

EVALUATION OF PROGNOSTIC FACTORS RELATED TO HEALING OF VENOUS ULCERATIONS OF LOWER EXTREMITIES

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Venous ulcerations occur in 1% of human population, being more frequent in the population over 65 years of age. The aim of this study was to evaluate the prognostic factors related to healing of venous ulcerations of the lower extremities treated with multi-layer bandage.

The research was based on the prospective randomized study conducted at the Outpatient Clinic for Dermal and Sexual Diseases and Medical Center in Doljevac during the period from 2007 until 2008. The research involved a group of 50 patients of both sexes with venous ulcerations of the lower extremities. Patients were followed up for 24 weeks from the beginning of the treatment.

Out of a total of 50 patients, 30 (60%) were of female sex and 20 (40%) of male sex. The mean age of the patients was 63.3±6.32 years. In thirteen patients (26%), there was no complete healing of chronic venous ulcerations. Locoregional characteristics of ulcerative changes indicated no significant difference in the average number of ulcers, their localization, duration, and average surface. The analysis made by Kendall's tau_b correlation coefficient showed that sex and localization had no significant correlation with the healing of ulcerative changes. Infection and swelling of the lower leg showed poor but significant positive correlation with a change in the healing rate ($p < 0.05$). Pearson's correlation coefficient showed a significant positive correlation between the number ($C = 0.5$) and surface ($C = 0.7$) of ulcerative changes with the healing rate ($p < 0.001$).

Venous ulceration treatment is a big social and medical problem. The number and surface of ulcerative changes present the most important healing prognostic factors. *Acta Medica Mediana* 2010;49(1):22-26.

Key words: venous ulcerations, healing rate, prognostic factor

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Introduction

Venous ulcerations occur in 1% of human population, that occurs more frequently in people older than 65 years of age. The occurrence ratio in relation to sex shows more significant occurrence in females - ratio of 3:1 (female: male). (1-3) Venous ulceration treatment is a big social and medical problem due to high treatment costs and manifold emotional problems of people suffering from this illness. Direct economic costs of venous ulcers treatment range from 750 million of \$ to 1 billion of \$ on the annual level throughout the world (2,4). Average price of venous ulceration treatment during life of one patient exceeds the amount of 40.000\$ (1-3).

There are various therapy treatment modality options for VU. The most popular and the most used at the same time is compression dressing (bandages) introduced by Unna 1885 (5). Certain number of modifications of this technique have been introduced and the most recent research has shown that the constant pressure application

of 20-40 mmHg on lower extremities has shown the best results in venous ulceration treatment (6,7). However, in spite of compression bandage modality, certain number of venous ulcerations have had unsatisfactory results in regard to this treatment modality.

Within 24 week therapy, the adequate therapy response ranged from 30 to 60% VU, while 70% to 85% were healed during one year of VU treatment (7-8).

Based on clinical experience available in literature, certain clinical parameters have been defined, especially those which may indicate prognosis of venous ulceration healing. Potential risk factors are: sex, race, socio-economic status, age, venous filling index (based on pletismography), ulceration surface, ulceration depth, level of present granulation tissue and fibrin in ulceration, duration of ulceration treatment, number of ulceration, localization of ulceration, patient mobility, ankle mobility, presence of chronic diseases diabetes, chronic heart diseases, injuries of the lower extremities, thyroid gland disease, etc)

Aim

The basic goal of this research has been set bearing in mind the very frequency of venous ulceration in clinical practice of dermatologists and their great impact on total morbidity whereas exact etiopathogenetic mechanisms have not been clarified yet: to determine and evaluate

factors of healing rate for venous ulcerations of lower extremities with patients treated with multilayer compression bandage.

Materials and methods

Research was based on the prospective randomized study at Outpatient Clinic for dermal and sexual diseases and Medical Center in Doljevac during the period from 2007 until 2008. Research involved a group of 50 patients of both sexes with venous ulcerations of the lower extremities. Patients were monitored for 24 weeks from the very beginning of treatment. Ulcerations were treated by the use of multiple layer compression bandage and the use of elastic stocks. Local treatment of ulceration was done with local antiseptics and antibiotics (according to biogram and antibiogram) three times a week, as well as hydrocolloid dressings.

