

META-ANALYSIS AND SYSTEMATIC REVIEW OF RADIO FREQUENCY ABLATION VS TRENDLENBURG SURGERY FOR VARICOSE VEINS

Surgery

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ABSTRACT

Background: Chronic venous insufficiency leading to varicose veins is one of the problems faced by adults. Minimally invasive endovenous procedures have been recently introduced for treating varicose veins to reduce postoperative pain, speedy recovery and improve quality of life compared to standard surgery. A systematic review and meta- analysis was conducted in this study to compare clinical outcomes between radio frequency ablation [RFA] and Trendelenburg surgery. **Methods:** A systematic review and meta-analysis was performed according to PRISMA guidelines. A literature search was carried out, and RCTs comparing RFA versus Trendelenburg were included. **Results:** The literature search was carried out .Eleven RCTs were chosen among the 155 articles shortlisted. RFA had advantages over surgery in lowering duration of surgery (MD = - 1.3 (95%CI: -0.7, -2.4) for RFA and -1.5 (95%CI:-0.7, - 3.0) for surgery)and return to normal activities (MD of -2.7 days(95%CI:-6.0,0.6) for RFA and MD of -4.9days (95%CI:- 7.1,-2.7) for surgery, lowering complications such as hematoma(RR= 0.4 (95%CI:0.1,0.8) and 0.5 (95%CI:0.3,0.8) for RFA and surgery, superficial thrombophlebitis, paresthesias, bleeding. **Conclusion:** The study concluded that RFA had lower chance of hematoma formation ,wound infection ,risk of bleeding , paresthesias and postoperative pain . The duration of surgery and duration of hospital stay is also decreased with RFA. However RFA had a higher chance of burns and skin pigmentation according to this study .

KEYWORDS

Radiofrequency ablation ,trendelenburg surgery ,varicose veins

INTRODUCTION

The purpose of the venous system is primarily to return blood back to the heart so that it can be delivered into the pulmonary circulation. Chronic venous insufficiency refers to a condition where the veins struggle to effectively pump deoxygenated blood back to the heart, leading to stasis due to a compromised musculo-venous pump. Varicose vein are subcutaneous dilated vein 3 mm in diameter or larger. They are frequently elongated and tortuous, with intermittent blowouts but are defined by the presence of reflux and may be straight and uniform tubes morphologically. This condition is more prevalent in India, especially among males.

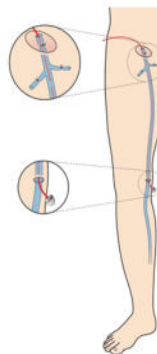
Varicose veins can occur due to either the vessel wall or valve pathology. It primarily affects individuals who have to stand for prolonged time during work. Venous problems arise when venous pressure increases, impeding blood flow due to factors like valve incompetence, perforator dysfunction and venous blockade.

These patients typically experience swelling and leg pain, which can severely limit their normal daily activities. They describe aching, heaviness, throbbing, burning or bursting over affected areas and sometimes the whole limb .This condition can significantly impact their quality of life especially since it can progress and lead to complications of venous hypertension such as skin ulceration. To ensure a proper diagnosis, classification of severity and effective management of varicose veins, conducting a physical examination and venous study is essential.

Many patients opt for surgery either due to failure of conservative management or for cosmetic purpose. Compression stockings relies on graduated external pressure to improve deep venous return and reduce venous pressures. Varicose vein surgery is a routine and common procedure, crucial for training surgeons. However, the traditional principles have faced challenges with the introduction of new minimally invasive techniques like ultrasound-guided foam sclerotherapy (UGFS), endovenous laser therapy (EVLT) and radiofrequency ablation (RFA) over the last decade. Endothermal ablation technologies replaced surgical ligation and stripping as the gold standard treatment once randomised trials demonstrated that they were marginally safer, have extremely high technical efficacy, offer superior quality of life post procedure (with a rapid recovery) and equivalent improvements in quality of life in the longer term. The techniques are cost-effective as they can be performed as an outpatient under local anaesthetic. The basic concept is that a treatment device is

