Hemodynamic basis of stasis ulceration—A hypothesis

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Approximately 25% of patients with stasis ulceration have normal or below normal ambulatory venous pressures. A reflux index was calculated by multiplying postexercise pressures by Valsalva-induced foot venous pressure elevation. In patients with stasis ulceration, reflux index was found to have an excellent negative predictive value with a clear discriminant line between normal limbs and those with ulcers. Increasing incidence of stasis ulceration was demonstrated with increasing reflux index value. Even when ambulatory venous pressure was within the normal range, the index was found to be abnormal in ulcerated limbs because Valsalva-induced foot venous pressure was elevated in these limbs. Conversely, some patients with stasis ulceration and normal Valsalva foot venous pressure elevation were found to have abnormal ambulatory venous pressure values, yielding an elevated reflux index. Preliminary analysis indicates that reflux index may be a better predictor of surgical outcome after valve reconstruction procedures than either ambulatory venous pressure or Valsalva-induced foot venous pressure elevation. The concept of reflux index is a hypothesis that attempts to explain inconsistencies observed in implicating ambulatory venous hypertension as the sole determinant of venous reflux. (J VASC SURG 1991;13:491-5.)

It is generally accepted that ambulatory venous hypertension is the basis of stasis ulceration in reflux venous insufficiency. Although an association between the two entities has been shown in individual small series,[1-6] an incontrovertible relationship from a large data base has not been established. Nicolaides and Yao[7] showed an increasing incidence of stasis ulceration with increasing ambulatory venous hypertension in a large group of patients. However, these limbs comprised a variety of venous abnormalities that included reflux, obstruction, and a combination. In our own experience of over 600 patients with reflux venous insufficiency, we have noted that approximately 25% of patients with stasis ulceration had ambulatory venous pressures of 50 mm Hg or less.[8] Other investigators (Kistner RL, personal communication) have also noted a similar lack of consistent relationship between ambulatory hypertension and stasis ulceration. Certain surgical procedures that have only minimal effect on postexercise pressures are nonetheless successful in healing stasis skin changes. Such procedures include saphenous vein stripping (in selected patients),[9-13] Linton perforator ligation,[14,15] and valve reconstruction procedures.[8] It has been established that an improvement of only 12 mm Hg is obtained on average after valve reconstruction, despite the fact that excellent ulcer healing is obtained.[8]

These observations have prompted us to suggest that ambulatory venous hypertension may not be the only factor responsible for the generation of stasis ulceration.[8] Other parameters, such as velocity of reflux (water hammer effect), may be important. Various reports confirm the presence of a high-velocity perforator beneath venous ulcers.[16-19] Limited ligation of such perforators has been reported to have led to the healing of ulceration,[20-22] although postexercise pressures were likely unaffected.

We have previously noted that a different pressure measurement, namely Valsalva-induced foot venous pressure elevation, appeared to define a refluxive population that was somewhat different from ambulatory venous pressure measurement.[23] It is suggested that the Valsalva-induced foot venous pressure reflects aspects of reflux not measured by the traditional ambulatory venous pressure measurement. Consequently, we propose an index of venous reflux that incorporates both mechanisms of venous pressure elevation.

MATERIAL AND METHODS

Five hundred eighty-six of 1342 patients investigated for suspected chronic venous insufficiency over

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Table I. Comparison of toe-stands and calf compression techniques in measuring ambulatory venous pressure

	Calf compression(†)			*Toe-stands(†)*		
Group	*No.*	*% drop (mean ± SD)*	*Recovery time seconds (mean ± SD)*	*No.*	*% drop (mean ± SD)*	*Recovery time seconds (mean ± SD)*
Healthy "normal" limbs	18	51% ± 8%*	>20 sec NS	18	64% ± 14%*	>20 sec NS
Limbs with symptoms of chronic venous insufficiency	44	38% ± 17%**	16 ± 6 NS	44	46% ± 23%**	15 ± 6 NS

*$p < 0.01$
**$p < 0.01$
NS, Not significant.
(†)Without tourniquet. See text for values with tourniquet.

a 12-year period in the laboratory were determined to have reflux (often bilateral) without obstruction. Among these, 407 limbs underwent ascending and descending venography. Of the total, 113 limbs had class III stasis skin changes and frank ulceration.[24] All of these limbs had a complete set of laboratory parameters in addition to ascending and descending venography.

