Is malignancy effective in the healing time of pressure ulcers in intensive care patients?

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Abstract
Aim: In this study, we aimed to investigate the duration of wound healing and an effective treatment management approach to patients with or without malignancy receiving wound care to provide effective wound care and to accelerate discharge.

Material and Methods: Three hundred and forty-five patients who were treated in our clinic were included in the study. Records of patients with pressure ulcers among those who stayed in the Surgical Intensive Care Unit between January 1, 2018 and January 1, 2020 were accessed. Patients’ pressure ulcers were graded on the Waterlow scale and standardized therapies were applied according to the grades. Dates of admission to the Intensive Care Unit (ICU), the pressure ulcers grades, comorbidities, laboratory values, administered treatment protocols and treatment response times were retrieved from the records and evaluated.

Results: The patients were divided into two groups: patients with malignancy (Group M, n = 78) and those without malignancy (Group NM, n = 73). Comparison of all parameters according to pressure ulcer stages revealed a significantly low albumin level in malignant patients with Stage 2 and 3 pressure ulcers when compared to the non-malignant patients (Group M/Group NM, Stage 2 p<.01 and stage 3 p = 0.015). In malignant patients with low albumin levels and Stage 2 pressure ulcers, the wound healing time was prolonged statistically significant (Group M/Group NM, 13.28±5.64/11.50±6.34 days, p = 0.047). No significant difference was established in the mean duration of wound healing between patients with and without malignancy when groups were taken up in general (Group M/Group NM: 8.00±6.49 / 6.67±6.35 days, p = 0.52).

Discussion: Malignancy does not play a role in the duration of wound healing in malignant and non-malignant patients treated in the intensive care unit at Stage 1 pressure wounds. Furthermore, there is a difference in the duration of wound healing between malignant and non-malignant patients, even for Stage 2 and 3 pressure ulcers on the Waterlow scale.

Keywords
Critical Care, Pressure Ulcer, Neoplasms, Wounds and Injuries
Malignancy and pressure ulcers

Introduction
Pressure ulcers are a syndrome that can cause significant morbidity and mortality, but can be prevented when the necessary precautions are taken. Pressure ulcers are a common complaint in geriatric patients due to pathological changes resulting from comorbidities. Selecting an appropriate approach to the treatment of pressure ulcers requires knowledge of the pathophysiology of the event. Pressure ulcers increase the length of hospital stays, morbidity and mortality, contributing therefore to increased healthcare costs [1–5].

Both intrinsic and extrinsic factors are involved in pressure ulcer formation, with the main pathology being interrupted blood flow and hypoxia due to pressure in the affected area [6, 7]. The pressure gradient at the arterial and venous ends of capillaries supports tissue perfusion. The disruption of capillary circulation due to pressure leads to hypoxia, triggering wound formation. With advanced age, the amount of collagen and elastin in the dermis decreases, and skin perfusion decreases [8].

Previous studies have reported that age is not a cause of pressure ulcer formation, but should be considered as a significant risk factor in the presence of other accompanying risk factors and chronic diseases, among which, malignancy is one such risk factor [9]. There is a chronic catabolic process. Low blood counts, and neutrophils, in particular, predispose patients undergoing malignancy treatment to infections. Different products are available for wound care that are selected depending on the characteristics of the wounds in question [10]. The main principle behind the prevention of pressure ulcers is to identify at-risk patients in advance, and take appropriate measures to relieve pressure. The best-known scales for grading pressure ulcers are the Norton Scale (1962), the Gaggin Scale (1973), the Knoll Scale (1985), the Waterlow Scale (1985) and the Braden Scale (1987) [11]. The Braden Scale assesses six parameters, including sensory perception, activity, mobility, moisture, nutrition and friction-shear, and produces a maximum score of 23. A score of 15–18 indicates mild risk, 13–14 moderate risk, 10–12 high risk and 0–9 very high risk. Patient risk assessments require an assessment of all patient data. Factors that should not be ignored when managing wound care include treatment of existing systemic diseases, treatments for changes in laboratory values, general condition, drug interactions and side effects experienced by the patient.

For Stage 1 pressure ulcers, it will be sufficient to prevent the progression of the lesion by relieving pressure. For Stage 2 pressure ulcers, no debridement is required, although it is important to keep the wound area non-infected and to provide a suitable moist environment. Stage 3 and 4 pressure ulcers often require debridement. Selection of products suitable for the characteristics of the wound, antibiotic treatment if infection is present, a combination of passive and active closure products when necessary, and surgical treatments may be required.

