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**Paper:**

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## **Title**

A prospective cohort study of prognostic factors for the healing of heel pressure ulcers

## **Abstract**

*Background:* pressure ulcers, 25–30% of which are on the heels are a major burden to patients and healthcare systems. A better understanding of factors associated with healing is required to inform treatment and research priorities.

*Objectives:* to identify patient and pressure ulcer characteristics associated with the healing of heel pressure ulcers.

*Study design and setting:* patients with heel pressure ulcers were recruited to a prospective cohort study in a large teaching hospital in the UK, with a maximum 18-month follow-up. Cox proportional hazards model regression analysis was used to identify prognostic factors for healing.

*Results:* one hundred and forty of 148 patients recruited were analysed. They had 183 pressure ulcers: 77 ulcers healed, 5 were on limbs amputated prior to ulcer healing, 88 were on patients who died prior to healing, 11 were present at the end of the study and 2 were lost to follow-up. The median time to healing was 121 (range 8–440) days. Of 12 variables associated with healing ( $P \leq 0.2$ ), multi-variable analysis identified two factors which were independently predictive of healing including the presence of a severe (versus superficial) ulcer (hazard ratio = 0.48,  $P < 0.1$ ) and the presence of peripheral arterial disease (hazard ratio = 0.40,  $P < 0.1$ ).

*Conclusions:* increased ulcer severity and the presence of peripheral arterial disease significantly reduced the probability of healing. Treatments for heel pressure ulcers should consider the severity of the ulcer and the presence of peripheral arterial disease.

*Keywords:* pressure ulcer, cohort study, heel, wound healing, prognosis, older people

## **Introduction**

Pressure ulcers (PUs) usually occur over bony prominences such as the heel and sacrum [1] where there is little soft tissue. PUs result in significant suffering and morbidity to patients [2] and are costly to the healthcare provider. In the UK costs to the health and social care system are estimated as £1.77 billion [3], costs in the USA range between \$9.1 and \$11.6 billion per year [4].

Interventions for healing PUs include offloading the pressure, wound treatments and correcting intrinsic factors, e.g. malnutrition. A Cochrane systematic review of support surfaces for treating heel PUs identified only one study and did not find evidence to recommend any specific type of support surface [5]. No studies have been identified which provide sufficient evidence for other healing interventions [6].

Very few prognostic factor studies have been performed to study PU healing and none has looked at heel ulcers specifically [6–8].

Most of the available evidence on the process of wound healing is based on in vitro studies of acute wounds [9, 10]. The effects of systemic and wound conditions on acute wound healing are limited and are relatively unknown for PUs [6]. This study examined the healing of heel PUs as they are a common location, the anatomy differs from other body sites and lower limbs are prone to peripheral arterial disease (PAD) [11], neuropathy [12] and oedema [13] which are likely to affect PU healing and aimed to identify prognostic factors for healing heel PUs.

## **Methods**

This was a single centre, prospective cohort study. Following informed consent/Consultee Agreement [14], patients aged  $\geq 18$  years with at least one heel ulcer of minimum Grade 2 [15] of any duration were recruited from elderly care, medical and surgical wards. Participants had baseline assessments and weekly follow-up while in hospital and monthly postdischarge until 18 months, ulcers healed, death or amputation. Patients were ineligible if it was thought unethical to approach them.

An a priori sample size of 200 was based on the expected healing rate and the number of variables considered in the regression model, based on Harrell et al.'s rule of thumb (10 events per variable) [16].

The study was approved by Leeds West Research Ethics Committee in June 2006. Variables were identified through a review of PU, diabetic foot ulcer and venous leg ulcer healing prognostic factor studies. Please see Supplementary data available in Age and Ageing online, Appendix 1, Table S1, for information on the derivation of variables. These included age, gender, ethnicity, speciality, co-morbidity, nutritional status, smoking, medication, pain, individual Braden risk scale factors, neuropathy, arterial disease, ulcer severity, size, duration and tissue type and surrounding skin condition. All data assessments were undertaken by a consultant nurse (E.M.).

The primary outcome was time to healing for each ulcer. Data were censored due to loss to follow-up, death, amputation of the affected limb, withdrawal from the study or the end of follow-up (18 months).

Cox proportional hazards regression was used to measure the hazard ratio (HR) of potential prognostic factors. The ulcer level analysis took into account non-independence of bilateral heel ulcers and included tests of proportional hazards assumption, collinearity, statistical and clinical quality [17]. See Supplementary data available in Age and Ageing online, Appendix 2, for details of analysis process.

## **Results**

One hundred and forty-eight patients with 183 PUs were recruited during a 2-year period (August 2007 to August 2009). Following consent/Consultee Agreement, eight patients were withdrawn and no follow-up data were collected (Figure 1), resulting in analysis population of 140 patients.

Half the patients were male, mean age 80 years, most were in Elderly Care speciality.

See Supplementary data available in Age and Ageing online, Appendix 1, Tables S2, S3 and S4, for full details of outcomes for variables (patient demographics, clinical factors and ulcer-related variables, respectively).

