An international survey on the interpretation of pigmentation using the C class of the Clinical, Etiological, Anatomical, Pathophysiological Classification

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Abstract

Skin changes over the gaiter area like pigmentation, lipodermatosclerosis and eczema are a clinical sign of advanced chronic venous disorder. This is documented as C_4 in the Clinical, Etiological, Anatomical, Pathophysiological (CEAP) classification. The hypothesis was that there is great variability whether skin changes are recorded as early or advanced disease. The aim was to evaluate different patterns of skin changes by delegates at 3 international venous conferences. Seven high-definition, A4-sized, color photographs were taken of untreated legs with skin changes from patients attending a public hospital venous clinic. They all had venous disease confirmed on duplex with deep or superficial vein reflux >0.5 s. The photographs were displayed and a questionnaire was provided. Delegates familiar with CEAP were asked to choose from 3 C class options for each photograph. The responses were summarized by grouping them into mild (C_{0-3}) and severe (C_{4-6}). A total of 117 delegates completed the questionnaire from 30 countries. A percentage of 60 had practiced phlebology >10 years. The percentages of responders scoring mild (C_{0-3}) and severe disease (C_{4-6}) were: mild/severe=3/96 (photo 1), 65/33 (photo 2), 31/67 (photo 3), 56/34 (photo 4), 74/21 (photo 5), 89/10 (photo 6) and 37/59 (photo 7). The median percentage measure of agreement was 36.8 [95% confidence interval (CI): 24.8-48.9]. The range was 23.2 (95% CI: 10.5-36.0) to 94.8 (95% CI: 90.7-98.9), P<0.001/image, Fisher exact test). This indicates a significant difference of opinion between the appearances of mild and severe clinical disease. Clinical decisions using the C class as a sign of advanced disease may be unreliable if used alone for recording severity, grouping patients or rationing treatment.

Introduction

The Clinical, Etiological, Anatomical, Pathophysiological (CEAP) classification for chronic venous disorders (CVD) was set up following an international ad hoc committee.[1,2] It was revised in 2004 when it was stated that revision of CEAP is an ongoing process and that recommendations for change in the CEAP standard be supported by solid research.[3] In 2007, a Joint Statement of the American Venous Forum and the Society of Interventional Radiology reported that this revision should be included as a baseline patient characteristic prior to endovenous treatments.[4] This would facilitate comparison between the results of different studies and improve the overall quality of research on venous disease.

The C component is the most widely used part of the CEAP classification and it is based solely on clinical appearance. Skin changes secondary to CVD are classified as C_4 with C_{4a} representing pigmentation or eczema and C_{4b} representing lipodermatosclerosis (LDS) or atrophie blanche. In 2004, a questionnaire study without photographs was sent to 3681 phlebologists around the world. They concluded from 206 responders that future work would be required on discriminating between C_1 and C_2 varicose vein sizes and which C (C_{1-3}) to assign for corona phlebectatica.[5,6] Discrepancies on the C placement of varicose veins of differing sizes were also apparent in an inter-observer reproducibility study between 3 clinicians on 54 limbs.[7] In that study there was disagreement between C_0 and C_2 or C_1 and C_2 in 13 legs (24%) but only in 6 legs (11%) between C_2 and C_4 or C_3 and C_4. The above studies[5-7] suggest that further clarification should focus on the definitions of C_{0-3} rather than the later stages. Furthermore, it has been commented in an international consensus from experts that patients with more advanced venous disease were most reliably classified.[8]

The hypothesis in this study is that pigmentation is also difficult to classify and that any discrepancy could have greater clinical significance if it spans several points across the 8-point C scale. This is because wide variations in the interpretation of skin changes could inappropriately place a leg into a mild (C_{0-3}) or severe (C_{4-6}) category. The aim was to investigate the definition of C_4 by asking dedicated phlebologists to use their judgment and experience to classify 7 color photographs of skin changes using the C of CEAP.