Student *t* test (for paired data when appropriate) was used. For reproducibility of techniques, intraclass coefficients were used.[25]

A postexercise (simulated) venous pressure measurement test was performed with the patient standing. After a needle had been inserted into a dorsal foot vein and resting pressure measured through a transducer affixed to the foot, the technologist compressed the calf manually several times. Usually five to six compressions resulted in a pressure level that was reaching a plateau. This was recorded as ambulatory pressure after simulated exercise. It was suggested that this modification of the original toe-stand technique might have resulted in an artificially low postexercise pressure, and that this difference in technique might have been the basis for the normal or low exercise pressures noted in some patients with stasis ulceration. To investigate this possibility, the manual calf compression method was compared to the traditional toe-stand technique in a group of normal volunteers as well as in patients with chronic venous insufficiency. The mean postexercise percentage drop with calf compression (with and without tourniquet) was 56% and 51%, respectively, and with toe-stand was 71% and 64%, respectively (Table I). It is important to note that the manual compression technique appeared to yield the *higher* mean postexercise pressure and lower percentage drop suggesting that this technique understates the incidence of normal exercise pressures and percentage drops in the presence of stasis ulceration. The reproducibility of the two techniques was also assessed by repeating the tests on the same limb after a few weeks' interval. The intraclass correlation coefficients for the two methods were 0.6 for calf compression and 0.4 for toe-stands (Table II).[25] Obviously, there was less variation in postexercise pressures when manual compression was used. This is not too surprising in that manual compression eliminates the potentially variable voluntary effort by the patient.

Through the same needle puncture used for ambulatory venous pressure measurement above, the resting venous pressure in the *supine* position was measured. At this point the patient was asked to exert and sustain a Valsalva effort of 30 to 40 mm Hg by blowing against a tube connected to a manometer; a rapid rise in the foot venous pressure in the supine position was noted. The resulting elevation in foot venous pressure from resting levels was recorded. On repetitive testing in 18 normal limbs, the value remained normal in 100% of patients. The intraclass correlation coefficient on repetitive testing in 24 reflux patients was 0.97. The technique is obviously highly reproducible (Table II). The Valsalva measurement was also examined before and after a valve reconstruction procedure. A dramatic drop in Valsalva-induced foot venous pressure was invariably noted after successful valve reconstruction.

RESULTS

The relationship between ambulatory venous pressure and Valsalva-induced foot venous pressure in 113 ulcerated limbs is depicted graphically in Fig. 1. It can be seen that a number of stasis ulcers (22%, or 25 ulcers) occurred in the presence of "normal" ambulatory venous pressure, that is, 50 mm Hg or less. With Valsalva-induced foot venous pressure, again 15% (17 ulcers) were noted to occur when this parameter was within the normal range (4 mm Hg o

Table II. Reproducibility of techniques

Group	*Ambulatory venous pressure* — *Calf compression % drop (mean ± SD)*	*Ambulatory venous pressure* — *Toe-stands % drop (mean ± SD)*	*Valsalva-induced foot venous pressure* — *Elevation mm Hg (mean ± SD)*
Normal limbs	$n = 18$	$n = 18$	$n = 18$
First test	51 ± 8	64 ± 14	1.8 ± 0.7
Second test	56 ± 7	71 ± 17	1.7 ± 0.9
Intraclass coefficient	0.6	0.4	0.3
Symptomatic limbs	$n = 19$		$n = 24$
First test	37 ± 16 Recovery time 17 ± 4 sec		10.2 ± 5.7
Second test	46 ± 11 Recovery time 17 ± 5 sec		11.7 ± 6.5
Intraclass coefficient	0.7 0.7 for Recovery time		0.97