No previous studies related to wound healing in intensive care patients with malignancy were identified in the literature. We believe that such a study on wound healing would serve to guide the treatment of patients in the future due to the large malignant patient population in our oncological hospital. The present study investigates whether malignancy has an effect on the healing of pressure ulcers in intensive care patients, and is conducted based on our belief that such a study of wound healing could serve as a guide in the treatment of patients in the future, due to the large malignant patient population of our oncological hospital.

Material and Methods
Following approval from the local ethics committee and informed consent from the patients, the records of patients with pressure ulcers among those who stayed in the Surgical Intensive Care Unit between January 1, 2018 and January 1, 2020 were accessed. Three hundred and forty-five patients who were treated in our clinic were included in the study. A further 126 patients with pressure ulcers who needed surgical debridement, mechanical ventilation and/or vacuum-assisted closure (VAC) were also excluded. The remaining patients were examined in 2 groups: those with malignancy (Group M, n = 108) and those without malignancy (Group NM, n = 111). Patients with diabetic wounds and those who died during treatment (30 patients in group M, 38 patients in group NM) were excluded from the study. Therefore, 78 patients in group M and 73 patients in group NM were included in the study.

Patients’ pressure ulcers were graded using the Waterlow scale, and standard treatment methods were applied according to the grades [12]. Dates of admission to the Intensive Care Unit (ICU), the pressure ulcers grades, comorbidities, laboratory values, administered treatment protocols and treatment response times were retrieved from the records and evaluated.

For Stage 1 pressure ulcers, the pressure was relieved by changing the position every two hours, and transparent film dressings and barrier cream were applied. (Figure-1)

For Stage 2 pressure ulcers, if the wound was exuding, hydrofiber + hydrocolloid dressings were applied and changed every other day. If the wound was moist, a hydrocolloid dressing was applied for 3–5 days.

For Stage 3 pressure ulcers, if the wound was necrotic and non-exuding, the dressing was changed after autolytic debridement or surgical debridement with a hydrogel dressing, and hydrofiber + hydrocolloid dressings were applied every 2–3 days. If the wound was exuding, hydrofiber + hydrocolloid dressings were applied for 2–3 days and changed every other day as needed. If the wound was moist, hydrofiber + hydrocolloid dressings were applied, and changed every 2–3 days as needed.

For Stage 4 pressure ulcers, negative pressure therapy (VAC) was administered after surgical debridement.

The study included cases with Stage 1, 2 and 3 pressure ulcers according to the Waterlow scale. Cases requiring surgical debridement (stage 4) were not included in the study. The healing time was counted from the day of initial diagnosis. The time taken for the wound to heal and regress to a lower Waterlow scale stage with appropriate treatment was compared (Stage 3 to 2, Stage 2 to 1, Stage 1 to 0).

For both groups of patients, laboratory values, treatment protocols and healing processes of pressure ulcers during treatment were retrieved from available intensive care records and evaluated retrospectively.

For statistical analysis, IBM SPSS Statistics for Windows (Version 25.0. Armonk, NY: IBM Corp.) was used. Prior to the
analysis, the assumption of normality for all data was assessed with the Shapiro-Wilk test. Numerical data were expressed in median and minimum-maximum values, and categorical data in numbers (percentage). The Chi-square test was used to compare categorical variables, and the Mann-Whitney U test to compare numerical data between the two groups. The study was conducted at a 95% confidence interval.

Results
The distribution of age, gender and the ASA (American Society of Anesthesiologists) scores was statistically similar in the malignant and non-malignant patient groups (p = 0.67; p = 0.11, p = 0.18, respectively, Table 1). Likewise, there was no statistically significant difference in healing, leukocyte, CRP, albumin, pressure ulcer stage and ASA score between the two groups (Table 1). Comparison of all parameters according to pressure ulcer stages revealed a significantly low albumin level in malignant patients with Stage 2 and 3 pressure ulcers when compared to the non-malignant patients (Group M / Group NM, Stage 2 p<0.01 and stage 3 p = 0.015, Table 2).

