Varicose Veins

Aspects on Diagnosis and Surgical Treatment

LENA BLOMGREN
Dissertation presented at Uppsala University to be publicly examined in Hörsalen, St Görans Sjukhus, St Görans plan 1, Stockholm, Wednesday, September 7, 2005 at 09:00 for the degree of Doctor of Philosophy (Faculty of Medicine). The examination will be conducted in Swedish.

Abstract


Treatment for varicose veins (VV) is insufficiently evidence based and recurrence rates are high. The aim of this thesis was to study the long-term results after VV surgery, risk factors for recurrences and the effect of preoperative duplex scanning on recurrence rate, quality of life (QoL) and costs.

In a follow-up study 89 patients with 100 legs operated on for VV 6–10 years earlier were re-examined with duplex, in 13 cases also with varicography. 57% had incompetent vessels in the groin visible with duplex, equally well defined by varicography. Residual branches could not be differentiated from new vessel formation. The recurrence rate did not correlate to the surgeon’s level of experience or perioperative difficulties at primary surgery.

In a prospective randomized study 293 patients (343 legs) were operated on for primary VV with or without preoperative duplex. Duplex was done postoperatively, at 2 months and 2 years. QoL was measured with SF-36 preoperatively, at 1 month, 1 year and 2 years.

After 2 years the number of reoperations were 2 in the group with preoperative duplex and 14 in the group without (p=0.002). Incompetent veins were seen in the saphenofemoral or saphenopopliteal junction in 19 and 53 legs respectively (p<0.001).

Preoperative QoL was worse in the VV patients compared to a reference population, and was normalised 2 years postoperatively. The improved surgical result in the duplex group was reflected in a significantly higher QoL.

The lower costs for redo surgery in the duplex group did not offset the costs for duplex, partly due to more extensive primary surgery.

A significant proportion of recurrences after 2 years was new vessel formation and progression of disease. Preoperative perforating vein incompetence did not influence recurrence rate, and was abolished without specific interruption in 60% at 2 years postoperatively.

Keywords: Varicose veins, Venous insufficiency, Surgery, Duplex, Quality of life, Cost analysis

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List of Papers

This thesis is based on the following papers, which are referred to in the text by the Roman numerals given below (I–V):


III  Blomgren L, Johansson G, Bergqvist D. Quality of life after surgery for varicose veins and the impact of preoperative duplex - results based on a randomized trial. *Submitted*


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<tr>
<td>APG</td>
<td>Air plethysmography</td>
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<td>AVP</td>
<td>Ambulatory venous pressure</td>
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<tr>
<td>CEAP</td>
<td>Clinical Etiology Anatomy Pathophysiology (classification system)</td>
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<td>CVD</td>
<td>Chronic venous disease or disorder</td>
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<td>CVI</td>
<td>Chronic venous insufficiency</td>
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<td>DVI</td>
<td>Deep venous insufficiency</td>
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<td>DVT</td>
<td>Deep venous thrombosis</td>
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<td>ELT</td>
<td>Endovenous laser treatment</td>
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<td>GSV</td>
<td>Great saphenous vein</td>
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<td>HHD</td>
<td>Hand held doppler</td>
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<td>ITT</td>
<td>Intention to treat</td>
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<td>PP</td>
<td>Per protocol</td>
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<td>PVI</td>
<td>Perforating vein incompetence</td>
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<td>RFA</td>
<td>Radiofrequency ablation</td>
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<td>QoL</td>
<td>Quality of life</td>
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<td>SEPS</td>
<td>Subfascial endoscopic perforator surgery</td>
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<td>SF-36</td>
<td>Short form 36 (QoL questionnaire)</td>
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<td>SFJ</td>
<td>Saphenofemoral junction</td>
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<td>SPJ</td>
<td>Saphenopopliteal junction</td>
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<tr>
<td>SSV</td>
<td>Small saphenous vein</td>
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<tr>
<td>SVS</td>
<td>Superficial venous surgery</td>
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<td>VV</td>
<td>Varicose veins</td>
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Introduction

Varicose veins (VV) are common and surgery for VV one of the most frequently performed operations, in Sweden approximately 6–10 000 per year within the national health care system. The complaints of the individual patient with VV are varying, from cosmetic aspects to painful non-healing ulcers. Costs for treatment of VV and their consequences are vast, both for society and individual patients. In contrast to the common occurrence is the lack of evidence based treatment for VV, in surgery as well as in alternative treatments such as venoactive drugs, sclerotherapy and new minimally invasive methods. Recurrence rates after surgery are high, and suggested causes are inadequate diagnosis and surgical technique. The increased interest in venous research during the last decade has so far not improved the long-term results.

The overall aim of this thesis is to evaluate the results of current surgical treatment of patients with VV, to identify potentially amenable risk factors for recurrence and to analyse whether the introduction of preoperative duplex scanning of diseased veins does influence the outcome.

Definitions

Venous research has been hampered by the lack of precise definitions. One reason may be the “normality” of the condition, many people have VV without being patients. Subsequently many papers report the results in terms of VV and venous disease as two separate entities (Evans 1998, Kurz 2001).

An attempt to create a common language for research and clinical use is the CEAP (Clinical Etiology Anatomy Pathophysiology) classification for chronic venous disorders (CVD), developed in 1994 by an international ad hoc committee of the American Venous Forum (Beebe 1996). The classification is based on clinical manifestations (C), etiologic factors (E), anatomic distribution of disease (A) and underlying pathophysiologic findings (P).

However, the terminology used may still be confusing, as the term CVD includes the whole spectrum of morphologic and functional abnormalities of the venous system, which means that also telangiectases in healthy individuals will be classified as a disorder or disease, whereas the term chronic venous insufficiency (CVI) is reserved for more advanced disease with oedema or skin changes.
The CEAP classification is increasingly used in venous research, but has been criticised for being complex and difficult to use, thus revisions are continually made (Carpentier 2003, Eklöf 2004). Often only the clinical class of CEAP is used, and so is also the case in the present studies.

Clinical (C) classes of CEAP

C0. No visible or palpable signs of venous disease.
C1. Telangiectases or reticular veins.
C2. Varicose veins; subcutaneous dilated veins 3 mm in diameter or larger.
C3. Oedema.
C4. Changes in skin and subcutaneous tissue secondary to chronic venous disease:
   C4a. Pigmentation or eczema.
   C4b. Lipodermatosclerosis or atrophie blanche.
C5. Healed venous ulcer.
C6. Active venous ulcer.

Another area of confusion in venous research is the anatomical nomenclature. In this thesis the recommendations of an international interdisciplinary consensus statement from Rome 2001 is used (Caggiati 2002), but this was not accepted by all editors for the papers included. Subsequently the great saphenous vein (GSV) is termed “the long saphenous vein”, and the small saphenous vein (SSV) is termed “the short saphenous vein” in one of the papers.

Figure 1. The relationship between superficial, perforating and deep veins of the leg. Drawing by Lena Lyons. (From Lindgärde: Kärlsjukdomar. Studentlitteratur, 2005. With kind permission.)
Anatomy and physiology

The veins of the leg are divided into a superficial and deep system, and the perforators connecting them, Figure 1. The anatomy of the superficial and perforating veins are shown in Figure 2.

From the venules to the pelvic veins, the veins contain valves that can resist gravitational and muscle pressure and direct the blood flow towards the heart. The driving force in the venous system is the inflow from the arteries, the muscle pump of the foot and calf, and the intrathoracic variations in pressure.

Besides serving as conduits for the blood, the veins also have a storage function and are part of the regulatory system of the body temperature. The venous endothelium has a large total surface with a variety of functions such as release of substances involved in coagulation and fibrinolysis. The diameter of the vein varies with total blood volume, temperature, body posture, sympathetic tone of the nervous system, and the presence of pathological conditions (Jogestrand 2002, Norgren 2004). Thus even in completely normal veins, the volume of blood in the veins of the legs can vary considere-
bly, which makes the contribution of the increased volume from diseased vein difficult to predict.

Pathophysiology

The exact aetiology of VV is not known. The affected vein wall has a lower content of collagen than healthy veins, and histological studies of VV have demonstrated a disruption of the organisation of the extracellular matrix and smooth muscle architecture (Jones 1999). VV also display a greater inflammatory cell infiltrate than normal veins (Ono 1998). VV have been shown to develop both in an antegrade and retrograde direction, so the progression of disease may be due to a combination of the inherent wall weakness and the haemodynamic forces with increased venous hypertension (Labropoulos 1997).

The fundamental pathophysiologic event in venous insufficiency is the reflux, the retrograde flow due to leaking venous valves. This leads to a delayed emptying of blood from the leg, which thus contains a greater volume than normal, and to venous hypertension.

The chain of events from venous hypertension to skin changes or to a venous ulcer is not yet delineated. Several theories have been proposed, the most popular being the theory that white cells accumulating due to the venous stasis will become activated and release toxic substances deleterious to the skin and subcutaneous tissue (Coleridge Smith 1996). However not all patients with venous hypertension develop skin changes, and although there is a correlation with the degree of venous dysfunction there is a considerable overlap between groups (Iafrati 1994, Milne 1994, Schmid-Schönbein 2001). The muscle pump is involved, factors within the coagulation and fibrinolysis system, disturbances in tissue remodelling and other factors still unknown, making some individuals more vulnerable (Rosfors 1990, Herouy 1999, Blomgren 2001).

Previously it was considered that only reflux in the deep venous system or postthrombotic changes could lead to the development of a venous ulcer. Investigations with duplex ultrasound have shown, however, that a substantial part of ulcer patients have insufficiency mainly in the superficial system, thus amenable to VV surgery (Labropoulos 1995).

Epidemiology

The most thorough study of the prevalence of venous disease in recent years is the Edinburgh Vein Study, where 1566 subjects from the general population, 18–64 years of age, were examined clinically and with duplex. In the study the prevalence of telangiectases and reticular veins was more than
80%, VV were interestingly found more often in men, 40%, than in women, 32%, and CVI was found in men in 9% and in women in 7% (Evans 1999).

Figures in Sweden are not known, but the prevalence of an open or healed venous ulcer in Sweden has been studied by Nelzén et al, and was estimated to 2% (Nelzén 1996). According to the statistics of the National Board of Health and Welfare, 11 000 operations for VV were performed in 1994, and 5 500 in 2002. The latter figure includes only hospitals, and there are an increasing number of operations performed in small private practices, so the figure is probably higher.

Costs

The economical impact of venous disease is vast. In France the costs of venous disease represented 2.6% of the total health care budget in 1995, in the UK the corresponding figure was 2%, and in Belgium the annual spending on venotropic drugs alone amounted to one billion BEF in 1995 (van den Oever 1998, Bosanquet 1999). It has been estimated that more than 1% of the total health care budget in the western world is spent on the treatment of leg ulcers, of which venous ulcers are in a majority (Nelzén 2000).

Costs for treatment of VV are covered in a varying degree by the social security system. In Sweden there is no national consensus regarding what patients are entitled to surgery within the national health care system, but most surgeons would agree on the practice that patients with skin changes are treated in hospitals within the national health care system and patients with VV and cosmetic complaints pay for the treatment themselves in private practice. Patients with symptomatic VV are treated depending on the resources and traditions at the local hospital, or according to the opinion of the examining physician, which means that there are considerable variations in policy.

Symptoms, signs and quality of life

Many VV are asymptomatic, and the patient’s complaint purely cosmetic. When symptoms occur, they are often described as heaviness, swelling, aching, restlessness, cramps and itching. These symptoms are not specific for venous disease, however, and the correlation with venous disease complex. In the Edinburgh Vein Study there was better agreement between symptoms and reflux as defined by duplex than there was between symptoms and visible VV on clinical examination, and there was poor agreement between the presence of skin changes and symptoms. When examined with duplex, superficial and mixed venous reflux were increasingly found in subjects with more severe varices visible on clinical examination, but there was no corre-
lation between the presence of telangiectases and reticular veins and the presence of reflux (Bradbury 1999).

Patients with more advanced CVI develop skin changes typically situated in the lower part of the calf, often on the medial side just cranial to the ankle. Hyperpigmentation, eczema, lipodermatosclerosis and ulcer may coexist or develop separately. Historically it was considered that one distinguishing feature between arterial and venous ulcers was pain, which was thought to be absent or minor in venous ulcers. However studies have shown that many patients with venous ulcers have very severe pain, requiring medication with opiates (Hofman 1997).

Several studies have addressed the quality of life (QoL) of patients with venous ulcers, which is lower than in the general population (Franks 1999, Kurz 2001). The impact of VV on QoL has traditionally been considered low, and patients with VV without skin changes have thus been assigned a low priority within the national health care systems.

