Recurrent venous leg ulcers: clinical analysis of an experience

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ABSTRACT

Despite recent advances in wound care, varicose ulcers of lower limbs remain frequent and display a high rate of recurrence. In this paper, we examined the clinical, surgical histories and associated diseases of 133 patients with venous ulcers of the lower limbs, which were recurrent in 56 cases. The analysis of potential risk factors for recurrence showed that the presence of recurrent varicose veins, a previous deep venous thrombosis, orthopedic problems, previous orthopedic procedures, obesity and age lower than 60 are potential risk factors for ulcer recurrence. Furthermore, the association of one or more risk factors increased the likelihood of relapse, from 22.7% with no risk factors to 33% with 2 risk factors, up to 57.5% with 3 risk factors, and up to 81.3% with 4 risk factors or more. Venous ulcers require close follow-up and continuous elastic compression, close collaboration by the patient and specific focus on risk factors.

INTRODUCTION

A varicose ulcer is a skin lesion located under the knee or foot, occurring in presence of a venous disease of the lower limbs that does not heal within two weeks;[1] in 25% of patients, therapy is destined to fail.[2] The economic burden on the National Health System is heavy and it is estimated that in some European countries the treatment of ulcers affects up to 1% of the health budget.[3]

Most ulcers are of venous origin, are caused by venous hypertension,[4] and the mainstay of treatment is compression therapy;[5] however, recurrence is not uncommon and is a difficult problem. Despite recent advances in the technology of dressings and varicose veins surgery, the problem of varicose ulcers is open; not only these lesions need long periods of treatment, but often undergo a recurrence, which is even more difficult to treat. As of today, medical therapy has no definitive solutions, while superficial reflux surgery, both *open* and endovascular, has shown to reduce ulcer recurrences;[2,3] however the problem of failures remains and results of follow-up are disappointing. Many factors contribute to the pathogenesis of recurrence; obesity, walking difficulties, poor compliance or lack of elastocompressive therapy have been reported as responsible for long-term failure. In this paper, we examined patients affected by varicose vein ulcers, both primitive and recurrent, in order to analyze their clinical characteristics and to identify the risk factors responsible for treatment failure.

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MATERIALS AND METHODS

133 patients affected by varicose ulcer of the lower limbs were examined at our Ulcer Therapy Center of the San Filippo Neri Hospital in Rome, from January 2014 to December 2017, and were enrolled in our study.

Criteria for admission were: i) a history of deep vein thrombosis (DVT) or superficial venous thrombosis (SVT) of the lower limbs; ii) history of surgery for varicose veins of the lower limbs; iii) varicose veins of the lower limbs at physical examination.

All patients underwent an anamnestic interview and analysis of their clinical records. Patients with arterial or lymphatic pathology were excluded from the study. In a database we included medical history, varicose veins surgery, previous episodes of phlebostatic ulcer and relative healing times, episodes of DVT or SVT; orthopedic problems and related surgery have also entered our analysis. The patients underwent a cycle of dressings, with a 4-layer elastocompression bandage until ulcer healing.

RESULTS

Results of the study are shown in the Supplementary Tables 1-14. The population examined is described in Supplementary Tables 1 and 2; 56 patients had recurrent ulcers.

51% of patients with recurrent ulcers had a previous history of DVT, compared to 35% of patients with primary ulcers. Associated diseases are reported in Supplementary Tables 3-8.

Data about oral anticoagulation are reported in Supplementary Table 9.

Surgery for varicose veins is reported in Supplementary Table 10, recurrence of varicose veins is summarized in Supplementary Table 11.

Orthopedic problems and orthopedic surgery are listed in Supplementary Tables 12 and 13.

The average healing time of ulcers and recurrences are shown in Supplementary Table 14; minimum follow-up was 6 months, maximum 2 years.

Data analysis

The analysis was almost exclusively based on the construction of contingency tables whose significance is given by the Chi-Square test. The only exception was the analysis of average healing time, whose statistical significance was evaluated through the comparison test between the averages (Anova and Fisher F).

The population examined was quite old, with about 70% of subjects aged over 70 and only 6% under 50. On average, 42.1% of patients had a recurrent ulcer; analysis of various potential risk factors showed that only some of them were statistically significant. In particular and in order of importance: i) recurrent varicose veins, the most significant (recurrence for 73% of patients with recurrent varicosis *vs* less than 35% in primitive ulcers); ii) previous DVT, very significant (recurrence for about 51% of patients with DVT against 35% in the absence of DVT in the history); iii) orthopedic surgery, very significant (relapse for 59% of patients who had undergone orthopedic surgery, against about 39%); iv) obesity, very significant (recurrence for almost 53% of the obese compared to 34% of the non-obese); v) the age group is rather significant (recurrence for more than 58% of subjects under the age of 60 compared to 40% of subjects over 60); vi) orthopedic problems, quite significant (about 48% of patients with orthopedic problems compared to 37%).

The other potential risk factors such as SVT and associated diseases such as hypertension, heart disease, diabetes, atrial fibrillation, chronic bronchopneumopathy and oral anticoagulant therapy are definitely not statistically significant.

In this context, we search for something more in recurrence risk, searching for a *combined risk factor* given by the possible co-presence and interdependence of single factors identified as *influential* in recurrence.

This *overall risk result* was the sum of the six individual factors in order of significance; this combined risk factor was most significant, showing a strong direct relationship between the number of simultaneously present factors and the probability of recurrence.

