Factors affecting the evolution of type III shunts of the Greater Saphenous Vein after the first step of the CHIVA 2 strategy.

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Abstract

The CHIVA 2 strategy is a two-step surgical procedure for treating type III venous-venous shunts in the territory of the Greater Saphenous Vein (GSV). The first step consists in disconnecting the incompetent GSV tributary, either N3 or N4. Once a new N2 re-entry perforator vein has developed, or the GSV incompetence has reached the pre-existing N2 re-entry perforator vein, both documented by the re-appearance of GSV reflux during the follow-up, the second step of the CHIVA 2 strategy, i.e. the closure of the saphenous-femoral junction, can be performed.

In this paper we addressed the intriguing question of whether it was possible to identify the pre-operative factors able to favourably affect the hemodynamic stability of type III shunts of the GSVs treated by the only first step of the CHIVA 2 strategy.

Our data show that the pre-operative GSV anterograde flow, detectable all along the GSV course even soon after the first step of the procedure, plays a pivotal role in ensuring the hemodynamic stability of the treated GSV, which may not need the second step up to 45% of cases.

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Keywords: Varicose veins, CHIVA 2 strategy, Greater Saphenous Vein, Venous Hemodynamics.

Introduction

The CHIVA 2 strategy [1,2] is a conservative and hemodynamic surgical procedure for treating varicose veins in the territory of the Greater Saphenous Vein (GSV). This kind of procedure is applied essentially in the case of type III venous-venous shunts (fig. 1A and 2A) that represent the most frequent hemodynamic pattern of varicose veins [3]. These shunts share with type I venous-venous shunts the escape point from the deep venous system, generally represented by the Saphenous-Femoral Junction (SFJ), but contrary to type I shunts, no GSV re-entry perforator vein is detectable proximally to the origin of the most distal incompetent GSV tributary.

This apparently speculative detail actually affects the CHIVA strategy, because in the case of type III shunts disconnecting the escape point and the incompetent GSV tributaries at the same time often results in non-draining GSVs [4], as there is no GSV re-entry perforator vein which drains back the blood coming from the SFJ into the deep venous system. The absence of a re-entry perforator vein negatively affects the stability of the system resulting in an increased tendency to develop recurrences [4].

Thus, the CHIVA 2 strategy was conceived as a two-step procedure [2, 5], whose first step consists in the disconnection flush with the GSV of the tributary, either N3 or N4, leading to the re-entry perforator vein (fig. 1B and 2B), without performing any surgical gesture on the SFJ. As the first step of the CHIVA 2 strategy leaves the SFJ open, the finding of a GSV calibre more than 7 mm is considered as a contra-indication, given the risk of GSV thrombosis and the consequent risk of pulmonary embolism [2]. The first step of the CHIVA 2 strategy is aimed at re-modelling the GSV hemodynamics by promoting the development of a new GSV re-entry perforator vein, or the progression of the GSV incompetence till the pre-existing GSV re-entry perforator vein. In other words, the first step of the CHIVA 2 strategy is aimed at transforming a type III venous-venous shunt into a type I shunt. The development of the new GSV re-entry perforator vein, or the progression of the GSV incompetence till the pre-existing GSV re-entry perforator vein, are both documented by the re-appearance of GSV reflux during the follow-up (fig. 1C and 2C). Once the GSV re-entry perforator vein has developed, or the GSV incompetence has reached the pre-existing GSV re-entry perforator vein, the second step of the CHIVA 2 strategy, i.e. the closure of the SFJ [1, 6], can be performed without resulting in non-draining GSVs [4] (fig. 1D and 2D).

In some cases, the re-appearance of GSV reflux after the first step of the CHIVA 2 strategy may also be due to the "jump" of the GSV tributary ligature, which means that the aim of the first surgical gesture of the CHIVA 2 strategy has failed: however, a detailed discussion on how to address the issue is beyond the scope of this paper.

The re-appearance of GSV reflux after the first step of the CHIVA 2 strategy has been poorly investigated and for short follow-ups, so that the results reported in the literature are quite conflicting. For instance, at 6-month follow-up Zamboni et al. [7] reported GSV reflux in 15% pts. while Escribano et al [8] reported GSV reflux in 92% pts. Further, at least according to our experience, not all the pts. undergone the first step of the CHIVA 2 strategy will necessarily undergo the second step.

