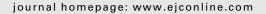


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Wounds and survival in cancer patients

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ABSTRACT

A number of validated and objectively based prognostic models are available for use in cancer care. The quest for additional prognostic factors continues in order to increase their accuracy. To date, none has considered the effect that wounds may contribute to assessing survival. This study serves to demonstrate that certain wound classes affecting cancer patients carry associations with survival. As a prospective observational study, based on a sequential case series of 418 advanced cancer patients, all cutaneous and wound issues were documented and monitored. Three hundred and seventy seven patients were followed until their deaths. Univariate and multivariate survival analyses were performed using hazard ratios (HRs) derived from Cox-proportional hazard models. Forty-four percent of patients presented with at least one wound at referral. Patients with wounds displayed worse overall survival than those without wounds ($p \le 0.0001$). A significant interaction was seen between pressure ulcers (PU's) and sex (p = 0.0005). After controlling for the cooccurrence of wounds, age, sex, Charlson comorbidity index and PPSv2, statistically significant increased risk of death was observed for female patients with PU's (HR 2.00, p = 0.0002), but not for males with PU's (HR 0.83, p = 0.328). Malignant wounds were not associated with decreased survival (HR 1.17, p = 0.285). The presence of all other wounds was associated with decreased survival (HR 1.48, p = 0.002). In summary, the presence of PU's in female cancer patients and 'other' wounds in all cancer patients correlates with reduced survival. Therefore, this data should be incorporated into existing prognostic models or used in conjunction with them in order to enhance prognostic accuracy.

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1. Introduction

Prognostication is currently experiencing a renaissance within health care. Once regarding solely as a craft, prognostication is evolving into both a science and an art. The science of prognostication relates to the computation of survival predictions, while the art of prognostication relates to the ability of physicians to communicate such data to the patient and their families. When relying solely on clinical experience and intuition, physicians demonstrate a poor prognostic accuracy with a tendency to overestimate survival by a factor of 5.3.2 The implications for accurate prognostication are multiple and significant. 1,3,4 It behooves physicians to embrace and advance prognostication as a core clinical skill as it

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ultimately helps patients to 'live their lives the way they want to'.¹ The consequences of inadequate attention to prognostication are considerable and include delayed transitioning of patients to a completely palliative mode of care along with the resultant high rates of late-stage futile interventions.¹,³,⁴

Prognostic models for newly diagnosed cancer patients are generally based on the degree of disease burden as evidenced by clinical, imaging, laboratory, tumour histology and molecular features. 1,3-6 An example is the SEER (Surveillance, Epidemiology and End-Results) programme of the National Cancer Institute which publishes survival data from populationbased cancer registries. Such models have demonstrated high levels of accuracy in providing estimates of long-term survival. However, they tend to be less accurate in predicting short-term survival in advanced cancer. A number of validated tools or instruments, based on the performance status, have been employed in advanced cancer. They include the Karnofsky Performance Status Score⁷ (KPS) and the Palliative Performance Scale⁸ (PPS). Both the performance status tools are metric scales ranging between 0% (dead) and 100% (fully ambulatory and healthy). Several studies have demonstrated that KPS correlates with survival in cancer patients. A recent meta-analysis has also demonstrated strong associations between PPS and survival.9 A systematic review of prognostic factors concluded that of 136 different variables derived from 22 studies, performance status was the most robust predictor of survival, followed by dyspnea, dysphagia, xerostomia, anorexia and cognitive impairment. 10 Examples of integrated prognostic models applicable in cancer care include the Palliative Prognostic Index¹¹ (PPI) and the Palliative Prognostic Score¹² (PaP). PPI integrates PPS with clinical signs and symptoms (oral intake, edema, dyspnea and delirium). The Palliative Prognostic (PaP) Score integrates KPS with clinical signs and symptoms (dyspnea, anorexia, total white blood cell count and lymphocyte%), together with clinical prediction of survival (CPS) which is an estimate generated by a physician. These tools, instruments and models although helpful continue to lack a desired level of accuracy. As a result, more prognostic factors need to be discovered, and perhaps, greater attention to subset analysis needs to be given. Importantly, none of the aforementioned prognostic tools, instruments and models consider the association of wounds with survival.

