

# **Plethysmographic features of venous reflux and impaired venous outflow do not influence the results of treatment of venous leg ulcers**

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**Abstract Background:** There is a need for a diagnostic tool to predict the clinical outcome of venous leg ulcer patients, as a prognosis of healing based only on clinical data has not appeared to be satisfactory. **Methods:** All patients were managed in the specialized leg ulcer clinic. Air-plethysmographic assessment of the venous reflux and the venous outflow was performed in 129 legs with an active ulcer. Results of air-plethysmography were compared to clinical data and time of healing of the ulcers. **Results:** Venous reflux and parameters of venous outflow did not correlate with the results of treatment of ulcerations. **Conclusions:** Assuming that the correct compression therapy is applied, venous reflux or impaired venous outflow do not influence the healing of venous leg ulcers.

**Key words:** Leg ulcer • plethysmography • venous reflux

## **Introduction**

Venous ulcers of lower legs constitute not only a significant medical problem, but also an economic and social one too. Due to the long treatment period, the condition consumes a disproportionate amount of the healthcare budget - approx. 1.5-2% in Western European countries and ulcer treatment poses a significant burden for the patient's family. Efficient treatment of ulceration would reduce these burdens to some extent; however, despite certain progress in treatment of the disease, treatment effects are still unsatisfactory [13, 15].

As only some patients require advanced treatments, (in the majority of patients standard dressing and compression bandage would suffice) it should be determined, as early as at the commencement of treatment, which patients have poor prognosis on early healing. However, despite numerous studies, there is still no reliable prognostic factor.

Ulcers with poor baseline prognosis should be treated with sophisticated treatments (e.g. skin grafts, bioartificial skin substitutes, cytokines and growth factors), instead of the current recommended scheme of 12-months standard treatment and application of modern methods only if the previous treatment failed.

To date several unfavourable factors related to prolonged healing have been defined, e.g. insufficiency of calf muscle pump determined by plethysmography [14]. The aim of this paper was to evaluate other parameters of plethysmographic examination (assessment of patency and venous outflow) and to determine whether they correlate with treatment outcome.

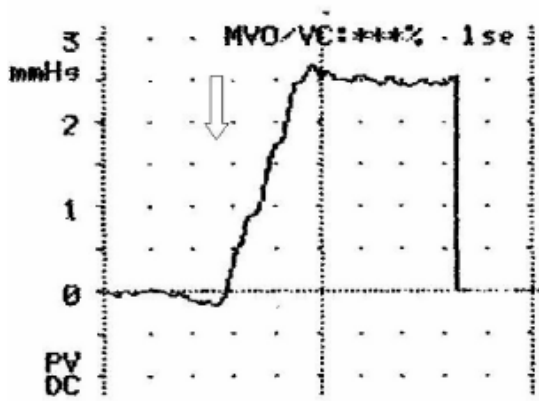


Fig. 1. Assessment of venous reflux. The arrow indicates the moment when the limb examined assumed vertical position.

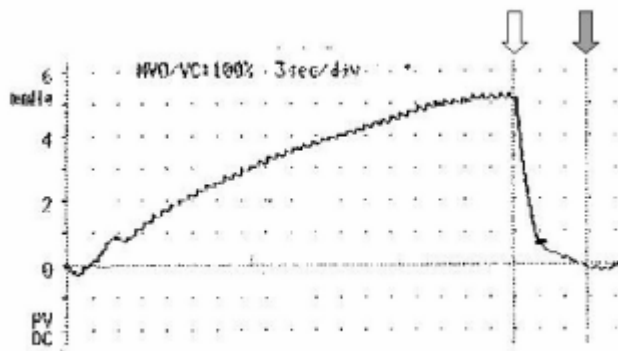


Fig. 2. Regular venous outflow from the limb: VOF-3 – 100%. First arrow: moment of release of thigh cuff; second arrow – 3 s.