Thus, in this paper we addressed the intriguing question of whether it was possible to identify the pre-operative factors able to favourably affect the hemodynamic stability of type III shunts of the GSVs treated by the only first step of the CHIVA 2 strategy, at least for a reasonably long follow-up.

Subjects and Methods

Three-hundred-eighteen patients (pts.) with varicose veins in the GSV territory due to a type III venous-venous shunt and without deep venous system diseases, nor pelvic escape points draining into the GSV, nor incompetent perforator veins along the GSV incompetent segment, were included in the study.

All pts. showed a GSV calibre less than or equal to 7 mm and could safely undergo the peripheral time of the CHIVA 2 procedure. The operation was performed under local anaesthesia and pts. left the surgery about one hour after the procedure. No adverse event occurred, either peri-operatively or during the follow-up, that was scheduled 1 week, 1 month, 6 months and then every year after the operation. All pts. included in the study showed a follow-up more than or equal to 1 year.

Obesity was defined as a Body Mass Index more than or equal to 30. With regard to the CEAP classification [9], we only considered the item C, as the other CEAP items were the same for all the pts. included in the study (Ep, As and Pr). GSV calibre was assessed at the thigh level, about 15 cm from the groin [10]. The incompetence of the GSV was classified as "short", if the origin of the incompetent GSV tributary was within the proximal half of the thigh, and as "long", if the origin of the incompetent GSV tributary was below [2, 5]. Both anterograde GSV flow, during muscle contraction, and reflux, during muscle relaxation, were assessed using the dynamic test known as Vasculab manoeuvre [11]. Pre-operative GSV anterograde flow was defined as an anterograde flow detectable all along the GSV course, particularly in the competent segment (fig. 3), also involving the SFJ, even soon after the disconnection of the incompetent GSV tributary. GSVs with hypoplastic segments, in which the anterograde flow was not detectable, were considered as not-showing an anterograde flow, unless the hypoplastic GSV segments were by-passed by a straight longitudinal N4. Further, also GSVs in which the anterograde flow was only detectable in some segments, were classified as not-showing an anterograde flow.

Finally, our 318 pts. were divided into two subgroups: pts. who showed the re-appearance of GSV reflux at any time during the follow-up, either due to the development of the GSV re-entry perforator vein or to the “jump” of the GSV tributary ligature or both, and pts. who never showed GSV reflux throughout the follow-up.

Statistical analysis was performed using the STATA 10.0 software (College Station, Texas, USA) and conducted in two steps. First, univariate analysis was performed to ascertain possible statistically significant differences between pts. who showed the re-appearance of GSV reflux at any time during the follow-up and pts. who never showed GSV reflux throughout the follow-up. Then, all variable showing a statistically significant difference were entered into a stepwise ($p<0.05$) multivariate logistic regression model to assess the strength of the association (Odds Ratios and related 95% CI) of each independent variable with the re-appearance of GSV reflux throughout the follow-up, that was considered as the dependent variable.

Results

In the whole group the mean follow-up was 8.5 ± SD 14.5 yrs. (range 1-30 yrs.).

Table 1 shows the characteristics of the whole group and of the two subgroups according to the presence (n. 245, 77%) vs. absence (n. 73, 23%) of GSV reflux throughout the follow-up, along with the univariate analysis.

Table 2 shows the stepwise ($p<0.05$) multivariate logistic regression model on factors affecting the re-appearance of GSV reflux throughout the follow-up. Higher CEAP C scores showed a modest/moderate positive association, while female sex showed a moderate/strong negative association and pre-operative GSV anterograde flow showed a very strong negative association.

An ancillary analysis was also conducted on the 175 pts. in which the femoral valve had been assessed. Of these, 120 (69%) showed a functioning femoral valve, evenly distributed ($p=0.623$) between pts. who showed the re-appearance of GSV reflux throughout the follow-up (92 over 136, 68%) and pts. who did not (28 over 39, 72%). The stepwise multivariate logistic regression conducted on this subgroup provided results completely comparable to those obtained in the whole group.

