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REVIEW

LATEST FRONTIERS OF HEMODYNAMICS, IMAGING AND TREATMENT OF OBSTRUCTIVE VENOUS DISEASE

Hemodynamics and volume changes of the venous system

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ABSTRACT

The venous system is aimed to drain tissues, to modulate thermoregulation, and to refill the heart regardless of posture or muscular activity. The organs of the venous system are the pathways that transport the blood from microcirculation to the right atrium, and the pumps, respectively cardiac, respiratory and valvulo-muscular, that move it. This article revises the physiological mechanisms of blood distribution and blood motion within the venous system.

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Key words: Hemodynamics - Veins - Blood circulation.

The venous system is aimed to drain tissues, to modulate thermoregulation, and to refill the heart regardless of posture or muscular activity.[1]

The organs of the venous system are the pathways that transport the blood from microcirculation to the right atrium, and the pumps, respectively cardiac, respiratory and valvulo-muscular, that move it. The venous system adapts permanently the direction, flow, and pressure of blood return. It maintains a transmural pressure favorable to drainage, adapts superficial venous flow to the needs of thermoregulation, and modulates venous blood volume available for the heart.[1]

Chronic venous insufficiency is the incapacity of the venous system to ensure all or part of the functions previously defined. Around 75% of blood volume is distributed in the venous system according to complex regulation based on physic mechanisms. This chapter revises the physiological mechanisms of blood distribution and blood motion within the venous system.

Basic physics

It is a widespread opinion that fluid motion within a conduit is produced by the pressure difference or gradient between the two ends. If this were to be true when we stood a closed-end cylinder vertically and filled it with a fluid, we should expect upward motion in the fluid from the bottom, where the pressure on the cylinder walls is greater, to the top, where the pressure on the cylinder walls is less. In reality, the fluid in the cylinder is completely stationary. The pressure against the cylinder walls (defined as lateral pressure) represents only one part of the total energy of this system; another part is the gravitational potential energy linked to the height level that the fluid occupies (hydrostatic pressure). Since lateral pressure, greater at the bottom and less at the top, is perfectly offset by hydrostatic pressure, greater at the top, less at the bottom, then total energy is absolutely identical in all parts of the system,

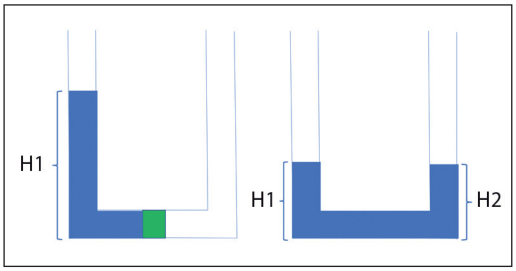

Figure 1.—Principles of communicating vessels. The fluid is distributed in the 2 cilinders, once the green diaphragm has been removed according to a hydrostatic pressure gradient (H1 equal H2) (modified from Franceschi *et al.*[1]).

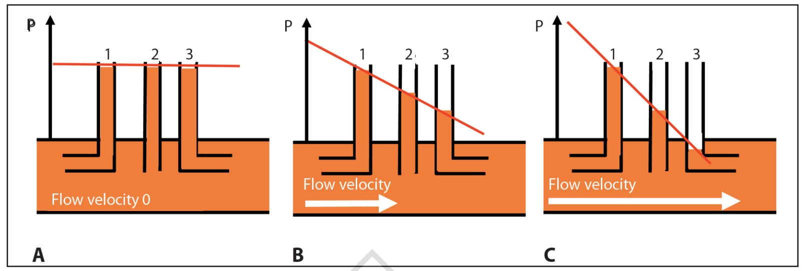

Figure 2.—The experiment of Pitot. A) No fluid motion and the fluid is equally distributed; B) the fluid motion determines a fluid velocity which of course increases the kinetic energy component of the Bernoulli theorem. To maintain a constant energy in the system the lateral pressure is decreased causing aspiration of fluids toward the main conduit; C) increased velocity in the main conduit proportionally increases the aspiration of fluid toward the main conduit (modified from Franceschi *et al.*[1]).

the fluid is stationary.[1-3] Now let us imagine two cylinders placed vertically, connected to each other through a conduit with a removable rigid diaphragm installed internally at the level of the base of the cylinders. If the height of the fluid within the cylinder on the right is greater than the height of the same fluid in the left cylinder, then an energy gradient exists between these two systems. The hydrostatic pressure is greater in the right than in the left cylinder because the fluid on the right is at a higher level. The energy gradient depends solely on the inequality of the levels within the two cylinders. Therefore, it is logical to expect fluid motion from the right cylinder to the left cylinder whenever the rigid diaphragm that separates the two systems is removed (principle of communicating vessels) (Figure 1).