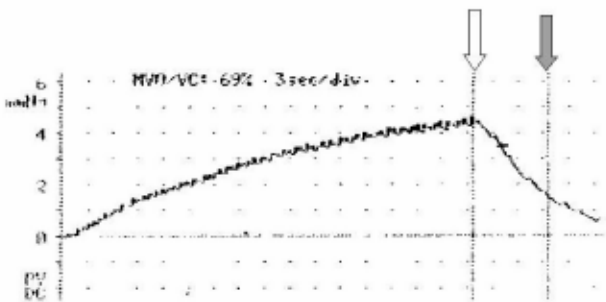


Fig. 3. Abnormal venous outflow from the limb: VOF-3 – 69%. First arrow: moment of release of thigh cuff; second arrow – 3 s.

### Clinical material

The study involved 129 limbs with ulcerations in 95 patients. All the patients were treated on an out-patient basis in Vascular Disease Clinic between 2003-2005. The age of the patients varied from 33 to 88 years; the mean age was 66.2 years. The study population comprised 66 women and 29 men (69.5% vs. 30.5%). Duration of ulceration varied from one week to 25 years with median amounting to three months. Diameter of ulcers varied from 1 to 30 cm, with median of 4 cm. If there were several ulcers on a

limb, analysis involved the biggest one. An ulcer's diameter was defined as distance between margins measured along the longest axis. Venous aetiology of ulceration was determined on the basis of symptoms revealed in clinical examination (localisation, presence of varices, oedemas, typical skin discolorations, etc.); the diagnosis was confirmed by Doppler examination. In some patients venous insufficiency was the predominant pathology; however, they were also diagnosed with other conditions which may affect the healing process (history of diabetes, rheumatoid arthritis, leukaemia or vasculitis) – there were 30 such cases. Patients with typical ulcers related to arterial ischaemia or diabetic foot (e.g. toe or heel necrosis) or without foot necrotic lesions but with no peripheral pulse on the limb or ankle-arm index below 0.8 were not included into the study. Final treatment effect was available for 123 ulceration cases, other patients prematurely terminated treatment due to various reasons.

### Methodology of plethysmographic examination

Plethysmography was performed by means of Hadeco Smartdop-20EX apparatus (Hayashi Denki Co., Kawasaki, Japan) with air-plethysmographic probe PV-20. The basic element of the apparatus is an air chamber that surrounds the examined limb. As veins provide the only portion of the limb that is able to change its volume significantly and rapidly, each change of limb volume is roughly equal to the change of veins' volume. Changes of limb volume resulting from filling or emptying veins lead to changes of pressure in the air chamber [3, 10, 11, 14]. The pressure changes may be calculated into volume units on the basis of the apparatus calibration made before the examination. Usually a single chamber made of non-stretch material. However, for examination of patients with venous ulceration, an air chamber comprising two connected sphygmomanometer cuffs was used. Such a chamber is easier to apply on pathologically deformed limbs (so called "champagne bottle" legs), and thus avoid formation of artefacts during examination. The air chamber is filled with air up to pressure of 6-8 mmHg (the pressure must not be higher to prevent vein collapse). Then the apparatus is calibrated by means of addition of small amount of air into the chamber (10 and 20 mL) and measurement of resulting pressure increase [14].