Materials and Methods

Study design

This was an international observational study involving experienced phlebologists familiar with the CEAP classification. The majority of delegates were vascular

surgeons/angiologists with an interest in phlebology. There were no responders whose main practice was dermatology. They were asked to complete a short questionnaire in order to grade 7 photographs on the C of CEAP. These photographs were displayed on a table, placed at strategic locations, throughout the duration of 3 international venous conferences: the Royal Society of Medicine venous forum (RSM-VF), the European Venous Forum (EVF) and the venous section of the World Congress of the International Union of Angiology (IUA). Participants were either self-selected when they took an interest in the display table or when known specialists, prominent in the venous world, were invited specifically to complete the questionnaire.

Patients

All 7 photographs were from patients with

leg symptoms who were attending the varicose vein clinic at a single public hospital. Patients were referred in the later stages of their disease because uncomplicated varicose veins do not fill the referral criteria under the current public health rationing system. Five patients had duplex evidence of reflux in the saphenous trunks greater than 0.5 s[9] without evidence of deep venous reflux. Two photographs were taken from the same patient (leg elevated and dependant) who had a previous calf vein thrombosis with significant tibial vein reflux. None of the patients had a healed venous ulcer or had received endovenous intervention for their condition.

Photographs

The photographs were high-resolution, taken at close range and printed in color on high-quality photographic A4 print-paper (Figures 1-7). Dissimilar backgrounds were chosen to avoid direct comparisons between the pictures. Each photograph was cropped to highlight the gaiter and ankle areas. The first photograph of lipodermatosclerosis was used as a quality control to determine the standard of the participants at classifying skin changes and to familiarize them with the task. The remaining 6 were selected to highlight controversial areas in the C-class. Although they were considered to be representative of venous disease, it is for the reader to decide on the prevalence of these skin changes in their day-to-day practice. All 7 photographs were displayed simultaneously on a table which enabled each participant to pick them up and view each from different angles in order to make their judgment. Conferring was not forbidden and occurred occasionally. A copy of the clinical classification of the revision of CEAP summary was also placed on the table for information purposes to remind each person of its precise wording as shown below.[3]

Clinical classification (C class)

According to CEAP classification, C class is divided as follows:
- C_0: no visible or palpable signs of venous disease;
- C_1: telangiectasies or reticular veins;
- C_2: varicose veins;
- C_3: edema;
- C_{4a}: pigmentation or eczema;
- C_{4b}: lipodermatosclerosis or *atrophie blanche*;
- C_5: healed venous ulcer;
- C_6: active venous ulcer.

Questionnaire design

The questionnaire occupied half a page of A4 paper from which participants were asked to check 9 boxes and state their country of practice (Figure 8). This restriction on 10 questions/replies was purposeful to prevent lapses of concentration or questionnaire fatigue thereby ensuring data quality with maximal completion.[10] Participants were given 3 C-class options for each photograph from which to pick their answer. They also had the option of stating an alternative C-class option or checking the *don't know* box for whatever reason, including poor quality of photographs. The question on whether a clinical history would influence their judgement was included because it is uncertain whether clinicians should rely on clinical appearance alone or use supplementary information in deciding the C of CEAP. This may be relevant because pigmentation could be the result of treatment. Discoloration could also be caused by extensive telangectasiae following a deep venous thrombosis (DVT). The clinical history in both of these situations may encourage an enthusiastic C class score of C_{4a} rather than C_0 or C_1.

Data analysis

Data were transferred manually from the questionnaires onto spreadsheets at the end of the study and then imported into the IBM® SPSS® statistics software version 19 (IBM Corp., Armonk, NY, USA) for statistical analysis. The results on the C-class determination from the 7 pictures were reported in a similar way to how the C of CEAP is used to stratify patients in clinical trials: percentages in each C-class and/or stratification into mild and severe venous disease. Similarly, the results were reported in two ways. Firstly, specifically, as the percentage of responders choosing each C class (frequency distribution). Secondly, generally, as the percentage choosing mild (C_{0-3}) or severe (C_{4-6}) venous disease (binary outcome). The percentage agreement between mild *versus* severe disease was determined using the risk difference value of the Fisher exact test. Full agreement, where all the raters scored either mild or severe, would be represented as 100%, whereas equivalence would be represented as 0% agreement.

