Prediction of healing in patients with venous leg ulcers

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ABSTRACT

Background. The treatment of venous leg ulcers is often prolonged. This is perceived as unsatisfactory by patients who desire more precise information about the prognosis. There is a need for predictive information about the most likely expected outcome of treatment. This information may not only aid the counseling of patients but also the allocation of resources. A predictive score system based on clinical aspects of leg ulcers has been suggested, but not independently tested.

Methods. This study was conducted as a prospective study of patients referred to a hospital to assess the predictive value and accuracy of a previously proposed predictive test (scores 0 - 10). A score of 5 or less in the proposed predictive index was associated with complete or partial healing (P= 0.04).

Results. No significant correlation was found between any of the general biochemical factors at first presentation and ultimate wound healing. Initial wound size correlated significantly with final wound size and rate of healing. The study confirmed that ulcer area and duration as well as patients age can be combined in a predictive score for the rate of wound healing. The variation of outcomes for a given score was, however, widely suggesting that the proposed test might be of a rather limited use as a guide to the prognosis of individual patients. Routine examination of general biochemical factors in patients with venous leg ulcers does not appear to have a significant predictive value with regard to the outcome of ulcer treatment.

KEY
WORDS

clinical test,
out-come,
predictive
value,
quality
assurance,
leg ulcer

Introduction

Biophysical and clinical investigations into the pathogenesis of leg ulcers give valuable predictive information and make a clinically useful classification possible (1, 2, 3, 4, 5). A number of new treatments have become available but conservative therapy most often remains a lengthy process. Patients frequently wish to have an information about the prognosis. Such information is rarely published and may vary greatly between institutions, making historical or bibliographical references less useful in the actual counseling of the patient. There is therefore a practical need for methods, which can give this information.

In addition to accuracy, it is important that a predictive test functions in a routine clinical setting, i.e.

Table I. The results of routine biochemical testing in patients with venous leg ulcers.

Test	Value (mean ± SD)	Reference range	No. of test with low value (minimum value)	No. of tests with high values (maximum value)
Hemoglobin (mmol/l)	7.83 ± 0.90	7 - 10	8 (6.0)	0
White Blood cell count (*10⁹/l)	6 ± 2	3 - 9	0	3 (10)
Sodium (mol/l)	140 ± 3	136 - 146	2 (132)	0
Potassium (mmol/l)	4,0 ± 0,36	3.5 - 5.0	6 (3.2)	0
Creatinine (mmol/l)	0,094 ± 0,022	0.040 - 0.110	0	10 (0.183)
Glucose (mmol/l)	6,33 ± 2,32	4.0 - 8.4	0	2 (17.3)
Albumin (mmol/l)	585 ± 87	600 - 830	22	0 (257)
ASAT (U/l)	14 ± 8	10 - 14	11 (3)	15 (37)
Alkaline phosphatase (U/l)	211 ± 61	80 - 275	0	6 (400)

while subject to the unpredictable variations in therapy and to various external factors such as e.g. infection. A predictive test has limited value if it only works in a strictly controlled environment - it must be rugged to be of any use.

A prognostic index to predict time of healing has been suggested based on ulcer area, ulcer duration, patient's age and possible deep vein involvement as measured by photoplethysmography (6). The test has, however, not been independently validated. It was therefore decided to study the predictive value of this test to a group of patients undergoing routine treatment.

In contrast to physical measurements of e.g. blood pressure, the significance of biochemical investigation was not similarly investigated and therefore remains unclear at present. Anecdotal reports and clinical impression suggest those biochemical investigations of e.g. albumen or hemoglobin may, occasionally, be useful in practical management of patients with leg ulcers.

We have therefore assessed the usefulness of the proposed prognostic index in routine treatment and undertaken a simple evaluation of the predictive value of general biochemical factors in the routine management of venous leg ulcers.

Table II. The outcome of routine treatment of venous leg ulcers compared with pre-treatment assessment according to Skene et al. [6]. *Lower scores are related to a better average rate of healing (P= 0.04). Ulcers in the high score group increased at an average rate of 2 cm² per month.*

Score	N	Complete healing (%)	Partial healing (%)	No healing or worsening (%)	Healing cm²/month (mean & 95% confidence intervals)
-5	15	10 (67)	3 (20)	2 (13)	25 (198 (-239 - 636)
5	15	10 (67)	4 (26)	1 (7)	24 (-10 - 58)
6-	15	5 (34)	4 (26)	6 (40)	-2 (-16 - 12)

Materials and methods

This study was conducted as a part of the quality assurance project at the department of dermatology of a tertiary referral center. A total of 79 consecutive new patients referred to the Department of dermatology at Rigshospitalet 1992-95 for the treatment of leg ulcers were studied. All patients had their ankle/brachial blood pressure ratio or the distal blood pressure (toe) measured. Blood samples were drawn for routine analysis of the factors listed in Table I, and the outline of the ulcers was traced for calculation of wound area.

Ulcers were classified according to the following definitions (7, 8):

Venous ulcer: Arm/ankle index > 0.8 or toe blood pressure > 60 mm Hg. In cases where patients objected to measurement of distal blood pressure or where the ulcers prevented measuring, the following clinical definition was used: Warm, clinically well-perfused feet were taken to indicate a predominantly venous cause of leg ulcers if the patient was not diabetic and did not suffer from connective tissue diseases.

The following patients were excluded: 7 with arteriosclerotic ulcers, 4 with diabetic ulcers, 2 with unclassifiable ulcers, 7 due to skin grafting and 8 were lost during follow-up. Only patients fulfilling the above mentioned criteria for venous ulceration were studied.