Our recent prospective study demonstrated high prevalence and incidence of cutaneous and wound-related issues, as well as their co-occurrence, among advanced cancer patients. 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 22.4% of patients followed by malignant wounds occurring in 14.5% of patients. The following wound classes were also identified with each occurring with a prevalence of less than 10%: traumatic wounds, iatrogenic wounds, infected/inflammatory wounds, venous leg ulcers, diabetic foot ulcers and arterial leg/foot ulcers.

This study investigates the association between multiple wound classes and survival in advanced 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 methods in the setting of advanced cancer.

2. Patients and methods

2.1. Study population

A consecutive cohort of all new referrals to a regional palliative medicine programme in Toronto, Canada, was assembled prospectively between 1st May 2005 and 30th June 2006. Referrals included both cancer patients and patients with advanced non-cancer disorders. Patients were referred for palliative medical management and eventual end-of-life care. This study focuses on the 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 customised MicrosoftTM Access 2007 database. This was done on an accrual basis.

2.2. Measurement

All patients were examined within 24 h of the initial referral, the baseline for the study. At this examination basic demographic data were collected, the primary cancer diagnosis was recorded, performance status was measured using the Palliative Performance Scale (PPSv2)⁸ and an inventory of the patient's wounds was made in terms of type, location, morphology and symptoms.

The primary cancer diagnoses were classified as breast, gastrointestinal (gastric, oesophageal, small intestine, colorectal, biliary, pancreatic and liver), genitourinary (prostate, renal, bladder and ureter), gynaecologic (cervix, ovarian and uterine), head and neck (oral, laryngeal and salivary gland), haemato-lymphatic (all leukaemias, lymphomas and myeloma), lung (non-small cell, small cell and mesothelioma), primary brain tumours, primary skin cancers (melanomas and squamous cell cancers) and others (sarcoma, carcinoid and metastatic adenocarcinoma of unknown primary source).

The wound types were tabulated and, prior to data analysis, grouped into the following six major classes based on the logical groupings and class size: malignant wounds (fungating, malignant ulcers, nodules/induration, zosteriform and mixed), pressure ulcers (National Pressure Ulcer Advisory Panel stages I, II, III, IV and unstageable), traumatic wounds (abrasions, lacerations, hematomas and thermal burns), iatrogenic wounds (radiotherapy burns, surgical wound dehiscences, chemotherapy-induced skin necrosis and 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). Given the small number of traumatic wounds, iatrogenic wounds, lower limb ulcers and infected and inflammatory wounds, it was deemed appropriate to consolidate them 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. ^{14–17} The Charlson comorbidity index

was calculated retrospectively according to the published guidelines. 18,19

2.3. Ethical considerations

This study involved analysis of a palliative medicine database developed by the principal author. The database was anonymised and bears no links to patients. This study was approved by the research ethics board of the William Osler Health Centre in Toronto, Canada.

2.4. Statistical analysis

Only patients with cancer were included in this study. Patient characteristics were summarised with means and percentages. Means were compared with t-tests and percentages were compared with Pearson χ^2 tests. The prevalence of the wound classes was calculated together with the degree to which wound classes co-occurred. For each primary diagnosis the percentage of patients that had a particular wound class present at referral were calculated and compared among diagnoses using the Pearson χ^2 tests.

Survival time was calculated from referral (baseline) to death. Patients discharged from the programme, or still alive at study end, were censored at last follow-up. The Kaplan-Meier survival curves were produced to show the survival experience of patients with wounds at referral relative to wound-free patients. The median survival of these two groups was compared using a log-rank test. Separate univariate Cox models were fitted to find the unadjusted associations of each wound class with survival relative to

wound-free patients. A multivariate Cox model was used to model the three wound classes simultaneously. The independence of wound effects relative to other traditional prognostic indicators, namely age, sex, PPSv2 (coded as less than 50 versus 50 or more) and the Charlson comorbidity index, was tested in a Cox model with age and the Charlson comorbidity index treated as continuous variables. Two-way interactions of age, sex and PPS with the three wound classes were included if (1) they were significant at the 5% level in a randomly chosen training set of half the data and (2) remained significant in the remaining data as well as in the full data set. This was done to reduce the false positive rate due to multiple testing. One interaction, between sex and pressure ulcers, was identified in this way. Results of the Cox models were presented in terms of hazard ratios (HRs) with 95% confidence intervals and Wald p-values.

