Heterogeneity hampers the identification of general pressure injury risk factors in intensive care populations: a predictive modelling analysis.

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Abstract

Objective: To determine risk factors for pressure injury in distinct intensive care subpopulations according to admission type (Medical; Surgical elective; Surgery emergency; Trauma/Burns).

Methodology/Design: Predictive modelling using generalised linear mixed models with backward elimination on prospectively gathered data of 13 044 adult intensive care patients.

Settings: 1110 intensive care units, 89 countries worldwide.

Main outcome measures: Pressure injury risk factors.

Results: A generalised linear mixed model including admission type outperformed a model without admission type (p=0.004). Admission type Trauma/Burns was not withheld in the model and excluded from further analyses. For the other three admission types (Medical, Surgical elective, and Surgical emergency), backward elimination resulted in distinct prediction models with 23, 17, and 16 predictors, respectively, and five common predictors only. The Area Under the Receiver Operating Curve was 0.79 for Medical admissions; and 0.88 for both the Surgical elective and Surgical emergency models.

Conclusions: Risk factors for pressure injury differ according to whether intensive care patients have been admitted for medical reasons, or elective or emergency surgery. Prediction models for pressure injury should target distinct subpopulations with differing pressure injury risk profiles. Type of intensive care admission is a simple and easily retrievable parameter to distinguish between such subgroups.

Keywords
Area Under Curve; Intensive Care Units; Patient Admission; Prediction model; Pressure injury; Pressure Ulcer; Risk Assessment; Risk Factors

Implications for Clinical Practice

- Intensive care unit patients constitute a highly heterogeneous population in which a “one size fits all” approach can lead to widely divergent results.
- Pressure injury risk factors in critically ill patients cannot be defined for a general, mixed intensive care population, but should be considered in distinct subgroups according to risk profiles.
- Pending a clear delineation of intensive care subpopulations, the type of admission to the intensive care unit can be used to help identifying the risk of pressure injury in critically ill patients.

Introduction

Pressure injuries are localised lesions of the skin and/or underlying tissues due to pressure or pressure combined with shear (National Pressure Injury Advisory Panel et al., 2019). They cause pain and disability, thereby negatively impacting the quality of life of affected patients (Gorecki et al., 2009), and have been associated with mortality (Labeau et al., 2021). By extending the length of hospital stay (Dealey et al., 2012, Demarre et al., 2015) and by the substantial additional treatment-related costs they require, pressure injuries are moreover a major economic burden for healthcare systems worldwide (Demarre et al., 2015, Guest et al., 2017, Nguyen et al., 2015).

As compared to general hospitalised populations, intensive care unit (ICU) patients are at significantly higher risk for pressure injury due to several predisposing factors, including inherently reduced mobility, debilitated condition, burdening comorbidities, effects of acute organ failure, and the multiple devices needed for their diagnosis and treatment (Cox, 2017, Coyer et al., 2017a, Lin et al., 2021, Soodmand et al., 2019, Tatucu-Babet and Ridley, 2021). As such, many risk factors for pressure injury in ICU patients are intrinsic, and therefore unmodifiable (Edsberg et al., 2014). It is therefore pivotal to target risk factors that are extrinsic and thereby modifiable to successfully prevent severe pressure injuries in the critically ill (Llaurado-Serra and Labeau, 2020, Powers et al., 2020).

The identification of specific risk factors is also crucial for the development of valid and reliable ICU-specific risk assessment scales, which are currently lacking (Zhang et al., 2021). Due to the considerable differences in clinical characteristics, treatment, and medical device use between ICU patients and the general hospitalised population, the risk assessment tools commonly used in general hospitalised populations underperform when applied to ICU patients (Ahtiala et al., 2016, Cho and

Noh, 2010, Hyun et al., 2013). Almost all have high sensitivity but low specificity when applied to critically ill patients, and are therefore not recommended to be used in the ICU (Alderden et al., 2018, Kottner and Dassen, 2010).

