SAPHENOUS SPARING TREATMENTS SHORT REVIEW

Are saphenous sparing treatments beneficial to the hemodynamics of the venous system?

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Abstract This short review analyzes first the hemodynamic changes that follow destructive procedures, such as stripping or endovascular techniques, and conservative procedures, such as the CHIVA Cure. Then, the effects of the hemodynamic changes resulting from conservative and destructive procedures are compared with respect to the course over time of the varicose disease, mainly focusing on the occurrence of recurrences and their different hemodynamic characteristics. The results show that both conservative and destructive procedures significantly improve the plethysmographic reflux parameters till their normalization. However, destructive procedures reduce the compliance of the lower limb, which expresses an impaired drainage of the superficial tissue, as documented by the typical occurrence of recurrent varicose veins without a detectable trans-compartmental reflux point that are never found after conservative procedures. On the contrary, conservative procedures, when appropriately performed based upon the type of the venous shunt, preserve the drainage of the superficial tissues making the incompetent venous system more hemodynamically stable, which results in a significantly less frequent occurrence of recurrences.

Keywords varicose veins, sparing surgery, CHIVA, venous hemodynamics, recurrent varicose veins

From the patho-physiological point of view, venous disease, either due to obstruction or reflux, is characterized by the increase in the trans-mural pressure (TMP) due to the increase in the lateral venous pressure (LVP)[1]. In the case of superficial reflux, it has been shown that these hemodynamic changes trigger an inflammatory process of the endothelium characterized by a cytokine cascade with activation of matrix metalloproteinases leading to a sustained remodeling of valves and venous wall resulting in valve incompetence, massive fibrosis of the media and its fusion with the adventitia[2, 3].

The hemodynamics of superficial venous insufficiency is commonly investigated by using duplex ultrasound (DUS) and plethysmography (PG). DUS is used to identify the venous reflux, defined as a retrograde flow lasting more than 0.5s in the greater saphenous vein, 0.3s in the perforators veins and 1.0s in the common femoral vein[4], and to characterize the type of venous-venous shunts (location of the escape point, course of the incompetent superficial veins and location of the re-entry perforating vein, i.e. the point through which the retrograde superficial flow re-gains the deep venous system)[5]. While DUS mainly provides “qualitative” information, that are, however, absolutely critical to correctly plan the strategy of conservative procedures, PG provides “quantitative” information, such as reflux parameters and lower limb compliance. The most studied reflux parameter is the venous filling index (VFI), calculated by dividing the 90% venous volume (VV90) by the 90% venous filling time (VFT90), i.e. the time needed to reach the VV90 once the orthostatic posture has been reassumed after leg veins have been emptied with the subject in supine position and

the lower limb elevated at 45 degrees[6]. With regard to lower limb compliance, it is generally assessed at calf level with the subject in the supine position by using the venous occlusion technique and it is calculated as the derivative of the pressure-volume curve during the deflation phase, for pressure between 60 and 10 mmHg [7, 8, 9]. As calf compliance is assessed during the deflation phase, once the occlusion is removed and the venous system is left free to empty out, calf compliance is affected not only by the elastic properties of the venous wall and of the lower limb tissues, but also by the overall draining capability of the venous system of the lower limb.

In the case of greater saphenous vein (GSV) incompetence, which is the most frequent cause of superficial venous insufficiency, destructive procedures suppress the venous reflux, by either removing (stripping) or occluding (endovascular procedures) the GSV. Park, et al.[10] have, in fact, retrospectively investigated a very large series of patients (more than 1,600 limbs) who had undergone either high ligation plus stripping or radio-frequency ablation for GSV incompetence. Authors compared the plethysmographic parameters recorded preoperatively and 1-month after the procedure and found that reflux parameters were significantly improved ($p<0.001$).

With regard to conservative procedures, they dramatically reduce the flow of the venous reflux by disconnecting the GSV from the escape point(s), as in the CHIVA 1 procedure, for type I shunts, and in the second step of the CHIVA 2 procedure, for type III shunts[5, 11-14]. Indeed, the flow of the venous reflux can also be reduced by occluding the GSV arch just partially, as with Office Based CHIVA[15]. Further, since the origin of the CHIVA, it is an established notion that conservative procedures may also hemodynamically suppress the venous reflux by disconnecting from the GSV the branch where the re-entry perforator vein is located, without disconnecting the GSV from the escape point, as in first step of the CHIVA 2 procedure for type III shunts. With this regard, it has been described a diagnostic test to preoperatively check the reflux suppression by finger compression of the GSV branch where the reentry perforator vein is located[11, 13], which was given the name "reflux elimination test"[16]. In this last paper, authors also showed that the plethysmographic reflux parameters significantly improved ($p<0.001$) 1 and 6 months after the first step of the CHIVA 2 procedure. Other two papers on factors affecting venous ulcer healing in patients undergone conservative procedures have confirmed that the plethysmographic reflux parameters were significantly improved ($p<0.001$) when the CHIVA strategy had been appropriately selected based upon the type of the venous-venous shunt[17, 18].

