Biophysical constraints in varicogenesis

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Introduction

In the last years Varicogenesis (VG) has become a frequent topic of discussion in phlebological magazines. Available evidences support partially an evolution starting from the periphery or Ascending VG (AVG) or in opposition starting from the centre or Descending VG (DVG).
Laboratory findings show ubiquitous biochemical and histological alterations,, above and under the incompetent valves, located also in segments not participating clinically to the disease.
VG can be linked to the structure of the vascular net. It can be spontaneous or secondary to interventions (surgery. Sclerotherapy), events (trauma, thrombosis) influencing the network. The analysis or the reflux structure helps in understanding the starting mechanisms which worsen a pre-existing chronic varicose disease (CVD) and in analysing how these mechanisms interact with local and biochemical factors.

Goals

To clarify the link between the network structure and the origin/evolution of CVD. This knowledge helps to formulate a hypothesis on VG.
To analyse the biophysical constraints in the venous network, which can be the cause of VG evolution.

Definitions

An hemodynamic venous map (MEV) contains Paths and Cycles.
A path connects the periphery to the centre. Inside a cycle the fluid transport is highly inefficient and it comes back to the starting point. Cycles can be direct or indirect. The Cycle Index (CY) show the connectivity exuberance.

Material and methods

A 1st group is constituted by a limited number of patients, examined two or more times by the same operator in a time interval ranging from 2 to 25

years. MEVs are compared in order to localise the anatomic and hemodynamic changes occurred in the venous network.
For each MEV the number of paths (P) and cycles (S) and CY are computed.
The comparison method takes into account the learning curve and the technical and diagnostic evolutions occurring in the time interval.

A 2nd group is constituted by a greater number of patients, always observed by the same operator and undergone to a single MEV.
It's possible to estimate the past and the future of the VG, starting from a single observation, which allows the drawing of simplified curves, which however become more rich and detailed in case of multiple observations.
The estimate is provided by VG curves (VGCs) drawn from the paths (P-VGC) and the cycles (S-VGC) (VNet 2.0, Aquarius s.r.l.).
The mathematical burden of computation is complex and relies on the intensive use of matrix calculus and graph theory theorems.

Results
A common effect in all examined MEVs is the increase of CY, P and S.
Depending on the calibre and the length, cycles have a greater/smaller clinical expression. In observed cases, there are cycles of minimal length, others have a much greater one.

The extensive evaluation of the VGCs is actually in progress.
Some examples of VGCs are provided, with unique and multiple observations.
The behaviour ot S-VGC and P-VGC in the first steps of VG is very interesting and shows not predicted relationships between paths and shunts.

Extreme cases match with a hemodynamic effect

- equally divided between all venous segments
- concentrated in an unique segment

The 2nd case is subjected to a sudden worsening, but it's also more easily cured, as the the therapeutic effect can be targeted.

Discussion

VG depends on the structure of the network, which causes the evolution direction.
As a consequence, the AVG/DVG theories and discussions about don't have much value.
The structure of the network acts as a predisposition (as familiarity) or as a facilitating factor for the evolution of CVD.
The evolution/worsening is a stepwise phenomenon:

1. elementarily at the level of each segment and valve apparatus

2. with visible effects on paths and cycles
3. with the appearance of clinical signs

The activation of one of these steps presupposes the previous, but not the following ones. More simply, VG proceeds following sequentially the points in the table.

Some segments cannot invert their flow alone and this is a practical example of dependence of VG on the structure of the network: valve incompetence can be masked, as a reflux isn't detectable owing to a missing re-enter point.

Another interesting hypothesis suggests that a superficial CVD can worsen by sudden events.
Several cycles could be separated by short competent segments. The sudden failure of some of these segments could cause the clinical/instrumental starting point of an important reflux. i.e., a hemodynamical great CVD could be present in all its components minus one, being at the moment clinically mute.

Phlebodynamometry and pletismography show that normally peripheral districts have a high pressure regimen only after a prolonged orthostatism, as valves open physiologically and the gravitational column acts completely on limb extremity.
In the more frequently observed dynamical conditions instead, valves close physiologically, so that the venous segments, emptied by muscle contraction, don't fill completely and consequently the peripheral venous pressure is lower than in orthostatism.
In addition, some instrumental observations show the development of a conspicuous iliac pressure (extreme tension of the iliofemoral valve during Valsalva) which transmits insignificantly to the common femoral vein (CFV) (continuous anterograde GSV flow during Valsalva, with open terminal SFJ valve), witness of a CFV pressure lower than in GSV.

As a consequence, a high pressure develops in peripherical veins eften after a central valve failure, able to transmit an elevated pressure also in the first phases of the dynamical manoeuvres.

Conclusions

AVG/DVG theories could be far from reality, as VG seems to proceed biologically in an ubiquitous manner and biophysically in a “spotlike” manner.

Biological factors of VG are important.

However, in order to be effective,

any biological factor must act through a physical interface.

The experimental observation of the increase of Metalloproteinase 2 and 9 with a consequent wall dilation in veins subjected to high tension seams to be the missing good chain link between VG biochemistry and biophysics. Retrieving the points in the network which present an increased tension is therefore essential to the study of VG.

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