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Epidemiology and outcome of pressure injuries in critically ill patients with chronic obstructive pulmonary disease: A propensity score adjusted analysis ☆,☆☆

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ABSTRACT

Background: Pressure injuries are a frequent complication in intensive care unit (ICU) patients, especially in those with comorbid conditions such as chronic obstructive pulmonary disease (COPD). Yet no epidemiological data on pressure injuries in critically ill COPD patients are available.
Objective: To assess the prevalence of ICU-acquired pressure injuries in critically ill COPD patients and to investigate associations between COPD status, presence of ICU-acquired pressure injury, and mortality.
Study design and methods: This is a secondary analysis of prospectively collected data from *DecubICUs*, a multinational one-day point-prevalence study of pressure injuries in adult ICU patients. We generated a propensity score summarizing risk for COPD and ICU-acquired pressure injury. The propensity score was used as matching criterion (1:1-ratio) to assess the proportion of ICU-acquired pressure injury attributable to COPD. The propensity score was then used in regression modeling assessing the association

☆ **Clinical Trial Registration:** DecubICUs was registered at ClinicalTrials.gov (NCT03270345).
☆☆ **Tweet:** #ICU patients with #COPD have significantly higher risk pressure injury; those that develop pressure injury are at higher risk of mortality

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of COPD with risk of ICU-acquired pressure injury, and examining variables associated with mortality (Cox proportional-hazard regression).
Results: Of the 13,254 patients recruited to *DecubICUs*, 1663 (12.5%) had documented COPD. ICU-acquired pressure injury prevalence was higher in COPD patients: 22.1% (95% confidence interval [CI] 20.2 to 24.2) vs. 15.3% (95% CI 14.7 to 16.0). COPD was independently associated with developing ICU-acquired pressure injury (odds ratio 1.40, 95% CI 1.23 to 1.61); the proportion attributable to COPD was 6.4% (95% CI 5.2 to 7.6). Compared with non-COPD patients without pressure injury, mortality was no different among patients without COPD but with pressure injury (hazard ratio [HR] 1.07, 95% CI 0.97 to 1.17) or COPD patients without pressure injury (HR 1.13, 95% CI 1.00 to 1.27). Mortality was higher among COPD patients with pressure injury (HR 1.35, 95% CI 1.15 to 1.58).
Conclusion and implications: Critically ill COPD patients have a statistically significant higher risk of pressure injury. Moreover, those that develop pressure injury are at higher risk of mortality. As such, pressure injury may serve as a surrogate for poor prognostic status to help clinicians identify patients at high risk of death. Also, delivery of interventions to prevent pressure injury are paramount in critically ill COPD patients. Further studies should determine if early intervention in critically ill COPD patients can modify development of pressure injury and improve prognosis.

What is already known

- Chronic obstructive pulmonary disease (COPD) is a condition that frequently leads to intensive care unit (ICU) admission and is characterized by multi-morbidity including hormonal, metabolic and musculoskeletal derangements.
- ICU patients are at high risk of pressure injuries because of their severity of acute illness and often debilitated physical condition.
- No epidemiological data on pressure injuries in ICU patients with COPD are reported.

What this paper adds

- COPD constitutes an important risk factor for ICU-acquired pressure injuries.
- ICU patients with COPD who developed ICU-acquired pressure injuries are at an increased risk of death.

1. Introduction

Pressure injuries are localised lesions to the skin and/or underlying tissues caused by mechanical stress (pressure or pressure combined with shear) (National Pressure Ulcer Advisory Panel, 2019). They usually occur at bony prominences such as the heels or sacral region but can develop anywhere on the body. Intensive care unit (ICU) patients have a higher prevalence of pressure injury compared to other hospitalised patients (Coyer et al., 2017). A systematic review and meta-analysis reported the upper and lower 95% confidence intervals (CI) of the cumulative incidence were 9.4 to 27.5% (Chaboyer et al., 2018) in studies using skin inspection (gold standard) to identify pressure injury in the ICU. Pressure injuries occur in ICU patients due to multiple comorbidities, acute clinical conditions, and ICU treatments (Labeau et al., 2021; Sala et al., 2021; Lin et al., 2021). Pressure injury more frequently affects those with acute organ derangements such as cardiovascular instability requiring vasopressor agents and acute respiratory failure requiring invasive mechanical ventilation and sedation, analgesia, and/or neuromuscular blockade agents (Nedergaard et al., 2018). Critical illness also threatens skin integrity by systemic inflammation and associated catabolic processes triggering muscle wasting and weight loss. Presence of underlying chronic disease associated with immobility, tissue ischemia, and malnutrition also increases the risk of pressure injury (Jaul et al., 2018). In the context of critical illness, the occurrence rate of pressure injury is strongly associated with case-mix and particular risk profiles thereby compromising the predictive value of risk scores (Deschepper et al., 2021a, 2021b; Zhang et al., 2021).

