Stage-related implications of community-acquired pressure injuries for the acute medical inpatients

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Abstract

Aims: To analyse the prevalence of any-stage pressure injuries at hospital admission and their impact on short-, mid- and late-term mortality. Patient characteristics associated with pressure injuries and the impact on hospital costs were also investigated.

Background: In medical patients acutely admitted to hospital, no study analysed the presence of pre-existing pressure injuries and the related short- and long-term mortality according to the overall stages of severity thereof.

Design: Retrospective cohort study following the STROBE guideline.

Methods: In a population of 7217 acute medical inpatients, the presence and staging of pressure injuries were assessed at hospital admission. The impact of pressure injury on 30-, 180- and 365-day mortality was analysed by multivariate Cox regression models.

Results: The prevalence of community-acquired pressure injuries was 14.9% (stage-1: 8.1%; stage-2: 3.5%; stage-3: 1.6%; stage-4: 1.1%; unstageable: 0.5%). Hemiplegia/paraplegia, anaemia, poor functional status, high nutritional risk, clinical instability and systemic inflammatory response, but not hydration status, were found to be associated with the occurrence of stage-2-and-above pressure injuries. An increasing difference was found in Diagnosis-Related Groups (DRG) weight according to pressure injury stages. A distinct and progressively increasing risk-of-death for any-stage pressure injury was shown after 365-days. A significantly increased mortality risk for all considered time intervals was found for unstageable and stage-4 pressure injuries.

Conclusions: In acute medical inpatients, the presence of community-acquired pressure injuries is part of a multidimensional clinical complexity. The presence and staging of pressure injuries have an independent dramatic impact on of early-to-late mortality and hospital costs.

Relevance to clinical practice: This study documented as community-acquired pressure injuries are highly prevalent and represents an independent predictor of outcomes in strict dependence of the progression of thereof stage. The presence of community-acquired pressure injuries should be interpreted as a critical marker of frailty and increased vulnerability.

KEYWORDS
Comorbidity, DRG weight, hydration, inflammation, mortality, nursing, nutrition, pressure injuries, stages

1 | INTRODUCTION

Pressure injuries (PIs) are tissue damages of different levels of severity caused by shear, friction, unrelieved pressure or the joint effect of these factors (National Pressure Ulcer Advisory Panel, European Pressure Ulcer Advisory Panel, & Pan Pacific Pressure Injury Alliance, 2014). The pathogenesis of PIs is multifactorial and involves vascular, degenerative, immune, inflammatory and metabolic changes (Jaul, 2010). PI prevention requires a comprehensive approach, particularly for older patients presenting functional impairment and multiple comorbidities (Jaul, 2014). Therefore, PI occurrence is strictly dependent on the provided healthcare, and the prevention and treatment thereof are challenging, especially for nurses who are called to identify vulnerable patients based on specific risk factors (Garcez Sardo et al., 2016). The occurrence of PIs is considered to be an indicator of poor-quality nursing care (Isis Montalvo, 2007). Once they appear, PIs can have a dramatic impact on the patient's health, causing prolonged pain and distress, a longer stay in healthcare facilities, increased costs and poorer outcomes (Jaul et al., 2018). In particular, PIs have been shown to be associated with short- and long-term mortality in both hospitals and nursing homes (Takahashi, 2008; Thomas et al., 2013). Therefore, the presence and severity of PIs may have a specific prognostic power, together with many other factors that notably contribute to the prognosis, such as age, nutritional status and comorbidity burden.

2 | BACKGROUND

A number of patients are admitted to hospital with pre-existing PIs (community-acquired PIs, or CAPI), while others can develop PIs during their hospital stay (hospital-acquired PIs, or HAPI) (Graves & Zheng, 2014). This distinction has relevant implication both on clinical and economic reasons.

CAPI have been documented in patients living at home and in healthcare facilities such as nursing homes (Corbett et al., 2017; Worsley et al., 2016). Clearly, patients are hospitalised for an acute disease, not for a CAPI, but the presence thereof might affect the clinical course and impact relevant outcomes (Hahnel et al., 2017).

Furthermore, CAPI have become an increasing economic interest for healthcare organisations worldwide. Since PIs represent a specific expenditure item when coded as a secondary diagnosis in Diagnosis-Related Groups (DRGs), a healthcare organisation may no longer warrant such reimbursement for PIs unless they were present on admission, as PIs are considered to be reasonably preventable by ensuring appropriate patient care (VanGilder et al., 2010).

What does this paper contribute to the wider global clinical community?

- Community-acquired pressure injuries (CAPI) are highly prevalent among acute medical inpatients
- The presence of CAPI on hospital admission should be interpreted as a marker of frailty and increased vulnerability
- The presence and staging of CAPI are strong independent predictors of early-to-late mortality

It is essential to document the presence of PIs at the time of hospital admission to distinguish those already present from those acquired during the hospital stay. A complete skin inspection and a PI risk assessment are therefore recommended as soon as possible (and no later than eight hours) after hospital admission to identify and document the presence of PIs and implement appropriate interventions (National Pressure Ulcer Advisory Panel et al., 2014). Regrettably, while a large number of studies on the prevalence and incidence of HAPI have been published, only a few studies considered the prevalence and characteristics of patients presenting CAPI at hospital admission, so this should be considered a vital research field (Latimer et al., 2019).

Among studies assessing PIs within eight hours of admission in hospitalised patients, the reported prevalence of CAPI ranged from 10.3 to 16.0% for acute medical or geriatric patients (Díez-Manglano et al., 2016; Khor et al., 2014; Garcez Sardo et al., 2016) to 61.5–66.5% for patients suffering from advanced or terminal illnesses and requiring palliative care (Jaul & Calderon-Margalit, 2015; Jaul et al., 2016). Inclusion criteria limited CAPI prevalence to PIs of at least stage-2 (Khor et al., 2014) or stage-3 and stage-4 (Jaul & Calderon-Margalit, 2015; Jaul et al., 2016), while among studies that included patients with stage-1-to-stage-4 PIs, unstageable injuries were not considered (Díez-Manglano et al., 2016; Garcez Sardo et al., 2016). As far as can be seen from the retrieved literature, no study has analysed CAPI prevalence and the related short- and long-term mortality according to the complete PIs staging.

