.3%)	2 (16.7%)	4.444*	0.035	S
	Yes	5 (41.7%)	10 (83.3%)			
	Pain in complication	3 (25.0%)	9 (75.0%)	6.000*	0.014	S
	Swelling in complication	3 (25.0%)	8 (66.7%)	4.196*	0.041	S
	Abnormal skin Color	2 (16.7%)	0 (0.0%)	2.182*	0.140	NS
	Bleeding	1 (8.3%)	0 (0.0%)	1.043*	0.307	NS

P-value > 0.05: Non significant; P-value < 0.05: Significant; P-value < 0.01: Highly significant
*: Chi-square test

Complications were significantly more common in the Polidocanol group (83.3% vs. 41.7%, P = 0.035). Specifically, pain (75% vs. 25%, P = 0.014) and swelling (66.7% vs. 25%, P = 0.041) were significantly higher with Polidocanol. However, abnormal skin color and bleeding showed no significant difference between the groups. **(Tab. 10)**

ILLUSTRATIVE CASES

Case 1:

A 5-year-old female patient with vulval venous malformation causing pain and disfigurement, underwent Polidocanol injection.

- The size pre-management was 8 cc.
- It decreased to 2 cc 6 months after management.
- Pain decreased according to NRS From 10 pre-management to 3 post management.
- Minor local complications occurred as regards the procedure in the form of slight swelling and redness.

