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Cost-Effectiveness of Current and Emerging Treatments of Varicose Veins

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ABSTRACT

Objectives: To analyze the cost-effectiveness of current technologies (conservative care [CONS], high-ligation surgery [HL/S], ultrasound-guided foam sclerotherapy [UGFS], endovenous laser ablation [EVLA], and radiofrequency ablation [RFA]) and emerging technologies (mechanochemical ablation [MOCA] and cyanoacrylate glue occlusion [CAE]) for treatment of varicose veins over 5 years. **Methods:** A Markov decision model was constructed. Effectiveness was measured by re-intervention on the truncal vein, re-treatment of residual varicosities, and quality-adjusted life-years (QALYs) over 5 years. Model inputs were estimated from systematic review, the UK National Health Service unit costs, and manufacturers' list prices. Univariate and probabilistic sensitivity analyses were undertaken. **Results:** CONS has the lowest overall cost and quality of life per person over 5 years; HL/S, EVLA, RFA, and MOCA have on average similar costs and effectiveness; and CAE has the highest overall cost but is no more effective than other therapies. The incremental cost per QALY of RFA versus CONS was £5,148/QALY. Time to return to work or normal activities was significantly longer after HL/S than after other procedures. **Conclusions:** At a threshold of £20,000/QALY, RFA was the treatment with highest median rank for net benefit, with MOCA second, EVLA third, HL/S fourth, CAE fifth, and CONS and UGFS sixth. Further evidence on effectiveness and health-related quality of life for MOCA and CAE is needed. At current prices, CAE is not a cost-effective option because it is costlier but has not been shown to be more effective than other options.

Keywords: cost-effectiveness, economic evaluation, endothermal, varicose veins, vascular.

Introduction

Varicose veins (incompetence of the great saphenous vein [GSV] and its tributaries) carry a considerable burden of disease for patients and health services. Symptoms can be discomforting, painful, and unsightly, and in serious cases can impair mobility and lead to elevated risk of ulcer [1]. Reported incidence of varicose veins ranges from 20% to 64% of the total population. Residual varicosities (spider veins), which are in many cases associated with varicose veins, can affect up to 80% of adults.

Treatment for varicose veins can offer substantial health-related quality-of-life (HRQOL) improvements to patients. The market is characterized by many competing modalities, and innovation continues to be rapid. Established treatments of varicose veins include conservative care (CONS) (such as compression stockings), high-ligation surgery (HL/S) (usually stripping and ligation of the great and small saphenous veins), ultrasound-guided foam sclerotherapy (UGFS), endovenous laser ablation (EVLA), and radiofrequency ablation (RFA) [2]. To these can be added emerging technologies of mechanochemical ablation (MOCA) [3] and cyanoacrylate glue occlusion (CAE) [4]. Interventional treatments aim to occlude the GSV and in most cases this will relieve the underlying cause of the symptoms. If symptoms do recur, re-intervention may be considered. Residual varicosities may in some cases also be treated during the index treatment or alternatively in a follow-up session [5].

This study develops an economic model of current and emerging technologies for treatment of varicose veins. The model draws together evidence from published literature to estimate the costs of the initial treatments, re-treatments for varicosities

Conflicts of interest: The authors have no conflicts of interest.

The authors have attempted to limit the potential for bias at all stages of the design and analysis. The study protocol was prepublished in PROSPERO. The review was conducted and reported according to the guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses as well as the Cochrane guidelines.

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and re-interventions for treatment failure, and HRQOL over 5 years. Key input variables for the model are estimated when possible from systematic reviews and meta-analyses of randomized controlled trials (RCTs), conducted according to recognized protocols [6,7]. The economic analyses are conducted according to guidelines for evaluation of health care programs [8]. The structure of the article is as follows. In the Methods section, we first describe the model structure and justify re-interventions and re-treatments as the principal measures of effectiveness. Next, we present the methods and results of the systematic review and evidence synthesis to obtain each of the key inputs used in the model. In the Results section, we show the 5-year predictions of costs and quality-adjusted life-years (QALYs) from the base-case model and sensitivity analyses. Finally, we discuss the implications for current practice and further research.

Methods

Overview

This study evaluates the cost-effectiveness of therapeutic options for varicose veins in adult patients requiring treatment in the upper leg for incompetence of the GSV (the "truncal" vein). Health outcomes are measured in QALYs, and the cost perspective is that of the UK National Health Service (NHS) and the social care system at 2015 prices. The time horizon of the decision model is 5 years. This is considered to be the maximum time over which recurrence of index symptoms is likely to occur, and is the longest follow-up of any published RCT in this area [9–11]. Costs and QALYs are discounted at 3.5% per year [12]. The treatments compared are CONS, HL/S, EVLA, RFA, UGFS, MOCA, and CAE.