3 | THE STUDY

3.1 | Aims

The main purposes of the present investigation are to analyse the prevalence and staging of PIs at the first skin assessment upon hospital admission in a population of acute medical patients and to

explore the impact of CAPI presence and staging on short-, mid- and late-term mortality, adjusting for factors that describe the multi-dimensional complexity of acutely hospitalised patients. As a secondary aim, the clinical and demographic patient characteristics associated with stage-2-and-above CAPI are analysed. Finally, the impact of CAPI of any stage on hospital costs is investigated.

3.2 | Design

This was a retrospective cohort study conducted in the University Hospital of Trieste, Italy following the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guideline (Supplementary File).

3.3 | Participants

All consecutive acute patients who were admitted from the Emergency Department (ED) to the Internal Medicine Department over a period of one year (between October 15, 2015 and October 14, 2016) were considered for eligibility. Patients were excluded if the possible presence of PIs was not documented at hospital admission.

3.4 | Data collection

3.4.1 | Pressure injuries documentation

During the first nursing assessment at hospital admission (i.e. within two hours), all of the patient's skin was observed to document the possible presence of PIs. This early evaluation was ensured by the fact that all the patients included in the study were transferred from the ED to a dedicated departmental nursing-led facility (i.e. 'Shared Admission' service) for a preliminary in-depth assessment and medical-nursing stabilisation before being transferred to their respective wards. The anatomical sites and the stage of all present PIs were documented using the classification system recommended by the US, European and Pan Pacific advisory committees on pressure ulcers prevention and treatment (National Pressure Ulcer Advisory Panel et al., 2014). Briefly, a stage-1 pressure ulcer is identified by a non-blanchable erythema, a stage-2 presents a partial-thickness skin loss, a stage-3 has a full-thickness skin loss and a stage-4 has a full-thickness tissue loss. Pressure ulcers presenting with slough or escara are classified as unstageable pressure injuries. Finally, PIs characterised by a purple or maroon localised area of intact skin (or a thin blister or thin eschar over a dark wound bed) were classified as suspected deep-tissue injury (sDTI); sDTIs were never documented in our study population. In patients presenting more than one PI, that of a higher stage was recorded for the study purpose. Where injuries of any stage were observed together to unstageable ulcers, the latter category was recorded, as their true depth (and thus stage) could not be determined at that moment.

Data were collected by the professional group belonging to the 'Shared Admission' service, consisting of expert nurses with at least three years of clinical nursing practice and trained to assess and document PIs stages using the classification system described above.

3.4.2 | Study covariates

Data on the patient's age and sex, variables describing the patient's nutritional and hydration conditions, inflammation, clinical acuity, functional status and comorbid conditions were collected as being potentially associated to the presence of PIs and to a higher risk of mortality (Coleman et al., 2014; Defloor, 1999; Saghaleini et al., 2018).

The Charlson Comorbidity Index (CCI) was used to assess the presence of multiple comorbidities (Charlson et al., 1994). The CCI considers 19 comorbid conditions scored as 1, 2, 3 or 6. The sum of all scores determines the CCI (ranging from 0–24): the higher the CCI, the higher the possible impact on mortality and resource-use. Moreover, the presence of the following diseases was considered: congestive heart failure, dementia, chronic obstructive pulmonary disease, diabetes with chronic complications, hemiplegia or paraplegia and the existence of any primitive or metastatic cancer.

The serum albumin level is commonly used as an indicator of nutritional status in patients with PIs; however, the level thereof can be affected by other conditions, particularly inflammation (Sugino et al., 2014). Therefore, the patients were categorised according to the Glasgow Prognostic Score (GPS), a prognostic marker based on relative C-reactive protein and albumin levels (Maurício et al., 2013; Namiuchi et al., 2015; Stepanova et al., 2015): 0 (CRP ≤10 mg/L and albumin ≥3.5 g/dL); 1 (CRP >10 mg/L and albumin ≥3.5 g/dL or CRP ≤10 mg/L and albumin <3.5 g/dL); or 2 (CRP >10 mg/L and albumin <3.5 g/dL). In addition, the Instant Nutritional Assessment (INA) (Seltzer et al., 1979) was computed to identify patients who were malnourished or at risk of malnutrition (Pablo et al., 2003) according to one of the four groups defined on the basis of serum albumin level and blood lymphocyte count: group 1 (albumin ≥3.5 g/dL; lymphocytes ≥1.5 cells ×103/μL), group 2 (albumin ≥3.5 g/dL; lymphocytes <1.5 cells ×103/μL), group 3 (albumin <3.5 g/dL; blood lymphocytes ≥1.5 cells ×103/μL) and group 4 (albumin <3.5 g/dL; lymphocytes <1.5 cells ×103/μL).

The Nutritional Risk Screening 2002 (NRS-2002) (Kondrup et al., 2003) was calculated to identify patients at risk of malnutrition. NRS-2002 identifies at-risk patients based on body mass index (BMI) <20.5 kg/m^2, recent weight loss or reduced dietary intake and the severity of the disease. An additional point was assigned to patients aged 70 years or older. An NRS-2002 ≥ 3 was identified as a prognostic factor for early and late mortality (Sanson et al., 2020).

Serum osmolarity is widely accepted as being an accurate reference standard for hydration status in older patients (Thomas et al., 2008; Volkert et al., 2019). Serum osmolarity was calculated based

on the equation by Khajuria and Krahn (2005), which has been previously validated in several different populations of older adults (Hooper et al., 2015). The presence of current dehydration was considered for a serum osmolarity of >300 mmol/L (Volkert et al., 2019).

Renal function was defined based on the estimated glomerular filtrate rate (eGFR) calculated using the formula by Levey et al. (2009). Renal function was defined as moderately or severely decreased for an eGFR of <60 mL/min/1.73 m^2, as this threshold was found to be a marker of an increased risk of mortality (Van Pottelbergh et al., 2013).