Alongside basic anamnestic data and physical check-up, appropriate functional diagnostics examinations were also applied.

Patients were monitored for: sex, age, body mass index (BMI) to measure total obesity level, ratio waist/heap to measure obesity level, surface and depth of ulceration, localization and number of ulcerations, level of present granulation tissue and fibrin in ulceration, duration of disease, surface condition and deep venous system (using color doppler ultrasonic test and functional tests of the venous system: Trenendelenburg's test; Pether's test; Lowenberg's test; Homan's test, presence of chronic diseases.

Ankle brachial pressure index was monitored (ABPI) by using a color doppler sonography.

Patients treated with immunosuppressives who had had ulcers together with dermal vasculitis, pyoderma gangraenosum and other neutrophilic dermatosis were excluded from this study.

Data had been processed by using Standard descriptive statistical methods (mean value, Standard deviation and percentual presence). This paper will show several types of applied tests depending on the group size, type of disease and type of distribution (Pearson's correlation coefficient, Kendall's tau_b correlation coefficient). Excel 2002 in Windows XP setting was used and the results are shown in tables and graphs.

Results

Total of 50 patients with chronic venous ulceration were tested. Basic characteristics of patients are shown in Table 1.

Out of a total number of tested patients, 30 (60%) were of female sex and 20 (40%) of male sex. Average age of patients was 63.3±6.32 years of age where male population was older. Average values of BMI were significantly higher in females as well as waist/ heap ratio($p<0.01$)

During the 24 week monitoring what was noticed was that 13 patients (26%) did not have full

healing of chronic venous ulcerations of the lower extremities. The group of patients whose ulcerations were not healed comprised 8 women and 5 men.

Table 1. Basic characteristics of patients

	female	male	total
Number of patients	30 (60%)	20 (40%)	50 (100%)
Not-healed ulcerations	8	5	13(26%)
age (year)	62.2±7.04	64.9±5.8*	63.3±6.32
BMI (kg/m ²)	29.3±3.2**	27.3±2.9	28.5±3.1
ratio waist/ heap	1.03±0.09**	0.9±0.04	1.01±0.06
Limb ulcers no.	2±1	1.6±0.7	1.8±0.11
Right leg	15	9	24 (48%)
Wound duration (day)	16.06±6.6	17.7±4.5	16.7±5.1
Area (cm ²)	8.2±5.8	9.7±6.8	8.8±6.1
ABPI	1.23±0.45*	0.99±0.29	1.13±0.40

* $p<0.05$; ** $p<0.01$

Characteristics of prognostic factors in relation to sex of tested patients were analysed in relation to locoregional characteristics of ulcerative changes. Table 2 shows loco-regional ulcerative changes.

