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Cardiac output and vasodilation in the vasovagal response: An analysis of the classic papers

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Abstract

The simple faint is secondary to hypotension and bradycardia resulting in transient loss of consciousness. According to Ohm's law applied to the circulation, $BP = SVR \times CO$, hypotension can result from a decrease in systemic vascular resistance (SVR), cardiac output (CO), or both. It is important to understand that when blood pressure (BP) is falling, SVR and CO do not change reciprocally as they do in the steady state. In 1932, Lewis, assuming that decreased SVR alone accounted for hypotension, defined "the vasovagal response" along pathophysiologic lines to denote the association of vasodilation with vagal-induced bradycardia in simple faint. Studies performed by Barcroft and Sharpey-Schafer between 1940 and 1950 used volume-based plethysmography to demonstrate major forearm vasodilation during extreme hypotension and concluded that the main mechanism for hypotension was vasodilation. Plethysmographic measurements were intermittent and not frequent enough to capture rapid changes in blood flow during progressive hypotension. However, later investigations by Weissler, Murray, and Stevens performed between 1950 and 1970 used invasive beat-to-beat BP measurements and more frequent measurements of CO using the Fick principle. They demonstrated that CO significantly fell before syncope, and little vasodilation occurred until very late in the vasovagal reaction. Thus, since the 1970s, decreasing cardiac output rather than vasodilation has been regarded as the principal mechanism for the hypotension of vasovagal syncope.

Keywords

Heart rate; Blood pressure; Cardiac output; Stroke volume; Systemic vascular resistance; Orthostasis; Vasovagal syncope; Central blood volume; lower body negative pressure

Introduction

Syncope is defined as a transient loss of consciousness secondary to global cerebral hypoperfusion and is characterized by rapid onset, short duration, and spontaneous complete recovery.¹ During vasovagal syncope (or fainting), the fall in blood pressure (BP) is mediated initially by decreased cardiac output (CO) with or without vasodilation. The decrease in CO is secondary to stroke volume reduction. When bradycardia and withdrawal of sympathetic vasoconstrictor activity occur, they are relatively late events, by which time BP is already low. There has been much debate as to whether decreased CO or vasodilation is the dominant hypotensive mechanism preceding vasovagal syncope.^{2,3}

Tilt testing was first used by Weiss et al⁴ for investigating orthostasis and by Graybiel and McFarland⁵ as a means of studying tolerance to decreased venous return as a determinant of fitness for military aviation. In 1986, Kenny, Sutton, and coworkers⁶ introduced tilt testing as a means of diagnosing vasovagal syncope. Since then, cardiologists, physicians, and researchers have adopted this approach to evaluate the hemodynamics of vasovagal syncope and other conditions related to orthostatic intolerance.¹ In the 1980s, Penaz and Wesseling introduced the Finapres or volume clamp method, which allowed continuous noninvasive measurement of finger arterial pressure. Thus, rapid changes in arterial pressure could be obtained accurately. Pulse wave analysis subsequently allowed the computation of relative changes in stroke volume (SV) and thereby calculated relative changes in CO and systemic vascular resistance (SVR). These scientific developments enabled clinicians and researchers to study noninvasively the vasovagal responses on a beat-to-beat basis.^{7,8} In addition, direct nerve recordings from the leg using the microneurographic technique enabled continuous monitoring of efferent vasoconstrictor sympathetic activity. Observations obtained from relatively small numbers of cases have demonstrated changes in sympathetic vasoconstrictor tone during vasovagal syncope, but this is only activity directed toward the leg.³

Despite these developments, the mechanisms underlying vasovagal syncope are still being debated.^{2,3} Most arguments rely on the classic experiments performed before the 1980s. These results emphasized that vasodilation is the dominant mechanism initiating the vasovagal response

We performed an in-depth critical overview of the classic literature related to the mechanisms underlying vasovagal syncope to provide a comprehensive historical summary.

