

ORIGINAL ARTICLE

Theoretically Optimised Sizing of Constrictive External Meshes for the Elimination of Diameter Irregularities in Vein Grafts

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Abstract

Objective: Tight-fitting external meshes were shown to suppress the development of flow-limiting narrowing in saphenous vein bypass grafts. Key to this phenomenon is diminution of circumferential wall stress and elimination of luminal irregularities through diameter reduction. Since over-constriction leads to insufficient flow and premature occlusion, optimal mesh diameters strike a balance between eliminating diameter irregularities and strangulating the grafts. The current study aimed at determining the minimum number of mesh diameters that could optimally protect a maximum proportion of human saphenous vein graft recipients.

Methods: Dimensions of 118 saphenous veins were assessed in 100 patients undergoing coronary bypass surgery. Two theoretical methods were used to identify the number of mesh diameters required while limiting the maximum constriction to 50%, preventing vein distension and restricting the smallest mesh diameter to 3.0mm. The mathematical method facilitated data selection and analysis for each vein followed by identification of suitable mesh diameters and vein classification. Recursive partitioning was utilised in the statistical analysis integrating mesh diameter identification and vein classification.

Results: With two mesh diameters, diametric irregularities could be eliminated in 87.3% of the veins without additional treatment. 96.6% of the veins were accommodated after disregarding narrow vein section with outer diameters less than 3.0mm and dividing harvested vein sections in the 12.7% of veins requiring additional treatment. Limited benefit was associated with extending the number of mesh diameters from two to four whereas five and more diameters did not appear useful. The mathematically proposed mesh diameters (3.0, 3.3, 3.6, 3.9mm) agreed well with the statistical solutions (3.0, 3.3, 3.5, 3.9mm). The maximum constriction degree ranged between $27.8\pm 9.5\%$ and $36.7\pm 8.8\%$ for the different solutions, exceeding the required smoothing constriction of $26.0\pm 11.1\%$.

Conclusions: The clinical relevance of this study is seen in the finding that two mesh diameters suffice for aorto-coronary vein grafts whereas four mesh sizes are likely to fulfil the requirements in the peripheral application. The classification algorithms used may easily be implemented in practical guides for mesh size selection in the operation theatre and the clinical diameter measurement may be reduced to a single recording supported by the indication that saphenous veins rarely exhibited a more than two-fold diameter variation.

Key words: Coronary artery bypass graft, vein graft, external support, saphenous vein diameter, diameter optimisation, focal intimal hyperplasia

Notations

Symbol	Unit	Description
C	%	Constriction degree
C_S	%	Constriction degree required for complete smoothing of vein
C_R	%	Constriction degree obtained through external reinforcement
D	mm	Inner diameter of mesh
D_i^+	mm	Maximum inner diameter of mesh for a vein
D_i^-	mm	Minimum inner diameter of mesh for a vein
l	-	Number of vein sub sets and number of mesh diameters required to accommodate all n veins
n	-	Total number of veins considered for the analysis
n_k	-	Number of veins in a sub set
OD	mm	Outer diameter of a vein
OD_{max}	mm	Maximum outer diameter of a vein
OD_{min}	mm	Minimum outer diameter of a vein
p_o	%	Permissible distension of a vein
p_u	%	Permissible constriction of a vein
x_j	-	Position of OD measurement along a vein
δ_i	mm	Admissible range of inner mesh diameter for a vein
Δ	mm	Admissible range of inner mesh diameter for a set of veins
Δ_k	mm	Admissible range of inner mesh diameter for a sub set of veins

1. Introduction

For several decades saphenous vein grafts have been the most widely used arterial bypass conduits. Although the overall patency of saphenous vein grafts is distinctly better than that of synthetic conduits, the failure rate of vein grafts is still sobering when compared with artery grafts. The main reason for the failure of vein grafts is the development of diffuse [1] and focal intimal hyperplasia [2]. The triggers for diffuse intimal hyperplasia are low shear stress at the blood interface [3] and high circumferential wall stress [4] - both related to the relatively large diameter of vein grafts as compared to their target arteries [3, 4]. Eddy flow as a consequence of luminal irregularities was shown to be the reason for focal intimal hyperplasia [5].

Attempts to constrict vein grafts with external meshes in order to reduce circumferential stress and increase shear stress go back several decades. Similarly, vein graft constriction with the goal of eliminating diameter irregularities was reported as early as in the 1960s [6]. Since then, many investigators have followed up on this concept [6-11]. More recently, our own group demonstrated that in order to achieve optimal suppression of intimal hyperplasia the degree of constriction needs to be even higher than previously thought [12]. However, this experimentally based demand for a distinct diameter reduction of vein grafts needs to be weighed against clinical reports of higher occlusion rates in vein grafts that show narrowings of less than 3.0mm [13]. Therefore, optimal mesh-constriction of vein grafts would attempt the 'smoothing' of diameter irregularities while preserving a minimum vein graft diameter of 3.0mm.

As much as an infinite number of mesh diameters would guarantee an individually optimized mesh support for each vein, clinical and commercial realities dictate to limit the diameter-range of devices. The guiding principle along which diameter ranges should be restricted is to find the optimal balance point between the proportion of patients benefiting and the number of available diameters. Given the clearly defined individual requirements – namely to eliminate irregularities without constricting beyond 3.0mm – the success of an attempt to narrow the diameter range will depend on the accuracy and completeness with which the entire anatomical spectrum is taken into consideration. In the case of human saphenous vein grafts it is the knowledge of diameter changes over the course of the harvested vein and a representative picture of the variability between individuals. While more than a million saphenous vein grafts are annually used for peripheral and coronary artery bypass operations, anatomical data are scarce. We therefore analyzed the saphenous veins of 100 consecutive patients undergoing coronary artery bypass surgery. The subsequent determination of the minimum number of mesh diameters, and their values, fulfilling the constriction criteria for a maximum number of

patients followed two independent approaches, namely a mathematical data analysis and classification and a descriptive statistical method utilising a recursive partitioning model.

2. Materials and Methods

2.1 Human Saphenous Vein Data Acquisition

In 100 consecutive patients undergoing aorto-coronary bypass grafting, the outer diameter (OD) of 118 saphenous veins was recorded every 2cm along the length using a vernier calliper during post-harvest in situ leakage-test distension. The saphenous vein was harvested from one leg in 83 patients and from both legs in 17 patients. For one patient of the latter group, two vein segments were harvested from one leg and one vein segment from the other leg. These veins were subsequently used in 2.0 ± 0.8 distal vein anastomoses out of a total 3.6 ± 1.3 distal anastomoses per patient to supplement other internal mammary artery and radial artery bypass grafts. Patient demographics (sex, race, age) and risk factors (weight, nutritional state, hypertension, diabetes and smoking) were also recorded. The measurement procedure was approved by the human ethics committee of the University of Cape Town with informed consent obtained from all patients.