Table 2. Loco-regional ulcerative changes characteristics

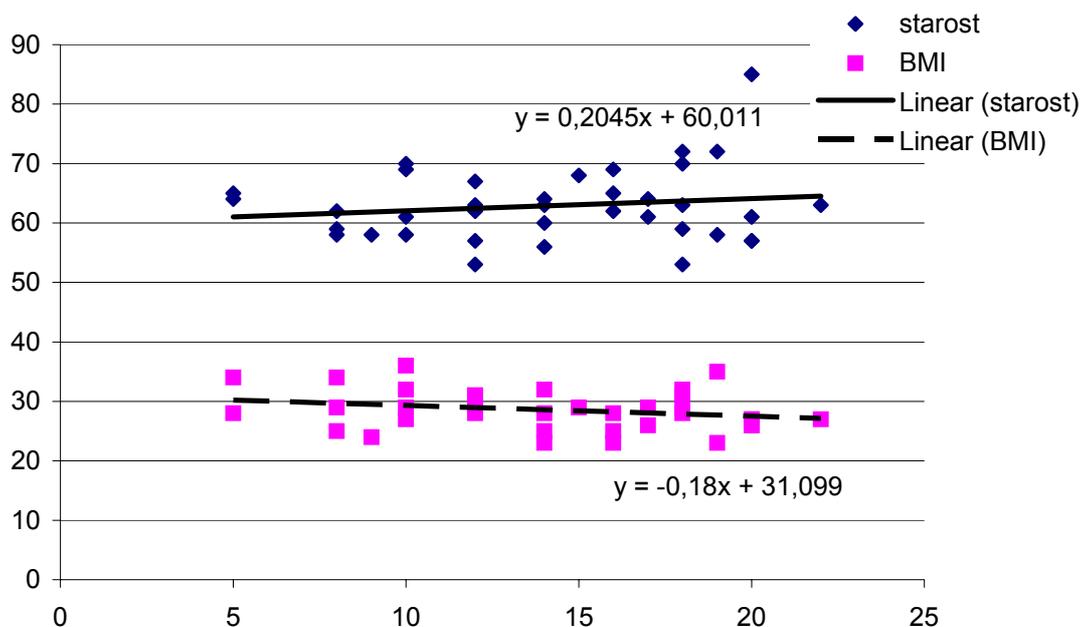
Loco-regional complications of ulcers	Female (%)	Male (%)
dermatitis	53.0	60.0
lipodermosclerosis	26.0	25.0
infection	63.3	75.0
limb edema	50.0	80.0
>50% of wound covered with fibrin	36.7	45.0
>50% of wound covered with eschar	83.0	85.0

Loco-regional characteristics of ulcerative changes indicated that there was no significant difference in the average number of ulcers, their localization, duration and average surface.

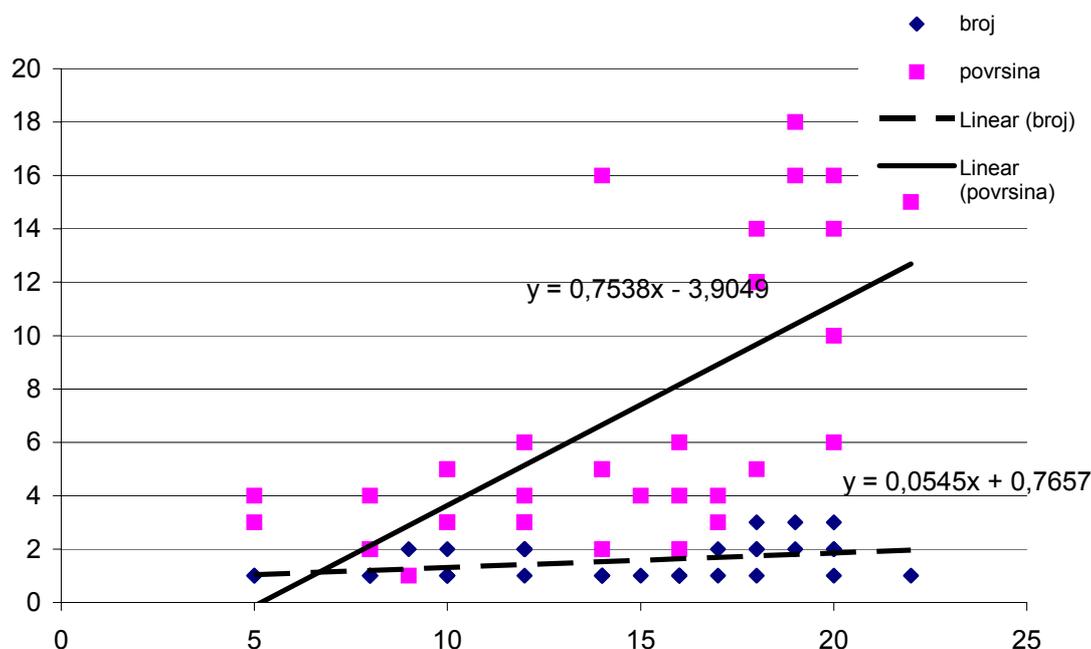
Analysis of prognostic factors and their impact on healing was made for all patients who were healed during 24 week treatment of chronic venous ulcerations using standard therapy protocol.