Methods

Referenced papers were selected by hand searches of our own databases. For focused searches, PubMed was used as the preferred database. All available studies were checked for

relevance to the present review. For the mechanisms involved in orthostatic BP control in healthy subjects, we refer to standard texts.^{2,9}

Historic overview

During World War I, Cotton and Lewis¹⁰ studied recruits with “the irritable heart” or “the effort syndrome,” in whom fainting was frequent. Findings from 8 soldiers (age 21–28 years) who fainted during medical examinations were presented with vivid descriptive precision and with great care. Heart rate (HR) was measured by counting the radial pulse or auscultation of the heart, and BP was determined using an arm cuff and stethoscope.

In 6 soldiers, the faint was elicited during blood sampling while in the sitting position; in the other two subjects, fainting occurred while they were standing for physical examination. Fainting was dramatic and included complete loss of consciousness and prolonged post-faint hypotension associated with persistent-marked bradycardia, lightheadedness, and nausea. Cotton and Lewis¹⁰ attributed the attacks to inhibitory cardiac impulses, that is, bradycardia and loss of contractility.

In a critical re-evaluation of his work, in 1932 Lewis¹¹ explored the idea that the vagus nerve was responsible not only for the slowing of the heart but also for simultaneous impairment of cardiac contractility. In a famous lecture entitled “Vasovagal syncope and the carotid sinus mechanism,” he stated that vagal stimulation did not cause appreciable weakening of the force of ventricular contractions in animal experiments and that atropine injection into a human subject during the attack increased the HR up to and beyond normal levels but not BP, so the patient remained pale and not fully conscious. Lewis concluded that “undoubtedly the main cause of fall in BP in attacks, and the enfeeblement or loss of pulse, is independent of the vagus and lies in the blood vessels.” He further stated “the cause of syncope is mainly vasomotor and not vagal, but the vagus adds impressively to the clinical picture by inducing conspicuous slowing of the heart and gastric manifestations.” Lewis reaffirmed the descriptive term “vasovagal syncope” introduced by Gowers along pathophysiologic lines to denote association of vasodilation and bradycardia. For Gowers (1845–1945), vasovagal was a purely descriptive term for episodes of a variety of gastric, respiratory, and cardiac symptoms, which he ascribed to vagal activity together with complaints of pallor and coldness, which he attributed to vasomotor activity.¹² It is important to be aware that Lewis’ opinion on the decisive role of vasodilation was based on clinical reasoning and not on actual measurements of cardiovascular variables.

Experiments during World War II: Documentation of vasodilation during massive hemorrhage-induced fainting

By mid-20th century, the development of intra-arterial BP measurements in humans made possible the study of syncope using beat-to-beat monitoring. In addition, right-sided cardiac catheterization was introduced for intermittent CO measurements and water bath plethysmography for forearm blood flow (FBF) measurement. Fick and thermodilation measurements of CO provide average values over a time interval of 30–60 seconds. Individual measurements using waterbath plethysmography for FBF took 10–20 seconds.

With the availability of mean BP and CO and the application of Ohm's law to the circulation ($\text{mean BP} = \text{CO} \times \text{SVR}$), SVR is calculated (Figure 1). Using these methods, scientists were able to obtain average values for CO (and SVR) over a 30- to 60-second time interval during vasovagal reactions induced in the laboratory.^{13–16} It should be appreciated that SVR is calculated (not measured) and that it represents total SVR, which in turn comprises several parallel vascular beds.

The first evidence for systemic vasodilation during fainting was provided by Barcroft et al,^{13,14} who studied syncope as a model for hemorrhagic circulatory shock in combatants during World War II. In his 1975 Campbell oration entitled "Adventures in physiology at Queen's University, Belfast, in World War II," Barcroft¹⁷ gave a dramatic description of the events. He reported studying 7 healthy male volunteers (age 20–30 years) who fainted during venesection, with or without thigh tourniquet inflation to trap blood in the legs. Before severe hypotension occurred, CO (measured with the Fick method) had decreased by ~40% (from ~5 L/min to ~3 L/min). In 5 of 7 subjects, CO did not decrease further during the actual faint when systolic blood pressure (SBP) was very low (<50 mm Hg) (Figure 2). Recovery was protracted and achieved by interrupting the venesection and deflating the tourniquets.¹³