Whenever energy is applied to a high-compliance vascular system, the gradient is capable to overcome inertia and produce the flow inside the conduit.[1-3]

Castelli's law (a development of the equation of continuity) states that flow velocity is inversely proportional to the area of the conduit sections. This means that if the area of a conduit section is reduced, flow velocity increases and conversely, if the area of a conduit section is increased, flow velocity decreases. In addition, if the conduit divides into several branches and the sum of the area of the sections in the different branches is greater than the area of the section in the main conduit, then flow velocity will decrease; conversely, if several branches unite to form one conduit and the sum of the area of the sections in the different branches is greater than the area of the section in the main conduit, then flow velocity increases.[1-4]

Whenever flow is produced in a conduit, the total energy of the system is represented by the sum respectively of the lateral and hydrostatic pressure, as in the case of a closed-end cylinder in a vertical position, but also by the kinetic energy produced by fluid motion.

According to Bernoulli's principle, the sum of the three energetic components above is constant at any point. This means that in a hydrodynamic system (with the fluid in motion) the sum of the first two components is decreased proportionately by the velocity of the fluid. This concept is very well expressed by the experiment of Pitot tubes (Figure 2).[1]

Although blood is not a Newtonian fluid and the venous vessel is not an ideal conduit, the Bernoulli theorem, the communicating vessel phenomenon and the Castelli's law are fundamental principles to be taken into consideration. The main limitation is not in the interpretation of the phenomena, rather in the impossibility to calculate hemodynamics with the same precision of ideal fluid dynamics.

Venous drainage in static conditions

Pitot tubes experience summarizes all the concepts expressed until now. Regarding blood distribution in supine posture and static conditions, Figure 2A shows how it is regulated by the principle of communicating vessels. This means that the individual relaxes supine, the hydrostatic pressure is equalized in the body and the blood is distributed equally within the venous system. If the individual puts their legs in the air, getting higher up respect the right atrium, the hydrostatic pressure becomes negative and the blood redistributes more in the head and trunk (Figure 3).[1-10] Changing posture to the

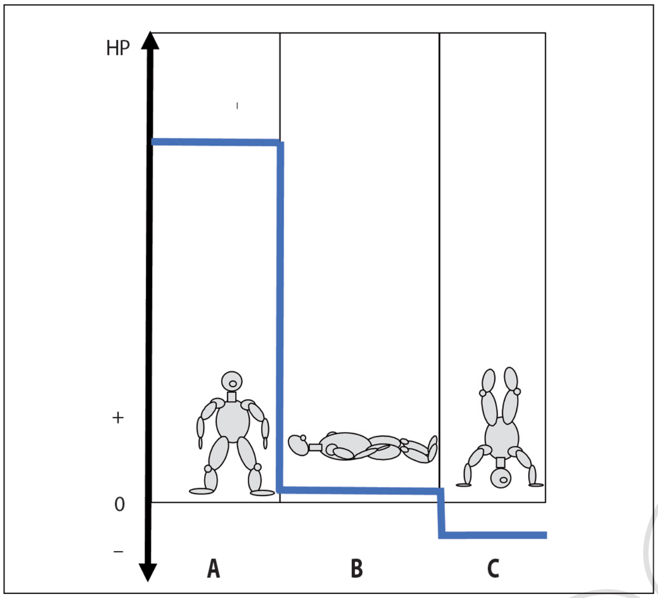

Figure 3. —A) In healthy and CVD subjects the hydrostatic pressure (HP) in orthostatic conditions is dependent from the distance between the ankle and the right atrium; B) if the person is in supine posture the blood is distributed equally within the venous system and the hydrostatic pressure is low and balanced in all segments; C) finally, if the person puts their legs higher compared to the heart, the HP becomes negative.

