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REVIEW

A Systematic Review and Meta-analysis of Thrombotic Events Following Endovenous Thermal Ablation of the Great Saphenous Vein

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WHAT THIS PAPER ADDS

The incidence of thrombotic complications following endovenous thermal ablation (EVTA) of varicose veins is uncertain. In this systematic review and meta-analysis, it was found that endovenous heat induced thrombosis, deep venous thrombosis, and PE occur infrequently after great saphenous endothermal ablation. However, given the large numbers of patients that undergo endothermal ablation, there is a need for further research on the natural history, management, and burden of these thrombotic events.

Objectives: A systematic review and meta-analysis was performed to determine the incidence of thrombotic events following great saphenous vein (GSV) endovenous thermal ablation (EVTA).

Methods: MEDLINE, Embase and conference abstracts were searched. Eligible studies were randomised controlled trials and case series that included at least 100 patients who underwent GSV EVTA (laser ablation or radiofrequency ablation [RFA]) with duplex ultrasound (DUS) within 30 days. The systematic review focused on the complications of endovenous heat induced thrombosis (EHIT), deep venous thrombosis (DVT), and pulmonary embolism (PE). The primary outcome for the meta-analysis was deep venous thrombotic events which were defined as DVT or EHIT Type 2, 3, or 4. Secondary outcomes for the meta-analysis were EHIT Type 2, 3, or 4, DVT and PE. Subgroup analyses were performed for both the RFA and EVLA groups. Pooled proportions were calculated using random effects modelling.

Results: Fifty-two studies (16,398 patients) were included. Thrombotic complications occurred infrequently. Deep venous thrombotic events occurred in 1.7% of cases (95% CI 0.9–2.7%) (25 studies; 10,012 patients; 274 events). EHIT Type 2, 3, or 4 occurred in 1.4% of cases (95% CI 0.8–2.3%) (26 studies; 10,225 patients; 249 events). DVT occurred in 0.3% of cases (95% CI = 0.2%–0.5%) (49 studies; 15,676 patients; 48 events). PE occurred in 0.1% of cases (95% CI = 0.1–0.2%) (29 studies; 8223 patients; 3 events). Similar results were found when the RFA and EVLA groups were analysed separately.

Conclusion: Thrombotic events occur infrequently following GSV EVTA. Given the large numbers of procedures worldwide and the potential for serious consequences, further research is needed on the burden of these complications and their management.

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INTRODUCTION

There has been rapid growth in the use of endovenous thermal ablation of varicose veins. In 2013, the National Institute for Health and Care Excellence (NICE) recommended endovenous thermal ablation (EVTA) as the preferred treatment option for symptomatic varicose veins.[1] This treatment modality causes heat induced vessel wall injury with thrombotic and fibrotic occlusion[2] leading to concerns regarding the potential for venous thromboembolism (VTE).[3] Although the complications of deep venous thrombosis (DVT) and pulmonary embolism (PE) are thought to be rare, the Society for Vascular Surgery recommends that patients undergo early post-procedural

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duplex scanning to detect potential thrombotic events.[2] Notably, the European Society for Vascular Surgery does not make such a recommendation.[4]

The routine use of duplex surveillance has led to the description of a new form of localised post-operative DVT which is termed endovenous heat induced thrombosis (EHIT)[5] and refers to the extension of thrombus from the ablated superficial vein into the deep vein. Four subtypes of EHIT have been described: Type 1, thrombus flush with the junction between superficial and deep vein; Type 2, thrombus extension into the deep vein, cross sectional area $\leq$50%; Type 3, thrombus extension into the deep vein, cross sectional area $>$50%; Type 4, complete occlusion of the deep vein. EHIT is a relatively new entity, little is known about its natural history or potential clinical relevance. In the literature, reported rates of EHIT vary from 0% to 8%[2,6] with no clear consensus on its management.

Given the large numbers of EVTA procedures that take place worldwide, and the potential for severe complications, it is important that healthcare providers appreciate the true rate of VTE complications. Such information may help to guide decision making for individual patients and may streamline research on methods of VTE prevention. For these reasons, a systematic review and meta-analysis of the incidence of VTE complications following great saphenous vein (GSV) EVTA was performed.