In recent years the number of studies dedicated to the identification of risk factors that are independently associated with pressure injury in ICU patients has increased, but yielded differing results (Cox et al., 2020, Sala et al., 2021, Wenzel and Whitaker, 2021). While this disparity in findings may be due to diverging definitions and measurements, the considerable heterogeneity of the ICU population may be among the causes with largest impact. Many studies investigating risk factors have targeted the general ICU population (Alderden et al., 2017, Cox et al., 2020, Sala et al., 2021), but risk factors may differ among distinct types of ICU subpopulations due to differing patient profiles (Deschepper et al., 2021). As an example, the characteristics of ICU patients admitted for elective cardiac surgery may differ substantially from those of medical patients admitted due to exacerbation of chronic obstructive pulmonary disease, which in turn may differ from patients admitted with multiple trauma or burns. To distinguish between subpopulations, the type of ICU admission might be an appropriate parameter.

We hypothesised that the risk of pressure injury development will differ according to whether patients have been admitted to the ICU due to medical conditions, for elective surgery, emergency surgery, or due to trauma / burns; and that distinct subpopulation-specific risk factors may thus enhance predicting the risk of pressure injury.

Methods

Study design and data collection

For this risk prediction modelling study, we used prospectively gathered data from the DecubICUs database. DecubICUs was a prospective, observational, cross-sectional, one-day point-prevalence study on pressure injuries in adult (≥ 18 years) ICU patients with follow-up for outcome assessment (length of ICU and hospital stay, and survival status) until hospital discharge (maximum 12 weeks). Data were collected on 15 May 2018 (Labeau et al., 2021). The study was registered at ClinicalTrials.gov (NCT03270345).

Data management

All variables regarding patient admission to the ICU available from the dataset were considered for inclusion in our analyses on the basis of their empirical support in the literature as pressure injury risk factors, and of their clinical relevance. After exclusion of variables identified as highly correlated by multicollinearity testing, 42 potential predictors of pressure injury were identified: Country, Days in ICU before study day, Age, BMI indicating normal weight, BMI indicating obesity, BMI indicating underweight, BMI indicating pre-obesity, Admission type medical, Admission type elective surgery, Admission type emergency surgery, Admission types trauma and burns, Malignancy, Minimal heart rate, Minimal body temperature, Maximal body temperature, Minimal mean arterial pressure, Maximal lactate, Minimal leukocytes, Maximal leukocytes, Minimal platelets, Minimal potassium, Maximal potassium, Minimal sodium, Maximal sodium, Bilirubin, Sex, Chronic Obstructive Pulmonary Disease, Acquired Immune Deficiency Syndrome, Heart failure, Peripheral vascular disease, Renal failure, Diabetes, Cirrhosis, Immunocompromised, Vasopressor use, Mechanical ventilation on study day, Renal replacement, Pressure injury on ICU admission, Braden moisture score, Braden mobility score, Braden friction and shear score, Braden activity score, Braden sensory perception score, and Braden nutrition status score. All cases with missing values for any of these variables were excluded from further analyses.

The dichotomous variable ‘Pressure Injury on admission’ was defined as presence of at least one pressure injury of all Stages on ICU admission, i.e. Stage I (nonblanchable erythema), Stage II (partial thickness skin loss), Stage III (full thickness skin loss), Stage IV (full thickness tissue loss), Unstageable, or Suspected Deep Tissue Injury (National Pressure Injury Advisory Panel et al., 2019). We categorised the variables ‘Age’ and ‘Days in ICU before study day’ to enhance insight in intervals where a potential association with pressure injury might change or break. Age categorisation was adapted from a risk prediction development study for general hospitalised patients (Perneger et al., 2002) into 18-49 years, 50-59 years, 60-69 years, 70-79 years, or ≥80 years. ICU length of stay was categorised into 0-1 days, 2-4 days, 5-12 days, or ≥12 days by relying on the Critical Care Statistics of the Society of Critical Care Medicine (Society of Critical Care Medicine, s.d.).

‘Admission type’ was either Medical, or Surgical Elective, or Surgical Emergency, or Trauma / Burns. For analysis and interpretation purposes, a separate dichotomous variable was created for each admission type.

Statistical Analysis

Admission type as important risk factor

We used generalised linear mixed models analysis to predict the occurrence of a pressure injury acquired in the ICU, of all Stages, with the variable ‘Country’ as random effect. We calculated the Akaike Information Criterium (AIC) and used analysis of variance (ANOVA) to test the difference between models with and without 'Admission type'.