2.2 Mathematical Data Analysis

The method for the mathematical data analysis has been described in detail previously [14]. Briefly, for each vein the minimum and maximum outer diameter (OD_{min} , OD_{max}), representing the narrowest and widest point of the vein, were identified along the harvested length.

Complete smoothing of diameter irregularities can be achieved by reducing the maximum to the minimum outer diameter. The associated smoothing constriction degree, C_S , is:

$$C_S = \left(\frac{OD_{max} - OD_{min}}{OD_{max}} \right) \cdot 100 . \quad (1)$$

The constriction of a vein with an external mesh beyond the smoothing constriction degree was allowed up to a maximum constriction degree of $C_R = 50\%$. This limit proved to be feasible and to provide the desired biological response of vein grafts, i.e. mitigation of intimal hyperplasia [12]. For each vein, the mesh diameter range for can now be formulated as

$$\delta_i = [0.5 OD_{i,max} , OD_{i,min}] = [D_i^-, D_i^+] \quad \text{with } i = 1, 2, \dots, n \quad (2)$$

where D_i^- and D_i^+ are the minimum and maximum allowable inner mesh diameter. (It should be noted that the minimum mesh diameter depends on the maximum vein diameter and vice versa.)

Exceptions: All veins with either a maximum OD exceeding the minimum OD by more than 100% ($OD_{max} > 2OD_{min}$) or a minimum OD smaller than 3.0mm ($OD_{min} < 3.0\text{mm}$) were

subjected an additional preliminary analysis described below. Veins with $OD_{\max} > 2OD_{\min}$ did not allow complete smoothing with the proposed maximum limit for constriction whereas $OD_{\min} < 3.0\text{mm}$ receded the typical outer diameter of internal mammary artery (IMA) grafts which was proposed as lower limit for saphenous vein grafts in the coronary position [12].

The diameter range for an external mesh that accommodates all n veins is

$$\Delta \in \left[\max_i D_i^-, \min_i D_i^+ \right]. \quad (3)$$

where $\max_i D_i^-$ and $\min_i D_i^+$ are the minimum and maximum allowable inner mesh diameter and the minimum mesh diameter has to be smaller than or equal to the maximum mesh diameter:

$$\max_i D_i^- \leq \min_i D_i^+. \quad (4)$$

If Eq. (4) is not satisfied, more than one mesh is required for the n veins. In this case, the set of n veins needs to be divided in two, or more, sub sets with n_k veins such that Eq. (4) is satisfied for each sub set. The mesh diameter range, Δ_k , for each sub set of veins is then derived as

$$\Delta_k \in \left[\max_i D_i^-, \min_i D_i^+ \right]_k \quad \text{with } k = 1, 2, \dots, l \text{ and } i = 1, 2, \dots, n_k. \quad (5)$$

where l is the total number of vein sub sets. Overlap between the mesh diameter ranges of different vein sub sets was allowed.

With the aim of minimising the number of mesh diameters required, four mesh diameters $D_1 < D_2 < D_3 < D_4$ were proposed. The assignment of a vein to a mesh diameter was performed with two alternative classification algorithms prioritizing either the smallest or the largest mesh suitable for the vein's mesh diameter range δ_i . The alternative prioritisation resulted in different constriction degrees for the vein.

The distribution of veins amongst the proposed mesh diameters was evaluated with the following parameters: 1) number of veins assigned to each mesh diameter; 2) mean reinforcement constriction degree for each mesh diameter; 3) ratio of reinforcement constriction degree to smoothing constriction degree per mesh diameter, and 4) mean reinforcement constriction degree for the entire set of veins over all mesh diameters.

2.3 Descriptive Statistical Data Analysis

In situ OD profile data of the cohort of 118 saphenous veins described above was additionally examined using a statistical approach to derive an optimal selection of mesh diameters for the cohort of saphenous veins under scrutiny.

Hypothetical deployment of tailored 'zero-distension' meshes

The extent of constriction for each vein was determined at each 2cm interval based on hypothetical deployment of a mesh with an inside diameter equal to the minimum OD for each vein, thereby avoiding any distension along the entire length for all veins. The extent of constriction at each 2cm interval was calculated according to:

$$C = \frac{(OD - OD_{\min})}{OD}, \quad (7)$$

where OD represents the outer diameter at each 2cm interval and OD_{\min} represents the minimum OD of each vein.

Hypothetical deployment of a single 'zero-distension' mesh

The extent of constriction for each vein was determined at each 2cm interval based on hypothetical deployment of a single 'one-diameter-fits-all' mesh with an inside diameter equal to the minimum OD of the entire cohort of veins. The extent of constriction was calculated according to:

$$C = \frac{(OD - 2.1\text{mm})}{OD} \quad (8)$$

where OD represents the outer diameter at each 2cm interval and the value 2.1mm represents the minimum OD recorded for all veins in the study cohort.

Partition modelling of veins based on the ratio OD_{\max}/OD_{\min}

In order to optimise the number and sizing of meshes the technique of recursive partitioning was applied to the vein data. This method, deployed by the statistical software package JMP (version 6.0.3, Cary; NC), veins based on a proposed relationship between the OD_{\min} and OD_{\max}/OD_{\min} ratio for each vein, and created a tree of optimal OD_{\min} cut-points for prediction of OD_{\max}/OD_{\min} ratios within the cohort of veins studied. This was performed using an iterative process where all possible cut-points (and thus groupings) were examined. The process was manually advanced until a desired fit (e.g. a plateau in R^2 values) was seen to be reached with the minimum number of partitions. The suggested cut-points were then hypothetically combined in the same sequence seen in the partitioning to simulate single, double, triple and quadruple solutions with the choice of mesh being determined by each vein's OD_{\min} and the extent of constriction determined as before.

2.4 Data Analysis for Outlier Veins

Veins excluded from the analysis due to $OD_{\min} < 3.0\text{mm}$ and $OD_{\max} > 2 OD_{\min}$, respectively, were assessed individually with respect to all OD measurements along the harvested length, i.e. not only OD_{\min} and OD_{\max} , to identify treatments that allow for utilisation of the entire vein or

parts thereof as mesh constricted grafts. Such treatments included dividing of the vein and removal of excessively narrow segments, respectively. Resulting vein segments that qualified for mesh reinforcement were subjected to dimensional analysis and mesh diameter assignment as described above. Vein segments shorter than 10cm were not considered for the dimensional analysis due to insufficient length for the construction of a coronary bypass graft.

3. Results

3.1 Vein Dimensions and Influence of Patient Demographics and Cardiovascular Disease Risk

The average length of the 118 harvested veins was 28.4 ± 9.5 cm with a minimum and maximum length of 10 and 52cm, respectively. The minimum and maximum OD over all 118 veins was 2.1 and 6.5mm with an average minimum and maximum OD of 3.50 ± 0.61 mm and 4.77 ± 0.75 mm.

