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Wounds and Survival in Noncancer Patients

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Abstract

Background: Currently available prognostic models for noncancer patients lack high levels of discrimination. Therefore, the quest for additional prognostic factors must continue. To date, none have utilized the occurrence of wounds as a prognostic factor.

Methods: As a prospective observational study, based on a sequential case series of 189 advanced noncancer patients, all wounds were documented. One hundred seventy patients were followed until their deaths. Univariate and multivariate survival analyses were performed using hazard ratios (HRs) derived from Cox proportional hazard models.

Results: Seventy-eight percent of patients presented with at least one wound at referral. Patients with wounds displayed worse overall survival than those without wounds ($p = 0.009$). Survival analysis for the full postreferral period revealed a violation of the proportional hazards assumption for pressure ulcers and the Palliative Performance Scale version 2 (PPSv2). In order to address this finding, early deaths (within 14 days of referral) were assessed separately from later deaths (more than 14 days after referral). After controlling for the cooccurrence of wounds, age, gender, Charlson comorbidity index, and PPSv2, pressure ulcers were associated with statistically significant increased risk of death for patients of sufficient health to survive at least 2 weeks after referral (HR 2.42, $p = 0.003$), while other wounds were associated with greater levels of mortality over the full postreferral period (HR 1.96, $p = 0.0001$).

Discussion: The occurrence of pressure ulcers and other wounds are correlated with reduced survival in patients with advanced noncancer illness. These data merit incorporation into existing prognostic models or used in conjunction with them to enhance prognostic accuracy.

Introduction

In developed countries with aging demographics there are more deaths from advanced noncancer illness than from cancer.[1] Yet, patients suffering from noncancer advanced illness are generally referred for palliative medical management late in their disease trajectory or not at all.[2–5] A leading cause of this phenomenon is the difficulty associated with prognostication. When relying solely on clinical experience and intuition, physicians demonstrate poor prognostic accuracy with a tendency to overestimate survival by a factor of 5.3.[6] The consequences of inadequate attention to prognostication are considerable and include delayed transitioning of patients to a completely palliative mode of care, significant unmet needs pertaining to pain, symptom, and psychosocial issues, and high rates of late-stage futile interventions.[7–9] Therefore, it is incumbent upon health care professionals to embrace and advance prognostication as a core clinical skill.[7]

A number of validated tools or instruments, based on performance status, have been used in the prognostication of advanced noncancer patients. The most commonly used is the Palliative Performance Scale (PPS) which is a modification of the Karnofsky performance Scale. PPS ranges between 0% (dead) and 100% (fully ambulatory and healthy).[10] A recent meta-analysis has also demonstrated strong associations between PPS and survival.[11] A systematic review of 11 qualifying prognostic models in patients with noncancer diseases concluded that those that estimate survival of less than 6 months have generally poor discrimination and cannot be recommended without further validation.[12] As a result, there is a need for additional prognostic factors, and perhaps, greater attention to subset analyses. Importantly, none of the aforementioned prognostic tools, instruments, and models

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considers the association of multiple wound classes with survival. The significance of wounds as prognostic factors in patients with advanced cancer has already been demonstrated.[13]

Our recent prospective study demonstrated high prevalence and incidence of cutaneous and wound-related issues, as well as their co-occurrence, among advanced noncancer patients.[14] This study also identified 43 different wound types and classified them into 9 distinct classes. The most prevalent wound class was pressure ulcers occurring in 71.3% of patients followed by traumatic wounds (skin tears, abrasions, and hematomata) occurring in 25.8% of patients. The following wound classes were also identified with each occurring with a prevalence of less than 10%: iatrogenic wounds, infected/inflammatory wounds, venous leg ulcers, diabetic foot ulcers, and arterial leg/foot ulcers.

This study investigates the association between wounds and survival in advanced non-cancer patients. The clinical assessment of wounds has the potential to serve as a simple and cost-efficient method to augment and refine the prognostic accuracy of existing prognostic tools, instruments, and models in the setting of non-cancer advanced illness.

Patients and Methods

Study population

A consecutive cohort of all new referrals to a regional palliative medicine program in Toronto, Canada, was assembled prospectively between May 1, 2005 and June 30, 2006. Referrals included both cancer patients and patients with advanced noncancer disorders. Patients were referred for palliative medical management and eventual end-of-life care. This study focuses exclusively on the non-cancer patients. All patients or their substitute decision makers provided consent to have their clinical data registered in a research database. The data collected were entered on a customized Microsoft™ Access 2007 database (Microsoft, Redmond, WA). This was done on an accrual basis.