In the presence of anaemia, oxygen supply to the body tissues can be compromised, thereby increasing the risk for PI development. Moreover, anaemia is a documented risk factor for mortality, particularly when associated with renal dysfunction (Kajimoto et al., 2016). Patients were thus categorised according to their haemoglobin levels into two groups: mild or non-anaemic: ≥11 g/dL; or moderate or severe anaemia: <11 g/dL (World Health Organization, 2011).

PI onset can be triggered by hemodynamic instability, which compromises tissue perfusion and oxygenation (Black et al., 2011). The Modified Early Warning Score (MEWS) (Subbe et al., 2001) was employed to assess patient criticality upon hospital admission on the basis of five physiological vital signs (i.e. systolic blood pressure, heart and respiratory rate, body temperature and level of consciousness) and patients were stratified according to the following risk categories: low (≤ 2), intermediate (3–4) and high (≥ 5).

The Norton Scale (Norton et al., 1962) was computed to consider the patient's overall functional status according to their mental condition, activity and mobility capacities and the presence of urinary or bowel incontinence. The Norton Scale is a widely used tool to assess the risk of PI development and was found to be associated with long-term mortality in elderly patients (Justo et al., 2012). Patients with a Norton score of <14 were considered to have a high or very high risk.

For all patients, the condition of those who survived or died was assessed up to one year after their hospital admission, and when applicable, the date of the patient's death was recorded to compute mortality rates at different time intervals.

3.4.3 | Study endpoints

The impact of every-stage PIs on hospital length-of-stay and on all causes for short-, mid- and late-term mortality (30, 180 and 365 days following hospital admission, respectively) was considered as primary study endpoints.

To investigate the demographic factors and the acute and chronic conditions that are potentially associated with CAPI in this population, a dichotomic secondary endpoint was established. Since studies documented that, although clinically relevant, the identification of stage-1 PIs is challenging so these lesions may be confused with other skin injuries and misclassified (Defloor et al., 2006), the cumulative prevalence at hospital admission of stage-2-and-above PIs, including unstageable PIs (i.e. the '2+PI' group), was considered. Patients admitted with stage-1 PIs or without any PIs were included in the '1-PI' group.

The impact of CAPI on hospital costs was investigated via the DRG weight (DRGw), a classification system for inpatient charges used as a marker for resource intensity of the acute treatment based on appropriate weighting factors related to each DRG. By way of an example, DRGw may be 0.5223 for an uncomplicated cardiac arrhythmia (DRG 139), 0.84616 for urinary tract infections (DRG 320), 1.82965 for acute ischaemic stroke (DRG 559) and 3.78905 for an endocarditis (DRG 126).

4 | ETHICAL CONSIDERATIONS

This research is part of the PROPOSING IDEAS (PROgnostic factors of Poor hospital Outcome based on clinical Severity, nutrItional and NursinG indexes IDEntified on AdmiSsion in elderly/frail patients) study, approved by the Regional Bioethics Committee of Friuli Venezia Giulia, Italy (protocol number: 28,217; date of approval: 31/7/2018). The research was conducted according to the Declaration of Helsinki. At hospital admission, all enrolled patients authorised the use of their clinical data for study purposes.

4.1 | Data analysis

The continuous variables were displayed as medians and interquartile ranges (IQRs) and the nominal variables as numbers and percentages. Comparisons between the groups were analysed via an χ^2 test, nonparametric Mann–Whitney's U test for independent samples or Kruskal–Wallis test adjusted by the Bonferroni correction for multiple pairwise comparisons, as appropriate. Univariate logistic regression was used to estimate the unadjusted association between 2+PIs and the study variables. Variables related to the presence of 2+PIs with a p-value <0.1 in the univariate models were tested via multiple forward stepwise logistic regression models. Since both age and CCI were non-normally distributed, a square-root transformation was performed to achieve a more normal data distribution; only the CCI resulted better distributed after the transformation. Results of all logistic regression analyses were presented as odds ratio (OR) and 95% confidence intervals (CI). For the final model, the adequacy of the adjustment was analysed via a likelihood-ratio χ^2 test and the coefficient of the determination was calculated based on the Nagelkerke R^2.

The different time of death according to the presence and stage of the PIs was explored. Observations were censored until 30, 180 or 365 days after hospital admission (i.e. known survival). Unadjusted analysis was carried out by comparing crude Kaplan–Meier curves and a Mantel–Cox log-rank test was used to calculate the differences in survival rates between groups. Multivariate Cox regression models with forward stepwise selection adjusted for confounders known to affect mortality (see the 'Study covariates' section) were subsequently used to estimate the patient's risk of death at the same time intervals. The results were presented as a proportional hazard ratio (HR) and 95% CI; cumulative hazard adjusted curves were drawn, as well.

TABLE 1 Characteristics of the entire study population and differences between patients who presented pressure injuries of stage 2 and over (2+PU) and those who did not (1-PU).