Table III. Valsalva foot venous pressure elevation and reflux index in normal refluxive and valve reconstructed limbs

	Normal limbs	*Refluxive limbs*	*Ulcerated limbs*	*Valve reconstructed limbs* — *Surgical preoperative*	*Success postoperative*	*Surgical preoperative*	*Failure postoperative*
Valsalva foot venous pressure mm Hg (mean ± SD)	1.8 ± 0.7 $n = 18$	7.9 ± 5.1 $n = 63$		9.2 ± 5.3 $n = 41$	4.2 ± 2.5 $n = 41$		
		$p < 0.001$			$p < 0.004$		
Reflux index (mean ± SD)	70 ± 39 (range 1-150) $n = 42$	192 ± 144 $n = 294$	547 ± 359 $n = 113$	715 ± 389 $n = 17$	318 ± 208	442 ± 213 $n = 12$	594 ± 355
		$p < 0.0001$	$p < 0.0001$		$p < 0.02$		NS

less). There is an apparent lack of correlation between the two parameters with a wide scatter of the plotted points. This suggests that these two variables are independent of each other in ulcerated limbs.

Reflux index was calculated by multiplying post-exercise pressure by Valsalva-induced foot venous pressure elevation.

Reflux index in healthy volunteers is shown in Table III. Based on these findings, a value of 150 was chosen as the upper limit of normal for reflux index. The distribution of stasis ulcers based on this index is shown in Fig. 2. With a reflux index of 150 as the discriminant value, 98% of all stasis ulcers fell beyond this line. Only 2% of ulcers had a reflux index value of less than 150. Patients with lesser degrees of reflux without ulceration had a mean reflux index value of 192 compared to 547 for ulcerated limbs (Table III).

It is clear that the incidence of ulcer progressively increases with increasing reflux index (Fig. 2). The incidence of stasis ulceration was virtually 100% when the index was over 1000. Reflux index had a false-negative rate of only 2% for stasis ulceration, compared to 16% for Valsalva and 22% for post-exercise pressure (Figs. 1 and 2). In a preliminary analysis of reflux index in patients undergoing valve reconstruction procedures, it appears that this parameter can be used as a predictor of surgical outcome. The preoperative and postoperative reflux index values in a group of patients undergoing valve reconstruction for stasis ulceration are shown in Table III. There was a reduction of 44% (mean) in

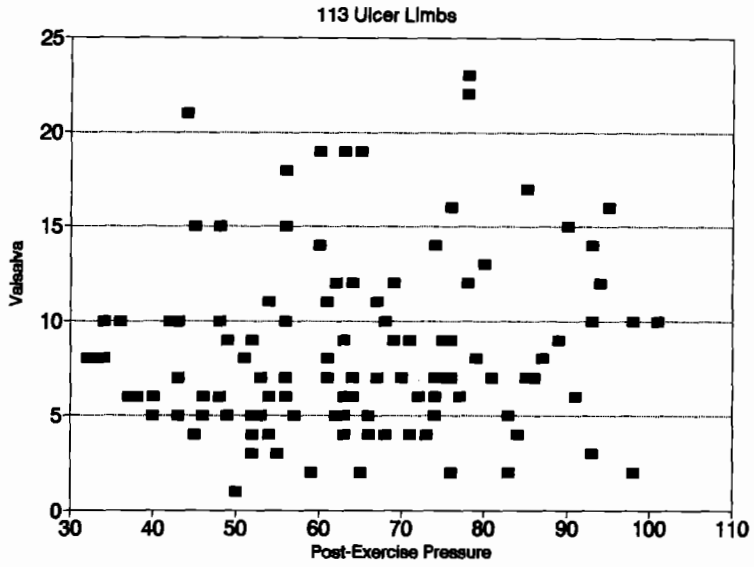

Fig. 1. Relationship between Valsalva-induced foot venous pressure elevation and ambulatory venous pressure in 113 ulcerated limbs. Twenty-five limbs have ambulatory pressures of 50 mm Hg or less. Seventeen limbs are shown to have Valsalva-induced foot venous pressure elevation of 4 mm Hg or less.