Measurement

All patients were examined within 24 hours of the initial referral, the baseline for the study. At this examination basic demographic data were collected, the primary diagnosis and concomitant conditions were recorded, performance status was measured using the Palliative Performance Scale, version 2 (PPSv2)[10] and an inventory of the patient's wounds was made in terms of type, location, morphology, and symptoms.

The primary diagnoses were classified as renal (diabetic and hypertensive renal failure, benign obstructive uropathy, polycystic kidney disease), cardiovascular (coronary artery disease, congestive heart failure, valvular heart disease, aneurysm), neurodegenerative (all forms of dementia, Parkinson's, amyotrophic lateral sclerosis, anoxic encephalopathy), cerebrovascular (thromboembolic, hemorrhagic), respiratory (chronic obstructive pulmonary disease [COPD], asthma, bronchiectasis, pulmonary fibrosis, pulmonary embolism), hepatic (cirrhosis, hepatitis), and infectious diseases (sepsis, TB, HIV/AIDS). In addition to the primary diagnosis, up to nine concomitant diagnoses were classified using the same system.

The wound types were tabulated and, prior to data analysis, grouped into the following five major classes: pressure ulcers (National Pressure Ulcer Advisory Panel stages I, II, III, IV, and unstageable), traumatic wounds (abrasions, lacerations, hematomas, thermal burns), iatrogenic wounds (surgical wound dehiscences, Foley catheter-induced hypospadius), infected and inflammatory wounds (abscesses, bacterial (cellulitis), viral (zoster), pemphigus, pemphigoid, vasculitis, and pyoderma gangrenosum), and lower limb ulcers (venous leg ulcers, arterial leg ulcers, gangrene, and diabetic foot ulcers involving the walking-contact surfaces of the foot). Wounds affecting the posterior aspect of the heel were classified with the pressure ulcer class as they are generally observed in bedbound patients. Given the small numbers of traumatic wounds, iatrogenic wounds, lower limb ulcers, and infected and inflammatory wounds, these classes were consolidated into a class named "other" wounds.

After their baseline assessment patients were treated in a supportive and palliative manner and were followed until their deaths. All wounds were managed by a specialist wound management team consisting of a specialist wound physician and advanced practice nurse in accordance with available best-practice protocols.[15–18] The Charlson comorbidity index was calculated retrospectively according to published guidelines.[19,20]

This study involved analysis of a palliative medicine database developed by the principal author. This study was approved by the research ethics board of the William Osler Health Centre in Toronto, Canada.

Statistical analysis

Only patients with noncancer advanced illness were included in this study. All wounds present at referral were classified into two classes: pressure ulcers and other wounds. A patient could have both types of wounds at the same time. Patient characteristics were summarized with means and percentages and compared between patients with and without each wound class. Means were compared with t tests and percentages with Pearson χ^2 tests. The prevalence of the wound classes were compared between those with and without each of the diagnoses recorded at referral using Pearson χ^2 tests.

Survival time was calculated from referral (baseline) to death. Patients discharged from the program, or still alive at study end, were censored at last follow-up. Kaplan-Meier survival curves were produced to show the univariate survival experience of patients with and without each wound class and the curves were compared using log-rank tests. Univariate Cox models were fitted relating survival time to each of the wound classes individually and a multivariate Cox model considered the two classes jointly. Another multivariate Cox model was fitted that further adjusted the results for age (continuous), gender (male versus female), the Charlson comorbidity index (continuous), and PPSv2 (<30 versus ≥ 30). Note that one of the assumptions of Cox models is that the relative hazard of death after referral is the same for all time periods after referral. If the relative hazard of death changes over time this assumption is violated. We tested the proportional hazard assumption using Grambsch and Therneau's test,[21] which indicated that two of the variables in the multivariate model, pressure ulcers and PPSv2, violated the assumption. Further investigation using Schoenfeld residual plots[21] and survival curves indicated that for these two vari-

Table 1. Association of Patient Characteristics with Wound Status at Referral for Pressure Ulcers and Other Wounds