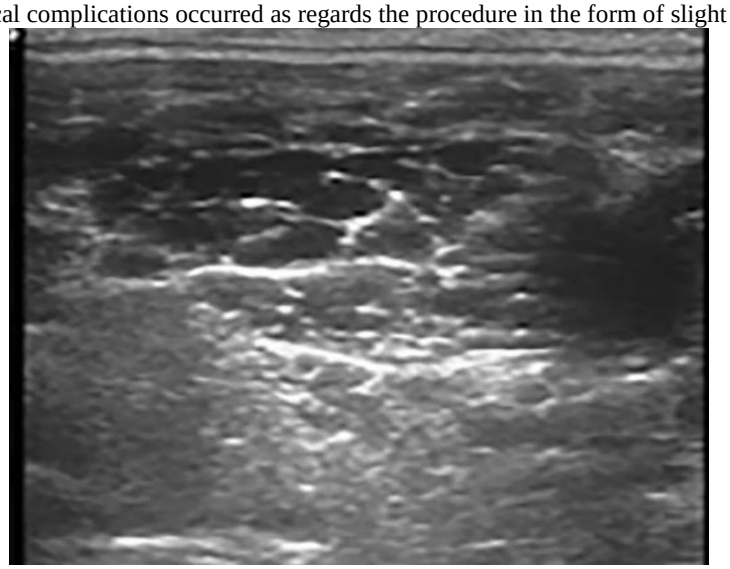

Figure (1): The Ultrasound appearance of the lesion

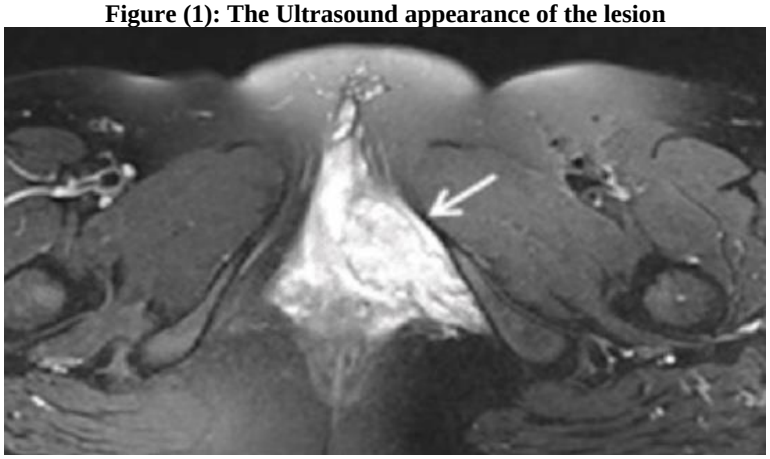

Figure (2): MRI appearance of the lesion

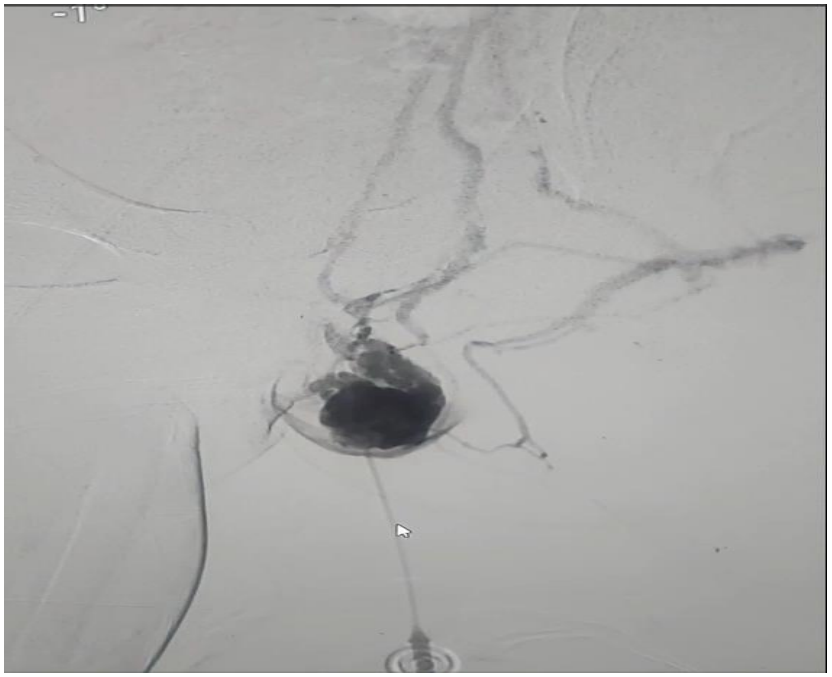

Figure (3): Injection of contrast within the lesion under fluoroscopic guidance

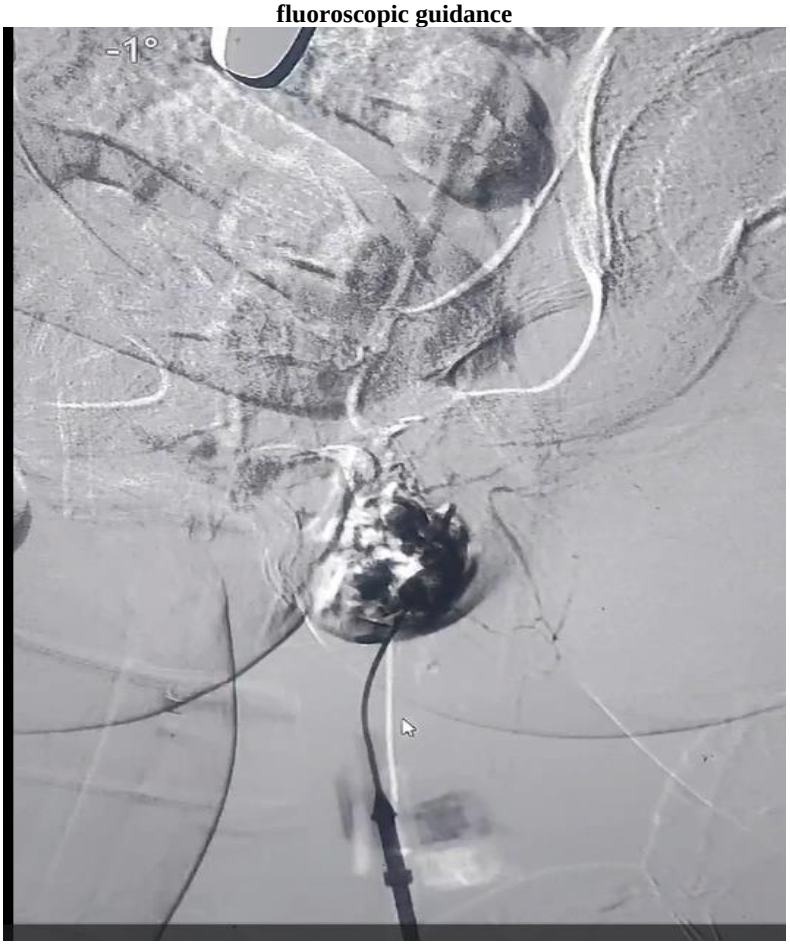

Figure (4): Fluoroscopic appearance of the lesion after injection of the sclerosant

Case 2:

A 17-year-old male patient with right knee venous malformation causing pain, swelling and disfigurement, underwent Bleomycin injection.

- The size pre-management was 12 cc.
- It decreased to 8 cc 6 months after management.
- Pain decreased according to NRS from 8 pre-management to 4 post management.
- No local complications occurred as regards the procedure.