Results

Participant characteristics

A total of 117 delegates completed the questionnaire out of the 120 that were returned. Three were excluded because the answers to the 7 picture questions were incomplete. It was interesting that 2 responders ticked multiple boxes for each question in line with the recommendations of the advanced CEAP. In this case the single highest descriptor was used for the clinical classification.[3] Delegates of 30 different nationalities completed this questionnaire, the top 5 being: UK (17), Italy (16), USA (10),

Figure 1. The control image depicting lipodermatosclerosis. Survey result: C_4 (16%), C_{4a} (39%), C_{4b} (42%).

Figure 2. Corona phlebectatica paraplantaris with an ankle flare. Survey result: C_1 (16%), C_2 (48%), C_{4a} (28%).

Figure 3. Pigmentation over extensive varicose veins. Survey result: C_1 (0%), C_2 (29%), C_{4a} (66%).

Czech Republic (8) and France (7). This distribution reflected the location of the conferences: London (RSM-VF: 20/117 responders, 17%), Florence (EVF: 63/117 responders, 54%) and Prague (IUA: 34/117 responders, 29%).

The experience of the delegate was determined by their number of years in phlebology practice which were: less than 2 (6%), between 2 and 10 (31%), between 10 and 30 (43%), over 30 (17%) and failure to answer (3%). Of the 27 original members of the *ad hoc* committee on the revision of the CEAP classification,[3] 12 (44%) were recognized and invited in person into the study. Nine members completed the questionnaire and 3 were unable to take part for whatever reason. A further index of experience was provided by the answers to the quality control picture 1 depicting lipodermatosclerosis. A total of 96% of delegates recognized this correctly as $C_4/C_{4a}/C_{4b}$, with 3% as edema (C_3) and 1% checking *don't know* for whatever reason.

C class response stratification

The percentage of participants checking each of the three given choices is displayed in the legends underneath each picture for convenience (Figures 1-7). Pictures 4, 5 and 7 caused the greatest amount of uncertainty with the percentage of participants checking the *don't know* box at 10%, 5% and 4%, respectively. The full spectrum is illustrated in Table 1.

Mild and severe response stratification

The percentages of participants scoring mild (C_{0-3}) and severe disease (C_{4-6}) for each photograph from 1 to 7 were: mild/severe=3/96 (photo 1), 65/33 (photo 2), 31/67 (photo 3), 56/34 (photo 4), 74/21 (photo 5), 89/10 (photo 6) and 37/59 (photo 7), respectively. Apart from the control picture 1 which was classed as severe according to 96% of participants, there was a significant lack of agreement between mild and severe clinical disease for the remaining legs. The percentage agreement (risk difference) of mild *versus* severe disease is displayed in the last column of Table 1. There was clinical uncertainty in classifying picture 2 (Figure 2) with 32% of participants choosing advanced disease. However, when the same leg was elevated in picture 6 (Figure 6), this was reduced to 10%.

Importance of a clinical history

In response to the influence a clinical history had to judgment of C class (Figure 8) the participants chose YES (67%), NO (26%), don't know (3%) with 4% leaving this question unanswered. The fact that two-thirds of participants stated that they would use a history was surprising because the C of CEAP was designed to be judged solely from clinical appearance.