![Figure 3. Illustration by John Gay of the varicose veins in the right leg of a 56-year-old woman. From the lecture “On varicose disease of the lower extremities”, 1866.](image)

**Diagnosis**

The most important investigation in a patient with VV is a thorough clinical examination including a detailed history with possible differential diagnoses in mind. Some physicians will supplement this with an examination with hand held doppler (HHD) to screen for the presence of venous reflux in the GSV and SSV.

Phlebography was the most common investigation historically when a more detailed map of the vein anatomy was needed, but is an invasive inves-
tigation with a small risk of anaphylaxis and has largely been replaced by duplex (see below). However, with the advent of endovascular techniques, phlebography has a new role, especially for patients with deep venous thrombosis (DVT) and postthrombotic lesions. The injection of contrast can be given in an antegrade or retrograde fashion, depending on the indication, and also directly into the VV, varicography (Corbett 1984).

Phlebography or duplex will mainly provide anatomical descriptions of where the incompetent vessels are located but will not evaluate the global venous insufficiency of the leg, although pressure or volume of flow can be measured in individual vessels (Neglen 2004).

When the haemodynamic effects of VV are investigated in terms of venous hypertension and increase of blood volume in the leg, functional investigations such as ambulatory venous pressure (AVP) measurement, air plethysmography (APG), photoelectrophysmography (PPG) and foot volumetry are used (Norgren 2000, Marston 2002, Danielsson 2003).

Depending on the severity of CVI, different levels of testing has been proposed (Nicolaides 2000, Eklöf 2004):

- **Level I**: clinical examination, may include HHD
- **Level II**: non-invasive testing: duplex and if appropriate a plethysmographic method
- **Level III**: invasive or complex imaging studies: venography, venous pressure measurements, computerised tomography, magnetic resonance imaging.

Although not specifically reported, there is reason to believe that most patients with VV are examined clinically only. The sensitivity and specificity of clinical tests are not acceptable (Wills 1998, Kim 2000). The use of HHD in skilled hands is accurate in most cases for the GSV, but not for the SSV which more often has a variable anatomy and is difficult to discriminate from the popliteal vein due to its proximity (Smith 2002, Wong 2003).

**Duplex scanning**

Duplex, colour Doppler ultrasound, has its name as it combines the ultrasound imaging with pulsed Doppler spectral waveform analysis that is colour-encoded and superimposed on the image, thus creating an image with the anatomy of the vascular segment and the flow pattern. The duplex technology has developed rapidly the last decade, and it is now possible to examine even small vessels with accuracy. Duplex is non-invasive, but can be combined with invasive treatment such as injection of drugs or insertion of catheters. As veins vary in diameter depending on the posture of the body, temperature and sympathetic tone etc, it is important that the examination is
performed according to a standardised protocol, especially so as it is examiner dependent and has a long learning curve (Haenen 1999).

The definition of pathological reflux is >0.5 s in most studies, and it has been shown that 93% of all reverse flow in normal subjects was within the 0.5 s cut-off (Lagattolla 1997). The duration of reverse flow in normal subjects has however been shown to be longer in the proximal deep veins, <1 s, and shorter in the deep veins of the calf, <0.3 s (Labropoulos 2003).

Duplex scanning has virtually replaced all other forms of non-invasive venous assessment in clinical practice, and is used frequently in more advanced CVI or recurrent VV. It is not routinely used for all VV patients, as it requires specially trained technologists, is time consuming and thus expensive.

Indications for treatment

In private practice, many patients will seek advice mainly for cosmetic complaints. Within the national health care system the most common indications for treatment of VV are relief of symptoms and the prevention or cure for venous ulcers and skin changes. There is a considerable variation in practice as even the benefit of surgery for ulcer patients has been questioned. However, in a recent randomized study, superficial venous surgery (SVS) and compression was more effective in preventing recurrence of venous ulcers than compression alone (Barwell 2004). Concerning symptomatic patients without skin changes there are at present no general recommendations concerning who will benefit from surgery.

In some patients recurrent bleeding from otherwise asymptomatic VV mandates treatment. It has also been suggested that VV may be a risk factor for DVT, and thus some patients seek treatment as a prophylactic measure. However, the increased risk is small, and is by itself not an accepted indication for treatment (Saarinen 1999, Edmonds 2004, Kyrle 2005).

Treatment options

When treatment of VV is considered, there are two targets, the cosmetic appearance and the venous hypertension. For treatment of minor varicosities of cosmetic concern sclerotherapy and/or surgery is employed, and for telangiectases and reticular veins also laser therapy.

The mainstay for relief of the venous hypertension is compression, with stockings or bandages, by which the diameter of the veins and thus the volume of blood within them is reduced and the outflow of venous blood from the leg is improved. Compression therapy is effective in alleviating symptoms and in healing of venous ulcers (Cullum 2001).
The second way to relieve venous hypertension is to remove the diseased vessels. This can be achieved in two principally different ways, by surgery (see below) and by obliteration with sclerotherapy or catheter techniques.

In sclerotherapy, a sclerosant agent is injected in the VV and an inflammatory reaction is induced in the vessel wall that makes the vein obliterate. There are different drugs, techniques and traditions in sclerotherapy in different countries which make comparisons difficult with other forms of treatment. In a Cochrane report the reviewers’ conclusion was that there were few randomized studies, that there was insufficient evidence to preferentially recommend the use of sclerotherapy or surgery and that there needs to be more research that specifically examines both costs and outcomes for surgery and sclerotherapy (Einarsson 1993, Rigby 2004). However, there was a trend for sclerotherapy to be evaluated as significantly better than surgery at one year; after one year the benefits with sclerotherapy were less, and by three to five years surgery had better outcomes. The use of foam sclerotherapy in recent years has been reported as more efficient than conventional sclerotherapy in eradicating venous reflux, with long-term results comparable to surgery in selected subjects (Belcaro 2003). However, for all forms of sclerotherapy, as for surgery, there is a concern for post treatment DVT as there is an activation of the coagulation system (Ikeda 1996).

Obliteration with catheter techniques is used with heat applied with radiofrequency, radiofrequency ablation (RFA) or with endovenous laser treatment (ELT). Studies have reported less postoperative pain and faster recovery compared with surgery (Rautio 2002, Min 2003), and hopes were raised that recurrences would be less due to the minor surgical trauma and subsequent lesser formation of new vessels (Pichot 2004). Recent studies have shown, however, that the prevalence of new vessel formation after RFA is similar compared to surgery, and that RFA carries a high rate of post treatment DVT, 16% (Salles-Cunha 2004, Hingorani 2004, Mozes 2005). The commercial and research interests in catheter techniques are intense, thus refinement of these methods is to be expected.

The use of venotonic drugs for treatment of VV is controversial. In a Cochrane review, it was concluded that horse chestnut seed extract and pentoxiphyllin may relieve venous symptoms, but there is a lack of more rigorous randomized controlled studies to assess the efficacy (Jull 2002, Pittler 2004).

Surgery
The basic principles for surgical treatment of VV is the removal of diseased vessels and/or the ligation of leaking connections between the deep and the superficial venous system. Removal of veins may seem unnatural for the patients, but is compatible with an improved venous circulation, as there is
an abundance of veins in the legs and the blood flow will be redirected to the healthy veins with healthy valves.

The removal of the GSV, so called stripping, has been questioned as the patient may be deprived of future graft material for arterial bypass surgery. Thus many surgeons have advocated ligation of the saphenofemoral junction (SFJ) only when the GSV is diseased, as it has been shown that this procedure alone or in combination with ligation of selected perforators may diminish the volume harboured in the GSV, and it may even regain competence and be preserved for future grafting (Hammarsten 1990, Zamboni 1998). However a diseased GSV may not be suitable as graft material, and the long-term results after high ligation only are inferior to removal of the GSV (Dwerryhouse 1999, Winterborn 2004).

Another drawback with removal of the GSV is that there is a risk of nerve damage in the calf. An alternative is removal of the GSV above the knee, which may lower the risk of recurrence compared to high ligation only, and save the GSV in the calf for future use (Holme 1996). Still there is a concern that the remnant distal GSV may cause recurrences (Morrison 2003). One study has even suggested that a remnant GSV above the knee, e.g. in cases with duplicated GSV, correlates with the development of deep venous insufficiency (DVI) (MacKenzie 2004).

Removal of the SSV is considered a more difficult operation, as the anatomy at the saphenopopliteal junction (SPJ) is variable and the surgical dissection is more difficult with the proximity of the tibial nerve (Winterborn 2004). In most hospitals the SPJ is marked preoperatively with duplex technique.

Removal of branch varicosities, local phlebectomies, may seem a mere cosmetic measure, but local VV can harbour large volumes of blood and thus contribute considerably to the venous congestion in the lower leg. Local phlebectomies can be performed via minute stab incisions and hooks, leaving a satisfactory cosmetic result (Ramelet 2002). Traditional local excisions with large incisions should be avoided.

Division of perforating veins has a long tradition, but the precise indication for perforator surgery is not defined (Cocket 1988, van Neer 2003). Perforating vein incompetence (PVI) have been associated with recurrent VV, and in analogy with ligation of the SFJ and the SPJ it has been considered that disrupting incompetent perforating veins will lower the pressure on the superficial veins and prevent recurrences (Zamboni 1998, Rutherford 2001). Furthermore, perforators are considered crucial for the development of skin changes and ulcers (Bianchi 2003). Incisions in diseased skin for perforator division has a poor healing rate, and thus techniques have evolved where the perforators are divided subfascially, either through a distant surgical incision, or endoscopically (subfascial endoscopic perforator surgery, SEPS). However, at present there is no evidence that perforator surgery improves the healing of ulcers better than SVS alone (Tenbrook 2004).
The reports concerning haemodynamic improvement after perforator surgery alone are contradictory (Åkesson 1990, Rhodes 1998). Studies have shown that perforators may regain competence without specific interruption when the superficial incompetence is removed, these findings are questioned by others (Mendes 2003, van Rij 2003). Thus the indication for perforator surgery is still controversial.

Some patients with VV have a combination of superficial and deep venous insufficiency. Traditionally these patients were considered unsuitable for SVS but contemporary studies have shown that similar to perforators, some deep veins may regain competence when the overload from the superficial system is removed (Sales 1996, Ciostek 2004). Also contrary to previous opinion, SVS may even be beneficial in cases of deep venous obstruction (Raju 1998). Deep venous reconstructions are performed with a variety of methods, in patients with varying patterns of reflux and randomized studies are scarce. In a Cochrane review 2004 the authors evaluated the use of ligation and valvuloplasty, and concluded that there was insufficient evidence to recommend this treatment to patients with primary valvular incompetence (Hardy 2004).

The rate of postoperative DVT after SVS varies in different studies, rates between 0% and 5% have been reported (Bohler 1995, van Rij 2004).

Recurrences after treatment

The recurrence rate after all kinds of treatment for VV is high. After surgery the figures vary depending on the length of follow-up, between 20–70%, and it has been estimated that 20% of operations for VV is for recurrences (Bradbury 1993, Fischer 2001). At present, there are three possible mechanisms discussed as causative: inadequate surgery, progression of disease and neovascularisation.

Inadequate surgery may be due to inadequate planning of the operation or inadequate surgical technique. Many patients are operated on after clinical examination only, and this may be insufficient for the choice of procedure. It has also been suggested that SVS often is performed by junior surgeons, who may misinterpret the anatomy (Lees 1997).

Patients with VV have an inherent abnormality of the vein wall, and after surgery the disease may progress in other segments of the veins, thus new VV develop in veins that were seemingly normal at surgery (Kockx 1998, Kostas 2004). It has also been proposed that the redirected venous flow after SVS will strain the susceptible veins and then surgery per se would precipitate the recurrences (Turton 1999).

Neovascularisation was first observed in rats, where small newly formed vessels reconnected the deep femoral vein and tributaries after surgical division (Glass 1987). With more refined methods of investigations, such as
varicography and duplex, it has been observed also in humans, and when examined prospectively neovascularisation seem to constitute a substantial part of recurrences (Stonebridge 1995, van Rij 2003). However, the definition is not established, as small vessels left at primary surgery may resemble newly formed vessels (Geier 2005). Neovascularisation has also been studied histologically, and defined as tortuous vessels with lack of mural nerves (Nyamekye 1998). This has been questioned lately, as no other group has reproduced these results (El Wajeh 2004).