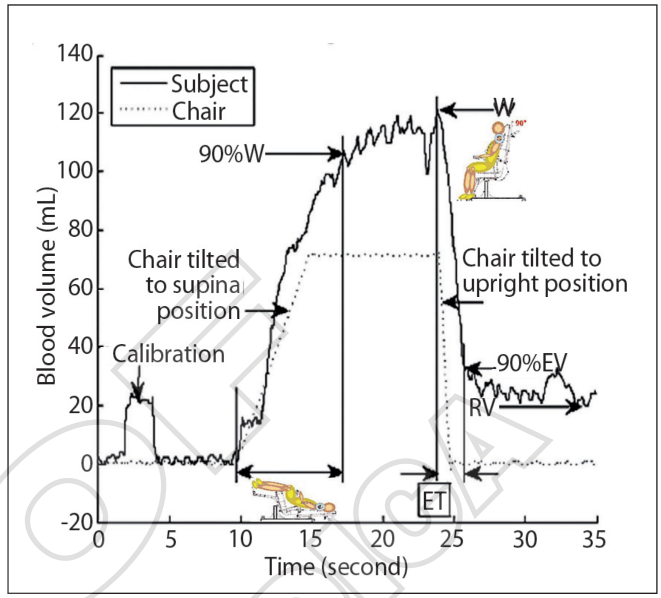

Figure 4.—After calibration in the subject in supine posture the neck volume is progressively filled by the blood coming from the lower part of the body into a plateau (VV and 90% VV). By tilting the subject in upright, blood is rapidly drained giving the possibility to assess the ejected volume (EV) and the little residual volume (RV) (modified from Zamboni *et al.*[12]).

fixed orthostatic condition, 70% of the blood is located below the diaphragm line. Approximately after 30 s the valves are open and the static blood is in free communication within the venous system. Of course, in the latter condition the venous ankle pressure raises and ultimately equals the height of the blood column between the right atrium and the ankle (Figure 3).[1-10]

The same happens in the upper part of the body. If you should put a plethysmography collar around the neck you measure the blood volume in different postural and gravitational conditions (Figure 4). When the subject is tilted backwards into the supine position, the sensor collar is able to detect the redistribution of blood coming from the sub-diaphragmatic part of the body into the IJVs, causing the blood to pool and plateau (Figure 4). The filling phase shows a plateau permitting the calculation of the filling time (FT) as well as respectively of the venous volume (VV), and 90% VV. When the subject is returned to the upright position, the gravitational gradient meant that the blood could readily escape through the cervical veins with the result that they exhibited a short ejection time (ET), with corresponding big ejection volume (EV, 90% EV) and a little residual volume (RV) (Figure 4).[11, 12]

The experiments above tell us that the hydrostatic pressure varies continuously according to the postural changes. Looking at the large veins of the body, in the iliac veins and in the inferior vena cava the hydrostatic pressure is rarely negative. It accounts for 3-8 cmH_2O in supine position, with values between 20-40 cmH_2O in standing. Moreover, in the jugular veins the pressure is negative in upright, exactly as in the legs when they are higher compared to the heart. Low pressure regimen and the big variability of pressure in the large veins both suggest that stents with high radial force may be useless and overstressing the venous wall.

The hierarchy of the venous emptying in hemodynamic conditions

Getting back to Pitot tubes in Figure 2B, C it is clearly depicted that when the fluid is in motion the lateral pressure is decreased proportionally to the increment of the velocity in order to maintain constant the total

