e-ISSN: 0975-5160, p-ISSN: 2820-2651

Available online on www.ijtpr.com

International Journal of Toxicological and Pharmacological Research 2023; 13(9); 6-13

Original Research Article

Short-Term Outcomes of Mechanochemical Ablation Versus Trendelenburg Procedure for Varicose Veins: A Randomised Control Trial

Swathi Vellaichamy[1], Narenkumar A[2], Sarathganesh S[3], Gokul D Yatheendranathan[4]

[1]Senior Resident, Department of General Surgery, Shri Sathya Sai Medical College and Research Institute, Sri Balaji Vidyapeeth (Deemed to be University), Ammapettai, Chengalpet District, Tamil Nadu, 603108

[2]Associate Professor, Department of General Surgery, Shri Sathya Sai Medical College and Research Institute, Sri Balaji Vidyapeeth (Deemed to be University), Ammapettai, Chengalpet District, Tamil Nadu, 603108

[3]Strategy Consultant, IQVIA, Bangalore, India

[4]Associate Professor, Department of General Surgery, Shri Sathya Sai Medical College and Research Institute, Sri Balaji Vidyapeeth (Deemed to be University), Ammapettai, Chengalpet District, Tamil Nadu, 603108

Received: 28-06-2023 / Revised: 21-07-2023 / Accepted: 26-08-2023

Corresponding author: Dr. Gokul D Yatheendranathan

Conflict of interest: Nil

Abstract:

Introduction: Varicose veins is a common disease of the lower limbs, affecting predominantly the great saphenous system. Various methods are in place for effective management of varicose veins. Trendelenburg operation with stripping of the vein has long been considered as the gold standard of treatment. However, in the era of minimal access surgery, it is necessary to study the wide application of various endovenous procedures and its effectiveness against the standard of care. In our study we have compared the effectiveness of mechanochemical endovenous ablation (MOCA), using Flebogrif™, a newer non thermal endovenous therapy with conventional surgery.

Methods: Randomised control trial was conducted among 71 patients undergoing mechanochemical endovenous ablation using Flebogrif™ and conventional surgery for the treatment of great saphenous varicose veins. Factors such as blood loss, pain scores, return to mobility, duration of hospital stay, incidence of surgical site infection, recanalization rates, and cost were compared between the groups.

Results: Age, Gender, and Diagnosis weren't significantly different between the groups. Patients undergoing mechanochemical endovenous ablation had lower blood loss, lesser pain scores in early post-operative period and earlier return to mobility. They also had significantly decreased length of hospital stay as compared to the conventional surgery group. However, cost of the surgery was found to be more in the endovenous group. Further, on follow up the recanalization rates in the endovenous group was found to be significantly higher than the conventional surgery group. However, patients with recanalization presented back with only minimal or no symptoms. Ulcer healing, complications, and Pain scores at one month and six months were not significantly different between the groups.

Conclusion: Mechanochemical endovenous ablation is preferred over conventional surgery for the treatment of great saphenous varicose veins. It can be performed under local anaesthesia and ensures better early post-operative outcomes as compared to the Trendelenburg operation with stripping of the veins.

Keywords: Mechanochemical endovenous ablation, Trendelenburg operation, stripping of veins, varicose veins.

Introduction

Varicose vein is a common disease of the lower limbs caused by weak or damaged vein walls and valves, affecting predominantly the great saphenous venous system.[1] Epidemiological studies have shown that the prevalence of varicose veins is about 21% in adults.[2] The spectrum of symptoms of great saphenous vein varicose veins range from simple cosmetic complaints, all the way to blackish discolouration of the skin and ulcers.[3] Quality of life studies revealed major disability and social impairment besides its chronicity and relapse.[4] The treatment options vary ranging from simple compression stockings to day-care procedures like ultrasound-guided foam sclerotherapy, endovenous laser ablation, radiofrequency ablation, emerging techniques such