Chronic obstructive pulmonary disease (COPD) is amongst the most common comorbid conditions of patients admitted to the ICU (Akkutuk et al., 2014) with the proportion ranging from 10 to 25% depending on local case-mix (Schmidt et al., 2014; Funk et al., 2013). COPD is a chronic inflammatory lung disease which is considered a systemic disease (Agusti and Soriano, 2008). Multimorbidity including hormonal, metabolic and musculoskeletal derangements are common (Machado et al., 2021; Laghi et al., 2009; Ishikawa et al., 2021). In the context of critical illness, COPD represents an independent risk factor for unfavorable outcomes including increased length of ICU stay, prolonged ventilator weaning, muscle wasting and interrupted skin integrity (Majewski et al., 2017), ICU readmission, and death (Funk et al., 2013; Rouze et al., 2020; Koulenti et al., 2015). As such, the typical COPD patient profile is characterized by a progressively debilitated physical condition reflecting a risk for pressure injury.

For that reason, we hypothesized that critically ill patients with COPD have an increased risk for developing pressure injury and that this may be associated with an increased risk of death. Our objectives were (i) to assess the prevalence of pressure injury in critically ill patients with COPD as a comorbidity or as a primary ICU admission diagnosis around the world, (ii) to investigate to what extent COPD constitutes an independent risk factor for pressure injury acquisition during ICU stay, (iii) to assess the proportion of pressure injury prevalence attributable to COPD, and (iv) to model relationships between COPD, ICU-acquired pressure injury, and hospital mortality.

2. Methods

2.1. Study design

We performed a secondary analysis of the DecubICUs study (NCT03270345), a multinational, prospective, observational one-day, point-prevalence study of pressure injury in adult ICU patients conducted in 1117 ICUs and 90 countries (Labeau et al., 2021). Data were collected anonymously on all patients aged ≥18 years present in a participating ICU from 0:00 to 23:59 on the study day (15 May 2018); there were no exclusion criteria. Patients were followed until hospital discharge (maximum of 12 weeks) to assess survival status. A detailed description of the study protocol and data handling are reported elsewhere (Labeau et al., 2021). Ethics approval was granted by ethics committees or institutional review boards at the hospital, regional or national level (Labeau et al., 2021).

2.2. Variables and definitions

Demographic and clinical data included ICU admission type, principal ICU admission diagnosis, mechanical ventilation on admission, and presence of pressure injury at time of ICU admission. Comorbidities, including COPD defined as Global Initiative for Chronic Lung Disease (GOLD) (Global Initiative for Chronic Obstructive Lung Disease Global Strategy for the Diagnosis, 2017) Stage ≥1, were documented from the medical record. Severity of acute illness on the point-prevalence day was assessed using physiological data including the Simplified Acute Physiology Score (SAPS) II (Gall, 1993). Pressure injury risk was evaluated using the Braden scale (Bergstrom et al., 1987).

Pressure injury overall and by body site was determined by direct observation using the international staging definitions, i.e. Stage I to IV, Unstageable, and Suspected Deep Tissue Injury (National Pressure Ulcer Advisory Panel, 2019). Data collectors recorded all pressure injuries. ICU-acquired pressure injuries were defined as those not present on ICU admission but present on the point prevalence day.

2.3. Statistical analysis

We used chi-square or Mann Whitney U tests for univariate comparisons of demographic and clinical characteristics and patient outcomes. Pressure injury prevalence was calculated as the proportion (95% CI) of the study cohort who had at least one pressure injury on the point prevalence day. ICU-acquired prevalence was calculated as the proportion who had at least one pressure injury identified as ICU acquired.