3. Results

3.1. Patient characteristics

Cancer patients (418) were referred to the programme during the study period (Table 1). Slightly over half of the patients (53.6%) were male. The mean age at referral was 73 years (standard deviation 13 years, range 19–99). The majority of referrals were Caucasian (86.1%) with the rest being Black (5.5%), South Asian (4.3%), East Asian (3.6%) and Hispanic (0.5%). The most frequent primary diagnoses were gastrointestinal (31%) and lung cancer (24%), followed by genitourinary (9%), breast (7%), haemato-lymphatic (6%), gynaecologic (5%), primary brain tumours (4%), primary skin cancers (3%),

Table 1 – Association of patient characteristics with wound status at referral.							
	Patients with wounds $N = 184$	Wound-free patients $N = 234$	р				
Sex N (%)							
Female	89 (45.9%)	105 (54.1%)	0.477				
Male	95 (42.4%)	129 (57.6%)					
Age							
Mean ± SD	74.3 ± 12.3	72.2 ± 13.4	0.093				
Race N (%)							
Caucasian	151 (41.9%)	209 (58.1%)	0.033				
Other	33 (56.9%)	25 (43.1%)					
Main cancer diagnosis N (%)							
Gastrointestinal	49 (37.4%)	82 (62.6%)	< 0.0001				
Lung	37 (37%)	63 (63%)					
Genitourinary	14 (36.8%)	24 (63.2%)					
Breast	19 (65.5%)	10 (34.5%)					
Haemato-lymphatic	17 (73.9%)	6 (26.1%)					
Gynaecologic	7 (33.3%)	14 (66.7%)					
Primary brain tumours	6 (33.3%)	12 (66.7%)					
Primary skin cancers	12 (92.3%)	1 (7.7%)					
Head and neck	9 (69.2%)	4 (30.8%)					
Others	14 (43.8%)	18 (56.2%)					
PPSv2 N (%)							
PPSv2 < 50	89 (57.4%)	66 (42.6%)	< 0.0001				
PPSV2 ≥ 50	93 (36%)	165 (64%)					
The Charlson comorbidity index							
Mean ± SD	9.0 ± 2.5	8.9 ± 2.6	0.771				

head and neck (3%) and other (8%). Women accounted for 39% of gastrointestinal cases, 37% of lung cases, 18% of genitourinary cases, 97% of breast cases, 39% of haemato-lymphatic cases, 100% of gynaecologic cases, 56% of primary brain tumour cases, 46% of primary skin cancer cases, 31% of head and neck cases and 66% of other cancer cases. 44% of All patients presented with one or more wounds at referral. The association of patient characteristics with wound status at referral is given in Table 1. A higher percentage of non-Caucasian patients than Caucasians presented with wounds (56.9% versus 41.9%, p = 0.033) as did a higher proportion of patients with PPSv2 less than 50 (57.4% versus 36%, p < 0.0001). Wound occurrence was associated with cancer diagnosis (p < 0.0001): patients with primary skin cancers, haemato-lymphatic cancer, head and neck cancer and breast cancer had the highest percentages for presenting with wounds (92.3%, 73.9%, 69.2% and 65.5%, respectively). Sex, age and the Charlson comorbidity index did not differ significantly between patients with wounds and those wound-free.

3.2. Wound classes

It was decided to use three wound classes, as shown in Fig. 2, in order to balance the numbers of patients. Pressure ulcers were the most common wound class occurring in 22.7% of all patients, followed by 'other' wounds (21.5%), and malignant wounds (14.8%). The number of patients in whom each wound class co-occurred with other wound classes is also shown. Nearly 50% of patients in each wound class also had wounds from one or more of the other wound classes.

None of the pressure ulcers had undergone malignant transformation into marjolin ulcers.²⁰ All the malignant wounds seen in this study represented cutaneous metastases rather than primary neoplasms. Of the 184 patients who presented with wounds none died directly from consequences related to any of their wounds.

Table 2 displays the distribution of wound classes relative to the particular cancer diagnosis. Statistically significant associations were noted with malignant wounds (p < 0.001), and with other wounds (p < 0.001). The cancer diagnoses with the highest proportions of patients with malignant wounds were primary skin cancers (53.8%), breast (48.3%) and head

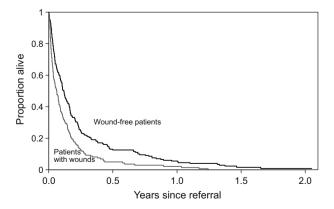


Fig. 1 – The Kaplan–Meier survival curves showing the survival experience of patients with wounds at referral relative to wound-free patients.

and neck cancers (46.2%). The cancer diagnoses with the highest proportions of patients with other wounds were haemato-lymphatic cancers (65.2%), primary skin cancers (53.8%) and head and neck cancers (30.8%).