Statistical analysis suggested that patient gender was the sole demographic factor influencing vein dimension while race, age, height, weight and nutritional state did not significantly affect vein diameter. Of the 100 patients entered into the study, 36 were female and 64 were male. The mean weight and mean BMI were 80.1 ± 17.4 kg and 28.7 ± 5.1 kg/m². Patient nutritional status was classified as normal ($18.5 \leq \text{BMI} < 25$ kg/m²) in 22 of patients, overweight ($25 \leq \text{BMI} < 30$ kg/m²) in 49 patients, obese ($30 \leq \text{BMI} < 40$ kg/m²) in 25 patients and extremely obese ($\text{BMI} \geq 40$ kg/m²) in 4 patients. The majority of patients were of mixed race (66%) with the remainder being either White (29%) or Indian (5%). The presence of major cardiovascular risk factors, specifically hypertension, diabetes and smoking was not predictive for outer vein diameter.

3.2 Mathematical Classification

A mean constriction of $26.0 \pm 11.1\%$ (range: 0 - 57.2%) was required for complete smoothing of the 118 veins according to Eq. (1). A constriction of 26% or less was sufficient for smoothing for 64 veins. The distribution of veins according to the smoothing constriction degree in increments of 5% is illustrated in Figure 1. The largest proportion of veins required moderate constriction of 20-30% to achieve diameter smoothing whereas only one vein exceeded the upper constriction threshold of 50%.

With the proposed limits for distension and constriction, the individual mesh diameter range condition of $\text{OD}_{\text{max}} \leq 2\text{OD}_{\text{min}}$ was satisfied for 117 veins as follows: $\text{OD}_{\text{max}} < 2\text{OD}_{\text{min}}$ for 115 veins allowing for a permissible mesh diameter range and $\text{OD}_{\text{max}} = 2\text{OD}_{\text{min}}$ for 2 veins, requiring a single value for the permissible mesh diameter.

For 15 veins, the upper limit of the mesh diameter range D_i^+ exceeded $OD_{\min} = 3.0\text{mm}$. One of these veins additionally exhibited $OD_{\max} > 2OD_{\min}$. These 15 veins were excluded from this analysis and subjected alternative treatment (see below).

For the remaining 103 veins, the individual mesh diameter ranges δ_i based on the conditions of no distension and maximum constriction of 50% are illustrated in Figure 1.

The mean minimum mesh diameter D_i^- was $2.44 \pm 0.36\text{mm}$ (range: 1.65 - 3.25mm) and the mean maximum mesh diameter D_i^+ was $3.64 \pm 0.52\text{mm}$ (range: 3.0 - 5.5mm). The overall maximum value of the minimum mesh diameter (3.25mm) exceeded the overall minimum value of the maximum mesh diameter (3.0mm). Hence the condition for a single mesh diameter range, $\max_i D_i^- \leq \min_i D_i^+$, was not satisfied. Hence a single mesh diameter, or diameter range, did not exist for these 103 veins under the proposed conditions for vein constriction and distension.

Four mesh diameters $D_1 = 3.0\text{mm}$, $D_2 = 3.3\text{mm}$, $D_3 = 3.6\text{mm}$ and $D_4 = 3.9\text{mm}$ were proposed to accommodate the 103 veins with their respective mesh diameter ranges presented in Figure 2.

The classification of these veins with small mesh diameter priority (maximising the constriction degree) to the proposed mesh diameters resulted in assignment of 95 and 8 veins to the mesh diameters of 3.0mm and 3.3mm, respectively, while the 3.6 and 3.9mm meshes did not receive any vein (see Table 1).

For the classification of the veins with large mesh diameter priority (minimising the constriction degree), it was distinguished between two (3.0, 3.3mm), three (3.0, 3.3, 3.6mm), and four (3.0, 3.3, 3.6, 3.9mm) mesh diameters. The distribution of veins to the different mesh diameters and the resulting constriction degrees for these three options is summarized in Table 1.

Complete diameter smoothing, i.e. $C_R/C_S \geq 1$, was ensured in the proposed solutions with the zero-distension condition, whereby the upper limit of the mesh diameter must not exceed the minimum vein diameter for any vein. Values of $C_R/C_S > 1$ indicated that the mesh reinforcement constricted a vein more than required for complete smoothing. The closest match between reinforcement constriction and smoothing constriction was obtained with large mesh diameter priority classification and the four-mesh solution (grand mean C_R/C_S : 1.20 ± 0.36), followed by the three-mesh and two-mesh solutions (C_R/C_S : 1.31 ± 0.47 and 1.47 ± 0.60). Classification with small mesh diameter priority for maximum downsizing resulted in the largest reinforcement to smoothing constriction ratio (C_R/C_S : 1.69 ± 0.72) utilizing the two smallest mesh diameters.

3.3 Descriptive Statistical Classification

Tailored 'zero-distension' meshes

Hypothetical application of external meshes equivalent in diameter to the corresponding OD_{min} of each vein resulted in a mean maximum constriction of $26.0 \pm 11.1\%$ (range 0 to 57.1%) (Figure 1). Whereas this solution is an unpractical one, since 86 differently sized meshes were required to accommodate the 118 veins accepting a tolerance of 0.1mm, the fact that 117 veins were constricted by 50% or less suggested a phenomenon intrinsic to the lengths of human saphenous vein harvested, namely that OD_{max} rarely exceeds OD_{min} by more than 100%. This finding was confirmed by the relationship between OD_{min} and OD_{max} illustrated in Figure 3 for each vein together with tolerance thresholds. The accommodation of all but one vein argues for a constriction limit of not less than 50%. Therefore, without limiting the number of available mesh diameters and by calculating the proportion of veins with an upper tolerance interval not exceeding 50%, simply applying a mesh with a fully distended internal diameter equal to the OD_{min} of the vein, both the 'zero-distension' and '50% maximum constriction' rules were seen to be met in 99% of veins with 95% confidence.

Single 'zero-distension' mesh

Hypothetical application of a single external mesh with an internal diameter equivalent to the overall $OD_{min} = 2.1\text{mm}$, avoided: a) the requirement for an excessive number of mesh solutions and (b) any distension which would have occurred at a point where the vessel OD was smaller than the inner diameter of the applied mesh. This approach, however, clearly failed due to widespread and excessive constriction (75% of veins experienced greater than 50% constriction and 25% more than 60% constriction, see Figure 4).