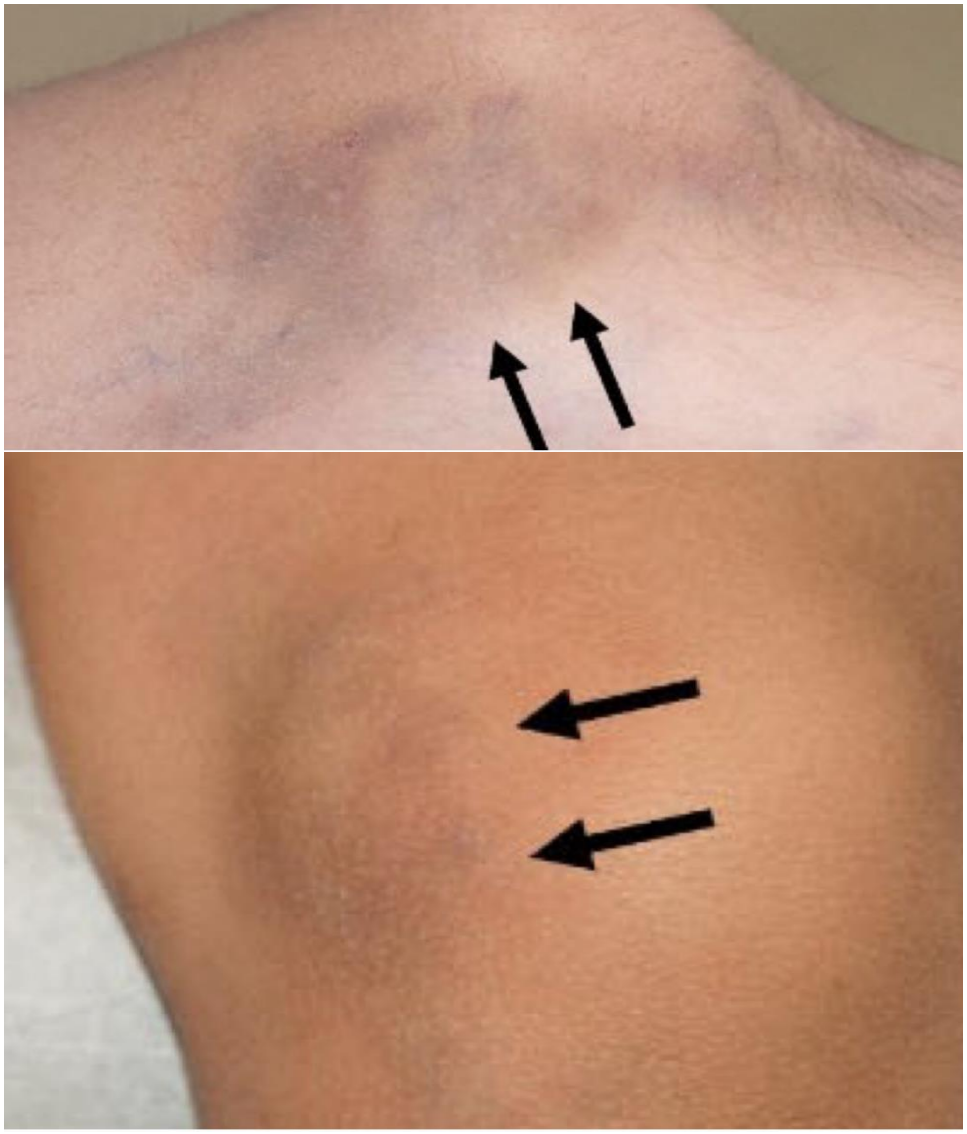

Figure (5): Appearance of the lesion

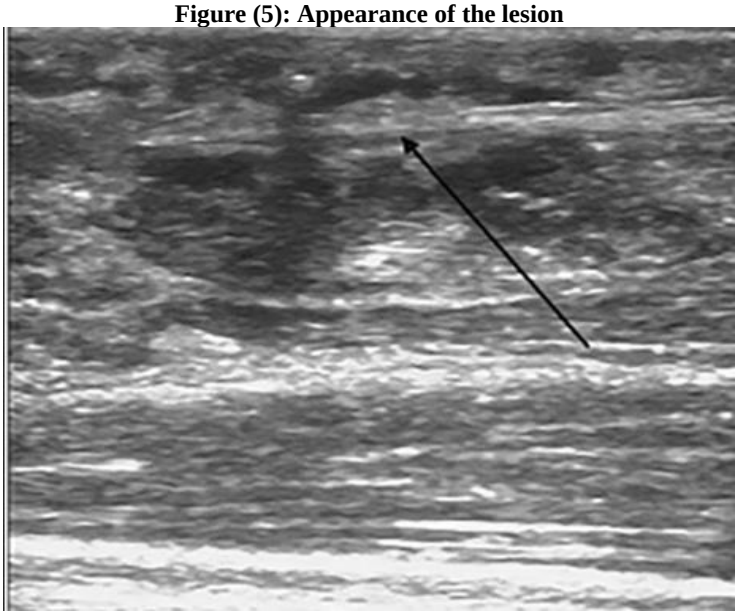

Figure (6): Ultrasound appearance of the lesion

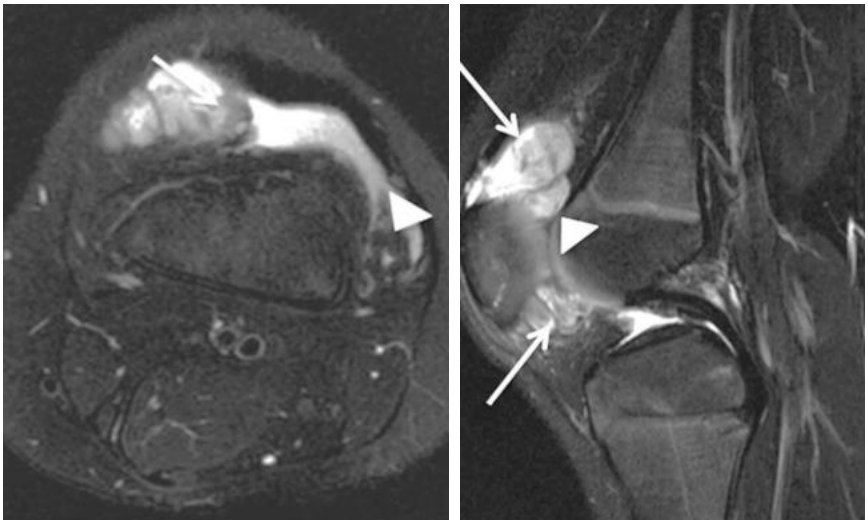

Figure (7): MRI appearance of the lesion

Figure (8): Injection of contrast within the lesion under fluoroscopic guidance

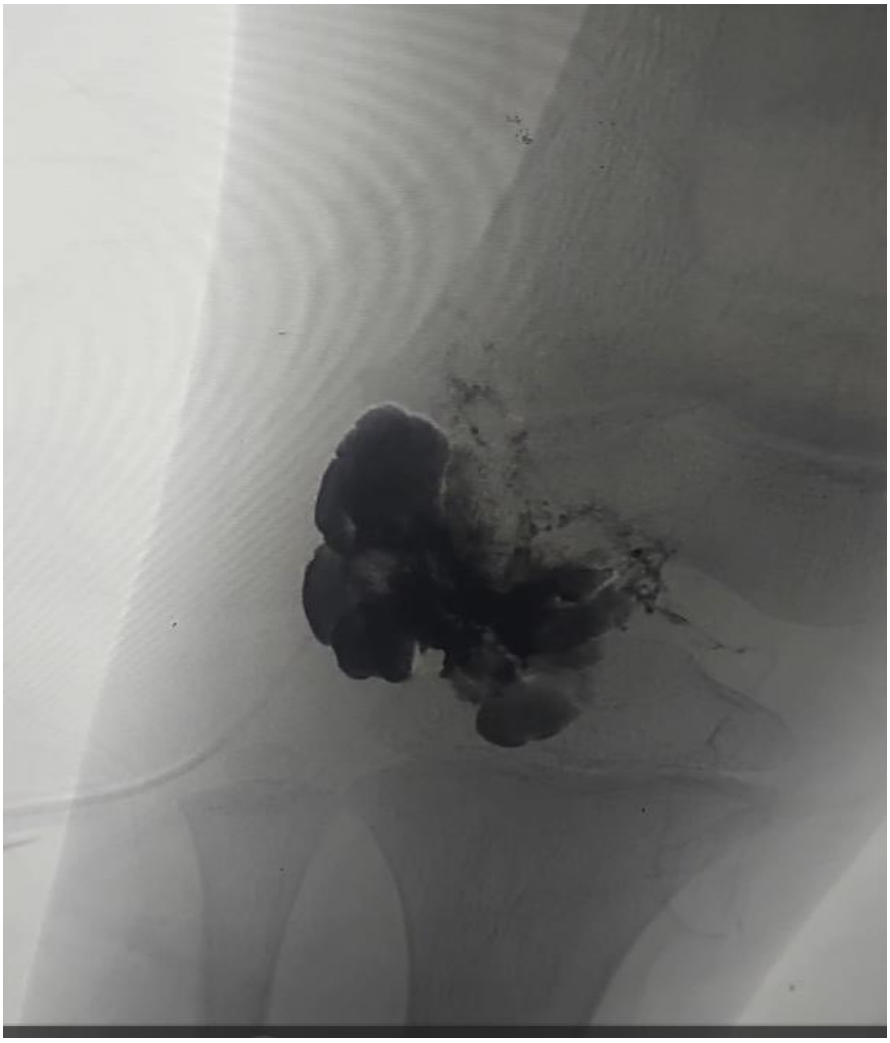

Figure (9): Fluoroscopic appearance of the lesion after injection of the sclerosant

DISCUSSION

Venous malformations (VMs) account for 70% of vascular malformations and are the most prevalent among such pathologies ***(Sadick et al., 2018)***. VMs are congenital conditions that can manifest at various ages, even in later stages of life. Patients with VMs commonly experience symptoms such as swelling, pain, and cosmetic disfigurement, which significantly impact their quality of life. These malformations consist of abnormally connected tortuous dilated veins and can occur in any part of the body, with a higher incidence in the lower extremities ***(Ni et al., 2024).***

VMs have physical and psychological impacts on the patients: Their physical impact is characterized by pain, swelling, and dysfunction, while their psychological impact is characterized by changes in the appearance arising from these malformations. Surgical resection was previously considered as an important conventional treatment for VMs; however, due to the complex structure of the lesion, which often infiltrates the surrounding tissues, a recurrence of VMs was often observed even after their curative resection ***(Hu et al., 2022).***