Associations were found between PPSv2 and the prevalence of pressure ulcers and 'other' wounds. 40.6% of Patients with PPSv2 < 50 had pressure ulcers versus 12% of patients with PPSv2 \geq 50 (p < 0.0001). 28.48% of Patients with PPSv2 < 50 had 'other' wounds versus 17.4% of patients with PPSv2 \geq 50 (p = 0.009). There was no association between PPSv2 and malignant wounds as 14.8% of patients with PPSv2 \leq 50 had malignant wounds versus 14.7% of patients with PPSv2 \leq 50 (p = 0.976).

3.3. Survival

Three hundred and seventy seven of the 418 study patients (90.2%) were followed until their death. The programme discharged 38 patients who were thus lost to follow-up. The most common reason for discharge was transfers to other hospitals, nursing homes or hospices. Three patients remained alive as at the date of database lock on 20th September 2007. The median time-to-death was 32 d.

As shown in Fig. 1, patients with wounds at referral had a worse prognosis with a median time-to-death of 23 versus 43 d for wound-free patients ($p \le 0.0001$). 41% of Wounded patients survived one month or longer and 12% survived 3 months or longer. For wound-free patients, the percentages were 60% and 25%, respectively.

The association of the different wound classes with survival was explored using Cox-proportional hazard models. Table 3, on the left, provides the results of separate univariate models for each wound class, compared to wound-free patients. All wound classes demonstrated significantly worse survival than wound-free patients. Results of a multivariate model which considers all three wound classes simultaneously is shown in Table 3, on the right side. In this model the presence of pressure ulcers was highly associated with early death, with the hazard ratio of 1.85 (95% confidence

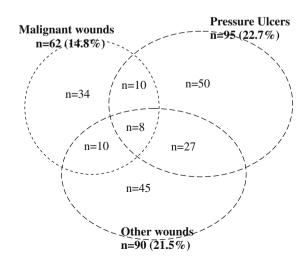


Fig. 2 – Venn diagram showing the number of patients that experienced each of the three wound classes and the interrelationships among the three classes.

Table 2 –	Percentage	e ot patients that had w	rabie 2 – Percentage of patients that had wounds from each wound class according to cancer diagnosis	id class according	to cancer diagno	SIS.				
Lung N = 100		ast Gastro-intestinal 29 N = 131	Breast Gastro-intestinal Haemato-lymphatic Genito-urinary $N=29$ $N=131$ $N=23$ $N=38$	Genito-urinary N = 38	Gynae-cologic N = 21	Primary brain tumours N = 18	Primary skin cancers N = 12	Head and neck N = 13	Others N = 32	d
Malignant wounds	spunon									
Absent	Absent 89.0 51.7	89.3	87.0	100.0	90.5	100.0	46.2	53.8	84.4	<0.001
Present	11.0 48.3	10.7	13.0	0.0	9.5	0.0	53.8	46.2	15.6	
Pressure ulcers	ers									
Absent 79.0	79.0 79.3	79.4	82.6	71.1	76.2	83.3	46.2	84.6	71.9	0.329
Present	21.0 20.7	20.6	17.4	28.9	23.8	16.7	53.8	15.4	28.1	
Other wounds ^a	ıdsa									
Absent	Absent 82.0 82.8	84.0	34.8	81.6	76.2	77.8	46.2	69.2	87.5	<0.001
Present	Present 18.0 17.2	16.0	65.2	18.4	23.8	22.2	53.8	30.8	12.5	
a Includes	traumatic w	a Includes traumatic wounds, iatrogenic wounds, lower limb ulcers		and infected/inflammatory wounds.	ounds.					

interval (CI) 1.44–2.37, p < 0.001) indicating that the hazard of death is 85% higher in patients with pressure ulcers than in patients without pressure ulcers. Other wounds (HR = 1.35, 95% CI 1.05–1.73; p = 0.019) were also associated with earlier death. Malignant wounds were not associated with earlier deaths when accounting for the co-occurrence of wounds.

