



Risk Factors of Varicose Ulcer-A Case Control Study in A Tertiary Care Institution

Authors

Dr Rajendran C. V.¹, Dr Thomas. P. K.², Dr Lydia Mary³

¹Additional Professor, Dept of General Surgery, Government Medical College Trivandrum, Kerala

²Additional Professor, Department of General Surgery, Government Medical College Trivandrum, Kerala

³Resident, Department of General Surgery, Government Medical College Trivandrum, Kerala

Abstract

Background: *The incidence of ulceration in varicose vein patients is on an increasing trend. The predisposing factors of venous ulceration is less understood. In this study we have tried to analyze the risk factors for development of ulcer in patients with varicose veins.*

Materials and Methods: *This is a case control study conducted under department of General Surgery, Government Medical College Trivandrum. A total of 150 patients were studied. Equal number of males and females were included in the study.*

Objectives: *The objective of our study was to find out the factors associated with increased risk of ulceration in patients with varicose veins.*

Result and Conclusion: *The various risk factors like smoking, increased BMI, venous reflux, dermatitis and flat foot were analysed. Obesity and superficial venous reflux were not significantly associated with increased risk of ulceration in our study.*

Keywords: *varicose veins, reflux, ambulatory venous hypertension, BMI.*

Introduction

Varicosity is the tax we pay for our upright posture that we have attained through evolution¹. Varicose veins mostly affects the lower limbs due to the venous pooling which occurs due to gravity². It remains asymptomatic in a major percentage of population but can become a surgical problem once the veins become enormously tortuous and when ulceration occurs³. The incidence of varicose vein amounts to more than 5% of population, and 1% have or have had venous ulceration⁴⁻⁶.

The accepted cause of venous ulceration now is known to be Ambulatory Venous Hypertension⁷. Primary valve incompetence of the saphenous

vein, incompetence of perforators, or obstruction or incompetence of deep veins are the major reasons of venous hypertension⁸⁻¹⁰. Almost 75% of all chronic leg ulceration are due to varicose veins¹¹. The unsightly venous ulcer is very difficult to heal and cause considerable morbidity¹². The chronic pain and disability leads to decreased quality of life (QOL). A good percentage (around 3%) of total expenditure on health care is being diverted for treating chronic venous ulcer patients¹¹.

Since the incidence of varicose veins increases with age, the incidence of this disease can be expected to rise in the near future as the life expectancy is on the rise¹³. This in combination

with the high cost of ulcer treatment is going to eat away a major part of our budget in the coming years. Hence strategies for preventing leg ulceration has to be given top priority to save our economy.

As shown in the Scottish leg ulcer project attempts to improve the ulcer healing rates due to venous ulcer by conventional methods of treatment has not been successful¹⁴. For planning a definite prevention / treatment protocol, clinical and other factors which increase the risk of ulceration has to be identified. Certain studies have been done in this field which include few cross sectional studies.¹⁴⁻¹⁷ Leg and foot ulcer prevalence and investigation and sample based studies of ulcer patients which were to some extent successful in picking up some factors which increase the risk of ulceration. All these studies have been observational case series. There is a lacking of controlled studies comparing factors in patients who develop ulceration with those who do not. The aim of this study is to determine in subjects with varicose veins the characteristics of varicose vein disease and other factors associated with an increased risk of ulceration. The objective of this study was to find out the factors associated with increased risk of ulcerations in patients with varicose veins.

Materials and Methods

We conducted this study in the department of surgery medical college Trivandrum after taking approval from the institutional ethics committee. Informed consents were taken from all participants. Precautions were taken to safeguard the confidentiality of the patients at all stages of the research. Throughout all phases of the study, we adhered to declaration of Helsinki.

