Author's response to reviews

Title: Reproducibility and day time bias correction of optoelectronic leg volumetry: a prospective cohort study

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Author's response to reviews: see over
Dear Editor, dear Reviewers

Thank you very much for your precious comments that give us the opportunity to improve our manuscript. We have revised our paper according to your suggestions. Please find our comments below.

Editorial Requests:

1. Please revise your abstract so that it contains some contextual information in addition to the research aims of your study.

We thank you for this suggestion and have revised our manuscript accordingly (page 3, abstract, line 2-4)

Reviewers comments

Reviewer 1

General remarks.
The subject researched is very relevant: reproducibility of a measuring device for legs. A second outcome parameter is daytime variability in hairdressers. The question is well proposed, the methods are appropriate described. The limitations are clearly stated and the manuscript is relevant.

As discussed and shown as limitation, only intra observer variability is studied. Why no inter observer variability, which give more strong information about the validity of this device.

We agree that interobserver reliability would be interesting to investigate. However, the optoelectronic device is a computer supported automatic measurement tool where the impact of observer relevant measurement bias should be fairly remote. In our study, all measurements where performed by one same observer, therefore we are not able to report inter observer variability.
Patients were seen by a vascular medicine specialist. The results of this consultation are mentioned as the “c” from CEAP. Is that correct? Ultrasound duplex scanning was not performed. What is the reason? We all know that duplex finding are essential in investigating venous insufficiency and especially when is focussed on edema, a more functional investigation is crucial. This item should be discussed and mentioned as limitation.


Yes indeed, we used the clinical classification (C) of the CEAP classification. We agree that duplex evaluation is essential in investigating venous disease and leg edema. However, our main question focused on the reliability of the volumetry measurements and therefore we did not consider any further information to be relevant for this issue. We have revised our manuscript explaining that the study population included relatively young subjects working mainly in standing position, most of them without any clinical evidence of superficial venous reflux. (page 15, limitations line, 11-12)

An exclusion criterion was deep venous thrombosis and arterial insufficiency. Was duplex performed or wrist/ankle pressures and which score is abnormal?

Clinical evaluation was performed and exclusion criteria were based on personal history and clinical examination. This has been addressed in the method part (page 5, study population, line 19-20).

Was a power calculation performed to state the sample size of the study population?

No, there was no power calculation. This was not required according to the focus of our investigation.

In the study a cohort of patients with risk on swelling was chosen. The authors presume that hair dressers are at risk. Why was there no control group, eg housewives without CVI or office clerks? Please explain in the discussion.

Yes, we presumed that persons with standing position at work are considered as being at risk for CVI (Ziegler et al, Wien Klin Wochenschr. 2003 Sep 15;115(15-16):575-9, reference added in the manuscript = Reference number 20). It would actually be interesting to compare different populations, eg. standing versus sitting working subjects according to their daily leg volume change. However, this present work did not aim to compare different working groups.

In the discussion (line 2) there is stated that all participants are healthy. But according the the “c” in CEAP, 74.6% had C1, 9.5% had C2 and even 7.9% had already clinically edema. So I the statement “healthy” should be reconsidered. Therefore more precise duplex finding should be very illustrative. In the discussion this item of “C” should be discussed more intensely and not just mentioned in the limitations. This finding is to important.

We do agree that subjects with CEAP C2 and more cannot be considered as “healthy”. Therefore, we adapted the method section (page 5, study population, line 16) and the
discussion (page 11, line 13 and page 15, limitations, line 10-12) accordingly. However, we believe that “C” classification is not of substantial importance for our specific investigation which was focused on the reliability of the leg volume measurement tool.

In the conclusion (line 11): reliability is just stated by intra-observer variability.

Thank you for this precious comment, we adapted the conclusion accordingly (page 16, conclusions, line 5-6).
Reviewer 2

Minor Essential Revisions

1. Were participants studied at the same or at different daytimes during the 1st and the 2nd visits?

Participants could decide themselves, at what daytime they would come for the 2 visits. According to their working shifts, most participants came for both visits either in the morning or in the afternoon. This point has been clarified under study protocol (page 6, study protocol, line 23-25).

2. The formula for the time correction should be clarified. For example if t1=12 and t2=24, is delta equals 12 or -12?

Thank you for this precious comment and important point. We added an illustrative example in order to clarify the use of the formula (page 9-10, relation between day time of measurement and leg volume, line 21-9).

Major Compulsory Revisions

1. Relationship between day time of measurement and the leg volume is highly questionable. If each participant was studied at different time during the 1st and 2nd visits, this difference is a large component of the difference between V1 and V2. If this was done at the same day time during these visits, then it is unclear how the potential confounding was addressed, i.e. having proportionally more larger legs studied in the afternoon etc.

As mentioned above, the participants could choose themselves at what time they wanted to be examined at the 2 different study days. Therefore, most of them were examined at rather slightly differing day times at the 2 visits. Our observation of daytime bias and leg volume change was indeed and very interestingly confounded by the body mass index (this point has been added in the Result part, page 9, relation between day time of measurement and leg volume, line 9-10), suggesting that in general more obese participants attended the visits at a more advanced daytime. Nevertheless, the correlation between leg volume difference and daytime of measurement difference was not modified after adjusting for BMI, age, sexe, and CEAP class (clarified under: page 9, relation between day time of measurement and leg volume, line 13-14 and page 13, discussion line 8 and 13-14).

2. The rapid volume change in 30-second time indicates possible lack of reliability of measurements.

We agree that the observed volume increase during the 2nd volume measurement could represent a lack of reliability. However, as outlined in our discussion, we strongly suggest that this observation can be entirely explained by the physiological phenomenon of orthostatic leg volume increase, since our participants were sitting for 15 minutes before performing the measurements in a standing position. Over time repeatability can also be increased by using the mean of several measurements (in our case two measurements) at each visit.

However, your comment is justified and underlines the importance of standardized measurements including early orthostatic leg volume increase most probably as part of physiological filling of the venous system.
3. This paper does not provide us with very basic information as it relates to reliability of the test. What was actual repeatability? If any repeated measurement done 30 sec or more apart results in a significant difference, the repeatability is extremely poor. What is reproducibility? The only aspect of reproducibility that was addressed is doing the test 3 weeks apart. What about a different operator?

We understand this comment and would like to reply the following: Despite the fact, that the second measurement was significantly higher than the first one, reliability of the volume measurement expressed as analytic coefficient of variance is still very high. Unlike blood markers like CRP, which can be assessed twice in the same blood sample to calculate analytic coefficient of variance, it is not possible to measure leg volume twice instantaneously with the currently available methods. On the other hand, when a single volume measurement is analyzed twice, by a single or another observer, the result is exactly the same since data analysis is automatically performed by the software program. This has to be taken into consideration, as suggested in the conclusions, by applying a strictly standardized measurement protocol and by taking the mean of several measurements. This point has been added in the conclusion section (page 16, conclusion, line 12-13).

We would be very pleased if this manuscript might be considered suitable for publication in your outstanding journal.

Thank you for your generous consideration.

Sincerely,

Rolf Engelberger, MD