Partition modelling of veins based on OD_{max}/OD_{min}

Figure 5 shows the result of successive splits and demonstrated increasing R^2 values until a plateau was reached. This confirmed the lack of additional benefit of further partitioning vessels beyond the fourth split. The result of these partitions proposed mesh diameters of 3.5, 2.7, 3.9 and 3.3mm in that order. The assumption of these mesh diameters revealed acceptable constriction ($C_R < 50\%$) but with a moderate degree of distension in the case of the deployment of a single 3.5mm mesh, rendering the single-mesh solution unsuitable. However, the combination of 3.5mm and 2.7mm mesh accommodated all veins without distension and

with not more than 50% constriction. Addition of the third 3.9mm and fourth 3.3mm mesh diameter into the solution did not appear to affect the extent of constriction, as shown in Figure 6 (A-D). Since an OD of less than 3.0mm (the typical OD of IMA grafts) was considered impractical, the smallest mesh diameter of 2.7mm was replaced with 3.0mm, in conjunction with exclusion of 15 veins with $OD_{\min} < 3.0\text{mm}$ to comply with the condition of no distension. Cases of undesired vein distension were again observed for the single 3.5mm mesh diameter, while the solutions with more than one mesh sufficed for all veins (Figure 6 E-H). The distribution of veins amongst the mesh diameters ordered 3.5, 3.0, 3.9 and 3.3mm was 41.7% and 58.3% for the two-mesh solution, 22.3%, 58.3% and 19.4% for the three-mesh solution and 22.3%, 36.0%, 19.4% and 22.3% for the four-mesh solution.

3.4 Analysis of Outlier Veins

Figure 7 illustrates the OD along the length for the 15 veins excluded from the analysis due to $OD_{\min} < 3.0\text{mm}$ (all 15 veins) and $OD_{\max} > 2 OD_{\min}$ (vein #25), respectively. The harvested length of these veins was $27.3 \pm 9.6\text{cm}$ and the smoothing constriction degree was $36.4 \pm 12.0\%$.

For 8 veins, $OD < 3.0\text{mm}$ occurred within proximity of one end. Seven of these veins qualified for external meshing after removal of an end segment of 2cm (veins 69 and 105), 4cm (veins 6, 46, 65 and 98) and 6cm (vein 81) length. For one vein (vein 25), the removal of a 2cm segment with $OD < 3.0\text{mm}$ resulted in a remaining length of 8cm and rendered the vein too short for grafting, although the smoothing constriction degree was reduced from 57.1% to 28.6%.

In seven veins, segments with $OD < 3.0\text{mm}$ occurred in the mid section of the vein and repeating throughout the entire length, respectively. Four veins (#41, 54, 112 and 113) qualified for an external mesh after removing between 40.0 and 55.0% of the harvested length. For the remaining three veins (#59, 89 and 105), treatment resulted in segments shorter than the 10cm length required for coronary grafting.

In total, 11 vein segments that can receive external mesh reinforcement were obtained from the 15 veins. The length of these segments was $20.6 \pm 8.9\text{cm}$ and the smoothing constriction degree was $19.8 \pm 11.5\%$. The distribution of the vein segments to the proposed mesh diameters and resulting constriction degrees are summarized in Table 1.

4. Discussion

In this study, a theoretical approach was developed for the optimised sizing of constrictive external meshes for the elimination of diametric irregularities, and the prevention of dilation, of human saphenous vein grafts. With the aim of identifying the most suitable mesh diameters and optimizing the mesh diameter selection for each vein, a mathematical method and descriptive statistics were employed comparatively to analyse the dimensional variability of 118 human saphenous veins harvested for clinical coronary artery bypass procedures and to cluster the dimensional data of the veins.

The two methods complemented each other in the sense that the statistical method requires a sufficiently large number of veins to generate reliable data for the mesh diameter selection but may be used for inferential statistical assessment of the proposed solutions whereas the mathematical method can be utilised for mesh diameter selection for any number of veins but is not able to statistically indicate the validity probability of the proposed solutions for a larger patient population.

The mean constriction degree required to smooth diametric irregularities of a vein by reducing OD_{max} to OD_{min} was $26.0 \pm 11.1\%$. This constriction degree sufficed for 54.2% of the veins where as the remaining 45.8% required a higher degree of constriction for diameter smoothing. Only one of the 118 veins required more than 50% constriction (57.1%) which indicated that saphenous veins rarely exhibit maximum outer diameters that exceed twice the minimum outer diameter. This is an important indication for the clinical use of constrictive external meshes: Recording the diameter of the harvested vein in theatre, for assignment of the suitable mesh diameter, can be limited to a single measurement of either the minimum or the maximum diameter yet ensuring that the maximum constriction of 50% will not be exceeded in 99.2% of veins.

Merely two mesh diameters were required to eliminate diametric irregularities in the 117 veins with $C_s \leq 50\%$ without violating the conditions of maximum constriction of 50% and zero distension. Assuming a lower limit for the outer diameter of aorto-coronary vein grafts of 3.0mm, the typical diameter of IMA grafts [12], 14 veins were unsuitable for the constrictive smoothing proposed. Preparative treatment allowed using 11 of these small-calibre veins with constrictive external meshes. 96.6% of the veins (114 of 118) and 94.4% of the total harvested vein length were accommodated with two mesh diameters 3.0mm and 3.3mm for the constrictive elimination of diameter irregularities.

The mesh diameters of the mathematical solutions (3.0, 3.3, 3.6 and 3.9mm) agreed well with the statistically proposed diameters (3.0, 3.3, 3.5 and 3.9mm) even though the approaches of the two methods were different. The mathematical method facilitated a two-stage approach,

namely a) data selection (OD_{\min} and OD_{\max}) and analysis for each vein and b) interactive identification of mesh diameters and data classification based on OD_{\min} and OD_{\max} . In contrast, the statistical method followed a single-stage partitioning approach without prior data reduction, hence utilising the full OD data set of each vein, and without user interaction for the mesh diameter identification. The smallest mesh diameter proposed (2.7mm) was, however, replaced with minimum mesh diameter of 3.0mm for the application of the statistical solution.

Similar results of the two methods were also observed with regard to the decrease of the overall constriction degree (mathematical: 8.9% and 14.7% vs statistical: 9.0% and 16%) associated with the extension of the number of mesh diameters from two to three and four, respectively. This finding is affirmative of the robustness of the two methods and their solutions, in particular as the overall constriction degrees of the mathematical method with large-mesh-diameter priority (2 meshes: $32.6 \pm 9.0\%$, 3 meshes: $29.7 \pm 9.1\%$, 4 meshes: $27.8 \pm 9.1\%$) were based on the maximum constriction degree for each vein, using OD_{\max} and OD_{\min} only, while the statistical overall constriction degrees (2 meshes: $20.0 \pm 8.2\%$, 3 meshes: $18.2 \pm 7.8\%$, 4 meshes: $16.8 \pm 7.1\%$) utilised the mean constriction degree, incorporating all OD measurements, for each vein. Additionally, the mathematical two- and three-mesh solutions comprised different diameter combinations (2 meshes: 3.0, 3.3mm; 3 meshes: 3.0, 3.3, 3.6mm) compared to the statistical solutions (2 meshes: 3.0, 3.5mm; 3 meshes: 3.0, 3.5, 3.9mm). The reason for these differences is the use of an ordered assignment sequence of mesh diameters for the mathematical method (3.0, 3.3, 3.6, 3.9mm) compared to an unordered assignment sequence (3.5, 3.0, 3.9, 3.3mm) inherent in the statistical method.

