Clinicopathological Evidence That Neovascularisation is a Cause of Recurrent Varicose Veins*

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Objectives: Recurrent varicose veins may result from poor initial surgical technique or progression of varicosities in collateral veins. In some cases new veins may develop at the saphenofemoral junction (neovascularisation) and cause recurrent saphenofemoral incompetence. This was a histological study of recurrent varicose veins.

Design: This clinicopathological study included 20 patients (median age 55 years) who had surgery for recurrent saphenofemoral incompetence.

Materials and methods: A total of 28 legs had groin re-exploration with repeat flush saphenofemoral ligation. The venous tissue block from the saphenofemoral region (including the proximal thigh varicosity) was excised and orientated for histological analysis. Evidence of neovascularisation was sought using routine histological sections and $100 immunohistochemistry.

Results: At operation, thin-walled, serpentine neovascular veins were detected clinically as the principal cause of recurrence in 19 groins. In five groins recurrence was due to a residual missed vein at the saphenofemoral junction, and in four recurrence was caused by cross groin collaterals. On histological sections, evidence of neovascularisation was present in 27 of 28 groins. In eight it co-existed with the veins missed at the original operation but it was the sole identified cause of recurrent saphenofemoral incompetence in 19 (68%) groins.

Conclusions: Neovascularisation was the principal cause of recurrent saphenofemoral incompetence in this series.

Introduction

Recurrent saphenofemoral incompetence, first reported by Langenbeck,1 is the major cause of recurrent varicose veins.2-4 It is associated with persisting symptoms and patient dissatisfaction and represents a major drain on health care resources. The cause of recurrent incompetence at the saphenofemoral junction is controversial but most authors blame failure to perform adequate dissection of the saphenofemoral junction.5,6 In properly ligated groins varicosities may developed in pre-existing collateral veins.7-13 The growth of new veins at the saphenofemoral junction (neovascularisation) which then connect with an existing long saphenous or other residual thigh vein has been suggested as another cause, but this remains controversial and is variably reported.7,14,15,16

Histological evidence for new vein formation has been provided by Glass, both experimentally and clinically, after simple interruption of the long saphenous vein.17,18 A previous prospective study from this unit identified neovascularisation as the principal cause of recurrent varicose veins.16 The present study was designed to determine the significance of neovascularisation in recurrent saphenofemoral incompetence using clinical and histological assessment.

Materials and Methods

Twenty patients (10 men) who had surgery for recurrent varicose veins (eight bilateral) due to recurrent saphenofemoral incompetence were studied. Their median age was 55 years (range 36–83) and the median interval between initial and recurrent venous surgery was 11.5 years (range 3–46). At the original operation 19 groins had saphenofemoral disconnection alone and nine had additional stripping of the long saphenous vein in the thigh. Recurrent saphenofemoral incompetence was diagnosed by clinical assessment including hand-held Doppler ultrasonography. Recurrent saphenofemoral incompetence was diagnosed when calf squeeze and release resulted in significant reflux in the groin and in an accompanying thigh

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Varicosity. In nine equivocal cases the diagnosis was confirmed using colour duplex imaging.

At groin re-exploration a consultant vascular surgeon made a clinical assessment of the cause of the recurrent veins in the course of performing repeat flush saphenofemoral disconnection. A block of tissue from the region of the saphenofemoral junction (including the proximal aspect of the main thigh varicosity) was excised and orientated for histology using marker sutures.

The tissue block was sectioned transversely at 2 mm intervals. These sections were orientated, processed through paraffin wax and sectioned at 4 μ. The histological sections were stained with haematoxylin and eosin, elastin van Geison and reticulin stains. Further histological sections were prepared for S100 immunohistochemistry by routine streptavidin-biotin labelling and microwave antigen retrieval. The hypothesis of the study was that immature neovascular veins would be tortuous and thin-walled, and lack mural nerves on S100 staining. Similar sized normal veins were examined as controls using identical histological and immunohistochemical techniques.

Results

Preoperatively the diagnosis of recurrent saphenofemoral incompetence was made in 19 groins using hand-held Doppler ultrasonography. In nine legs which needed colour duplex imaging because of equivocal Doppler findings, all had recurrent saphenofemoral incompetence, three due to missed veins at the saphenofemoral junction and six due to neovascularisation alone.