inserted into the incompetent axial vein percutaneously. The vein is surrounded by tumescent local anaesthetic solution. This compresses the vein onto the treatment device, emptying it of blood. It also hydro-dissects tissues such as nerves away from the zone of injury. Finally, it acts as a heat sink, mopping up excess thermal energy to prevent remote damage. The treatment device then produces thermal energy that destroys the structure of the vein, resulting in permanent occlusion. The principles of traditional ligation and stripping (Figure 1) are to fully dissect the point of junctional incompetence and to remove the refluxing axial vein and dilated tributaries. RFA uses the same treatment principles, but an electromagnetic current is used to create the thermal energy. This device has a wire coil on the end of a treatment catheter (Figure 2). The generator passes an electrical current through the coil until the surrounding temperature reaches 120°C. This is then maintained for a treatment cycle of 20 seconds. The coil is then withdrawn for a set length and another treatment cycle is commenced. Radiofrequency ablation, a minimally invasive surgical option, has largely replaced the classical Trendelenburg operation. This shift is due to its lower risk of complications. This advancement has made it increasingly prevalent in managing varicose vein . Previous studies have extensively examined the effectiveness of various procedures for treating venous insufficiency, analysing outcomes ranging from short-term to long-term. The initial systematic review conducted in 2012 encompassed 28 randomized controlled trials (RCTs) to assess the short-term and mid-term results of endovenous procedures compared to traditional surgery.

Figure 1:



Saphenofemoral junction ligation and great saphenous vein stripping.

Figure 2:



Radiofrequency ablation with Cluselfast introducing the treatment catheter through a sheath. The distal 7 cm of the device comprises a metal coil.

Subsequent systematic reviews in 2017 and 2018 focused solely on long-term outcomes incorporating 12 and 9 RCTs with follow-up exceeding 5 years respectively. However, the 2017 meta-analysis only pooled outcome data from RCTs without directly comparing these outcomes between different intervention groups, potentially introducing bias. Similarly, the latest meta-analysis in 2018 faced challenges in discerning significant differences in recurrence rates among EVLA, RFA and traditional surgery due to limited sample sizes and study populations.

As a result, this systematic review and meta-analysis have been conducted with the objective of comparing clinical outcomes between RFA and trendelenberg surgery. Postoperative outcomes such as pain levels, time required to resume normal activities and work, as well as any complications such as wound infections, hematomas, paresthesia, ecchymosis, and deep venous thrombosis, will be compiled using all accessible data sources.

METHODS

This protocol is developed according to the Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) guidelines. The patient, intervention, comparator and outcome (PICO) method is used for assessing and selecting appropriate studies.

P - Patients with varicose veins

Intervention – Use of surgical techniques for varicose veins
Comparator - Radiofrequency ablation and Trendelenburg Outcome – Successful surgical outcomes

Search Strategy

The search was done in databases such as Medline, Embase, the Cochrane library, Scopus spanning from 2015 to January 2024, with subsequent updates every month until March 2024. Search terms are tailored to capture patients and interventions/comparators, encompassing terms like 'Varicose veins'[MeSH] OR 'Saphenous vein'[MeSH]; radiofrequency OR RFA OR endovenous OR EVLT OR EVLA OR laser OR sclerotherapy [MeSH] OR foam sclerotherapy OR UGFS OR stripping OR sapheno-femoral ligation OR surgery OR steam OR glue OR cyanoacrylate OR mechanochemical OR mechanochemical. These search criteria are combined using 'AND' and limited to clinical trials, studies involving humans, and articles published in English. Additionally, relevant studies were identified by reviewing the reference lists of previous meta-analyses and all eligible papers.

Study Selection

The study selection process is conducted by two independent authors. Initially, titles and abstracts were screened to assess eligibility criteria and full texts were reviewed if a decision cannot be made based on the initial screening. Any discrepancies in selection will be resolved through consensus by a third party. For studies with multiple publications, data will be amalgamated and treated as one publication for analysis purposes. Studies published from 2015-2024 as prospective RCTs for evaluating radiofrequency ablation and Trendelenburg for varicose veins were included.