Discussion

The CEAP classification remains the gold standard classification of CVD. This was confirmed in a recent review article at which they conducted a Medline analysis retrieving 266 publications using CEAP.[11] This review also discussed the limitations of CEAP firstly stating that CEAP was not a severity classification and then pointed out the controversial areas as C_{0-3}. The current study has demonstrated that the controversial areas can extend into the higher categories of CEAP. The reality is that C of CEAP is frequently used to group patients into categories and is also used to discriminate patients with mild and severe disease. The C_{4-6} group has been discussed as an individual disease.[12] The C stratification has been used in epidemiological studies,[13] longitudinal studies[14] and as a comparator against symptoms and signs,[15] quality of life questionnaires[16] and hemodynamic assessments.[17] Many clinical papers stratify patients' legs into mild/severe or uncomplicated/complicated based on this division between C_{0-3} and C_{4-6}.[18-24] This stratification is also used for rationing treatment in most public hospitals and in cost calculations.[25,26]

The CEAP and venous clinical severity score (VCSS) are different tools and do not measure the same items equally. The existence of similar items with different definitions revised or otherwise should be clear in the mind of the assessor to avoid substitution error. For example, C_2 uses a definition of >3 mm for a varicose vein whereas the VCSS uses a cut-off point of 4 mm.[27] Furthermore, pigmentation defined by the VCSS is more strict than the CEAP because *focal pigmentation over varicose veins does not qualify*, and a *focal low intensity (tan)* is not considered by the VCSS as indicative of significant skin pigmentation.[27] Eczema is C_{4a} but not a VCSS attribute unless it is synonymous with inflammation.

The current research demonstrates that there are substantial discrepancies in the clinical classification of CVD using the C of CEAP and the distinction between mild and severe venous disease is also unclear. Each photograph is commented upon below in order to focus on the controversial areas.

Picture 1: This is the control photograph which was correctly identified as $C_4/C_{4a}/C_{4b}$ by 96% of participants. A plaque of LDS is seen in the gaiter region with deeply situated varicose veins above this area. Although LDS is confirmed by palpation, this was not possible using photographs, a fact probably realized by 16% of participants who decided on choosing C_4 alone. Nevertheless, the highest percentage score was C_{4b} (42%) indicative of LDS.

Pictures 2 and 6: This is the same leg

Figure 4. Mild pigmentation with eczema at the gaiter region. Survey result: C_0 (32%), C_2 (21%), C_{4a} (34%).

Figure 5. Mild retro-malleolar pigmentation over a normal vein. Survey result: C_0 (50%), C_2 (16%), C_{4a} (21%).

Figure 6. The same as shown in Figure 2 but the leg is now elevated. Survey result: C_1 (86%), C_{4a} (8%), C_5 (2%).

dependent (Figure 2) and elevated (Figure 6) in a patient who has deep venous reflux in the calf veins following a DVT. The dependent ankle is discolored with a venous flare/corona phlebectatica and small varicose veins but on elevation pigmentation is not present which confirms the C_{1-2} status of this leg. The dependent leg was reported as C_{4a} by 28% of participants but this reduced to 8% after elevation. Elevation was used here to discriminate apparent pigmentation from venous congestion against true pigmentation from extravasation. Although corona phlebectatica is currently C_1 there are recommendations by many phlebologists to consider it as C_3.[6] The lack of a marker scale prohibits the sizing of varicose veins. This may be necessary for establishing if they are >3 mm in diameter, in which case they would belong to C_2. However, skin thickness and depth of vein should also be taken into consideration. For example it would be difficult to compare vein size in Figure 1 with those in Figure 2.

tion rather than basing a judgment on its presence or absence. This has been highlighted in this picture of gaiter telangectasiae where 56% of participants classified the accompanying hyperpigmentation as C_{4a}.

In cases of doubt there are two additional ways to evaluate pigmentation. The first is to

Table 1. Percentage of C classes chosen by 117 participants for each picture. The 3 given choices are highlighted in italics. Risk difference represents agreement, from no agreement (0%) to full agreement (100%).