METHODS

The review was registered with the International Prospective Register of Systematic Reviews (PROSPERO) (registration number CRD42018089260) and the protocol is available online.[7] Eligible studies were randomised controlled trials or case series which included at least 100 adults who underwent GSV ablation for symptomatic reflux via endovenous laser ablation (EVLA) or radiofrequency ablation (RFA) and had duplex ultrasound (DUS) surveillance scanning within 1 month of the procedure. Both prospective and retrospective studies were included and patients in eligible studies could additionally have concomitant treatment of non-truncal varicosities by phlebectomies or foam sclerotherapy and/or perforator ligation. Studies involving the treatment of GSV truncal reflux with EVLA or RFA combined with other modalities such as open surgical ligation of the saphenofemoral junction (SFJ) or other endovenous modalities were excluded. Similarly, studies that did not report on the incidence of DVT, PE, and EHIT were excluded as were studies that reported on treatment of a variety of superficial venous trunks (such as great saphenous, small saphenous, anterior accessory saphenous) without specifically reporting on patients who had great saphenous ablation in isolation. Eligibility was limited to studies that were reported in English. Regarding the sample size constraint that was imposed, eligibility was restricted to studies with at least 100 patients because VTE is thought to be an uncommon event. This cut off point was chosen arbitrarily; a previous review on the topic chose a minimum sample size of 150 for case series.[8]

MEDLINE was searched using the following search strategy comprising free text words: [(radiofrequency OR endovenous ablation OR laser) AND (great saphenous vein)] OR [endovenous heat induced thrombosis]. Embase was searched using the following search strategy comprising words using the "title, abstract, author keyword" option: [(radiofrequency OR endovenous ablation OR laser) AND (great saphenous vein)] OR [endovenous heat induced thrombosis].The search was first performed on April 5, 2017, and a final search for additional studies was performed on February 25, 2018. Two authors (D.H. and D.P.) screened titles and abstracts for eligibility. Full manuscripts of potentially eligible studies were obtained and examined to finalise eligibility. Uncertainties regarding eligibility were resolved by discussion between D.H. and D.P., and when necessary referral to another author (E.K.). The reference lists of eligible articles were scrutinised for additional eligible studies. Conference proceedings from the annual meetings of the Vascular Society of Great Britain and Ireland (2010–2017) and the Society for Vascular Surgery's Vascular Annual Meetings (2010–2017) were also searched for eligible studies that were published only in abstract form (S.K.). For each eligible study, data on the following aspects were extracted independently (D.H. and D.P.) and entered into an electronic spread sheet: author, publication year, study design, treatment modality, numbers of included patients and limbs, age and gender profile of patients, clinical classification of patients' chronic venous disease (CVD), positioning of the EVTA fibre or catheter tip in relation to the SFJ, use of peri-procedural anticoagulation, timing of the first post-procedural DUS, additional concomitant procedures, incidence of DVT, incidence of EHIT, incidence of PE. There were no predefined definitions for DVT or PE: the definitions provided in manuscripts were used if such definitions were provided. EHIT was defined using the classification system outlined in the Introduction.[5] Disagreements regarding extracted data were resolved by discussion between D.H. and D.P.

Outcomes for the systematic review were DVTs, EHIT of all types, and PE. The primary outcome for the meta-analysis was deep venous thrombotic events which were defined as DVT or EHIT Type 2, 3, or 4. Secondary outcomes for the meta-analysis were EHIT Type 2, 3, or 4, DVT, and PE. Additional subgroup analyses were performed for both the RFA and the EVLA groups.

The Down's and Black Tool was used for assessment of study quality.[9] This consists of a total of 27 questions that assess the quality of reporting and internal and external validity. It yields scores that may vary between 0 and 31, including a score of 0–5 for sample size justification. For the purposes of this review, the checklist was modified by giving 1 point for reporting a sample size calculation and 0 points for omitting this. Therefore, studies included in this review could have had scores ranging from 0 to 27, with higher scores indicating higher quality.

Statistical analyses were performed with StatsDirect version 3 (StatsDirect Ltd, Altrincham, UK).[10] Proportion meta-analyses using random effects modelling were used to

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