At present the relative contribution of these different causes for recurrences after VV treatment is poorly understood, and thus there is still insufficient evidence to recommend new treatment strategies.
Aims of the investigation

The overall aim of this thesis has been to study risk factors for recurrences after varicose vein surgery and the impact of preoperative duplex examination on outcome. The specific aims were:

To study the recurrence rate after current varicose vein surgery (Study I and V)

To compare the morphology of groin recurrences on duplex examination, with that at varicography and at surgery (Study I and V)

To validate a classification system for groin recurrences proposed by the Edinburgh group (Study I)

To identify potential risk factors for recurrences at primary surgery (Study I and V)

To study the impact of preoperative duplex examination on the rate of redo surgery and recurrences (Study II)

To study the impact of varicose vein surgery and preoperative duplex examination on quality of life (Study III)

To study the cost consequences of preoperative duplex examination (Study IV)

To prospectively study the changes in pattern of venous incompetence two years after varicose vein surgery (Study V)

To study the effect of varicose vein surgery on vein segments not specifically targeted at operation, such as perforators and the great saphenous vein in the calf (Study V)
Patients and methods

Patients

All patients were examined and treated within the ordinary clinical setting at the Departments of Clinical Physiology and Surgery at St. Göran’s Hospital, Stockholm.

In paper I, a retrospective analysis was made of medical records for all patients operated on for VV from 1990 to 1991, and those subjected to primary SFJ ligation and removal of the GSV were invited for re-examination.

The study population in papers II–V was recruited from patients with primary VV referred to St. Göran’s Hospital from October 1997 to July 2001. The exclusion criteria were age below 20 years or above 75 years, pure cosmetic complaints, previous venous surgery or sclerotherapy, history of suspected or manifest DVT, active or healed leg ulceration, peripheral arterial disease, previous significant trauma to the leg, severe concomitant disease and drug or alcohol abuse.

Study design

Paper I

The patients included were examined clinically and with duplex 6–10 years after VV surgery. In cases with a clinical indication for reexploration of the groin, varicography was performed prior to the operation.

The venous anatomy of the groin was studied, in order to classify recurrences according to a system proposed by the Edinburgh group (Stonebridge 1995) (Table 1). Operative findings were compared with duplex and varicography.

The original medical records were studied for the following possible risk factors for recurrence: sex and age, surgeon’s level of experience (surgical resident, general or vascular surgeon), perioperative difficulties (bleeding, technical problems) and postoperative complications (haematoma, thrombo-phlebitis, infection, lymph exudates).
Table 1. Classification of groin recurrences in 57 legs with duplex according to the Edinburgh system.

<table>
<thead>
<tr>
<th>Type</th>
<th>no of legs</th>
<th>subtype</th>
<th>no of legs</th>
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<tbody>
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<td>1</td>
<td>50</td>
<td>A</td>
<td>8</td>
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<td>B</td>
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<td>C</td>
<td>15</td>
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<td></td>
<td>B or C</td>
<td>17</td>
</tr>
<tr>
<td>2</td>
<td>9</td>
<td>A</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td></td>
<td>B</td>
<td>6</td>
</tr>
</tbody>
</table>

NB: the same leg can have more than one type of recurrence, hence the sum exceeds the no of legs.

Paper II–V

The patients were randomized to VV surgery with or without preoperative duplex. The 20 surgeons participating were instructed not to change their individual standard procedures for clinical examination, which to a varying extent included the use of HHD. Clinical status was classified according to the C part of the CEAP (Beebe 1996). After the decision to operate, the patients were randomized to preoperative duplex imaging (group D) or not (group ND) using sealed envelopes. If a bilateral operation was planned, both legs were assigned the same randomization.

In all patients a postoperative duplex was planned 1–2 months after surgery. After 2 years a clinical examination and a further duplex scan were planned.

The analyses focused on reflux at the SFJ and the SPJ, and the effect of surgical treatment on reflux in the GSV and SSV, as the removal of these segments was considered a crucial surgical decision. Results were analysed by intention to treat (ITT) when all legs were included, and as per protocol (PP) in the cases where the operation was performed according to the results of the preoperative scan.

QoL measurements were made four times: at the first visit, and at 1 month, 1 year and 2 years after surgery.

Duplex scanning

The duplex scans were done at the Department of Clinical Physiology, St. Göran’s Hospital. All examinations were performed according to a standard protocol by a vascular technologist supervised by a physician at the department.
With the patient in the supine position the venous flow was examined in the external iliac and common femoral vein, and the presence of spontaneous flow as well as respiratory variations were observed. Valvular function was evaluated in the femoral, popliteal and superficial veins of the thigh after manual distal compression with the patient upright with slightly flexed knee. Reflux with a duration of more than 0.5 s was considered significant. The veins in the lower leg, including the posterior tibial, the peroneal and the SSV, were evaluated with the patient in a sitting position. Perforating veins were considered incompetent if larger than 3 mm with bidirectional flow.

When analysing the duplex data, the following anatomical sites were studied: SFJ, SPJ, GSV above the knee, GSV below the knee, SSV, perforating veins in the thigh and calf, and deep veins. The segments examined were classified as incompetent, obliterated or competent, and for the GSV above the knee, the GSV below the knee and the SSV, this had to be more than half of the length of the segment. If remaining or new incompetent connections were found in a segment or site it was termed incompetent. If no colour flow was detected in an operated area, it was considered obliterated. Remnant vessels without reflux in an operated area were termed competent.

Varicography

Varicography was performed according to Corbett et al (Corbett 1984). Intravenous contrast medium was injected in the groin or in the upper portion of the thigh under continuous fluoroscopic control and simultaneous videotape recording with films taken at appropriate intervals. The films were evaluated by two independent radiologists.

Surgery

The operations were done by surgical residents, general surgeons and vascular surgeons, and the procedures were those predominantly performed at the time of the studies. Removal of the GSV was in paper I in most cases done from the ankle to the groin, whereas in papers II–V more often only from the groin to the knee. Stripping instruments were mainly conventional, but in the later part of the studies inversion stripping became more common. Removal of the SSV was made with stripping in some cases, and in others by segmental avulsions. Interruption of perforators was done in some cases, with extrafascial technique only. Local phlebectomies were done with local incisions and avulsions, in the later part of the studies mainly with minor stab incisions and hook phlebectomies. The majority of cases was done as day surgery, but some stayed overnight if longer operating times or elderly patients. DVT prophylaxis was given selectively when risk factors were pre-
sent, such as elderly patient, long operating time and contraceptive medication.

Quality of life

In paper III QoL was measured with the Short Form 36 (SF-36). The SF-36 is a well validated generic health related QoL instrument, where the QoL is calculated in eight domains, four physical: physical function (PF), role physical (RP), bodily pain (BP), general health (GH), and four mental: vitality (VT), social function (SF), role emotional (RE), mental health (MH) (Brazier 1992). SF-36 scores were compared with a reference group of 1921 subjects from the Swedish population matched for sex and age, with matched subgroups and between group D and ND.

Comment

When the trial started, the disease-specific instruments for measuring QoL in VV patients were not widely accepted, so the generic health-related questionnaire SF-36 was chosen. This may influence the sensitivity of the measurements.

Cost analysis

In paper IV direct costs related to the primary and redo procedures during a two-year period were estimated, and compared between group D and ND. All the prices were taken from the hospital accounting system 2004. The duplex cost paid was double if two legs were examined, and included costs for staff, physicians, colour flow duplex imagers and overhead costs. Operating room costs included salaries for the anaesthetic and theatre staff, drugs, material for cleaning and draping, gowns and gloves. The costs for surgeons’ time was based on the mean of their salaries (pay-roll taxes included). Extra operative costs consisted of preoperative mapping (which was routinely performed before short saphenous vein surgery), and stripping equipment. The cost for basic instrumentation was the same for all patients. Admission costs was the extra costs for patients admitted to the hospital overnight. Costs per outpatient visit included surgeons’ salary and overhead, and consisted of the first visit and the extra visit for those patients who came back to plan redo surgery. All costs for the reoperation were defined as for the primary surgery.

Comment

The cost analysis was limited to a direct comparison of costs between the two randomized groups. No cost-effect analysis was made, as information
about indirect costs were not available, and quality adjusted life years were considered difficult to estimate due to the complicated relation between QoL and surgical results.

Statistics
Sample size calculations in paper II were based on detecting a possible reduction of the recurrence rate from 40 to 20%. With 90% power at the 5% significance level, 120 patients were required in each group. To adjust for drop-outs, it was planned to randomize 300 patients.

Mean values between samples of normally distributed data were compared by means of the two-tailed independent samples t-test. Differences between variables that were not normally distributed were tested with the Mann-Whitney U-test and Kruskal-Wallis test. Comparison of proportions were made with $\chi^2$ and Fisher’s exact test, and for differences before and after surgery Wilcoxon Signed Ranks Test was used.

In Paper IV a regression analysis was carried out where the effect on total costs of age, gender and number of legs operated on was analysed.

Statistical significance was accepted at $p<0.05$.

Ethics
The studies was approved by the Ethics Committee at the Karolinska Hospital, Stockholm, Sweden. All participating patients gave their informed consent.
Results

Clinical characteristics of the study populations

Paper I
Eighty-nine patients (60 women and 29 men) were examined 6–10 years after ligation of the SFJ and removal of the GSV. Their mean age at the time of operation was 48 years (range 23–76). Altogether 100 legs were included in the study. Nine patients (ten legs) had been re-operated already (two re-explorations in the groin, eight local excisions). One patient had been treated with sclerosant injections.

Eighty-six legs had visible VV on clinical examination, of which 30 were in the groin, proximal thigh, or both. Clinical presentation according to CEAP was 0–6 (median 2). Skin changes such as hyperpigmentation, hypostatic eczema, pre- or postulcerative changes (CEAP 4–6) were present in 29 legs.

In 68 of the legs there were symptoms that the patients ascribed to the residual or recurrent VV (such as heaviness, oedema, pain), most of them minor (cosmetic or slight discomfort), and in 27 legs there was a clinical indication for a reoperation.

Paper II–V
Three hundred and eight patients were randomized, of whom 15 subsequently were excluded due to pregnancy, patient moved to remote region or inclusion criteria were violated. 293 patients, 343 legs, were operated on (Table 2).

In 191/209 legs removal of the GSV was done from the groin to just below the knee, and in 18 legs from the groin to the ankle.
Table 2. Base-line demographics and clinical characteristics of the trial groups, varicose vein surgery with and without preoperative duplex.

<table>
<thead>
<tr>
<th></th>
<th>Preoperative duplex</th>
<th>No preoperative duplex</th>
<th>p*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total no of legs</td>
<td>166</td>
<td>177</td>
<td></td>
</tr>
<tr>
<td>Male:Female</td>
<td>44:122</td>
<td>43:134</td>
<td>0.638</td>
</tr>
<tr>
<td>Mean age, yrs **</td>
<td>47.9(11.1) (24-72)</td>
<td>44.6 (12.4) (20-75)</td>
<td></td>
</tr>
<tr>
<td>CEAP class &gt;3</td>
<td>29</td>
<td>22</td>
<td>0.190</td>
</tr>
<tr>
<td>GSV removal</td>
<td>125</td>
<td>22</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>SSV removal</td>
<td>8</td>
<td>5</td>
<td>0.494</td>
</tr>
<tr>
<td>GSV+SSV removal</td>
<td>0</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Local phlebectomies only</td>
<td>33</td>
<td>89</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Bilateral surgery</td>
<td>18</td>
<td>32</td>
<td>0.024</td>
</tr>
</tbody>
</table>

* χ2 test
** values are mean (s.d.) (range)

Groin anatomy and nature of recurrences

In paper I duplex identified 57 legs (57%) with incompetent veins in the groin including 50 in the former SFJ and four from the femoral vein in the vicinity of the SFJ. In three cases it was not possible to visualize the confluence. A further 12 groins had a vessel emanating from the SFJ but without incompetence. None of the patients had post-thrombotic changes such as filling defects in the deep veins on duplex examination.

Fourteen legs were reoperated in the groin, 13 of these patients were examined with varicography. The varicographies and operative findings all confirmed the recurrence of insufficient veins in the groin found by the duplex examination.

In 54 of 57 recurrences duplex could distinguish between type 1 and 2 of the Edinburgh classification, i.e. whether or not there was an incompetent vessel entering the former SFJ. The subtypes were more difficult to classify, especially between type 1B, intact tributaries, and 1C, neovascularisation (Table 1), thus it was not possible to decide whether the recurrence was due to inadequate dissection at primary surgery or due to new vessel formation.

In comparison, in the study population in paper II–V 159 legs were operated on with ligation of the SFJ and removal of the GSV, and examined with duplex both at 2 months and 2 years after operation. 21 legs (13%) had incompetent veins in the groin after 2 years, of which only 2 legs at 2 months.

