Ulceration of the lower leg after total knee replacement
A FIVE-YEAR REVIEW
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Ulceration of the lower leg is considered to be a ‘hard’ clinical endpoint of venous thrombosis. Total knee replacement (TKR) is a significant risk factor for venous thrombosis of the leg and therefore potentially for ulceration.

We sent a postal questionnaire to 244 patients at a minimum of five years after TKR enquiring about the development of ulceration since their TKR. The overall incidence of ulceration, both active and healed, was 8.67% which is similar to that in the age-matched general population (9.6% to 12.6%), as was the prevalence of active ulceration. We also identified no clear association between venographically-confirmed postoperative deep-venous thrombosis (DVT) and the incidence and prevalence of ulcers at five years. We suggest that after TKR DVT is not a significant risk factor for ulceration of the leg and that perioperative chemical thromboprophylaxis may not be justified on these grounds.

Received 1 December 2000; Accepted after revision 23 May 2001

The clinical significance of venous thrombosis of the lower leg in joint replacement remains controversial. The most important consequence is fatal pulmonary embolism (PE). Several reports have shown that the incidence of fatal PE after total knee replacement (TKR) performed without chemical thromboprophylaxis is between 0.19% and 0.4%. Power calculations suggest that in order to demonstrate a clinically significant reduction of this rare event a study containing 100 000 patients would be required. The surrogate endpoints of venographically-detected deep-vein thrombosis (DVT) and PE, confirmed by a perfusion scan, are more common events and thus the clinically significant effects of treatment can be detected by smaller studies. These rely on the assumption that a reduction in non-fatal or asymptomatic thromboembolism will equate to a reduction in fatal embolic events. Although logical, this assumption may be flawed and has not been validated.

The other major clinical consequence of venous thrombosis is chronic morbidity related to venous insufficiency. Valvular disruption or venous occlusion contributes to reflux, vascular engorgement and venous hypertension. Insufficiency produces a variety of signs and symptoms including chronic discomfort, nocturnal cramps, skin changes and pigmentation, atrophie blanche and ulceration, representing the progression of the postphlebitic syndrome.

Ulceration of the lower leg is a significant cause of morbidity in the elderly population. Ulcers are difficult to manage, require prolonged treatment, and are often recurrent. They place considerable demands on health-care resources. Attempts at prevention are therefore desirable.

TKR is a significant risk factor for venous thrombosis of the lower leg. The presumed predisposition to the post-phlebitic syndrome and ulceration of the lower leg has been used as an argument in support of the use of chemical thromboprophylaxis, but there is little evidence in the literature as to the extent of this problem after TKR.

We have determined the prevalence of active ulceration and the overall incidence of active and healed ulcers of the lower leg after a minimum of five years following TKR performed without chemical thromboprophylaxis. Using a unique cohort of patients we have attempted to find an association between ulceration of the lower leg and postoperative thrombosis detected by intravenous contrast venography.

Patients and Methods

Patients were recruited from an ongoing prosthesis survival study which had been established by the senior author.
(PJG). All had had a TKR performed by him between 1992 and 1995. No routine chemical thromboprophylaxis had been used. After mid-1993, all patients entering the original trial had routine intravenous contrast venography seven to ten days after operation.

All the surviving patients with a follow-up of more than five years were contacted by postal questionnaire specifically enquiring:

Have you had a leg ulcer, if so which side?
Left/right/both/neither
If so, is this ulcer present at the moment?
Left/right/both/neither

Additional information was supplied describing a leg ulcer.

We identified and contacted 244 surviving patients (333 TKRs) and received 205 replies (84.0%), of which 12 had been completed by relatives or carers stating that seven patients were incapable of replying because of other medical problems such as a cerebrovascular accident, and that five had died after the questionnaire had been sent out. These replies were excluded from the analysis. Thus a total of 193 returned questionnaires was available. The mean age of the 193 patients at the time of response was 77.1 years (52 to 92) and 72 had received bilateral TKRs. Therefore, 265 limbs were available for assessment. It was possible to identify active and healed ulcers in all operated limbs.

