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Postural and Ambulatory Changes in Regional Flow and Skin Perfusion

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WHAT THIS PAPER ADDS

- Changes in regional flow and microcirculation are known to occur with a change in posture. Volumetric data acquired with modern instrumentation are in sharp variance from prior information. A salient new finding is the profound cutaneous deoxygenation in the lower limb by ≈40% that occurs in orthostasis. This powerful physiologic change is likely relevant to understanding the pathophysiology of limb ulceration and dysvascular syndromes, particularly those with orthostatic features such as venous ulcers and acrocyanosis.

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ABSTRACT

Background: Studies of orthostatic changes in cutaneous micro-perfusion have yielded conflicting results, likely from imprecision of legacy equipment.
Methods: Postural flow changes in the femoral vessels and cervical carotids were measured in healthy normal adults using duplex equipment. Nutrient skin flow was measured using Hyperspectral imager (OxyVu-2™), a newer non-touch measurement technology.
Results: There are regional variations in cutaneous capillary density, sparse in the abdomen but richer in the forehead and ankle. Orthostatic microvascular congestion displays regional variations reflective of the non-linear pressure–volume relationship in thin walled vessels. There is profound cutaneous deoxygenation (≈40% reduction) in the lower body starting at the level of the umbilicus and involving all levels below, in the erect posture; upper body is unaffected. Quantitative regional flow is preserved however, with an increase in pulse rate despite a velocity decrease in the femoral vessels. Increasing the arterio-venous gradient by calf-emptying maneuvers resulted in little improvement in cutaneous oxygenation unable to overcome the powerful orthostatic vasoconstriction.
Conclusion: There is intense orthostatic vasoconstriction and cutaneous deoxygenation of the lower limbs to a degree not previously suspected. This powerful mechanism may be relevant to an understanding of dysvascular syndromes, particularly those with strong orthostatic features.

Introduction

A change in posture from supine to erect in a six-foot man adds a hydrostatic (gravity) component of ±90 mm Hg to the arterial, capillary and venous conduits. Unregulated, resulting high pressures will dilate resistance arterioles and result in high fluid egress leading to an unsustainable disturbance of homeostasis.[1–3] A variety of compensatory mechanisms[1,4] come into play. Notably, vasoconstriction of resistance arterioles (∼200 μm in size) and precapillary sphincters occurs[1,5,6] decommissioning capillary units (negative recruitment) and reducing the overall size of the capillary bed by as much as 70% by one estimate.[3] The vasoconstriction results in an increase in peripheral resistance by about 30–40% while dropping cardiac output by a similar amount with opposing effects on arterial blood pressure.[5,7–9] The venous system behaves like a passive elastic reservoir with postural change; 500–700 ml of central blood volume pools in the distension of the distal venous tree, taking it 'off line' simulating blood loss from hemorrhage.[5,10–12] The orthostatic drop in cardiac output is variably offset by tachycardia of about 10–20 beats per minute[1,13] that persists till recumbency is resumed; volume-preserving renal mechanisms are inadequate to compensate.[5,11,13,14]

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The mechanism of the orthostatic arteriolar vasoconstriction is disputed. There is support for (and against) a pressure-mediated arteriolar myogenic response (Bayliss effect) and 'veno-arterial reflex' through local axon pathways triggered by venous distension.[3,5,13,15,16] The vasoconstriction is strong in muscle, weak or absent in the skin per previous work. Metabolic requirements of lower limb tissues remain largely unchanged with orthostasis. The combination implies underperfusion; prolongation of limb circulation time and capillary transit time have been reported.[5,17] and oxygen extraction increases by ±50%. Muscle oxygenation is reduced in the erect posture and does not improve with exercise,[17–19] likely due to increased oxygen consumption offsetting perfusion increase.

In the head and neck, the hydrostatic pressure in the arteries falls in orthostasis by ±30 mm Hg, but only a 7–10 mm Hg pressure drop occurs in the jugular veins which collapse (pressure cannot drop below zero in the collapsed vein) for a net loss of about 20 mm Hg driving pressure gradient.[2]

There are three horizontal vascular networks beneath the skin[20] (Fig. 1); the most superficial is nutrient, the middle thermoregulatory and the deepest in the subcutaneous tissue supplies the other two networks. Only the outermost nutrient network is relevant to skin perfusion and oxygenation. The clinical test of 'capillary fill' after blanching the skin involves the superficial nutrient network. The network is sensitive to even slight local pressure as can be verified visually.