Comment

One suggested purpose with the Edinburgh classification was to differentiate between recurrences due to residual VV, i.e. inadequate surgery, and ne-
ovascularisation. As the retrospective analysis failed to differentiate between subgroup 1B and C, this was not possible. However, the prospective study implies that inadequate surgery is a minor cause for recurrences in the operated groin.

Risk factors for recurrences at primary surgery

The recurrence rate in the study population of paper I did not differ significantly if the surgeon was a vascular or general surgeon or a surgical resident, or if there were perioperative complications at the primary operation. Neither was there any significant difference in the recurrence rate between men and women, nor between patients older or younger than the mean age.

Risk factors for recurrences were not specifically presented in papers II–V, but have been analysed subsequently. Also in this study population, the recurrence rate was similar regardless of the level of experience of the surgeon, and between male and female patients. However there was a difference between patients older or younger than the mean age, inasmuch that even though there was no difference in residual incompetence postoperatively, younger patients were reoperated more often.

Impact of duplex on surgical result

Intention to treat and per protocol

In 44/166 (26.5%) legs in study II the result of the preoperative duplex scan suggested that a different procedure than planned would be optimal. In 29 of these legs, the surgical procedures were amended accordingly, whereas in 15 legs the duplex findings were disregarded. The reasons for not operating according to the duplex findings included the patient’s wish for a minor operation and the surgeon’s doubt concerning the clinical significance of the duplex result. The operations performed are listed in Table 2.

Duplex results after two months

One hundred and sixty-six of the 177 legs that had surgery without preoperative duplex examination were rescanned 1-2 months postoperatively (Table 3). There was a significant difference in the number of legs with junctional incompetence between the two groups (p<0.001). Only 14 legs with preoperative duplex had junctional incompetence, including 8 legs where the insufficiency had not been treated surgically. In a per protocol analysis, of six legs with postoperative incompetence, reflux in one SSV was due to technical error, reflux in one GSV was not detected preoperatively but postopera-
tively, and in 4 legs, reflux was present in the SFJ with residual branches of which 2 were transient and had disappeared after 2 years and 2 were not examined again.

Table 3. **Duplex results 2 months after varicose vein surgery.**

<table>
<thead>
<tr>
<th></th>
<th>Preoperative duplex, ITT</th>
<th>Preoperative duplex, PP</th>
<th>No preoperative duplex</th>
<th>p*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Legs examined</td>
<td>160</td>
<td>146</td>
<td>166</td>
<td>0.268</td>
</tr>
<tr>
<td>SFJ reflux</td>
<td>10</td>
<td>5</td>
<td>37</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>SPJ reflux</td>
<td>4</td>
<td>1</td>
<td>9</td>
<td>0.143</td>
</tr>
<tr>
<td>SFJ and/or SPJ reflux **</td>
<td>14 (8.8%)</td>
<td>6 (4.1%)</td>
<td>44 (26.5%)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Duplex group ITT(intent to treat) consists of the whole group. Duplex group PP (per protocol) includes only legs operated according to the duplex findings.

*χ² test between the duplex group ITT and the no-duplex group

** in 2 legs combined reflux

Results after two years

After 2 years, 292 legs (145 legs in group D, 147 in group ND), were examined again. In that time 2 legs in group D, and 14 in group ND had been scheduled for reoperation on the GSV or SSV (p=0.002). The indication for reoperation was persistent or recurrent symptoms in combination with the patient’s wish. None of the 151 legs treated according to the preoperative duplex findings were scheduled for reoperation within 2 years.

Ninety-five legs in group D and 112 in group ND had visible VV on examination (p=0.045). Eight legs in group D and 7 legs in group ND had visible veins in the groin, proximal thigh or both. Skin changes such as hyperpigmentation, eczema, pre- or postulcerative changes (CEAP 4 and 5) were present in 15 legs in group D, and in 19 legs in group ND (p=0.492). One hundred and ninety legs of the 292 examined, 65%, were improved in clinical class of CEAP, 104 legs in group D and 86 in group ND (p = 0.018).

Two hundred and fifty-six legs were examined with duplex 2 years after operation, 127 in group D and 129 in group ND. Of patients who had preoperative duplex reflux was seen in the SFJ or SPJ, or both in 19 legs (14 treated PP). In those with no duplex, reflux was seen in the SFJ or SPJ, or both in 53 legs (p<0.001) (Table 4).
Table 4. *Duplex results 2 years after varicose vein surgery.*

<table>
<thead>
<tr>
<th></th>
<th>Preoperative duplex, ITT</th>
<th>Preoperative duplex, PP</th>
<th>No preoperative duplex</th>
<th>p*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Legs examined</td>
<td>127</td>
<td>118</td>
<td>129</td>
<td>0.441</td>
</tr>
<tr>
<td>SFJ reflux</td>
<td>14</td>
<td>10</td>
<td>44</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>SPJ reflux</td>
<td>7</td>
<td>4</td>
<td>13</td>
<td>0.174</td>
</tr>
<tr>
<td>SFJ and/or SPJ reflux **</td>
<td>19 (15.0%)</td>
<td>14 (12.0%)</td>
<td>53 (41.1%)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Duplex group ITT (intention to treat) consists of the whole group. Duplex group PP (per protocol) includes only legs operated according to the duplex findings.

*χ² test between the duplex group ITT and the no-duplex group

** in 6 legs combined reflux

Impact of surgery and duplex on quality of life

Of the 293 originally included patients, 237 (81%) completed all SF-36 questionnaires, preoperatively and 1 month, 1 year and 2 years after surgery. Preoperative mean age in this group was 47 (22–73) years, 169 (71%) were women. 45 patients had bilateral surgery, 16 in group D and 29 in group ND (p=0.03). Skin changes were present in 43 (18%), with no significant difference between group D and ND.

Two hundred and fifty patients attended the follow-up visit after 2 years, 130 in group D and 120 in group ND. In comparison with preoperatively, 115 patients in group D stated that their operated limb(s) were improved, 11 unchanged and 4 worse, the corresponding figures in group ND were 101, 16 and 3 (NS).

The group of patients who did not complete all SF-36 questionnaires scored lower than the complete responders in GH preoperatively (p=0.01), and at 1 month (p=0.01), but there were no significant differences in physical scores at 1 and 2 years. In mental scores the non-complete responders scored lower at 1 month in VT (p=0.003), SF (p=0.005), RE (p=0.02) and MH (p<0.001), at 1 year lower in VT (p=0.04), and at 2 years no difference was found. The group of non-complete responders is excluded from the following analyses.

Comparison of study patients and reference group

The scores for the reference group and for the study population preoperatively and after 2 years, and comparisons with the reference group, are presented in Table 5 and 6.
Table 5. SF-36 scores preoperatively.

<table>
<thead>
<tr>
<th></th>
<th>Reference group</th>
<th>Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>Median</td>
</tr>
<tr>
<td>PF</td>
<td>86.6</td>
<td>95</td>
</tr>
<tr>
<td>RP</td>
<td>82.2</td>
<td>100</td>
</tr>
<tr>
<td>BP</td>
<td>72.8</td>
<td>84</td>
</tr>
<tr>
<td>GH</td>
<td>74.8</td>
<td>82</td>
</tr>
<tr>
<td>VT</td>
<td>68.5</td>
<td>75</td>
</tr>
<tr>
<td>SF</td>
<td>87.9</td>
<td>100</td>
</tr>
<tr>
<td>RE</td>
<td>86.3</td>
<td>100</td>
</tr>
<tr>
<td>MH</td>
<td>81.2</td>
<td>88</td>
</tr>
</tbody>
</table>

*Mann-Whitney.

Table 6. SF-36 scores at 2 years.

<table>
<thead>
<tr>
<th></th>
<th>Reference group</th>
<th>Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>Median</td>
</tr>
<tr>
<td>PF</td>
<td>86.6</td>
<td>95</td>
</tr>
<tr>
<td>RP</td>
<td>82.2</td>
<td>100</td>
</tr>
<tr>
<td>BP</td>
<td>72.8</td>
<td>84</td>
</tr>
<tr>
<td>GH</td>
<td>74.8</td>
<td>82</td>
</tr>
<tr>
<td>VT</td>
<td>68.5</td>
<td>75</td>
</tr>
<tr>
<td>SF</td>
<td>87.9</td>
<td>100</td>
</tr>
<tr>
<td>RE</td>
<td>86.3</td>
<td>100</td>
</tr>
<tr>
<td>MH</td>
<td>81.2</td>
<td>88</td>
</tr>
</tbody>
</table>

*Mann-Whitney.

Preoperatively men scored higher in GH (p=0.02) and RE (p=0.04), whereas women scored lower in BP (p<0.001), VT (p=0.001) and MH (p=0.03). The patients without and with skin changes (C-class of CEAP 0–3 and 4–5 respectively) did not differ in QoL from matched subpopulations in the reference group.

One month after surgery, VV patients scored significantly lower in BP (p<0.001), RP (p<0.001), and VT (p<0.001). After 1 year scores improved, and BP was even higher (p=0.04) than in the reference group.

After 2 years the only domain that differed significantly was MH (p=0.02), where VV patients scored lower. There was no gender difference, and no difference regarding the presence or absence of skin changes.
The effect of preoperative duplex

There was no significant difference when comparison was made between group D and ND in any SF-36 domain at any time. The results were the same when patients who were subjected to re-do surgery were excluded, and also when patients with unilateral and bilateral VV surgery were analysed separately. Both groups were significantly improved in BP (p=0.001 and 0.006 respectively) 2 years after surgery.

Comment

One reason for the lack of difference in QoL between the two randomized groups may be that SF-36 is a generic questionnaire and may be better to discriminate between different diseases, whereas when evaluating differences between treatments for the same disease, a disease specific questionnaire may be more appropriate (Smith 1999). Vein specific questionnaires have been developed, but were not available when planning the present studies (Launois 1996, Lamping 2003).

The impact of duplex on costs

As a whole, surgery was more extensive in group D, even though the duplex findings were ignored in 15 patients in that group ending in more minor procedures. More local excisions only were done in group ND. Women had more often minor procedures (p=0.001).

At 2 years, 16 patients had been scheduled for reoperation, 3 (2.0%) in group D, and 13 (9.0%) in group ND. Two patients in group ND were reoperated twice, one on the same leg, and one on both legs at separate times. There was no difference in the rate of reoperations between men and women (p=0.810).

Cost analysis

The prices used to cost the quantities, the mean value of quantities and the costs for the two groups are presented in Table 7. The quantities and costs include primary and redo surgery. The price paid for a duplex scan was SEK 1 990 for one leg, and SEK 3 980 when two legs were examined.
Table 7. Unit costs, mean quantities and mean costs/patient including primary and redo surgery.

<table>
<thead>
<tr>
<th>Identified costs</th>
<th>Price/unit</th>
<th>Units/patient</th>
<th>Costs/patient</th>
<th>Cost difference</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Preopera-</td>
<td>No preopera-</td>
<td>Preopera-</td>
<td>No preopera-</td>
</tr>
<tr>
<td></td>
<td>tive duplex</td>
<td>tive duplex</td>
<td>tive duplex</td>
<td>tive duplex</td>
</tr>
<tr>
<td>OPD visit</td>
<td>1 338</td>
<td>1.02</td>
<td>1.10</td>
<td>1 365</td>
</tr>
<tr>
<td>Duplex scan</td>
<td>1 990</td>
<td>1.14</td>
<td>0.12</td>
<td>2 272</td>
</tr>
<tr>
<td>ORT (hours)</td>
<td>4 870</td>
<td>1.64</td>
<td>1.62</td>
<td>7 994</td>
</tr>
<tr>
<td>Surgeon (hours)</td>
<td>670</td>
<td>0.80</td>
<td>0.79</td>
<td>539</td>
</tr>
<tr>
<td>Preop mapping</td>
<td>950</td>
<td>0.06</td>
<td>0.05</td>
<td>58</td>
</tr>
<tr>
<td>Strip equipment</td>
<td>225</td>
<td>0.84</td>
<td>0.63</td>
<td>189</td>
</tr>
<tr>
<td>Basic instrument</td>
<td>153</td>
<td>1.02</td>
<td>1.10</td>
<td>156</td>
</tr>
<tr>
<td>Hospital admission</td>
<td>3 300</td>
<td>0.09</td>
<td>0.17</td>
<td>312</td>
</tr>
<tr>
<td>Surgeons admin.</td>
<td>168</td>
<td>1.02</td>
<td>1.10</td>
<td>171</td>
</tr>
<tr>
<td>Total costs</td>
<td>13 056</td>
<td>11 216</td>
<td>1 840</td>
<td></td>
</tr>
</tbody>
</table>

Costs in SEK, based on prices 2004. The costs include primary and redo surgery. OPD = out patient department, ORT = operating room time.