Characteristics	Whole population	1-PU	2+PU	*p*-value
Age (years)[a]	82.0; 74.0–88.0	81.0; 74.0–88.0	87.0; 81.0–91.0	<0.001
Sex (female)[b§]	4117 (57.0%)	3810 (56.6%)	307 (62.8%)	0.008
Congestive heart failure[b]	1501 (20.8%)	1425 (21.2%)	76 (15.5%)	0.003
Dementia[b]	351 (4.9%)	290 (4.3%)	61 (12.5%)	<0.001
COPD[b]	782 (10.8%)	749 (11.1%)	33 (6.7%)	0.003
Diabetes (with complications)[b]	158 (2.2%)	149 (2.2%)	9 (1.8%)	0.585
Hemiplegia or paraplegia[b]	55 (0.8%)	43 (0.6%)	12 (2.5%)	<0.001
Any primitive cancer[b†]	525 (7.3%)	502 (7.5%)	23 (4.7%)	0.023
Metastatic solid cancer[b]	312 (4.3%)	300 (4.5%)	12 (2.5%)	0.035
Charlson index[a]	3.0; 2.0–4.0	3.0; 2.0–4.0	3.0; 2.0–5.0	<0.001
Norton index <14[b]	2042 (36.0%)	1669 (31.6%)	373 (94.9%)	<0.001
NRS–2002 ≥ 3[b]	2764 (38.3%)	2465 (36.6%)	299 (61.1%)	<0.001
Current dehydration[b]	3263 (50.1%)	2998 (49.3%)	265 (62.4%)	<0.001
eGFR <60 mL/min/1.73 m^{2} [b]	2878 (40.8%)	2666 (40.5%)	212 (45.3%)	0.040
Anaemia (moderate to severe)[b]	2104 (29.8%)	1889 (28.6%)	215 (45.6%)	<0.001
Glasgow Prognostic Score[b]				<0.001
GPS =0	1751 (26.2%)	1738 (27.7%)	13 (3.1%)	
GPS =1	2159 (32.3%)	2110 (33.6%)	49 (11.7%)	
GPS =2	2783 (41.6%)	2427 (38.7%)	356 (85.2%)	
Instant Nutritional Assessment[b]				<0.001
INA =1	1109 (16.8%)	1101 (17.8%)	8 (1.9%)	
INA =2	2030 (30.8%)	2003 (32.5%)	27 (6.5%)	
INA =3	786 (11.9%)	711 (11.5%)	75 (18.0%)	
INA =4	2661 (40.4%)	2355 (38.2%)	306 (73.6%)	
Modified Early Warning Score[b]				<0.001
MEWS ≤2	3264 (45.3%)	3186 (47.4%)	78 (16.1%)	
MEWS 3–4	1989 (27.6%)	1893 (28.2%)	96 (19.8%)	
MEWS ≥5	1949 (27.1%)	1639 (24.4%)	310 (64.0%)	

a: median; interquartile range [Mann–Whitney's U test]. b: number (percentage) [χ^2 test]. PU: pressure ulcers. COPD: chronic obstructive pulmonary disease. NRS-2002: Nutritional Risk Screening 2002.

GPS: Glasgow Prognostic Score. INA: Instant Nutritional Assessment. MEWS: Modified Early Warning Score.

§compared to males (whole population: n = 3100, 43.0%; 1-PU: n = 2918, 43.4%; 2+PU: n = 182, 37.2%).

†including leukaemia and lymphoma. eGFR: estimated glomerular filtrate rate.

The overall statistical significance of the model was tested via likelihood χ^2 statistics. The assumption of the Cox model was assessed by comparing the log-log transformation versus the log of survival time of the Kaplan–Meier curves for the PI subgroups, which showed approximately parallel curves without any intersection with time, such that a proportional hazard constant was assumed over time.

Given the high number of statistical comparisons performed for each variable, to reduce the type-1 error rate for an alpha-level

TABLE 2 Variables associated with the occurrence of pressure injuries of stage-2 and over.

Variable	Unadjusted OR (95% CI)	*p*-value	Adjusted OR (95% CI)	*p*-value
Age	1.064 (1.052–1.076)	<0.001	e.f.m.	
Sex (female)	1.292 (1.069–1.562)	0.008	e.f.m.	
Congestive heart failure	0.685 (0.533–0.881)	0.003	e.f.m.	
Dementia	3.164 (2.361–4.241)	<0.001	e.f.m.	
Chronic obstructive pulmonary disease	0.578 (0.402–0.829)	0.003	e.f.m.	
Diabetes with chronic complications	0.828 (0.420–1.633)	0.586	/	
Hemiplegia or paraplegia	3.911 (2.049–7.466)	<0.001	5.116 (2.128–12.298)	<0.001
Any primitive cancer†	0.612 (0.399–0.940)	0.025	e.f.m.	
Metastatic solid cancer	0.539 (0.300–0.967)	0.038	e.f.m.	
Charlson comorbidity index	1.580 (1.328–1.879)	<0.001	e.f.m.	
Norton index <14	40.295 (25.601–63.422)	<0.001	20.357 (12.0378–34.424)	<0.001
Nutritional Risk Screening 2002 ≥ 3	2.721 (2.253–3.285)	<0.001	1.551 (1.179–2.042)	0.002
Current dehydration	1.704 (1.392–2.087)	<0.001	e.f.m.	
eGFR <60	1.218 (1.009–1.471)	0.040	e.f.m.	
Anaemia (moderate to severe)	2.093 (1.733–2.529)	<0.001	1.510 (1.143–1.995)	0.004
Glasgow Prognostic Score =0	1		1	
Glasgow Prognostic Score =1	3.105 (1.679–5.741)	<0.001	e.f.m.	
Glasgow Prognostic Score =2	19.610 (11.237–34.223)	<0.001	5.426 (2.876–10.236)	<0.001
Instant Nutritional Assessment =1	1		1	
Instant Nutritional Assessment =2	1.855 (0.840–4.097)	0.126	e.f.m.	
Instant Nutritional Assessment =3	14.517 (6.961–30.277)	<0.001	e.f.m.	
Instant Nutritional Assessment =4	17.882 (8.831–36.213)	<0.001	e.f.m.	
Modified Early Warning Score ≤2	1		1	
Modified Early Warning Score 3–4	2.071 (1.528–2.808)	<0.001	e.f.m.	
Modified Early Warning Score ≥5	7.726 (5.985–9.973)	<0.001	1.906 (1.329–2.734)	<0.001

eGFR: estimated glomerular filtrate rate. OR: odds ratio. CI: confidence interval. e.f.m.: excluded from the final regression model
†including leukaemia and lymphoma.

of $p < 0.01$ was set to determine statistical significance. Statistical analyses were performed using SPSS Statistics for Windows, version 23.0 (IBM Corp., Armonk, NY, US).

5 | RESULTS

During the study period, 7423 patients were admitted to the study setting and assessed for inclusion. Twenty-nine subjects (0.4%) were excluded because the presence of PIs was not assessed early after admission, and 177 (2.4%) were excluded because the staging of the PIs was not documented. The final study population was thus 7217 patients. All patients were Caucasian, so possible misclassifications due to darkly pigmented skin were excluded.