There was a wide range in ulcer duration prior to recruitment (0–1475 days). A quarter of the patients had neuropathy in the affected foot and only 38% had an ulcer on a limb with adequate arterial supply. There were similar numbers of superficial and severe ulcers and a wide range in ulcer size (0.24–43.14 cm<sup>2</sup>). The most common tissue type was necrotic, 28% of patients had healthy skin surrounding the ulcer and 25% reported their ulcer painful.

Seventy-seven ulcers healed, 5 were on limbs amputated prior to ulcer healing, 88 were on patients who died prior to healing, 11 were present at the end of the study and 2 were lost to follow-up. The median time to healing was 121 (range 8–440) days.

See Supplementary data available in Age and Ageing online, Table S5, for details of the univariate analysis. Analysis identified the following variables which reached significance at  $P \leq 0.2$ : specialities of 'Elderly' and 'Vascular', PAD (as comorbidity), prescribed nutritional, analgesic or respiratory medication, PAD (as ABPI), ulcer severity, area, tissue type and erythema/maceration of surrounding skin.

The variables: speciality of Elderly Care, PAD (comorbidity), prescribed nutritional, analgesics and respiratory medication, ulcer severity, ulcer area and gender, were entered in the multi-variable model. Other variables were excluded due to small numbers of observations (erythema, skin maceration), collinearity with other variables (vascular speciality and tissue type) or missing data.

Two variables emerged as significant: severity (HR: 0.48) 95% confidence interval 0.30–0.75  $P = 0.001$  and PAD (HR: 0.40) 95% confidence interval 0.20–0.81  $P = 0.010$ .

This suggests that in a heel ulcer population, having a severe rather than a superficial ulcer, after controlling for the confounding effects of the presence of all other variables in the model, is associated with half (HR = 0.48) the chance of healing over time (95% CI: 0.3–0.8). The presence of PAD, also significantly reduces the chance of healing over time (HR: 0.4, 95% CI: 0.2–0.8) (Table 1).

## **Discussion**

This is the first study to identify prognostic factors for healing of heel PUs. Two factors were identified: the severity of the ulcer and the presence of PAD, both of which have clinical validity.

Three previous studies have examined PU healing prognostic factors including two retrospective studies [7, 8] and one prospective cohort study of patients with Grade  $\frac{3}{4}$  PUs [6]. None reported heel data. With the exception of Berlowitz et al. [7], who found PU severity to be prognostic for healing, other factors identified as independently prognostic of PU healing did not emerge in multi-variable modelling in our study of heel PU healing. However, the relevance of PAD in predicting outcomes has been identified in two prospective cohort studies of patients with diabetic foot ulcers [18, 19], confirming its validity.

There are a number of strengths of this study including the prospective design, minimal missing data, the population was externally valid, the inclusion criteria were broad, comparisons of screened and recruited patients identified the main difference being those who were near death were not recruited (Figure 1), the study used the endpoint of time to complete healing had a long duration of follow-up (18 months) and continued to collect data following hospital discharged. The use of relative assent/Consultee agreement enabled those who lacked capacity, e.g. due to dementia, to be included, thus improving the external validity.

Study limitations include: the sample size was not met due to time constraints; variables selected were likely correlated or surrogates for other measures, e.g. speciality and co-morbidity, however given the lack of evidence, the exploratory

nature of this study and a concern for not overlooking important potential factors led to collection of a broad range of variables.

A high number of patients died prior to healing. Similarly, a high proportion of patients were screened but not recruited as they were close to death (39%). This may also be related to the age of the population. Although no association can be derived in this study, the notion of 'skin failure' as constituent of 'multi-organ failure' associated with death has been proposed by other authors [20]. This censoring impacted on the amount of data included for analysis.

The study has provided valuable information about heel ulcers which take a long time to heal, this will assist healthcare professionals (and enable them to inform patients) to have realistic expectations about difficult to heal wounds. It will help inform resource needs and enable patients and their carers to make choices about treatments which will affect their quality of life. Given the dominance of PAD, questions need to be raised about current service configuration and the potential benefit of vascular assessment and referral for patients with heel ulcers. It will also help inform future research studies, in particular trial planning by identifying study follow-up requirements as well as prognostic factors for analysis.

This study has made an important contribution to the knowledge of healing heel PUs. Very few studies of prognostic factors for healing PUs on all body sites have been identified and no previous work has been carried out specifically for heel ulcers.

**Key points**

- PUs, particularly those found on the heel are predominately found in older people.
- Ulcer severity and the presence of PAD are independent prognostic factors for slower healing of heel PUs.

**Conflicts of interest**

None declared.

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**Supplementary data**

Supplementary data mentioned in the text is available to subscribers in Age and Ageing online



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Figure 1. Flow of participants.