Analysis made using of Pearson's correlation coefficient did not indicate any significant relation to patient's age, obesity expressed through BMI and change in healing rate (Graph 1.), although a trend of slower healing in older patients was noticed. Regression analysis is presented in Graph 1.

Correlation of the number and surface of ulcerative changes with healing rate is shown by regression linear trend on Graph 2.



Graph 1. Correlation of patient's age and obesity with change in healing rate



Graph 2. Correlation of the number and surface ulcerative changes with change in healing rate

Analysis made by Pearson's correlation coefficient shows significant positive correlation between the number (C=0.5) and surface (C=0.7) of ulcerative changes with healing rate (p<0.001); regression analysis is shown on Graph 2.

Correlation between sex, localization and local complications of chronic venous ulcerations with healing rate by Kendall's tau_b correlation coefficient is shown in Table 3.

Infection and swelling of the lower leg shows significant positive correlation with change in healing rate (p<0.05) whereas the presence of dermatitis and lipodermosclerosis does not show more significant impact regarding the level of fibrin settlements coverage or tissue on healing rate.

Table 3. Correlation of sex, localization and local complications of chronic venous ulcerations with healing rate

	Duration
sex	0.14
left/right leg	0.02
dermatitis	0.123
lipodermosclerosis	-0.236
infection	0.247*
limb edema	0.288*
>50% of wound covered with fibrin	0.06
>50% of wound covered with eschar	-0.09

*p<0.05

Discussion

Venous ulcerations (VU) are one of the most frequent vascular diseases in human population. They occur as complications of chronic venous insufficiency. Chronic venous insufficiency is responsible for the occurrence of 70% of chronic ulcerations of the lower extremities, especially those which do not heal within 6 weeks (9).

Venous ulceration treatment is a big social and medical problem due to high costs of treatment and many emotional problems that people who suffer from this disease have. Direct economic costs of venous ulceration treatment in the world range from 750 million of \$ to 1 billion of \$ on the annual level (10). Average price of venous ulceration treatment during life span of one patient exceeds the amount of 40.000\$ (9-11).

Venous ulcerations occur in 1% of human population; they are frequently found in persons older than 65 years of age. The ratio of occurrence depending on the sex show a significant occurrence in females ratio 3:1 (female: male). (10)

This study shows that out of 50 tested patients, 30 (60%) were females and 20 (40%) males. Average age of patients was 63.3±6.32 years where male population was somehow older. Average values of BMI were significantly higher in females and the waist/hip ratio ($p<0.01$).

It was noted during the 24 week monitoring that 13 patients (26%) did not have full healing of chronic venous ulcerations of the lower extremities. The group of patients in whom ulceration healing failed comprised 8 women and 5 men with no statistical importance.

Loco-regional characteristics of ulcerative changes indicate that there is no significant difference in average number of ulcers, their localization, duration and average surface.

In this study, patients were classified into two groups according to the level of present tissue granulation and fibrin in ulceration (group I <50% and group II >50% of ulceration covered by fibrin and/or granulation tissue).

Higher coverage of ulceration with fibrin is somehow more present in males compared to females, but with no statistical importance. Ulceration coverage with a scar was found in over 50% of patients of both sexes.

Loco-regional characteristics of chronic venous ulcerations included identification of local complications such as dermatitis, lipodermosclerosis and infection.

Statistical analysis showed that lipodermosclerosis was significantly higher in males compared to females ($p<0.05$) while other local complications did not show any significant difference in frequency between sexes.

Lower leg swelling is often registered in patients of both sexes without significant statistical difference.

Analysis of prognostic factor impact of healing rate was done in all patients who had chronic venous ulceration healed during 24 week treatment monitoring. Analysis carried out according to Kendall's tau_b correlation coefficient

showed that sex and localization have no significant correlation with healing rate of ulcerative changes.