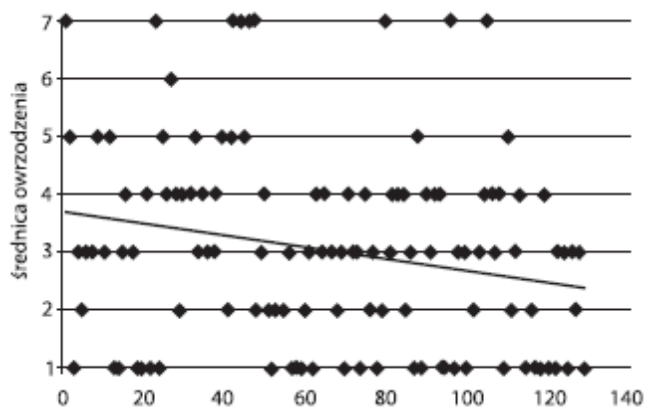


Fig. 4. Volume of venous reflux vs. ulcer diameter. Statistically insignificant differences (Spearman's rank test:  $p > 0.05$ ). 1 – < 1 cm; 2 – 1-2 cm; 3 – 2-5 cm; 4 – 5-10 cm; 5 – 10-20 cm; 6 – > 3/4 circumference; 7 – entire limb circumference.

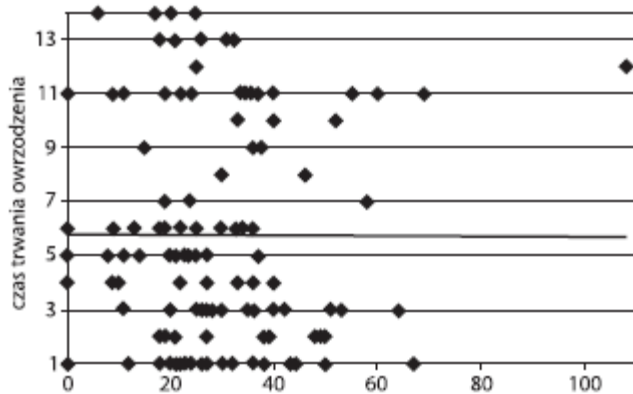


Fig. 5. Volume of venous reflux vs. duration of ulceration presence. Statistically insignificant differences (Spearman's rank test:  $p > 0.05$ ). 1 – 1 week; 2 – 2 weeks; 3 – 2 weeks-1 month; 4 – 1-2 months; 5 – 2-3 months; 6 – 3-6 months; 7 – 6-9 months; 8 – 9-11 months; 9 – 12-18 months; 10 – 18-24 months; 11 – 2-5 years; 12 – 5-10 years; 13 – 10-20 years; 14 – >20 years.

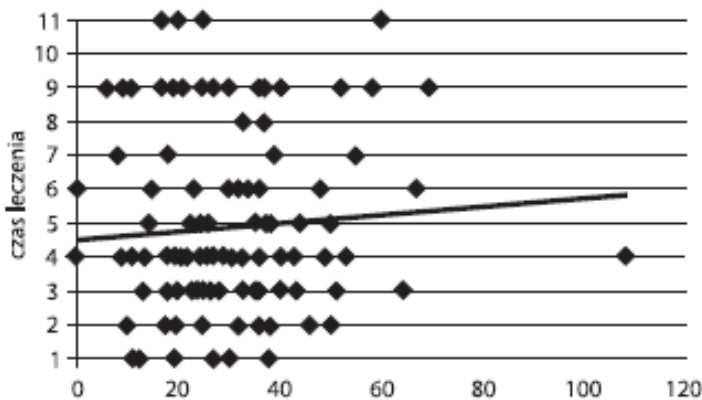


Fig. 6. Volume of venous reflux vs. duration of ulceration healing. Statistically insignificant differences (Spearman's rank test:  $p > 0.05$ ). 1 – 1 week; 2 – 2 weeks; 3 – 2 weeks-1 month; 4 – 1-2 months; 5 – 2-3 months; 6 – 3-6 months; 7 – 6-9 months; 8 – 9-11 months; 9 – 12-18 months; 10 – 18-24 months; 11 – over 24 months.

### Assessment of venous reflux

Examination was performed in a sitting position. To determine the presence and volume of venous reflux the examined limb was lifted up and then, after stabilisation of air chamber pressure, lowered. Venous reflux volume was calculated on the basis of curves obtained during calibration of the plethysmographic apparatus (Fig. 1).