The fact that the only the two smallest mesh diameters were utilised with small-mesh-diameter priority mathematical solution demonstrates potential of the three- and four-mesh solutions to accommodate larger vein diameters than those observed in this study focussing on saphenous veins harvested for coronary artery bypass procedures. The elimination of diameter irregularities is however expected to offer similar advantages in coronary and in peripheral applications. The harvest of longer vein segments for peripheral grafting (total: 68.6 (61 – 74)cm; calf part: 34.5 (31 – 37)cm; thigh part: 34.0 (30 – 37)cm; standard deviations not provided) [15] compared to aorto-coronary grafts (28.4 ± 9.5 (10 – 52)cm, this study) in conjunction with a flaring vein diameter from the knee towards the thigh [16] offers the proposed solutions for peripheral applications.

If constrictive external mesh support of vein graft aims, besides the elimination of diametric irregularities, also at matching the diameters of host vessel and graft in order to mimic native arterial flow conditions [12], the desired constriction degree may additionally be dictated from site-specific host vessel dimensions in the coronary and peripheral vasculature. While smaller constriction degrees are likely to provide host-graft matched diameters in the peripheral

application with larger-diameter host vessels, larger constriction degrees will be required for the coronary application when grafting small-calibre coronary arteries.

5. Conclusions

In this study related to the constrictive external support of vein grafts, we showed with two independent theoretical methods that merely two diameters of a support mesh prove sufficient to fully eliminate diametric irregularities in 96.6% of the saphenous veins harvested in 100 coronary artery bypass patients. While a maximum constriction of the outer diameter of 26% was required on average for the diametric smoothing of the veins studied, constriction was allowed up to 50% whereas distension was not permitted. The similarity of the solutions of up to four mesh diameters derived with the two dissimilar analysis methods underlined the robustness of the solution approaches and verified the results. The relevance of this study for the clinical application of constrictive external vein graft support is seen in the indication that a mesh support device will suffice with two sizes for aorto-coronary vein grafts and four sizes will be likely to fulfil the demands for the peripheral application. Furthermore, the algorithms used for assignment of a vein to the most suited mesh diameter, based on the minimum and maximum outer vein diameter, lend themselves for the development of an easy-to-use guide for mesh size selection in the operation theatre. This guide may furthermore utilise the finding that the outer diameter of a saphenous vein rarely varies more than two-fold along the harvested length. This minimises, in connection with the 50% constriction limit, the number of diameter measurements required to identify the suitable mesh size for a vein to a single recording during the harvest procedure.

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Table 1. Vein distribution and constriction degrees for mathematical 2-, 3-, and 4- mesh diameter solutions for the 117 veins not requiring more than 50% constriction for complete smoothing (top) and for usable segments of the 15 veins requiring additional preliminary treatment due to $OD_{min} < 3.0\text{mm}$ or $OD_{max} > 2 OD_{min}$ (bottom).

ALL VEINS				
	SMDP 2 - 4 meshes	2 meshes	LMDP 3 meshes	4 meshes
Excluded				
n	14	14	14	14
D ₁ [mm]	3.0			
n	95	27	27	27
C _R [%]	35.8±8.6	29.6±9.8	29.6±9.8	29.6±9.8
C _R /C _S	1.68±0.71	1.09±0.38	1.09±0.38	1.09±0.38
D ₂ [mm]	3.3			
n	8	76	25	25
C _R [%]	47.7±1.4	33.7±8.4	31.2±9.4	31.2±9.4
C _R /C _S	1.81±0.92	1.61±0.60	1.16±0.16	1.16±0.16
D ₃ [mm]	3.6			
n	0	N/A	51	18
C _R [%]			29.0±8.4	26.8±9.4
C _R /C _S			1.50±0.53	1.11±0.11
D ₄ [mm]	3.9			
n	0	N/A	N/A	33
C _R [%]				24.3±8.4
C _R /C _S				1.38±0.48
Overall				
n	103	103	103	103
C _R [%]	36.7±8.8	32.6±9.0	29.7±9.0	27.8±9.5
C _R /C _S	1.69±0.72	1.47±0.60	1.31±0.47	1.20±0.36
EXCLUDED SMALL CALIBER VEINS				
	SMDP 2 - 4 meshes	2 meshes	LMDP 3 meshes	4 meshes
D ₁ [mm]	3.0			
n	11	7	7	7
C _R [%]	26.0±9.0	24.5±10.4	24.5±10.4	24.5±10.4
C _R /C _S	1.29±0.38	1.10±0.18	1.10±0.18	1.10±0.18
D ₂ [mm]	3.3			
n	0	4	3	3
C _R [%]		21.4±6.6	22.8±7.4	22.8±7.4
C _R /C _S		1.30±0.13	1.30±0.13	1.30±0.13
D ₃ [mm]	3.6			
n	0	N/A	1	0
C _R [%]			10.0	
C _R /C _S			-	
D ₄ [mm]	3.9			
n	0	N/A	N/A	1
C _R [%]				2.5
C _R /C _S				-
Overall				
n	11	11	11	11
C _R [%]	26.0±9.0	23.4±9.0	22.7±9.7	22.1±10.9
C _R /C _S	1.29±0.38	1.16±0.19	1.16±0.19	1.16±0.19

SMDP: Small Mesh Diameter Priority Classification

LMDP: Large Mesh Diameter Priority Classification

Figure Legends

Figure 1. Distribution of maximum constriction and smoothing constriction degree C_s , respectively, of saphenous veins assuming reduction of the maximum outer diameter OD_{max} to match the minimum outer diameter OD_{min} .

Figure 2. Graph showing the admissible mesh diameter range δ_i for 103 veins that qualify without preliminary treatment for constrictive smoothing on the conditions of no distension and maximum constriction of 50%. The mesh diameter ranges are ranked according to maximum (primary ranking parameter) and minimum mesh diameter (secondary ranking parameter). The dashed horizontal lines indicate the proposed mesh diameters $D_1 = 3.0\text{mm}$, $D_2 = 3.3\text{mm}$, $D_3 = 3.6\text{mm}$ and $D_4 = 3.9\text{mm}$.

Figure 3. Maximum to minimum OD relationships of saphenous veins distended during leak testing. Tolerance 'fronts' for constriction ranging from 10 to 50% are shown to accommodate increasing numbers of veins.