as mechano-chemical ablation[MOCA] and cyanoacrylate glue occlusion[CAE] to the gold standard of care, Trendelenburg operation with stripping of the vein.[5] Despite being the standard of care, Trendelenburg operation with stripping of the vein comes with a plethora of immediate complications such as pain, haematoma and possible saphenous nerve injury, and has a high recurrence rate of 18 to 40% after five years.[6] Mechanochemical endovenous ablation (MOCA) is a novel technique which uses a rotating wire or deployable hooks to create mechanical damage and the infused sclerosant (sodium tetradecyl sulphate) causes chemical damage to the endothelium of the blood vessels with no thermal energy.[7] MOCA is a safe, relatively cheaper and effective substitute to standard-methods such as surgical-treatment, thermal-ablation, etc. in the management of saphenous varicosity.[5] Mechanochemical endovenous ablation was associated with decreased post-procedural pain and faster-recovery than open or thermal procedures.[8] Thermal ablative modalities can cause local tissue damage due to the heat produced. However, there is no thermal energy exposure in MOCA and as a result, it can be performed without any requirement for even tumescence anesthesia.[4]

In our study, we have performed a randomized clinical trial amongst 71 patients and compared the effectiveness of Mechanochemical endovenous ablation (MOCA), using Flebogrif™, a newer non thermal endovenous therapy, with conventional surgery.

Methods:

Study setting: A single centre randomised control trial between mechanochemical ablation and conventional surgery for primary great saphenous varicose veins between the time period of December 2019 to June 2021, in a tertiary care centre. Shri Sathya Sai Medical College and Research Institute's Human Ethics Committee approval was obtained before the start of the study. Patients were included in the study after obtaining informed and written consent.

CTRI registration number: CTRI/2020/07/026683

Institute human ethics committee approval number: 2019/542

Patient recruitment: 71 patients were included in the study. In patients having bilateral disease, only one leg was treated and included in the study. Recruitment process is mentioned in Figure 1. Both sexes above the age of 18 with varicosity of great saphenous vein with CEAP classification grade II and above were included in the study.[9] Exclusion criteria were Secondary varicose veins, recurrent varicose veins, pregnancy or congenital anomalies or patients who are medically unfit to undergo the procedure, diameter of GSV > 1.2 cms, varicose veins with ABI < 0.9 cms, allergy to sclerosant.[10]

Randomization*:* Non blinded, simple random sampling. 39 patients were grouped under conventional surgery and 32 patients underwent mechanochemical ablation.

Pre-operative assessment: Before the procedure, all patients were clinically examined by the surgeon, USG Venous duplex scan was done to determine SFJ incompetence and reflux.

Study Procedure: Patients who were allocated conventional surgery underwent high flush ligation of the saphenous femoral junction, along with ligation of the tributaries and stripping of the GSV. Open Surgery was done under spinal anaesthesia. In Mechanochemical ablation group, the procedure was done using Flebogrif™ catheter, under local/spinal anaesthesia depending on patient compliance, 4F sheath was inserted at a level just below the knee, through which the Flebogrif™ catheter was inserted up to the SFJ. It was then retracted by a cm and then deployed and pulled down. The metallic barbed wires damage the vein wall as it makes is way distally. After pulling it 2 cms distal to the SFJ, only then chemical ablation was done using 3% sodium tetradecyl sulfate injection after preparing foam (1ml solution + 4ml air) by slowly withdrawing the catheter through the length of the GSV. Perforator incompetence in both groups were treated using foam sclerotherapy injections. Compression bandage was applied to the treated limb post procedure in both the groups.

Post operative assessment and follow up: Patients were followed up for a period of 6 months. Patients were given oral NSAIDs on the night of surgery and thereafter only when required, on the basis of pain. Both groups were assessed for per operative variables such as amount of blood loss, evaluation of pain score before administration of analgesics using VAS score on day of surgery, post operative day 1, and day 5, [11] hospital stay duration measured in days, post-operative complications such as bruises, paraesthesia, haematoma, DVT, skin infections, and cost of procedure. Late findings such as pain score at 1 month and 6 months after surgery and ulcer healing at end of 6 months were assessed.