Backward elimination to simplify and optimise the models

For each Admission type a separate model was fit. To simplify the models and optimise their performance, we used feature selection with backward elimination on the basis of the Area Under the Receiver Operating Curve (AUC). The AUC was calculated on a test set (1/5th of the dataset) and the models were trained on a training set (4/5th of the data). The backward elimination process consisted of two major steps. First, for each of the three models (patients with admission types Medical, Surgical Emergency, or Surgical Elective) the variables were ranked according to their predictive value by removing alternately each predictor from the model. Subsequently, the variables with the least predictive value were removed from the model one by one until this no longer resulted in an improvement in AUC. These two steps were repeated for all three models as long as they resulted in improving the respective final AUCs.

Statistical analysis was performed using R statistical software 3.6.1. (R_Core_Team, 2017). Prevalence data are reported as percentage (95% confidence interval [CI]).

Ethical approval

The DecubICUs data was collected after approval by established national, regional or local ethics committees and/or institutional review boards (Labeau et al., 2021).

Results

The complete DecubICUs database included 13 254 patients residing in 1117 ICUs (90 countries – 6 continents). After removing all cases with missing values for any of the 42 potential predictors, the final dataset consisted of 13 044 patient records from 89 countries (1110 ICUs): 6375 patients admitted to the ICU for medical reasons (48.9%); 2570 for emergency surgery (19.7%); 2944 following elective surgical procedures (22.6%); and 1155 patients admitted for trauma / burns (8.8%).

Admission type as important risk factor

Overall prevalence of ICU-acquired pressure injury (all stages) in the study cohort was 16.18% (95% CI 15.56 –16.82) (Labeau et al., 2021). The prevalence of pressure injuries according to admission type was 17.4% (95% CI 16.24 – 18.08) for patients with Medical admission; 9.67% (95% CI 8.66 – 10.78) for Surgical-elective admission; 20.01% (95% CI 18.52 – 21.59) for Surgical-emergency admission; and 19% (95% CI 16.80 – 21.30) for patients admitted for Trauma / Burns.

Generalised linear mixed models including versus not including patients' type of admission to the ICU differed significantly (p=0.004; Table 1). The lower AIC for the model including the admission types highlights its higher performance. Both models are described in detail in Supplementary material_1.

Table 1. Results of the ANOVA on the generalised linear mixed models per Admission type (full dataset)

	Number of variables	AIC	Chi-square	p
Mixed model without Admission types	56	8745		
Mixed model with Admission types	59	8738	13.51	0.0037

Legend: AIC, Akaike Information Criterium

Admission type 'Trauma / Burns' was not withheld in the generalised mixed model (Supplementary material_1) and therefore excluded from further analyses.

Backward elimination to simplify and optimise the model

Backward elimination performed on the three remaining subsamples (i.e., patients with admission types Medical, Surgical Emergency, or Surgical Elective) both simplified the models and improved all respective AUCs (Table 2), with larger improvements for the two surgical subsamples.

Table 2. Results of the backward elimination on AUC and number of predictors in the models

Admission type	Number of predictors at onset	Number of predictors in the best model	AUC at onset	AUC best model	Number of Backward elimination rounds
Medical	38	23	0.7856	0.7927	9
Surgical Elective	38	17	0.8561	0.8797	10
Surgical Emergency	38	16	0.8489	0.8760	6

AUC: Area Under the Receiver Operating Curve

The effects (odd ratio’s) and significance levels for all variables in all three models are shown in Table 3. The AUCs resulting from each step of the backward elimination are in Supplementary material_2. While the three distinct models contain 23, 17 and 16 predictors, they only have five predictors in common (length of ICU stay before the study day, maximal lactate levels, diabetes, male sex, and body mass index indicating underweight, Table 3), thereby illustrating that the set of predictors defining a risk profile for pressure injury development during the ICU course highly depends on the type of ICU admission.