Prior studies of posture-related skin perfusion changes with a variety of techniques have yielded wide ranging contradictory results[5,15] probably due to methodological and instrumentation deficiencies. All prior methods perturb the superficial network by significant local pressure exerted by the measuring probe or device (volumetry, photoplethysmography, laser Doppler, transcutaneous oxymetry) or by thermal heating (heated oxymetry probe, heat from contact light source in photoplethysmography). One photoplethysmographic probe in common use measured 3 g without and 13 g with attached cables in our laboratory, and would exert even more pressure when pressed to the skin with an adhesive tape. All prior techniques including remote thermometry and laser Doppler flowmetry access one or more of the deeper vascular networks in their metrics and are prone to error.[15]

Hyperspectral imaging, a new semi-quantitative non-invasive technology derived from the space program, has found wide application in industrial and medical fields, notably in monitoring skin perfusion in diabetes and other ischemic conditions.[21–25] The remote sensing avoids many of the problems with older techniques and is specific for skin nutrient micro-perfusion.

Substantial orthostatic cutaneous deoxygenation is demonstrated with this technology with broad implications for the pathogenesis of lower limb ulceration and cutaneous dysvascular syndromes.

Methods

Instrumentation

The hyperspectral imaging device (OxyVu-2™, HyperMed inc. Watertown, MA.) is non-touch except for the nearly weightless (3 mg) paper target to center the light source. An incorporated remote thermal sensor assures normal conditions. Reflected light from each *pixel* (0.1 mm × 0.1 mm) over a 94 mm × 94 mm area (~1 million pixels) outside the central target is spectrally analyzed for oxyhemoglobin and deoxy hemoglobin. Internally calculated mean values of relative concentrations compared to a known standard are reported as arbitrary units proportional to micromoles of chromophore present per liter of tissue. The information is semi-quantitative yielding percentage change with perturbation. A false color-coded image is presented as well. Two parameters of microcirculation are used in this study: 1. total hemoglobin (Hb, the sum of oxy and deoxy hemoglobin) is a surrogate for blood volume and a measure of density of the vascular bed and its congestion; and 2. tissue hemoglobin percent oxygen saturation (S_TO_2) = [100% × (Oxy-Hb/Hb)] displayed by the instrument is an index of tissue perfusion.

Duplex measurements of regional vessel flow were made with Logiq9™ scanner (GE medical systems, Waukesha, WI) with 7L vascular probe. The method described by Li[26] in estimating mean flow was used. It has an error rate of ≈5% with good tolerance for practical variations that occur in insonation angle, flow rate and pulsatality. Maximum flow velocity in the center of the color flow channel was recorded with pulsed Doppler signals over several