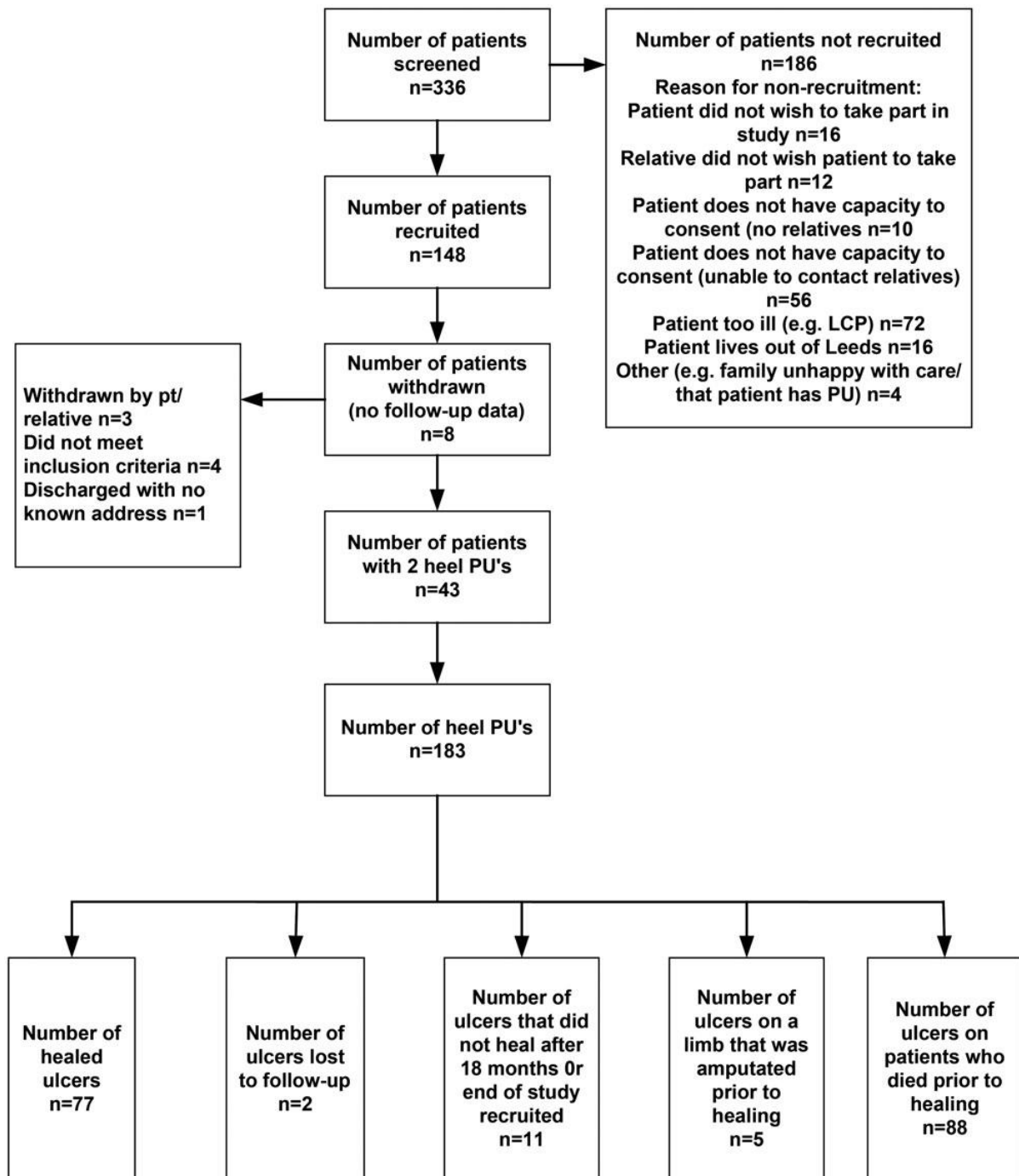


Table 1. Patient baseline variables

Variable/ Attribute		Total number of patients (140)
Age (years)	Mean (SD)/median (range)	80 (14.0)/84 (20–102)
Gender	Male/female	66 (47%)/74 (53%)
Ethnicity	White British	135 (96%)
	Asian	2 (1.5%)
	Afro-Caribbean	2 (1.5%)
	Eastern European	1 (1%)
Speciality	Care of the elderly	91 (65%)
	Vascular	17 (12%)
	Orthopaedics	11 (8%)
	Neurosciences	8 (6%)
	General surgery	9 (6%)
	Diabetology	4 (3%)
Haemoglobin	Mean (SD)/median (range)	10.9 (1.7)/11 (6.7–15.9)
	Missing	1
Smoking	Current/previous/never	14 (10%) / 67(48%) / 59(42%)
Medication	Anticoagulants/antiplatelet	112 (80%)
	Cardiovascular	93 (66%)
	Endocrine	53 (38%)
	Nutrition	77 (55%)
	Steroids	12 (9%)
	Analgesics	101 (72%)
	Antibiotics	32 (23%)
	Gastrointestinal	98 (70%)
	Central nervous system	75 (54%)
	Respiratory	23 (16%)
	Obstetrics, gynaecology and urinary tract	10 (7%)
	Other	12 (9%)