In malignant patients with low albumin levels and Stage 2 pressure ulcers, the wound healing time was statistically significantly increased (Group M / Group NM, 13.28±5.64 / 11.50±6.34 days, p = 0.047, Table 2). CRP levels were lower in the NM Group than in the M Group (p=0.018).

Albumin levels were lower in malignant patients with Stage 3 pressure ulcers than in the non-malignant group (Group A / Group B: 2.18 ±0.23/ 1.05±1.20 g/dl, p =0.01, Table 2). This finding was statistically significant (p<0.05).

Furthermore, in patients with malignancy, the healing time of Stage 3 pressure ulcers was statistically significant (Group M/ Group NM: 13.75±5.79/7.90±6.31 days, p=0.009, Table 2).

No significant difference was established in mean duration of wound healing between patients with and without malignancy when groups were taken up in general (Group M / Group NM: 8.00±6.49 / 6.67±6.35 days, p = 0.52, Table 1).

Discussion
In the present study, the wound healing time was similar in both the malignant and non-malignant patient groups. When the groups were compared separately according to the pressure ulcer stages, albumin levels were found to be low in malignant patients with Stage 2 and 3 pressure ulcers. The healing time of Stage 2 and 3 pressure ulcers was significantly delayed in malignant patients with low albumin levels.

Ricci et al. discussed the significance of having an albumin level of >3 g/dl and a prealbumin level of >20 mg/dl in wound treatment [13]. In the present study, when the groups were compared separately according to the pressure ulcer stages, albumin levels were found to be low in malignant patients with stage 2 and 3 pressure ulcers. Although the healing time of Stage 2 pressure ulcers was statistically insignificant in malignant patients with low albumin, it was observed to be delayed numerically. In addition, malignant patients with stage 3 pressure ulcers had low albumin levels along with a statistically prolonged healing time.

They recommend the optimization of protein, vitamin and mineral intake, and correction of albumin and prealbumin

Table 1. Characteristic features of the cases

| Variables | Group M (n=78) Mean ± SD | Group NM (n=73) Mean ± SD | p value |
|-----------|--------------------------|--------------------------|---------|
| Age       | 62.12 ± 8.68             | 63.95 ± 19.29           | 0.67    |
| Wound healing (day) | 8.00 ± 6.49 | 6.67 ± 6.35 | 0.22   |
| Gender    | female: 48, male: 30     | female: 44, male: 29    | 0.11    |
| ASA Scores| ASA 2= 3                 | ASA 3=4                 | 0.001*  |
| WBC (4-10×103 cells/UL) | 8888.46 ± 4290.67 | 8598.0 ± 2626.10 | 0.79    |
| CRP (0-5 mg/L) | 207.85 ± 155.89 | 203.90 ± 136.07 | 0.93    |
| Albumin (3.5-5.2 g/Dl) | 1.84± .86 | 2.07 ± 6.7 | 0.32    |

Table 2. The time taken for the wound to heal and to regress to a lower Waterlow scale stage with appropriate treatment were compared

| Grade of wound | Variables | Group M (n=78) Mean ± SD | Group NM (n=73) Mean ± SD | p value |
|----------------|-----------|--------------------------|--------------------------|---------|
| 1              | Age       | 60.890 ± 6.945           | 62.000 ± 18.566          | 0.862   |
|                | Wound healing (days) | 4.330 ± 1.320 | 3.750±0.960 | 0.382   |
|                | WBC (4-10×103 cells/UL) | 9066 ± 4189 | 8660 ± 3075 | 0.754   |
|                | CRP (0-5 mg/L) | 165.550 ± 169.620 | 197.580 ± 151.530 | 0.382   |
|                | Albumin (3.5-5.2 g/Dl) | 2.120 ± 0.435 | 2.430 ± 0.670 | 0.310   |
|                | n         | 27                       | 36                       |         |
| 2              | Age       | 63.820 ± 10.320          | 69.710 ± 13.700          | 0.179   |
|                | Wound healing (days) | 13.280 ± 5.640 | 11.500 ± 6.340 | 0.047*  |
|                | WBC (4-10×103 cells/UL) | 9172 ± 4875 | 7218 ± 2497 | 0.211   |
|                | CRP (0-5 mg/L) | 252.27 ± 144.51 | 152.43 ± 120.58 | 0.018*  |
|                | Albumin (3.5-5.2 g/Dl) | 1.930 ± 0.190 | 2.540 ± 0.600 | 0.0155* |
|                | n         | 33                       | 21                       |         |
| 3              | Age       | 61.500 ± 7.990           | 53.500 ± 45.960          | 1       |
|                | Wound healing (days) | 13.750 ± 5.790 | 7.900 ± 6.510 | <0.009* |
|                | WBC (4-10×103 cells/UL) | 9150 ± 4001 | 9900 ± 1555 | 0.857   |
|                | CRP (0-5 mg/L) | 238.670 ± 152.750 | 275.500 ± 85.560 | 0.857   |
|                | Albumin (3.5-5.2 g/Dl) | 1.050±1.200 | 2.180 ± 0.230 | 0.001*  |
|                | n         | 18                       | 16                       |         |