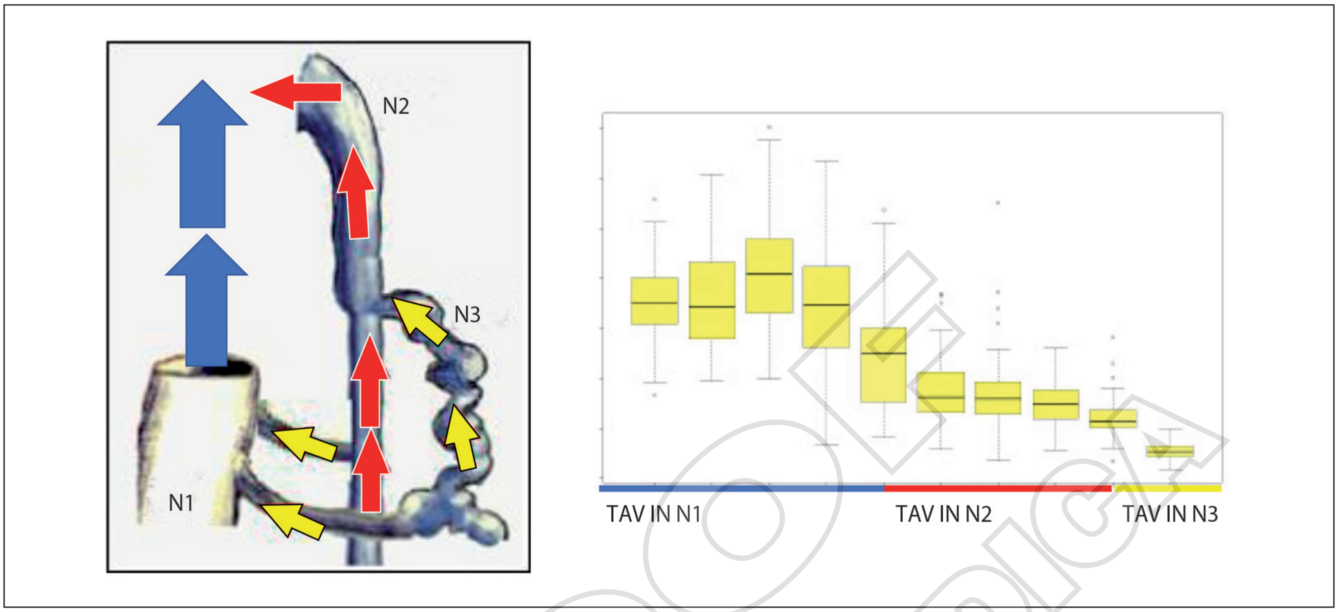

Figure 5.—Muscular contraction transduce energy to the deep veins, resulting in higher time average velocity (TAV) in network 1 (N1). The latter is composed respectively of the iliac veins and the femoral popliteal and tibial axes. TAV is proportionally reduced respectively in network 2 (N2), which is composed of the great and short saphenous vein, and in the subcutaneous tributaries (N3). The TAV gradient explains why the N3 tributaries drain into the N2 and N1, according to the Bernoulli theorem and Venturi effect (modified from Gianesini *et al.*[13]).

energy of the system. Velocity is the second hierarch of the venous system, out of the force of gravity. Flow velocity depends from the valvulo muscular, cardiac and respiratory pumps which transmit kinetic energy to the blood in the venous system. The dominance of one pump upon the others depends from the location of the venous segment and from the posture.

The venous conduit with higher blood flow velocity becomes the main collector where the blood is drained from the other segments of the venous network, exactly as in the Pitot' tubes. For instance in the lower limbs the muscular contraction favourites higher velocity in the deep venous compartment with lower lateral pressure, a mechanism which literally aspirates inward the blood from the saphenous and the superficial veins.[1, 13]

Blood flow velocity regulates the order of emptying each other of the various compartments of the venous system. An exemplification of this concept is well established in the lower limbs, where the emptying of the compartments takes place by means of energy gradients that are activated during muscular systole.

Muscle contraction applies different amounts of energy to compartments AC1 (sub fascial deep venous system), AC2 (great and short saphenous vein), and AC3 (subcutaneous veins above the superficial fascia).[1, 14] Muscle contraction brings about an energy application that is converted into levels of kinetic energy that differ in the respective compartments. Maximal energy in the AC1 means higher flow velocity and drop in lateral pressure which literally aspirate blood from AC2 and AC3 (Figure 5).[14] The different anatomical venous networks resulted to be associated with different velocity values, which follow the drainage hierarchical order: a tendency that is evident looking at the decreasing values reported in Figure 5.