On the 5th day, 1st month and 6th month, clinical examination and USG venous duplex scan was done to determine great saphenous vein recanalization rates. Partial recanalization was defined as evidence of persistent reflux in <50% of the length of the vein treated and complete recanalization was defined as evidence of persistent reflux in >50% of the length of the vein treated. The standard criterion for reflux was used: at least 0.5 second of reflux.[12]

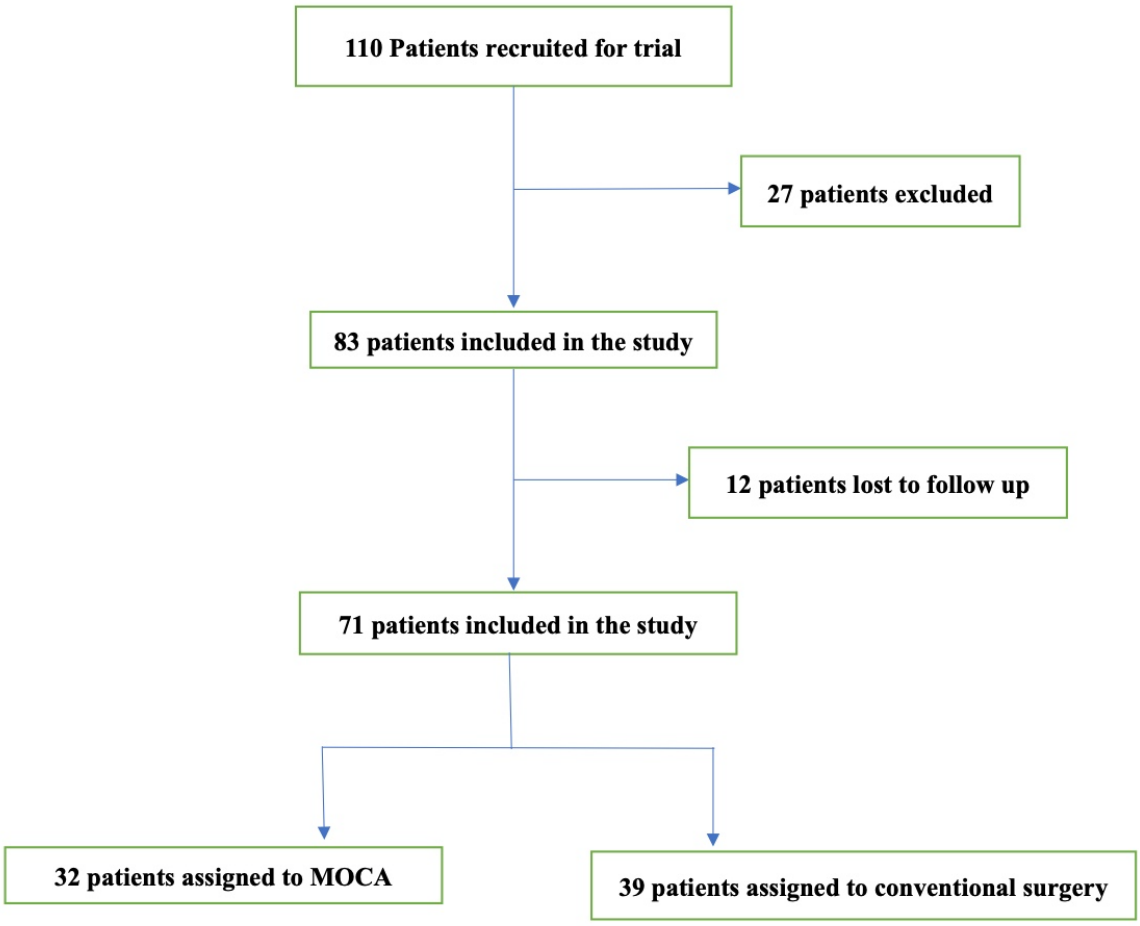

Figure 1: Patient recruitment process

Statistical analysis: Pearson's correlation test and chi square test were used for test of significance. P-values less than 0.05 were considered statistically significant. Data was analysed using SPSS software version 16.

Results

A total of 71 patients with GSV incompetence who required surgical intervention and consented to participate in the study were evaluated between December 2019 to June 2021. The mean age of the patients was 42.66 years ± 9.88. Patients belonging to both groups were homogenously equivocal in most respects like age, gender etc. There was no crossover between the two groups during the study. Demographic parameters are included in Table 1.

