VENOUS INSUFFICIENCY REVIEW

Significant features characterizing the nature of varicose vein disease

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Abstract The following features characterize varicose vein disease: 1) Venous reflux, 2) Inherent weakness of the vein wall, 3) Tendency to recurrence. Venous reflux is the most important pathological hemodynamic phenomenon causing ambulatory venous hypertension and evoking chronic venous insufficiency; it is released by the ambulatory pressure gradient, which arises during calf pump activity between thigh and lower leg veins. Inherent weakness of the vein wall entails increased vein distensibility. The impaired vein wall structure is not able to resist the dilatation force of the hydrostatic and intra-abdominal pressure; the veins in the lower extremity subsequently dilate, become incompetent, and tend to form varicose veins. Abolition of saphenous reflux removes the hemodynamic disturbance but it simultaneously generates preconditions for reflux recurrence. This run of events is triggered by the drainage of venous blood from the thigh saphenous system into deep lower leg veins, which occurs during calf pump activity. The dividing line of the ambulatory pressure gradient that is located in healthy people just below the knee joint is displaced into the thigh between the femoral vein and the incompetent thigh saphenous system; in this way, pressure gradient between the femoral vein and the incompetent saphenous system occurs and starts the chain of events that evokes reflux recurrence. Hindrance of the untoward drainage at the knee level would prevent generation of this prerequisite for reflux recurrence.

Keywords Varicose vein disease, venous reflux, reflux recurrence, weakness of varicose vein wall, venous pressure

Introduction

Varicose vein disease has been characterized by three important features: venous reflux, inherent deficient structure of the venous wall, and tendency to recurrence. Venous reflux running through the incompetent saphenous system into deep lower leg veins is the most important hemodynamic phenomenon in primary varicose veins. It interferes with the physiological decrease in ambulatory venous pressure in the veins below the knee and causes ambulatory venous hypertension. The coaction of the deficient vein wall structure and the intravenous hydrostatic as well as intra-abdominal pressure induces dilatation of varicose veins. The valve leaflets in the dilated vein cannot close anymore; the so called *relative valve incompetence* occurs. It can be reversible. The venous diameter diminishes after abolition of reflux[1-4], and the valves can retrieve their competence.

The therapeutic procedures used for treatment of varicose veins are pointed at interruption of saphenous reflux. Nevertheless, neither of the therapeutic methods is able to achieve definite healing of varicose veins and to prevent recurrences. Thus, the tendency to recurrence is an unfavorable, embarrassing feature of varicose vein disease. The real reason for this tenacious tendency to recur has not yet been ascertained; nevertheless, it seems probable that a hemodynamic phenomenon – the drainage of venous blood from incompetent thigh saphenous system into deep lower leg veins – may trigger the run of events that cause

recurrent reflux[5]. With this in mind, a conception of the therapeutic procedure aimed at contravening this tendency to recurrence has been laid out.

Venous reflux

Venous reflux is the most common cause of venous hemodynamic disorders. Initially, incompetence of deep and calf perforating veins has been generally regarded as the most important pathological phenomena responsible for the development of chronic venous insufficiency, whereas significance of saphenous reflux has been underestimated. However, strong saphenous reflux is able to induce the severest ambulatory venous hypertension and evoke the severest congestive symptoms of chronic venous insufficiency, as documented by venous pressure measurements and plethysmography[6-12]. On the other hand, the pathogenetic significance of different deep venous segments differs substantially. So incompetence of iliac veins is generally thought to be hemodynamically irrelevant. In regard to femoral vein incompetence, opinions differ considerably ranging between denying its hemodynamic importance[13-16], and emphasizing that it is the main cause of the most serious form of chronic venous insufficiency[17-21]. Based on the results of venous pressure measurement, Höjensgard and Stürup[13] claimed that since no decrease in pressure occurs in the popliteal vein, there is no tendency to retrograde flow in the femoral vein. In studies presenting results after femoral valve repair, superficial vein surgery was mostly performed contemporaneously[17-21], so that the real hemodynamic improvement attributable to the femoral valve repair could not be plausibly evaluated. On the other hand, plethysmographic measurements evidenced that in patients with simultaneous great saphenous vein and femoral vein incompetence the abolition of saphenous reflux alone without influencing the femoral incompetence removed the hemodynamic disorders[16,22,23]. Thus, it can be resumed that incompetent valves in the femoral/popliteal vein do not induce per se the hemodynamic disturbance; femoral/popliteal vein incompetence becomes hemodynamically effective in combination with either deep lower leg veins incompetence or saphenous vein incompetence. As concerns incompetence of deep lower leg veins, it causes an irreparable damage to the calf muscle venous pump and is hemodynamically of prime importance.

The term "venous reflux" has not so far been unambiguously perceived, which impairs the comprehension of the venous hemodynamics. Some venous flows in the lower extremity are mistakenly denoted "reflux", although they have nothing to do with venous reflux, e.g. the outward flow within calf perforators and the systolic outward flow through the incompetent saphenous-popliteal junction. Therefore, the following definition of venous reflux is proposed.