A fundamental outcome was the detection of a constantly slower TAV in the tributaries system compared to the saphenous and deepest one. In this scenario the Venturi's effect must be taken into consideration, with a suction action exerted on the slower flow by the fastest one (Figure 5).

When we apply the hierarchy based on kinetic energy in other part of the body it happens the same, although the pump transducing energy for the blood motion is different. For instance, in the internal jugular vein two pumps are active, respectively the cardiac and the respiratory pump. Both accelerates the blood flow through the main route draining the brain, and interest-

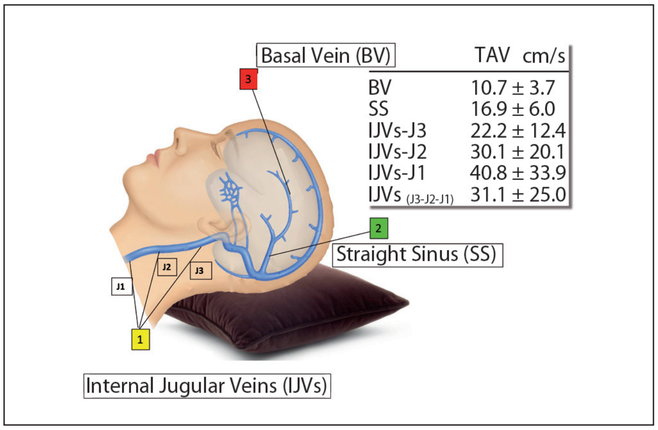

Figure 6.—Also in the head and neck system the main collectors, the internal jugular veins, constitute compartment one. It exhibits the higher TAV, which is progressively increased from J3 to J1 thanks to the activation of the respiratory and cardiac pumps. According to the Bernoulli Theorem and Venturi effect, the TAV gradient allows the aspiration of blood respectively from the parenchima veins of compartment 3 to the sinusal veins of compartment 2. Finally, the TAV gradient allows the aspiration of the intracranial veins into the main collectors of the neck.

ingly, close to the chest there is the highest flow velocity.[15, 16] The gradient of velocity from the cerebral deep veins to the sinusal veins, and that from the latter to the jugulars determines a hierarchy also at this level (Figure 6). We may consider the parenchymal veins as the venous compartment 1. Haemodynamics was assessed in the basal vein (BV) of Rosenthal because more frequently insonated by the means of transcranial ECD. There is a significant difference between the latter time average velocity (TAV) and that measured in the dura mater sinuses constituting the compartment 2 (straight sinus, SS).[14] Finally, the TAV was even more higher in the compartment 3, represented by the IJVs, permitting to aspirate the blood from the intracranial veins to the extracranial level. In addition, the blood flowing in the collaterals veins of the neck is aspirated into the IJVs in consequence of the progressive increased velocity. The kinetic energy is improved by both the cardiac and the respiratory pumps, very active when the blood is close to the chest. Accordingly, TAV increases along the neck and the flow rate as well. The latter has been measured progressively increased from the jugular foramen to the subclavian outlet (Figure 6).[16]

The above lesson learned explains us why the restoration of blood flow obstruction in the large veins permits to improve the haemodynamics in all the veins draining into the main collector path.