Adequate correction for confounding was pursued through propensity score adjustment. A propensity score is a versatile method to control for confounding and is particularly useful when the number of potential confounders is high (Fitzmaurice, 2006; Brookhart et al., 2006; Blot et al., 2007). The basic principle is to reduce this large number of confounding covariates to a single variable that summarizes all the relevant information about the confounders, i.e. the propensity score. We used logistic regression to generate a propensity score summarizing potential risk for COPD and risk for ICU-acquired pressure injury. The following covariates were considered for building the propensity score: country, World Bank economy status, ICU admission type, age, sex, body mass index, underlying comorbidities other than COPD (heart failure, peripheral vascular disease, renal failure, cirrhosis, malnutrition, diabetes, malignancy, and steroid therapy), Braden score, length of ICU stay before point prevalence day, and need for major organ support (i.e. mechanical ventilation at ICU admission, renal replacement therapy, and vasopressor use). These covariates were selected based on their relationship with pressure injury risk based of the DecubICUs database (Labeau et al., 2021), or alternatively, based on a plausible relationship with pressure injury risk (e.g. diabetes). No feature selection was applied given the relatively conservative number of predictors and the adequate dataset size that minimised the risk of overfitting. Patients with missing values were not included in the regression model.

Propensity score-adjustment was used in three ways. First, the propensity score was used to adjust for confounding in a logistic regression model that assessed the impact of COPD on the risk of ICU-acquired pressure injury on the total cohort. The relationship with ICU-acquired pressure injury (dependent variable) with the propensity score and COPD was reported with odds ratio (OR), 95% confidence interval (CI) and regression coefficient (B).

Second, the propensity score was used as the matching criterion in a matched cohort analysis to assess the proportion of ICU-acquired pressure injury attributable to COPD as underlying disease. In this matched cohort analysis (1:1 matching ratio) cases were designated as COPD patients and matched controls as non-COPD patients. For matching on the propensity score, a 1% deviation (± 0.01) was allowed creating matched pairs with a nearly identical risk of acquiring pressure injury during the ICU stay. In fact, concerning pressure injury risk, the only clinical difference between cases and matched controls is the presence, respectively absence, of COPD. This permitted calculation of the proportion of ICU-acquired pressure injury attributable to COPD by subtracting the crude pressure injury rate of controls from that of cases (WENZEL, 1988; Blot et al., 2003a, 2003b).

Third, propensity score adjustment was applied in a Cox proportional-hazard regression model to assess the relationship between COPD, ICU-acquired pressure injury, and hospital mortality at 12 weeks from study day. In this model, we examined mortality in four patient groups defined according to their COPD/pressure injury status: (i) non-COPD patients *without* ICU-acquired pressure injury (i.e. reference category); (ii) non-COPD patients *with* ICU-acquired pressure injury; (iii) COPD patients *without* ICU-acquired pressure injury; and (iv) COPD patients *with* ICU-acquired pressure injury. This model was executed on the total cohort (n = 13,254). Results of the model were reported as hazard ratios (HR) and 95% CI. In addition, based on these Cox regression outcomes, survival curves were created according to the Kaplan Meier method.

Observational studies are susceptible for potential unmeasured or uncontrolled confounding. For that reason, we calculated the E-value for our logistic and Cox proportional-hazard regression models using the VanderWeele & Ding approach (VanderWeele and Ding, 2017). The E-value is defined as the minimum strength of association, on the relative risk, odds ratio or hazard ratio scale, that an unmeasured confounder would need for both the independent covariate (e.g. COPD) and outcome variable (e.g. pressure injury) to fully explain away the association between risk factor and outcome. We calculated the E-value for both the observed association estimate (after adjustments for confounding) and the lower limit of the 95% CI.

3. Results

3.1. Study cohort and pressure injury prevalence

The DecubICUs cohort included 13,254 patients recruited from 1117 ICUs and 90 countries. Of these 13,254 patients, COPD was an underlying condition in 1663 (12.5%); 333 (20.0%) were admitted for acute COPD exacerbation. Compared to ICU patients without COPD, COPD patients were older, more commonly admitted for medical reasons, had higher severity of acute illness, and had more underlying conditions (Table 1). COPD patients had a longer ICU and hospital length of stay and increased in-hospital mortality (Table 2).