5.1 | CAPI prevalence

The prevalence of any-stage PIs upon hospital admission was 14.9% (n = 1073); specifically, the prevalence of stage-1, stage-2, stage-3, stage-4 and unstageable PIs was 8.1%, 3.5%, 1.6%, 1.1% and 0.5%, respectively. Therefore, the prevalence of 2+PIs was 6.8% (n = 489).

5.2 | Risk factors associated with CAPI occurrence

Table 1 shows the characteristics of the entire study population and the differences between patients who presented 2+PIs and those who did not. In subgroup comparisons via a univariate logistic regression analysis (Table 2), all considered variables except for complicated diabetes showed a statistically significant association with the occurrence of 2+PIs. In a multivariate analysis (likelihood-ratio 1437.737; Nagelkerke R^2 0.357), the association was confirmed for the presence of hemiplegia/paraplegia, moderate-to-severe anaemia, Norton index <14, NRS-2002 ≥ 3, GPS =2 and MEWS ≥5.

5.3 | Impact of CAPI on patient outcomes

Data for hospital mortality and LOS were available for 7091 patients (98.3%). The median LOS was 7.0 days (IQR 4.0–12.0) for the entire

population. For patients who were discharged alive from the hospital, the median LOS was 7.0 days (IQR 4.0–11.0) and was longer for 2+PIs patients (1-PIs: 7.0 days, IQR 4.0–11.0; 2+PIs: 8.0 days, IQR 5.0–13.3; $p < 0.001$). After stratifying the population according to the presence of PIs and the possible stages thereof, a significant overall difference between the groups was found ($p < 0.001$); however, Bonferroni-corrected pairwise comparisons revealed that LOS only differed significantly between the no pressure injuries and stage-1 PIs ($p = 0.001$) and the no pressure injuries and stage-2 PIs ($p < 0.001$) subgroups (Figure 1).

Overall hospital mortality for the study population was 10.3% ($n = 729$). The cumulative mortality rate was 14.1% ($n = 1003$), 30.0% ($n = 2127$) and 37.7% ($n = 2676$) after 30, 180 and 365 days after hospital admission, respectively. After stratifying the population according to the presence of PIs and the possible stages thereof, the cumulative risk-of-death was analysed through crude Kaplan–Maier curves. After 30 and 180 days, a clear and progressive increase in the risk of death from stage-1 and stage-2 PIs, and a further risk increase for upper-stage PIs without, however, a clear distinction between the different stages were noticed (Figure 2a and 2b). This finding was similar for one-year mortality, but the risk increase appeared similar for stage-2 and stage-3 PIs, as well as for stage-4 and unstageable PIs (Figure 2c).

In adjusted multivariable Cox regression models, a significant increase in mortality risk for all considered time intervals was detected for unstageable and stage-4 PI (although the latter showed a $p = 0.013$ for 30-day mortality, which slightly exceeded the established threshold). Overall, compared to patients admitted without PIs, a more distinct and progressive increase in risk-of-death for all-stages PIs was observed after 180 and 365 days (Table 3 and Figure 2d–f).

5.4 | Impact of CAPI on hospital costs

A significant difference was found in DRGw according to the presence and stage of the PIs ($p < 0.001$). Compared to patients admitted without PIs (DRGw 0.88761, IQR 0.75176–1.13944), a post hoc analysis revealed a Bonferroni-corrected statistically higher DRGw for those admitted with any-stage PIs that slighting exceeding the defined significance threshold for unstageable PIs: stage-1: 0.93045, IQR 0.80247–1.15005 ($p = 0.004$); stage-2: 1.02700, IQR 0.83828–1.22435 ($p < 0.001$); stage-3: 1.08472, IQR 0.84616–1.22435 ($p = 0.004$); stage-4: 1.13944, IQR 0.87995–1.29552 ($p < 0.001$); unstageable: 1.04804, IQR 0.85930–1.494 ($p = 0.017$).

6 | DISCUSSION

The main result of the present investigation was that, in our population of acute medical inpatients, the presence and staging of CAPI were strong independent predictors of early-to-late mortality, as showed by multivariable analyses adjusted for factors that describe both the disease-specific and non-disease-specific multidimensional complexity of acutely hospitalised medical patients. To the best of our knowledge, this is the first study that demonstrates the impact

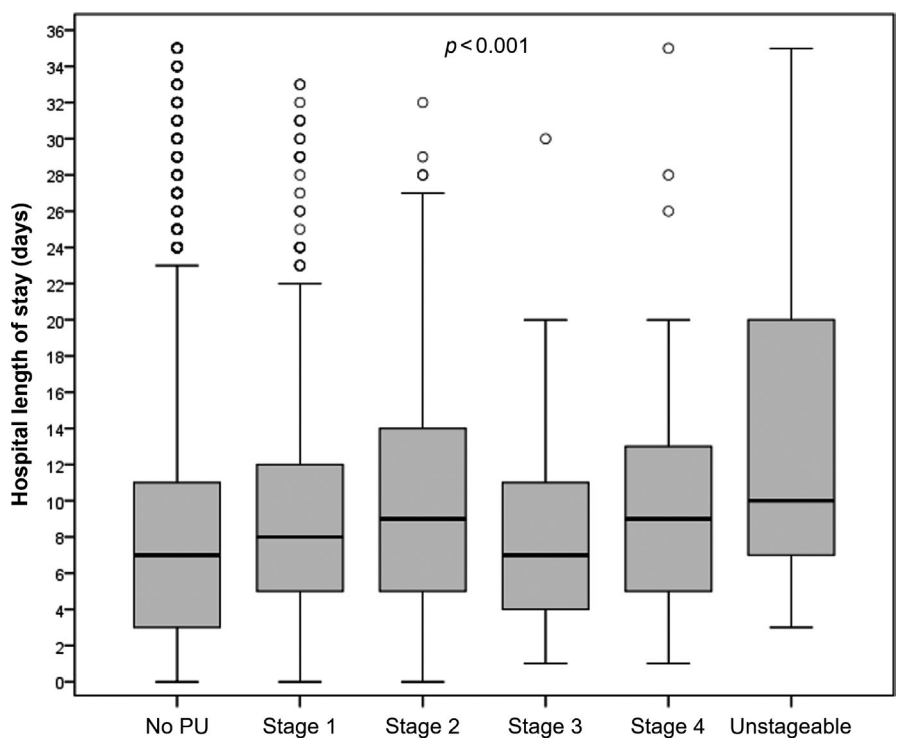

FIGURE 1 Length of hospital stay according to the presence and staging of community-acquired pressure injuries (PI). Black horizontal line inside the boxes: median. Boxes height: interquartile range. Whiskers: 1.5 × interquartile range. Circles: outliers.