Table 3. Three distinct models of predictors of pressure injury according to admission type

	Medical admission		**Surgical Elective admission**		**Surgical Emergency admission**	
Predictor	**Odds Ratio [Confidence interval]**	**p**	**Odds Ratio [Confidence interval]**	**p**	**Odds Ratio [Confidence interval]**	**p**
Length of ICU stay before study day						
0-1 days	*Reference*		*Reference*		*Reference*	
2-4 days	1.71 [1.22 - 2.40]	0.0017	2.49 [1.33 - 4.68]	0.0045	1.89 [1.16 - 3.07]	0.0108
5-12 days	3.88 [2.88 - 5.22]	<0.0001	5.00 [2.96 - 8.45]	<0.0001	4.17 [2.70 - 6.42]	<0.0001
≥12 days	7.78 [5.78 - 10.46]	<0.0001	16.94 [10.26 - 27.96]	<0.0001	7.79 [5.10 - 11.91]	<0.0001
Male sex	1.18 [0.99 - 1.40]	0.0684	1.40 [0.98 - 1.99]	0.0611	1.20 [0.92 - 1.56]	0.1871
Age						

18-49 years					*Reference*	
50-59 years					1.43 [0.95 - 2.15]	0.0852
60-69 years					1.37 [0.93 - 2.01]	0.1123
70-79 years					1.78 [1.19 - 2.66]	0.0052
≥80 years					1.37 [0.85 - 2.20]	0.1963
BMI underweight	1.41 [0.99 - 2.03]	0.0590	1.69 [0.76 - 3.73]	0.1975	1.77 [0.96 - 3.27]	0.0658
BMI pre-obesity	1.07 [0.89 - 1.28]	0.4969	0.98 [0.68 - 1.39]	0.8900		
Minimal mean arterial pressure					0.99 [0.99 - 1.00]	0.1836
Minimal heart rate	1.00 [1.00 - 1.01]	0.3299			1.01 [1.00 - 1.02]	0.0594
Minimal body temperature	0.88 [0.78 - 1.00]	0.0453			1.21 [1.01 - 1.46]	0.0429
Maximal body temperature	1.14 [1.01 - 1.29]	0.0343				
Maximal lactate	0.98 [0.93 - 1.03]	0.3876	0.89 [0.81 - 0.99]	0.0261	0.95 [0.87 - 1.03]	0.2033
Minimal leukocytes	1.00 [0.98 - 1.01]	0.7047			0.99 [0.97 - 1.01]	0.4431
Minimal potassium	0.94 [0.81 - 1.08]	0.3860	0.92 [0.67 - 1.27]	0.6093		
Minimal sodium			0.98 [0.94 - 1.03]	0.3898	0.97 [0.94 - 1.01]	0.0978
Maximal sodium			1.03 [0.98 - 1.08]	0.2104	1.04 [1.00 - 1.07]	0.0433
Heart failure			1.49 [0.97 - 2.30]	0.0715	1.05 [0.72 - 1.55]	0.7840
Renal failure			1.07 [0.64 - 1.76]	0.8042		
Acquired Immune Deficiency Syndrome	2.10 [0.80 - 5.48]	0.1302	0.62 [0.04 - 10.19]	0.7404		
Peripheral vascular disease	1.19 [0.84 - 1.68]	0.3343				
Diabetes	1.02 [0.84 - 1.24]	0.8313	1.26 [0.84 - 1.90]	0.2662	1.06 [0.77 - 1.45]	0.7135
Cirrhosis	0.93 [0.58 - 1.47]	0.7468				
Immunocompromised	1.08 [0.82 - 1.42]	0.6038	1.76 [0.98 - 3.16]	0.0602		
Mechanical ventilation on study day	1.64 [1.34 - 2.01]	<0.0001				
Renal replacement	1.47 [1.17 - 1.84]	0.0011	1.67 [0.99 - 2.80]	0.0532		
Braden moisture score						
Mild risk (15-18)	*Reference*				*Reference*	
Moderate risk (13-14)	1.15 [0.80 - 1.66]	0.4513			1.11 [0.66 - 1.87]	0.6880
High risk (10-12)	0.98 [0.70 - 1.38]	0.9164			0.67 [0.42 - 1.07]	0.0944
Very high risk (≤9)	0.70 [0.49 - 1.02]	0.0610			0.53 [0.32 - 0.88]	0.0142
Braden friction and shear score						
Mild risk (15-18)	*Reference*		*Reference*			
Moderate risk (13-14)	0.67 [0.55 - 0.82]	0.0001	0.56 [0.37 - 0.83]	0.0044		
High risk (10-12)	0.52 [0.39 - 0.70]	<0.0001	0.41 [0.23 - 0.73]	0.0026		
Braden activity score						
Mild risk (15-18)	*Reference*		Reference			
Moderate risk (13-14)	0.79 [0.60 - 1.04]	0.0962	1.03 [0.62 - 1.72]	0.9094		
High risk (10-12)	0.49 [0.29 - 0.82]	0.0070	0.42 [0.17 - 1.06]	0.0655		
Very high risk (≤9)	0.30 [0.12 - 0.78]	0.0135	0.46 [0.06 - 3.80]	0.4731		
Braden sensory perception score						
Mild risk (15-18)	*Reference*					
Moderate risk (13-14)	0.83 [0.66 - 1.06]	0.1348				
High risk (10-12)	0.98 [0.77 - 1.26]	0.8781				