Currently, sclerotherapy is the preferred treatment option for VMs, and various sclerosing agents are used to treat them ***(Cao et al., 2023; Park et al., 2016).*** Absolute ethanol is considered the most effective agent, but it has a higher incidence of postoperative complications than other agents. In recent years, the efficacy of bleomycin and polidocanol for VMs has gained considerable recognition ***(He et al., 2023; Yang et al., 2020).*** Bleomycin causes damage to endothelial cells by eliciting intravascular inflammatory responses and vascular fibrosis ***(Zhang et al., 2013).*** Polidocanol is a sclerosing agent widely used in foam sclerotherapy for VMs. However, the effect of the two sclerosants alone is poor, and the lesion volume was reduced by no more than 70% ***(Cao et al., 2023; He et al., 2023).***

Unfortunately, the evaluation of treatment efficacy has focused on changes in lesion size, with a lack of emphasis on subjective findings, such as symptom improvement and appearance ***(Hu et al., 2022).*** Therefore, further studies are needed to evaluate the efficacy and safety of bleomycin and polidocanol in treating VMs.

This randomized clinical trial was conducted on 24 patients with peripheral low flow vascular (venous) malformation who randomly classified into 2 groups: group A: 12 patients subjected to Polidocanol injection, group B; 12 patients subjected to Bleomycin percutaneous injection, at 'Interventional radiology unit' at the Radiology Department "Ain Shams University hospitals", Cairo, Egypt, to compare between Bleomycin and polidocanol injection in the treatment of peripheral venous

malformations as regard the reduction in size/session, number of sessions used, postprocedural pain and complications.
Among the studied patients, the median age of the studied patients was 10 (IQR: 6.5–15) years ranged from 3 to 45 years. There were 14 males (58.3%) and 10 females (41.7%).