Picture	C_0	C_1	C_2	C_3	C_4	C_{4a}	C_{4h}	C_5	Don't know	Mild/severe*	P value°	Risk difference % (CI: 95%)
1	-	-	-	2	*16*	*39*	*42*	-	1	3/113	<0.0005	94.8 (90.7-98.9)
2	-	*16*	*48*	1	-	*28*	2	2	3	76/38	<0.0005	33.3 (21.1-45.6)
3	-	*0*	*29*	1	-	*66*	1	-	3	36/78	<0.0005	36.8 (24.8-48.9)
4	*32*	-	*21*	3	-	*34*	-	-	10	65/40	0.0009	23.8 (10.7-36.9)
5	*50*	4	*16*	4	-	*21*	-	-	5	87/24	<0.0005	56.8 (45.9-67.6)
6	-	*86*	1	1	-	*8*	-	*2*	1	104/12	<0.0005	79.3 (71.5-87.2)
7	-	*21*	*15*	1	-	*56*	3	-	4	43/69	0.0008	23.2 (10.5-36.0)

*Ratio in absolute numbers of C_{0-3}/C_{4-5}; °Fisher exact test. CI, confidence interval.

Figure 7. Telangectasiae and reticular veins with infra-malleolar pigmentation. Survey result: C_1 (21%), C_2 (15%), C_{4a} (56%).

Figure 8. The questionnaire which delegates were asked to complete. Picture 1 is Figure 1 and likewise for the remaining 6 illustrations.

bologists to consider it as C_3.[6] The lack of a marker scale prohibits the sizing of varicose veins. This may be necessary for establishing if they are >3 mm in diameter, in which case they would belong to C_2. However, skin thickness and depth of vein should also be taken into consideration. For example it would be difficult to compare vein size in Figure 1 with those in Figure 2.

Picture 3: Obvious mid-calf pigmentation over extensive varicose veins was reported by only 66% of participants using C_{4a} in comparison to the 29% who reported C_2. This may be because pigmentation in CEAP is defined as *brownish darkening of the skin* and *occurs in the ankle region but may extend to leg and foot*.[3] Should pigmentation arising de novo over a mid-calf varicose vein without having extended from the ankle be classed as C_{4a}? These factors may explain the reluctance of choosing C_{4a} as an option.

Pictures 4 and 5: These legs demonstrate mild (Figure 4) and very mild (Figure 5) degrees of pigmentation with eczema. This is reflected in the percentage of participants choosing C_0 at 32% and 50%, respectively. Once again, it has been left for the observer to decide on what constitutes *brownish darkening* and how much eczema is significant to qualify as C_{4a}. Both patients also had a normal looking vein present beneath the medial malleolus which may have prompted the choice of C_2 at 21% and 16%, respectively.

Picture 7: Many patients have different baseline skin colors which may cause additional problems in defining increased pigmenta-

make a comparison with the *normal* other side because this will indicate the natural color of the skin. The second is to elevate the leg to confirm a real pigmentation that does not disappear.

A published limitation of CEAP is that the patient's venous history is not taken into account.[28] The C class according to the current definition is about clinical appearance, not medical history. It is clear from the current study that 67% of participants would use a clinical history in making their judgment on C. This supports the rationale of this study because the C of CEAP is nothing more than clinical appearance and was not intended to co-ordinate historical features. However, in everyday practice the judgment of a C class cannot be devoid of a clinical history. Pigmentation in the gaiter region may have other etiological factors like post-inflammatory hyperpigmentation occurring after trauma or a skin infection. Similarly, eczema may be caused by an allergic reaction or an insect bite rather than venous insufficiency. A C_2 classification assessed by a doctor in the morning may become a C_3 in the evening. These may only become apparent from the clinical history. Furthermore, the presence of minor reflux within a small caliber vein may not be enough to cause pigmentation. It would be interesting if a group of dermatologists were asked to complete the survey since they have a focused interest in pigmentation disorders.

The pictures represent legs seen in common practice, which are difficult to classify because of lack of agreement using the C class. Improvements in C stratification could be

made by defining the controversial areas as this work has demonstrated. A consensus statement from a panel of experts using published photographs may improve the reliability and agreement of CEAP.