	Pressure ulcers			*Other wounds*		
	Present n = *132*	*Absent* n = *57*	p	*Present* n = *74*	*Absent* n = *115*	p
Gender			0.1873			0.4021
Female	83 (73.5%)	30 (26.5%)		47 (41.6%)	66 (58.4%)	
Male	49 (64.5%)	27 (35.5%)		27 (35.5%)	49 (64.5%)	
Age			0.0220			0.6259
Mean ± SD (range)	81.7 ± 10.7	77.5 ± 13.3		79.9 ± 12.3	80.8 ± 11.3	
Range	(28.5–102.7)	(34.9–97.7)		(34.9–98.4)	(28.5–102.7)	
Race			0.3871			0.9712
Caucasian	109 (71.2%)	44 (28.8%)		60 (39.2%)	93 (60.8%)	
Other	23 (63.9%)	13 (36.1%)		14 (38.9%)	22 (61.1%)	
Main diagnosis			0.0285			0.0127
Renal	3 (60%)	2 (40%)		2 (40%)	3 (60%)	
Cardiovascular	19 (51.4%)	18 (48.6%)		18 (48.6%)	19 (51.4%)	
Neurodegenerative	38 (76%)	12 (24%)		18 (36%)	32 (64%)	
Cerebrovascular	45 (78.9%)	12 (21.1%)		14 (24.6%)	43 (75.4%)	
Respiratory	7 (70%)	3 (30%)		3 (30%)	7 (70%)	
Hepatic	6 (46.2%)	7 (53.8%)		10 (76.9%)	3 (23.1%)	
Infectious Diseases	14 (82.4%)	3 (17.6%)		9 (52.9%)	8 (47.1%)	
PPS v2			0.1300			0.1399
PPS ≥30	56 (64.4%)	31 (35.6%)		39 (44.8%)	48 (55.2%)	
PPS <30	76 (74.5%)	26 (25.5%)		35 (34.3%)	67 (65.7%)	
Charlson comorbidity index			0.0007			0.0840
Mean ± SD	7.0 ± 2.3	5.8 ± 1.9		6.9 ± 2.3	6.4 ± 2.1	

SD, standard deviation; PPS v2, Palliative Performance Scale version 2.

ables separate hazard ratios (HRs) were needed for the first two weeks after referral and for the period after that. We thus partitioned the time axis into these two periods and estimated the HRs for each period separately as described in.[22] Results are presented for the full period and the two separate periods with HRs and 95% confidence intervals and Wald p values. Univariate Cox model results are presented in a similar way for comparison.

Results

Patient characteristics

One hundred eighty-nine noncancer patients were referred to the program during the study period (Table 1). Slightly over half of the patients (59.8%) were female. The mean age at referral was 80 years (standard deviation, 12 years; range, 29 to 102). The majority of referrals were Caucasian (81%) with the rest being black (4.8%), South Asian (11.1%), East Asian (1.6%), and Hispanic (1.6%). The most frequent primary diagnoses were cerebrovascular (30.2%) and neurodegenerative (26.5%), followed by cardiovascular (19.6%), infectious (9.0%), hepatic (6.9%), respiratory (5.3%), and renal (2.6%). PPSv2 ranged from 10 to 60 with median 20; the Charlson comorbidity index ranged from 2 to 12 with median of 6.

Wound classes

Wounds were identified in 148 patients (78%) at referral. As shown in Figure 1, 132 patients had pressure ulcers and 74 patients exhibited other wounds. The latter comprised 51 patients with traumatic wounds, 33 with lower limb ulcers, 5 with iatrogenic wounds and 4 with infected and inflammatory wounds (note subgroup numbers do not add up to group totals as some patients contributed wounds to more than one class).

The association of patient characteristics with wound status at referral is given in Table 1. The presence of pressure ulcers was significantly associated with greater age and higher scores on the Charlson comorbidity index. Patients with infectious, cerebrovascular, neurodegenerative, and respiratory disease as primary diagnosis had a higher probability of having pressure ulcers that the other diagnoses. Patients with hepatic disease as primary diagnosis had a higher prevalance of other wounds (77%) than the other diagnoses ($p = 0.0127$).