Likely, a retrospective study included 55 patients diagnosed with common sporadic VMs. In this study, there were 31 female and 24 male patients with mean age, 18.8 years ranged from 2 to 60 years ***(Yang et al., 2020).***

Slightly similar to our results, a retrospective study that 138 patients with suspected VMs. Among their patients, 58 were male and 80 were female. The age range was 3 to 65 years, with a mean age of 27.86 years ***(Ni et al., 2024).*** Also, a retrospective study that was conducted on 51 patients diagnosed with VMs, the patients included 17 males and 34 females, ranging in age from 5 to 65 years of age (mean, 26.8 ± 13.5 years) ***(He et al., 2023)***

.
In the current study, the upper limb was the most affected site (46.2%), followed by the lower limb (30.8%) and trunk (23.1%). This contrasts with the study by ***Zhan et al. (2020)*** where the lower limb was more frequently involved (68.4%) compared to the upper limb (31.6%) ***(Zhan et al., 2020).*** Similarly, ***Kim et al.*** reported a higher prevalence of VMs in the lower extremities (69.4%) than in the upper extremities (30.6%) ***(Kim et al., 2022).*** These discrepancies may result from differences in study populations or referral patterns.

Pain was common in our patients (70.8%), and swelling or disfigurement occurred in 91.7% of cases. Limb dysfunction affected 16.7% of patients. These findings are consistent with ***Zhan et al.,*** who reported pain and/or numbness in 65.8% of patients and limb movement disorders in 5.26% ***(Zhan et al., 2020). Kim et al.*** also identified pain as the most common symptom (68.1%) ***(Kim et al., 2022). Ni et al.*** further corroborated these observations, noting that common symptoms included pain, swelling, abnormal skin color, and functional limitations ***(Ni et al., 2024).***

Sclerotherapy was equally divided between Bleomycin and Polidocanol (50% each) in our study. The median number of sessions was two (IQR: 1–2), with some patients requiring up to five sessions. In contrast, ***Zhan et al.*** reported a median of four sclerotherapy sessions (range: 1–10) ***(Zhan et al., 2020). Kim et al.*** found that 16.7% of patients underwent sclerotherapy alone, while 11.1% received combined treatments such as sclerotherapy plus phlebectomy or coil embolization ***(Kim et al., 2022).*** These variations in treatment approaches and session numbers may reflect differences in lesion characteristics, treatment protocols, or healthcare resources across studies.

Sclerotherapy involves injecting a sclerosing agent into the affected area to cause the lesion to shrink ***(Liu et al., 2024).*** In the current study, there was reduction in lesion size over time. Prior to treatment, the median lesion size was 9 cm^3 with an interquartile range (IQR) of 5.5–13.5 cm^3, and the lesion sizes ranged from 4 to 20 cm^3. One month after treatment, there was a notable decrease, with the median lesion size reducing to 4 cm^3 (IQR: 3–8 cm^3) and a range of 2–15 cm^3.

The observed reduction in lesion size among our studied patients aligns with findings from previous studies on sclerotherapy for venous malformations (VMs). In a retrospective study by ***Nevesny et al.*** that included 26 patients with venous malformations (VMs) and lymphatic malformations (LMs) who underwent bleomycin sclerotherapy. Out of 26 patients, 15 (57%) had VMs. Sclerotherapy resulted in a ≥50% volume reduction in 64% of VMs ***(Nevesny et al., 2021).*** Similarly, ***Spence et al.*** study of 37 patients with facial VMs were treated by percutaneous sclerotherapy with bleomycin, reported that percutaneous sclerotherapy with bleomycin led to objective size reductions in facial VMs, with 11 out of 32 lesions showing a marked decrease (≥50%) and 10 showing minor improvements (<50%) ***(Spence et al., 2010).*** Furthermore, a study by **Ahmad** demonstrated that sclerotherapy using bleomycin and sodium tetradecyl sulfate achieved complete obliteration in 16 patients, with significant size reductions in others ***(Ahmad, 2019).***

Among studied patients, initially, the median pain score was 8 (IQR: 6–9), decreasing to 5 (IQR: 4–6) one month post-treatment, and further declining to 0 (IQR: 0–3) at six months. Similarly, a study by ***Mimura et al.*** evaluated the safety and efficacy of polidocanol sclerotherapy in 31 patients with painful venous malformations (VMs). They reported a significant reduction in mean pain scores from 6.6 ± 2.5 before treatment to 2.4 ± 2.9 after treatment ($P < .001$). Notably, 89.7% of patients experienced pain improvement at a mean follow-up of 46 months ***(Mimura et al., 2009).***

Likely, a retrospective review of 152 patients with VMs treated with electrochemotherapy combined with polidocanol foam (ECP) and bleomycin polidocanol foam (BPF), the preoperative mean VAS scores were 5.50 ± 0.99 in the BPF group and the mean postoperative was 1.29 ± 1.17 showed significant reduction in pain ***(Liu et al., 2024).***

Furthermore, a comprehensive review by ***Ali & Mitchell*** analyzed outcomes of VM sclerotherapy across multiple studies. They found that 35.4% of patients experienced significant pain improvement, 17.2% had moderate improvement, and 12.9% reported mild improvement. However, 17.2% experienced no change, and 7.7% reported worsening pain ***(Ali & Mitchell, 2017).***

As regard patient satisfaction, at one month post-treatment, all 24 patients (100%) reported a partial response. By six months post-treatment, patient satisfaction improved significantly, with 13 patients (54.2%) achieving a complete response. Meanwhile, 10 patients (41.7%) still reported a partial response. Only 1 patient (4.2%) had a stable condition, showing no further improvement.

