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## THE INFLUENCE OF VASOACTIVE DRUGS ON THE OCCURRENCE OF PRESSURE ULCERS IN THE SURGICAL INTENSIVE CARE UNIT

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### ABSTRACT

**Background:** A pressure ulcer (pressure injury) occurs when tissue loading and/or loading duration exceeds individual tissue tolerance. Risk factors for pressure ulcer development include mobility/activity limitations, skin condition, perfusion, circulation, oxygenation, moisture/microclimate, age, and diet. Patients in the intensive care unit (ICU) have additional risks for the development of pressure ulcers, such as the use of vasoactive drugs, prolonged treatment in the ICU, the presence of comorbidities (diabetes, cardiovascular diseases, hypotension), prolonged mechanical ventilation, hemodialysis and sedation, which confirms the complex nature of pressure ulcer development.

**The aim:** To examine the influence of vasoactive drugs on the incidence of pressure ulcers in the surgical intensive care unit.

**Subjects and methods:** The subjects were all patients with pressure ulcers treated in the surgical ICU, Clinic for Anesthesiology, Resuscitation, Intensive Care and Pain Therapy, University Hospital Center Zagreb over a 3-year period. All subjects were assessed for pressure ulcer risk using the Braden scale.

**Results:** The incidence of pressure ulcers was 5.7%, with no significant differences in gender or age. The most common risk factors included pressure, friction, traction, hypotension, and anemia. In most subjects, the pressure ulcer occurred in the ICU, formed in the sacrum, gluteal, and ischial regions, and was observed in stage II. Vasoactive drugs were used in all subjects. Noradrenaline was most commonly used.

**Conclusion:** Vasoactive drugs were used in all subjects, which indicates their association with decubitus. In future research, it is necessary to specify the dose, the time of application, to study each individual vasoactive drug, their synergistic effects, and to include all patients treated in the ICU, in order to examine the difference between patients with/without pressure ulcers with regard to the use of vasoactive drugs.

**Key words:** pressure ulcer, vasoactive drugs, Braden scale, intensive care unit.

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## INTRODUCTION

Pressure ulcers (pressure injuries) develop when tissue loading and/or duration of loading exceeds the individual tissue tolerance (1). The European Pressure Ulcer Advisory Panel (EPUAP) defines pressure ulcers as localized damage to the skin or subcutaneous tissue caused by pressure, shear or friction forces, or a combination thereof (2). Risk factors for pressure ulcer development include mobility/activity limitations, skin status, perfusion, circulation, oxygenation, humidity/microclimate, age and nutrition (1). Patients in the ICU have additional risks for pressure ulcer development, such as the use of vasoactive drugs, prolonged ICU treatment, the presence of comorbidities (diabetes, cardiovascular disease, hypotension), prolonged mechanical ventilation, haemodialysis and sedation, which confirms the complex nature of pressure ulcer development (3). Pressure ulcers, although preventable, today represent a significant problem for both the patient and his family (pain, longer hospitalization, reduced quality of life, economic costs), and for the healthcare system (need for greater resources – increased treatment costs). Globally (204 countries), the number of prevalent cases of pressure ulcers in 2019 was 0.85 million (4). Age-standardized prevalence rates were 11.3 per 100,000 population, and incidence was 41.8 per 100,000 population. The global prevalence rate of pressure ulcers increases with age, peaking in the age group 80 to 84 years for men and 85 to 89 years for women, with decreasing patterns in older age groups. In the last 30 years, global age-standardized incidence and prevalence rates have decreased (with significant regional

differences), although pressure ulcers still represent a significant global health problem (4). No consolidated data were found for the incidence and prevalence of pressure ulcers in Croatia; different studies have reported different incidence rates of pressure ulcers ranging from 0.4 to 38% (5). Huljev et al. report that the incidence of pressure ulcers in hospitalized patients reaches 38%, and in patients treated in the ICU 33% (6). According to another source, the incidence of pressure ulcers in seriously ill patients treated in the ICU ranges from 3.3% to 53.4%, with a prevalence ranging from 13.1% to 45.5% (7).

Knowledge of risk factors for pressure ulcer development enables the identification of patients at increased risk, which enables timely provision of preventive measures (8). A systematic review of articles in the Cochrane Library, CINAHL, MEDLINE and Embase databases, from January 2008 to September 2022, identified 37 risk factors for pressure ulcer development in hospitalized adult patients, among which the main risk factors were diabetes, length of surgery or length of stay in the ICU, use of vasoactive drugs and low hemoglobin levels. Other risk factors included: the presence of comorbidities (anemia, cancer, cardiovascular disease, diabetes, kidney disease, respiratory disease, and others), older age, increased body mass index, type of hospital admission, use of certain medications (sedatives, steroids, vasoactive drugs), low nutritional status, skin status, surgical factors (number of operations, duration of surgery), use of medical devices, mobility, presence of force, pressure, traction, pain, low blood pressure, and poor tissue oxygenation (9).