*Venous reflux in the lower extremity is a **diastolic, retrograde/centrifugal, pathological flow of venous blood** within incompetent venous channel(s) connecting both poles of the **ambulatory pressure gradient** that arises during the diastolic phase of the calf pump activity and amounts to **37.4 ± 6.4 mm Hg**[24,25], may be **> 33± 11.8 mm Hg**[26]. The higher pole of the pressure gradient lies in the popliteal, femoral or iliac vein, the lower pole in deep lower leg veins. Reflux exceeds the duration of the physiological centrifugal streaming lasting 200-300 milliseconds, takes more than 0.5 second, and stops as soon as the pressure difference has been equalized. It can also be provoked by increased intra-abdominal pressure propagating into the iliac, femoral, and popliteal vein. Reflux interferes with the physiological decrease in pressure arising during calf pump activity in deep and superficial veins of the lower leg and foot. **Venous reflux causes ambulatory venous hypertension**, the degree of which depends on the intensity of the centrifugal flow expressed in ml/s.*

According to the above mentioned definition, the venous reflux is a centrifugal/retrograde, diastolic, pathological flow streaming downward the great saphenous vein and inward within calf perforators into the deep lower leg veins and causing ambulatory venous hypertension. The fact that the venous reflux within calf perforators is an inward, not outward flow has been evidenced by venous pressure measurements; the diastolic pressure in the great saphenous vein is about 13 mm Hg higher than in the posterior tibial vein[8,13,26]. In addition, the inward refluxing streaming within incompetent calf perforator was proven by direct electromagnetic flow measurement[27]. The outward flow within calf perforators is no pathological reflux; it is a systolic, physiological, centripetal/orthograde flow, which streams toward the heart and does not cause any hemodynamic disorder. Calf perforators are innocuous structures, even if enlarged and incompetent, because they are connected to the lower pole of the ambulatory pressure gradient[24]. Similarly, the systolic outward flow through the incompetent saphenous-popliteal junction is also no reflux; it continues in the orthograde direction via the Giacomini vein, the great saphenous vein, and the femoral vein toward the heart; it cannot stream in the retrograde direction toward deep lower leg veins because the systolic pressure in deep lower leg veins is much higher than in the popliteal vein. The refluxing flow downward the small saphenous vein occurs only in the diastolic phase, during which the pressure in deep lower leg veins is quite lower than in the popliteal vein.

Triggering the venous reflux

In the quiet standing position the hydrostatic pressure causes venous hypertension in the veins of the lower extremity; the pressure is equally high in superficial and deep veins[13,26]. No reflux takes place in the veins. Vis a tergo, the remaining heart energy of about 15-20 mm Hg is the motive force propelling venous blood in the orthograde/centripetal direction toward the heart. Venous reflux in the lower extremity is triggered by the ambulatory pressure gradient[25,28], which is generated during calf pump activity between thigh veins with higher pressure and the lower leg veins with lower pressure. The dividing line of the ambulatory pressure gradient is located just below the knee at the beginning of the popliteal vein, as accrues from the direct venous pressure measurements in the posterior tibial vein and the popliteal vein[13,26]. Thus, the incompetent reflux-carrying vein must connect both poles of the ambulatory pressure gradient, i.e. the popliteal, femoral, profunda femoris, or iliac vein with one of the deep veins of the lower leg. Venous reflux takes place during calf muscle relaxation or during calf pump activity (a series of calf muscle contractions and relaxations). Höjensgard and Stürup[13] measured the venous pressure successively in the posterior tibial and popliteal veins. Whereas the high hydrostatic pressure decreased considerably during calf pump activity in the posterior tibial vein, the pressure in the popliteal vein did not decrease; it oscillated but remained at the same high level found in the quiet standing position. Arnoldi[26] measured the venous pressure simultaneously with two catheters, one lying in the posterior tibial and the other in the popliteal vein; he reported pressure difference of 33 ± 11.8 mm Hg occurring between these veins during calf pump activity. Recek and Pojer[25] found a similar pressure gradient of 37.4 ± 6.4 mm Hg.

Hemodynamic consequence of saphenous reflux

Saphenous reflux interferes with the physiological decrease in ambulatory pressure. Depending on its intensity, it causes more or less pronounced ambulatory venous hypertension, congestive symptoms, and chronic venous insufficiency. Interruption of saphenous reflux at any level removes the hemodynamic disorder of any degree of severity and restores physiological hemodynamic values, as proven by plethysmography and venous pressure measurements; this conspicuous therapeutic result has been achieved in spite of the presence of large incompetent calf perforators[29,30], which clearly documented that saphenous reflux was responsible for the hemodynamic disorder, not incompetent calf perforators. Unfortunately, this excellent immediate hemodynamic effect abates in the course of time due to the development of recurrent reflux[30].