Table 8 presents the costs for the two groups subdivided into primary operation and reoperation costs.

Table 8. Mean value of the total direct costs for primary and redo surgery in the two groups.

<table>
<thead>
<tr>
<th>Total costs</th>
<th>Preoperative duplex</th>
<th>No preoperative duplex</th>
<th>Cost difference</th>
<th>p*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>145</td>
<td>145</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Primary surgery</td>
<td>12 827 (7 177-33 685)</td>
<td>9 856 (3 909-24 883)</td>
<td>2 971</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Redo surgery</td>
<td>229 (0-17 236)</td>
<td>1 360 (0-41 029)</td>
<td>-1 131</td>
<td>0.011</td>
</tr>
<tr>
<td>Total costs</td>
<td>13 056 (7 177-33685)</td>
<td>11 216 (3 909-47 778)</td>
<td>1 840</td>
<td>0.003</td>
</tr>
</tbody>
</table>

Costs in SEK, based on prices 2004. Range in parentheses. *t-test
The increase in costs in group D for the primary surgery was SEK 2,971, which is explained by increases in costs for the duplex examination, operating room time and stripping equipment. The decrease because of lower costs for reoperations was SEK 1,131, which resulted in a mean net increase of SEK 1,840 for group D. The savings in reoperation costs do not offset the increase in the primary operation cost, during the two-year follow-up period.

Men had a higher total cost, SEK 13,325, than women, SEK 11,732 (p=0.024).

Comment
In this study we have only included direct medical costs, i.e. the expenses of the care-giver. Indirect costs for patients such as loss of productivity were not considered. The main reason for that was that reliable information about days lost at work was not available. However, the loss of productivity would probably be higher in group D at the first operation due to more extensive procedures, and lower for redo surgery as recurrences were less frequent.

Changes in patterns of venous reflux after varicose vein surgery
One hundred and sixty-six legs were examined preoperatively with duplex, 326 legs 2 months after surgery and 257 legs after 2 years. One hundred and twenty-six legs were examined on all three occasions, and 251 legs at 2 months and 2 years. The patients lost to follow-up had declined further examinations. Those who were reoperated during follow-up were excluded in the following analysis.

Perforating vein incompetence
103/126 legs were not operated on with perforator interruption. 42 of these had perforating vein incompetence (PVI) in the calf preoperatively and 61 had no PVI. The presence of PVI in the calf preoperatively, not surgically targeted, did not influence the distribution of venous incompetence after 2 years in any other segment than in the PVI themselves (Table 9).

When comparing the prevalence of PVI in the total number of legs, PVI was found in the thigh preoperatively in 7% (12/166), after 2 months in 3% (9/326) and after 2 years in 2% (5/265). The corresponding figures for the calf was 48% (80/166), 27% (88/326) and 32% (82/257). The limbs with PVI at 2 months and 2 years were however only partly identical (Table 10).
Table 9. Comparison of prevalence of venous incompetence in different segments 2 years after varicose vein surgery in legs with and without preoperative PVI.

<table>
<thead>
<tr>
<th>Incompetent segments after 2 years</th>
<th>PVI preop (42 legs)</th>
<th>No PVI preop (61 legs)</th>
<th>p*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Deep veins</td>
<td>2 5</td>
<td>0 0</td>
<td>0.164</td>
</tr>
<tr>
<td>SFJ</td>
<td>3 7</td>
<td>9 15</td>
<td>0.194</td>
</tr>
<tr>
<td>GSV thigh</td>
<td>5 12</td>
<td>3 5</td>
<td>0.177</td>
</tr>
<tr>
<td>GSV calf</td>
<td>12 29</td>
<td>21 34</td>
<td>0.532</td>
</tr>
<tr>
<td>SPJ</td>
<td>1 2</td>
<td>3 5</td>
<td>0.460</td>
</tr>
<tr>
<td>SSV</td>
<td>2 5</td>
<td>4 7</td>
<td>0.528</td>
</tr>
<tr>
<td>PVI thigh</td>
<td>2 5</td>
<td>1 2</td>
<td>0.362</td>
</tr>
<tr>
<td>PVI calf</td>
<td>17 40</td>
<td>11 18</td>
<td>0.012</td>
</tr>
<tr>
<td>None</td>
<td>11 26</td>
<td>18 30</td>
<td>0.713</td>
</tr>
</tbody>
</table>

The 103 legs in the table were examined with duplex preoperatively, after 2 months and 2 years postoperatively, and were not operated on with perforator interruption. 

SFJ, saphenofemoral junction; GSV, great saphenous vein (distal to the SFJ); SPJ, saphenopopliteal junction; SSV, short saphenous vein (distal to the SPJ); PVI, perforating vein incompetence.

* = χ² test

Table 10. Development of perforating vein incompetence in 251 legs examined with duplex at both 2 months and 2 years.

<table>
<thead>
<tr>
<th></th>
<th>2 months n</th>
<th>2 years n</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>PVI</td>
<td>no PVI</td>
</tr>
<tr>
<td>PVI thigh</td>
<td>6</td>
<td>3</td>
</tr>
<tr>
<td>no PVI thigh</td>
<td>245</td>
<td>242</td>
</tr>
<tr>
<td>PVI calf</td>
<td>68</td>
<td>40</td>
</tr>
<tr>
<td>no PVI calf</td>
<td>183</td>
<td>41</td>
</tr>
</tbody>
</table>

PVI, perforating vein incompetence.

n = number of legs
A larger proportion of legs had reversal of PVI in the calf during follow-up, 28/68 (41%) than new PVI, 41/183 (22%) (p=0.003). The difference was even larger when analysing 103 legs that were not subjected to perforator interruption and that were examined preoperatively and twice postoperatively, where 25/42 legs (60%) had abolished PVI in the calf and 11/61 legs (18%) had new PVI in the calf after 2 years (p<0.001) (Table 11).

Table 11. Development of perforating vein incompetence in the lower leg in 103 legs not subjected to perforator interruption where duplex was done preoperatively, at 2 months and 2 years.

<table>
<thead>
<tr>
<th>Preop</th>
<th>n</th>
<th>2 mo postop n</th>
<th>2 yrs postop n</th>
</tr>
</thead>
<tbody>
<tr>
<td>PVI</td>
<td>42</td>
<td>PVI 19</td>
<td>no PVI 7</td>
</tr>
<tr>
<td>no PVI</td>
<td>61</td>
<td>no PVI 23</td>
<td>PVI 5</td>
</tr>
</tbody>
</table>

Abolished PVI from preop – 2 years: 7+18/42 = 60%, new PVI from preop – 2 years: 3+8/61 = 18% (p<0.001)

When the legs subjected to GSV removal were analysed separately, the figures were also comparable, with abolished PVI in the calf in 21/36 legs (58%), and new PVI in 8/44 legs (18%) (p<0.001). Similar differences were observed for PVI in the thigh, but the numbers were too small to make a meaningful analysis.

The fraction of legs without PVI in the calf after 2 years was not significantly lower when perforator interruption had been done (p=0.591). Sixty-four of the 126 legs, that were examined preoperatively, after 2 months and after 2 years, had PVI in the calf preoperatively. 22/64 legs were operated on with extrafascial ligation of the perforators. 15/22 legs (68%) had no remaining PVI at 2 months, and 13 legs (59%) no PVI at 2 years. 42/64 legs with PVI in the calf preoperatively were not subjected to perforator ligation, of these 23 legs (55%) had no PVI at 2 months and 25 legs (60%) no PVI after 2 years.
137/166 legs that were examined preoperatively with duplex had no skin changes (CEAP 2–3), and 29 legs had skin changes (CEAP 4–5). The prevalence of PVI in the calf in legs with CEAP 2–3 was 66/137 (48%) and in legs with CEAP 4–5 14/29 (48%) (p=0.992). Two years after surgery 224/257 legs examined with duplex were classified as CEAP 0–3 and 33/257 as CEAP 4–5. The prevalence of PVI in the calf was 63/224 (28%) and 19/33 (58%) respectively (p<0.001). When summarising all incompetent segments, there was no difference between legs with and without skin changes preoperatively, but after 2 years the group with skin changes had more incompetent segments than those without (unpublished data).

The saphenofemoral and saphenopopliteal junctions

One hundred and fifty-nine of the 251 legs examined with duplex at both 2 months and 2 years had been operated on with removal of the GSV, of which 151 were obliterated in the SFJ at 2 months. Ten legs were operated on with removal of the SSV. All ten were obliterated at the SPJ at 2 months.

Ninety-two legs were operated on without GSV removal, of these 63 had normal findings in the SFJ at 2 months. Of 241 legs operated on without removal of the SSV, 226 had a normal SPJ at 2 months. A comparison of the development of the duplex findings in the legs where the SFJ and the SPJ were surgically obliterated or normal at 2 months is made in Table 12.

<table>
<thead>
<tr>
<th>Duplex findings at 2 months</th>
<th>n</th>
<th>Duplex findings at 2 years</th>
<th>n</th>
</tr>
</thead>
<tbody>
<tr>
<td>SFJ obliterated</td>
<td>151</td>
<td>incompetent obliterated</td>
<td>17 (11)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>competent</td>
<td>133</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>1</td>
</tr>
<tr>
<td>SFJ competent</td>
<td>63</td>
<td>incompetent obliterated</td>
<td>11 (18)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>competent</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>51</td>
</tr>
<tr>
<td>SPJ obliterated</td>
<td>10</td>
<td>incompetent obliterated</td>
<td>4 (40)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>competent</td>
<td>6</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>0</td>
</tr>
<tr>
<td>SPJ competent</td>
<td>226</td>
<td>incompetent obliterated</td>
<td>3 (1)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>competent</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>226</td>
</tr>
</tbody>
</table>

Numbers in brackets are percentages.

SFJ, saphenofemoral junction; SPJ, saphenopopliteal junction.
Neovascularisation, identification of new vessels where previously obliterated, was more common in the SPJ than in the SFJ (p=0.027). Progression of disease, new incompetence in previously normal vessels, was more common in the SFJ (p<0.001).

Remnant great saphenous vein
Fifty-nine of the 126 legs that completed all three duplex scans had reflux in the GSV from the groin to the ankle according to the preoperative duplex. Fifty-six of these were subjected to GSV removal of which 50 legs from the groin to just below the knee. After 2 months 17/50 (34%) legs had remaining reflux in the GSV below the knee, and 22/50 (44%) after 2 years, thus reflux was abolished in 28/50 (56%) legs after 2 years. In the 33 legs where reflux was abolished at 2 months, in 16 legs this was due to postoperative thrombophlebitis and occlusion, and in 17 cases due to reversal of reflux.

In comparison there were 49 legs where preoperative duplex did not show any reflux in the GSV below the knee, of which 30 legs were subjected to proximal removal of the GSV to the knee and in 19 legs other segments than the GSV were operated on. At 2 months 2/30 and 0/19 were incompetent in the GSV below the knee, and after 2 years the corresponding figures were 6/30 and 4/19. A larger fraction of legs thus had abolished reflux in the GSV below the knee during follow-up, 28/50 (56%) than new reflux in the GSV below the knee, 10/49 (20%) (p<0.001).

Fifteen of the 18 legs with removal of the GSV from groin to ankle were examined again at 2 years. The pattern of incompetent segments was similar compared to the legs subjected to proximal removal only, however the figures for the different segments were considered too small for analysis.

209 of the original 343 legs were subjected to GSV removal, 202 of these were examined at 2 months and 11 legs had remaining reflux in the GSV above the knee without DVI. 163 of the stripped legs were examined again at 2 years, and all 5 examined of the original 11 had remaining reflux in the GSV above the knee without DVI. Further 2 legs had developed reflux in the GSV above the knee of which one also had developed DVI (unpublished data).