Despite the documented fall in CO, Barcroft et al concluded that the hypotension was mainly secondary to generalized vasodilation because SVR was estimated to be 20%–30% below baseline. This finding was supported by a large (2–3 times baseline) increase in FBF during a fully developed faint. In the prolonged phase of post-faint hypotension, HR, CO, and SVR were markedly decreased whereas FBF was increased.^{13,14,17} Brigden, Howarth, and Sharpey-Schafer reproduced this finding during tilt-induced syncope.¹⁵ Using waterbath plethysmography, they demonstrated a 2- to 3-fold increase in FBF during a fully developed faint. Based on the literature available at the time, Barcroft and Edholm concluded that the behavior of the forearm circulation probably is a reliable index of what was happening elsewhere in skeletal muscle. They made calculations suggesting that it was quite possible that the fall in total body SVR could be entirely accounted for by muscle vasodilation and that the initial splanchnic and skin vasoconstriction of hemorrhage persisted during a faint.^{13,14} In the 1950s, data on the importance of the splanchnic bed for orthostatic BP were demonstrated by the effects of sympathectomies in the splanchnic area. These sympathectomies were performed to treat hypertension.¹⁸ Vasodilation was documented to also occur in the splanchnic bed during vasovagal syncope.¹⁹ These observations prompted Edholm²⁰ to change his view about exclusive vasodilation in skeletal muscle in a state-of-the-art discourse on the visceral circulation in 1952. He concluded that vasodilation may also occur in the splanchnic bed, but that "unfortunately our knowledge of the alterations and of the actual volume of blood in the splanchnic bed are at present grossly inadequate."

The analysis of Barcroft et al was based on infrequent hemodynamic measurements. For example, the analysis of 1 faint consisted of only 4 CO and 6 BP measurements (by arm cuff inflation) over 16-minutes (Figure 2). Data from only 2 subjects were documented. A Fick CO measurement took ~30–60 seconds and so could not be used to measure rapid changes during fainting. The Fick principle requires a hemodynamic "steady state," which was not achieved during these experiments.

The FBF measurements by plethysmography also were intermittent, blood flows were recorded at 1-minute intervals during the faint, and individual measurements took 10–20 seconds. On average, the last measurement of FBF before the fully developed faint demonstrated values similar to control. SBP had decreased to about 80 mm Hg, a level consistent with presyncope.^{13,14} This was followed by a marked increase in FBF during syncope, which persisted during post-faint hypotension. Barcroft and Edholm were careful to reduce the collecting pressure (to <30 mm Hg) in the plethysmography arm to make sure blood could still flow into the forearm when perfusion pressure fell to very low levels.^{13,14}

Further studies confirmed that vasodilation occurred primarily in the muscles of the forearm and not in the skin or the hand. Because vasodilation did not occur in a sympathectomized arm, it was thought to be “actively” mediated by sympathetic vasodilator fibers.^{13,14,17} This concept was subsequently challenged, and other mechanisms including sympathetic vasoconstrictor withdrawal and circulating vasodilators were suggested instead.^{2,3}

Additional experiments showed that muscle tensing and movement during an impending faint could reverse development of hypotension. The effect was attributed to an increase in the amount of blood available for the heart to pump.¹⁵ Sharpey-Schafer et al²¹ further commented “there seems to be some truth in the popular belief that fainting may be prevented by taking a grip on oneself.” In 1946, Engel and Romano²² also emphasized the importance of muscle tension and commented that the sensation of muscle weakness before fainting was typical. Studies of the relationship between intramuscular pressure, venous return, and orthostatic tolerance were performed in the 1930s. Henderson et al²³ documented in relaxed biceps muscle decreased intramuscular pressure after prolonged bedrest (38%), after surgery (35%), with voluntary hyperventilation (28%), and in the absence of air movement over the skin (31%). These situations are strongly associated with decreased orthostatic tolerance and increased tendency to faint. In addition, intramuscular calf pressure was shown to be 50% lower in fainters compared with nonfainters during head-up tilt.²⁴ Although these interesting results from early studies have never been confirmed, it is likely that an increase in muscle tension augments intramuscular pressure, thus reducing venous distension and blood pooling, in turn increasing central blood volume (CBV).² Accordingly, a recent study of the beneficial effects of tensing leg and abdominal muscles in aborting a vasovagal faint have documented that the main effect of these maneuvers is a mechanically induced instantaneous increase in venous return and CO.²⁵ The effect is similar to inflating an antigravity suit (Figure 3).