In COPD patients, the overall prevalence of pressure injury was higher than non-COPD patients (36.4% [95% CI 34.1 to 38.7] vs. 25.2% [95% CI 24.4 to 26.0]), as was the prevalence of ICU-acquired pressure injury (22.1% [95% CI 20.2 to 24.2] vs. 15.3% [95% CI 14.7–16.0]). Pressure injury prevalence of COPD patients was higher across all pressure injury severity stages (Table 2).

3.2. ICU-acquired pressure injury and body location

In the COPD-cohort (n = 1663), 710 ICU-acquired pressure injuries were identified in 368 COPD patients with 162 (44%) patients with more than one ICU-acquired pressure injury Fig. 1. shows frequencies and proportions of ICU-acquired pressure injuries at the affected body sites in COPD and non-COPD patients. In both COPD and non-COPD patients, the most common regions for pressure injury were the sacral region and the heels.

Table 1
Characteristics of ICU patients with or without chronic obstructive pulmonary disease (COPD).

		Non-COPD patients (n = 11,591)	COPD patients (n = 1663)	P
Demographics and admission data				
Economy*				<0.001
	Low- & lower-middle income economy	510 (4.4)	43 (2.6)	
	Upper-middle income economy	4410 (38.0)	536 (32.2)	
	High income economy	6671 (57.6)	1084 (65.2)	
Age, years		63 (49 – 73)	71 (63 – 79)	<0.001
Sex, male		7138 (61.6)	1046 (62.9)	0.308
Admission type				
	Medical	5429 (46.8)	1072 (64.5)	<0.001
	Surgical, elective	2713 (23;4)	265 (15.9)	<0.001
	Surgical, emergency	2347 (20.2)	262 (15.8)	<0.001
	Trauma & burns	1102 (9.5)	64 (3.8)	<0.001
Body Mass Index (BMI)				
	Underweight (BMI <18.5)	576 (5.0)	104 (6.3)	0.026
	Normal (BMI 18.5 – 24.9)	4693 (40.5)	594 (35.7)	<0.001
	Pre-obesity (BMI 25 – 29.9)	3936 (34.0)	484 (29.1)	<0.001
	Obesity (BMI ≥30)	2386 (20.6)	481 (28.9)	<0.001
Severity of acute illness				
Respiratory diagnosis leading to ICU admission		2069 (17.9)	743 (44.7)	<0.001
Acute exacerbation of chronic pulmonary disease** as admission diagnosis		180 (1.6)	333 (20.0)	<0.001
SAPS II score		32 (22 – 45)	37 (27 – 48)	<0.001
Mechanical ventilation at admission		6389 (55.3)	980 (59.0)	0.004
Vasopressor use		3010 (26.0)	472 (28.4)	0.040
Renal replacement therapy		1221 (10.6)	182 (11.0)	0.629
Sedation use		3550 (30.7)	538 (32.4)	0.167
Muscle relaxant use		467 (4.0)	76 (4.6)	0.307
Comorbidities				
AIDS		52 (0.4)	4 (0.2)	0.301
Heart failure		1344 (11.6)	408 (24.5)	<0.001
Impaired mobility		1407 (12.1)	273 (16.4)	<0.001
Peripheral vascular disease		514 (4.4)	148 (8.9)	<0.001
Renal failure		1176 (10.1)	240 (14.4)	<0.001
Diabetes mellitus		2408 (20.8)	434 (26.1)	<0.001
Malnutrition		538 (4.6)	113 (6.8)	<0.001
Cirrhosis		391 (3.4)	42 (2.5)	0.069
Malignancy (i.e., solid tumor, metastatic or hematologic cancer)		1315 (11.3)	194 (11.7)	0.700
Immunosuppressed status (i.e., chemotherapy, chronic steroid use, or other immunosuppressive agents)		831 (7.2)	137 (8.2)	0.117
Corticosteroid therapy		355 (3.1)	94 (5.7)	<0.001
Pressure injury risk (Braden scale categories)				0.079
No risk (19 – 23)		1443 (12.5)	192 (11.6)	
Mild risk (15 – 18)		3207 (27.8)	482 (29.1)	
Moderate risk (13 – 14)		2145 (18.6)	329 (19.9)	
High risk (10 – 12)		3430 (29.8)	498 (30.1)	
Very high risk (≤9)		1295 (11.2)	153 (9.3)	

ICU: intensive care unit. SAPS: Simplified Acute Physiology Score. AIDS: acquired immunodeficiency syndrome Data are reported as n (%) or median (interquartile range, 1st – 3rd quartile).