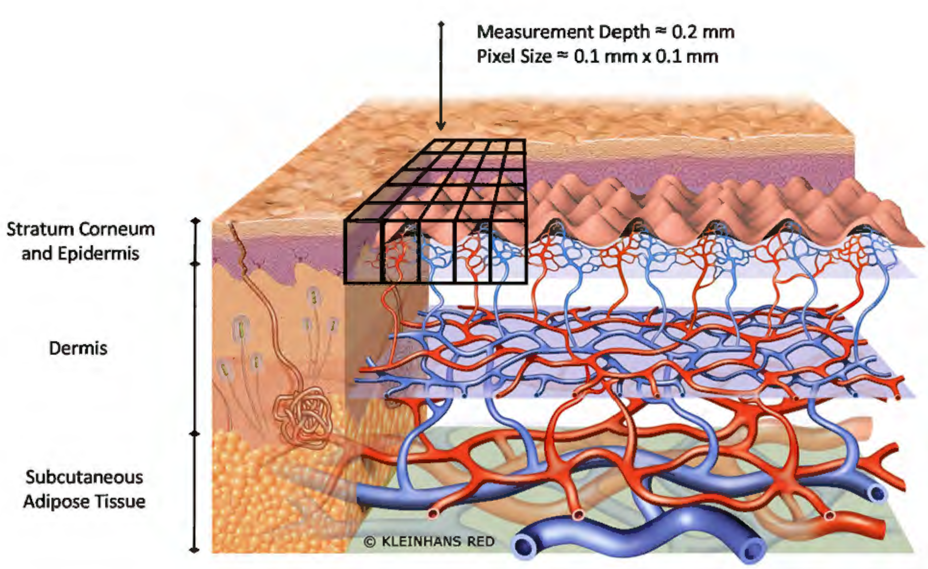

Figure 1. Vascular anatomy of skin. There are three vascular networks, but only the most superficial network is nutrient (see text). The OxyVu-2™ instrument targets only the nutrient network (grid). (By permission, Kevin Schomacker P.h.D.; HyperMed, Inc. and www.scf-online.com, Skin Care Forum 40, Cognis GmbH - now part of BASF).

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pulse cycles and averaged yielding Time averaged velocity or TAV. Mean flow velocity is half of TAV. Volumetric flow per pulse wave (Pulse flow volume) was then calculated from this and flow channel diameter (2D). Minute flow volume was derived from pulse flow volume and heart rate displayed by the scanner.

Measurements were taken at controlled room temperature of 22° Celsius in a small windowless room with high-flow air conditioning. Intra-subject comparative measurements were completed in about an hour minimizing temperature variations. Skin surface temperatures at points of measurement showed intra-subject variation of ≈0.3° and inter-subject variation of ≈1° on average.

A photoplethsymography (PPG) probe (Parks inc. Aloha, Oregon) was used to measure heart rate and pulse amplitude in calf exercise experiments.

Normal subjects

Healthy young (Median 22; range 20–32 years, Male/female ratio: 1.2/1) adult volunteers with normal body mass index (≤25) and no current or past venous symptoms or signs were recruited for the study.

Informed consent and institutional review board approval was obtained.

Measurements

Arterial inflow

Carotid (common, external and internal), common femoral and superficial femoral artery flow parameters were measured in the supine and 5 min after assuming the erect position.

Microvascular skin measurements

(a) *Postural changes*. Skin markers to center the light were placed on the ankle 1 inch above and ½ inch anterior to the medial malleolus, mid-calf, lower thigh, upper thigh, mid abdomen 2" lateral to umbilicus, over the xiphisternum, chest over 2nd rib and on the forehead. Initial measurements were made with the patient supine and then 5 min after assuming the erect posture (standing).

(b) *Calf pump action*. Resting measurements in the ankle site were taken with the subject in the erect position. and after three different calf pump emptying maneuvers: 20 manual calf squeezes, 10 toe stands and 5 min on a treadmill (3 mile/hr, 0 grade) Measurements were also made in the supine position before and after 20 manual calf squeezes.

Statistical Analysis

Flow and perfusion data were assessed through a series of linear mixed models.[27] This approach adjusts for within subject dependence due to multiple related measurements. The normality assumption was reasonable in each case through inspection of normal quantile plots. Interaction terms with *p*-values less than 0.20 were excluded for parsimony. *P*-values less than 0.05 were considered significant. All statistical analyses were performed using Statistical Analysis System™, Version 9.2, (SAS Institute Inc., Cary, North Carolina).

Results

Regional flow measurements

Supine and erect flows in the various arteries of the lower limb and cerebro-vascular circulations are shown in Table 1. Net change with posture is shown in (Fig. 2). Flow velocity and pulse volume flow decreased by 24% and 25%, respectively, in the common femoral artery on assuming the erect position ($P < 0.01$). Minute flow volume changes little from supine to erect due to pulse rate increase. In the superficial femoral artery, flow velocity decreased significantly ($P < 0.03$) with pulse flow volume trending lower but not reaching significance probably due to the sample size.

In the neck, (Table 1 and Fig. 2) time TAV is decreased significantly ($P < 0.03$) in the external carotid arteries) but not in the common and internal carotid arteries. Pulse volume flow and minute flow volume did not change significantly with position in any of the neck arteries.