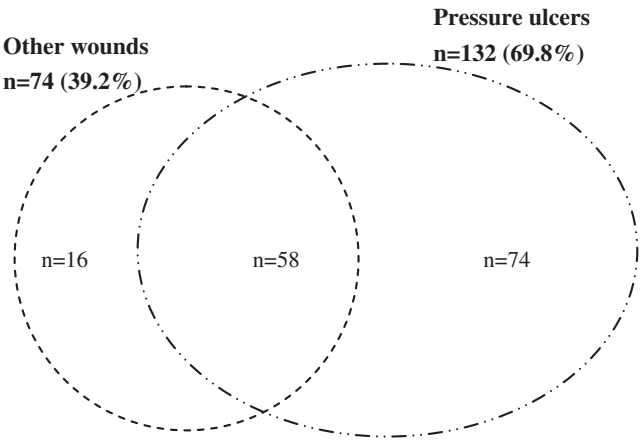

FIG. 1. Venn diagram showing the number of patients who had pressure ulcers and/or other wounds at referral.

Table 2. Percentage of Patients who had Pressure Ulcers (left) or Other Wounds (right), by Presence or Absence of Particular Diagnoses at Referral

	Pressure ulcer(s) present			*Other wound(s) present*		
Diagnosis	*Yes*	*No*	p	*Yes*	*No*	p
Renal						
Present	26 (63.4%)	15 (36.6%)	0.311	23 (56.1%)	18 (43.9%)	0.012
Absent	106 (71.6%)	42 (28.4%)		51 (34.5%)	97 (65.5%)	
Cardiovascular						
Present	71 (70.3%)	30 (29.7%)	0.884	43 (42.6%)	58 (57.4%)	0.302
Absent	61 (69.3%)	27 (30.7%)		31 (35.2%)	57 (64.8%)	
Neurodegenerative						
Present	97 (79.5%)	25 (20.5%)	<0.0001	44 (36.1%)	78 (63.9%)	0.241
Absent	35 (52.2%)	32 (47.8%)		30 (44.8%)	37 (55.2%)	
Cerebrovascular						
Present	81 (81%)	19 (19%)	0.0004	31 (31%)	69 (69%)	0.015
Absent	51 (57.3%)	38 (42.7%)		43 (48.3%)	46 (51.7%)	
Respiratory						
Present	66 (71%)	27 (29%)	0.740	35 (37.6%)	58 (62.4%)	0.674
Absent	66 (68.8%)	30 (31.2%)		39 (40.6%)	57 (59.4%)	
Hepatic						
Present	11 (57.9%)	8 (42.1%)	0.232	12 (63.2%)	7 (36.8%)	0.024
Absent	121 (71.2%)	49 (28.8%)		62 (36.5%)	108 (63.5%)	
Infectious diseases						
Present	54 (75%)	18 (25%)	0.225	30 (41.7%)	42 (58.3%)	0.579
Absent	78 (66.7%)	39 (33.3%)		44 (37.6%)	73 (62.4%)	

This table considers both main diagnosis and concomitant diagnoses.

There were no statistically significant associations between PPSv2 and the prevalence of pressure ulcers or "other" wounds ($p = 0.13$, $p = 0.14$).

Table 2 displays the association of the wound classes with all the diagnoses recorded at referral: main as well as concomitant diagnoses. When all diagnoses are considered, significantly more patients with cerebrovascular or neurodegenerative diagnoses had pressure ulcers than patients without these diseases (81% versus 57%, $p = 0.0004$ and 80% versus 52%, $p < 0.0001$, respectively). Significantly more patients with renal or hepatic diagnoses had other wounds (56% versus 35%, $p = 0.012$ and 63% versus 37%, $p = 0.024$, respectively), while patients with cerebrovascular disease were less likely to have other wounds than patients without the disease (31% versus 48%, $p = 0.015$).

Survival

Of the 189 study patients, 170 (90%) were followed until their death. The program discharged 18 patients who were thus lost to follow-up. The most common reason for discharge was transfers to other hospitals, nursing homes, or hospices. One patient remained alive as at the date of database lock on September 20, 2007. The median time-to-death was 10 days. Of the 148 patients who presented with wounds none died directly from consequences related to any of their wounds.