Very high risk (≤9)	0.67 [0.50 - 0.90]	0.0075				
Braden nutrition status score						
Mild risk (15-18)	*Reference*				*Reference*	
Moderate risk (13-14)	0.96 [0.72 - 1.28]	0.7781			0.79 [0.54 - 1.16]	0.2287
High risk (10-12)	0.90 [0.67 - 1.20]	0.4586			0.85 [0.58 - 1.25]	0.4120
Very high risk (≤9)	1.25 [0.73 - 2.12]	0.4125			0.27 [0.09 - 0.87]	0.0282
Braden mobility score						
Mild risk (15-18)			*Reference*		*Reference*	
Moderate risk (13-14)			0.48 [0.32 - 0.73]	0.0006	0.77 [0.57 - 1.04]	0.0891
High risk (10-12)			0.44 [0.26 - 0.76]	0.0034	0.63 [0.43 - 0.91]	0.0153
Very high risk (≤9)			0.26 [0.09 - 0.73]	0.0103	0.39 [0.18 - 0.86]	0.0199
Pressure injury on ICU admission	0.32 [0.25 - 0.42]	<0.0001				

Legend: ICU, intensive care unit; BMI, body mass index

In each of the three separate models, ICU length of stay before the study day has a large, gradually increasing, effect, with the largest effect in the model for patients admitted to the ICU following elective surgery. In the model for patients with medical admission, entering the ICU with a pressure injury that had previously developed was shown to protect against developing new pressure injuries in the ICU (OR 0.32, 95% CI 0.25 – 0.42; p<0.0001). There is no uniform effect of the various components of the Braden scale.

Discussion

We found clear differences in pressure injury risk factors depending on whether patients were admitted to the ICU for medical reasons, after elective surgery, or after emergency surgery, with different effect sizes and significance levels for identical predictors among these three groups. Common risk factors identified for patients of all three admission types were length of ICU stay, maximal lactate levels, diabetes, male sex, and a body mass index indicating underweight. From our data, patients admitted for trauma or burns showed to be an ill-defined subpopulation with a divergent set of predictors. The latter may be due to the relatively small number of trauma / burns patients in our dataset (n=1155; 8.8%) as well as to the fact that trauma / burns patients constitute a very heterogeneous ICU population.

Length of ICU before the study day was shown to have a large effect in all three models, thus reinforcing previous findings which identified duration of ICU stay before pressure injury development as risk factor for pressure injury (Alderden et al., 2020, Labeau et al., 2021, Lima Serrano et al., 2017, Schuurman et al., 2009). ~~For the medical population, presence of a pressure injury on ICU admission was found to be a protective factor against developing ICU-acquired pressure injury~~ Being admitted to the ICU with a pressure injury that had previously developed, appeared to protect medical patients from developing new pressure injuries in the ICU (OR 0.32, 95% CI 0.25 – 0.42; p<0.0001). This finding may be associated with the use of additional preventive measures and heightened awareness among ICU nurses upon admittance of patients who already have developed pressure injury pre-ICU admission. For the impact of the various Braden score components, no clear, unambiguous pattern was identified. While, for example, the friction and shear score was shown to have an important effect in the models for the medical and surgical elective patients, it was not retained in the model for those admitted to the ICU following emergency surgery. This finding supports earlier claims against the undifferentiated use of the Braden scale in critically ill patients (Chen et al., 2017, Han et al., 2018, Kottner and Dassen, 2010, Lima-Serrano et al., 2018).