Cutaneous microcirculation

Capillary density/filling

Total hemoglobin resident in the supine position in the capillary network for the various locations are shown in (Fig. 3). The values reflect anatomical density of capillary units and their degree of filling. The density/filling is mean 86 ± 19 at the ankle gradually declining to a nadir in the mid abdomen ($P < 0.0005$ vs. ankle) and increasing thereafter at the xiphisternum ($P = 0.05$ vs. ankle). There is a gradual increase in the upper chest skin similar to values in the calf ($P = 0.3$ vs. ankle), rising even more in the forehead which has a greater capillary density fill than the ankle ($P < 0.0001$ vs. ankle).

Microvascular changes in orthostasis

Congestion/decongestion

Microvascular volume increases, i.e., gets congested in the lower limb and trunk up to the xiphisternum ($P < 0.01$ in each case) on

Table 1
Orthostatic flow changes in femoral and carotid arteries.

Artery	(*n*)	Supine Time Averaged Velocity cm/s ± SD	Erect Time Averaged Velocity cm/s ± SD	Supine Pulse Flow Volume[a] mL ± SD	Erect Pulse Flow Volume[a] mL ± SD	Supine [b]Minute Flow Volume[a] mL ± SD	Erect [b]Minute Flow Volume[a] mL ± SD
CFA	18	13.72 ± 4.0	**10.45 ± 4.01	3.4 ± 1.4	**2.6 ± 1.1	199.6 ± 82.5	199.5 ± 98.7
FA	18	11.16 ± 4.87	*8.64 ± 3.42	1.7 ± 0.9	1.2 ± 0.6	99.3 ± 63.6	104.3 ± 50.4
CCA	10	27.87 ± 3.03	28.13 ± 4.76	4.5 ± 1.9	4.0 ± 0.8	290.5 ± 153.6	341.4 ± 152.7
ICA	14	27.67 ± 5.73	24.36 ± 6.17	2.6 ± 0.7	2.3 ± 0.7	163.5 ± 46.9	190.2 ± 62.6
ECA	15	18.73 ± 7.73	*14.86 ± 3.08	1.1 ± 0.5	0.9 ± 0.3	85.0 ± 41.4	87.0 ± 55.8

CFA – Common Femoral Artery, FA – Superficial Femoral Artery, CCA – Common Carotid Artery, ICA – Internal Carotid Artery, ECA – External Carotid Artery.
n = number of vessels.
*$P < 0.05$, **$P < 0.01$.
[a] See text for calculation of volumetric flow.
[b] Derived from Heart Rate × Pulse Flow Volume.

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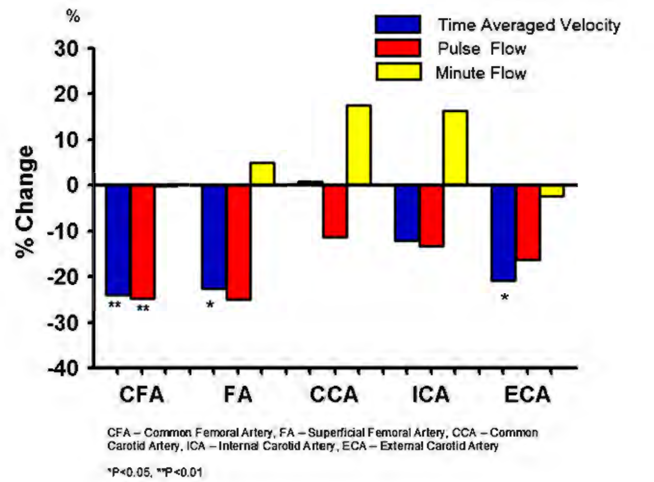

Figure 2. Net postural change in lower limb and cerebro-vascular flows. Data derived from Table 1. "n" values are the same as Table 1.