Pts. showing pre-operative GSV anterograde flow had a significantly lower rate of re-appearance of the GSV reflux throughout the follow-up when compared to pts. who did not (79 over 144, 55% vs. 166 over 174, 95%, $p<0.001$).

Among the 245 pts. who showed the re-appearance of GSV reflux throughout the follow-up, 171 (70%) developed a GSV re-entry perforator vein, 59 (24%) a “jump” of the GSV tributary ligature and 15 (6%) both. The distribution of GSV re-entry perforator veins, “jumps” of the GSV tributary ligature and both was not significantly different ($p=0.087$) between pts. who showed a pre-operative GSV anterograde flow (59 over 79, 75%, 19 over 79, 24% and 1 over 79, 1.3% respectively) and those who did not (112 over 166, 67%, 40 over 166, 24% and 14 over 166, 8.4%, respectively).

Women showed a significantly lower rate of re-appearance of the GSV reflux when compared to men (187 over 254, 73% vs. 58 over 64, 91%, $p=0.004$). Further, women also showed a significantly lower CEAP C score (mean 2.88 ± SD 0.66 vs. 3.04 ± 0.91, $p=0.021$) and a smaller, though not statistically significant GSV caliber (mean 5.91 ± SD 0.90 vs. 6.12 ± 0.69, $p=0.083$).

Finally, in the whole group after the 1^{st} step of the procedure the mean reduction of the GSV caliber was 1.96 ± SD 1.04 mm ($p<0.001$).

Discussion

In this paper we addressed the issue of whether it was possible to identify the pre-operative factors able to favourably affect the hemodynamic stability of type III shunts of the GSVs treated by the only first step of the CHIVA 2 strategy.

We found that pre-operative GSV anterograde flow showed a very strong negative association with the re-appearance of GSV reflux throughout the follow-up and that female sex showed a moderate/strong negative association, while higher CEAP C scores showed a modest/moderate positive association. In other words, pre-operative GSV anterograde flow and female sex prevent from the re-appearance of the GSV reflux, while higher CEAP C scores foster the re-appearance of GSV reflux.

Understanding how the pre-operative GSV anterograde flow might play a protective role against the re-appearance of GSV reflux after the first step of the CHIVA 2 strategy is quite challenging and needs first to focus on the hemodynamic effects of the first step of the procedure.

The disconnection of the incompetent GSV tributary leading to the re-entry perforator vein suppresses the GSV reflux, at least for a variable lapse of time, without changing the hydrostatic pressure in the GSV at the disconnection level.

Further, the disconnection of the incompetent GSV tributary leading to the re-entry perforator vein eliminates the "aspirating" effect of the muscular pump on the GSV and this has two effects:

- the static pressure does not act any more on the internal GSV wall, which reduces the trans-mural pressure, as documented by the reduction of the GSV calibre reported in the literature [10] and confirmed by our results;

- the dynamic pressure, too, does not act any more on the internal GSV wall, which eliminates the shear stress [7]. The decrease in the shear stress causes the leucocyte adhesion to the endothelium which triggers an inflammatory process [12] able to damage the GSV competent valve located below the origin of the ligated incompetent GSV tributary, thus resulting in the descending progression of the GSV incompetence. Further, the inflammatory process may also be responsible for the "jump" of the GSV tributary ligature. In fact, a "jump" may be due either to the incompetence of a previously competent GSV tributary (rectilinear "jump"), as a consequence of the inflammatory involvement of its ostial/parietal valve, or to the formation of new vessels (tortuous "jump"), as a consequence of the local production of the Vascular-Endothelial Growth Factor and fostered by the presence of granulation tissue resulting from the surgical gesture.

In other words, the first step of the CHIVA 2 strategy shows a sort of "paradox effect", because on one side, it improves the GSV hemodynamics in terms of static (lateral) pressure, but, on the other, it fosters the evolution towards the re-appearance of the GSV reflux, due either to the progression of the GSV incompetence, till reaching a newly-developed or pre-existing GSV perforator vein able to act as an efficient re-entry, or to the "jump" of the GSV tributary ligature.

Coming to the GSV anterograde flow, although sometimes cannot be detected at Doppler examination, due to the limitations of the technique that cannot detect speeds less than 6cm/sec. it is, actually, always present, as documented by the B-Flow and, especially, by the B-Flow HD.