INCLUSION CRITERIA includes studies comparing outcomes between RFA vs trendelenberg, studies involving patients with great saphenous vein reflux, reporting at least one of the following outcomes -anatomical success, postoperative pain, wound infection, ecchymosis, deep vein thrombosis, time to resume normal activities and work, clinical recurrence and quality of life. Studies are excluded if they lack sufficient data for meta-analysis, those which were not in English and retrospective studies.

Statistical Analysis

Data were aggregated for comparisons where at least three studies were available. Risk ratios (RRs) and their corresponding 95% confidence intervals (CIs) were calculated and combined. In instances where a cell had zero occurrences, a continuity correction was applied. The DerSimonian and Laird method was used to pool RRs in the presence of heterogeneity, while the inverse variance method was employed when homogeneity was observed. Continuous data, such as mean differences (MDs), were estimated and pooled using an unstandardized approach.

Heterogeneity was assessed using the Q test and the I^2 statistic. If either I^2 was equal to or greater than 25% or if the Q test yielded a significant result, the random-effects model was utilized. Covariates such as mean age, follow-up time and wavelength were included in a meta-

regression analysis to explore potential sources of heterogeneity. If a covariate was found to reduce I^2 , a subgroup or sensitivity analysis focusing on that factor was conducted.

Risk Of Bias

Two independent researchers will evaluate studies for potential bias using the Cochrane Collaboration's tool. This tool comprises seven domains: random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessors, incomplete outcome reporting, selective outcome reporting and other sources of bias. Any discrepancies in assessment will be resolved by a third party.

Outcomes

The definition of anatomical success was initially established as incomplete vein stripping for open surgery, as well as the presence of GSV non-occlusion with or without reflux diagnosed through duplex scan. The primary outcome measure was the inability to eliminate reflux in the axial vein.

As MIEPs and surgical procedures employ distinct mechanisms to eradicate refluxes, each method possesses unique definitions of failure. For RFA, primary failure was identified as recanalization diagnosed through the duplex scan including incomplete stripping, inadequate removal of intended veins, or recanalization. The count of primary failures after the study was utilized for data analysis.

Secondary outcomes were clinical recurrences assessed by physical examination, post operative complications (wound infection, paresthesia, superficial thrombophlebitis, haematoma, or Ecchymosis) post operative pain, time return to normal activities or work. If a study reported both time return to normal activities and time to work, the former was used.

RESULTS

155 RCTs from MEDLINE, scopus, cochrane library were identified (figure 3). 70 duplications were found among them and the remaining are screened out, leaving 11 studies for data extraction (figure 3). All the studies are comparing Radio Frequency ablation with conventional surgery.

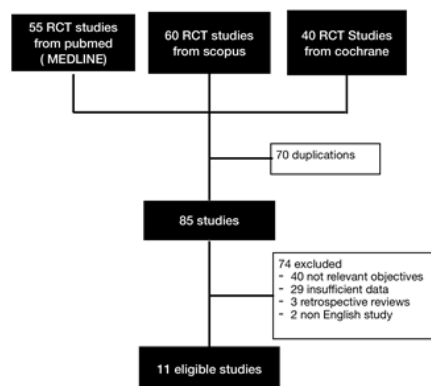


Figure 3 : studies selection flow

General characteristics of the eligible studies are presented in table 1. Most of the sample size ranges in between 60 to 100 patients. The mean age ranges from 40-50 yrs. Most patients included in the study were of CEAP C2 category.

Duration Of Surgery

Three out of eleven studies showed that RFA takes longer duration compared to that of conventional surgery, but the remaining studies favoured the RFA. The mean deviation is -1.3 (95%CI:-0.7, -2.4) for RFA and -1.5 (95%CI:-0.7, -3.0) for surgery. (table 2)

Table 1 : General Characteristics of eligible studies

Source (year of publication)	Study population	Mean age	Study period	Country	Anaesthesia
Rathnaganapathi (2022) ¹	100	45	2017-2019	India	RA
S kedara Harshita (2023) ²	200	46	2021-2023	India	RA