In fact, from 22.7% in patients with any single factor to 33.3% of patients who have one or two factors, the probability of ulcer recurrence rises to 57.7% for patients who present three until at 81.3% for patients who have four or more at the same time.

Finally, regarding healing time, only relapse and arterial hypertension showed a statistically very significant influence, while for all others the relationship was only apparent. Moreover, relapse and hypertension show a strong and significant interaction between them. While healing time is shorter for patients at first episode of ulcer compared to recurrent ulcers (on average 57 days *vs* 87), as well as for patients not suffering from hypertension compared to hypertensive patients (on average 58 days *vs* 90), there is also an intensification of these effects when relapse and arterial hypertension are combined together. In these patients, healing time ranges from a minimum of 52 days on average for first-episode ulcer patients and non-hypertensive patients, up to 112 days on average for hypertensive patients with recurrence.

DISCUSSION

Varicose ulcers account for about 70% of ulcers of lower limbs in outpatient observation; incidence is 1% in the western population, which rises to 3% in *over 65*.[2,4,6] In 30% of cases, these lesions don't heal within 6 months and identification of risk factors is crucial for prognosis.[6] Despite recent advances in dressings technology and wound care, recurrences are not uncommon and represent a problem for the specialist and the patient; medical literature information indicates that high elastic compression levels are the key for treatment success,[5,7,8] though patient intolerance to elastic stockings often proves a penalizing factor. Keeping these considerations in mind, we believe it is important to have a *risk profile* for patients who are more likely to suffer an ulcer relapse; our study examined the patients' clinical histories to have a first instance prognostic index, just at the moment of the first diagnostic approach. In our experience, women show a prevalence both for primitive ulcers and recurrences, as already highlighted by other authors.[9] Another significant figure is the high percentage (42.1%) of *recurrent* ulcers; this means that almost half the patients of an outpatient clinic are those who have greater therapeutic difficulty and longer healing times. In our analysis of recurrence risk factors, recurrent varicose veins was the most important prognos-

tic index; a recurrent ulcer in 73% of patients with recurrence *vs* less than 35% in the group of primitive ulcers seems to underline a more difficult *phlebological history*, which needs strict and rigorous follow-up and, when necessary, an active treatment of varicose syndrome. Another noteworthy aspect concerns patients with recurrent ulcers who suffered a DVT, 51% as against 35%, a figure that appears significant and that had already been underlined by other authors.[9-13] The percentage of orthopedic operations in patients with recurrent ulcers (59% *vs* 39%) can be explained with the altered posture and therefore a distorted dynamic of the sural pump and venous return, in addition to the possibility of a postoperative DVT, which sometimes remains undetected. We know how the patient's mobility and the effectiveness of the venous calf pump affect the ulcer, in particular the motility of the ankle joint,[6] with obvious consequences on healing.[9] Also the significant incidence of orthopedic problems in recurrent ulcers (48% *vs* 37%) correlates with walking dynamics; exercise programs for ankle joint motility have been shown to improve calf function, with good results on ulcer healing,[7,11,14,15] and we believe that this should become part of the follow-up program for phlebopathic patients. Among the comorbidities in our experience, obesity, often mentioned as a risk factor for ulcers, influenced the recurrence, causing problems in hemodynamics of the limb.[7,11,13] Patient age group also turned out to be quite important, since the data showed higher relapse incidence in younger patients (58% *vs* 40%), due perhaps to a more active lifestyle implying a greater likelihood of trauma. The analysis of the results showed us that, when the most significant risk factors are combined, the probability of recurrence is 22.7% for patients with a single risk factor, while it raises to 81.3% for 4 or more factors; this may allow the identification of patients whose follow-up should be strict and therapy more aggressive. We were surprised by the substantial equality of patients in oral anticoagulation therapy between the two groups examined; we expected more relapses due to the ease with which a trauma or an infection may evolve into a recurrent ulcer.[4] The average healing time of recurrent ulcers, 87 days compared to 57 of primitive ulcers, shows that we face not only an invalidating disease that tends to become chronic; the percentage of recurrences that we observed up to now (but which we think will grow over time) is 26% for recurrent ulcers and 5% for primitive ones, an indication that there is still much to do for a definitive resolution of this disease. In fact, it is highly probable that recurrences increase during follow-up and that recurrence of the ulcer is a negative prognostic factor,[16] which certainly does not justify optimism. Obviously, surgery has a role in preventing recurrences; studies on surgery of the superficial veins in ulcers has shown a reduction in ulcers recurrences.[3] Finally, we were surprised by the data concerning the influence of arterial hypertension on healing time, which are generally not detected in medical literature; we believe that, in addition to the very probable circulatory damage due to the hypertensive disease, drugs taken by these patients may play a role in delayed healing, and we intend to verify this data in a further analysis.

CONCLUSIONS

Recurrent ulcers are an increasing problem in outpatient care and need special attention due to the discomfort they cause to the patient and the need for long and often painful treatment. Identifying patients with *high recurrence risk* is important to devise adequate follow-up programs and to educate the subjects on healthy lifestyles helping to maintain a good function of the venous calf pump. In our experience a positive anamnesis for DVT, the presence of recurrent varicose veins after surgical treatment, orthopedic problems and the related operations, obesity and patient age were significant markers for risk of ulcer recurrence; in these the average healing time was significantly higher than in primitive ulcers. This must be pointed out to patients beginning the treatment, in order to avoid excessively optimistic expectations. The planning of a close follow-up will be pivotal to monitor the evolution of the disease and correct existing risk factors so as to prevent ulcer relapses.

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