All patients were treated according to the routine regimen used in the Department, consisting of a short-stretch double-layer compression bandage (Comprilan®, Beiersdorf, Germany) applied daily, and ointment dressings (changed on alternate days) or hydrocolloid dressings changed as appropriate. Treatment was however not standardized and variations therefore occurred dependent on various factors, e.g. infection, or minor differences in the approach by different physicians. It was expected that a clinically useful test would be accurate even under these conditions.

After a period (mean: 18 months; 95% confidence interval 14 - 21 months) of treatment the wound area was measured, and the rate of healing in cm² per month calculated.

The following correlations were studied: The ability of biochemical factors to explain wound size or wound duration, and the predictive value of biochemical testing for assessment of wound size 18 months later.

Three patients had concomitant diseases (1 blind patient, 2 patient with rheumatoid arthritis). Patients' ability to walk at the time of the first examination varied from normal (21 patients), to partial (necessitating support or cane, 11 patients) to wheel chair bound (7 patients), while no specific information on mobility was available for the remaining 11 patients

Six patients were lost to follow-up, leaving a subgroup of 45 patients available for the study of the previously proposed prognostic index. The index was calculated for each ulcer at the start of the investigation, and these scores were compared with actual outcome 18 months later. The original index was calculated by adding scores for ulcer size, ulcer duration, patient's age and deep vein involvement as measured by photoplethysmography. The scores ranged 0 - 5 for area, 0 - 2 for ulcer duration, 0 - 3 for patient's age and 0 - 0.5 for deep vein involvement, giving a total range of 0 to 10.5 in steps of 0.5 points. We modified the score and performed the calculation without the photoplethysmography, which is not available in our department. Because of photoplethysmography's contribution to the overall index is very low, its omission was not considered to impair the results. The modified score has a range of 0 - 10 in steps of 1 point. The index scores were grouped into two categories: < 6 based on the data suggested by Skene et al., and the rate of healing compared. The numbers of patients showing complete healing, partial healing and no healing or actual worsening were also compared.

Non-parametric statistics (Mann Whitney and Kruskall-Wallis test), Chi-square tests as well as multiple linear regression analysis were used.

Results

The 51 patients had a mean age ± standard deviation of 74.1 ± 13.8 years and a sex ratio of 1 : 1.8 (18 men/32 women). The mean size ± standard deviation of the ulcers was 25.9 ± 62,9 cm², and the mean ulcer duration ± standard deviation was 55.8 ± 116.2 months. No significant correlation was found between the baseline biochemical studies and wound area or wound duration at the first consultation. A number of biochemical abnormalities were found, see Table I, but none correlated with wound healing or ultimate wound size.

The proposed predictive test showed significantly more patients with a score of <5 had complete healing of their ulcers (P = 0.04) as can be seen from Table II.

General physical parameters showed a significant correlation with the outcome of treatment. Multiple linear regression analysis showed that patients' age, ulcer duration and wound size are significantly correlated to both final wound size (P < 0.001) and rate of healing (P = 0.002). Initial wound size was, however, the one physical component, which was most significant, and correlated to both final wound size and rate of healing (P < 0.001).

Discussion

Conservative leg ulcer therapy is usually a long process and patients' expectation to know the prognosis is justified. Benchmarking, i.e. comparison with other centers is difficult, as the outcome of routine treatment is rarely reported. This may be of lesser importance as the experience can vary considerably both between and within different institutions. Prognosis should therefore

ideally be established for individual patients by the use of appropriate testing. Multiple linear regression analysis confirmed that patient's age, ulcer duration and ulcer size are significantly correlated to both final wound size and rate of healing.

The predictive ability of the index was compared with the outcome of treatment. Three groups were identified: patients with completely healed ulcers, patients with partially healed ulcers, and patients with unchanged or increasing ulcer area. Statistically significant differences were seen, suggesting that the test was able to predict the outcome of treatment in patients. A score of 5 or less was found to be predictive of a better average rate of healing but not of a higher likelihood of complete healing, as can be seen from Table II. The number of patients was insufficient for further stratification of scores, and the variation of outcomes for a given score was large (wide confidence intervals of the mean healing rate). The proposed test may therefore only be of limited use as a guide to the prognosis of individual patients.

Biochemical factors, which could hypothetically either promote or slow down the healing of ulcers were studied as possible predictive parameters. No correlation to wound size or ulcer duration was seen, and the predictive value of the chosen biochemical investigations was not significant. Few biochemical abnormalities were seen, and the majority of these were thought to be clinically insignificant, see Table I. Two cases of hyperglycemia were found by the screening. No other new diseases were discovered by routine testing, but this may be due to the setting in a tertiary referral center where patients have usually been seen by several physicians prior to referral. Potentially initiating and potentially predisposing factors were studied. Hypothetical initiators of healing, such as e.g. hemoglobin did not show any correlation to the rate of wound healing, nor did potential inhibitors, such as sodium, potassium or albumen which could predispose to ulceration by increasing e.g. edema. Abnormal tests did not have a discernible negative influence on the wound healing. In contrast to the information obtained by biophysical investigation of the vessels, general biochemical investigation does therefore not appear to have any significant value for the description or prospective assessment of treatment outcome of venous leg ulcers (9).

The results suggest that in good accordance with clinical experience, the ulcer size at the initial evaluation may be the most important prognostic factor. The results do not support the inclusion of specific tests to the standard biochemical investigations except for glucosuria in patients with venous leg ulcers in a tertiary referral center. If general biochemical parameters have any influence on the treatment outcome of venous leg ulcers, it is speculated that this occurs only in conjunction with other and clinically relevant factors.

More accurate information about the prognosis of individual patients is an important aspect of quality assurance in dermatology (10). This study suggests that even in areas where the outcome is clearly defined (healing of ulcers) the current methodology be still not sufficiently developed.

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