The application of Pearson's correlation coefficient did not show any significant correlation between patient's age and obesity expressed through the BMI and abdominal obesity expressed through the relation W/H with change in healing rate, although a trend of slower healing in elderly persons is evident.

This analysis showed significant positive relation between the number ($C=0.5$) and area ($C=0.7$) of ulcerative changes in healing rate ($p<0.001$). Analysis carried out according to Pearson's correlation coefficient indicated significant negative correlation with ABPI and a change in healing rate ($C=0.61$; $p<0.001$).

A number of researchers have been engaged in identification of the most significant prognostic parameters related to chronic venous ulceration healing rate. Most of these studies have taken into account up to one hundred patients.

Some authors (12) have shown that the duration length of ulceration and total ulceration surface correlate with the healing rate of chronic venous ulceration, [it is in compliance with the results obtained in this study. Chaby et al. (13) have shown outstanding correlation between healing rate of chronic venous ulceration and ulceration surface. Certain number of studies are not in compliance with results present herewith and according to findings obtained in one of these studies (14) ulceration surface is not a prognostic factor of healing rate of chronic venous ulceration.

Data obtained in this study confirm the findings of the study (15) that involved the analysis of 100 patients with chronic venous leg ulceration. The study has shown that the healing process is much faster when calibrated compression bandage is used for patients with small surface ulceration and short duration of ulceration.

Younger age and absence of deep venous insufficiency is a more favorable prognostic factor of venous leg ulceration healing.

Margolis, Berlin, and Strom (16) have shown that a larger surface and longer duration of ulceration are a bad prognostic parameter for healing rate of venous ulceration of lower extremities, accompanied with previously performed operations on a leg venous system, implanted heel and knee ankle prosthesis, with ankle brachial pressure index less than 0.8, and the presence of fibrin settlements on more than 50% of ulceration surface.

Analysis made by Kendall's tau_b correlation coefficient shows that sex and localization have no significant correlation with the healing rate of ulcerative changes. Infection and swelling of the lower leg show poor but at certain extent significant positive correlation with change healing rate ($p<0.05$).

Pearson's correlation coefficient shows significant positive correlation between the number ($C=0.5$) and surface ($C=0.7$) of ulcerative changes with the healing rate ($p<0.001$).

Apart from these usual prognostic factors that play a role in healing ulcerations what should be kept in mind are other specific conditions that

not only increase risk occurrences/appearances but also the very success of healing (17).

Conclusion

Based on the review of available literature and results obtained from this research, it may be

concluded that venous ulceration of the lower extremities are significant medical and social-economic problem because of disability that develops in patients and also because of significant economic resources, which must be provided by the community for treatment of these patients.