Changes induced by the exercise pressor reflex through sympathetically mediated constriction take 5–10 seconds to reach a full effect] and do not play a role in the instantaneous beneficial effect of muscle tensing. The reflex effect induced by muscle tensing that is beneficial is a decrease in vagal tone with an instantaneous increase in HR.²⁵

Role of reduced cardiac output during vasovagal syncope

The hemodynamic importance of fall in CO during a faint was addressed exhaustively in the 1950s in a study of 8 male university students by Weissler et al.¹⁶ Fainting was induced by tilt after the subjects took oral nitrate while they were supine. During head-up tilt, 500–1000

cc of blood pools below the diaphragm. Intravascular blood volume may also decrease because of transcapillary filtration into the interstitial spaces of dependent parts.^{2,9} Nitrates in the doses used by Weissler et al are venodilators and will increase the pooling of blood.⁴ An intra-arterial line was placed to measure BP continuously, and CO was determined by dye dilution, which allowed its more rapid estimation (~30 seconds). The first figure in the study by Weissler et al indicates that dye dilution CO provided a time average of rapid changes during BP fall (Figure 4). A practical problem here was that the dye dilution method did not allow continuous recording of BP at the same time as arterial blood was sampled for CO measurement.

A sudden and rapid fall in BP was observed at the moment of fainting. Figure 1 in the publication by Weissler et al suggests that subjects were returned to supine when loss of consciousness was imminent (Figure 4). At the moment of presyncope (and tilt down), mean BP was 38 mm Hg. As soon as the subjects were supine, BP and HR recovered promptly.

The postulated mechanism underlying the faints was vasodilation: SVR decreased by 50%, whereas the decrease in CO *during tilt* was minor (about 15%). Weissler et al used the stable hemodynamic values during the 3- to 10-minute tilt period as control; however, compared with supine control, the decrease in CO was at least 40% during presyncope. In view of these observations on CO, Weissler et al considered the fall in SVR to be the essential element of orthostatic vasovagal syncope. Because Weissler et al were familiar with studies showing that, in the event of a fall in SVR, the arterial pressure was maintained by an increase in CO (studies in patients with A-V shunts),²⁶ they emphasized “a striking feature of the observation on vasodepressor syncope reported here is the failure of CO to rise in the face of decreased peripheral resistance.” Weissler et al argued that the failure of CO to rise could not simply be explained by bradycardia at the time of faint and considered a decrease in SV secondary to decreased cardiac filling or a decrease in contractility. Weissler et al favored the first of these explanations because inflating an antigravity suit caused an immediate increase in BP with full recovery (Figure 3), whereas atropine (1.6–2.4 mg) was ineffective.

In additional studies, Weissler et al²⁷ reported on the effects of posture and atropine on CO in 6 young adult male subjects. They documented that atropine (2 mg) administered to subjects in the supine position increased HR by an average of 44 bpm. The HR increase correlated with a 2-fold rise in CO and an increase in mean BP from 79 mmHg to 86 mmHg. However, after administration of atropine to subjects in the upright position, no effect was observed on CO or BP despite a greater increase in HR. When pooling of blood in the upright posture was prevented by sustained inflation of an antigravity suit, cardiac responsiveness to atropine in tilted subjects was partly restored.¹⁶ Prompt recovery and reversal of hypotension also were noted when negative pressure breathing (to increase venous return) was applied at the time of presyncope. Syncope could no longer be induced by the tilt–nitrate procedure after rapid infusion of 1 L 5% albumin in saline.¹⁶

Weissler et al concluded that central blood volume (CBV), that is, the reservoir of blood available in the 4 cardiac chambers and in the pulmonary and great thoracic vessels, is an

important determinant of cardiac responsiveness. When CBV is low, ventricular filling is diminished and CO cannot be maintained by increasing HR.