Figure 4. Maximum constriction degree along the length of veins following hypothetical constriction to an overall diameter of 2.1mm corresponding to the minimum outside diameter overall for all veins. No distension occurs although more than 50% constriction is seen along the full length in more than 75% of harvested veins.

Figure 5. Impact of recursive partitioning of veins into subgroups grouped by OD_{min} and based on separating veins into distinct clusters maximally separated by their OD_{max}/OD_{min} ratios. After the fourth split, little benefit is derived as shown by the effect of the split on R^2 suggesting maximally a five mesh solution.

Figure 6. Solutions based on recursive partitioning to define mesh diameters showing extent of constriction along the length of veins. Final choice of mesh diameters was based on the minimum OD for each vein. No benefit was observed beyond a double mesh solution. The different solutions assumed the following mesh diameters: single mesh 3.5mm (A), two meshes 3.5mm and 2.7mm (B), three meshes 3.9mm, 3.5mm and 2.7mm (C), four meshes 3.9mm, 3.5mm, 3.3mm and 2.7mm (D). Charts E through H represent identical analyses but with the minimum mesh diameter of 2.7mm replaced by 3.0mm and any vein exhibiting a minimum OD of less than 3.0mm excluded.

Figure 7. Graphs of OD along the length of veins excluded from the analysis due to $OD_{\max} > 2 OD_{\min}$ (vein #25) or $OD_{\min} < 3.0\text{mm}$. The threshold $OD_{\min} = 3.0\text{mm}$ is indicated in each graph.

Figures

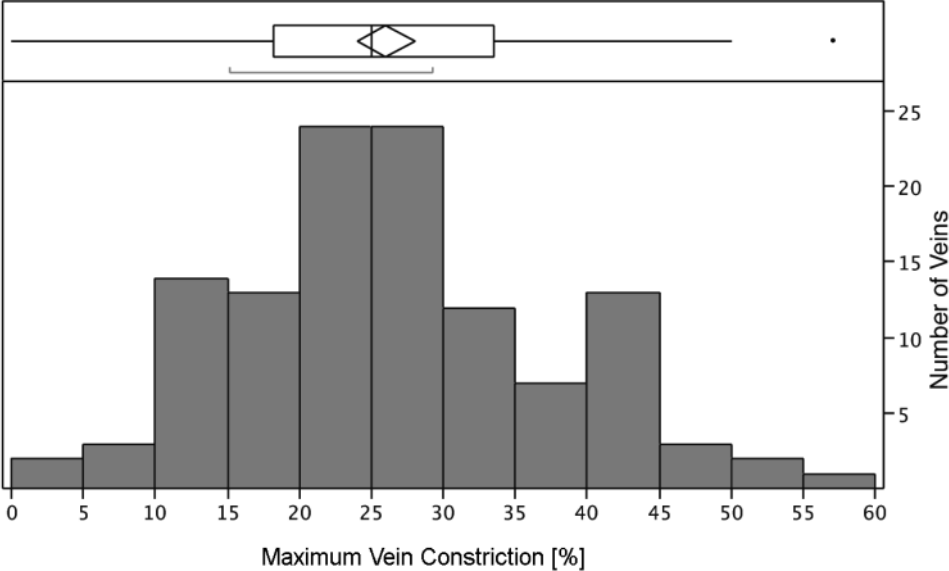


Figure 1. Distribution of maximum constriction and smoothing constriction degree C_s , respectively, of saphenous veins assuming reduction of the maximum outer diameter OD_{max} to match the minimum outer diameter OD_{min} .