Patients admitted to the ICU are at higher risk for developing pressure ulcers compared to patients admitted to general hospital wards. Patients treated in the ICU have the highest rates of hospital-acquired pressure ulcers, which often develop due to the presence of serious illnesses, immobility, and medical interventions. They are associated with longer ICU stays and increased mortality (7). No single risk factor for developing pressure ulcers can explain the occurrence of pressure ulcers in the ICU. Multiple risk factors contribute to the development and progression of pressure ulcers, which are often life-threatening and worsen (14). Some studies support the use of vasoconstrictors as a potential risk factor, but a synthesis of the available evidence is incomplete. In a systematic review by Tang et al. on the effects of vasoconstrictors on pressure ulcer development, pressure ulcers occurred in 10.9% of the population receiving vasoconstrictors and in 3.5% of the population not receiving them (8). It was found that the use of vasoconstrictors increased the risk of pressure ulcers in intensive care patients by almost twofold. The aim of this study is to examine the influence of vasoactive drugs on the incidence of pressure ulcers in the surgical intensive care unit.

## SUBJECTS AND METHODS

### Procedures and participants

A cross-sectional study was conducted with historical data. The subjects were 191 patients with pressure ulcers treated in the ICU for surgical patients, at the Clinic for Anesthesiology, Resuscitation, Intensive Care and Pain Therapy of the Clinical Hospital Center Zagreb, over a three-year period, from January 1, 2021 to December

31, 2023. Data were collected from the BIS, and a retrospective data analysis was applied. Data were collected on gender, age, underlying medical diagnosis, presence of comorbidities, present exogenous and endogenous risk factors for pressure ulcer development, assessment of risk for pressure ulcer development, time of pressure ulcer onset, stage of pressure ulcer at first observation and discharge, pressure ulcer localization, use of vasoactive drugs, and pressure ulcer treatment. Data were collected during April 2024. Approval was obtained from the ethics committee of the University Hospital Center Zagreb for the purposes of this study.

### Statistical analysis

Descriptive statistics methods were used in data processing. Categorical data are presented as absolute and relative frequencies. Numerical data are presented as arithmetic mean and standard deviation. Differences or associations between categorical variables were tested using the Chi-square test, and when necessary, Fisher's exact test. All P values are two-sided, and the significance level was set at 0.05. Statistical analysis was performed using the MedCalc software system (version 14.12.0, Med Calc Software bvba, Ostend, Belgium).

## RESULTS

### Sample description

In the three-year period, 191 patients with pressure ulcers were treated in the surgical ICU. Table 1 shows the number of patients with pressure ulcers treated in the surgical ICU in the individual years observed. The fewest subjects with pressure ulcers were in 2021 (5.19%), and the most in 2023

(6.29%). The incidence in the three-year period was 5.7%.

**Table 1.** *Number of patients with pressure ulcers treated in the surgical ICU*

Year	Number (%) of respondents	
	Total number of treated	Patients with decubitus ulcers
2021.	1233	64 (5,19)
2022.	1007	57 (5,66)
2023.	1113	70 (6,29)
<b>Total</b>	3353	191 (5,70)

Table 2. shows the gender and age of the respondents. There were no statistically significant differences between the respondents with regard to gender and age, although there were slightly more men

(52.88%) compared to women (47.12%) and slightly more respondents in the age group 65 to 74 years (31.41%) compared to the other observed age groups.

**Table 2.** *Gender and age of respondents*

Demographic characteristics		Number (%) of respondents	P*
Gender	Female	90 (47,12)	0,43
	Male	101 (52,88)	
Age	< 65 years	42 (21,99)	0,14
	65 – 74 years	60 (31,41)	
	75 – 84 years	50 (26,18)	
	> 85 years	39 (20,42)	
<b>Total</b>		191 (100,0)	

\* chi-square test

### Risk factor for ulcer formation

Table 3. shows the presence of endogenous risk factors for pressure ulcers. Hypotension 188 (98.43%) and anemia

(59.69%) were present in statistically significant numbers of subjects (Chi square test,  $P < 0.001$ ).

**Table 3.** *Endogenous risk factors for pressure ulcers*

Endogenous risk factors for pressure ulcers	Number (%) of respondents	P*
Immobility	65 (34,03)	
Incontinence	78 (40,84)	
Malnutrition	18 (9,42)	
Anemia	114 (59,69)	
Hypotension	188 (98,43)	
Neurological diseases	19 (9,95)	< 0,001
Cardiovascular diseases	49 (25,65)	
Diabetes	53 (27,75)	
Disorders of consciousness	54 (28,27)	
Fever	3 (1,57)	

\* Chi-square test

Table 4. shows the time of onset of pressure ulcers. A statistically significantly higher number of subjects developed pressure ulcers in the ICU compared to

subjects who developed them before admission to the ICU (78.53%:21.47%) (Chi square test,  $P < 0.001$ ).