Table 4 displays the results of a multivariate model that adjusts for age, sex, the Charlson comorbidity index and PPSv2. While age and the Charlson comorbidity index were not significant, sex showed a highly significant interaction (p=0.0005) with pressure ulcers indicating a differential effect of pressure ulcers for men and women. According to this model, the deleterious effect of pressure ulcers was largely seen in women, with a hazard ratio of death of 2 for women with pressure ulcers relative to women without pressure ulcers and 1.85 relative to men with pressure ulcers. For men with pressure ulcers, the hazard of death was much smaller: relative to men without pressure ulcers it was 0.83; relative to women without pressure ulcers, it was 1.08. As in the earlier model 'other' wounds were also associated with earlier death in all patients.

4. Discussion

This is the first study investigating the relationship between multiple wound classes and survival in the cancer care arena. 44% of All patients presented with one or more wounds at referral. This study used three wound classes: malignant wounds, 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 50% of patients in each class. Thus, it is important to take into account the simultaneous effect of the wound classes when studying prognosis.

A higher percentage of non-Caucasian patients than Caucasian patients exhibited wounds. This is congruent with a number of studies that have demonstrated that blacks have a higher prevalence of pressure ulcers compared to caucasians. There was no significant difference in the survival of Caucasians with wounds relative to non-Caucasians with wounds (HR 0.94; 95% CI 0.70–1.26; p = 0.672).

The presence of all wounds at referral was associated with low performance status as measured by PPSv2, and reduced survival (median 23 versus 43 d) indicating that wounds are important indicators or markers of a patient's condition. Of the wound classes assessed, the prevalence of pressure ulcers was most strongly correlated with low levels of PPSv2. This is consistent with the results of a recent report, in cancer patients, that showed a strong correlation (r = 0.885; p < 0.001) between PPSv2 and Braden scores, the most commonly used risk assessment tool for pressure ulcers. The presence of pressure ulcers and 'other' wounds was significantly associated with earlier deaths in both the wound co-occurrence adjusted multivariate model and the multivariate model that adjusted for age, sex, the Charlson comorbidity index and PPSv2.

Pressure ulcers most commonly occur among patients with advanced illness within hospitals and nursing homes.²⁴

Table 3 – Univariate and multivariate Cox survival models using the wound classes as predictors. The first column gives separate univariate models for each wound class. The second column gives the results of a single multivariate Cox model with all wound classes in one model, which controls for the co-occurrence of wounds.

Univariate model for wound classes			Multivariate model for wound classes				
Factor	HR	95% CI	р	Factor	HR	95% CI	р
Malignant wounds				Malignant wounds			
Present versus absent	1.37	1.02-1.83	0.037	Present versus absent	1.14	0.86–1.51	0.356
Pressure ulcers				Pressure ulcers			
Present versus absent	2.07	1.60-2.67	< 0.001	Present versus absent	1.85	1.44-2.37	< 0.001
Other wounds ^a				Other wounds			
Present versus absent	1.72	1.33-2.22	<0.001	Present versus absent	1.35	1.05–1.73	0.019
a Includes traumatic wounds, iatrogenic wounds, lower limb ulcers and infected/inflammatory wounds.							

Table 4 – Multivariate Cox survival model using the wound classes as predictors, controlling for age, sex, the Charlson comorbidity index and PPSv2. The model incorporates a differential effect for pressure ulcers by sex.

Factor	HR	95% CI	р
Malignant wounds			
Present versus absent	1.17	0.88–1.56	0.285
Differential effect of pressure ulcers (PU) by sex ^a			
Women with PU versus women without PU	2.00	1.38–2.89	0.0002
Women with PU versus men without PU	1.55	1.07-2.24	0.020
Men with PU versus men without PU	0.83	0.58-1.20	0.328
Men with PU versus women without PU	1.08	0.75-1.54	0.688
Other wounds ^b			
Present versus absent	1.48	1.15–1.91	0.002
PPSu2			
<50 versus ≥ 50	2.85	2.23–3.65	<0.0001
The Charlson comorbidity index			
Per increment of 1	0.99	0.95–1.03	0.491
Age			
Per increment of 10 years	0.95	0.87–1.03	0.218

a p-Value for interaction: 0.0005.

They mostly affect increasingly bed-bound patients and most commonly 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 a 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. A case-matched cohort study of 33 cancer patients demonstrated a 39% mortality rate; the patients that died did so within a mean of 3 weeks after developing pressure ulcers. A case-matched cohort study of 30 cancer patients demonstrated a 39% mortality rate; the patients that died did so within a mean of 3 weeks after developing pressure ulcers.