Various pressure injury prediction models for critically ill patients were recently developed using different methodological approaches (Alderden et al., 2020, Alderden et al., 2018, Hyun et al., 2014, Ladios-Martin et al., 2020). In spite of a few common findings, they primarily show considerable differences in risk factors identified. Noteworthy in this regard is that the data used to build these models were from different ICU populations. Alderden and colleagues (Alderden et al., 2020, Alderden et al., 2018) used data from critical care patients admitted to a surgical or a cardiovascular surgical ICU, whereas Hyun et al. (2014) and Ladios-Martin et al. (2020) included general, mixed ICU populations. The differences in risk factors identified by these prediction models support our hypothesis that differentiating between ICU subpopulations is key to all research aiming at determining pressure injury risk factors in critically ill patients. This is also clearly reflected in the models resulting from our study, which found five common predictors for pressure injury only in medical, surgical elective, and surgery emergency ICU patients. While staffing levels, local protocols, availability and use of preventive measures, and differences in quality of care may contribute to these differences, our findings suggest that distinct ICU subpopulations have different risk factors for developing pressure injury.

Critically ill patients constitute a considerably diverse population, with high rates of multimorbidity and substantial differences in risk profiles and outcomes. There is a growing consensus that in the ICU a “one size fits all” approach can lead to widely divergent results (Maslove et al., 2017, Vincent, 2010). Recently, machine learning approaches (clustering analysis) have been used to try to unravel the heterogeneity of ICU populations (Geri et al., 2019, Vranas et al., 2017), but efforts to increase the interpretability of these findings are crucial before they can inform practice (Castela Forte et al., 2019). Meanwhile, patients' type of ICU admission, which has also been integrated in other predictive scoring systems used in critically ill patients (Le Gall et al., 1993, Lemeshow et al., 1993), is a simple and easily retrievable parameter researchers can use to distinguish ICU subpopulations.

Recently, it has been shown that pressure injury prediction models resulting from advanced machine learning approaches do not outperform models generated by classical statistical regression techniques (Ladios-Martin et al., 2020). Therefore, the current study combined statistical techniques with some best practices from the machine learning community to calculate the AUC performance measure. Regression techniques moreover offer the advantage that they provide clear insights into the generated model by providing effect sizes and significance levels, whereas machine learning techniques result in a list of predictors impacting on the model only (Shmueli, 2010). The backward elimination procedure enhanced the models' performance in terms of prediction, although only slightly. More importantly, however, it also considerably limited the number of predictors, resulting in models that can easily be used in clinical practice. Ideally, they are implemented in electronic health records systems that generate an early warning signal at the time the patient is admitted to the ICU or at any other time during the ICU stay.

The major strength of this study is that it is the first of which the results explicitly suggest that investing in further research into risk factors for pressure injury in general, mixed ICU populations should be avoided, and that specific subpopulations should be targeted. Moreover, the dataset used to calculate the models is, to our best knowledge, to date the largest dataset collected regarding pressure injuries and associated factors in critically ill patients worldwide. On the other hand, the study is based on point-prevalence data with inherent limitations associated with such study designs (Dale et al., 2021, Labeau et al., 2021, Labeau and Blot, 2021). A possible comment may be that for this analysis all pressure injury stages, Stage I included, were pooled. In previous reports Stage I pressure injuries were not considered as they are easily overlooked during skin assessment, and because they are considered reversible on the short term (Coyer et al., 2017b, Llaurado-Serra and Afonso, 2018). However, Labeau et al. demonstrated that – in the context of critical illness – even Stage I pressure injuries are independently associated with increased risk of mortality, thereby justifying their pooling with more severe pressure injuries (Labeau et al., 2021).

Conclusions

In critically ill patients, risk factors for pressure injury differ according to whether they have been admitted for medical reasons, or following elective surgery, or for emergency surgery. We recommend not to build prediction models for pressure injury on data from the general, considerably heterogeneous ICU population, but to target distinct subpopulations with differing pressure injury risk profiles. Type of admission to the ICU is a simple and easily retrievable parameter to distinguish between such subgroups.

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Conflicts of Interest

SB received grants or honoraria outside the submitted work from Pfizer and 3M.

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