The key outcome data used to inform the decision model are re-interventions, operative time, HRQOL, and time off work. These are based as far as possible on the synthesis of RCT data obtained from systematic review. Because this is a multiple technology appraisal, network meta-analysis (NMA) should be considered when appropriate [13]. The main assumption of NMA, in addition to those used in conventional random-effects meta-analysis, is consistency of treatment effects [7]. That is, for any three treatments A, B, and C, the treatment effect (on an appropriate linear scale) of B versus C is the same as that of A versus C minus the effect of A versus B. Consistency can be assessed statistically by observing whether the direct and indirect evidence agree with one another [14,15]. The network is more likely to be consistent if the distributions of patient characteristics (potential effect modifiers) are similar in all the studies [7]. The standard random-effects NMA model also assumes that studies are exchangeable; that is, between-study variance is the same for all treatment comparisons [14]. In this study, for outcomes for which these assumptions appear valid, we estimate model parameters from the RCT data using mixed treatment effects, and for outcomes for which an NMA appears inappropriate, we estimate model parameters from direct treatment effects using conventional random-effects meta-analysis.

Model Structure

The decision model is a Markov structure (Fig. 1). The principal measure of effectiveness of the treatments is re-intervention. Broadly, there are two reasons for a re-intervention. The first is the *re-treatment* of painful or unsightly varicose veins in the tributaries of the GSV at or near the surface, known as residual varicosities. It is assumed that these will be treated shortly after the first 6-week follow-up. The second is the *re-intervention* on the truncal vein. These re-interventions can occur if the index treatment has failed or symptoms have recurred and will take place between 6 months and 5 years after the index treatment. Varicose veins can be a painful and debilitating condition, but not life-threatening. Hence, mortality is not an outcome in the model.

Re-treatments of residual varicosities

Residual varicosities are usually unsightly but can also be symptomatic and painful. In most patients, treatment of the GSV will lead these to be significantly less prominent. This leads some practitioners not to treat these during the index procedure, but instead to "wait and see." Nevertheless, the Ambulatory Varicosity avUlsion Later or Synchronized (AVULS) study found that the most effective course of action (in terms of overall patient quality of life) is to treat the varicosities alongside the truncal treatment during the index procedure [5]. It is assumed in our model that concomitant phlebectomy or foam will be used to treat nontruncal varicosities as needed alongside all the surgical treatment options, except in UGFS because it does not use appropriate anesthetics to allow this strategy to be followed. This means that the rate of re-treatment of residual varicosities is greater after UGFS than after other interventional modalities [16]. In all treatment modalities, patients are re-assessed at a 6-week follow-up. If residual varicosities are still present and symptomatic, these will be treated by ambulatory foam [17].

Re-interventions on the truncal vein

Re-intervention on the truncal vein is an indicator of the failure of the initial treatment or a recurrence of serious symptoms. In the case of re-intervention, HRQOL is assumed to be impaired

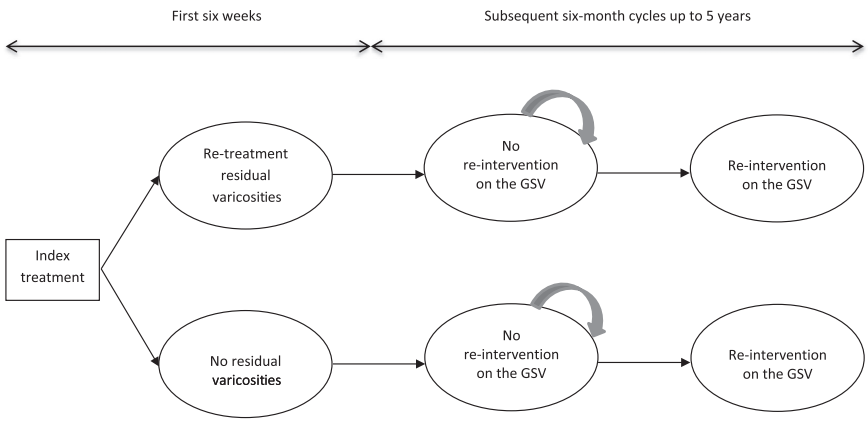

Fig. 1 – Structure of Markov model. Residual varicosities are re-treated at 6 weeks and re-interventions can occur up to 5 years after index procedure. GSV, great saphenous vein.