This study's univariate HR of 2.07 (95% CI 1.60–2.67) for pressure ulcers is comparable to the results of a European study of frail elderly out-patients (HR 1.92; 95% CI 1.52–2.43). After adjustment, a striking sex-mortality differential was demonstrated with women affected with pressure ulcers having worse survival than men with pressure ulcers by a factor of 1.85. The reasons for this sex-survival disparity are unclear and merit investigation. Although a diagnosis effect is

possible since nearly 100% of breast and gynaecologic cases were females these cancers per se are not known to have worse survival.²⁸ The preservation of statistical significance, for women affected with pressure ulcers, after adjustments for the Charlson comorbidity index and PPSv2, supports the conclusion that they represent an independent risk factor for decreased survival.

There are three main types of malignant wounds: primary skin neoplasms, cutaneous metastases from remote neoplasms and marjolin ulcers which are rare malignant transformations occurring within chronic pressure ulcers. The survival of patients with malignant wounds has been increasing over the past four decades. Data published in 1966 demonstrated that patients survived an average of only 3 months after the development of cutaneous metastases. Data published in 1993 demonstrated that patients survived an average of 11.27 months after the development of cutaneous metastases, with patients diagnosed with cancers of the lung, ovary and foregut faring the worst. This positive trend is clearly the result of advancements in oncologic

b Includes traumatic wounds, iatrogenic wounds, lower limb ulcers and infected/inflammatory wounds.

therapeutics over the past few decades, especially in breast cancer.

This study showed a 14.8% prevalence of malignant wounds and they tended to occur in patients with primary skin cancers, breast cancer and head and neck cancers. After adjusting for pressure ulcers, other wounds, age, sex, the Charlson comorbidity index and PPSv2, malignant wounds did not demonstrate statistically significant associations with decreased survival, with HR of 1.17 (95% CI 0.88–1.56; p = 0.285). A Canadian study³¹ published in 2000 and a Hong Kong based study³² published in 2007 also demonstrated that malignant wounds were not associated with decreased survival in advanced cancer patients. Thus, the presence of a malignant wound should not be automatically regarded as a disqualifying criterion for additional attempts at disease-modulating therapies.

The third 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 mostly in haemato-lymphatic malignancies, primary skin cancers and head and neck cancers. Traumatic wounds such as lacerations and abrasions were most common in haemato-lymphatic malignancies and were most likely related to skin atrophy caused by longterm corticosteroid usage. Surgical wound dehiscences and surgical wound infections represented half of all other wounds seen in patients with primary skin cancers. Radiation therapy burns were the most common of the iatrogenic wounds seen in patients with head and neck cancers. Almost half of the 'other wounds' occurring in lung cancer patients were iatrogenic and were caused by EGFR tyrosine kinase inhibitor usage. After adjusting for age, sex, the Charlson comorbidity index and PPSv2, other wounds demonstrated a HR of 1.48 (95% CI 1.15–1.91; p = 0.002).

The results of this study may be used to calculate estimated composite HR's. For example, a female cancer patient with a PPSv2 < 50 having a pressure ulcer and an 'other' wound carries a HR = 8.55 ($2.85 \times 2.00 \times 1.48$), compared to a HR = 1.00 for a female cancer patient of the same age and the Charlson index with a PPSv2 ≥ 50 and no wounds.

A limitation of this study is that it only considered patients in a large urban centre within a single developed nation. Therefore, the results may not be reflective of other settings or underdeveloped nations. Another limitation is lack of stratification according to the stage of pressure ulceration. The number of wounds within each class was not taken into account, only the presence or absence of the wound class at referral. In addition, this study did not consider wounds that occurred between baseline and death. All of these limitations should be subjects for future investigations.

The results of this study provide impetus to promote comprehensive and serial assessments of the cutaneous system as a core aspect and competency of clinical oncologic care. The diagnosis and monitoring of such lesions are a simple and low-cost means of providing valuable data that may be employed to enhance currently available prognostic tools, instruments and models. This study extends prognostic research by examining survival in the context of wounds. Any increase in our capacity to improve and facilitate prognostica-

tion will aid in timely transitioning patients from aggressive oncologic management to a completely supportive and palliative mode of care.

Conflict of interest statement

None declared.

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