Table 1: Demographic details

Variables	MOCA	TRENDELENBURG	p-Value
Number of patients, n (%)	32 (46%)	39 (54%)	
Age, years; mean +- SD	41.69 ± 9.81	43.64 ± 10.35	0.421
Male, n (%)	23 (71.87%)	27 (69.23%)	0.809
Female, n (%)	9 (28.12%)	12 (30.76%)	0.809
Bilateral Lower Limb Varicose Veins, n (%)	9 (28.12%)	4 (10.25%)	0.051
Left Lower Limb Varicose Veins, n (%)	16 (50%)	17 (43.58%)	0.051
Right Lower Limb Varicose Veins, n (%)	7 (21.87%)	18 (46.15%)	0.051

Pain improvement during the early post operative period was significantly better in the MOCA group (3.34 vs 5.10, p value: 0.001). However, as illustrated in Figure 2, the 6-month VAS scores for pain assessment showed the outcomes for both the procedures to be comparable (1.03 vs 1.08). This is clinically supported by earlier return to mobility in MOCA patients (Day 0, 87.5% vs 25.6%, p value: 0.001). Likewise, as represented in Table 2, the MOCA group had significantly shorter time of Hospital stay (0.53 vs 1.87, p value: 0.001).

Table 2: Operative and immediate post operative consequences

Variables	MOCA	TRENDELENBURG	p-Value
Blood Loss (mL); mean +- SD	32.34 ± 10.78	141.54 ± 27.68	0.001
Cost of Surgery (INR); mean +- SD	40,438.5 ± 618.92	12,820.51 ± 823.08	0.001
Anaesthesia			
Local Anaesthesia, n (%)	23 (71.87%)	0 (0%)	0.001
Spinal Anaesthesia, n (%)	9 (28.12%)	39 (100%)	0.001
Pain Score (VAS)			
Pain Score Day 0; mean +- SD	5.28 ± 1.28	6.74 ± 0.85	**0.001**
Pain Score Day 1; mean +- SD	3.34 ± 1.36	5.10 ± 1.27	**0.001**
Pain Score Day 5; mean +- SD	1.59 ±.98	2.51 ± 0.88	**0.001**
Pain Score 1 Month; mean +- SD	1.06 ± 0.35	1 ± 0.0	0.325
Pain Score 6 Months; mean +- SD	1.03 ± 0.18	1.08 ± 0.27	0.414
Mobility			
Mobility; 0 days, n (%)	28 (87.5%)	10 (25.64%)	0.001
Mobility; 1 day, n (%)	4 (12.5%)	29 (74.35%)	0.001
Hospital Stay n(%)			
	20 (62.5%)	0 (0%)	0.001
	9 (28.12%)	10 (25.64%)	0.001
	2 (6.25%)	27 (69.23%)	0.001
	1 (3.12%)	1 (2.56%)	0.001
	0 (0%)	1 (2.56%)	0.001
	0.53 ± 0.88	1.87 ± 0.77	0.001

The need for spinal anaesthesia was significantly lower for the MOCA group. Only 28.12% of MOCA patients required spinal anaesthesia, as against all Trendelenburg operation patients requiring spinal anaesthesia.

During our follow-up, there were no major systemic complications and no reinterventions. We observed five surgical site infections (12.82%) in the Trendelenburg group and no such issues in the MOCA group Table 3. However, there were no statistically significant differences between the two groups regarding other complications such as wound bruising, seroma, superficial thrombophlebitis, or suture granuloma. Ulcers were more common with MOCA patients (90.62% vs 82.05%), and the healing at the end of 6 months did not show any statistical difference between the groups.