* Economy: categorised according to the 2016 World Bank classification (https://data.world bank.org/indic ator/SH.XPD.CHEX.GD.ZS).

** The database did not allow discriminating between acute exacerbations of COPD and other chronic pulmonary diseases. In non-COPD patients this may include patients with acute exacerbation for asthma, cystic fibrosis, … but not COPD. In COPD patients this may include acute exacerbation of COPD or other chronic pulmonary conditions.

3.3. Relationship between COPD and ICU-acquired pressure injuries

The propensity score ranged from 0.011 to 0.773 (very low to high-risk, respectively) for pressure injury acquisition in the ICU. Due to missing values, we were unable to generate a propensity score for 221 patients, including 22 with COPD. As a summary statistic representing all potential risk factors except COPD, the propensity score itself was strongly associated with ICU-acquired pressure injury risk (OR 635, 95% CI 406 to 995; B 6.46). Notwithstanding, after propensity score-adjustment, COPD remained positively associated with risk of an ICU-acquired pressure injury (OR 1.40, 95% CI 1.23 to 1.61; B 0.34). E-value calculation indicated that the observed OR of 1.40 could be explained away by an unmeasured confounder associated with both COPD and ICU-acquired pressure injury by an OR of 1.65 (lower limit 95% CI 1.46), but weaker confounding could not do so.

Of the 1663 COPD patients, we were able to match 1640 cases (23 patients not matched within a 1% deviation in propensity score). Prevalence of ICU-acquired pressure injury in cases and matched controls was 22.1% and 15.7%, respectively. As such, the proportion of ICU-acquired pressure injury attributable to COPD was 6.4% (95% CI 5.2% to 7.6%).

3.4. Hospital mortality

Unadjusted mortality rates for COPD and non-COPD patients are shown in Table 2 Table 3. shows the propensity score-adjusted Cox regression modeling reporting on the mortality risk relative of non-COPD patients *without* pressure injuries. Compared with this reference group, mortality was higher among COPD patients *with* pressure injury. E-value calculation indicated that the observed HR of 1.35 could be explained away by an unmeasured confounder

Table 2
Outcomes of ICU patients with or without chronic obstructive pulmonary disease (COPD).

Outcomes	Non-COPD patients(n = 11,591)	COPD patients(n = 1663)	p
Pressure injuries			
Overall	2921 (25.2)	605 (36.4)	<0.001
Pressure injury present at ICU admission	1144 (9.9)	237 (14.3)	<0.001
ICU-acquired	1777 (15.3)	368 (22.1)	<0.001
ICU-acquired pressure injuries			
Stage I ICU-acquired pressure injury	852 (7.4)	192 (11.5)	<0.001
Stage II ICU-acquired pressure injury	826 (7.1)	171 (10.3)	<0.001
Stage III ICU-acquired pressure injury	353 (3.0)	69 (4.1)	0.017
Stage III or higher* ICU-acquired pressure injury	613 (5.3)	123 (7.4)	<0.001
Stage IV ICU-acquired pressure injury	180 (1.6)	39 (2.3)	0.018
Unstageable ICU-acquired pressure injury	221 (1.9)	37 (2.2)	0.380
Suspected deep tissue injury	219 (1.9)	50 (3.0)	0.003
Length of stay and mortality			
Length of ICU stay, days	11 (4 – 27)	13 (5 – 33)	<0.001
Length of hospitalization, days	19 (9 – 40)	22 (11 – 42)	<0.001
In-hospital mortality	2465 (23.4)	464 (30.9)	<0.001

ICU: intensive care unit.
* includes Stage III, Stage IV, unstageable pressure injury, and suspected deep tissue injury.

