Pinch skin grafting or porcine dermis in venous ulcers: a randomised clinical trial

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Abstract

Chronic venous ulcers are common, and even with effective compression or elevation large ulcers may take months to heal. Pinch skin grafting may allow healing from epithelial islands throughout the surface area of the ulcer, and a prospective randomised trial was therefore conducted comparing this treatment with porcine dermis dressings.

Most patients were treated as outpatients, 25 ulcers being randomised to treatment with pinch skin grafts and 28 to treatment with porcine dermis. Though the groups were well matched, the mean healing rate in the first week was 15 cm² for pinch skin grafts compared with 3.5 cm² with porcine dermis ($p < 0.02$). By life table analysis 64% of ulcers treated by pinch grafts were healed at six weeks and 74% by 12 weeks compared with 29% and 46% of ulcers, respectively, treated with porcine dermis dressings ($\chi^2 = 4.1$; $p < 0.05$). All ulcers that failed to heal within 12 weeks included an area posterior to the medial malleolus, where local compression may have been inadequate.

Pinch skin grafting improves the rate of healing in large venous ulcers and is a simple technique that may be performed as an outpatient procedure under local anaesthesia.

Introduction

Venous or gravitational ulcers are extremely common, affecting between 1% and 2% of the elderly population.¹ They represent a persistent clinical problem to the general practitioner, his district nurse, and various outpatient clinics. As a wide range of specialties are concerned in their treatment, including surgery, dermatology, geriatrics, and rheumatology, not surprisingly the subsequent results range from good to distressingly poor. The combination of slow or non-existent healing and frequent recurrence produces unacceptable morbidity and consumes considerable time and health service resources.²

Gravitational ulcers are a consequence of either gross venous incompetence or failure of the calf pump due to paralysis or immobility. The resulting venous and capillary hypertension increases permeability producing tissue oedema and perivascular deposition of fibrin.³ These combine to impair diffusion of oxygen and metabolites resulting in tissue necrosis and ulcer formation. The basic principles of early treatment are to reduce oedema and increase venous return by a combination of elevation and elastic compression.⁴ As leg ulcers are very common, treatment must be available either in the community or in the outpatient department. Treatment requiring special skills or a period of inpatient care is conceivable for only a small proportion of sufferers.

A wide variety of local applications have been advocated to

expedite re-epithelialisation. Topical agents include antiseptic, debriding, or nutrient activities,^{5,8} and dressings may be occlusive or permeable and impregnated by various substances.⁹⁻¹¹ The effect of these remains poorly evaluated but excellent healing rates of 1.72 and 1.8 cm² a week have been obtained with biological dressings using porcine dermis.^{10,12} These compare favourably with other techniques including bed rest, vertical leg drainage, "Bisgaard treatment," and compression with topical medications.^{10,12-15} Nevertheless, even when the ideal environment has been maintained the time to complete healing will depend on the size of the ulcer, which may epithelialise only from the edge. Skin grafting offers rapid re-epithelialisation^{16,17} but sheets of split skin graft require special skill in their use, may lead to donor site problems, and tend to be lifted by discharge in venous ulcers. Pinch skin grafts have the advantage that they may be placed in areas of healthy granulation tissue in incompletely prepared ulcers and are not lifted by discharge.¹⁸

We have compared the rates of healing in chronic venous ulcers randomised to treatment with either pinch grafting or porcine dermis dressings. All patients received identical high compression bandaging and most were treated as outpatients.

Patients and methods

Over 10 months 51 consecutive new patients with 60 chronic leg ulcers of at least six months' duration were seen in the venous ulcer clinic and entered the study. To establish the cause of the ulceration all patients underwent full clinical examination, arterial and venous Doppler investigation, photoplethysmography, and biopsy if indicated. Blood was taken when appropriate to exclude diabetes or rheumatoid disease. Of the 60 ulcers, 57 were confirmed as venous; four patients refused the study, however, so that 53 legs were available for randomisation to treatment with pinch graft or porcine dermis. Each ulcerated leg was randomised separately using random number tables to prepare a sequence of sealed envelopes which were opened after the ulcers had been prepared and consent obtained. Multiple ulceration on one leg was treated as a single ulcer of area equal to the sum of individual ulcers.

Preparation of ulcers—On presentation most ulcers were oedematous and contained slough. Preparation by compression bandaging was usually required over two weeks before the application of pinch grafts or porcine dermis. The ulcer base was cleaned mechanically, washed in saline, dressed with a non-adherent contact dressing (N-A; Johnson and Johnson Ltd), and covered with an adequate layer of absorbent Velband (Johnson and Johnson Ltd). In 18 elderly patients with difficult social circumstances and deep necrotic ulcers hospital admission and leg elevation were required to achieve a granulating base.