The venography results were retrieved from the Department of Radiology. The prevalence of active ulcers, the total number and the incidence were calculated. Binomial confidence intervals (95%) were also calculated. A comparison of the incidence of ulcers in the DVT-positive and DVT-negative groups was performed using Fisher’s exact test.

The incidence of ulcers was the percentage of patients who had developed ulceration since TKR and therefore included healed and currently active lesions. The prevalence was the percentage of patients with active ulceration at the time of completing the questionnaire.

Results

For the purpose of analysis, all knees were considered in isolation. We identified 18 healed ulcers and five which were currently active. The overall incidence of ulcers was 8.67% (23/265) (95% confidence interval (CI) 5.6 to 12.7) and the prevalence of active ulcers was 1.89% (5/265) (95% CI 0.32 to 4.47).

The inclusion of both limbs of patients with bilateral TKR raised concerns regarding possible bias and loss of independence. Consequently, we performed an analysis in which the second operated limb of a bilateral TKR was eliminated. Similar findings were obtained with an overall incidence of 9.8% (95% CI 6.03 to 14.9) and active prevalence of 1.6% (95% CI 0.32 to 4.47). We therefore concluded that this bias was theoretical and of limited significance.

Of the 265 limbs on which we had a completed questionnaire, 141 had had postoperative venography. Of these 64 (45.3%) had no DVT, 69 (48.9%) had a below-knee DVT and eight (5.7%) an above-knee DVT. In this cohort of 141 TKRs, nine (6.38%) healed and two active ulcers (1.42%) were identified with an overall incidence of 7.80% (11/141). These were divided into DVT-positive and DVT-negative groups and rates of ulceration were calculated (Table I). Analysis using Fisher’s exact test suggested that there was no evidence that postoperative DVT increased the risk of venous ulceration (p = 0.07).

Discussion

Several large studies have described the overall prevalence of active ulceration to be between 0.11% and 0.4%. These figures, however, do not reflect the prevalence in the elderly population; 90% of ulceration of the lower limb occurs in those over 60 years of age, and in the UK this represents 18.1% of the total population. It is therefore possible to calculate the prevalence of ulceration in the older age group (Table II). This is similar to the age-matched figures for prevalence observed by Cornwall et al and Nelzen, Bergqvist and Lindhagen (Table III). Combining the upper and lower estimates from these studies, the prevalence of active ulceration in the general population over the age of 60 years will lie between 0.69% and 3.2%.

Using identical reasoning the overall incidence of ulceration in the over-60 age group is 11.04% (1.8% for the entire population). The incidence of 0.69% (1/141) for TKRs in the 60 to 69 age group is similar to that of 0.9% (1/107) for TKRs in the over-60 age group of the general population.

We have described the prevalence of active ulceration in the general population. It is therefore possible to calculate the incidence of ulceration in the general population.

Table I. Comparison of rates of ulceration (%) in DVT-positive and DVT-negative subgroups

<table>
<thead>
<tr>
<th></th>
<th>DVT-positive</th>
<th>DVT-negative</th>
<th>p value</th>
<th>Odds ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Active ulceration</td>
<td>Active ulceration</td>
<td>Active ulceration</td>
<td>p value</td>
<td>Odds ratio (95% CI)</td>
</tr>
<tr>
<td>1.30 (1/77)</td>
<td>1.56 (1/64)</td>
<td>1.00</td>
<td>0.83 (0.01 to 66)</td>
<td></td>
</tr>
<tr>
<td>Overall ulceration</td>
<td>Overall ulceration</td>
<td>Overall ulceration</td>
<td>p value</td>
<td>Odds ratio (95% CI)</td>
</tr>
<tr>
<td>3.90 (3/77)</td>
<td>12.5 (8/64)</td>
<td>0.07</td>
<td>0.28 (0.05 to 1.26)</td>
<td></td>
</tr>
</tbody>
</table>