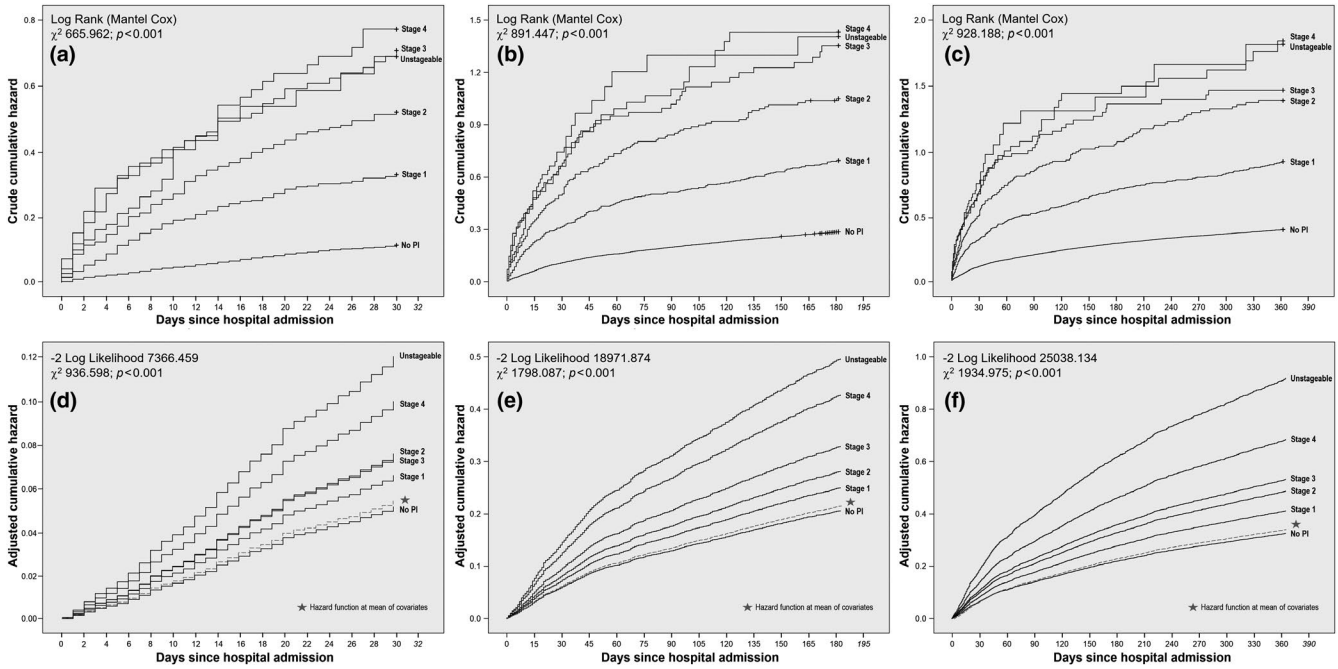

FIGURE 2 Unadjusted (a-c) and adjusted survival curves (d-f, multivariate Cox regression analysis) at different time interval from hospital admission for patients admitted with community-acquired pressure injuries.

of short-to-long-term mortality of CAPI according to the overall stages of severity thereof.

A similar progressive impact on adjusted mortality risk consistent with the progression of PI severity (staging) clearly emerged from our data; the data highlighted some interesting, peculiar differences, however. In particular, despite the limited prevalence, patients who were admitted presenting stage-4 or unstageable PIs showed a risk-of-death that was more than doubled in all considered time intervals. Conversely, the prognostic power on mortality of stage-2 and stage-3 PIs showed a similar, not-significant and indistinguishable impact on short-term mortality. Some authors indicated that unstageable PIs corresponded to a stage-3 or stage-4 PI once slough or eschar is removed (Schank, 2015), which suggests a reliable and predictable correspondence between these injuries. However, other studies found that, based on the healing evolution, only two-thirds of unstageable PIs are consistent with full-thickness wounds, while the remaining correspond with partial-thickness wounds, thus implying that the current definition of unstageable PIs as full-thickness injuries may be inaccurate (Zaratkiewicz et al., 2015). We believe that these considerations risk diverting attention from the most relevant aspect related to unstageable PIs. Indeed, until the basis of the wound is exposed by removing the slough/eschar, the depth of an unstageable PI cannot be determined and, most importantly, a specific treatment cannot be initiated.

In daily clinical practice, a patient's overall condition, as well as organisational issues, often prevents a prompt and complete removal of eschar or slough, particularly in bedridden, unstable subjects. A delayed or incomplete debridement may lead to a worsening PI stage and the occurrence of critical complications (Jung & Lee, 2020), with a potentially negative impact on the patient's outcome. A study that followed patients with CAPI for one year showed that healing time was significantly longer ($p < 0.001$) for patients with an unstageable PI, compared to patients with stage-3 and stage-4 PIs (10.0 months vs 7.7 months) (Guest et al., 2018). Based on these considerations and on our findings that demonstrate the independent association thereof with patient outcome, unstageable PIs should be considered as the most fearsome condition and treated with the highest priority.