The anterograde flow results from a complex interplay of the residual pressure, which generates a continuous flow, with the action of several pumps, that superimpose a phasic component: the thoraco-abdominal pump is responsible for the phasic changes that occur at rest during breathing or speaking, and the peripheral pumps are responsible for the phasic changes that occur during walking or upstanding. Interestingly, it has been shown [13] that during walking the systolic phase lasts much longer than the diastolic phase.

Thus, the protective role of the GSV anterograde flow might be explained by the fact that the anterograde flow maintains an adequate shear stress avoiding, or limiting, the inflammatory process that is responsible for the descending progression of the GSV incompetence and/or for the "jump" of the GSV tributary ligature, and, hence, for the re-appearance of the GSV reflux. Interestingly, it has been shown [14] that the suppression of the oscillatory component of the reflux results in a favorable modulation of the inflammatory endothelial phenotype that mitigates the inflammatory process responsible for the sustained damaging of venous valves and wall.

With regard to the protective role of female sex against the re-appearance of the GSV reflux, it may be explained by the fact that women, compared to men, seek for treatment in earlier stages of the diseases, as documented by the significantly lower CEAP C score and the smaller, though not statistically significant GSV caliber.

Finally, with regard to the fostering effect of higher CEAP C scores on the re-appearance of GSV reflux it may be explained by the fact that higher CEAP C scores are expression of more advanced disease, which is associated with more severe inflammatory endothelial phenotypes [11].

Conclusions

Our data show that the pre-operative GSV anterograde flow, detectable all along the GSV even soon after the first step of the CHIVA 2 strategy, plays a pivotal role in ensuring the hemodynamic stability of the treated GSV, which may not need the second step of the procedure up to 45% of cases, at least for a reasonably long follow-up.

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Tables

Table 1 - Characteristics of the whole group and of the two subgroups, with univariate analysis.					
		Whole Group (n.318)	**Presence of GSV reflux at any time of the follow-up** (n.245, 77%)	**Absence of GSV reflux throughout the follow-up** (n.73, 23%)	*p (*)*
Age at operation, (yrs), mean ± SD		52 ± 14,4	52 ± 14.0	51 ± 15,5	*0.337*
Female sex, (Y/N), n.(%)		254 (80)	187 (76)	67 (92)	***0.004***
Obesity, (Y/N), n.(%)		25 (8)	20 (8)	5 (7)	*0.714*
	2, n.(%)	85 (27)	55 (22)	30 (41)	
	3, n.(%)	186 (58)	147 (60)	39 (53)	
CEAP Classification - item C	4 a, n.(%)	4 (1)	4 (2)	0 (0)	***0.008***
	4 b, n. (%)	39 (12)	35 (14)	4 (5)	
	5, n.(%)	0 (0)	0 (0)	0 (0)	
	6, n.(%)	4 (1)	4 (2)	0 (0)	
GSV caliber, (mm), mean ± SD		5.96 ± 0.79	6.05 ± 0.78	5.75 ± 0.77	***0.004***
Long GSV Incompetence, (Y/N), n.(%)		259 (81)	209 (85)	50 (68)	***0.001***
Pre-op GSV Anterograde Flow, (Y/N), n.(%)		144 (45)	79 (32)	65 (89)	***0.001***

(*) From Student "*t*" test or Pearson "*chi-square*" test, as appropriate.

Table 2 - Stepwise (p<0.05) multivariate logistic regression model of factors affecting the re-appearance of GSV reflux throughout the follow-up.

(Number of obs 318, LR chi-square 99.94, Prob > chi-square 0.000, Pseudo R2 0.292)

	OR (95%CI)	***p***
Female sex (Y/N)	0.198 (0.074 - 0.526	*0.001*
CEAP Classificaion (score 2-6)	2.072 (1.238 - 3.470)	*0.006*
Pre-op GSV Anterograde Flow (Y/N)	0.055 (0.025 - 0.124)	*0.001*

GSV caliber and Long GSV Incompetence were discarted by the model (p 0.075 and 0.265, respectively).