**Table 4.** *Time of onset of pressure ulcers*

Time of onset of pressure ulcers	Number (%) of respondents	P*
Before admission to the ICU	41 (21,47)	
In the ICU	150 (78,53)	< 0,001
<b>Total</b>	191 (100,0)	

\* Chi-square test

Vasoactive drugs were used in all subjects with pressure ulcers. 1 vasoactive drug was used in 115 (60.21%) subjects, 2 in 53 (27.75%) subjects, 3 in 19 (9.95%) subjects, and 4 in 3 (1.57%) subjects.

Table 5. shows the vasoactive drugs used. Statistically, the most commonly used drug was noradrenaline, in 190 (99.48%) subjects (Chi square test,  $P < 0.001$ ).

**Table 5.** *Vasoactive drugs used*

Vasoactive drugs used	Number (%) of respondents	P*
Adrenaline	20 (10,47)	
Noradrenaline	190 (99,48)	< 0,001
Vasopressin	50 (26,18)	
Dobutamine	32 (16,75)	

\* Chi-square test

Table 6. shows a comparison of the stage of pressure ulcers at discharge with respect to the number of vasoactive drugs administered. No statistically significant

association was observed between the number of vasoactive drugs administered and the stage of pressure ulcers (Chi square test,  $P = 0.41$ ).

**Table 6.** Comparison of pressure ulcer stages at discharge with respect to the number of vasoactive drugs administered

Stages of pressure ulcers at discharge from the ICU	Number (%) of respondents			P*
	1 drug	2 drugs	3 drugs	
Stage I	23 (27,06)	4 (18,18)	0 (0,0)	0,41
Stage II	43 (50,59)	14 (63,64)	5 (62,50)	
Stage III	14 (16,47)	3 (13,64)	2 (25,0)	
Pressure ulcer of unknown depth	1 (1,18)	0 (0,0)	1 (12,50)	
Suspicion of deep tissue injury	3 (3,53)	1 (4,54)	0 (0,0)	
No pressure ulcers	1 (1,18)	0 (0,0)	0 (0,0)	
<b>Total</b>	85 (73,91)	22 (19,13)	8 (6,96)	

\* Chi-square test

## DISCUSSION

The results of a study on the influence of vasoactive drugs on the occurrence of pressure ulcers in the surgical intensive care unit of the Clinical Hospital Center Zagreb over a three-year period showed a low incidence (5.7%), which is within the range established by previous studies. In this study, there were no statistically significant differences in the gender and age of the subjects, which was also established by previous studies (4, 14). Patients treated in the ICU are known to have the highest rates of hospital-acquired pressure ulcers. The incidence of pressure ulcers in the ICU ranges from 3.3% to 53.4% (10). Results vary depending on the methodology and study site. A study conducted in 90 countries in 1117 ICUs reported a prevalence of pressure ulcers acquired in the ICU of 16.2% (12). In a study by de Oliveira Ramalho et al., the

incidence of pressure ulcers in the ICU in patients with Covid-19 was 30.2% (13). In a global study of pressure ulcer incidence and prevalence, there were no significant differences by gender (6). In a study of pressure ulcer prevention strategies in adult acute care settings in the United States in 2018/2019, there were equal numbers of men (50%) and women (49.4%) and 0.6% of unknown gender, with a mean age of 64.29 years (14).

In this study, among endogenous risk factors, hypotension and anemia were present in a statistically significant number of subjects, which confirms the findings of previous studies (9, 13).

In this study, the majority of subjects developed pressure ulcers in the ICU compared to subjects who developed them before admission to the ICU, confirming that the ICU is a place of treatment and care with an increased risk for developing

pressure ulcers compared to other hospital settings (7). The risk assessment for pressure ulcers using the Braden scale was performed in all subjects.

In this study, vasoactive drugs were used in all subjects. 60.21% of subjects used 1 drug, 27.75% used 2 drugs, 19.95% used 3 drugs, and 1.57% used 4 vasoactive drugs. The most commonly used drug was noradrenaline, either alone or in combination with vasopressin. From the above, it can be concluded that the use of vasoactive drugs is associated with the development of pressure ulcers. Vasopressor infusion is commonly administered to patients in intensive care to improve perfusion in shock, with consequent peripheral vasoconstriction, which may pose a risk for the development of pressure ulcers (15). Pressure ulcers have been shown to be associated with the use of vasoactive drugs (16), and vasopressor infusion has been shown to independently predict the development of pressure ulcers (17, 18). The exact mechanism by which vasoactive drugs may influence the development of pressure ulcers is unclear. Critically ill patients may experience hemodynamic changes during turning, leading to conditions such as cardiac arrest, and the use of vasoactive drugs may exacerbate hemodynamic instability. For this reason, nurses/technicians may reduce the frequency of turning patients who are receiving vasoactive drugs. They constrict peripheral blood flow to maintain blood flow to vital organs, thereby reducing peripheral blood flow and increasing the risk of developing pressure ulcers (19). Vasopressors are difficult to study because of the variability in their effects on peripheral circulation related to the dose