* : p<0.05

Figure 1. 72-years old male patient with stage 3 pressure wound under the heel on the left side of the figure, 14 days after wound care treatment in the middle of the picture (stage 2 ), 16 days after wound care treatment on the right side of the figure (stage 1).
levels, and stress the necessity of reaching target nutritional values through calorie calculations, high-protein diets and, if necessary, tube gastrostomy and jejunostomy [13]. This is also important for the success of treatment in patients treated with a turning flap. In the present study, the albumin value was <3 g/dl in malignant patients with stage 2 pressure ulcers, and wound healing time was prolonged, although not significantly. This absence of a significant prolongation in wound healing may suggest the effectiveness of the applied wound care, even in malignant patients with low albumin levels. Reed et al. investigated the factors affecting the formation of pressure ulcers in hospitalized patients with a randomized, prospective study of 2,771 patients from 47 centers [14]. The authors identified confusion and low albumin to be risk factors for the development of pressure ulcers. The stage of pressure ulcers, presence of indications for resuscitation, presence of malnutrition, body mass index, albumin level, mental state, presence of urinary or fecal incontinence, and presence of pneumonia on chest radiography were considered risk factors. In the absence of fecal incontinence, an albumin level of <3 g/dl and the presence of confusion were found to be statistically significant in the formation of pressure ulcers. In the present study, we found no difference in ASA scores, pressure ulcer stages, leukocyte counts, CRP or healing times between the malignant and non-malignant patients, while a low albumin level in malignant patients with Stage 2 pressure ulcers was noted.

In a multicenter randomized controlled study, the etiology of pressure ulcers was examined in 6,155 patients, of whom 97% had stage 2 and eight patients had stage 3 pressure ulcers [15]. More pressure sores were observed in acute patients, the elderly, and patients undergoing orthopedic and vascular surgeries. The risk factors for pressure ulcer formation were investigated in a prospective cohort study of 213 in patients over the age of 65 years. In this population, appetite, continence, skin condition and age, all of which are among the Waterlow risk factors, were considered more important in risk identification than the other Waterlow risk factors [16]. Cancer diagnosis was found to be positively associated with pressure ulcer formation, while the presence of Parkinson's disease had the opposite effect. In the present study, no difference was found in the healing times of the pressure ulcers of the malignant and non-malignant groups. The limitations of this study include the fact that the general condition of the majority of malignant patients admitted to the postoperative surgical intensive care unit worsened, and they underwent mechanical ventilation or died. The number of patients who were discharged or transferred to inpatient service upon improvement in their general condition, and the number of patients meeting our criteria were not high, resulting in a small number of patients with wound healing. When patients were classified according to pressure ulcer stage, the number of patients per group was not equal and also low. However, there was no statistically significant difference in healing times in stage 1 and 2 pressure wounds. Therefore, there was a statistically significant difference in healing times in stage 3 pressure wounds.

Conclusions
Malignancy does not play a role in the duration of wound healing in malignant and non-malignant patients treated in the intensive care unit for pressure wounds. Therefore, malignancy no longer plays a role in the duration of wound healing in malignant and non-malignant patients treated in the intensive care unit at stage 1 pressure wounds. However, there is a difference in the duration of wound healing between malignant and non-malignant patients, even for stage 2 and 3 pressure ulcers on the Waterlow scale. The healing time of stage 2 and 3 pressure ulcers was statistically significantly in malignant patients with low albumin. We believe that optimizing albumin levels in patients with malignancies is essential for the effective advanced pressure wound care.

Animal and human rights statement
All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. No animal or human studies were carried out by the authors for this article.

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Conflict of interest
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