Table 3: Post operative complications and Ulcer healing

Variables	MOCA	TRENDELENBURG	p-Value
Complications			
None reported, n (%)	28 (87.5%)	33 (84.6%)	0.092
Seroma, n (%)	0 (0%)	3 (7.7%)	0.092
Wound Bruising, n (%)	3 (9.4%)	0 (0%)	0.092
Superficial Thrombophlebitis, n (%)	1 (3.1%)	0 (0%)	0.092
Suture Granuloma, n (%)	0 (0%)	1 (2.6%)	0.092
Surgical site Infection, n (%)	0 (0%)	5 (12.82%)	0.045
SSI - Grade 1, n (%)	0 (0%)	1 (2.56%)	0.044
SSI - Grade 2, n (%)	0 (0%)	4 (10.25%)	0.044
Ulcer			
Absence of Ulcer, n (%)	3 (9.37%)	7 (17.94%)	0.166
Presence of Ulcer, n (%)	29 (90.62%)	32 (82.05%)	0.166
Decrease in size of ulcer at 6 months, mean +- SD	86.33% ± 8.62%	79.43% ± 10.77%	0.359

The most significant difference between the two groups though, is that even at 6 months post procedure, no recanalization was observed in the Trendelenburg group as compared to 15.63% of patients who had partial recanalization in the MOCA group Table 4.

Table 4: Recanalization rates

Variables	MOCA	TRENDELENBURG	p-Value
3rd Day			
0% Recanalization, n (%)	31 (96.87%)	39 (100%)	0.451
25% Recanalization, n (%)	1 (3.12%)	0 (0%)	0.451
1 Month			
0% Recanalization, n (%)	28 (87.5%)	39 (100%)	0.037
10% Recanalization, n (%)	2 (6.25%)	0 (0%)	0.037
20% Recanalization, n (%)	1 (3.12%)	0 (0%)	0.037
25% Recanalization, n (%)	1 (3.12%)	0 (0%)	0.037
6 Months			
0% Recanalization, n (%)	27 (84.37%)	39 (100%)	0.015
10% Recanalization, n (%)	1 (3.12%)	0 (0%)	0.015
20% Recanalization, n (%)	1 (3.12%)	0 (0%)	0.015
30% Recanalization, n (%)	2 (6.25%)	0 (0%)	0.015
50% Recanalization, n (%)	1 (3.12%)	0 (0%)	0.015

Discussion

Mechanochemical ablation using Flebogrif™ is a relatively new technique for management of varicose veins. It is minimally invasive and induces closure by a combination of mechanical damage to the endothelium in veins with chemical damage and fibrosis due to injected sclerosant infusion. It can be done under local anaesthesia and alleviates the need for tumescent anaesthesia unlike other thermal endovenous techniques. Ultimately the risk of injury to surrounding tissue and heat related injuries are minimised.[13]

Open Trendelenburg operation consists of ligation of the incompetent vein at the SFJ with stripping of the vein. This method is still considered the gold standard of varicose vein surgery and Van Den Bermer and Moll believe that this is the standard against which results of all other treatment for varicose veins must be judged.[14]

In our study, among the subjects, 39 (54.93%) underwent Trendelenburg procedure and 32 (45.07%) underwent MOCA for varicose veins. Age, gender, and bilaterality were not significantly different between the Mechanochemical endovenous ablation and Trendelenburg groups. Hence the role of confounding on the study outcomes were ruled out.

In the MOCA group there was a higher proportion of patients who underwent the procedure under local anaesthesia and about 9 patients in the MOCA group had to be converted to spinal anaesthesia because of non-compliance and anxiety, whereas in the Trendelenburg group, all patients underwent the procedure under spinal anaesthesia, the difference was statistically significant ($p < 0.05$).

Blood loss**:** The mean Blood Loss (ml) among MOCA group was lower and statistically significant compared to Trendelenburg group. J F Thompson et al, also stated that the mean blood loss in Trendelenburg surgery was 133+/-78ml (Range – 5 to 430 ml),[15] which is significantly higher than any endovenous procedure where the blood loss is only while cannulating the vein.