### Assessment of venous outflow

Examination was performed in a supine position. To determine whether venous outflow from the limb was regular, an additional broad cuff was applied on the patient's thigh that was filled with air up to pressure of 80-100 mmHg (to completely close venous outflow from the limb and not to compromise arterial inflow). After inflation of the thigh cuff, limb volume was increasing due to dilatation of venous bed until certain stable

maximum value was maintained. Then air was released from the thigh cuff with simultaneous registration of the curve of limb volume decrease.

Venous outflow fractions after 1 sec. and 3 sec. were calculated (VOF-1 and VOF-3) as a percentage ratio of air chamber pressure drop after 1 sec. and 3 sec. to the difference between baseline pressure and maximum pressure. In healthy individuals VOF-3 is 95-100%. Lower values indicate venous outflow disorders (additional tests may differentiate between deep vein occlusion and superficial vein occlusion) (Fig. 2-3).

### Statistical methods

For statistical calculations a MS Excel spreadsheet (Microsoft, Richmond, USA) with specialised statistical features (<http://udel.edu/~mcdonald/statintro.html>) was used. Data were analysed by means of Spearman's rank test and differences were considered statistically significant for degree of freedom-dependent significance level  $p > 0.05$ .

### Results

Assessment of venous reflux: No statistically significant correlations between the venous reflux volume and ulcer diameter or duration of ulcer presence before treatment in a specialised clinic were found. Also volume of venous reflux had no effect on the duration of ulceration healing. Actually ulcerations on limbs with higher reflux volume healed slightly slower than ulcerations associated with insignificant reflux; however, the differences were statistically insignificant. Thus, considering results of this study, volume of the venous reflux does not seem to have any effect on the course of healing of venous ulcers of lower legs (Fig. 4-6).

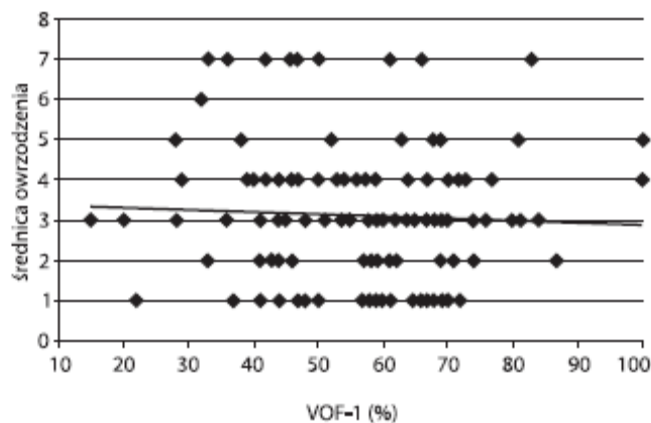


Fig. 7. Parameters of venous outflow (VOF-1) and ulceration diameter. Statistically insignificant differences (Spearman's rank test:  $p > 0.05$ ).

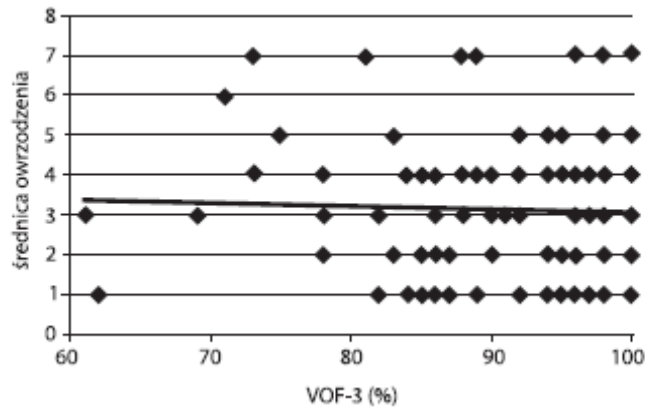


Fig. 8. Parameters of venous outflow (VOF-3) and ulceration diameter. Statistically insignificant differences (Spearman's rank test:  $p > 0.05$ ).