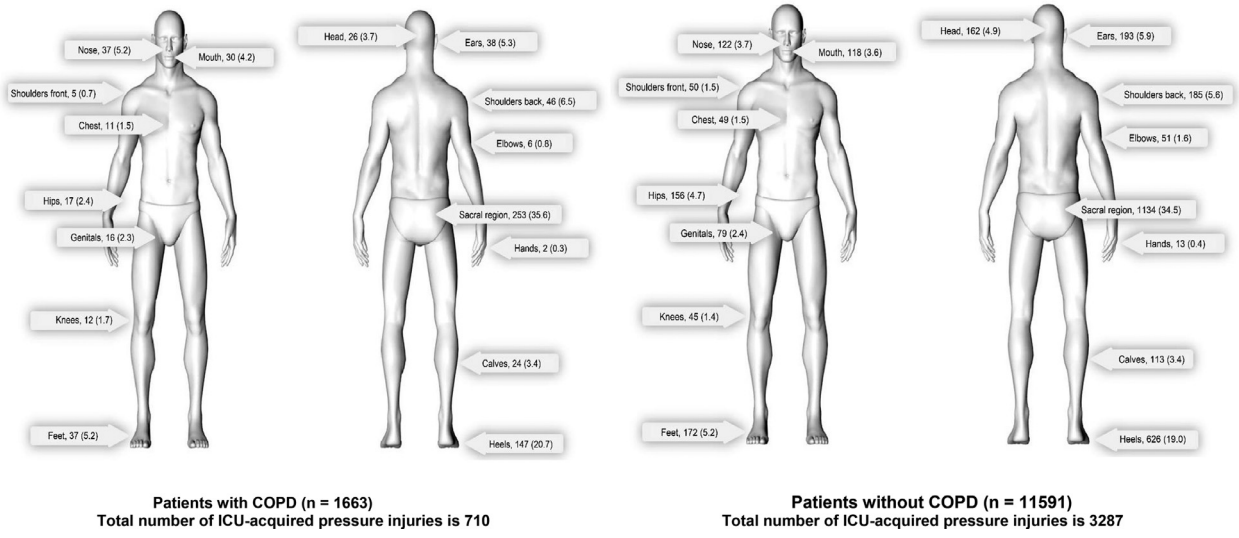

Fig. 1. Number (%) of ICU-acquired pressure injuries by body site in patients with and patients without chronic obstructive pulmonary disease (COPD).

Table 3
Propensity score-adjusted mortality risk according to chronic obstructive pulmonary disease (COPD) and pressure injury status.

Risk factor	Hazard ratio(95% confidence interval)	p
COPD and pressure injury status		
Non-COPD patient without pressure injury	Reference	–
Non-COPD patients with pressure injury	1.07 (0.97–1.17)	0.183
COPD patients without pressure injury	1.13 (1.00–1.27)	0.058
COPD patient with pressure injury	1.35 (1.15–1.58)	<0.001
Propensity score	17.1 (12.3–23.9)	<0.001

associated with both COPD plus ICU-acquired pressure injury and mortality by an HR of 2.1 (lower limit 95% CI 1.37), but weaker confounding could not do so. Compared with the reference group, mortality was not increased in non-COPD patients *with* pressure injury nor in COPD patients *without* pressure injury. Kaplan Meier survival curves are shown in Fig. 2.

4. Discussion

We performed this secondary analysis of data from the DecubICUs study, the largest epidemiological study of pressure injury in the ICU to date, to explore relationships between COPD, pressure injury, and mortality. We found the prevalence of overall pressure injury was higher in COPD patients, as was ICU-acquired pressure injury. Prevalence was higher across all pressure injury severity stages. COPD was an independent risk factor of developing ICU-acquired pressure injury with an attributable risk of 6.4%. Additionally, pressure injury in COPD patients was associated with increased risk of in-hospital mortality.