Findings on stage-2 and stage-3 PIs solicited some interesting thoughts, as well. These PI stages are relatively limited-depth wounds, having as a common feature the involvement of only the skin with loss limited to epidermis and dermis (i.e. stage-2) or at-most to hypodermis (i.e. subcutaneous fat and connective tissue, stage-3), while muscle, tendon and bone-tissue are not exposed. When stage-2 and stage-3 PIs are managed in a timely fashion according to the appropriate standards of care, it is possible to effectively avoid the progression thereof to higher stages and improve the patient's outcome (Eaton, 2005; Kramer & Kearney, 2000; Palese et al., 2015). These premises seem to be strengthened by our findings, which highlighted that stage-2 and stage-3 PIs indicated a mortality risk that is closer to stage-1 than to stage-4 or unstageable PIs.

Surprisingly, stage-1 PIs, which are often not taken into consideration in PI research, also showed an increasing impact on mortality, compared to patients without PIs. A stage-1 PI is characterised by intact skin, so it is considered to be a less-severe condition based on the premise that a PI always starts at skin level and only subsequently involves deeper tissues. This conception could be misleading, since soft tissues are more prone to ischaemia than epidermis, such that a deep PI could originate at the subcutaneous and muscular level long before involving the skin (Bethell, 2003). Based on this pathophysiologic premise and on the independent impact thereof on

TABLE 3 Results of stepwise Cox regression of mortality at different time interval from hospital admission on study variables.

Predictor	30-days mortality HR (95% CI); *p*-value	180-days mortality HR (95% CI); *p*-value	365-days mortality HR (95% CI); *p*-value
Age	e.f.m.	1.022 (1.015–1.029); <0.001	1.024 (1.019–1.030); <0.001
Sex (female)	e.f.m.	0.839 (0.747–0.943); 0.003	0.840 (0.759–0.931); 0.001
COPD	0.640 (0.457–0.897); 0.009	e.f.m.	e.f.m.
Any primitive cancer†	2.855 (2.196–3.712); <0.001	3.034 (2.572–3.580); <0.001	2.972 (2.561–3.449); <0.001
Metastatic solid cancer	4.344 (3.246–5.813); <0.001	5.693 (4.650–6.971); <0.001	5.430 (4.495–6.560); <0.001
Charlson index	1.652 (1.391–1.962); <0.001	1.471 (1.322–1.637); <0.001	1.393 (1.268–1.529); <0.001
Current dehydration	1.695 (1.403–2.049); <0.001	1.299 (1.157–1.459); <0.001	1.268 (1.147–1.403); <0.001
Anaemia‡	e.f.m.	e.f.m.	1.199 (1.079–1–332); 0.001
GPS =0	1	1	1
GPS =1	1.702 (1.138–2.546); 0.010	1.791 (1443–2.223); <0.001	1.519 (1.285–1.795); <0.001
GPS =2	3.063 (2.103–4.459); <0.001	2.927 (2.384–3.594); <0.001	2.176 (1.851–2.557); <0.001
Norton index <14	2.418 (1.930–3.028); <0.001	1.903 (1.657–2.184); <0.001	1.733 (1.538–1.953); <0.001
MEWS ≤2	1	1	1
MEWS 3–4	1.589 (1.224–2.062); <0.001	1.250 (1.078–1.450); 0.003	1.339 (1.180–1.520); <0.001
MEWS ≥5	2.427 (1.894–3.111); <0.001	1.594 (1.378–1.844); <0.001	1.587 (1.397–1.802); <0.001
NRS 2002 ≥ 3	1.493 (1.236–1.803); <0.001	1.403 (1.249–1.577); <0.001	1.313 (1.186–1.453); <0.001
Pressure injuries: none	1	1	1
Stage–1	*1.277 (0.974–1.674); 0.077*	*1.225 (1.023–1.467); 0.028*	1.269 (1.082–1.489); 0.003
Stage–2	*1.468 (1.046–2.060); 0.027*	1.403 (1.103–1.784); 0.006	1.504 (1.211–1.867); <0.001
Stage–3	*1.453 (0.905–2.333); 0.122*	1.621 (1.155–2.275); 0.005	1.629 (1.175–2.259); 0.003
Stage–4	*1.933 (1.148–3.254); 0.013*	2.006 (1.370–2.937); <0.001	2.075 (1.466–2.938); <0.001
Unstageable	2.333 (1.288–4.227); 0.005	2.496 (1.568–3.974); <0.001	2.842 (1.847–4.373); <0.001

HR: hazard ratio. CI: confidence interval. e.f.m.: excluded from the final model.

COPD: chronic obstructive pulmonary disease. GPS: Glasgow Prognostic Score. MEWS: Modified Early Warning Score. NRS 2002: Nutritional Risk Screening 2002

†including lymphoma and leukaemia.

‡moderate to severe.

patient outcome found in the present study, we think that stage-1 PIs should not be underestimated and should be considered to be a relevant risk factor, especially considering the relevant prevalence thereof.

The present study had a secondary aim to investigate patient characteristics associated with CAPI and the impact thereof on hospital costs. Our findings revealed that patients presenting an impaired functional status, clinical instability, systemic inflammatory

response, moderate-to-severe anaemia and high nutritional risk were more likely to be acutely admitted to hospital with pre-existing PIs. CAPI should thus be considered to be a strong marker of the patient's overall fragility and complexity at the time of hospital admission and strongly predictive for a higher short- and long-term mortality rate. This complexity was also associated with a significantly increasing DRGw consistent with the worsening PI stage, which corresponded to progressively increasing expenditures for the National Health System. This finding is in line with previous surveys, which showed that the cost of treatment increases dramatically with PI-stage increase; for example, Dealey et al. (2012) reported that the expected cost in the UK was about 1200, 5200, 9000 and 14000 pounds-per-patient to heal a stage-1, stage-2, stage-3 and stage-4 PI, respectively. In a study conducted in Spain on a population of patients with PIs who were hospitalised in internal medicine units, Díez-Manglano et al. (2016) reported that DRGw was significantly higher ($p < 0.001$) in patients with PIs of any stage (2.10 ± 0.96) than in patients without PIs (1.58 ± 0.96). To our knowledge, the present study is the first to report the impact of stage-by-stage CAPI on DRGw.