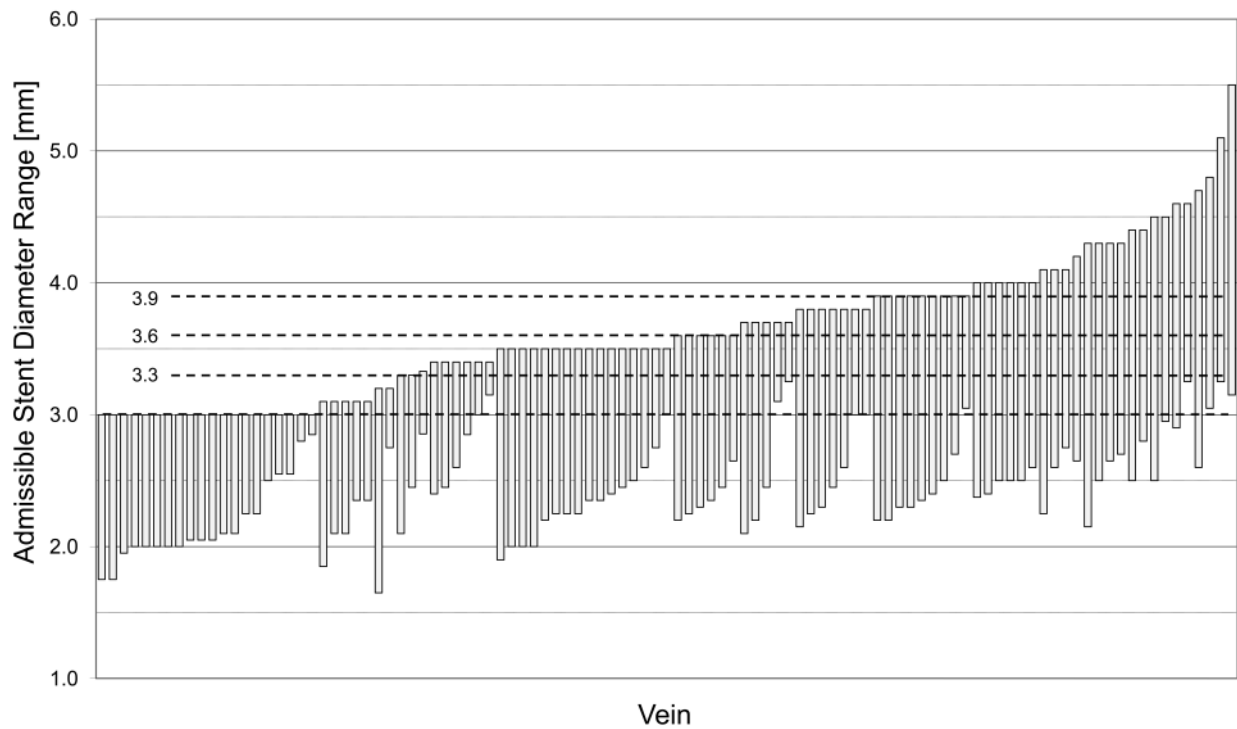


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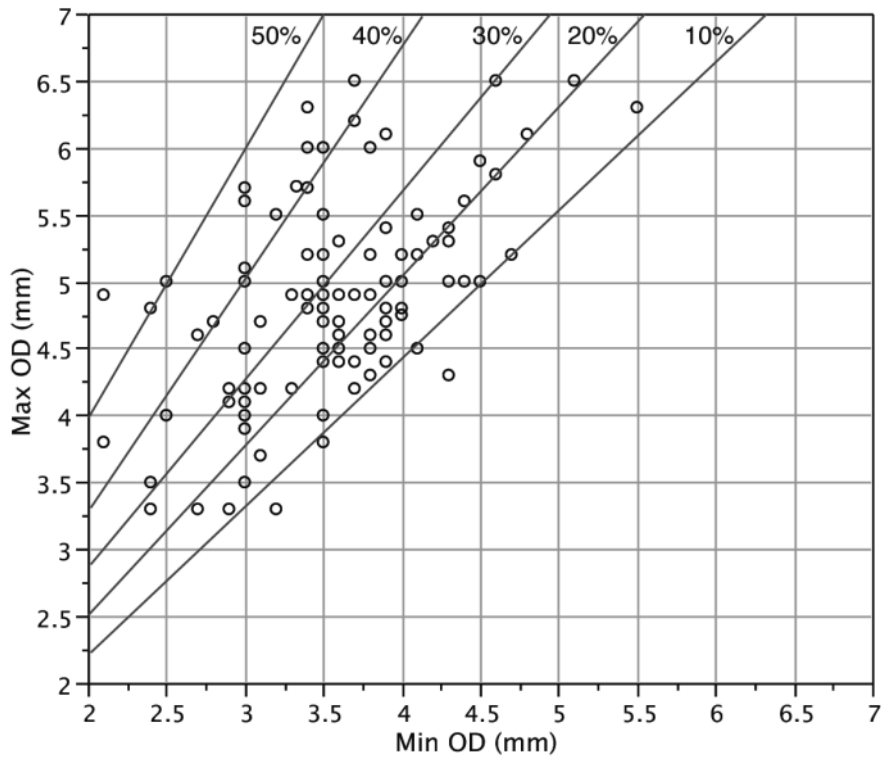


Figure 3. Maximum to minimum OD relationships of saphenous veins distended during leak testing. Tolerance 'fronts' for constriction ranging from 10 to 50% are shown to accommodate increasing numbers of veins.

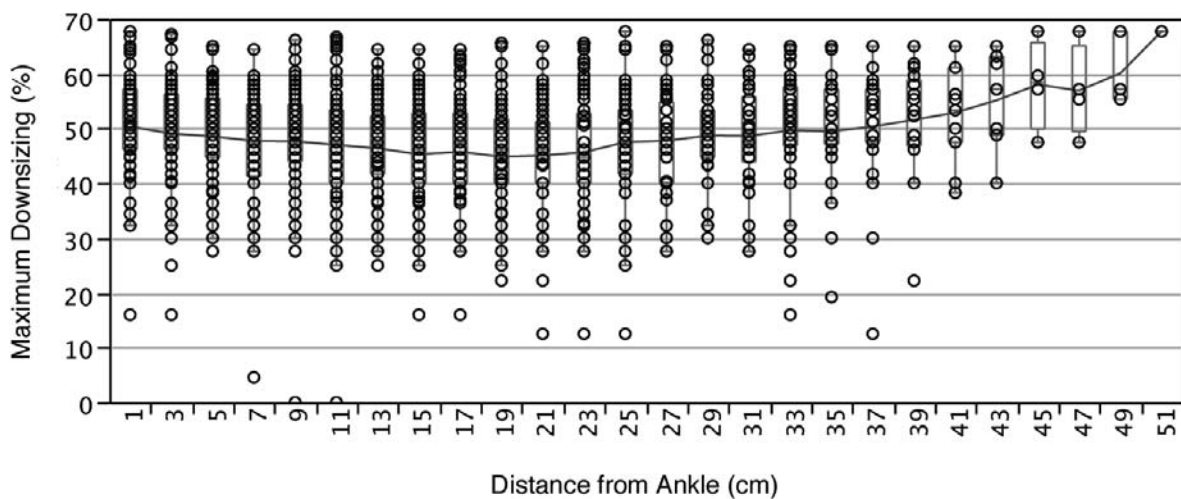


Figure 4. Maximum constriction degree along the length of veins following hypothetical constriction to an overall diameter of 2.1mm corresponding to the minimum outside diameter

overall for all veins. No distension occurs although more than 50% constriction is seen along the full length in more than 75% of harvested veins.

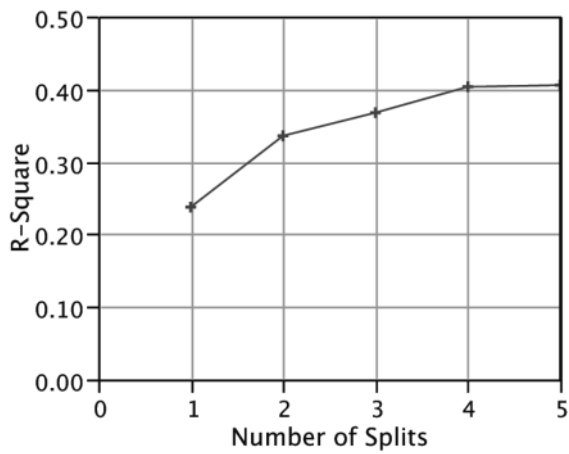


Figure 5. Impact of recursive partitioning of veins into subgroups grouped by ODmin and based on separating veins into distinct clusters maximally separated by their ODmax/ODmin ratios. After the fourth split, little benefit is derived as shown by the effect of the split on R² suggesting maximally a five mesh solution.