Compression bandaging—A standard two or three layer compression bandage was applied during preparation and throughout the study. When Velband had been used extensively because of profuse discharge this was compressed by a layer of crepe bandage allowing precise application of the subsequent elastic layers. The next layer consisted of Elset bandage (Seton Ltd) applied with two thirds overlap at the ankle and one half overlap at the upper calf. Finally, to prevent movement of the bandage and maintain compression over one week a layer of cohesive elastic Coban (3M Health Care Ltd) was applied. Measurements in healthy volunteers showed graduated compression maximal near the ankle at 45 mm Hg. This degree of compression is not required when the leg is raised in elderly patients during inpatient care, and for these patients the outer layer of Coban was therefore omitted. All patients were given illustrated instruction sheets and advised to walk two or three miles (3-5 km) a day when possible and at other times to keep the legs raised. As soon as full healing had been achieved below knee Sigvaris elastic stockings (Camp Ltd) were fitted.

Pinch skin grafts and porcine dermis—Pinch skin grafts 0.5 cm diameter and of partial thickness at the periphery and full thickness centrally were taken from the thigh under local anaesthesia. They were placed on areas of

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healthy granulation tissue leaving a maximum distance between epithelial edges of less than 15 mm. In eight patients grafts failed to take over areas larger than 10 cm² and re-grafting was performed. Lyophilised porcine dermis was soaked in sterile isotonic saline for one minute and then trimmed precisely to cover the granulating area and replaced as required on weekly review. Non-adherent dressings (N-A) were then applied before compression bandaging.

Follow up and ulcer measurement—The ulcer was photographed and accurately measured at weekly intervals. The margin of all ulceration on each leg was traced on to transparent polyethylene sheets and transferred to card of uniform weight, which was trimmed and precisely weighed, allowing calculation of the ulcer area. The first measurement was taken before randomisation but after preparation to give a granulating base. Subsequent measurements were at seven day intervals until complete healing, defined as confluent epithelial cover, or up to 12 weeks, when the treatment was judged to have failed.

Analysis of results—Results were expressed in three ways: (a) the reduction in ulcer area was calculated as a percentage of the initial area; (b) the healing rate was taken as the re-epithelialised area of ulcer expressed in cm² a week; (c) complete healing was analysed by the life table method throughout the study period. Means are presented with standard errors (SEM). The non-parametric Mann-Whitney U test was used to compare the two study groups with respect to ulcer size and healing rates. Time to complete healing was compared by χ^2 analysis and the log rank test on life table plots. Pinch skin grafting is invasive and we considered that the number of ulcers healing by a given time would need to be more than doubled to be clinically important. Statistical power was calculated as recommended by Peto *et al.*¹⁹ We needed to heal 40 legs to achieve an 80% chance of detecting this improvement in ulcer healing with a significance of $p < 0.05$.

Results

Of the 53 chronic venous ulcers available for the study, 25 were randomised to treatment with pinch skin grafts and 28 to treatment with porcine dermis dressings. The treatment groups were closely comparable, with a wide range of age, ulcer size, and time since the ulcer last healed but no significant differences between groups (table I). All ulcers had been active for at least six months, with a mean duration of over 3.5 years. Inpatient preparation of large and sloughy ulcers was required for social reasons in 18 cases, eight of which were subsequently randomised to treatment with pinch skin grafts and 10 to treatment with porcine dermis dressings.

TABLE I—Distribution of risk factors after randomisation

	Age (years)		Ulcer size (cm ²)		Time since last healed (months)	
	Mean	SEM	Mean	SEM	Mean	SEM
Pinch skin grafts (n=25)	71.1	3	41	16	49	16
Porcine dermis (n=28)	75.0	2	32	11	39	11

Reduction in ulcer size—By one week ulcers treated with pinch skin grafts and porcine dermis were reduced to 51% and 70%, respectively, of the initial ulcer size ($p < 0.05$) (fig 1). It is difficult to be precise about the viability of pinch grafts at one week, but this advantage over porcine dermis was maintained throughout the study with the proportion of initial ulcer size reduced to 36% at two weeks and only 2% at 12 weeks compared with 62% at two weeks and 15% at 12 weeks, respectively ($p < 0.01$). Most of the pinch grafts took more or less completely at their first application. In seven of the eight exceptions re-grafting at three to five weeks was required for grafts that had failed in the posterior medial malleolar area in ulcers that subsequently remained unhealed at 12 weeks.

Healing rate—The healing rate in the first week was 15 cm² with pinch grafts compared with 3.5 cm² for porcine dermis (fig 2). This initial difference is explained by the area of viable pinch grafts. Nevertheless, healing rates in the second to fourth weeks were also improved with pinch grafts, the rate in the second week being 8.5 cm² compared with 2.5 cm² in the porcine dermis group ($p < 0.05$). As over half of the ulcers treated by pinch skin grafts had healed by six weeks and the mean proportion of the initial ulcer size was less than 15%, not surprisingly the ulcer healing rate expressed in absolute units fell in the second half of the study. Age had no important effect on healing rate and did not influence viability of pinch skin grafts. Healing rate was similar in the two treatment groups in ulcers of less

than 10 cm², the advantage of pinch skin grafting being largely confined to ulcers larger than 10 cm².