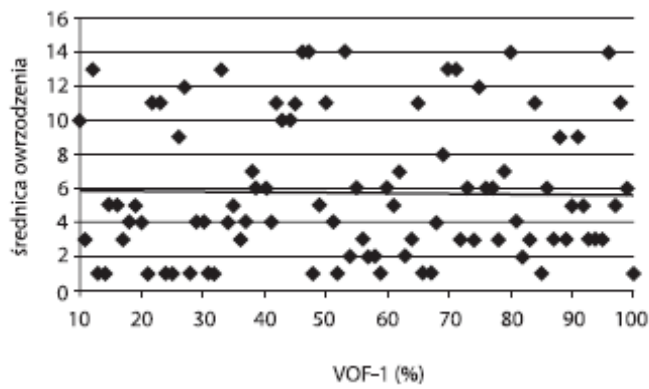


Fig. 9. Parameters of venous outflow (VOF-1) and duration of ulceration presence. Statistically insignificant differences (Spearman's rank test:  $p > 0.05$ ).

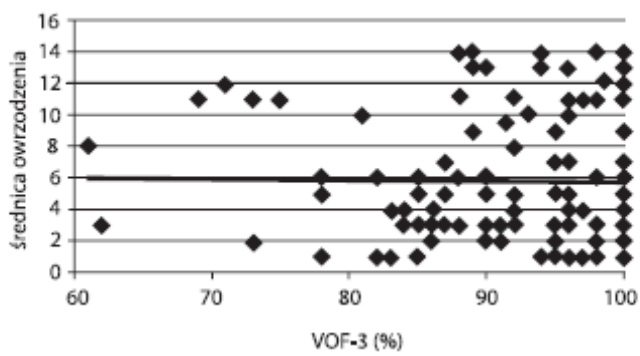


Fig. 10. Parameters of venous outflow (VOF-3) and duration of ulceration presence. Statistically insignificant differences (Spearman's rank test:  $p > 0.05$ ).

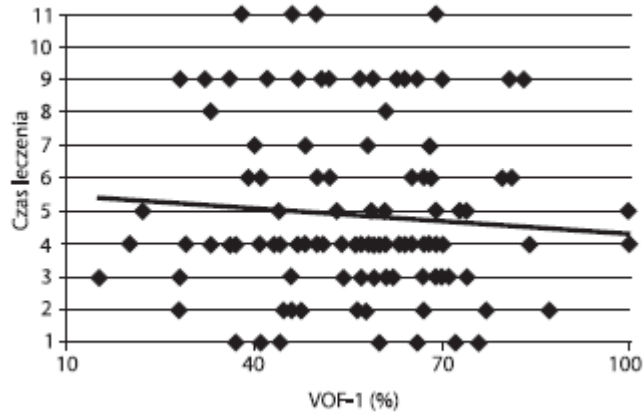


Fig. 11. Parameters of venous outflow (VOF-1) and duration of ulceration healing. Statistically insignificant differences (Spearman's rank test:  $p > 0.05$ ). 1 – 1 week; 2 – 2 weeks; 3 – 2 weeks-1 month; 4 – 1-2 months; 5 – 2-3 months; 6 – 3-6 months; 7 – 6-9 months; 8 – 9-11 months; 9 – 12-18 months; 10 – 18-24 months; 11 – over 24 months.