Altogether, these data show that, in patients with GSV incompetence, plethysmographic reflux parameters are considerably improved after both destructive and conservative procedures. Accordingly, the first message to take home is that to reduce the pathogenic effects of the venous reflux on lower limb tissues it is not necessary removing, or destroying, the GSV, which, instead, can be spared and possibly used later in life as an arterial graft. In fact, the retrograde flow detected within the GSV after conservative procedures is not "per se" a limit to its use as a graft[19, 20], GSV rarely shows bulges that, in any case, can be "repaired"[19] and the GSV fragmentation, foreseen in the original description of the conservative procedures[5], is seldom necessary in clinical practice (in authors' experience less than 2% of cases over more than 3,000 operated GSVs, personal unpublished data). Interestingly, the TMP reduction due to the dramatic decrease in the reflux flow, decreases the GSV caliber[21] and "maintains" the normal histologic architecture of the venous wall[22]. Further, the suppression of the oscillatory component of the reflux favorably modulates the inflammatory endothelial phenotype and mitigates the inflammatory process responsible for the sustained damaging of venous valves and wall[2].

The second message to take home from the papers that have investigated the effects of destructive[10] and conservative[16-18] procedures on plethysmographic reflux parameters comes out from the analysis of the figures reported in the papers. In fact, VV reduction after both destructive and conservative procedure was around 25-30%, while VFI reduction was 75% after destructive procedures[10] and around 45-50% after conservative procedures[16-18]. As VFI is the ratio of VV to VFT, the greater VFI reduction found after destructive procedures, in spite of the VV reduction comparable to that found after conservative procedures, is necessarily due to the greater increase of VFT after destructive procedures, although rough data on VFT are not reported in the papers. This strongly suggests that destructive procedures impair the venous drainage of the lower limb. In fact, once the escape point has been closed, independent of the performed procedure, the filling of lower limb veins, which is only due to the "vis a tergo", depends on the arterial-venous gradient. Accordingly, the longer VFT found after destructive procedures is explained by the reduced arterial-venous gradient, which, in the absence of peripheral artery disease, is due to the increase in the pressure on the venous side resulting from the impaired venous drainage.

Other studies on venous compliance also support the thesis that destructive procedures impair the venous drainage of the lower limb. Skoog, et al.[23] have, in fact, shown that, in patients with GSV incompetence, calf

venous compliance was significantly reduced 1 month after GSV radio-frequency ablation. The compliance reduction is related to the increased resistance to the outflow of the superficial tissues which slows down the flow speed and increases the LVP and, hence, the TMP. As venous compliance shares an inverse relationship with the TMP, the reduction of the venous compliance found after destructive procedures results in an increase in the TMP. Once the "hemodynamic reserve" (supra- and trans-fascial network)[24] has been exceeded, the increase in the TMP triggers the occurrence of recurrences, that, typically, never exhibit a detectable trans-compartmental escape point[25]. Further, observations from everyday clinical practice show that patients with primary varicose veins exhibit few DUS detectable perforating veins, either incompetent or not, while after GSV stripping patients show more perforating veins with respect to the preoperative assessment, independent of whether they present with recurrent varicose veins[26] or not. This suggests that once the lower limb has been deprived of its physiological, low resistance draining system, i.e. the GSV, the superficial tissues of the lower limb seek somehow to empty out and that perforating veins represent the "hemodynamic reserve" for the drainage of the superficial venous system.

With regard to conservative procedures, other observations from everyday clinical practice support the thesis that these procedures preserve the venous drainage of the lower limb. In fact, after the procedure, high resolution DUS shows a spontaneous, slow velocity, retrograde, breath-phasic flow in the thigh GSV, when the subject lays in supine position, which represents the rest drainage of the superficial tissues [https://www.studioflebologicocappelli.it/deflusso-post-chiva/]. Further, pulsed doppler DUS shows a double anterograde flow in the GSV thigh tributaries, when the subject performs a dynamic test in upright position. The diastolic component of the anterograde flow, which is never detectable when the escape point is open, represents the ability of the muscle pump to create a diastolic depression gradient between the GSV tributary and the re-entry perforator vein, which allows the drainage of the superficial tissues through the preserved retrograde GSV during exercise. These observations highlight the concept that the GSV retrograde flow detectable after conservative procedures is only fed by the superficial tissue outflow, and that, on the contrary, the GSV retrograde flow found in patients with an open escape point, is also fed by a relevant hemodynamic overload through the escape point itself. Thus, it is not surprising that the GSV retrograde flow resulting from conservative procedures shows a much lower pathogenic potential than the GSV retrograde flow found in patients with an open escape point.