Patients with wounds displayed worse overall survival than those without wounds ($p = 0.009$). As shown in Figure 2 (top), patients with pressure ulcers at referral had a worse survival than patients without pressure ulcers ($p = 0.006$) but this difference was only evident about 2 weeks after referral. In patients who died within 2 weeks of referral the overlapping curves indicate similar rates of death in those with

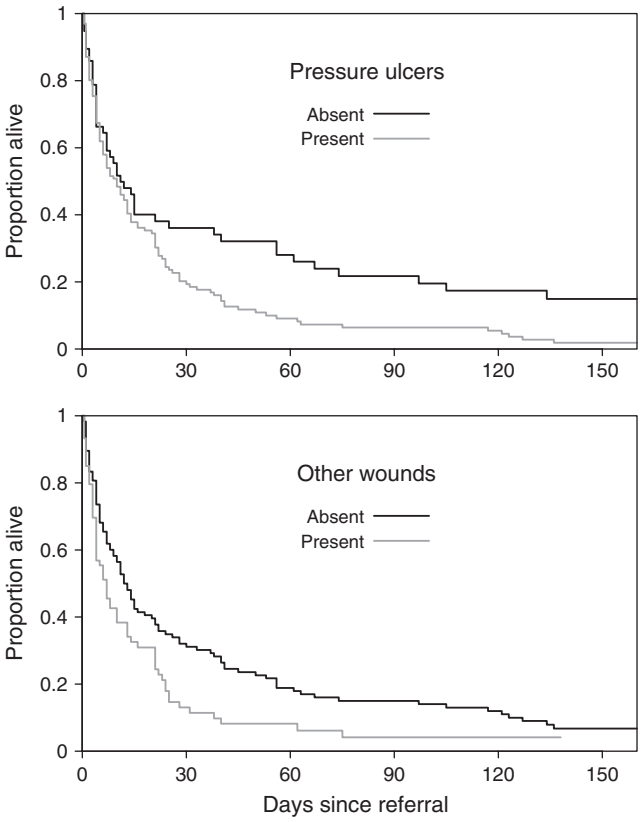

FIG. 2. Kaplan-Meier survival curves showing the survival experience of patients with and without pressure ulcers (**top**) and other wounds (**bottom**).

Table 3. A: Univariate Cox Survival Model for Other Wounds. B: Univariate Cox Survival Model for Pressure Ulcers. C: Multivariate Cox Model for Both Pressure Ulcers and Other Wounds, Which Controls for the Co-occurrence of Wounds

A	*Death over full postreferral period*		
Factor	*HR*	*95% CI*	p
Other wounds[a]: present vs absent	1.77	1.15–2.75	0.0103

B	*Death over full postreferral period*			*Death within 14 days after referral*			*Death more than 14 days after referral*		
Factor	*HR*	*95% CI*	p	*HR*	*95% CI*	p	*HR*	*95% CI*	p
Pressure ulcers: present vs absent	1.74[b]	1.17–2.58	0.0060	1.27	0.78–2.05	0.3307	2.80	1.46–5.4	0.0021

C	*Death over full postreferral period*			*Death within 14 days after referral*			*Death more than 14 days after referral*		
Factor	*HR*	*95% CI*	p	*HR*	*95% CI*	p	*HR*	*95% CI*	p
Pressure ulcers: present vs absent	1.57[b]	1.11–2.22	0.0115	1.16	0.76–1.77	0.5012	2.62	1.46–4.72	0.0013
Other wounds[a]: present vs absent	1.49	1.08–2.05	0.0142	1.46	1–2.13	0.0527	1.74	0.97–3.11	0.0620

[a]Includes traumatic wounds, iatrogenic wounds, lower limb ulcers, and infected/inflammatory wounds.
[b]This hazard ratio is a non-representative average over time since there is evidence of non-proportionality.
There was evidence that the proportional hazards assumption was violated for pressure ulcers. To address this problem deaths within 14 days of referral were modeled separately from later deaths in models that included pressure ulcers.
HR, hazard ratios; CI, confidence interval.

and without pressure ulcers. As a result the probability of surviving 10 days or more is similar between groups (48% versus 52% in those with and without pressure ulcers) but bigger differences are seen when 30 or 90 day survival is considered (19% versus 35%; 6% versus 20%).

The presence of nonpressure ulcer wounds at referral was also associated with worse survival (Figure 1, bottom) with a median time to death of 7 days versus 12 days for patients without such wounds ($p = 0.009$). Thirty-eight percent of patients with other wounds survived 10 days, 12% survived 30 days and 4% survived 90 days or more versus 56%, 31%, and 14%, respectively for patients without these types of wounds.