delivered and the receptors targeted (13). Future studies should specify the dose, time of administration, study each individual vasoactive drug separately, and consider their synergistic effects. In this study, no statistically significant association was observed between the number of vasoactive drugs administered and the stage of pressure ulcers, probably because only patients with pressure ulcers were included. Future studies should include all patients treated in the ICU, in order to examine the difference between patients with and without pressure ulcers with regard to the use of vasoactive drugs.

## CONCLUSIONS

The incidence of pressure ulcers in the three-year period in the surgical ICU was low (5.7%). There were no statistically significant differences between the subjects with respect to gender and age, although there were slightly more in the age group 65 to 74 years (31.42%) compared to the other observed age groups. Of the endogenous risk factors, hypotension and anemia were statistically significantly more common in the majority of subjects. A statistically significantly higher proportion of subjects developed pressure ulcers in the ICU (78.53%) compared to subjects who developed pressure ulcers before admission to the ICU (21.47%). Vasoactive drugs were used in all subjects. 60.21% of subjects used 1 drug, 27.75% of subjects used 2 drugs, 19.95% of subjects used 3 drugs, and 1.57% of subjects used 4 vasoactive drugs. Statistically, the most commonly used drug was noradrenaline, either alone or in combination with vasopressin.

In future research, it is necessary to specify the dose, time of administration,

specifically study each individual vasoactive drug, their synergistic effects, and include all patients treated in the ICU, in order to examine the difference between patients with and without pressure ulcers with respect to the use of vasoactive drugs.

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## UTJECAJ VAZOAKTIVNIH LIJEKOVA NA POJAVU DEKUBITUSA U JEDINICI KIRURŠKOG INTENZIVNOG LIJEČENJA

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### SAŽETAK

Uvod: Dekubitus (ozljeda od pritiska) nastaje kada opterećenje tkiva i/ili trajanje opterećenja premašuje individualnu toleranciju tkiva. Čimbenici rizika za razvoj dekubitusa uključuju ograničenja pokretljivosti/aktivnosti, stanje kože, perfuziju, cirkulaciju, oksigenaciju, vlagu/mikroklimu, dob i prehranu. Bolesnici u jedinici intenzivnog liječenja (JIL) imaju dodatne rizike za razvoj dekubitusa, kao što su primjena vazoaktivnih lijekova, produljeno liječenje u JIL-u, prisutnost komorbiditeta (dijabetes, kardiovaskularne bolesti, hipotenzija), produljena mehanička ventilacija, hemodijaliza i sedacija, što potvrđuje kompleksnu prirodu razvoja dekubitusa.

Cilj: Ispitati utjecaj vazoaktivnih lijekova na incidenciju dekubitusa u jedinici intenzivnog kirurškog liječenja.

Ispitanici i metode: Ispitanici su bili svi bolesnici s dekubitusom liječeni na kirurškoj JIL-u Klinike za anesteziologiju, reanimatologiju, intenzivno liječenje i liječenje boli KBC-a Zagreb tijekom 3 godine. Svim ispitanicima je procijenjen rizik od dekubitusa pomoću Bradenove ljestvice.

Rezultati: Učestalost dekubitusa bila je 5,7%, bez značajnih razlika u spolu i dobi. Najčešći čimbenici rizika uključivali su pritisak, trenje, trakciju, hipotenziju i anemiju. Kod većine ispitanika, dekubitus se pojavio u JIL-u, formirao se u sakrumu, glutealnoj i ishijalnoj regiji, a uočen je u stadiju II. Kod svih ispitanika korišteni su vazoaktivni lijekovi. Najčešće se koristio noradrenalin.

Zaključak: Kod svih ispitanika korišteni su vazoaktivni lijekovi, što ukazuje na njihovu povezanost s dekubitusom. U daljnjim istraživanjima potrebno je precizirati dozu, vrijeme primjene, proučiti svaki pojedini vazoaktivni lijek, njihove sinergističke učinke, te obuhvatiti sve bolesnike liječene u JIL-u, kako bi se ispitala razlika između bolesnika s/bez dekubitusa s obzirom na primjenu vazoaktivnih lijekova.

**Ključne riječi:** dekubitus, vazoaktivni lijekovi, Bradenova ljestvica, jedinica intenzivnog liječenja.

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