The observation of Weissler et al that a full dose of atropine did not influence fainting attacks was confirmed by Murray and Shopshire,²⁸ who used progressive lower body negative pressure (LBNP) to decrease CBV. LBNP was introduced by Air Force researchers, such as Murray, as a means of studying tolerance to decreased venous return as a determinant of fitness for military aviation.⁵ Severe presyncope was used as an endpoint in these studies, similar to today's tilt testing. However, recent studies have documented that LBNP (traditionally performed in the horizontal position), although useful as a model to simulate loss of CBV (hemorrhage), is not a physiologic surrogate for tilt-induced orthostasis.²⁹

By applying LBNP to 7 young healthy males (age 25–40 years), Murray et al³⁰ were able to measure CO and FBF during a 3-minute period when the subjects were very close to syncope with a mean SBP of 76 mm Hg at the moment of dye injection to measure CO. Before syncope, CO decreased by about 50% from baseline, whereas SVR actually increased by 30%. FBF, now measured by strain gauge plethysmography with no collecting pressure adjustments, remained at baseline levels throughout presyncope. However, just before syncope, mean BP and calculated forearm vascular resistance fell. During presyncope, the increase in SVR occurred while FBF was constant, implying that resistance in the upper limbs might not be contributing to SVR. Epstein et al³¹ also obtained FBF measurements in 6 male volunteers aged 19–23 years during LBNP immediately before a fully developed vasovagal faint (mean BP 34 mm Hg, HR 47 bpm during syncope). They confirmed the observation of Murray et al that FBF remained at baseline levels during presyncope. Similarly, when mean BP fell rapidly before syncope, calculated forearm vascular resistance also fell on average by 62%.³¹

Thus, for the first time, systemic vasodilation reported by Barcroft et al, Sharpey-Schafer et al, and Weissler et al was not demonstrated.^{13–16} The important observation by Murray et al was confirmed by Stevens and Lamb,³² who studied 38 fit, young, Air Force personnel during presyncope (SBP 79–99 mm Hg) induced by LBNP, and recorded a fall in CO of 40%.

Again, SVR increased by ~30% from baseline. The results were similar when Stevens³³ suspended 41 subjects upright using a parachute harness. Mean SBP fell to 74 mm Hg and CO decreased by 40%, but SVR levels remained just above baseline. Therefore, vasodilation was no longer thought to be the dominant mechanism for hypotension during presyncope.

Murray, Stevens, and Epstein and coworkers all documented a gradual fall in central venous pressure (2–6 mm Hg from baseline) as LBNP increased, but no change in central venous pressure during the transition from presyncope to syncope. Based on the changes in venous tone in the forearm, Epstein et al³¹ concluded that venoconstriction occurs during vasovagal syncope. A decrease in cardiac contractility that changes the relationship between venous return and CO was another possible explanation.²

Table 1 summarizes the observations of the different studies. Note the small number of subjects, variability in the methods for inducing vasovagal syncope, differences in measurement techniques, and timing of measurements before syncope. Relative bradycardia was present in all studies, but pronounced cardioinhibition occurred only when the study protocol “allowed” fully developed faints. Pronounced bradycardia or asystole would clearly exacerbate the progressive fall in CO already underway during presyncope (see above).

Stevens³³ also demonstrated that instrumentation and its associated anxiety increased considerably the likelihood of a hypotensive reaction. This observation was consistent with earlier human studies showing vasodilation in skeletal muscles during emotional stress.^{21,34}

In studies using the combination of head-up tilt and LBNP, Newberry et al³⁵ emphasized variation in fainting responses (observed but not appreciated by Barcroft et al and Stevens) and the influence of ambient temperature.