Limitations

This is an observational study where patients with an indeterminate C class were selected deliberately because they would invoke disagreement between different participants. However, the objective of this study was to highlight controversial areas because recognition of a limitation is an essential step prior to an improvement. Although all the patients were photographed within the same week the true prevalence of their leg appearances and the extent to which these patients are representative of a diseased venous cohort should be determined by the readers' individual clinical practice. However, patients attend the clinic because of their varicose veins rather than hyperpigmentation *per se*.

A further limitation is that photographs are not patients. Differences in lighting, background and angles are known to have profound effects on the interpretation of varicose veins. The quality of the photographs appears poor from a professional viewpoint, and this is a factor which may have caused difficulties in participant's choice. However, an A4 photograph at high resolution is much better than its on screen image. Each participant had the option to check the *don't know* box, for whatever reason, but this rarely happened. Care was taken to ensure that each photograph accurately represented the clinical features of each patient. This may have advantages over questionnaire studies which use descriptors without photographs[5] and disadvantages in comparison to studies where patients are examined in a clinical setting.[7] However, the use of photographs outside a clinical setting may be beneficial because it standardizes the available information from which judgments are made. Clinicians are therefore less likely to have their judgments on the C of CEAP influenced by the patients' medical records, symptoms or duplex findings.

Conclusions

Clinical trials using the C class as a means of stratifying legs into mild and severe clinical disease should be interpreted with caution because of the difficulties in weighting the importance of pigmentation based solely on appearance. This information is of value in clinical situations where the C of CEAP may be used to ration treatment and in research situations were it is often used as a benchmark or comparator for hemodynamic and quality-of-

life validations. The results of this work have also indicated that the C of CEAP may be improved by using the same rater throughout clinical studies, unifying the CEAP definitions with those of the VCSS and by using leg elevation to discriminate between telangectasiae and pigmentation. This work also confirms that the C class should not be used as a severity classification.

References

1. Porter JM, Moneta GL. Reporting standards in venous disease: an update. International Consensus Committee on Chronic Venous Disease. J Vasc Surg 1995;21:635-45.
2. Beebe HG, Bergan JJ, Bergqvist D, et al. Classification and grading of chronic venous disease in the lower limbs. A consensus statement. Eur J Vasc Endovasc Surg 1996;12:487-91; discussion 91-2.
3. Eklof B, Rutherford RB, Bergan JJ, et al. Revision of the CEAP classification for chronic venous disorders: consensus statement. J Vasc Surg 2004;40:1248-52.
4. Kundu S, Lurie F, Millward SF, et al. Recommended reporting standards for endovenous ablation for the treatment of venous insufficiency: joint statement of The American Venous Forum and The Society of Interventional Radiology. J Vasc Surg 2007;46:582-9.
5. Antignani PL, Cornu-Thenard A, Allegra C, et al. Results of a questionnaire regarding improvement of 'C' in the CEAP classification. Eur J Vasc Endovasc Surg 2004;28: 177-81.
6. Uhl JF, Cornu-Thenard A, Carpentier PH, et al. Clinical and hemodynamic significance of corona phlebectatica in chronic venous disorders. J Vasc Surg 2005;42: 1163-8.
7. Uhl J-F, Cornu-Thenard A, Carpentier PH, et al. Reproducibility of the "C" classes of the CEAP classification. J Phlebol 2001;1: 39-43.
8. Allegra C, Antignani PL, Bergan JJ, et al. The "C" of CEAP: suggested definitions and refinements: an International Union of Phlebology conference of experts. J Vasc Surg 2003;37:129-31.
9. van Bemmelen PS, Bedford G, Beach K, Strandness DE. Quantitative segmental evaluation of venous valvular reflux with duplex ultrasound scanning. J Vasc Surg 1989;10:425-31.
10. Rathod S, LaBruna A. Questionnaire length and fatigue. ESOMAR Panel Research Conference, Budapest, 2005. Available from: http://www.esomar.org/web/research_papers/web-Panel_