Despite pressure injury being associated with multiple other risk factors, we convincingly showed that a significant proportion of the pressure injury prevalence could be attributed to COPD. Our data indicate that COPD is more than a "lung disease" and that this chronic condition affects the body beyond respiratory function including an inherent high risk for pressure injury development in the ICU setting. Other studies identify COPD as a risk fac-

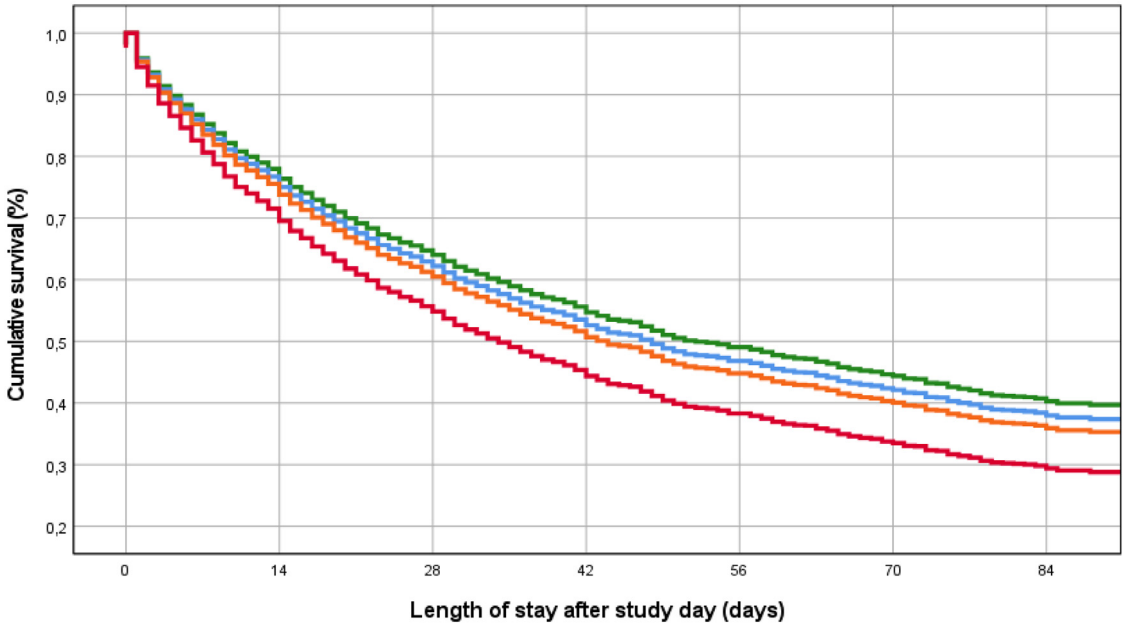

Fig. 2. Survival according to COPD and pressure injury status
Green line represent non-COPD patients without ICU-acquired pressure injuries; blue line represent non-COPD patients with ICU-acquired pressure injuries; orange line represents COPD patients without ICU-acquired pressure injuries; red line represents COPD patients with ICU-acquired pressure injuries.

tor for pressure injury in ICU patients. Hu et al. (2021). reported COPD to be associated with an increased risk of pressure injury at the sacral region (OR 3.2, 95% CI 1.3 to 8.0) with an association stronger than the Braden score and multiorgan dysfunction syndrome Argenti et al. (2021). also reported COPD to be associated with pressure injury risk in univariate analysis (OR 2.6, 95% CI 1.8 to 3.9) but these data were not further explored in multivariable analysis.

Reasons for the higher prevalence of pressure injury in COPD patients overall and ICU-acquired are likely multifactorial. Well-described risk factors for pressure injury are poor mobility, impaired skin perfusion, malnutrition, and an overall higher burden of underlying conditions, all of which are well-recognized features of COPD (National Pressure Ulcer Advisory Panel, 2019). In the COPDGene project (Maselli et al., 2019) commonly occurring comorbidities included chronic heart failure, osteoporosis, stroke, peripheral vascular disease, gastroesophageal reflux disease, coronary heart disease, hypertension, and stomach ulcers. In our study, more COPD than non-COPD patients had chronic heart failure, impaired mobility, peripheral vascular disease, chronic renal failure, diabetes mellitus, and malnutrition. COPD patients received more long-term corticosteroid therapy which causes skin thinning and atrophy contributing to pressure injury risk (Liu et al., 2013).