Table 3 shows the results of univariate Cox models for the two wound classes. The presence of pressure ulcers was associated with increased mortality in patients of sufficient health to survive 14 days after survival in both the unadjusted univariate model (HR 2.8, 95% confidence interval [CI] 1.46–5.4; $p = 0.0021$), and the model adjusted for the co-occurrence of wounds (HR 2.62, 95% CI 1.46–4.72; $p = 0.0013$). The presence of wounds other than pressure ulcers was associated with increased mortality in all patients, throughout the full postreferral period, in both the unadjusted univariate model (HR 1.77, 95% CI 1.15–2.75; $p = 0.0103$), and the model adjusted for the co-occurrence of wounds (HR 1.49, 95% CI 1.08–2.05; $p = 0.0142$).

Table 4 (left) displays the results of a multivariate Cox model for the two wound classes that adjusts for the co-occurrence of wound classes as well as for age, gender, Charlson comorbidity index, and PPSv2. Other wounds, male gender, higher Charlson scores, and PPSv2 less than 30 were significantly associated with higher hazard of death, with other wounds demonstrating a HR of 1.95 (95% CI 1.40–2.71; $p = 0.0001$). While this model is adequate for other wounds, age, gender, and Charlson scores, an omnibus test for non-proportionality was significant ($p = 0.004$) with the indication that pressure ulcers and PPSv2 could not be adequately represented with constant hazard ratios ($p = 0.001$, $p = 0.002$, respectively). Table 4 (right) shows that the presence of pressure ulcers is significantly associated with increased risk of death in patients who are of sufficient health to survive at least 2 weeks after referral (HR = 2.42, 95% CI 1.34–4.38; $p = 0.003$). Pressure ulcers are not associated with greater risk of death in patients who are close to death (HR = 0.81, $p = 0.345$; Table 4, middle). In contrast PPSv2 < 30 at referral is highly predictive of early death (HR = 5.66, $p < 0.00001$) but for patients still alive after 14 days the HR reduces to 1.56 ($p = 0.176$).

Discussion

This is the first prospective study investigating the relationship between multiple wound classes and survival in patients with advanced noncancer illness. Seventy-eight percent of all patients presented with one or more wounds at referral. This study used two wound classes: pressure ulcers and "other" wounds (summation of traumatic wounds, iatrogenic wounds, lower limb ulcers, and infected/inflammatory wounds). The co-occurrence of wounds from more than one class was common, having occurred in almost 40% of patients with wounds. Thus, it is important to take the simultaneous effect of the wound classes into account when studying prognosis.

Table 4. Multivariate Cox Survival Model for Pressure Ulcers and Other Wounds Adjusting for age, Gender, the Charlson Comorbidity Index, and PPSv2

	Death over full postreferral period			*Death within 14 days after referral*			*Death more than 14 days after referral*		
Factor	*HR*	*95% CI*	p	*HR*	*95% CI*	p	*HR*	*95% CI*	p
Pressure ulcers: present vs. absent	1.26[a]	0.88–1.81	0.214	0.81	0.51–1.27	0.345	2.42	1.34–4.38	0.003
Other wounds[b]: present vs absent	1.95	1.40–2.71	0.0001	1.99	1.34–2.94	0.001	1.99	1.08–3.69	0.028
Age: per increment of 10 years	1.09	0.96–1.24	0.185	1.15	0.97–1.36	0.117	0.97	0.79–1.20	0.789
Sex: male vs female	1.60	1.17–2.19	0.003	1.71	1.15–2.54	0.008	1.19	0.68–2.08	0.545
PPSv2: <30 vs ≥ 30	3.51[a]	2.51–4.91	<0.00001	5.66	3.59–8.90	<0.00001	1.56	0.82–2.96	0.176
Charlson comorbidity index: per increment of 1	1.09	1.01–1.18	0.032	1.09	0.99–1.20	0.082	1.14	0.99–1.32	0.060

[a]This hazard ratio is a nonrepresentative average over time since there is evidence of nonproportionality.
[b]Includes traumatic wounds, iatrogenic wounds, lower limb ulcers, and infected/inflammatory wounds.
In the model using the full follow-up period (left), pressure ulcers and PPSv2 violates the proportional hazards assumption. To address this problem deaths within 14 days of referral were modeled separately from later deaths (middle and right panels).
HR, hazard ratios; CI, confidence interval; PPSv 2, Palliative Performance Scale version 2.