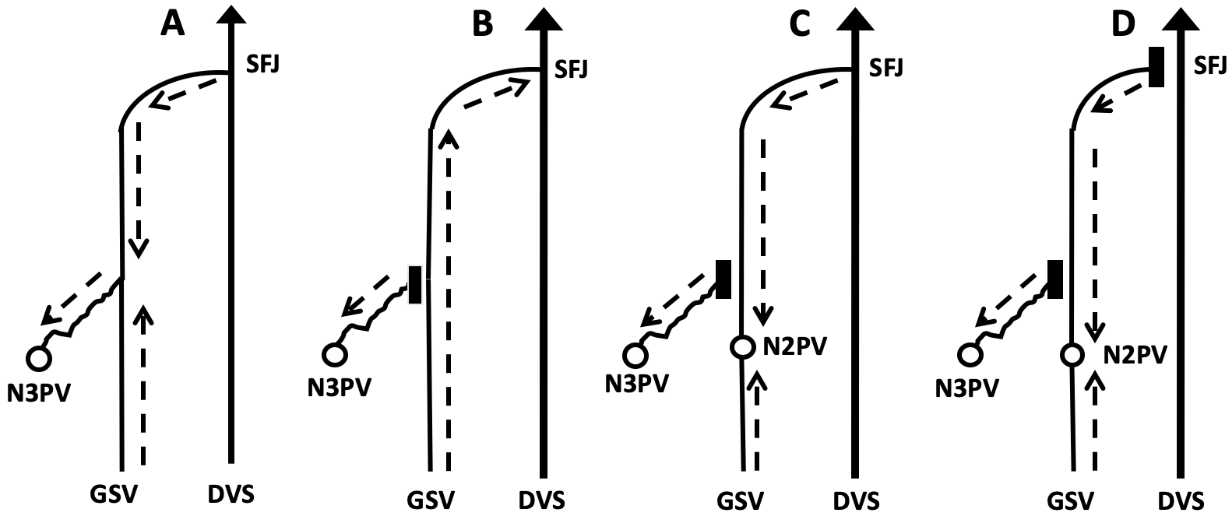

Figure 1

Figure 1 – A: Type III shunts with an incompetent N3 tributary draining into an N3 re-entry perforator vein; **B**: 1st step of the CHIVA 2 strategy; **C**: re-appearance of the GSV diastolic reflux due to the development of a new N2 re-entry perforator vein; **D**: 2nd step of the CHIVA 2 strategy.

GSV = Greater Saphenous Vein; SFJ = Saphenous-Femoral Junction; DVS = Deep Venous System; N3PV = N3 Perforator Vein; N2PV = N2 Perforator Vein.