COPD patients in our cohort had higher severity of acute illness as evidenced by higher SAPS II scores on the day of the point-prevalence study and more organ support (mechanical ventilation and vasopressor use) than non-COPD patients. This reflects an overall high burden of illness severity predisposing pressure injury development. Critical illness is associated with a hypercatabolic state and resultant nutritional deficiency. Wenzel and Whitaker (2021) recently reported that the time to pressure injury development for patients who did not achieve nutritional goals was shorter compared to those achieving nutritional goals. These findings highlight the importance of nutritional state and pressure injury (Tatucu-Babet and Ridley, 2021). The combination of chronic conditions associated with COPD and severity of acute illness contribute to a patient phenotype explaining the higher pressure injury prevalence at the time of ICU admission as well as ICU-acquired pressure injury among COPD patients.

One hypothesis generating finding is that critically ill COPD patients with pressure injury had a higher mortality risk. Previously, we reported independent and gradually increasing risk of mortality with increasing severity of pressure injury (Labeau et al., 2021). As such, the acquisition of pressure injury during ICU stay may reflect a debilitated condition leading to an unfavorable outcome. The relationship between pressure injury and mortality was also demonstrated in a recently published study from Finland including over 6000 critically ill patients (Ahtiala et al., 2020). In the 1980s Kennedy reported pressure injury to be predictive of impending death in intermediate care facilities with 56% of those developing a pressure injury dying within six weeks (Kennedy, 1989; Ayello et al., 2019). To the best of our knowledge, such a time-dependent relationship has not been described in the context of critical illness. Due to its point-prevalence approach also our study could not assess such an association. However, COPD is an independent risk factor for ICU mortality in critically ill patients with VAP (Makris et al., 2011) and for in-hospital mortality after ICU discharge (Madotto et al., 2021).

Our study has important strengths such as the large sample size which provides a current and worldwide epidemiology of pressure injury in critically ill COPD patients. We used robust analysis methods to assess known risk factors independently associated with pressure injury including propensity score adjustment and matching.

Study limitations are those inherent to point-prevalence studies such as the absence of exposure time for some variables such as mechanical ventilation and vasopressor use. However, while incidence data are better suited to evaluate effectiveness of prevention measures, prevalence data support insights in resource requirements and their allocation (Baharestani et al., 2009). Data collectors recorded COPD, defined as GOLD stage $\geq$1, from the medical record. As such we were unable to perform sensitivity analyses according to COPD severity. The database also did not allow discriminating acute COPD exacerbations from acute exacerbation of other chronic pulmonary diseases. Because of our

cross-sectional design, pressure injury prevention strategies such as patient positioning were not included in our analyses. Data were collected on a single day, therefore we could not account for any preventative strategies used prior to this. Finally, the propensity score may be suboptimal as we were unable to include known risk factors for COPD and pressure injury, such as smoking status. Smoking has previously been shown to be a risk factor for pressure injury in ICU patients, probably due to morphological changes resulting in decreased microvascular function and consequent worsening of the skin's natural defense (Nassaji et al., 2014). Consequently, our study may be subject to unmeasured confounding. However, E-values indicate that potentially unmeasured confounders would need to provide robust associations to reduce the observed relationships to non-significant proportions. Future studies aiming to assess specific risk factors for pressure injury should use a study design that enables collection of cumulative incidence data with sufficient attention to disease-specific aspects, details on preventive measures, and other contextual influences of care delivery (Deschepper et al., 2021a, 2021b).

5. Conclusion

In conclusion, our study demonstrates critically ill COPD patients are at higher risk than non-COPD patients for pressure injury, and when they occur, pressure injury in COPD patients is an independent risk factor for mortality. As such, pressure injury may serve as a surrogate for poor prognostic status in COPD patients and may help clinicians identify patients at high risk of death. Also, delivery of interventions to prevent pressure injury are paramount in critically ill COPD patients. Further studies should determine if early intervention in critically ill COPD patients can modify development of pressure injury and improve prognosis.

CRediT authorship contribution statement

IML, SOL, LR and SIB prepared the first draft.

SOL, SIB and MD analysed the data.

GF managed study registrations and the online platform for data collection.

SJB, WC, AKK, and LS provided first internal reviewer feedback.

All authors provided data, developed models, reviewed results, provided guidance on methods, and reviewed the manuscript.

IML, LR, SOL, SIB and MD finalised the manuscript on the basis of comments from all authors.

All authors approved the final version.

SOL, SIB, and GF had full access to all the data in the study. SOL and SIB had final responsibility for the decision to submit for publication.

Declaration of Competing Interest

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All other authors: no competing financial interests

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