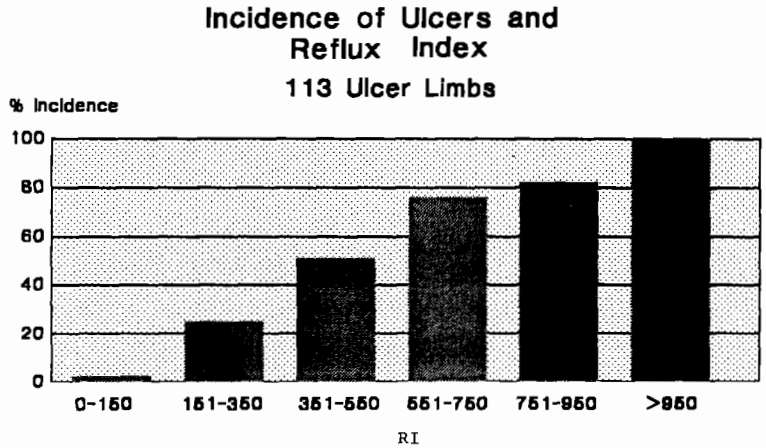

Fig. 2. Relationship between incidence of stasis ulceration and reflux index.

reflux index after successful valve reconstruction. Among surgical failures there was a mean *increase* of 34% after valve surgery. In some patients reflux index deteriorated over a period of time after initial improvement after valve reconstruction. After initial healing, ulcer recurrence was noted when there was deterioration of reflux index.

DISCUSSION

The concept that venous reflux causes stasis ulceration is well established. However, details of the pathophysiology of reflux are imperfectly understood. It is widely believed that ambulatory venous hypertension resulting from reflux are the basis of stasis ulceration. Accepting postexercise pressure as the sole parameter of reflux cannot be reconciled with many observations related to stasis ulceration as outlined above. In particular, approximately 20% to 25% of patients with stasis ulceration have ambulatory venous pressure values that are considered within the normal range. In the series presented herein, 25 limbs with stasis ulceration had normal ambulatory venous pressures (< 50 mm Hg). Twenty-three of these had abnormal Valsalva-induced foot venous pressure

elevation. In the same series 17 limbs had normal Valsalva-induced foot venous pressure elevation, 16 of which had abnormal values for postexercise pressures. It is clear that both parameters of reflux should be considered in the genesis of stasis ulceration. An index representing reflux was, therefore, calculated by multiplying these values as measured in individual patients. An excellent correlation between stasis ulceration and increasing reflux index can be demonstrated. It is more important to note that a good discriminant line between normal and abnormal limbs is available with this index, yielding an excellent negative predictive value for stasis ulceration. In contrast, the ambulatory venous pressure and Valsalva-induced foot venous pressure individually exhibit false-negative rates leading to poor negative predictive values. In approximately 60% of patients with stasis ulceration, both components of the index are abnormal. However, approximately 15% to 25% of limbs at each end of the bell-shaped curve have only one abnormal component, nonetheless producing an abnormal reflux index.

The Valsalva-induced foot venous pressure elevation may be seen to represent the capacity of the deep venous hypertension to be transmitted to the vessels of the skin and subcutaneous tissues in the periphery. If the communication between the deep and superficial compartments, that is, perforators, is small with competent valves, sudden changes in deep venous pressure caused by coughing and straining may be damped out before they are transmitted to the superficial tissues, including skin. If the communication is large with incompetent valves, reflux in the deep system has greater potential for transmission to the superficial compartment in an undamped fashion, producing substantial stasis damage.

One of the major criticisms leveled against valve reconstruction procedures is the poor correlation between ambulatory venous pressure measurements and surgical outcome. Reflux index may be a better predictor of surgical outcome after valve reconstruction.

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