This result aligns with findings from other studies. For instance, a systematic review and meta-analysis by ***De Maria et al.*** reported

an overall patient satisfaction rate of 91.0% (95% CI, 86.1–95.9%) following sclerotherapy for venous malformations of the head and neck ***(De Maria et al., 2020).*** Similarly, a study by ***Khaitovich et al.*** evaluated patient satisfaction after sclerotherapy of venous malformations in 153 patients. They found that 25% of patients reported being very satisfied, 36% satisfied, 32% not satisfied, and 7% very unsatisfied with treatment outcomes ***(Khaitovich et al., 2019).***

In contrast, a retrospective study by ***Çay et al.*** demonstrated that polidocanol sclerotherapy was safe and effective in VM treatment, with high satisfaction. Out of 232 patients, 116 (50%) patients reported significant satisfaction, 75 (32.3%) patients reported slight satisfaction, 24 (10.3%) patients reported unsatisfaction, and 17 (7.3%) patients reported significant dissatisfaction ***(Çay et al., 2023).***

Variations in patient satisfaction following sclerotherapy for venous malformations (VMs) can be attributed to several factors, including the choice of sclerosant agent, lesion characteristics, patient demographics, and assessment methodologies.

The present study observed a higher complication rate (62.5%) among patients undergoing sclerotherapy for venous malformations (VMs), with pain (50%) and swelling (45.8%) being the most common issues. In contrast, ***Ni et al.*** reported a lower complication rate of 22.5%, with swelling (10.14%) and pain (7.25%) as the predominant complications ***(Ni et al., 2024).*** Similarly, ***Yang et al.*** documented minor complications in 18.2% of patients, noting that while all patients experienced transient swelling and pain post-treatment, these were not classified as complications ***(Yang et al., 2020).***

The higher complication rate in the present study may be attributed to differences in sclerosant agents, treatment protocols, or patient selection criteria. Additionally, the classification of transient symptoms like pain and swelling as complications varies among studies, influencing reported rates.

In comparison between sclerosant agents, there was no significant difference in age distribution between the two groups, with a median age of 11 years (IQR: 8.5–15) in the Bleomycin group and 8.5 years (IQR: 5–15.5) in the Polidocanol group (P = 0.469, NS). The gender distribution was also comparable, with an equal proportion of females (41.7%) and males (58.3%) in both groups (P = 1.000, NS).

He et al. reported that the mean age in BPF group was 24.5 ± 15.7 years and the mean age in Polidocanol group was 28.0 ± 12.1 years. Most of patients in both BPF and Polidocanol groups were females (71.4%, 63.3%, respectively) ***(He et al., 2023).*** Also, in ***Liu et al.*** study, the mean age in BPF group was 26.77 ± 13.22 years and 26.12 ± 12.77 years in ECP. Male to female was 38/49 in BPF and 30/35 in ECP group, indicating that most of patients in both groups were females. Both age and gender showed no significant difference between the studied groups ***(Liu et al., 2024).***

Regarding lesion sites, the lower limb was affected in 50% of patients in the Bleomycin group but not in the Polidocanol group, whereas upper limb involvement was more common in the Polidocanol group (80%). However, this difference was not statistically significant. The presence of pain and swelling/disfigurement did not differ significantly between the two groups. Limb dysfunction was observed in 16.7% of patients in both groups, with no statistical difference. Finally, the median number of treatment sessions was 2 (IQR: 1.5–3) for Bleomycin and 2 (IQR: 1–2) for Polidocanol, with a range of 1–4 sessions for Bleomycin and 1–5 for Polidocanol, showing no significant difference between the two treatments.

In contrast, ***He et al.*** reported that the most commonly involved sites were the lower extremities in both the BPF and Polidocanol groups (57.7% and 47.05%, respectively). The most common symptom in both groups was pain (66.67% vs. 63.33%), followed by cosmetic disfigurement and swelling. The mean number of sclerotherapy sessions was similar between the BPF group (1.09 ± 0.3) and the Polidocanol group (1.03 ± 0.2), with no significant differences noted between the two groups ***(He et al., 2023).***
In this study, both Bleomycin and Polidocanol groups started with a median lesion size of 9 cm^3. At 1 month post-treatment, the median size reduced to 4 cm^3 in both groups. By 6 months, further reductions were observed (2 cm^3 for Bleomycin, 0 cm^3 for Polidocanol), but these differences were not statistically significant. Similarly, median pain scores decreased from 7 (Bleomycin) and 8 (Polidocanol) pre-treatment to 2 and 0, respectively, at 6 months, with no significant differences between the groups. These findings suggest that both agents effectively reduce lesion size and pain over time.