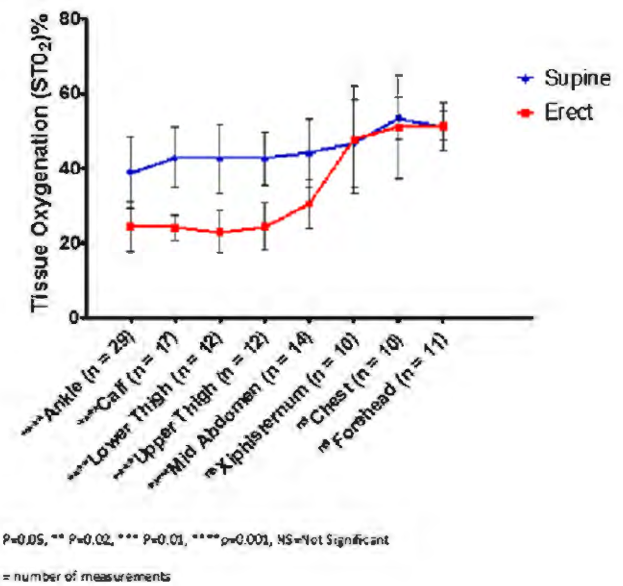

Figure 4. Regional variations in orthostatic cutaneous deoxygenation as measured by the OxyVu-2™ instrument. Note rather uniform decline in oxygen saturation in the erect position at all levels from ankle to mid abdomen.

assuming the erect posture (Fig. 3). The increase ranged from 30% to 45% (median 39%); the magnitude of congestion was similar (P = NS). At the chest level, congestive increase was only 11%, less than other locations caudad. There is no significant positional change in the forehead despite a fall in net arterio-venous gradient ($P = 0.06$).

Tissue oxygenation

Despite the increase in congestion, there is a profound fall in tissue oxygenation (range −32% to −48%) at all locations in the lower limbs and midabdomen ($P < 0.001$ in each case) on assuming the erect posture (Fig. 4). In contrast, tissue oxygenation remains unaffected in the xiphisternum, upper chest and forehead with postural change ($P > 0.5$ in each case).

Microvascular changes with calf pump action

A variety of calf-emptying maneuvers were tested for their coincident effect on heart rate and pulse waveform amplitude. Toe pulse photoplethysmographic waveform amplitudes and heart rate shown in Table 2 suggest that S_TO_2 changes with 10 toe stands and 20 calf squeezes reflect A-V gradient increase without induced cardiac and metabolic changes.

Skin oxygenation changed little with calf emptying in the erect position (Fig. 5) and remained well below resting supine levels shown in Fig. 4 for all but a few limbs; improvement was relatively better for supine calf squeezes with many limbs exceeding resting supine levels. Percentage S_TO_2 improvement with calf exercise (all 3 types) was greater for the left lower limb in the erect position and for the right in supine position. S_TO_2 increased more in the supine position than the erect even though estimated A-V gradient change was likely very much less.

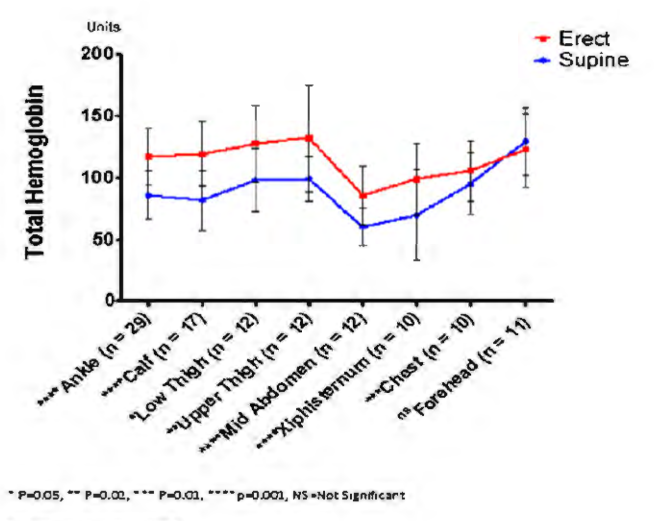

Figure 3. Regional variations in orthostatic microvascular congestion derived from OxyVu-2™ data: Note significant increase in hemoglobin content in the lower part of the body up to the xiphisternum on assuming the erect position.

Discussion

A change in posture from recumbent to erect results in profound changes in regional and microvascular skin flow. An orthostatic velocity reduction of lower limb flow was shown by Rushmer[14] but volumetric measurement was not available at the time. Data presented here show a significant reduction in common femoral pulse velocity (TAV) and pulse volume flows. But, minute flow is unchanged due to compensatory increase in pulse rate. Nevertheless, there is intense vasoconstriction in the lower trunk and lower limbs with resultant severe fall in dermal S_TO by about 40% of supine; Improvement with erect calf exercise is modest at best and still below resting supine levels (Fig. 5).