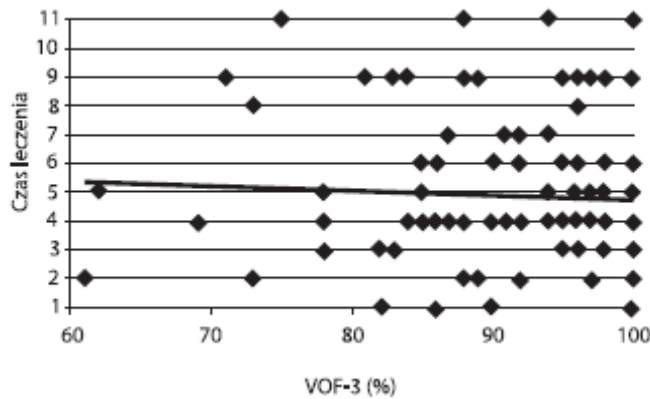


Fig. 12. Parameters of venous outflow (VOF-3) and duration of ulceration healing. Statistically insignificant differences (Spearman's rank test:  $p > 0.05$ ). 1 – 1 week; 2 – 2 weeks; 3 – 2 weeks-1 month; 4 – 1-2 months; 5 – 2-3 months; 6 – 3-6 months; 7 – 6-9 months; 8 – 9-11 months; 9 – 12-18 months; 10 – 18-24 months; 11 – over 24 months.

### Assessment of venous outflow

No statistically significant correlations between regular or abnormal venous outflow and ulcer diameter or duration of ulcer presence before treatment in specialised clinic were found. Similarly to the venous reflux, venous outflow parameters did not correlate with the duration of ulcer healing.

According to treatment results in the study population, it may be stated that venous outflow (i.e. presence of stenoses or occlusion with deep vein system) does not seem to have any effect on the course of healing of venous ulcers of lower legs (Fig. 7-12).

### Discussion

Venous outflow from lower limb depends mostly on the emptying of sural venous sinuses within the triceps muscle and other veins within the deep muscle compartment of the lower leg. Such emptying takes place during plantar flexion in ankle joint. Emptying of

foot and thigh veins is of secondary importance. Moreover, regular venous outflow from lower limb depends on the presence of competent valves, patency of main venous trunks and lack of reflux through incompetent superficial veins. With all the above elements maintained, venous blood may flow from the superficial vein system to the deep vein system and from distal to proximal veins, and then towards the heart. Each disorder of this fragile system may result in the development of venous hypertension and in turn, serious and long-lasting venous hypertension may result in ulceration [1, 4, 5, 7, 9, 14].

As venous hypertension in patients with chronic venous insufficiency (CVI) can result from a combination of venous reflux, outflow disorder and/or muscle pump insufficiency, plethysmography is recommended to provide an element of diagnostics for such patients, as this examination is able to assess each of the pathologies described. Pneumoplethysmography comprises several independent tests; each of them allowing the assessment of different variables of venous flow [6, 11].

Currently the majority of therapeutic decisions in phlebology are taken on the basis of anatomical examinations. Functional examinations are still undervalued. Thorough assessment of CVI patient should include clinical examination (history and physical examination), anatomical diagnostics (Doppler ultrasound and/or phlebography) [2, 10, 11] and functional diagnostics (e.g. plethysmography) [2, 10, 11, 17]. In fact most patients do not require such thorough assessment; however such extended diagnostics involving also functional tests are necessary in more complex cases (e.g. patient with ulceration). It should be highlighted that chronic venous insufficiency is not a mere blood vessel condition, but should be considered a composite clinical syndrome involving not only pathological venous circulation, but also lymph circulation disorder, skin lesions and abnormal function of skeletal system [1, 4, 8, 12, 14, 18]. Only such an approach may improve the outcome of treatment of the most serious form of chronic venous insufficiency.

It should be noted that contrary to venous hypertension resulting from muscle pump insufficiency, venous hypertension associated with reflux or occlusion may be significantly relieved by means of compression treatment. However, venous hypertension resulting from muscle pump insufficiency usually does not improve after compression treatment [14]. Results of the study indicate that venous reflux or venous occlusion symptoms revealed by plethysmography have no effect on the result of venous ulceration healing. It is probable that the appropriate compression treatment applied in the patient, which normalised venous pressure, enabled unhindered healing of the ulcerations [16].

## **Conclusion**

Venous reflux or venous occlusion symptoms revealed by plethysmography have no effect on the result of venous ulceration healing, provided that appropriate compression treatment is applied.

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