Study design was case control study. All patients with primary varicose veins of lower limb with superficial and perforator venous incompetence with ulceration who were either admitted to general surgery ward of Government medical college, Trivandrum or those who attend the outpatient clinic of general surgery department during one year period from 1st May 2014 to 30th

April 2015. We selected the controls from all patients both inpatient and outpatient, with primary varicose veins of lower limb with superficial and perforator venous incompetence without skin ulceration. All consecutive patients qualifying the criteria for cases and controls were recruited to the study. Information given in a study conducted by L Robertson et al, presented at the Twentieth American Venous Forum Annual Meeting, Charleston, SC, Feb 20-23 2008 and published at Journal of vascular surgery, 2008 was used to calculate the sample size of the present study. The study quoted above stated a odds ratio of 2.87 for dermatitis in causing ulceration in varicose veins. Sample size was calculated using formula $[\frac{z\alpha/2+z1-\beta}{2}]^2 \frac{[p1(100-p1)+p2(100-p2)]}{(p1-p2)^2} = 7.9$ when alpha is 0.05 and beta is 0.2. Case:Control ratio of 1:2. prevalence of exposure in control group is assumed to be 30%. The sample size calculated according to above formula was 50 cases and 100 controls.

We followed the CEAP classification to evaluate the site and severity of the varicose veins and ulceration¹⁸. Patients were examined in standing position after two minutes. Henceforth varicose veins were classified as: C0 no visible or palpable signs of venous disease, C1 telangiectases or reticular veins, C2 varicose veins, C3 edema and corona phlebectatica, C4 skin changes ascribed to venous disease for pigmentation, venous dermatitis, and lipodermatosclerosis), C5 skin changes ascribed to venous disease as above with healed ulceration, and C6 skin changes ascribed to venous disease as above with active ulceration. The Leg with ulcer was taken as the index leg and the leg with varicose vein in the control group. In this study, we excluded all patients with ulcers in the feet and those with absent posterior artery pulsations. Moreover all patients with features suggestive of diabetic ulcer and arterial ulcers were not recruited into the study. In addition, all known cases of hematological and neurological ulcers were excluded from taking part in the study.

All patients underwent duplex scanning of the superficial deep and perforate systems of the index leg. All examination including scanning was done using a standardized procedural protocol by trained professionals.

Outcome variable studied was presence or absence of ulceration. Other variables studied are potential risk factors like history of smoking, exercise, venous reflex in the duplex study, presence of lipodermatosclerosis, dermatitis, presence of flat foot apart from the basic demographic variables.

Data was collected using a combination of a semi structured questionnaire based interview, clinical examination, Lab investigations and from the charts. All data were collected by residents blind to the research question and protocol. All information collected in the case report forms were entered into an excel database.

Statistical analysis were done in graphpad statistical program and R. Univariate statistical analysis done with t test and chi square test or their nonparametric equivalent. Subsequently logistic regression modeling was done to find out the risk factors indecently associated with venous ulceration. A p value of less than 0.05 was taken as statistically significant.

Results

We recruited 150 patients who fulfilled the inclusion and exclusion criteria. Of these, 50(33.3%) patients were cases and 100(66.7%) controls. All were strictly followed up and there were no loss to follow up. The mean (SD) age reported for the whole sample we studied was 44.5(10.7) years. There were equal number of males and females in the study. The mean (SD) of BMI was 27.5(2.08). There were 46(30.7%) smokers in the whole sample. In this study, 71(47.3%) belonged to moderate exercise group, followed by 66(44%) with history of mild exercises and 13(8.6%) with severe exercise. Patients with superficial reflex alone constituted the largest subgroup in the study, followed by combined superficial and deep reflexes. Lipodermatosclerosis was present only in

17(11.3%) patients. Dermatitis was observed in 42(28%) of the patients. In the study, 22(14.7%) had flat foot.

Table 1 shows the baseline demographic features across cases and controls. Males were the predominant group in the controls where as there were more females in the case group. All other baseline parameters were comparable across the groups.