In the head and neck, postural hydrostatic changes are quantitatively modest (20–30 mm Hg) compared to the lower limb

Table 2
Pulse wave amplitude and heart rate with calf emptying maneuvers.

Parameter ($n = 9$)	Rest	10 Calf Squeezes	40 Calf Squeezes	10 Toe Raises	20 Toe Raises	40 Toe Raises
Mean Amplitude	5.6 mm	6.1 mm	5.6 mm	6.1 mm	*8.7 mm	*9.1 mm
Mean Heart Rate/min	61	61	63	62	66	*72

*$P < 0.05$, **$P < 0.01$, ***$P < 0.001$.
n = number of limbs.
Calf squeezes and 10 toe raises appear to have little cardiac effect.

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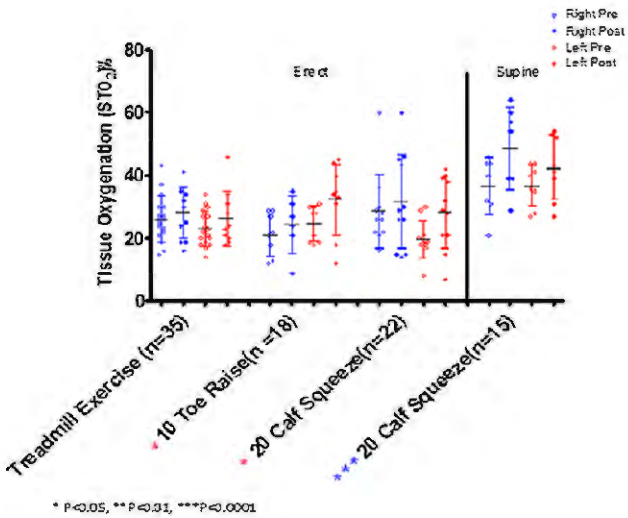

Figure 5. Change in tissue oxygen saturation with a variety of calf emptying maneuvers to increase the A-V gradient. "Pre" and "Post" in the figure key represent before and after calf-emptying maneuver. Note the difference between supine and erect position (see text).

(≈90 mm Hg) because the gravity component is less. However, there is a net loss of driving pressure in orthostasis unlike in the lower limbs. There are several anatomic and physiologic protective mechanisms that attempt to buffer the resulting fall in intracranial perfusion.[28,29] Importantly, there is little or no vasoconstriction due to autoregulatory mechanisms.[10,29–31] In this study, flow velocity decreased significantly in the external carotid artery with no change in pulse volume or minute flows. There was no significant change in velocity or volume flows in the common or internal carotid arteries. Vertebral flow was not measured in this study.

Velocity is inversely related to area for a constant volume flow. The superficial femoral vessels show a slight increase and the carotids show a slight decrease in area due to opposite postural changes in hydrostatic pressure. Postural area changes in this study were relatively small (≈5%) and therefore their effect on flow velocity was relatively minor; orthostatic changes in driving pressure gradient and in regional flow resistance (Poiseuille equation) have a far greater effect. These parameters differ substantially in neck vessels (with inter-carotid differences) from those in the superficial femoral arteries explaining regional differences in velocity and pulse volume flows with orthostasis.

The deterioration in tissue oxygenation despite preservation of minute flow volume in the lower limbs suggest that rate based low volume pulsatile flow is not as functionally efficient as high volume pulsatile flow (A-V shunting?). Fluid mechanical properties of collapsible tubes help explain reported postural microcirculatory changes.

Hydrostatic indifferent point (HIP)

On assuming the erect posture, extra-cranial veins empty, collapsing down to the base of the neck. The venous collapse would extend even farther down but for the negative intra-pleural pressure which keeps the great veins pulled open from collapse. The pressure of the proximal venous column 5–10 cm in length is therefore negative, does not exert downward pressure on the column below and does not contribute to the hydrostatic pressure measured at the foot level. A few centimeters below the diaphragm (xiphoid in this study), a hydrostatic indifferent point (HIP) is located where the venous pressure (say 10 mm for example) will remain unchanged when the person is tilted from horizontal to erect. All venous locations (and connected capillaries) below HIP will experience a pressure increase, and others above HIP a decrease in the erect position due to the addition or subtraction of the hydrostatic component respectively. Even though the venous pressure increases proportional to the distance caudad from HIP, increase in the venous congestion averaging about 27% was similar in all locations below HIP. This is because of the non-linear pressure volume relationship within collapsible tubes. By the time the pressure within reaches about 10 mm Hg they are nearly fully filled and any additional increment in pressure reflects only a minute, perhaps ±10%, incremental volume.