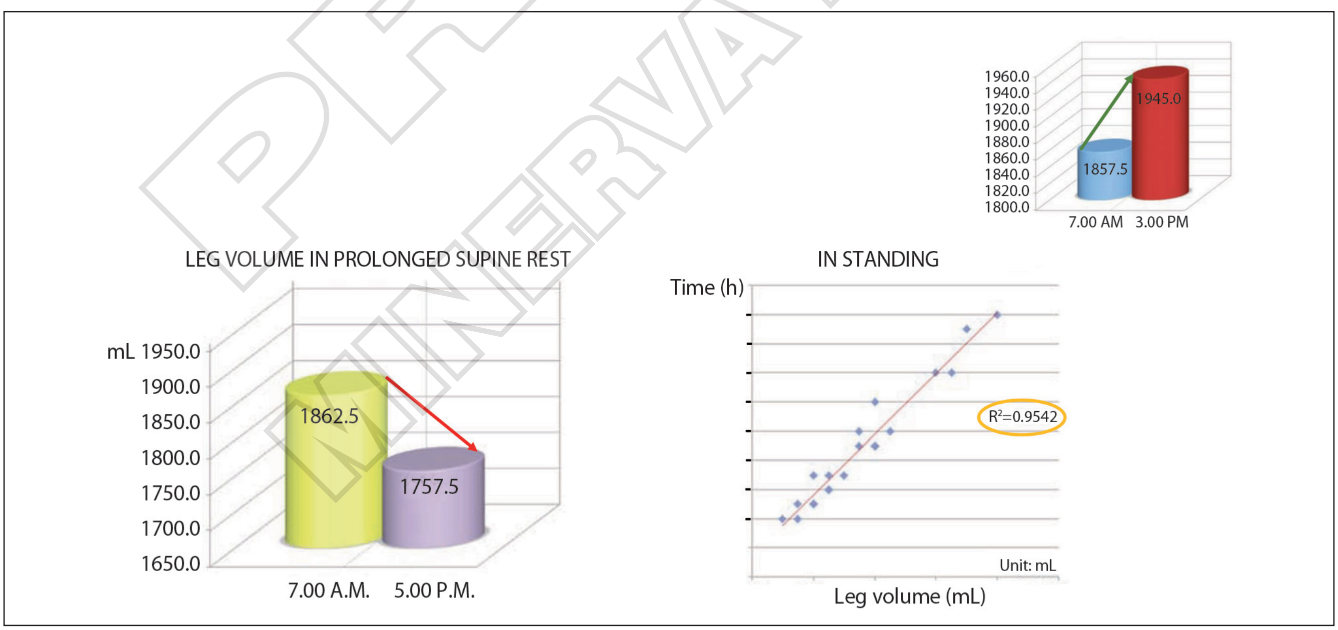

Figure 7.—A) Progressive decrease of lower limb volume prolonging the supine position for additional 10 hours after the normal wake time. The edema reduction correlates with the prolonged resting time; B) progressive increased volume in the lower limbs in healthy workers standing for 8 hours. It nicely correlates with the time of exposure to gravity (modified from Tessari *et al.*[17]).

Discussion

The venous system is a complex, low pressure, free communicating network of vessels, which contains 75% of the body's circulating blood. When a subject lies in the supine position, the absence of any gravitational gradient causes the blood to be evenly distributed throughout the system, similarly to the principles of the above communicating vessel experiment. However, when upright the distribution changes, and approximately 70% of the blood volume becomes located below the diaphragmatic line, due to the action of gravity.

If the subject is not mobile the blood is distributed in accordance with the hydrostatic pressure. Whether sitting or standing, the subject tends to accumulate overtime fluids and macromolecules in the venous and lymphatic system, and in the interstitium as well, of the lower extremity. The pivotal importance of the hydrostatic pressure was confirmed by the volume reduction, which was measured simply prolonging the time in the supine position in a group of healthy subjects after the wake. Tessari experimental observation represents an objective assessment of the old postural therapy for the prevention and treatment of the lower limbs edema. He found an even more pronounced lower limb volume reduction by the means of plethysmography from 7 a.m. to 5 p.m. in a group of healthy volunteers (Figure 7). This experiment in supine seems to exclude the presence of regulatory molecules for the very strong inverted correlation found, suggesting the pivotal role of gravity respect to regulatory molecules.

Quite the contrary he found a progressive edema increase in the lower extremities of healthy workers, which nicely correlates with the time of exposure to the gravity (Figure 7). Thus the gravitational gradient is the major force in determining the distribution of blood volume in the body.[17]

The pumps are the motor energy of the blood in the venous system.[18-23] The calf and thigh valvulo muscular pump activated by the walking permits the fragmentation of the hydrostatic pressure, with significant reduction of the venous pressure measured at the ankle. The hydrostatic pressure passes from values of 70-100 cmH_2O, according to the height of the subject, to 20-30 cmH_2O after 10 steps (Figure 8). In case of valve insufficiency the reduction of the hydrostatic pressure is insufficient and pressure at the ankle can be on average 20-40% less than in sitting or in standing. Paradoxically, in case of iliac-femoral vein obstruction the exercise might also cause an increased venous pressure (Figure 8).[18-23]

As we described above, the gravitational gradient is also of course important when we consider the brain outflow and the neck volume in different postures.