References

1. Abbade LP, Lastória S. Venous ulcer: epidemiology, physiopathology, diagnosis and treatment. *Int J Dermatol* 2005; 44(6): 449-56.
2. Vowden KR, Vowden P. The prevalence, management and outcome for patients with lower limb ulceration identified in a wound care survey within one English health care district. *J Tissue Viability* 2009; 18(1): 13-9.
3. Simka M. Seasonal variations in the onset and healing rates of venous leg ulcers. *Phlebology* 2010; 25(1): 29-34.
4. Vowden KR, Vowden P. The prevalence, management and outcome for patients with lower limb ulceration identified in a wound care survey within one English health care district. *J Tissue Viability* 2009; 18(1): 13-9.
5. Etufugh CN, Phillips TJ. Venous ulcers. *Clin Dermatol* 2007; 25(1): 121-30.
6. Herschthal J, Kirsner RS. Current management of venous ulcers: an evidence-based review. *Surg Technol Int* 2008; 17: 77-83.
7. Raju S, Neglén P. Clinical practice. Chronic venous insufficiency and varicose veins. *N Engl J Med* 2009; 360(22): 2319-27.
8. Barron GS, Jacob SE, Kirsner RS. Dermatologic complications of chronic venous disease: medical management and beyond. *Ann Vasc Surg* 2007; 21(5): 652-62.
9. Ricci MA, Emmerich J, Callas PW, Rosendaal FR, Stanley AC, Naud S, et al. Evaluating chronic venous disease with a new venous severity scoring system. *J Vasc Surg* 2003; 38(5): 909-15.
10. Posnett J, Gottrup F, Lundgren H, Saal G. The resource impact of wounds on health-care providers in Europe. *J Wound Care* 2009; 18(4): 154-61.
11. Jones KR. Why do chronic venous leg ulcers not heal? *J Nurs Care Qual* 2009; 24(2): 116-24.
12. Szewczyk MT, Jawień A, Migdalski A, Piotrowicz R, Grzela T, Brazis P. Predicting time to healing by anatomical assessment of venous pathology. *Med Sci Monit* 2009; 15(2): CR74-81.
13. Chaby G, Viseux V, Ramelet AA, Ganry O, Billet A, Lok C. Refractory venous leg ulcers: a study of risk factors. *Dermatol Surg* 2006; 32(4): 512-9.
14. Colgan MP, Dormandy JA, Jones PW, Schraibman IG, Shanik DG, Young RA. Oxpentifylline treatment of venous ulcers of the leg. *BMJ* 1990; 300(6730): 972-5.
15. Phillips TJ, Machado F, Trout R, Porter J, Olin J, Falanga V. Prognostic indicators in venous ulcers. *J Am Acad Dermatol* 2000; 43(4):627-30.
16. Margolis DJ, Berlin JA, Strom BL. Risk factors associated with the failure of a venous leg ulcer to heal. *Arch Dermatol* 1999; 135(8): 920-6.
17. Čojbašić I, Mačukanović-Golubović L. Modality of treatment in essential thrombocythemia. *Acta Medica Medianae* 2008;47(3):51-5.

EVALUACIJA PROGNOŠTIČKIH FAKTORA BRZINE ZARASTANJA VENSkih ULCERACIJA DONJIH EKSTREMITETA

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Venske ulceracije javljaju se kod 1% celokupne ljudske populacije, pri čemu se češće javljaju kod osoba starijih od 65 godina života. Osnovni cilj istraživanja bio je odrediti i evaluirati faktore brzine zarastanja venskih ulceracija donjih ekstremiteta kod bolesnika tretiranih višeslojnom kompresivnom bandažom.

Ispitivanja su vršena po tipu prospektivne randomizirane studije na Klinici za kožne i polne bolesti i u Domu zdravlja Doljevac u periodu 2007-2008. godine. Ispitivanje je obuhvatilo grupu od 50 bolesnika oba pola sa prisutnim venskim ulceracijama donjih ekstremiteta. Bolesnici su praćeni 24 nedelje od početka lečenja.

Od ispitivanog broja bolesnika 30 (60%) je bilo ženskog a 20 (40%) muškog pola. Prosečna starost bolesnika bila je 63.3±6.32 godine. Kod 13 bolesnika (26%) nije došlo do kompletnog zarastanja venskih ulceracija. Lokoregionalne karakteristike ulkusnih promena pokazuju da ne postoji značajna razlika u prosečnom broju ulkusa, njihovoj lokalizaciji, dužini trajanja i prosečnoj površini u odnosu na pol bolesnika. Urađena analiza Kendall's tau_b koeficijentom korelacije pokazuje da pol i lokalizacija nemaju značajniju povezanost sa brzinom zarastanja ulkusnih promena. Infekcija i otok potkolenice pokazuju značajnu pozitivnu povezanost sa brzinom zarastanja promena (p<0.05). Pearson-ov koeficijent korelacije pokazuje značajnu pozitivnu povezanost broja (C=0.5) i površine (C=0.7) ulceroznih promena sa brzinom zarastanja (p<0.001).

Venske ulceracije donjih ekstremiteta predstavljaju značajan medicinski i socio-ekonomski problem. Broj i površina ulceroznih promena predstavljaju najznačajnije prognostičke faktore brzine zarastanja venskih ulceracija. *Acta Medica Medianae* 2009; 48(1):22-26.

Ključne reči: venske ulceracije, brzina zarastanja, prognostički faktori