At operation, serpentine neovascular veins were the sole connection between a thigh varicosity and the common femoral vein in 19 groins. A residual vein missed at the previous operation was easily identified at the saphenofemoral junction in five groins. In four, small veins passed from the thigh, across the groin, towards the anterior abdominal wall. These have been termed cross groin collaterals.⁷

Histological analysis confirmed the presence of tortuous, thin-walled veins. They were less well structured compared with normal veins of equivalent size. One noticeable pathological feature, typical of immature veins, was the asymmetry of the vein wall, especially the thickness of the media (Fig. 1). Normal small veins in control tissue from primary varicose veins, mesenteric veins and veins from breast tissues (controls) all stained positive for mural nerves on S100 immunohistochemistry. In contrast, there was a complete absence of mural nerves in the neovascular veins (Fig. 2).

Neovascularisation was present in the tissue bridging the common femoral vein and the recurrent thigh varicosity by histological criteria in 27 of 28 groins examined. In 19 groins these were the sole connections but in eight groins the new veins coexisted with a missed vein at the saphenofemoral junction or a cross groin collateral. In one groin, the saphenofemoral junction appeared previously untouched and there was no evidence of new vein formation.

There was no significant difference in the interval between the first and second operations in patients with neovascularisation compared with those who had a residual missed vein in addition (mean 13.7 and 14.3 years, respectively.)

Discussion

Langenbeck¹ suggested that regeneration of the long saphenous vein at the site of transection could be
a cause of recurrent saphenofemoral incompetence. Although this was supported in an early report by Homans,29 the majority of studies have, until recently, blamed inadequate surgery or expansion of collateral veins as the principal cause of recurrent saphenofemoral incompetence.7,8,15,20

The phenomenon of neoangiogenesis, initially observed in the rabbit ear chamber model21,22,23 has recently been demonstrated after ligation of the rat femoral vein and after transection of the long saphenous vein in the lower part of the thigh in patients with varicose ulcers.17,18 In the latter study new vein formation was demonstrated by angiography, surgical assessment and histological examination of excised tissue.

The present study provides clinical and pathological evidence that neoangiogenesis occurs in patients with recurrent saphenofemoral incompetence. Many of the patients previously had saphenofemoral disconnection alone, whereas stripping of the long saphenous veins is presently recommended to reduce recurrence.18 This may have influenced the incidence of neoangiogenesis. The clinical findings were supplemented by histology because imaging methods alone cannot reliably diagnose neoangiogenesis. Mature neoangiogenic veins can have luminal appearances indistinguishable from collateral veins on duplex imaging. This failure to recognise neoangiogenic veins may have led to an underestimate of their incidence using imaging studies.7,24 Khaira et al. reported a high incidence of neoangiogenesis; in a study using colour duplex, 68% of recurrent saphenofemoral incompetence was due to neoangiogenesis.15

Histological analysis is a potentially more accurate method for identifying neoangiogenic veins although there is still no agreed definition. Features seen on routine staining such as vein tortuosity, small size and mural asymmetry have been used to diagnose neoangiogenesis but are suggestive rather than definitive.17,18 New veins lack the traversing intramural small nerves which are visible in mature veins. In this study the absence of intramural nerves on $100 stained sections provided further evidence that the veins have formed recently. It is accepted that negative demonstration of a focal structure, such as a mural nerve seen on $100 stained sections, is never entirely convincing but a more useful method for the diagnosis of neoangiogenesis is not yet available.

It should come as no surprise that new veins form after saphenofemoral disconnection. Angiogenesis is a feature of all healing wounds.25 Whether these early vessels go on to develop and cause clinical saphenofemoral recurrence probably depends on the presence of larger veins within reach of the developing vessels. Careful avulsion of all tributaries within the vicinity of the saphenofemoral junction during varicose vein surgery might minimise saphenofemoral recurrence by reducing the chances of developing neoangiogenic veins gaining communication with nearby tributaries or a residual long saphenous vein. However, this technique would have no effect if the new veins arise from the femoral vein close to the saphenofemoral junction. Further investigation of the source of neoangiogenic veins is important.

The present study provides clinical and histological evidence for neoangiogenesis as a major cause of recurrent saphenofemoral incompetence. The biological basis of neoangiogenesis means that it is unlikely to be prevented by surgical technique alone. Barrier methods are presently being investigated but future research could be aimed at the use of growth factor inhibitors to reduce or prevent the process of angiogenesis.

References


21 Sandison JC. Observations on the growth of blood vessels as seen in the transparent chamber introduced into the rabbit’s ear. Am J Anat 1928; 41: 475–496.