Table 1: Baseline comparison between cases and controls

| Variable | [ALL] N=150 | Cases N=50 | Controls N=100 |
|----------|------------------|------------------|------------------|
| Age | 44.5 (10.7) | 47.6 (9.81) | 43.0 (10.8) |
| gender: | | | |
| Male | 75 (50.0%) | 20 (40.0%) | 55 (55.0%) |
| Female | 75 (50.0%) | 30 (60.0%) | 45 (45.0%) |
| BMI | 27.5 (2.08) | 27.8 (2.19) | 27.3 (2.02) |
| SBP | 121 [114;128] | 122 [114;132] | 119 [114;128] |
| DBP | 76.0 [72.0;82.0] | 76.0 [72.0;82.0] | 76.0 [72.0;82.0] |

BMI-Body mass index, SBP-Systemic bp, DBP- Diastolic bp.

Table 2 shows the severity and effect of various risk factors for ulcer formation across the cases and controls. No significant difference was observed in the prevalence of flat foot in the cases compared to the controls. There was no significant association between smoking and the occurrence of the ulcer.

Table 2: Association between potential risk factors and venous ulceration

| variable | [ALL] N=150 | 1 N=50 | 2 N=100 | OR | p.ratio | p.overall |
|------------------------|-------------|------------|------------|------------------|---------|-----------|
| Smoking: | | | | | | 0.118 |
| Yes | 46 (30.7%) | 20 (40.0%) | 26 (26.0%) | Ref. | Ref. | |
| No | 104 (69.3%) | 30 (60.0%) | 74 (74.0%) | 1.89 [0.91;3.91] | 0.087 | |
| Exercise: | | | | | | 0.403 |
| Mild | 66 (44.0%) | 26 (52.0%) | 40 (40.0%) | Ref. | Ref. | |
| Moderate | 71 (47.3%) | 20 (40.0%) | 51 (51.0%) | 1.65 [0.81;3.42] | 0.171 | |
| severe | 13 (8.67%) | 4 (8.00%) | 9 (9.00%) | 1.43 [0.41;5.94] | 0.585 | |
| Reflux: | | | | | | 0.001 |
| Superficial | 104 (69.3%) | 25 (50.0%) | 79 (79.0%) | Ref. | Ref. | |
| Deep | 11 (7.33%) | 5 (10.0%) | 6 (6.00%) | 0.38 [0.10;1.47] | 0.156 | |
| combined | 35 (23.3%) | 20 (40.0%) | 15 (15.0%) | 0.24 [0.11;0.54] | 0.001 | |
| Lipodermato sclerosis: | | | | | | <0.001 |
| Present | 17 (11.3%) | 13 (26.0%) | 4 (4.00%) | Ref. | Ref. | |
| Absent | 133 (88.7%) | 37 (74.0%) | 96 (96.0%) | 8.10 [2.64;31.2] | <0.001 | |
| Dermatitis: | | | | | | <0.001 |
| Present | 42 (28.0%) | 26 (52.0%) | 16 (16.0%) | Ref. | Ref. | |
| Absent | 108 (72.0%) | 24 (48.0%) | 84 (84.0%) | 5.59 [2.61;12.4] | <0.001 | |
| Flat foot: | | | | | | 0.935 |
| Present | 22 (14.7%) | 8 (16.0%) | 14 (14.0%) | Ref. | Ref. | |
| Absent | 128 (85.3%) | 42 (84.0%) | 86 (86.0%) | 1.18 [0.43;3.00] | 0.740 | |

Figure 1: Association between reflux and ulceration.