The observations that BP and symptoms recovered within seconds by maneuvers that increased venous return (Figures 3 and 4) and that vasovagal syncope was never observed in patients with heart failure with fluid overload prompted Sharpey-Schafer et al²¹ to propose that, during a faint, a vigorously contracting empty atrium or ventricle might paradoxically stimulate cardiac receptors, which fire the afferent mechanism of the faint reflex. This theory is debated and will not be further addressed here.

Summary

1. Fewer than 10 young adult healthy males without a fainting history were studied in early laboratory studies (Table 1). Females, seniors, and patients were not studied. In addition, subjects were instrumented, which greatly influences fainting responses. Thus, the classic studies included only a selected healthy male population under highly invasive conditions.
2. The circulatory changes during a faint are rapid, and the time between onset of hypotension and loss of consciousness is crucial. Unfortunately, in the classic studies, this interval was often shorter than the time needed to perform CO and FBF measurements. The Fick CO measurements used in the classic studies took ~30–60 seconds, thus rendering precise measurement of rapid hemodynamic changes during fainting impossible. This may have led to underestimation of the fall in CO during syncope and overestimation of the role of systemic vasodilation (Figure 5).
3. The observations by Weissler and coworkers that, when CBV fell, CO did not increase by afterload reduction or

- tachycardia are fundamental to our understanding of the hemodynamic mechanisms underlying vasovagal syncope.
4. The discrepancies between the observations of Barcroft and coworkers and those of Murray/Epstein and coworkers on the role of changes in CO and SVR are secondary to a difference in severity of the fainting response (fully developed severe faint vs presyncope) and the exact timing of FBF measurements during the faint (Table 1). Pronounced cardioinhibition was observed only in the studies with fully developed faints. The importance of the different phases of vasovagal syncope was not appreciated in the early laboratory studies.
 5. Murray and Stevens and coworkers both demonstrated that, during presyncope, CO decreases by at least 40% without significant vasodilation in the systemic circulation. The discrepancy between minor forearm vasodilation and increase in SVR shown by Murray et al suggests that forearm vascular responses to hypotension during (pre)syncope differ from those in other vascular beds (splanchnic and lower extremity muscle beds). Data on the importance of the splanchnic bed for orthostatic BP regulation were known to be important at the time of the classic studies, and the complexity of performing measurements in this vascular bed were appreciated.

We conclude that the strong emphasis on vasodilation by Lewis as *the* defining mechanism of vasovagal syncope in combination with Barcroft's observations during fully developed "heroic" faints have overemphasized the role of vasodilation as the main mechanism underlying a vasovagal faint. Reduction in cardiac output, rather than vasodilation, may be the primary cause of the hypotension of vasovagal syncope.

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ABBREVIATIONS

BP	blood pressure
CBV	central blood volume
CO	cardiac output
FBF	forearm blood flow
HR	heart rate
LBNP	lower body negative pressure

SBP	systolic blood pressure
SV	stroke volume
SVR	systemic vascular resistance

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Figure 1.

Ohm's law: Mean arterial pressure = Cardiac output (CO) $\times$ Systemic Vascular Resistance (SVR). LA = left atrium; LV = left ventricle; RA = right atrium; RV = right ventricle; Venous pooling = accumulation of blood in the venous system.

Figure 2.

Vasovagal faint induced by venesection 1020 cc. Steeps fall in blood pressure (BP) and heart rate (HR) are observed at the moment of the faint. See text for details. CO = cardiac output. (Reproduced with permission from Barcroft H, Edholm OG, McMichael J, Sharpey-Schafer EP. Posthaemorrhagic fainting. Study by cardiac output and forearm flow. *Lancet* 1944; I: 489–491.) RAP = right atrial pressure; TPR = total peripheral resistance

Figure 3.

Aborting a vasovagal faint after antigravity suit inflation to 60 mm Hg. Note progressive fall in intra-arterial pressure. *Shaded section* indicates the period of inflation. Central venous pressure increases instantaneously after inflation. The increase in blood pressure (BP) is delayed by about 3 seconds due to the transit time from the right to the left ventricle. The increase in BP was solely explained by the increase in cardiac output (increase by a factor of 1.4). Note that deep sighs during the fall in pressure increase BP for 3–4 beats (effect of the thoracoabdominal pump). Brachial artery = intra-arterial pressure; CVP = central venous pressure; Resp. = respiration. (Reproduced with permission from Weissler AM, Warren JV, Estes EH, McIntosh HD, Leonard JJ. Vasodepressor syncope; factors influencing cardiac output. *Circulation* 1957;15:875–882.)