Time to complete healing—Of the 25 ulcers treated with pinch grafts, 16 were fully healed at six weeks compared with only eight of the 28 treated with porcine dermis ($\chi^2 = 6.69$; $p < 0.01$). Ultimately adequate compression bandaging will heal most ulcers, and the difference between the two treatment groups at 12 weeks was no longer statistically significant, with 18 of the pinch graft group healed compared with 13 of the porcine dermis group. The overall time to complete healing was calculated by the life table

FIG 1—Mean percentage of initial ulcer size in each treatment group plotted weekly throughout study. Bars are SEM.

FIG 2—Mean healing rates in the two treatment groups expressed as cm² of re-epithelialised ulcer a week. Bars are SEM.

method (fig 3). With pinch skin grafts the cumulative probability of healing at 12 weeks was 74% compared with 46% with porcine dermis ($\chi^2 = 4.1$; $p < 0.05$). Again, it was the increased healing during the first six weeks of the study that largely explained the difference between the two groups. Age had little effect on the proportion of patients achieving complete healing, only six of 16 patients aged over 80 failing to heal by 12 weeks. Failure to heal was associated with ulcers larger than 10 cm² and with the duration of previous ulceration, factors that were also related to each other. Of the 22 ulcers that failed to heal, 20 were larger than 10 cm² and had not been healed in the previous four years. No ulcer initially larger than 10 cm² healed by six weeks in the pinch skin graft group.

Unhealed ulcers—By 12 weeks 22 of the 53 ulcers had failed to heal. Of these, 18 included an area immediately posterior to the medial malleolus

FIG 3—Time to complete healing assessed by life table method plotting cumulative percentage of ulcers achieving complete healing against time.

(table II). Overall, 18 of 30 posterior medial malleolar ulcers failed to heal compared with only four of the 23 not including this area ($\chi^2=8.06$; $p<0.01$). These posterior medial malleolar ulcers were equally distributed between the two treatment groups, but in the pinch skin graft group all seven ulcers that failed to achieve complete healing included this area, where compression is difficult to apply.

TABLE II—Ulcers failing to heal by 12 weeks

	All ulcers		Posterior medial malleolar ulcers	
	No studied	No (%) unhealed at 12 weeks	No studied	No (%) unhealed at 12 weeks
Pinch skin grafts	25	7 (28)	13	7 (54)
Porcine dermis	28	15 (54)	17	11 (65)
Total	53	22 (42)	30	18 (60)

Discussion

Adequate compression bandaging performed by a limited number of trained staff may achieve healing in most chronic venous ulcers, even in an elderly population with ulcers of a mean duration exceeding three years. The type of dressing is probably less important, but in view of the age range and ulcer size in this patient population the 46% complete healing within 12 weeks obtained with porcine dermis compares favourably with other studies. The results with pinch skin grafting were nevertheless significantly better, showing that seeds of viable skin equally spaced over the surface of a granulating venous ulcer improve healing. This is particularly important, as inadequate bandaging on any single outpatient attendance may cause enough deterioration to delay healing by many weeks. The shorter the interval to complete healing the less likely this is to occur.

With porcine dermis the healing rate over the first six weeks was 2.5 cm² a week in this study and around 2 cm² a week in other studies.^{10,12} This appears better than the 0.9 cm² a week reported with the Bisgaard method¹⁰ and the 0.5 cm² a week obtained with various topical medications or vertical leg drainage, though the compression technique may be the main factor.^{13,15} The greatly improved healing with pinch skin grafts in the first week may be explained entirely by the area of skin that has been accepted as a graft. The continued healing of over 7 cm² a week for the first four

weeks shows the value of increasing the length of epithelial margin from which re-epithelialisation may occur by implanting islands of epithelium. We also found that the healing rate appeared to accelerate as the growing epithelial edges approached each other, suggesting that there may be an added effect due to the production of epithelial growth factors.

Large ulcers which had remained unhealed for many years were more difficult to treat successfully. To some extent the risk factors of age, size, and duration of ulceration were strongly related to each other, large ulcers having resisted treatment for longer. Age had little effect on subsequent healing, though we were aware that immobility due to previous paralysis or osteoarthritis resulted in ulcers that did not respond well to compression bandaging and which possibly required prolonged elevation. Ulcers involving the posterior medial malleolar area were particularly resistant to healing. This became apparent only with increased usage of pinch skin grafts where the grafts took and epithelialised the ulcer surface in all areas except the posterior medial malleolar region. Though low medial calf perforators have been implicated in the pathophysiology of ulcers in this area,²⁰ we believe that the skin and soft tissue posterior to the medial malleolus cannot effectively be compressed by standard bandaging techniques. Moreover, it is conceivable that compression bandaging may place pressure on all the surrounding tissues thereby promoting further oedema and perivascular fibrin deposition within this region.

In this randomised clinical study pinch skin grafting achieved more rapid healing of venous ulcers than dressings with porcine dermis. The procedure is simple and quick and may be performed as an outpatient procedure under local anaesthesia.^{2,18} Though there is little merit in applying grafts to ulcers of under 10 cm², the results dramatically improve the outlook in large or circumferential ulcers, where complete healing may be achieved in under one month. The grafts may even be placed on granulating tissue within an ulcer that has been less than perfectly prepared.

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