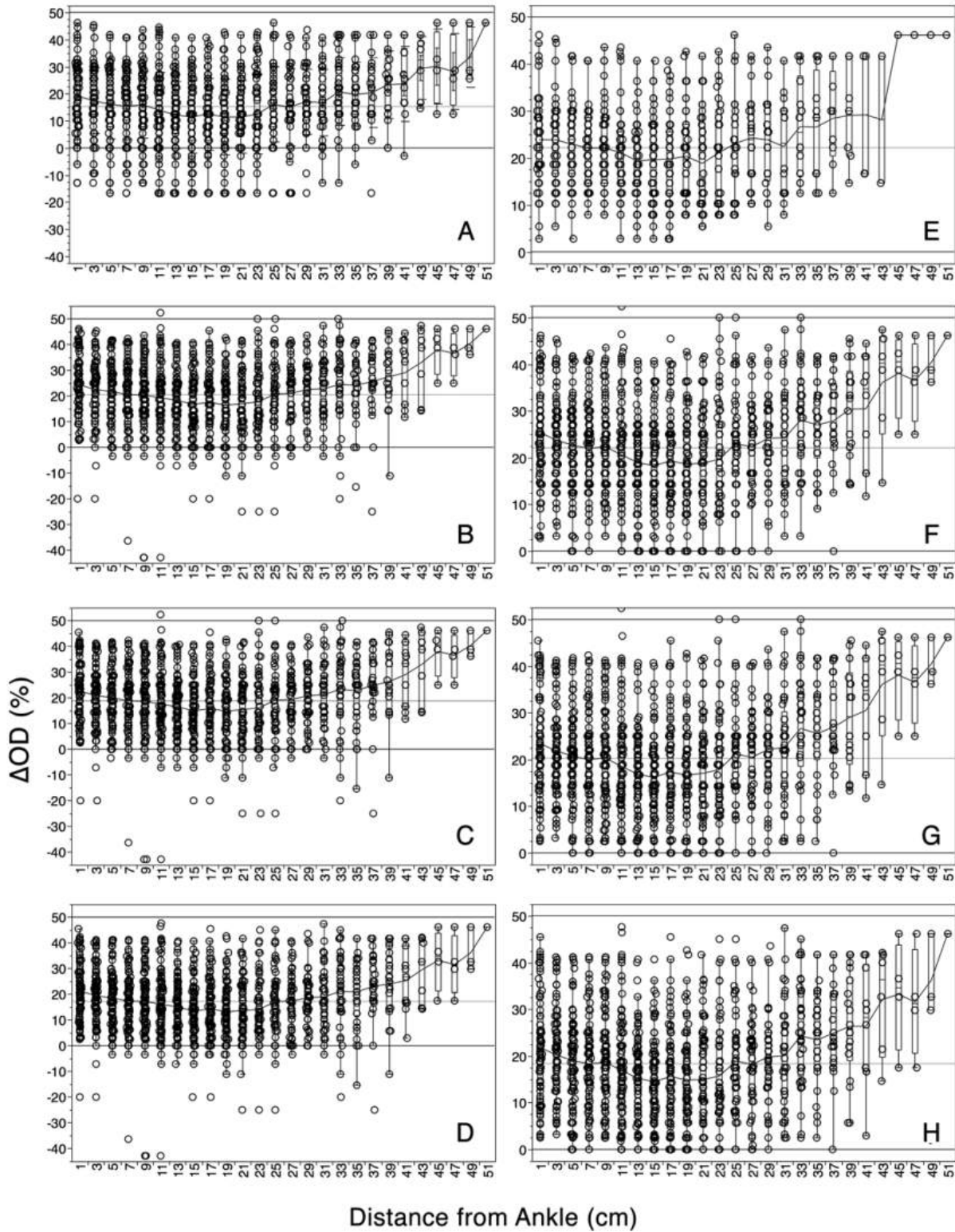


Figure 6. Solutions based on recursive partitioning to define mesh diameters showing extent of constriction along the length of veins. Final choice of mesh diameters was based on the minimum OD for each vein. No benefit was observed beyond a double mesh solution. The different solutions assumed the following mesh diameters: single mesh 3.5mm (A), two meshes 3.5mm and 2.7mm (B), three meshes 3.9mm, 3.5mm and 2.7mm (C), four meshes 3.9mm,

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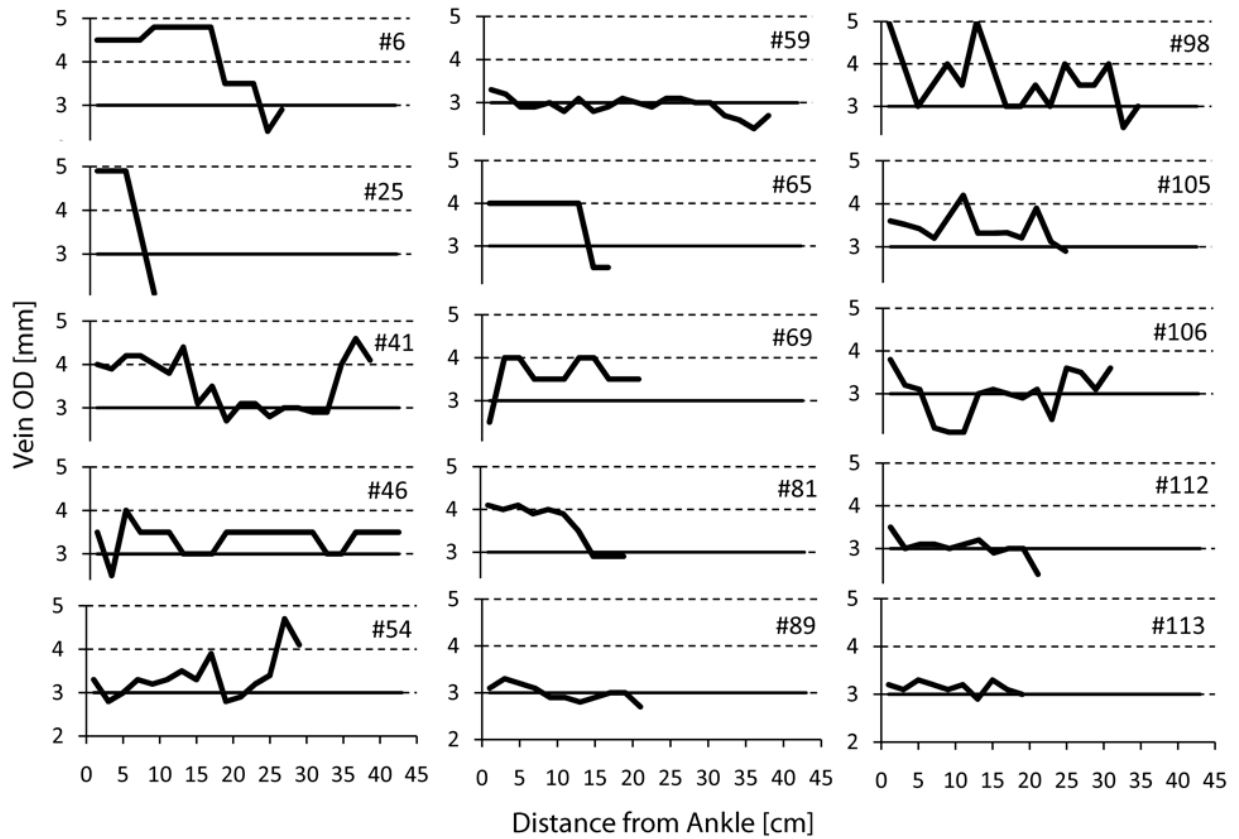


Figure 7. Graphs of OD along the length of veins excluded from the analysis due to $OD_{max} > 2 OD_{min}$ (vein #25) or $OD_{min} < 3.0mm$. The threshold $OD_{min} = 3.0mm$ is indicated in each graph.

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