The decrease in tissue oxygenation by ≈40% at various levels below HIP is due to arteriolar vasoconstriction with closing off of precapillary sphincters.[32] All locations at and above HIP experienced no reduction of tissue oxygenation on assuming the erect posture while locations below HIP suffered in this regard, suggesting a sharp linkage to venous pressure. The vasoconstrictory response was also non-linear showing no proportionality with orthostatic pressure increase (Fig. 4), which argues against vascular muscle stretch (Bayliss effect) as the initiating mechanism.[5]

There is discordance between levels of tissue hypoxemia and orthostatic congestion (Figs. 3 and 4). Hypoxemia from vasoconstriction was restricted to the level of abdomen and below while orthostatic congestion extended farther up to the upper chest which corresponds to the height of the venous column (not hydrostatic pressure column). This suggests that the receptors initiating the vasoconstrictory response are not stretch sensitive but pressure sensitive.

Microvascular congestion increased rather than showing a decrease in the ankle (and other locations) despite a fall in tissue oxygenation, an observation originally made in the pioneering work by Levick and Michel.[33] Closure of precapillary sphincters implies negative capillary recruitment (closure of units).[3] It appears that capillaries, though unperfused from the arterial side, can remain congested but functionally inert due to back filling from the venous side.

Increasing the arterio-venous pressure gradient by calf-emptying maneuvers yielded the same or greater fractional improvement in tissue oxygenation in the supine compared to the erect posture (Fig. 5). Since vascular resistance (R) is increased by an estimated 30–40% in the erect position a proportionately higher induced arterio-venous gradient (ΔP) would be necessary to yield the same improvement in perfusion (F) and tissue oxygenation per Poiseuille's law ($F = \Delta P/R$). However, calf emptying in the erect position results in an estimated ΔP three to five times greater than in the supine position. The discrepancy is probably due to the phenomenon of 'flow limitation' described below.

The Starling resistor

This curious flow phenomenon occurs in tubes subject to collapse from external pressure and is prevalent in a wide variety of biological flows.[32,34,35] The *transmural* pressure influences flow volume rather than the pressure gradient across the tube. When the outflow pressure is lowered below transmural pressure, collapse of the tube at a region near the outflow end occurs and 'flow limitation' ('choking' in hydraulics) prevails; further outflow pressure reduction has little effect and the flow remains fixed, i.e. Poiseuille equation no longer applies. Precapillary sphincters act as external compressive elements influencing transmural pressure.[32] Precapillary sphincters are constricted in the erect posture and transmural pressure is near critical closing pressure and prone to flow limitation. In the absence of arteriolar vasoconstriction in the supine position, a relatively smaller increase in A-V gradient by calf

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squeezes results in a much greater flow and skin oxygenation in the Poiseuille flow regimen. The curious difference between the right and left limb in venous egress was noticed by Lebow.[36] Most venous pathologies occur 3–5 times more commonly on the left side compared to the right likely related to the ubiquitous presence of iliac vein obstruction even in normal individuals.[37]

The intense orthostatic deoxygenation of lower limb skin may be relevant to pathophysiology of ischemic and venous ulcerations and cutaneous dysvascular syndromes of the lower limb such as acrocyanosis and erythromelalgia. An ischemic component to venous ulceration has long been proposed. In a broad review, Shami and colleagues[38] concluded that the evidence was often conflicting and did not support such a hypothesis. However, most studies in this area were carried out in the supine or erect position but not both; where positional change was monitored, only flow parameters and not oxygenation with error prone legacy equipment was measured. Current findings with more precise equipment show that there is profound reduction in dermal nutrient flow and deoxygenation with orthostasis. This suggests that positional restoration of nutrient skin flow is an alternative explanation for the healing of venous ulcers with leg elevation in addition to or instead of the traditional one of reduction of venous pressure.

Conflict of Interest

None.

Funding Source

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