S Subramonia and T lees(2009) ³	88	44	2008-2009	UK	RA
S hemachandar (2018) ⁴	100	47	2016-2018	India	LA
Sandeep Shrivastava (2023) ⁵	100	44	2016-2020	India	RA/ GA
G kavithal (2021) ⁶	60	46	2018-2020	India	RA
Gh.mustafa Dar (2020) ⁷	60	47	2017-2019	India	RA
Naithani v (2020) ⁸	207	48	2015-2020	India	RA
Ram Praveen (2023) ⁹	66	44	2020-2022	India	LA
Elkaffas(2015) ¹⁰	70	49	2010-2016	Uk	RA
Stoetter(2018) ¹¹	100	45	2019-2020	Us	GA / RA

Duration Of Hospital Stay

Duration of hospital stay is less with RFA in all the 11 studies with a pooled MD of -2.0 days (table 2)

Pain In 1st Week

It is calculated based on VAS (visual analogue scale).Most of the studies show that the pain during 1st week of post operative period is less with RFA compared to conventional surgery .The RFA caused significantly less pain than surgery with pooled MD of -0.8 (95% CI: - 1.5, -0.1)(table 2)

Return To Normal Activities

Return to normal activities was significantly longer for surgery compared with RFA with pooled MD of -4.9days (95%CI : - 7.1,-2.7) for surgery and -2.7 days (95%CI:-6.0,0.6) for RFA.(table 2)

Table 2: Comparison of post operative pain, return to normal activities and duration of surgery and hospital stay between RFA and trendelenberg

Out comes	No of studies	Total number of patients	Heterogeneity		I ²	MEAN DIFFERENCE(95%CI)
			Q	P value		
Duration of surgery	11	1131	7.33	0.198	31.7	-0.6(-1.3 , -1.5)
Duration of hospital stay	11	1131	11.65	0.341	59.2	-2.0(-2.1,-1.8)
Postoperative pain	11	1131	0.98	0.642	0	-0.8(-1.5,-0.1)
Return to normal activities	11	1131	38.23	0.000	87.1	-4.9days(- 7.1,-2.7)

Postoperative Complications

Haematoma

Effects of surgery vs RFA were highly heterogeneous in 7 studies with a pooled RR of 0.5 (95% CI :0.2 ,0.8) for surgery and 0.4 (95%CI:0.1, 0.8) for RFA suggesting that the risk of haematoma was 60% significantly less with RFA when compared with surgery .

Bleeding

Only 3 studies have showed the complication of bleeding with RFA having less risk compared to surgery

Table 3 :Methodological quality and risk of bias in included trials

STUDY	RANDOMIZATION	ALLOCATION CONCEALMENT	OUTCOMES	FOLLOW UP
Rathnaganapthi (2022) ¹	Unclear	Yes	Complete	Adequate
S kedara Harshita (2023) ²	Unclear	Yes	Complete	Adequate
S Subramonia and T lees(2009) ³	Random number table	Unclear	Complete	Adequate
S hemachandar (2018) ⁴	Unclear	Yes	Complete	Adequate
Sandeep Shrivastava (2023) ⁵	Random number table	Yes	Complete	Adequate
G kavithal (2021) ⁶	Random number table	Unclear	Complete	Adequate
Gh.mustafa Dar (2020) ⁷	Unclear	Unclear	Complete	Adequate
Naithani v (2020) ⁸	Unclear	Yes	Complete	Adequate
Ram Praveen (2023) ⁹	Random number table	Unclear	Complete	Adequate
Elkaffas(2015) ¹⁰	Computer generated	Yes	Complete	Adequate
Stoetter(2018) ¹¹	Computer generated	Yes	Complete	Adequate

Superficial Thrombophlebitis

Five studies have reported the complication of inflammation with surgery having high risk on comparison with RFA .The risk of superficial thrombophlebitis was 2.3 (95% CI:1.1, 5.0) times significantly higher in surgery than RFA.

Skin Burns And Pigmentation

Among the 11 studies RFA has shown more skin burns when compared to negligible cases with surgery . One study has shown the p value to be insignificant while the others were found to be significant.

Paresthesia

Four out of 11 studies reported paresthesias with both RFA and conventional surgery with pooled risk ratio of 0.3 .One study have shown higher incidence of paresthesia with conventional surgery alone.