Figure 4.

Vasovagal faint with recovery during a tilt test with marked hypotension and bradycardia. The period of measurement of cardiac output (CO; about 20 seconds) matching the rapid fall in blood pressure (BP) is indicated (i.e., the CO measurement is not a steady-state measurement). The exact matching of the CO with the fall in BP is the idealized situation because the dye dilution method does not allow BP to be recorded continuously at the same time as arterial blood is sampled for CO measurement. Note that deep sighs during BP fall increase BP for 3–4 beats (effect of increase in CO by the thoracoabdominal pump). (Reproduced with permission from Weissler AM, Warren JV, Estes EH, McIntosh HD, Leonard JJ. Vasodepressor syncope; factors influencing cardiac output. *Circulation* 1957;15:875–882.)

Figure 5.

Pulse wave analysis computation of cardiac output (CO) during the last minute of a vasovagal faint induced by tilt-table testing in 6 patients demonstrates that the magnitude of the fall in CO is very much dependent on both the blood pressure (BP) level and the length of time needed to measure CO. CO 60–30 s = 5.2 L/min; CO 30–15 s = 4.8 L/min; CO 15–0 s = 3.5 L/min.

Table 1

Summary of hemodynamic variables in the historical studies during (pre)syncope

	Patients (n, gender)	Age (years)	HR (bpm)	SBP (mm Hg)	Mean BP (mm Hg)	CO (%)	SVR (%)	FBF
Cotton and Lewis et al ¹⁰	8 M ^a	21–28	33–64	—	—	—	—	—
Barcroft et al ¹³	7 M ^b	20–30	40–60	50	—	–25%, –50%	–40%, –20%	2–3×
Barcroft and Edholm ¹⁴	9 M ^c	20–30	50	50	—	—	—	2×
Weissler et al ¹⁶	8 M ^d	Students	—	33–84	38	–14% (–7% to 37%)	–44% (–13% to 66%)	—
Murray et al ³⁰	7 M ^e	25–40	64	76	56	–53%	39%	NS
Stevens and Lamb ³²	38 M ^f	17–34	71	79	—	–43 %	20%	—
Stevens ³³	41 M ^g	23–34	71	74	57	–39%	+7% (NS)	—
Epstein et al ³¹	10 M ^h	19–23	47	—	34	—	—	NS

BP = blood pressure; CO = cardiac output; FBF = forearm blood flow; HR = heart rate; SBP = systolic blood pressure; SVR = systemic vascular resistance.

^aClinical observations. Undetectable pulse during the faint.

^bTourniquets and venesection. Volunteers. Actual data in only 2 subjects given. Fully developed prolonged faints. Fick CO measurement. Volume-based plethysmography.

^cTourniquets and venesection. Volunteers. Volume-based plethysmography. As typical values for the fully developed faint, Barcroft and Edholm give BP 50/30 mm Hg, mean BP 40 mm Hg, CO –40%.

^dTilt + nitroglycerin. Students. Fully developed faints. Control for changes in CO and SVR during syncope is 3–10 minutes after head-up tilt. Mean and range are given. Comparing post-faint values with CO at the faint, the decrease in CO is about 40%.

^eLower body negative pressure (LBNP). Trained volunteers. Hemodynamic measurements during presyncope. Dye dilution CO. Strain gauge plethysmography. NS compared to control.

^fLBNP. Air force personnel. Dye dilution CO. Hemodynamic measurements during presyncope.

^gUpright tilt while suspended in a standard Air Force parachute harness. Air Force pilots and navigators. Dye dilution CO. Hemodynamic measurements during presyncope. NS compared to control.

^hLBNP. Trained volunteers. Fully developed faints. FBF measured by strain gauge plethysmography just before the faint. NS compared to control.