1092_Questionnaire-length-and-fatigue.php Accessed: 12 July 2012.
11. Rabe E, Pannier F. Clinical, aetiological, anatomical and pathological classification (CEAP): gold standard and limits. Phlebology 2012;27:114-8.
12. Bradbury AW. Epidemiology and aetiology of C4-6 disease. Phlebology 2010;25:2-8.
13. Maurins U, Hoffmann BH, Losch C, et al. Distribution and prevalence of reflux in the superficial and deep venous system in the general population—results from the Bonn Vein Study, Germany. J Vasc Surg 2008;48:680-7.
14. Stucker M, Reich S, Robak-Pawelczyk B, et al. Changes in venous refilling time from childhood to adulthood in subjects with apparently normal veins. J Vasc Surg 2005;41:296-302.
15. Chiesa R, Marone EM, Limoni C, et al. Chronic venous disorders: correlation between visible signs, symptoms, and presence of functional disease. J Vasc Surg 2007;46:322-30.
16. Shepherd AC, Gohel MS, Lim CS, Davies AH. A study to compare disease-specific quality of life with clinical anatomical and hemodynamic assessments in patients with varicose veins. J Vasc Surg 2011;53: 374-82.
17. Lattimer CR, Azzam M, Kalodiki E, et al. Saphenous pulsation on duplex may be a marker of severe chronic superficial venous insufficiency. J Vasc Surg 2012;56:1338-43.
18. O'Hare JL, Parkin D, Vandenbroeck CP, Earnshaw JJ. Mid term results of ultrasound guided foam sclerotherapy for complicated and uncomplicated varicose veins. Eur J Vasc Endovasc Surg 2008;36:109-13.
19. Rasmussen LH, Lawaetz M, Bjoern L, et al. Randomized clinical trial comparing endovenous laser ablation, radiofrequency ablation, foam sclerotherapy and surgical stripping for great saphenous varicose veins. Br J Surg 2011;98:1079-87.
20. Darvall KA, Sam RC, Bate GR, et al. Changes in health-related quality of life after ultrasound-guided foam sclerotherapy for great and small saphenous varicose veins. J Vasc Surg 2010;51:913-20.
21. Neglen P, Egger JF, Olivier J, Raju S. Hemodynamic and clinical impact of ultrasound-derived venous reflux parameters. J Vasc Surg 2004;40:303-10.
22. Yamaki T, Nozaki M, Fujiwara O, Yoshida E. Comparative evaluation of duplex-derived parameters in patients with chronic venous insufficiency: correlation with clinical manifestations. J Am Coll Surg 2002;195:822-30.
23. Lattimer CR, Kalodiki E, Azzam M, Geroulakos G. Reflux time estimation on air-plethysmography may stratify patients

with early superficial venous insufficiency. Phlebology 2013;28:101-8.

24. Navarro TP, Delis KT, Ribeiro AP. Clinical and hemodynamic significance of the greater saphenous vein diameter in chronic venous insufficiency. Arch Surg 2002; 137:1233-7.

25. Lattimer CR, Kalodiki E, Azzam M, Geroulakos G. The Aberdeen Varicose Vein Questionnaire may be the preferred method of rationing patients for varicose vein surgery. Angiology 2013. [Epub ahead of print].

26. Ratcliffe J, Brazier JE, Campbell WB, et al. Cost-effectiveness analysis of surgery versus conservative treatment for uncomplicated varicose veins in a randomized clinical trial. Br J Surg 2006;93:182-6.

27. Rutherford RB, Padberg FT Jr, Comerota AJ, et al. Venous severity scoring: An adjunct to venous outcome assessment. J Vasc Surg 2000;31:1307-12.

28. Cornu-Thenard A, Uhl JF, Carpentier PH. Do we need a better classification than CEAP? Acta Chir Belg 2004;104:276-82.