Finally, once the more favorable effects of conservative procedures on the hemodynamics of the venous system have been established, it appears quite sensible to verify whether they also improve short- and long-term outcomes. Indeed, a small number of Randomized Controlled Trials (RCTs)[25, 27-29] and Metanalyses (MAs)[30, 31] have compared the results from destructive and conservative procedures. Generally speaking, RCTs comparing the results from all the various procedures used for the treatment of varicose veins unavoidably suffer from the "detection" bias (instrumental outcome assessors are not blind with regard to the performed procedure) and from the "performance" bias (the awareness of both participants and personnel with regard to the assigned treatment arm)[32]. Thus, all RCTs show a "moderate quality" evidence according to the GRADE criteria[33, 34], which does not mean at all that the treatment providing better results cannot represent a "strong, in favor" recommendation, as quality of the evidence and strength of recommendations are quite different concepts[35, 36]. Further, in some RCTs including the CHIVA cure[27, 29] there are relevant biases that affect the CHIVA arm, concerning both the selected CHIVA "strategy" (type III shunts treated by the CHIVA 1 procedure)[5, 11-14] and the surgical "tactic" (crossectomy instead of crossotomy)[5, 14, 37], so that these RCTs should not be taken into any consideration.

That being said, hereafter the results of the RCTs and MAs that have compared the results from destructive and conservative procedures are shortly reported. The RCT of Carandina, et al.[25] compared the results from GSV stripping and those from CHIVA Cure and found a significantly lower incidence of recurrences in the CHIVA arm. Parés, et al.[28], in their RCT with 3 arms (stripping with clinical marking, S-CM, stripping with duplex marking, S-DM, and CHIVA Cure) also found an incidence of recurrences significantly lower in the arm CHIVA with respect to the arm S-CM and to the arm S-DM. The MA of Bellmunt-Montoya, et al.[30] analyzed the three RCTs on the comparison between stripping and CHIVA Cure available at the time of the study[25, 27, 28] and found a significantly lower cumulative Risk Ratio for recurrences in favor of the CHIVA Cure. Finally, Guo, et al.[31] in their more recent "network" metanalysis of 39 RCTs concerning all available procedures to treat varicose veins, alone or in combination, found that the CHIVA Cure was associated with significantly higher Odds Ratios with regard to the successful treatment rate and significantly lower Odds Ratios with regard to the recurrence rate.

Altogether, the results from the aforementioned RCTs and MAs also controvert the widely held theory that the retrograde GSV flow resulting from crossectomy/

crossotomy, and more generally from any conservative procedures, might trigger the occurrence of recurrences[38].

In conclusion, this short review shows that GSV sparing treatments are actually beneficial to the hemodynamics of the venous system. In fact, although both destructive and conservative procedures improve, till normalization, the plethysmographic reflux parameters, destructive procedures seriously jeopardize the venous drainage of the lower limb. This makes the venous hemodynamics unstable, resulting in a more frequent occurrence of recurrences that are an expression of the need of lower limb superficial tissues to somehow empty out and that never show a trans-compartmental reflux point. On the contrary, conservative procedures, in spite of leaving a retrograde flow in the GSV, reduce the pathogenic effects of the reflux, due to the dramatic reduction of the reflux flow, and preserve the venous drainage of the lower limb. This makes the venous hemodynamics more stable and, consequently, results in a significantly less frequent occurrence of recurrences that always show a trans-compartmental reflux point.

Saphenous sparing treatments: bullet points

- To reduce the pathogenic effects of the venous reflux on lower limb tissues it is not necessary removing, or occluding, the GSV;
- The saphenous retrograde flow resulting from sparing treatments shows a much lower pathogenic potential than that found in patients with an open escape point;
- Contrary to destructive procedures, saphenous sparing treatments preserve the drainage of the superficial tissues of the lower limb;
- Saphenous sparing treatments result in a significantly lower incidence of recurrence over time than destructive treatments;
- Saphenous sparing treatments are actually more beneficial to the hemodynamics of venous system than destructive treatments.

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