Deep veins
No venous obstruction was found in any patient. None was treated for a DVT within the follow-up period, although one patient had a minor filling defect in one of the gastrocnemic veins at 2 months. When examined 1 month later the defect was unchanged. One patient had a superficial thrombophlebitis in the SSV reaching the SPJ at 2 months and was treated with warfarin for 3 months, and no sign of DVT was seen with duplex at 2 months or 2 years.
The prevalence of deep reflux was low, 5/166 (3%) legs preoperatively, 9/326 legs (3%) at 2 months and 11/257 (4%) at 2 years. Of the 126 legs that were examined preoperatively and twice postoperatively, 5 legs had deep reflux preoperatively, 3/5 had deep reflux at 2 months, and 4/5 at 2 years. 121/126 legs had no deep reflux preoperatively, 1 leg had reflux in a gastrocnemian vein at 2 months, but no deep reflux was seen in any of the 121 legs at 2 years.
Discussion

Long-term results after surgery for varicose veins

Safety and surgical results

Surgery for VV is common and often considered by doctors and patients as minor procedures with low risks. However, complications do occur, but most often minor, such as skin nerve injuries without clinical significance (Morrisson 2003). Postoperative DVT is a risk, and there are uncommon major complications such as injuries to the femoral artery or vein.

In the present studies the complications were not specifically studied, but no major complications were recorded in the follow-up. In the study population of paper I no post-thrombosis changes were seen on duplex examination (100 legs), and in the study population of papers II–V (326 legs after two months and 257 legs after two years) there was one patient with a minor filling defect in one of the gastrocneanic veins postoperatively that was considered clinically insignificant and left untreated, with no change at an extra control some month later. In a recent study the DVT rate after VV surgery was 5%, if sclerosant agents were injected in perforators 8%, and in another study after RFA the DVT rate was 16% (van Rij 2004, Hingorani 2004). Thus, in comparison VV surgery so far seem to be a safe option.

The low DVT rate after VV surgery in the present studies is interesting, and similar findings have been reported previously (Bohler 1995). Case selection may be a reason, as no patient in the prospective study and few in the retrospective study had a history of venous ulcers, and thus the majority suffered from a more benign disease. Cases may have been missed, but this is not probable, as the deep veins were scanned routinely for postthrombotic changes in all patients. One major contribution to the low DVT rate may be the rather aggressive policy of postoperative mobilization. The patients were encouraged to remove all bandages, to use a below-knee compression stocking and to start taking long walks already on the first postoperative day, and the majority resumed work within a week.

The recurrence rates after VV surgery were high in these studies just as in other reports (Bradbury 1993, Fischer 2001). In study I 57% had incompetent vessels in the former SFJ seen with duplex 6–10 years after high ligation, and in study II incompetent vessels were seen in the SFJ and/or SPJ in 28% after two years. However, the clinical significance of these recurrences
was varying. Many patients with residual or recurrent VV in study I and II were asymptomatic and did not wish to be operated again.

Quality of life
The high recurrence rate was in contrast to the high degree of satisfaction with the operative results amongst the patients. In the first study, 82% of the patients said that their operated leg was improved 6–10 years after surgery in comparison to the preoperative state, 11% unchanged and 6% worse, 1% did not remember. The corresponding figures for the second study population after two years was 87% improved, 10% unchanged and 3% worse.

Also when measured with the SF-36 questionnaire, there was a significant improvement of QoL after VV surgery. The VV patients in the second study population scored preoperatively lower than the reference population in the parameters Bodily pain, Vitality and Mental health, in spite of a higher score in General health. Two years after surgery there was no difference except for Mental health that was lower in the study population. There was, however, no difference between the two randomized groups, i.e. the significantly lowered rate of recurrences and redo surgery in the duplex group did not correspond to a higher QoL as measured with the SF-36. If a vein specific questionnaire had been used, the results may have been different.

The present studies corroborate the findings by other groups that surgery for VV does have a positive impact on the patients’ QoL, and that this effect remains for a long time (Baker 1995, Sam 2004). This is important in discussions regarding priorities within the national health care system.

The discrepancy between surgical results and patient satisfaction
One of the main aims of this thesis was to identify risk factors for recurrences after VV surgery amenable for therapy, and thus hopefully find ways to lower the need for redo surgery. However, the fact that a patient has VV visible on clinical examination or with an anatomical investigation such as duplex or phlebography does not mean that he or she has symptoms or signs that require treatment. In the present studies it was not uncommon that patients came back two years after surgery, with a residual incompetent GSV after an operation with local phlebectomies only, and the patient was still satisfied with the operation. Other patients with the same anatomical distribution of venous reflux postoperatively came back within a short time and asked for redo surgery as their symptoms had not improved.

The indication for primary and redo surgery in these studies was symptoms affecting daily life, and the decision to operate was made in a discussion between patient and surgeon where the patient’s subjective complaints were crucial. The surgeon could thus choose to disregard the duplex findings and base the decision on his or her clinical judgment. This may be question-
able in an era of evidence based medicine, but probably reflects the practice of many clinicians. The fact that the patients were satisfied with the results may favour this pragmatic approach.

Psychological factors may influence the measurements of QoL, also in the somatic domains. Nonspecific leg symptoms are often ascribed to what the patient can see with their own eyes, i.e. varicosities. Surgery has a potent placebo effect (Moseley 2002, McRae 2004), and when surgery has been performed and the visible part of the VV removed, non-venous symptoms may also improve. On the other hand, as symptoms are vague, some patients experience an improvement after VV surgery from symptoms they had ascribed to other conditions.

The discrepancy between symptoms, signs and duplex findings has been observed in previous studies (Bradbury 1999, Kurz 2001). Duplex will confirm the presence and extent of venous reflux, but may not confirm the degree of symptoms. Functional measurements like PPG, APG and foot volumetry can measure the venous hypertension and may be more accurate in predicting degree of CVI and symptoms (Nicolaides 1993, Danielsson 2003, Gohel 2005). Thus there is a need to revive the knowledge of these methods, and to continue research in the area.

Possible risk factors for recurrences

Inadequate preoperative investigations

The rate of redo surgery was lowered and the extent of residual venous reflux was less when preoperative duplex was used in comparison with clinical examination alone. HHD was not routinely used, and if appropriately used it might have changed results, however previous studies concerning the accuracy of HHD are conflicting (Kent 1998, Mercer 1998, Kim 2000, Rautio 2002, Smith 2002, Wong 2003). The SSV is difficult to assess with the HHD and anatomical variations, such as reflux emanating from an incompetent thigh perforator or non-saphenous branches from the SFJ, can be mistaken for GSV incompetence.

Presumably there is a considerable variation amongst physicians in the interest and knowledge of how to use HHD. A physician with a specific venous interest, using the HHD frequently, may reach a high accuracy in the diagnosis. In the clinical setting of this study, where VV patients were examined by surgeons with a mixed caseload, duplex however did improve the preoperative diagnosis of the anatomical extent of venous reflux.
Inadequate surgical technique and perioperative difficulties

In previous studies it has been found that the rate of recurrences is lower when VV surgery is performed by specialists (Lees 1997, Stucker 2004). In the present studies no significant difference could be found between surgeons with different levels of experience. The reason for this is not clear. Presumably there is a difference between an experienced and a novice surgeon, but the difference may have been blurred with time as other causes for recurrence, such as neovascularisation and progression of disease, became more important.

When studying the records, it was also found that in some cases where the surgical resident was in doubt of the surgical anatomy, he or she would call for help from a more experienced colleague, and thus parts of the operation would be performed under supervision. This reinforces the findings of others that appropriately trained even rather junior surgeons can perform VV surgery in a safe way (Turton 1997). One may furthermore assume that a senior surgeon with minor interest in VV surgery and inadequate surgical technique will perform worse than an adequately trained junior surgeon.

Possible consequences of inadequate surgical technique are perioperative complications such as major bleeding, incomplete removal of the GSV and wound complications. There were few such cases recorded in the studies, and these patients did not have a higher recurrence rate.

A topic for debate is the importance of thorough dissection in the groin, and the division of even minute branches around the SFJ to avoid the risk of these enlarging and transmitting the pressure from the femoral vein to superficial veins with inherent weakness that thus may become varicose (Turton 1999, Donnelly 2005). Such a meticulous approach has not lowered recurrences, however, and it has even been suggested that the surgical trauma might stimulate neovascularisation (Jones 1996, van Rij 2004).

Neovascularisation

The phenomenon of neovascularisation, i.e. the formation of new branching vessels from a previously obliterated vessel, is increasingly suggested as the most important cause for recurrences after VV surgery (Jones 1996, van Rij 2004). However, it is difficult to distinguish morphologically from enlarged branches left at previous surgery, and thus it has been proposed that the only reliable diagnostic criteria is histological examination (Nyamekye 1998, Geier 2005). The histological difference between remnant branches and newly formed vessels has been defined as the presence or absence of neural proteins (Nyamekye 1998). This has been questioned recently, as the findings have not been reproduced (El Wajeh 2004). One can speculate that small remnant branches with inherent varicose disease, that enlarge due to
continuing high venous pressure from an open connection with the deep veins, may also show a pathological composition of the vessel wall.

In the study population in paper I 57% had incompetent veins in the groin after previous removal of the GSV, but it was not possible to distinguish morphologically if these were new vessels or remnant branches that had enlarged with time. In study V 11% of the legs where the SFJ was obliterated, as seen with duplex two months postoperatively, had new incompetent veins in the groin at two years. This would support the hypothesis that a significant proportion of recurrences stem from neovascularisation.

One suggested cause for neovascularisation is the surgical trauma. In favour for this was the preliminary findings that non-surgical methods such as RFA did not induce neovascularisation (Pichot 2004). Long-term results have shown, however, that the rate of neovascularisation and recurrences are equal or higher after RFA than after surgery (Salles-Cunha 2004, Lurie 2005).

In study V neovascularisation was seen in 40% in the SPJ compared to 11% in the SFJ. If new vessel formation is stimulated by the extent of surgical dissection, this could explain the difference, as most surgeons find the SPJ more difficult to dissect out properly than the SFJ. However, the anatomy around the SPJ is more complex with the variations of gastrocnemic branches entering the SSV or the popliteal vein at different levels. These branches may have enlarged during follow-up and become incompetent, and may not be possible to distinguish from neovascularisation with duplex. The recurrences in the SPJ were more often a clinical problem than recurrences in the SFJ, as the recurrent veins in the groin in some cases had no connection to VV more distally and thus no transmission of venous pressure. SSV surgery thus still remains a surgical challenge, and the SSV may even be a more important target for alternative treatments than the GSV.

Different surgical strategies have been proposed to prevent neovascularisation. The avoidance of surgical dissection with techniques such as RFA and ELT has already been mentioned above. Implantation of barriers of PTFE (polytetrafluoroethylene) or silicone has been used with varying results (Bhatti 2000, de Maeseneer 2004). In a recent study the stump of GSV in the groin was invaginated to prevent contact of the venous endothelium with surrounding tissue and minimize the stimulus for angiogenesis, the recurrences were reduced but the numbers were small (Frings 2004). So far the optimal surgical technique is not defined, and a possible future strategy may be the combination of surgical, endovascular and pharmacological treatments, including the instillation of substances that may inhibit excessive neoangiogenesis (Agu 2002).
Perforating vein incompetence

The indication for division of incompetent perforating veins is controversial, but it has been suggested that remaining incompetent perforators can transmit the high pressure of the deep system to the superficial veins and thus become the starting point for new varicosities, e.g. from the Hunterian perforator in the thigh (Stonebridge 1995, Rutherford 2001). As the number of incompetent perforators has been seen to correlate with the degree of venous insufficiency, another indication would thus be to prevent or cure more advanced CVI with skin changes (Delis 1998). Studies have shown a high rate of ulcer healing after SEPS but no randomized studies have been published so far (Tenbrook 2004). It has also been shown that in patients with superficial and perforator incompetence, the PVI will be corrected by superficial surgery alone (Fitridge 1999, Mendes 2003).

In study V there was more PVI that resolved during two years follow-up than new PVI evolving. Furthermore, after two years the proportion of legs with reflux in the examined segments was not significantly different in the group of legs with and without PVI preoperatively, perforator surgery not performed. Thus, the presence of PVI could not be shown to be an independent risk factor for recurrence.

In the group of patients where skin changes were present, there were equal numbers with and without PVI preoperatively, but after two years the fraction of legs with PVI was larger in the group with skin changes than in the group without. The total burden of VV, calculated by adding the incompetent segments examined, was higher in the legs with PVI. This is a simple and rather crude score, so the data has to be interpreted with caution. It can, however, be hypothesised that PVI correlates with the total extent of venous reflux, and may not be a causative factor in itself. This has been described in previous reports (van Rij 2003, Delis 2004, Recek 2004).

It can further be hypothesised that PVI just as any other incompetent segment, in its early phase can be corrected if the total burden of venous hypertension is reduced, as is seen with deep insufficiency in combination with reflux in the SSV, or if the SFJ is ligated and the GSV regains competence (Hammarensten 1990). In more advanced CVI the PVI may be irreversible, but this is only clinically significant if there is elevated venous pressure in the segments connected to the perforator (van Neer 2003).