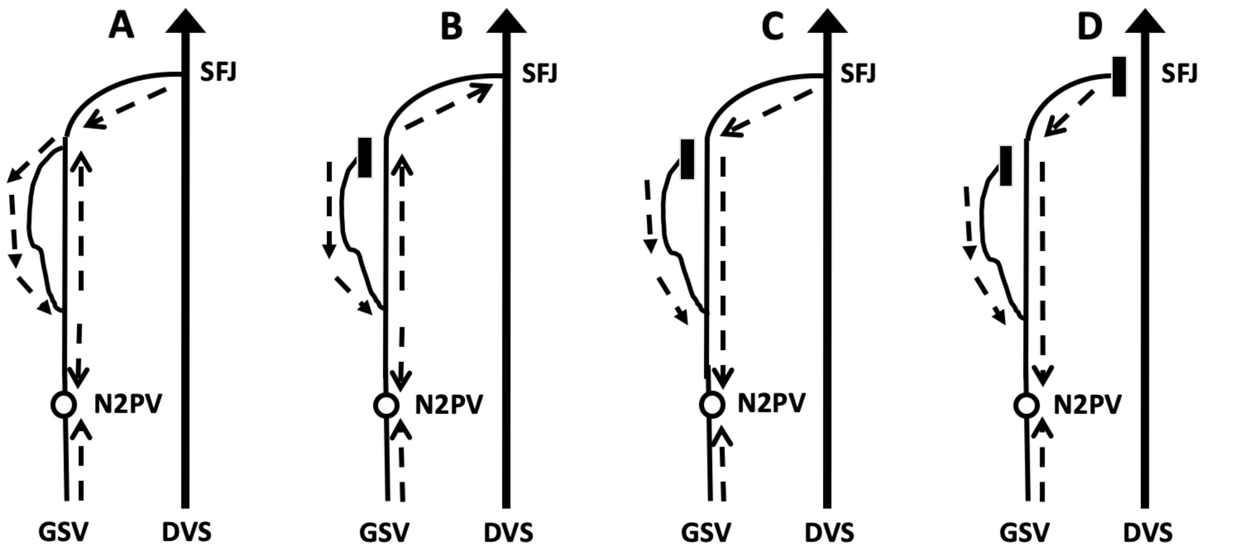

Figure 2

Figure 2 – A: Type III shunts with an incompetent N4 tributary draining into an N2 re-entry perforator vein; **B**: 1st step of the CHIVA 2 strategy; **C**: re-appearance of the GSV diastolic reflux due to the progression of the GSV incompetence till the pre-existing N2 re-entry perforator vein; **D**: 2nd step of the CHIVA 2 strategy.

GSV = Greater Saphenous Vein; SFJ = Saphenous-Femoral Junction; DVS = Deep Venous System; N2PV = N2 Perforator Vein.

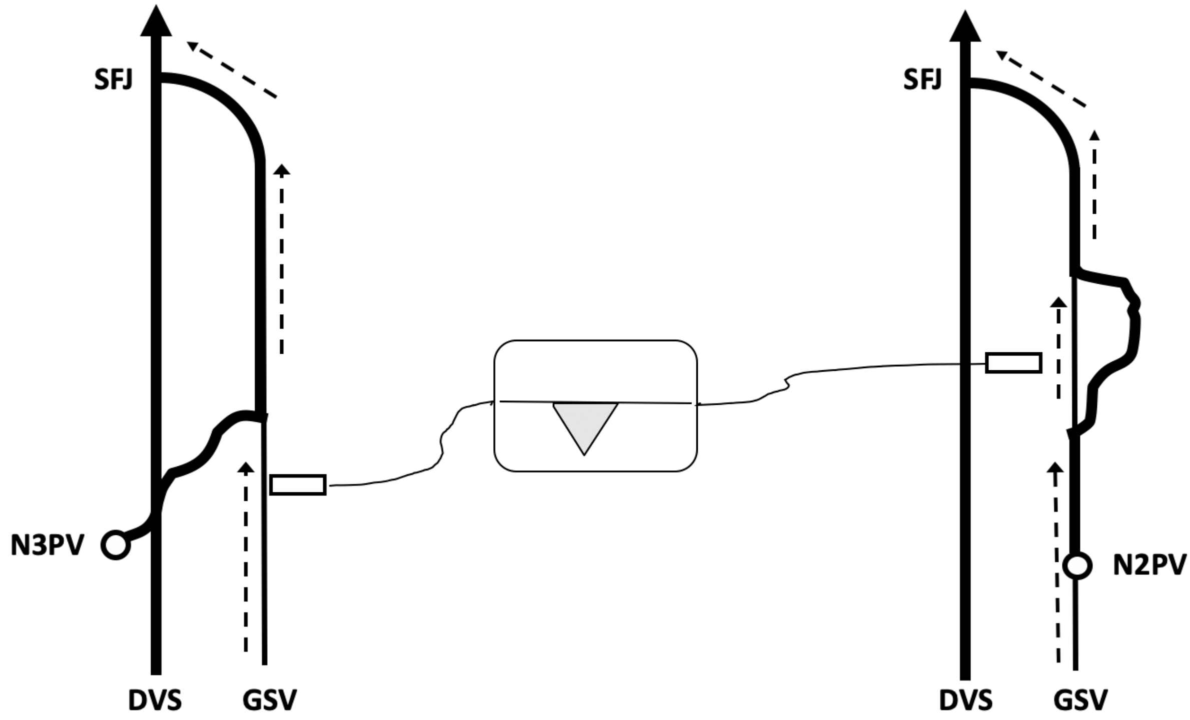

Figure 3

Figure 3 – Assessment of the anterograde GSV flow in the competent segment during the systolic phase of the Vasculab manoeuvre.

GSV = Greater Saphenous Vein; SFJ = Saphenous-Femoral Junction; DVS = Deep Venous System; N3PV = N3 Perforator Vein; N2PV = N2 Perforator Vein.