By comparison, in the cohort of patients with venous obstruction due to chronic cerebrospinal venous insufficiency, this drainage route appears to have been impaired in many of the patients, resulting in a prolonged ET and a higher RV, two parameters showed in Figure 4.

In particular, the prolonged ET appears to be a strong indicator of the presence of CCSVI, with cervical venous outflows on average 45% longer in CCSVI patients compared to the controls, when the chair is returned to the sitting posture. However, when using ET alone there is still considerable overlap between the two groups making diagnosis in the single case much more difficult.[11, 12]

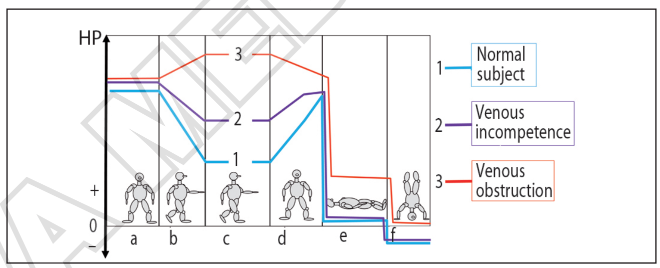

Figure 8.—The blue line shows how the hydrostatic pressure at the ankle (a) is decreased by the activation of the valvulo-muscular pump of the lower limbs (b-c). When the subject is standing the refilling time lasts in normal individuals more than 18 s (d). The valvulo-muscular pump is less efficient in case of valve incompetence (violet line), and paradoxically worse in case of obstruction of the iliac femoral segment (red line). However, elimination of gravity with proper postures (e, f) determines dramatic hydrostatic pressure reduction.

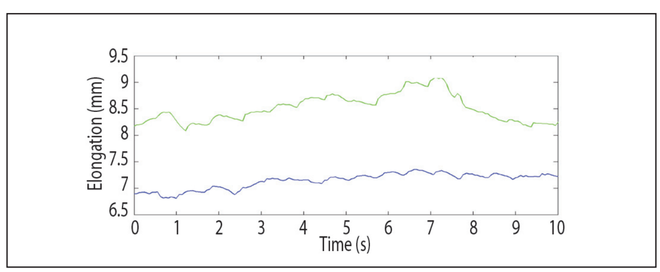

Figure 9.—The green curve shows the neck volume measured in supine position in a normal subject breathing in supine position. The volume variations express the modulation of the respiratory and cardiac pumps. The blue line shows a significant reduction of the blood content in the neck veins following forced inspiration, 70% of the vital capacity.

In addition, the activation of the pumps, and particularly of the respiratory pump, permit to document significant venous emptying thus confirming the role of the respiratory pump in cerebral venous return. The drained blood volume is increased in forced breathing (70% of the vital capacity) respect to normal individual breathing.[15] This because there is a modulation of the atmospheric pressure. When the subject breathes normally the pleural negativity is -3 cmH_2O respect to the atmospheric pressure, whereas in forced inspiration the pleural negativity rises up to -8 cmH_2O.[15]

The effect of the respiratory pump on the large veins of the neck can be assessed also by the means of cervical plethysmography (Figure 9).

Conclusions

Although blood is not a Newtonian fluid and the venous system is not a network of ideal conduits, the physics of fluids needs to be taken into consideration either for the diagnostic venous assessment or for the effect of our therapeutical attempts. Venous hemodynamics is regulated by the gravitational gradient of pressure and by the muscular, respiratory, and cardiac pumps. Blood flow velocity induced by the pumps is the physiologic regulator of the rigid, hierarchical, mono-directional order of emptying from the tissue to the main large veins connecting the right atrium. This hierarchical order, based on energy parameters of flow, explains how the surgical flow restoration in the large veins is beneficial for all the segments tributary of the main collectors. Surgery would be addressed in restoring the hierarchical order of emptying, independently from the techniques used.

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