Pressure ulcers most commonly occur among patients with advanced illness within hospitals and nursing homes.[23–26] They mostly affect increasingly bed-bound patients and have a propensity to involve the sacrum and the posterior aspect of the heel. Debate exists whether they are due to neglect and negligence, or whether they are unavoidable and part of the natural history of advanced illness. Although there is controversy over the link between pressure ulcers and increased mortality, consensus is growing that they are mostly predictors of impending death rather than a direct cause of death.[27]

Survival analysis for the full postreferral period revealed a violation of the proportional hazards assumption for pressure ulcers and the PPSv2. In order to address this finding, early deaths (within 14 days of referral) were assessed separately from later deaths (more than 14 days after referral). For deaths within 14 days of referral, pressure ulcers were not associated with greater levels of mortality. A potential explanation for this finding is the extremely late referral of end-stage patients, many of whom were actively dying at the point of referral as evidenced by extremely low PPSv2 at referral. Such patients are already on a steep decline from multi-organ failure, and the presence or absence of wounds at this point is unlikely to add to the accuracy of very late stage prognostication. However, for patients of sufficient health to survive at least two weeks after referral, pressure ulcers were associated with greater levels of mortality. Note that in the model adjusted for the factors age, gender, Charlson comorbidity index, and PPSv2, the HR for pressure ulcers reflects the unique contribution of pressure ulcers over and above that of the listed factors, In particular, it means that differences in survival in patients with and without pressure ulcers do not simply reflect the differences in PPSv2 and Charlson comorbidity index seen in Table 1. The preservation of statistical significance after controlling for age, gender, Charlson comorbidity index, and PPSv2, supports the conclusion that pressure ulcers represent an independent risk factor for decreased survival.

The results of this study are congruent with other studies that demonstrate increased mortality in patients with pressure ulcers. A retrospective cohort of a veterans administration hospital and long-term care unit experienced a 68.9% 6-month mortality rate.[28] An Italian observational cohort study involving frail elderly patients showed increased mortality in patients with pressure ulcers (HR 1.92, 95% CI 1.52–2.43, $p < 0.001$).[26] Two studies that looked at nursing home patients with pressure ulcers also demonstrated increased mortality associated with pressure ulcers, one showing a fourfold increase in mortality,[25] and the other showing an 88.1% greater death rate ($p < 0.001$) at 1 year.[27] However, none of these studies adequately controlled for other parameters associated with increased mortality or the co-occurrence of wounds.

The second class of wounds evaluated in this study, dubbed "other" wounds was a summation of the following groups: traumatic wounds, iatrogenic wounds, lower limb ulcers, and infected and inflammatory wounds. This conglomerate wound class tended to occur most in patients suffering from hepatic and renal diseases. "Other" wounds were associated with greater levels of mortality over the full postreferral period with no evidence of a differential hazard ratio by time period. The preservation of statistical significance after controlling for age, gender, Charlson comorbidity index, and PPSv2, supports the conclusion that "other" wounds also represent an independent risk factor for decreased survival.

A limitation of this study is that it only considered patients referred for consideration of palliative medical management in a large urban center within a single developed nation. Most patients were referred at a very late stage of their disease trajectory. Therefore, the results may not be reflective of other clinical settings. Another limitation is lack of stratification within pressure ulcers and "other" wounds. In addition, this study did not consider wounds that occurred between baseline and death. All of these limitations should be subjects for future investigations. Another limitation relates to the fact that the number of wounds within each class was not taken into account, only the presence or absence of the wound class at referral. However, one recent study has demonstrated that the summation of all types of ulcers was associated with increased mortality at 6 months with a HR = 1.32 (95% CI 1.07–1.63).[29] Unfortunately, that study did not disclose the proportions of the various wound classes or account for their co-occurrence.

The results of this study provide stimulus to promote comprehensive and serial assessments of the cutaneous system as a key aspect and competency in the clinical care in patients suffering from advanced noncancer illness. The diagnosis and monitoring of such lesions is a simple and low-

cost means of providing valuable data that may be used to enhance currently available prognostic tools, instruments, and models. This study enhances prognostic research in the noncancer setting by examining survival in the context of multiple wound classes. Improved prognostication in advanced non-cancer illness has the potential to allow for appropriate and earlier transitioning to a completely supportive and palliative mode of care with resultant improvements in comfort, dignity, and quality of life.

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Author Disclosure Statement

No competing financial interests exist.

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