Consistent with our results, a study by ***Liu et al.*** which reported that there was no significant difference in the percentage change of lesion volume and clinical response between the two groups (BPF Vs ECP: 76.91% ± 18.62% vs 75.89% ± 8.88%; *P* = .764). On the other hand, the reduction of VAS of pain in the BPF group was significantly higher than that in the ECP group (reduction of VAS: 4.21 ± 1.27 vs 3.46 ± 0.66; *P* = .008) ***(Liu et al., 2024).*** In contrast***, He et al.*** detected that preoperative MRI revealed the mean VM volume was 33.9 ± 30.4 mL for the BPF group and 28.2 ± 23.4 mL for the polidocanol foam group. The mean postoperative VM volume on MRI or ultrasound examination was 7.0 ± 6.0 mL for the BPF group and 12.8 ± 11.4 for the polidocanol foam group. The decrease in percentage of lesion volume in the BPF group was significantly higher than the polidocanol foam group (79.4 ± 1.6% vs 55.7 ± 6.1%; *P* < .001) **(*He et al., 2023).***

In the current study, at 1 month, all patients showed a partial response, but by 6 months, complete response was more frequent in the Polidocanol group (66.7% vs. 41.7%), while partial response was higher in the Bleomycin group (50% vs. 33.3%), with one patient in the Bleomycin group having a stable lesion; however, the difference was not statistically significant (P = 0.351). Complications were significantly more common with Polidocanol (83.3% vs. 41.7%, P = 0.035), particularly pain (75% vs. 25%, P = 0.014) and swelling (66.7% vs. 25%, P = 0.041), while abnormal skin color and bleeding showed no significant difference between groups.

Several studies have compared the efficacy and safety of polidocanol and bleomycin as sclerosing agents for treating venous malformations (VMs). ***He et al.*** detected that patient satisfaction scores were also higher in the BPF group (7.2 ± 1.1 vs. 5.7 ± 0.8; P < .001). Importantly, no major complications were observed in either group, and minor complication rates were comparable between the two ***(He et al., 2023).***

All patients in study by ***Yang et al.*** reported symptomatic improvement, with an excellent response in 58.2% and a good response in 36.4% of cases. Magnetic resonance imaging showed a mean lesion volume reduction of 84.6%. Minor complications occurred in 12% of procedures, with no major complications reported ***(Yang et al., 2020).***

Additionally, a study by ***Markovic et al.*** investigated the safety and efficacy of foam sclerotherapy using polidocanol in children with low-flow vascular malformations. The study reported a high rate of symptom improvement and lesion size reduction, with minor complications observed in a subset of patients ***(Markovic et al., 2020).***

CONCLUSION

In this randomized clinical trial, both Bleomycin and Polidocanol demonstrated comparable efficacy in reducing lesion size and alleviating pain over a six-month period. By one month, all patients in both groups exhibited partial responses. At six months, the Polidocanol group had a higher rate of complete response (66.7% vs. 41.7%), although this difference was not statistically significant (P = 0.351). While Polidocanol showed a trend toward more complete responses, it was associated with a significantly higher incidence of complications (83.3% vs. 41.7%, P = 0.035), particularly pain (75% vs. 25%, P = 0.014) and swelling (66.7% vs. 25%, P = 0.041). In contrast, Bleomycin had fewer overall complications, but still yielded effective clinical outcomes.