Pain score (VAS): In this study, the mean pain score (VAS) at Day 0, Day 1, and at Day 5 among MOCA group was significantly lower compared to the Trendelenburg group. But the mean pain score (VAS) at one month, and six months among MOCA group was not significantly different compared to the Trendelenburg group. SV Vun et al, observed significantly reduced pain scores with Mechanochemical endovenous ablation with a median pain score of 1 using VAS score.[16] Whereas Rautio et al, described the pain in open surgery using VAS with an average score of 3 on walking and 2.6 on standing and 1.4 at rest.[17] The difference in pain between the groups during only the early post operative period can be attributed to inflammation secondary to tissue injury due to the incisions made and not neuropathic pain.[18]

Mobility and Duration of Hospital Stay: All the patients who underwent MOCA under local anaesthesia were mobilised immediately after the procedure, patients who underwent the procedures under spinal anaesthesia were mobilised on the same or next day, a few patients owing to pain, did not mobilise on the 1st post operative day.

In this study, the mean Hospital Stay (Days) among MOCA group was 0.53 (± 0.88) which is lower by 1.34 and statistically significant compared to 1.87 (± 0.77) in Trendelenburg group. Most of our patients in the MOCA group were discharged on the same day of the procedure, and though Trendelenburg procedure is advocated as day care surgery, most of the patients had to stay longer due to delay in recovery from anaesthesia or post operative pain. G V Miller et al also stated in their article that day care Trendelenburg procedure was

difficult owing to patient's age, co-morbid conditions, delay in recovery from anaesthesia and unavailability of an attender at home.[19]

Complications: In this study, wound bruising was higher among the MOCA group, and seroma and wound infection was common among the Trendelenburg group. In both the groups, majority of the patients had no complications and the differences in complications were not significantly different. None of the patients in MOCA group had surgical site infections (SSI), as compared to the Trendelenburg group of whom 12.82% had SSI and the difference was statistically significant ($p < 0.05$). Similarly, Ramon R.J.P. van Eekeren et al, observed that immediate technical success rates with the MOCA-technique was 100% with no major adverse-events. Minor complications comprise of local ecchymoses at the site of the puncture and superficial phlebitis.[20] Schouten et al says apart from hematoma formation and minor wound infection, there are no severe complications,[21] concurring with our study.

Recanalization: In our study, among the MOCA group, on the 3rd day of follow-up, only 1 patient had partial recanalization compared to Trendelenburg group where none of them had recanalization and the difference was not statistically significant ($p > 0.05$). At 1 month of follow up 4 patients in the MOCA group (12.5%), had less than 25% partial recanalization compared to Trendelenburg group, where none of them had recanalization and the difference was statistically significant ($p < 0.05$). At 6 months follow up, among the MOCA group, 15.7% had partial recanalization without reflux compared to Trendelenburg group where none of them had recanalization and the difference was statistically significant ($p <0.05$). But none of the patients who had recanalization had symptoms of recurrent varicose veins and they did not require further treatment. Sari Vähäaho et al, observed that at 3 years, the occlusion-rate was significantly reduced with MOCA (compared with thermal ablative procedures) but the difference in quality of life was not significant. They also concluded that, considering the technical superiority, MOCA can be preferred as the management option of great saphenous veins insufficiency.[22] Witte et al, reported in a three year follow up after MOCA that recanalization occurred in 15% of total 102 treated limbs, and stated that though it is an effective modality of treatment, the anatomical success seemed to be declining over time.[23] Khor et al, studied for a year the effectiveness of MOCA for GSV, at 1month, 3 months and 1 year the occlusion rates were 90.8%, 86.9% and 84.8% respectively, they concluded that though the recurrence at 1 year was far more than expected, but it is tempered by the fact that the patients remained asymptomatic.[24] Though in our study there were no recurrences in the 6 months of follow up in the Trendelenburg group, Van Rij et al, stated that after high ligation of SFJ and stripping of the vein, there was recurrence due to inadequate surgery in 1% of the patients and after 3 years this recurrence increased to 23% mainly due to neovascularisation.[25]

Cost of surgery: The mean cost of surgery (INR) in our study among MOCA group was Rs. 40,437.5 (± 618.92) which is higher by Rs. 27,616.99 and statistically significant compared to Rs.12,820.51 (±823.08) in Trendelenburg group. The price of the catheter adds up to the total cost of the MOCA procedure even though the cost is cut down in many places like non requirement of higher forms of anaesthesia and shorter duration of stay in the hospital. The overall cost is very low in our centre for conventional surgery, because of it being a teaching institute with minimal cost for surgical procedures and stay. MOCA is also a cost-effective option in low resource settings where there is no need of investment in inventory.