Inherent weakness of the vein wall

Varicose vein disease embodies an inherent abnormality of the vein wall structure[31-35], which includes:

- Deficiency in collagen III synthesis
- Lack of elastin
- Fragmenting elastin
- Disproportion in collagen-to-elastin ratio

The inherent vein wall weakness entails increased vein wall distensibility, decreased vein wall contractility, and tendency to permanent dilatation. The impaired vein wall structure is not able to resist the dilatation force of the hydrostatic and intra-abdominal pressure; the veins subsequently dilate, become incompetent, and tend to form varicose veins.

The vein wall deficiency is a generalized phenomenon; it afflicts veins both in the lower and in the upper extremity. Nevertheless, varicose veins appear only in the lower extremity. This is because of the coaction of the hydrostatic and increased intra-abdominal pressure, which comes into effect only in the lower extremity, not in the upper extremity. Under the influence of the hydrostatic and increased intra-abdominal pressure the varicose veins tend to permanent dilatation. The consequence is incompetence of venous valves enabling centrifugal streaming, venous reflux.

Tendency to recurrence

Varicose vein disease has a pronounced tendency to recurrence. This is caused by a hemodynamic phenomenon that arises during calf pump activity. Once the saphenous reflux in the thigh has been abolished (e.g. by crossectomy), a pressure difference is generated during calf pump activity between the femoral vein and the incompetent thigh saphenous system. Treatment of varicose veins evokes namely a curious situation: it starts a new trouble while fixing the problem. Abolition of saphenous reflux removes the ambulatory venous hypertension of any degree of severity and restores normal hemodynamic values but at the same time it creates preconditions for reflux recurrence;

this phenomenon has been called *hemodynamic paradox*[5]. During calf pump activity, the venous blood is drained from the incompetent saphenous system of the thigh into deep lower leg veins, and the lower ambulatory venous pressure extends from deep lower leg veins into the thigh saphenous system. In this way, the dividing line of the ambulatory pressure gradient that is located in healthy people just below the knee, i.e. at the beginning of the popliteal vein, is displaced into the thigh between the femoral vein and the incompetent thigh saphenous system, and gives impetus to the process generating recurrent reflux. The run of events is as follows: pressure gradient –> increased flow through preformed tiny communicating venous channels between the femoral vein and incompetent superficial veins –> enhanced fluid shear stress on the endothelium of these venous communications –> release of vasoactive agent nitride oxide and vascular endothelial growth factor –> progressive dilatation of the communicating channels –> recurrent reflux[36-39]. This process has been called vascular remodelling.

How to counteract the tendency to reflux recurrence

As mentioned above, the undesirable run of events triggering reflux recurrence is induced by the drainage of venous blood from the thigh saphenous system into deep lower leg veins, which installs ambulatory pressure gradient between the femoral vein and incompetent segments of the thigh saphenous system. Thus, the tendency to recurrence can be counteracted by hindering this drainage; that would avert the process leading to the reflux recurrence. In addition, precluding the drainage of venous blood from superficial thigh veins into deep lower leg veins will prevent the development of ambulatory venous hypertension. Based on the behavior of the ambulatory venous pressure, it can be presumed that the external pressure of about 40 mm Hg applied just below the knee in the form of a rubber strip or a pneumatic or hydrostatic manchette would hinder the drainage during calf pump activity. The therapeutic procedure used in the treatment of primary varicose veins should include abolition of the source(s) of saphenous reflux (mostly at the saphenofemoral junction), which removes the hemodynamic disturbance and restores the physiological decrease in ambulatory venous pressure in the veins below the knee. The drainage should be inhibited by interruption of all incompetent subcutaneous venous channels at the knee level, where it can be done easiest and most effectively. All draining veins must pass here the confined space between the skin and the bone or musculature and are easily accessible to treatment. This therapeutic concept was lately published in detail[40].

Conclusion

Venous reflux, inherent defective structure of the vein wall, and the tendency to recurrence are characteristic features of varicose vein disease. Saphenous reflux is the most important pathogenic phenomenon causing ambulatory hypertension and evoking congestive symptoms as well as chronic venous insufficiency. It is triggered by the ambulatory pressure gradient, which is generated during calf pump activity between thigh and lower leg veins. The inherent vein wall deficiency causes increased venous distensibility and decreased contractility; the veins in the lower extremity tend to permanent dilatation due to the impact of the hydrostatic and increased intra-abdominal pressure on the defective vein wall structure. Vein dilatation entails valve incompetence and enables retrograde/centrifugal streaming of venous blood. Abolition of saphenous reflux removes the hemodynamic disturbance of any degree of severity but it simultaneously creates hemodynamic preconditions for reflux recurrence; this curious entanglement of events has been called hemodynamic paradox. The hemodynamic preconditions for reflux recurrence are induced during calf pump activity by the drainage of venous blood from the thigh saphenous system into deep lower leg veins; it follows that preclusion of this drainage would prevent this untoward run of events. With this in mind, conception of a new therapeutic strategy called *Hemodynamic Based Treatment of Varices* has been conceived[40]. This theoretical conception, which is based on proven hemodynamic evidences, could keep the reflux recurrence at bay.

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