The factors tested as being potentially associated to CAPI occurrence warrant further considerations. Impaired functional status as described by the Norton score is a well-known risk factor for PIs development; this was also confirmed in the present study. Among the considered diseases, only the presence of hemiplegia or paraplegia was found to be associated with 2+PI in an adjusted regression model. In particular, the presence of diabetes mellitus with neuro-vascular complications, which was previously documented as a strong risk factor (Demidova-Rice et al., 2012), failed to demonstrate any association with 2+PI.

Previous studies explored the association between PIs and nutritional risk according to NRS-2002 in different populations and showed that malnutrition is closely associated with the development of PIs (Alhaug et al., 2017; Lussi et al., 2018). More importantly, increased nutritional risk, functional dependence, clinical instability, comorbidities and age were all associated with higher short- and long-term mortality risk in our study. Since it is well-known that functional dependence can impair the patient's ability to self-feed and that energy requirements are increased in patients with PI (Cereda et al., 2011), an accurate evaluation of nutritional status and oral intake should be part of the initial assessment of each patient. It should also be noted that specific nutritional treatment reduces the economic burden of PIs (Cereda et al., 2017).

Although dehydration is widely considered to be a risk factor for the development of PIs and for the delayed healing thereof based on the pathophysiological assumption that water plays an essential role in the transport of nutrients and waste products (National Pressure Ulcer Advisory Panel et al., 2014), to our knowledge, no study has thus far considered the association between the presence of PIs and dehydration as described by serum osmolarity. In the present investigation, a condition of current dehydration was found to be significantly associated with 2+PI in bivariate analyses, but this association was not confirmed after adjustment for other relevant risk factors. It should be noted that, while serum osmolarity precisely reflects intracellular dehydration and is a good marker for assessing acute changes in hydration, it is less representative of chronic hydration status, since it constantly changes and therefore only describes the patient's current condition, not what has been present over time (Baron et al., 2015). Therefore, the issue of exclusively using serum osmolarity to assess hydration status in the setting of a PI without any clinical signs or symptoms of dehydration needs to be addressed in future studies.

The association of PI occurrence and clinical instability was previously reported, in particular as having an association with low perfusion (Black et al., 2011; Kirkland-Kyhn et al., 2017). The novelty of our finding is the confirmation of this association by using a comprehensive score (MEWS) to describe clinical instability, taking into account neurological, cardiovascular and respiratory parameters. Patients with PIs often present a systemic inflammatory response similar to that observed in the presence of acute infectious conditions (Cordeiro et al., 2005). Multifactorial anaemia due to either chronic inflammation associated with PI or nutritional deficiencies can be a concomitant finding that is heavily implicated in impaired PI wound-healing. Our findings are in agreement with previous data in the literature obtained in different populations that demonstrated the role of tissue ischaemia on PI development and recovery (Aloweni et al., 2019; Jaul et al., 2018).

6.1 | Limitations

This study has some limitations that must be taken into account when considering the results. The observational and retrospective design exposes the risk of bias, thereby requiring particular caution when considering the reported associations between predictors and outcome as causal. However, although in clinical research causality should be demonstrated by randomised controlled trials, causal inferences may be suggested also from observational study designs, provided they are taken into account relevant potential confounders, in the planning of the study and in data analysis, as well as in the interpretation of study findings (Gianicolo et al., 2020). In the present investigation, the impact of PIs staging on mortality risk was tested through Cox regression analysis taking into account several relevant confounders. Nonetheless, these associations should be explored more in-depth, taking the care received by the patients during their hospital stay into account. Finally, the study was conducted in a single hospital centre, which implies that facility-specific factors (e.g. available staff resources, local clinical pathways and organisational issues) may have influenced patient outcomes. These facts limit the external validity of our results, which should be generalised with caution.

7 | CONCLUSIONS

A high prevalence of CAPI was found in a large population of medical patients acutely admitted to the hospital. After adjusting for

other relevant conditions describing the patients' multidimensional complexity, the presence and staging of CAPI were found as strong independent predictors of early-to-late mortality. Despite a limited prevalence, the presence of stage-4 or unstageable PIs was associated to a more than doubled risk-of-death. However, an independent association with an increased risk-of-death was also demonstrated for stage-1 PIs. Moreover, CAPIs were associated with a progressive increasing in expenditures for the National Health System consistent with the worsening PI stage.

Further prospective studies are needed to explore the hospital pathway of patients who are admitted with pre-existing PIs in order to identify the impact of hospital care on relevant outcomes.

8 | RELEVANCE TO CLINICAL PRACTICE

In patients who are acutely admitted to Internal Medicine departments, the presence and staging of PIs at the time of hospital admission should be interpreted as a marker of frailty and increased vulnerability, and as a predictor of higher DRGw and, thus, of higher hospital costs. CAPI should be considered to be an independent predictor of mortality in strict dependence of the stage of the PI. In particular, the presence of stage-4 and especially of unstageable PIs should be considered to be red flags of the utmost importance because of the strong predictive power thereof on both short- and long-term risk-of-death.

A complete skin inspection at the time of hospital admission is therefore recommended to ensure prompt PI-detection in order to ensure appropriate interventions in the short-, medium- and long-term. Failing to document unstageable PIs may cause a delay in effective debridement, thereby leading to an inaccurate assessment and inaccuracy in determining the magnitude of tissue injury, thereby determining a potential negative impact on PI healing and affecting patient outcome.

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CONFLICT OF INTEREST

No conflict of interest has been declared by the authors.

AUTHORS' CONTRIBUTIONS

G. Sanson conceived the research; G. Sanson and M. Zanetti contributed to the study design; I. Barbin, D. De Matteis and I. Marzinotto contributed to the acquisition and analysis of the data; G. Sanson, I. Barbin and M. Zanetti contributed to the interpretation of the data; G. Sanson and M. Zanetti drafted the manuscript. All authors critically revised the manuscript, agree to be fully accountable for ensuring the integrity and accuracy of the work, and read and approved the final manuscript.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.