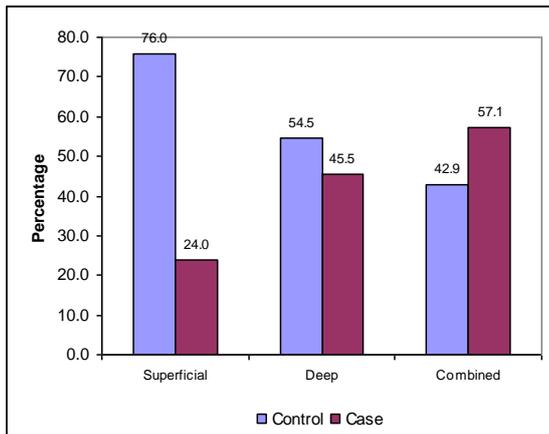
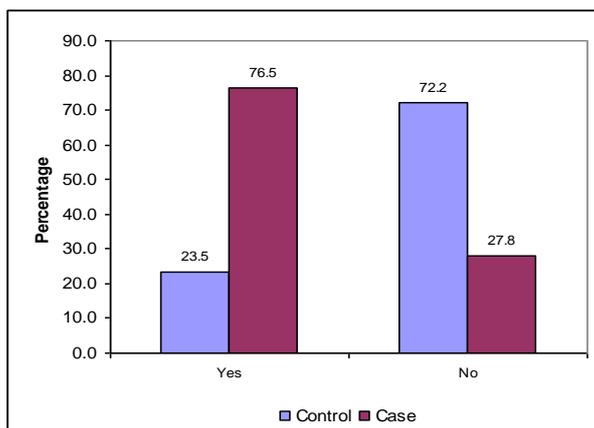


Figure 2: Association of lipodermatosclerosis and ulceration.



Discussion

In the study conducted by us a total of 50 cases and 100 controls were analysed. The risk factors were studied in both the study groups for their association with ulcer development¹¹. Body mass index, smoking, physical exercise, blood pressure, reflux in duplex scanning, lipodermatosclerosis, dermatitis and flat foot were the risk factors studied¹⁶.

International consensus committee protocol was used to assess the site and severity of venous disease which is based on clinical, etiological, anatomical and pathophysiological data (CEAP). The index leg was defined as the leg with ulceration in the ulcer group. In case of bilateral ulceration, the leg with more severe ulceration was taken as index limb. For control subjects, the index leg was the leg with more severe varicose veins.

The standing height of the subjects were measured without shoes to the nearest 5mm and weight without shoes was measured to the nearest 100 gms on a digital scale. For all subjects body mass index was calculated (Kg/ m²). In our study BMI of 25 to less than 30 was classified as overweight and subjects with BMI 30 or more, as obese in accordance with the WHO criteria. Right arm blood pressure of each subjects was measured by a Stethoscope and Sphygmomanometer. A Questionnaire was used to gather information on patients medical history, status, smoking history and physical exercise. Physical exercise were classified into mild, moderate, and heavy according to reference activities.

32 cases out of 50 cases had varicose veins involving the great saphenous vein only, 10 in small saphenous vein only, and the remaining 8 had varicosities affecting both the great and small saphenous veins. 72 cases out of 100 controls had varicose vein in the great saphenous vein only, 19 in small saphenous vein only and remaining 9 had bilateral varicosity.

Mean age group of our cases was 46.2 \pm 8.6 and of the control group was 42.9 \pm 9.7. 60% of cases studied were females while only 45% of control study group were females.

Obesity was not found to be a significant risk factor in our study (p=0.444). Though obesity is a significant risk factor for venous insufficiency, it is not a risk factor for ulceration as is shown in studies by C. V. Ruckley^{19,20}. In patients with skin changes of chronic venous insufficiency and reflux in deep veins, our study confirmed the association with increased risk of ulceration. Stuart et al studied 233 patient with venous disease and found that a history of active or healed ulcer was associated with reflux in deep vein, with 49% having reflux in their popliteal vein compared with only 15% of subjects with varicose veins (p= 0.002) . Welch et al also found that the frequency of reflux in the deep veins increased as the clinical symptoms progressed ,with increased incidence of class 3 ulcerations²⁰.

Superficial vein reflux was not significantly associated with increased risk of ulceration²¹. In

our study as well we expected the same results since we have selected our control group on the basis of visible varicose veins. (superficial reflux in 90% of cases and 93% in controls).

Acknowledgment

We sincerely thank Dr. I.P.Yadev for all the help rendered during the study and for the data analysis.

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