The role of perforator interruption thus still remains undefined, but the results of these and other studies suggest that in primary VV surgery it can be omitted. In patients with skin changes there may be a case for selective perforator surgery, and then SEPS is preferable to open perforator surgery, but the results of randomized studies are needed.
Remnant great saphenous vein

In the prospective study, the operating surgeons performed a partial removal of the GSV in the majority of cases and in a few cases removal from ankle to groin. In the legs where preoperative duplex showed an incompetent GSV below the knee, and where only removal above the knee was performed, incompetence was abolished in the remaining GSV in 66% at two months postoperatively, and after two years in 56%. These figures should be interpreted with caution, however, as it may be difficult for the vascular technologist to differentiate between a remnant GSV and saphenous branches when the continuity proximally is lost. In the majority of cases where the remnant GSV on the lower leg was incompetent, this was clinically insignificant. Thus in patients with uncomplicated VV, removal of the GSV above the knee is probably sufficient to relieve symptoms.

In a recent study it was observed that remnant GSV in the thigh correlated with the development of DVI when examining the patients two years after removal (MacKenzie 2004). It was not reported, however, if the patients were examined also shortly after surgery, and thus the insufficient vessels in the thigh may have developed postoperatively. In study V, few cases with deep insufficiency developed during follow-up, thus the correlation with remnant GSV in the thigh cannot be confirmed. However, it was noted that in the cases where insufficient vessels were seen in the medial thigh two years after removal, the majority had developed after the duplex two months postoperatively. These recurrences may be saphenous branches that have developed incompetence during follow-up, or they may be true remnant parts of GSV, due to incomplete surgery or duplicated GSV, that regained competence after surgery and subsequently developed incompetence again.

Postoperative changes and natural progression of disease

VV are progressive, and may develop in any part of the leg at any time, sometimes in an ascending fashion regardless of surrounding venous pressures, sometimes in a retrograde direction in response to increased venous pressure from leaking valves (Labropoulos 1997). In previous studies it has been shown, that a substantial part of recurrences stem from progression of disease (Smith 2001, Kostas 2004). That was also the case in study V. In legs where the SFJ was not operated on and normal two months after surgery, 17% had developed incompetence there at two years. In the SPJ this occurred in only 1%. This confirms the clinical observation that the SFJ is a predilective site for reflux due to varicose disease.

Another interesting finding in study V was that the haemodynamic changes induced by VV surgery continued for a long time, the postoperative pattern of venous reflux was not static. It was observed in all segments that competence was regained in many legs even after the duplex control two
months postoperatively. For perforators this was noticeable, as there were more perforating veins regaining competence between two months and two years postoperatively, 41%, than perforators developing new incompetence, 21%.

The fraction of legs with PVI was thus not identical at two months and two years postoperatively, due to these dynamic changes. If this has been the case in previous studies where proportions of legs with venous insufficiency have been compared after treatments, the results may have to be interpreted with caution. A group with reduced venous incompetence after follow-up may in part have been cured by an gradual indirect improvement in venous competence, and not by the direct intervention studied. The reverse is also possible, a group with significant venous incompetence after follow-up may in fact have been successfully treated but then developed new incompetence.

There may be difficulties also in interpreting the present results. Moderate venous insufficiency may have diurnal variations, and may vary with the examiner and factors such as temperature and physiological and psychological stress (Haenen 1999). However, the number of legs examined were sufficiently large to provide statistical significance to the differences observed.

The changes in venous physiology after treatment remains insufficiently understood. In light of these results and others it seems important to inform patients that VV is a dynamic disease, where a complete cure never can be promised, and where results after treatment have to be evaluated with patience.

Costs for varicose vein treatment and priorities in the health care system

During the last decade there has been an increasing interest in venous research and in the improvement of venous surgery. The development is similar to that of hernia surgery, which has moved from being a low priority area within surgery to a more evidence based discipline with lowered recurrence rates. However, so far the recurrence rates after VV surgery have not substantially improved, but the increasing interest has led to efforts in clinical practice to perform venous surgery in a more standardised way and surgeons participate in venous surgery training courses to improve their long-term results surgically and cosmetically with minimal complication rate.

Traditionally VV have been assigned a low priority in the Swedish health care system, and this is not unique for Sweden. “Varicose veins are the ‘Cinderella’ of surgery” (Wright 1999). For comparison, few would question that an asymptomatic hernia would be repaired within the national health care system, whereas symptomatic VV without skin changes would be referred to treatment in private practice paid in full by the patient. The reasons for the
low priority of VV are several: the idea/dogma that venous ulcers were caused by postthrombotic venous hypertension and not by VV, the notion that patients without skin changes often are exaggerating symptoms in order to be treated for a basically cosmetic disease, the surgical difficulties especially in redo surgery and the high recurrence rate. All of this can be questioned, as in spite of a considerable overlap regarding degree of symptoms and extent of VV, primary and recurrent VV do lower QoL and also impose a considerable cost for society when venous ulcers develop (Garratt 1993, Nelzén 2000).

When faced with a patient seeking advice for VV, the doctor therefore has not only to make a correct diagnosis, but also to evaluate if the patient’s symptoms merit treatment within the national health care system. There is no uniform agreement about this in Sweden. In most governmental hospitals, patients with venous ulcers or severe skin changes are always treated, and patients with pure cosmetic complaints never treated. For the patients with symptomatic VV without skin changes there is considerable variation in policy.

If a decision is made to operate the patient with VV, the surgeon may need some kind of anatomical investigation in order to resect the diseased venous segments correctly. In these studies, the use of duplex lowered the rate of redo surgery and extent of residual VV, but there was no corresponding decrease in costs, partly because the primary surgery became more extensive and expensive. A higher surgical quality of primary surgery was thus more costly, and furthermore it did not correspond to an increase in QoL as measured by SF-36. If duplex becomes more readily available, and cheaper, the cost equation becomes more favourable for its routine use.

To offset the duplex costs with present prices, 20 more reoperations would have had to be performed in the no-duplex group than in the duplex group, an increase in the rate of redo surgery from 10.3% to 24.1%. With a longer follow-up time preoperative duplex may be a cost-saving strategy compared with clinical examination only, due to fewer reoperations. However, the incidence of recurrences may not be linear, as a substantial part of recurrences were due to the formation of new VV. Consequently, if a longer follow-up period would have given an economic advantage to the duplex group is not evident.

**Gender differences**

In study II more women than men were operated on, and women were generally operated on for a less advanced disease. In previous population based studies, women have had a higher prevalence of VV than men (Franks 1992, Sisto 1995). In the Edinburgh Vein Study, however, where subjects randomly selected from the population were examined, the prevalence was higher in men (Evans 1999). The difference in prevalence may be due to
gender differences in the perceived presence of VV in studies using self reporting questionnaires (Laurikka 1995).

In the Edinburgh Vein Study it was found that symptoms in women correlated better with duplex findings than in men. It also seems that a slightly greater proportion of female patients develops skin changes (Evans 1999). Why this is so is not known, but it can be speculated that differences in the muscle pump of the leg and hormonal influence on a cellular level make women more prone to develop skin changes in response to the venous hypertension. If so, there would be a medical reason to operate on women earlier in the disease process.

Should all patients with varicose veins be examined with duplex preoperatively?

The recommendations for preoperative investigations in venous disease in current literature are not uniform, probably due to differences in tradition and experience regarding the available investigation modalities (Nicolaides 2000, Jogestrand 2002, Eklöf 2004, Norgren 2004). Duplex technology has expanded in the last decade, often at the expense of other investigations such as phlebography and functional assessment of the global venous function, and the knowledge of these latter techniques has been lost in many hospitals. Duplex provides a detailed anatomical map of the diseased segments, which makes the results easy to understand for the clinician and the patient. However, as in arterial disease, the presence of a diseased vascular segment does not imply a need for treatment. The diseased vascular segment, blocked or refluxing, may not cause a significantly lowered arterial pressure or raised venous pressure. Thus, if the patient’s symptoms do not merit treatment, duplex and other investigations are unnecessary.

When summarising the results of studies II–IV, it is found that preoperative duplex before VV surgery reduces the extent of residual varices and lowers the need for redo surgery, but this improved surgical result does not confer a corresponding increase in QoL as measured with SF-36, and the lowered costs for redo surgery do not match the increased costs at primary surgery. Furthermore a substantial part of recurrences develop after the operation and is not preventable with a more adequate preoperative diagnosis. Thus it is not evident whether or not preoperative duplex should be recommended for all VV patients, at least not within the national health care system.

If treatment is contemplated, the level of investigation depends on the severity of the patient’s symptoms and signs, but also on the general illness of the patient. Concomitant conditions may contraindicate surgery, and then the
anatomical distribution of CVI is not important but rather the functional status of the limb, in order to institute adequate compression therapy.

The economical aspects are important, and the level of investigation may have to be adapted to the actual economical resources. The tradition, knowledge and experience of the different investigation modalities of the vascular technologists and physicians is also vital for the choice of investigation. As there is no radiation involved in duplex imaging, and as it is non-invasive, there is no risk with the investigation that needs to be considered.

In conclusion, preoperative duplex examination is recommended in the majority of cases planned for VV surgery. Even in skilled hands the diagnostic accuracy of anatomical variations, especially for the SSV, is insufficient. If duplex scanning is not readily available, for geographical or economical reasons, it can be omitted in primary VV without skin changes, previous DVT or significant trauma to the leg, VV in proximity of the SSV or any other complicating factor. If duplex is omitted, the surgeon should be familiar with the use of HHD. However, the single most important investigation is still a thorough clinical examination, including a detailed history, performed by a dedicated physician with an open mind for alternative explanations for the patient’s complaint.
Conclusions

The rate of residual and recurrent varicose veins after surgery is still high. 57% had incompetent vessels in the groin after 6–10 years (study I). Two years after surgery only 21% showed no sign of venous reflux on the duplex examination (study V).

The morphology of groin recurrences as depicted by duplex examination correlated well with varicography and findings at surgery (Study I).

The classification system for groin recurrences proposed by the Edinburgh group could not be fully used as it was not possible to differentiate between neovascularisation and remnant vessels (Study I).

The recurrence rate was not influenced by the surgeon’s level of education or perioperative difficulties or complications (Study I and II), and it was not influenced by the presence of incompetent perforating veins not subjected to interruption (Study V).

Preoperative duplex examination lowered the rate of recurrences and redo surgery (Study II).

Patients with VV have a reduced physical quality of life as measured with SF-36, and surgery improves quality of life to the level of the reference population. Preoperative duplex examination does not further improve quality of life (Study III).

To the cost for preoperative duplex examination is added the cost for more extensive primary surgery, and this increased cost is not matched by the lowered cost of redo surgery (Study IV).

The changes induced in the venous system of the legs by surgery for VV were not static, a substantial part of the legs continued to improve from two months to two years postoperatively (Study V), and conversely a substantial part of recurrences were due to formation of new incompetent vessels in surgically obliterated sites and the progression of venous disease in previously normal vessels, recurrences that with present lack of etiological
knowledge cannot be prevented with improved surgical technique (Study I and V).

Perforating vein incompetence was abolished without perforator interruption in 60% after two years (Study V). Incompetence in the great saphenous vein below the knee was abolished after removal of the great saphenous vein above the knee in 44% (Study V).
Critical issues in research and treatment

The effect of standardised education in VV surgery and quality control of outcomes in governmental as well as in private practice needs to be assessed.

A more uniform protocol for prioritising patients with VV within the national health care system needs to be developed.

In this study the rate of postoperative DVT was lower than in other studies, presumably due to a policy of aggressive mobilisation and short time off work, as prophylactic low molecular weight heparins were given selectively, only in a few cases. The effect of the postoperative regime needs to be studied further, as the tradition of surgeons varies considerably.

The discrepancy between symptoms, clinical signs and duplex findings makes prioritising difficult. Global measurements of the venous function like PPG, APG and foot volumetry may be more accurate in predicting degree of CVI. However, these investigations are expensive, and if all patients with symptomatic VV would be examined this thoroughly, the expenses would be considerable. Thus, there is a need for a simple screening tool to evaluate the functional effect of the VV that is seen in the actual patient.

A substantial part of the venous segments with reflux became competent without interruption or removal when the total venous hypertension of the leg was reduced. There seems to be a point of no return, when the vessel wall is irreversibly damaged by the disease process. An interesting issue is if there is an optimal time for treatment in the individual patient.