Ulcer healing: In this study, the rate of healing of venous ulcer was compared between the two groups. 9.37% of the MOCA group and 17.94% of Trendelenburg surgery group had ulcer. In both groups ulcers were found to heal well after the procedure. However, the difference in the rate of healing at 6 months between the two groups was not statistically significant ($p > 0.05$). Kheirelseid EAH et al, did a review and meta-analysis of 1103 articles which studied the outcome of venous ulcer after varicose vein treatment and concluded that both open and endovenous surgeries aided in the ulcer healing process and were better than conservative approach.[26]

Our study was done using the Flebogrif™ catheter, though there are many studies regarding mechanochemical ablation, many of them were using ClariVein and the ones with Flebogrif™ were relatively sparse.

Limitations of our study is that we did not have long term follow-up for the recurrence and prognosis. Blinding was not feasible owing to the difference in procedures, anaesthesia and post-operative care which would have revealed the patients the groups they are in. Pain might have been over reported, to seek more attention and care from the treating surgeon/principal investigator.

Recommendations: Considering the lesser blood loss, lesser Pain scores (VAS), decreased duration of hospital stay, lower incidence of SSI Incidence, and higher probability of undergoing the procedure under local anaesthesia, mechanochemical endovenous ablation is preferred over open Trendelenburg surgery for the treatment of primary great saphenous varicose veins. Future multi-

centric randomised control trials in other resource limited settings with longer follow up will elucidate the true outcomes of mechanochemical ablation. Further studies with a focus on the cost-effective analysis is needed. Studies using Flebogrif™ with long term follow up is required.

Conclusion

Mechanochemical ablation is an effective and relatively safe method in treatment of primary great saphenous varicose veins, with lesser pain, lower complications, higher chance of undergoing the procedure as day care under local anaesthesia when compared to Trendelenburg surgery. Though partial recanalization may occur, patients are asymptomatic alleviating the need for repeat procedures.

References:

1. Lim CS, Davies AH. Pathogenesis of primary varicose veins. Br J Surg. 2009;96(11):1231-1242.
2. Maurins U, Hoffmann BH, Lösch C, Jöckel KH, Rabe E, Pannier F. Distribution and prevalence of reflux in the superficial and deep venous system in the general population--results from the Bonn Vein Study, Germany. J Vasc Surg. 2008;48(3):680-687
3. Campbell B. Varicose veins and their management. BMJ. 2006;333(7562):287-292.
4. van Eekeren RR, Boersma D, Holewijn S, et al. Mechanochemical endovenous Ablation versus RADiOfrequeNcy Ablation in the treatment of primary great saphenous vein incompetence (MARADONA): study protocol for a randomized controlled trial. Trials. 2014; 15:121. Published 2014 Apr 11.
5. Ammollo RP, Petrone A, Giribono AM, Ferrante L, Del Guercio L, Bracale UM. Early Results of Mechanochemical Ablation with Flebogrif® in great Saphenous Vein Insufficiency: does Polidocanol Concentration Affect Outcome? Transl Med UniSa. 2020; 21:47-51. Published 2020 Feb 20.
6. Perkins JM. Standard varicose vein surgery. Phlebology. 2009;24 Suppl 1:34-41.
7. Kim PS, Bishawi M, Draughn D, et al. Mechanochemical ablation for symptomatic great saphenous vein reflux: A two-year follow-up. Phlebology. 2017;32(1):43-48.
8. Boersma D, van Eekeren RR, Kelder HJ, et al. Mechanochemical endovenous ablation versus radiofrequency ablation in the treatment of primary small saphenous vein insufficiency (MESSI trial): study protocol for a randomized controlled trial. Trials. 2014; 15:421. Published 2014 Oct 29.
9. Lurie F, Passman M, Meisner M, et al. The 2020 update of the CEAP classification system and reporting standards [published correction appears in J Vasc Surg Venous Lymphat Disord. 2021 Jan;9(1):288]. J Vasc Surg Venous Lymphat Disord. 2020;8(3):342-352
10. Aboyans V, Criqui MH, Abraham P, et al. Measurement and interpretation of the ankle-brachial index: a scientific statement from the American Heart Association [published correction appears in Circulation. 2013 Jan 1;127(1): e264]. Circulation. 2012; 126(24): 2890-2909.
11. Langley GB, Sheppeard H. The visual analogue scale: its use in pain measurement. Rheumatol Int. 1985;5(4):145-148.
12. Toniolo J, Chiang N, Munteanu D, Russell A, Hao H, Chuen J. Vein diameter is a predictive factor for recanalization in treatment with ultrasound-guided foam sclerotherapy. J Vasc Surg Venous Lymphat Disord. 2018;6(6):707-716.
13. Tang TY, Kam JW, Gaunt ME. ClariVein® - Early results from a large single-centre series of mechanochemical endovenous ablation for varicose veins. Phlebology. 2017;32(1):6-12.
14. van den Bremer J, Moll FL. Historical overview of varicose vein surgery. Ann Vasc Surg. 2010;24(3):426-432.
15. Thompson JF, Royle GT, Farrands PA, Najmaldin A, Clifford PC, Webster JH. Varicose vein surgery using a pneumatic tourniquet: reduced blood loss and improved cosmesis. Ann R Coll Surg Engl. 1990;72(2):119-122.
16. Vun SV, Rashid ST, Blest NC, Spark JI. Lower pain and faster treatment with mechanico-chemical endovenous ablation using ClariVein®. Phlebology. 2015;30(10):688-692.
17. Rautio T, Ohinmaa A, Perälä J, et al. Endovenous obliteration versus conventional stripping operation in the treatment of primary varicose veins: a randomized controlled trial with comparison of the costs. J Vasc Surg. 2002;35(5):958-965.
18. Pogatzki-Zahn EM, Segelcke D, Schug SA. Postoperative pain-from mechanisms to treatment. Pain Rep. 2017;2(2):e588. Published 2017 Mar 15.

19. Miller GV, Lewis WG, Sainsbury JR, Macdonald RC. Morbidity of varicose vein surgery: auditing the benefit of changing clinical practice. Ann R Coll Surg Engl. 1996;78(4):345-349.
20. van Eekeren RR, Boersma D, Elias S, et al. Endovenous mechanochemical ablation of great saphenous vein incompetence using the ClariVein device: a safety study. J Endovasc Ther. 2011;18(3):328-334.
21. Schouten R, Mollen RM, Kuijpers HC. A comparison between cryosurgery and conventional stripping in varicose vein surgery: perioperative features and complications. Ann Vasc Surg. 2006;20(3):306-311.
22. Vähäaho S, Halmesmäki K, Mahmoud O, Albäck A, Noronen K, Venermo M. Three-year results of a randomized controlled trial comparing mechanochemical and thermal ablation in the treatment of insufficient great saphenous veins. J Vasc Surg Venous Lymphat Disord. 2021;9(3):652-659.
23. Witte ME, Holewijn S, van Eekeren RR, de Vries JP, Zeebregts CJ, Reijnen MM. Midterm Outcome of Mechanochemical Endovenous Ablation for the Treatment of Great Saphenous Vein Insufficiency. J Endovasc Ther. 2017;24(1):149-155.
24. Khor SN, Lei J, Kam JW, Kum S, Tan YK, Tang TY. ClariVein™ - One-year results of mechano-chemical ablation for varicose veins in a multi-ethnic Asian population from Singapore. Phlebology. 2018;33(10):687-694.
25. van Rij AM, Jiang P, Solomon C, Christie RA, Hill GB. Recurrence after varicose vein surgery: a prospective long-term clinical study with duplex ultrasound scanning and air plethysmography. J Vasc Surg. 2003;38(5):935-943.
26. Kheirelseid EA, Bashar K, Aherne T, et al. Evidence for varicose vein surgery in venous leg ulceration. Surgeon. 2016; 14(4):219-233.