Table II. Overall and calculated prevalence of ulceration (%) in the over-60 age group of the general population

<table>
<thead>
<tr>
<th>Author/s</th>
<th>Overall prevalence</th>
<th>Calculated prevalence</th>
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<tbody>
<tr>
<td>Callam et al</td>
<td>0.11</td>
<td>0.69</td>
</tr>
<tr>
<td>Cornwall et al</td>
<td>0.12</td>
<td>0.72</td>
</tr>
<tr>
<td>Hansson et al</td>
<td>0.2 to 0.4</td>
<td>1.08 to 2.16</td>
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</table>

Table III. Age-related prevalence (%) of active ulceration in the general population

<table>
<thead>
<tr>
<th>Age (yr)</th>
<th>Nelzen et al</th>
<th>Cornwall et al</th>
</tr>
</thead>
<tbody>
<tr>
<td>50 to 59</td>
<td>0.9 (21/23890)</td>
<td>-</td>
</tr>
<tr>
<td>60 to 69</td>
<td>1.5 (48/3140)</td>
<td>0.3</td>
</tr>
<tr>
<td>70 to 79</td>
<td>1.5 (43/2795)</td>
<td>0.7</td>
</tr>
<tr>
<td>80+</td>
<td>3.2 (63/1995)</td>
<td>2.1</td>
</tr>
</tbody>
</table>
The overall incidence of ulceration in this age group to be 9.8%, rising to 12.6% in the eighth decade.

The overall incidence of ulcers in our cohort was 8.67% (95% CI 5.6 to 12.7) suggesting that there is no difference between the general population and our patients. The prevalence of active ulcers in our cohort was 1.89% (95% CI 0.62 to 4.35) which is also similar to that for the general population (0.69% to 3.2%).

Two of our patients were under the age of 60 years. Their inclusion was not thought to bias the analysis, especially as the figures for Nelzen et al for ulceration in the 50- to 60-year age group (Table III) were included in our calculations to predict the rate of ulceration in the elderly population.

The overall incidence of ulceration in the DVT-negative group was 12.5% (95% CI 3.58 to 14.85) and in the DVT-positive group it was 3.90% (95% CI 0.06 to 8.47), but this difference is not statistically significant (p = 0.07).

The allocation to the DVT-positive or DVT-negative group was based on the venographic appearances at seven to ten days after operation. We have no data regarding those patients who went on to develop DVT after discharge. Reports suggest that the amount of conversion from DVT-negative to DVT-positive may be about 20% in the four weeks after TKR. Furthermore, the power of the analysis is limited by the small numbers in the venography subgroups. We therefore cannot state conclusively that venographically-detected perioperative DVT is not a risk factor for the subsequent development of ulceration.

Our findings indicate that the study population has been exposed to a significant risk factor for venous thrombosis of the leg. At least 53.2% of these patients had a thrombosis, as confirmed by venography. Despite the high rate of postoperative thrombosis, our sample does not appear to be at a greater risk of developing venous ulceration than an age-matched sample.

We accept that this group may be biologically younger than the age-matched cohort, since they were sufficiently fit to undergo TKR. In addition, we have no data regarding the rate of ulceration in those patients who have died. We also acknowledge that we cannot predict how many patients may progress to ulceration in the future. Nonetheless, venous ulceration of the leg, as a ‘hard’ clinical endpoint, does not appear to be increased by TKR at five years after surgery. We therefore conclude that reduction in venous ulceration of the leg cannot be used as an argument in support of chemical thromboprophylaxis in TKR.

A review of this cohort at ten years after surgery may throw further light on this continuing controversy.

No benefits in any form have been received or will be received from a commercial party related directly or indirectly to the subject of this article.

References