DISCUSSION

Removing the refluxing saphenous vein from the sapheno-femoral junction upto knee or up the leg, with individual ligation of the named saphenous branches at the groin, is the normal treatment for patients with symptomatic incompetent superficial veins¹². Endovascular obliteration of the vein with radiofrequency probes inserted inside the vein through a percutaneous puncture or a cut down in the upper leg is a newer technique.RFA is a minimally invasive procedure. Its potential early benefits, by avoiding groin dissection and GSV stripping, have been confirmed here. Our results suggest that most of the outcomes that we considered in this study were favourable towards RFA than conventional surgery .Primary failure of the ablated vein was a surrogate outcome of clinical recurrence. Other causes may play a role on clinical recurrence including below knee GSV reflux, reflux in tributaries, neovascularisation, saphenopopliteal reflux, non axial branches and perforator insufficiency.Recurrence at a new site of reflux is a natural progression of the disease.However,the incidence of reflux in tributaries and neovascularisation might differ between the procedures with and without sapheno-femoral ligation.RFA took significantly longer to perform than conventional surgery in one of the studies .This was due to tumescent infiltration and detailed duplex scanning before and after treatment.

Some authors have suggested that patients undergoing RFA may be less prone to neovascularization because the SFJ is left untouched¹³. Neovascularization is thought to be theconsequence of angiogenesis following tissue trauma due to surgical dissection, and it has been implicated as the main cause of recurrence in several studies. This is ultimately linked to the need for reintervention, which is a cause of patient dissatisfaction with the technique.It has been suggested that the observed high recurrence rates following conventional surgery are related to the technical inadequacy of the initial procedure . A larger number of recurrences has been associated with insufficiency in the below-knee GSV after stripping of the GSV to the knee only . It has been argued that the length of stripping should be dictated by the length of the refluxing vein and not by concerns over injury to the saphenous nerve.The superior success rate reported for conventional surgery in our study can be explained by the fact that stripping of the GSV was performed from the SFJ to the ankle level. However, full-length stripping remains controversial.

RFA involves considerably less tissue dissection and trauma. Patients who had RFA experienced considerably less pain, required less analgesia and were able to return to their activities more quickly. This improved confidence, lifestyle, social contacts, cosmesis, quality of life and satisfaction in the early days after the procedure. Driving is a good index of recovery from a procedure such as varicose vein surgery¹⁴. Most trial participants resumed driving significantly more quickly after RFA.For postoperative complications,RFA had significantly lower wound infections and hematoma,but similar paresthesia compared to surgery.Also RFA had significantly less pain scores than surgery with MD of - 0.4 and - 1.2 respectively,these are clinically significant with RFA . Return to work was significantly sooner with RFA than surgery .

The strength of our study was included only in RCTs, the most powerful design for therapeutic study. We considered all relevant outcomes in all techniques currently used nowadays. Treatment effects were mild to moderate heterogeneities with no evidence of publication bias. Therefore, our results should help physicians decide on the most appropriate interventions for their individual patients.

Current evidence based on randomized trials consistently demonstrates significant early benefits after RFA in suitable patients with varicose veins. Five-year outcomes from large cohort studies appear comparable to those after conventional surgery. It is important, however, to remember that conventional surgery, unlike RFA, may be performed on most patients irrespective of the configuration or distribution of varicosities, and that stripping of the GSV is effective in reducing long-term recurrence and risk of reoperation. The conventional procedure also improves Quality of Life and symptoms in most patients, and differs from RFA only in the extent of the improvement and in short-term morbidity¹⁵. Long-term results from this and other similar studies may throw more light on the consequences of leaving intact the superficial epigastric vein and other tributaries at the SFJ.

CONCLUSION

RFA took less time to perform than conventional surgery and it provides better results and significantly reduced recovery time in patients with varicose veins however the complication of skin burns and pigmentation was high with RFA. For a long time, trendelenberg surgery has been used to treat varicose veins, with varying degrees of success. Endovenous RFA has been proven to be a viable and effective alternative to surgery.

Conflicts Of Interest - none

Source Of Funding - none

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