REFERENCES

1. **Ahmad, S. (2019).** Efficacy of percutaneous sclerotherapy in low flow venous malformations-a single center series. *Neurointervention*, *14*(1), 53-60.
2. **Ali, S., & Mitchell, S. E. (2017).** *Outcomes of venous malformation sclerotherapy: a review of study methodology and long-term results.* Paper presented at the Seminars in Interventional Radiology.
3. **Cao, J., Liu, J., Zhang, X., & Wang, Z. (2023).** A systematic review and network meta-analysis of the effectiveness of sclerotherapy for venous malformation. *Journal of Vascular Surgery: Venous and Lymphatic Disorders*, *11*(1), 210-218. e213.
4. **Çay, F., Altunbulak, A. Y., Özbay, Y., Eldem, G., Çil, B. E., Vargel, İ., et al. (2023).** Clinical results of polidocanol sclerotherapy in venous malformation treatment: patient-perceived improvement and satisfaction. *Phlebology*, *38*(1), 36-43.
5. **De Maria, L., De Sanctis, P., Balakrishnan, K., Tollefson, M., & Brinjikji, W. (2020).** Sclerotherapy for venous malformations of head and neck: systematic review and meta-analysis. *Neurointervention*, *15*(1), 4-17.
6. **He, B., Yang, B., Nie, Q.-q., Zhang, J.-b., Chen, J., Liu, P., et al. (2023).** Comparison of polidocanol foam versus bleomycin polidocanol foam for treatment of venous malformations. *Journal of Vascular Surgery: Venous and Lymphatic Disorders*, *11*(1), 143-148.
7. **Hu, W., Liu, Z., Sun, J., Wang, L., Song, D., & Guo, L. (2022).** Effectiveness of polidocanol in the treatment of venous malformations: a meta-analysis. *Frontiers in Pediatrics*, *10*, 925318.
8. **Khaitovich, B., Kalderon, E., Komisar, O., Eifer, M., Raskin, D., & Rimon, U. (2019).** Venous malformations sclerotherapy: outcomes, patient satisfaction and predictors of treatment success. *Cardiovascular and Interventional Radiology*, *42*, 1695-1701.
9. **Kim, H., Joh, J., & Labropoulos, N. (2022).** Characteristics, clinical presentation, and treatment outcomes of venous malformation in the extremities. *Journal of Vascular Surgery: Venous and Lymphatic Disorders*, *10*(1), 152-158.
10. **Legiehn, G. M., & Heran, M. K. (2008).** Venous malformations: classification, development, diagnosis, and interventional radiologic management. Radiologic clinics of North America, 46(3), 545-597.
11. **Liu, J.-w., Ni, B., Gao, X.-x., He, B., Nie, Q.-q., Fan, X.-q., et al. (2024).** Comparison of bleomycin polidocanol foam vs electrochemotherapy combined with polidocanol foam for treatment of venous malformations. *Journal of Vascular Surgery: Venous and Lymphatic Disorders*, *12*(2), 101697.
12. **Markovic, J. N., Nag, U., & Shortell, C. K. (2020).** Safety and efficacy of foam sclerotherapy for treatment of low-flow vascular malformations in children. *Journal of Vascular Surgery: Venous and Lymphatic Disorders*, *8*(6), 1074-1082.
13. **Mimura, H., Fujiwara, H., Hiraki, T., Gobara, H., Mukai, T., Hyodo, T., et al. (2009).** Polidocanol sclerotherapy for painful venous malformations: evaluation of safety and efficacy in pain relief. *European radiology*, *19*, 2474-2480.
14. **Müller-Wille, R., Wildgruber, M., Sadick, M., & Wohlgemuth, W. A. (2018).** Vascular anomalies (part II): interventional therapy of peripheral vascular malformations. In RöFo-Fortschritte auf dem Gebiet der Röntgenstrahlen und der bildgebenden Verfahren (Vol. 190, No. 10, pp. 927-937). © Georg Thieme Verlag KG.
15. **Nevesny, F., Chevallier, O., Falvo, N., Guillen, K., Malakhia, A., Pellegrinelli, J., et al. (2021).** Bleomycin for percutaneous sclerotherapy of venous and lymphatic malformations: a retrospective study of safety, efficacy and mid-term outcomes in 26 patients. *Journal of Clinical Medicine*, *10*(6), 1302.
16. **Ni, B., Liu, J.-w., Fan, X.-q., He, B., Nie, Q.-q., Ye, Z.-d., et al. (2024).** Clinical outcomes and predictors of bleomycin polidocanol foam sclerotherapy treatment response in venous malformations. *Journal of International Medical Research*, *52*(1), 03000605231223441.
17. **Park, H. S., Do, Y. S., Park, K. B., Kim, K.-H., Woo, S. Y., Jung, S.-H., et al. (2016).** Clinical outcome and predictors of treatment response in foam sodium tetradecyl sulfate sclerotherapy of venous malformations. *European radiology*, *26*, 1301-1310.

18. **Sadick, M., Müller-Wille, R., Wildgruber, M., & Wohlgemuth, W. A. (2018).** *Vascular anomalies (part I): classification and diagnostics of vascular anomalies.* Paper presented at the RöFo-Fortschritte auf dem Gebiet der Röntgenstrahlen und der bildgebenden Verfahren.
19. **Spence, J., Krings, T., TerBrugge, K. G., & Agid, R. (2011).** Percutaneous treatment of facial venous malformations: a matched comparison of alcohol and bleomycin sclerotherapy. Head & neck, 33(1), 125-130.
20. **Sun, Y., Gu, H., Yang, X., Cai, R., Shang, Y., Hu, L., ... & Lin, X. (2020).** Bleomycin polidocanol foam (BPF) stability–in vitro evidence for the effectiveness of a novel sclerosant for venous malformations. European Journal of Vascular and Endovascular Surgery, 59(6), 1011-1018.
21. **Tessari, L., Cavezzi, A., & Frullini, A. (2001).** Preliminary experience with a new sclerosing foam in the treatment of varicose veins. Dermatologic surgery, 27(1), 58-60.
22. **Van Der Vleuten, C. J., Kater, A., Wijnen, M. H., Schultze Kool, L. J., & Rovers, M. M. (2014).** Effectiveness of sclerotherapy, surgery, and laser therapy in patients with venous malformations: a systematic review. *Cardiovascular and interventional radiology*, *37*, 977-989.
23. **Yamaki, T., Nozaki, M., Sakurai, H., Takeuchi, M., Soejima, K., & Kono, T. (2008).** Prospective randomized efficacy of ultrasound-guided foam sclerotherapy compared with ultrasound-guided liquid sclerotherapy in the treatment of symptomatic venous malformations. Journal of vascular surgery, 47(3), 578-584.
24. **Yang, X., Chen, H., Gu, H., Jin, Y., Hu, L., Hua, C., et al. (2020).** Interim results of bleomycin-polidocanol foam sclerotherapy as a highly efficient technique for venous malformations. *Journal of Vascular Surgery: Venous and Lymphatic Disorders*, *8*(6), 1066-1073.
25. **Zhan, T., Cai, F., Guo, P., Lian, Y., Zhuang, H., Zhang, J., et al. (2020).** Therapeutic evaluation of sclerotherapy for limb venous malformations: A case series. *Phlebology*, *35*(9), 663-671.
26. **Zhang, J., Li, H.-B., Zhou, S.-Y., Chen, K.-S., Niu, C.-Q., Tan, X.-Y., et al. (2013).** Comparison between absolute ethanol and bleomycin for the treatment of venous malformation in children. *Experimental and therapeutic medicine*, *6*(2), 305-309.