It was found that many perforators changed group during two years, some regained competence whereas some became incompetent. In many prospective studies, PVI has been reported as fractions of examined legs at different times. Thus conclusions may be misleading as to the development of venous disease, as the PVI studied may not be identical. The role of PVI and perforator interruption needs to be clarified in further prospective studies.

The inherent defect of the vessel wall of VV patients may bear resemblance of other diseases such as aneurysmal disease. Prospective studies where se-
The phenomenon of neovascularisation is still obscure. Possible treatments, surgical such as barriers, or pharmacological in the form of instillated anti-angiogenetic drugs, needs to be further addressed.
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Allmän information om åderbråck (varicer)

Varicer på benen är så vanligt förekommande att gränsen mellan normalvariant och sjukdomstillstånd är flytande. Tidigare forskning har angett att varicer är vanligare hos kvinnor än män, men det kan ha berott på att man till stor del låtit människor själva rapportera om man hade varicer eller ej, och att män i större utsträckning negligerat sina varicer. I en studie från Skottland publicerad 1999 där man kallat ett slumpmässigt urval på 1566 personer av normalbefolkningen till läkarundersökning och ultraljud hade männen varicer i 40% och kvinnorna i 32%. Vidare fann man att c:a 80% av befolkningen hade små ådernät på benen, med eller utan större varicer.

Varicer på benen utvecklas i de kärl som för blodet tillbaka till hjärtat, vene rarna. Vener har normalt klaffar. När man rör på musklerna i benet pumpas blodet uppåt, och mellan muskelrörelserna förhindrar klaffarna att blodet rinner tillbaka ner mot foten igen. I varicerna är kärlväggarna och klaffarna svagare, och blodet läcker neråt, s.k. reflux. Följden blir att en person med varicer har för mycket blod i benet och ett högre tryck i benets vensystem.

Varicer kan ge olika symtom och följdverkningar. Många människor känner inte av dem alls, ens om de är ganska utbredda. Andra människor har symtom som tyngd- och trötthetskänsla i benen, kläda, värk eller nattliga vadkrarper. Tyvärr är dessa symtom inte unika för varicer, utan kan också förekomma vid sjukdomstillstånd i t ex rygg, leder, muskler och nerver, vilket gör det svårt att bedöma om en patient kommer att förbättras av en variceroperation. En vanlig orsak till att patienter vill att deras varicer ska opereras är rädska för blodpropp. Risken för blodpropp i det djupa systemet är något ökad om man har varicer, men fortfarande inte mycket högre jämfört med en person utan varicer, varför detta ej är en indikation för operation.

Hos vissa människor orsakar det högre ventrycket en skada på hud och underhud, som kan yttra sig som eksem, missfärgningar, förhårdningar eller bensår. Ungefär 2% av befolkningen har eller har haft ett venöst bensår. Det är alltså en mindre del av dem med varicer som får sår. Patienter med venösa bensår har ofta besvärjliga smärtor, och såren har en tendens att komma tillbaka igen efter läkning. Skötseln av bensår kostar samhället stora summor årligen. Man beräknar att 1–2% av EU’s totala hälso- och sjukvårdsbudget går åt till bensårbehandling, och då är de venösa såren i majoritet. Studier med ultraljud har visat att många patienter med bensår har vanliga varicer,
och nyligen har studier också visat att man med vanlig varicerkirurgi kan åstadkomma mer permanent läkning av dessa bensår än med konservativ behandling med lindor eller kompressionsstrumpor. Tyvärr kan man inte med nuvarande kunskap förutsäga vilka varicerpatienter som kommer att utveckla bensår.


Vid operation av varicer tar man helt enkelt bort de sjuka kärlen. Vensystemet är ett rikt utvecklat nät i flera skikt i benet, så även om man tar bort varicerna så finns det tillräckligt många vener kvar för att transportera blodet. Dock vill man helst undvika att ta bort vener i onödan, eftersom friska vener kan användas som reservdelar till by-passkirurgi. Varicerkirurgi har liksom andra operationer risker för komplikationer, bl.a. för blodpropp i det djupa vensystemet, vilket i tidigare studier angetts till c:a 5%.

Själva operationsmetoderna är väsentligen oförändrade sedan många år, men är omdiskuterade. Det vanligaste ingreppet är att operera bort en större ven från ljumsken till underbenets insida, s.k. stripping. Motsvarande operation görs ibland på vadens baksida på en mindre ven. Små åderbråck kan tas bort via minisnitt, s.k. lokala extirpationer. Ett annat vanligt ingrepp är perforantligatur, där förbindelser mellan det ytliga och djupa vensystemet, s.k. perforanter, delas, med öppen teknik eller tithålsteknik. Perforanterna har ansetts ha betydelse för utveckling av sår och nya varicer, recidiv, men än så länge finns inga studier som verkliga visar att så är fallet.

Efter operation av varicer är recidivfrekvensen skiftande i olika studier beroende på hur lång tid man följer patienterna, men ligger mellan 20–70%. Orsakerna till recidiv är flera. Kirurgi som inte varit tillräckligt noggrann och dålig kartläggningsav riskerar före operation har föreslagits. De senaste åren har också olika forskargrupper visat att det bildas nya varicer i de opererade områdena efter en tid, och tidigare friska vener utvecklas till varicer.

Forskningen om och utredningen av varicer har revolutionerats det senaste decenniet med utvecklingen av duplex, ultraljud med doppler, som både kan kartlägga blodkärlen anatomiskt och mäta flöden och flödesriktningar. Duplex används allmer inför operation, och ger en detaljerad karta av varicerna så att kirurgen vet exakt vilka kärl som är sjuka, vilket kan vara svårbedömt vid vanlig kroppssundersökning. Duplex är tidskrävande och kräver högspecialiserad personal, vilket gör att det är dyrt. Det har därför hittills inte ansetts rimligt att undersöka alla varicerpatienter med duplex inför operation.
Syfte med avhandlingen

Syftet med de studier som ingår i avhandlingen var att studera långtidsresultat efter operation p.g.a. varicer och möjliga riskfaktorer för recidiv, t.ex. kirurgens utbildningsnivå, bristande diagnostik inför operationen och tekniska svårigheter. Värdet av preoperativ duplexundersökning avseende recidivfrekvens, livskvalitet och kostnader analyserades. Själva kirurgins påverkan på vensystemet på sikt studerades också, framför allt de vener med kvarvarande oåtgärdad reflux.

Metoder

I studie I undersöktes 89 patienter som opererats på 100 ben 6–10 år tidigare p.g.a. av varicer med klinisk undersökning samt duplex. Undersökningen fokuserade på ljumsken, då recidiv är vanliga efter strippingoperationer och reoperation i ljumsken kan vara tekniskt svårt. De patienter som behövde reopereras undersöktes också med kontraströntgen, s.k. varikografi. Undersökningens foton jämfördes med operationsfotot, och ett klassifikationssystem från en forskargrupp i Edinburgh användes för att om möjligt kunna avgöra orsaken till recidivet. Ursprungsjournalerna studerades avseende kirurgens utbildningsnivå, och svårigheter vid operationen eller komplikationer efteråt.

I studierna II–V ingår samma grupp av 293 patienter (343 ben), där hälften lottades till att som komplement till den vanliga kliniska undersökningen före operationen genomgå en noggrannare kartläggning med duplex. Efter operationen har alla deltagande patienter kallats till en ny duplex efter 1–2 månader, samt efter 2 år ett läkarbesök och duplex. De båda grupperna har jämförts avseende recidivfrekvens och reoperationer (studie II), livskvalitet enligt formuläret SF-36 (studie III), och kostnader (studie IV). Duplexfynden har jämförts mellan de olika tillfällena för att studera hur omfattningen av reflux i benets vensystem påverkats under de 2 åren efter operationen (studie V).

Resultat av studierna

Långtidsresultat efter varicerkirurgi

I studie I hade 57% nya varicer i ljumsken vid duplexundersökning 6–10 år efter operationen. De flesta av dessa recidiv gav dock ej symtom, och patienterna önskade ej ny operation. Motsvarande siffra i studie V efter samma typ av operation, hög underbindning och stripping, var 13% efter 2 år. Majoriteten av patienterna i studie V, 79%, hade kvarvarande eller nya varicer någonstans på benet, dock var det i många fall små recidiv, och även här hade många av patienterna inga symtom. Av de 326 ben som undersöktes med duplex 2 månader efter operationen hade ingen en behandlingskrävande djup blodpropp.
**Duplex och kontraströntgen**

Resultaten av undersökning med duplex, kontraströntgen och operationsfynd korrelerade väl i studie I.

**Duplex påverkan på recidivfrekvensen**

I studie II sjönk frekvensen reoperationer efter 2 år betydligt i den grupp som undersöktes med duplex före operation, 1% jämfört med 9% i den grupp som ej gjort preoperativ duplex, och vid undersökning med duplex efter 2 år sågs också färre större recidiv i den duplexundersökta gruppen, 15% respektive 41%.

**Livskvalitet och varicer**

I studie III fann man att varicerpatienterna hade sänkt livskvalitet jämfört med normalbefolkningen före operation, men hade normaliserats vid mätning efter 1 och 2 år efter operationen. Det var ingen skillnad beroende på om man opererats med eller utan duplex före operation. Orsaken kan vara att det valda frågeformuläret var för allmänt hållet och ej specifikt konstruerat för just varicerpatienter, eller att symtom och utbredning av varicer korrelerar dåligt. Ett flertal patienter med utbredda varicer två år efter operation var ju ändå nöjda och önskade ej ny operation.

**Duplex och kostnader**

De direkta kostnaderna, d.v.s. kostnader för duplex, personal och läkare, material, vårdplatser och mottagningsbesök, beräknades i studie IV. Den vinst i form av minskade reoperationskostnader som genererades i duplexgruppen kunde ej väga upp de initiala duplexkostnaderna. Dessutom medförde duplex att patienterna i duplexgruppen genomgick mer omfattande ingrepp, med längre operationstid, som därmed också blev dyrare.

**Riskfaktorer för recidiv**

I studie I fanns det ingen korrelation mellan kirurgens erfarenhet och risken för recidiv, inte heller med komplicationser i samband med ingreppet. Klassifikationssystemet från Edinburgh gick ej att använda fullt ut så tillvida att inte gick att avgöra utifrån kärlns utseende i ljumsken om recidivet berodde på kvarlämnade kärl eller om det berodde på nyutväxta kärl. Som jämförelse så opererades 159 ben med s.k. hög underbindning i ljumsken i studie II–V. 21 ben (13%) hade recidiv i ljumsken efter 2 år, varav endast i 2 fall detta funnits redan vid kontrollen efter 2 månader, i de övriga var duplexresultatet invändningsfritt. Således hade majoriteten av dessa recidiv utvecklats efter operationen.

I studie V fann man att perforanter med reflux var vanligt förekommande före operation, och mindre vanligt efter operation trots att man inte specifikt åtgärdat dem, och en hypotes är att det minskade totala venösaa trycket har
gjort att refluxen genom perforanterna upphört. De perforanter som hade reflux 2 månader efter operation var endast delvis de samma som de med reflux efter 2 år. Detta skulle tala för att omställningsprocessen efter en operation tar lång tid, och samtidigt är varicen sjukdomen progressiv så att nya vener blir påverkade.

**Slutsatser**

- Recidivfrekvensen var hög efter operation p.g.a. varicen.
- Recidiven kunde kartläggas lika väl med hjälp av duplex som av kontraströntgen.
- Det gick inte att avgöra enbart utifrån recidivens utseende på duplex eller röntgen om varicen bestod av nybildade eller kvarlämnade kärl.
- Recidivfrekvensen påverkades ej av kirurgens utbildningsnivå eller svårigheter vid operationen, och inte heller av kvarlämnade perforantvener med icke åtgärdad reflux.
- Preoperativ undersökning med duplex minskade frekvensen av reoperationer och recidiv.
- Patienter med varicen har lägre livskvalitet än normalbefolkningen, livskvaliteten normaliseras efter operation och kvarstår så efter två år. Preoperativ duplexundersökning ökade inte livskvaliteten ytterligare, trots lägre recidivfrekvens.
- De ökade kostnaderna för duplex motsvarades ej av de minskade reoperationskostnaderna i duplexgruppen, och operationerna där var längre och dyrare.
- Den förbättring av veners funktion som åstadkommts av operationen fortsatte upp till två år efteråt, samtidigt som nya varicen bildades p.g.a. progress av varicen sjukdomen och nybildade kärl. Dessa nya varicen kan ej förebyggas med nuvarande kunskap.
- Efter variceroperationen blev även många av de vener som inte specifikt åtgärdades, t.ex. perforanter med reflux, normaliserade.
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