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## Early Low Level of Procalcitonin Is Associated with a Favorable Outcome in a Case of a Surviving Patient with 80% Body Surface Area Thermal Burn

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Statistical Analysis C  
Data Interpretation D  
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**Patient:** Male, 28-year-old  
**Final Diagnosis:** Burn wound  
**Symptoms:** Pain • dyspnea  
**Medication:** —  
**Clinical Procedure:** —  
**Specialty:** Anesthesiology • Critical Care Medicine • Surgery

**Objective:** Unusual clinical course

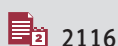
**Background:** Burns covering a large skin surface area represent a life-threatening condition due to the release of cytokines and the activation of a systemic inflammatory response, as well as the potential for septic complications. Outcome for these patients is related to the burn surface, age, and coexisting diseases. Although some severity scores are available, such as the Abbreviated Burn Severity Index (ABSI), Baux score, R-Baux score, Boston score, and Belgian Outcome Burn Injury (BOBI) score, none can provide a solid picture of the final outcome. Recent studies claim that procalcitonin, a known sepsis marker, can assist in estimating a burn patient's chance of survival from the time of admission, and can also assist in estimating the chance of sepsis occurrence during hospitalization.

**Case Report:** In this manuscript we report the case of a 28-year-old man who suffered burn injuries on approximately 80% of his body surface due to poor handling of a gasoline can in August 2018. Despite high severity index scores and early high values of C-reactive protein, we noticed a low level of early procalcitonin. In this case, as well in our previous experience, early low procalcitonin was associated with a favorable outcome.

**Conclusions:** Early procalcitonin values might prove to be a promising prognosis marker in some cases of extensive burns.

**Keywords:** Burns • Injury Severity Score • Procalcitonin

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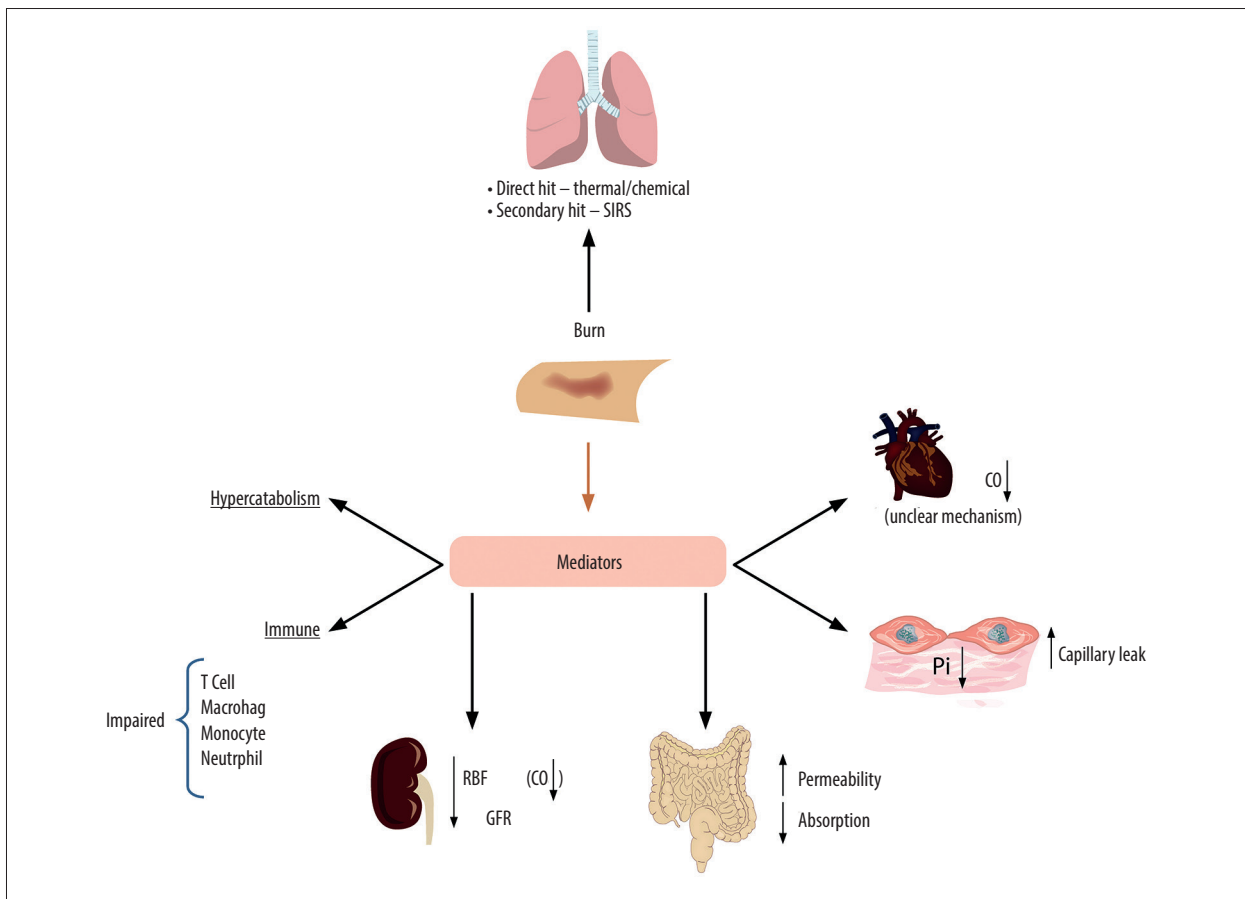
## Background

Burns have been mentioned in medical documents since antiquity; the first writings about how to address this issue appeared in 1600 BCE, recommending resin, honey, tinctures, wine, and myrrh. Ambroise Pare performed the first burn wound excision, but 2 centuries passed before Reverdin made the first burn excision followed by skin grafting, in 1869 [1]. Burns are caused by physical factors such as thermic agents (scalds, flame, contact), electrocution, radiation, or chemical factors such as acids or bases. A systemic inflammatory response induced by the cytokines released from the burn lesion takes place in response to the burn. The magnitude of this response is influenced by the patient's previous health condition. A systemic inflammatory response generally occurs in the case of a burn on >30% of the total body surface area (TBSA). Systemic reactions include: depressed cardiac contractility, decreased preload due to the leakage of water into the interstitium, increased capillary permeability, impaired lung function (including acute respiratory distress syndrome-ARDS) by direct or secondary hit, decreased immune response, and hypermetabolism (Figure 1).

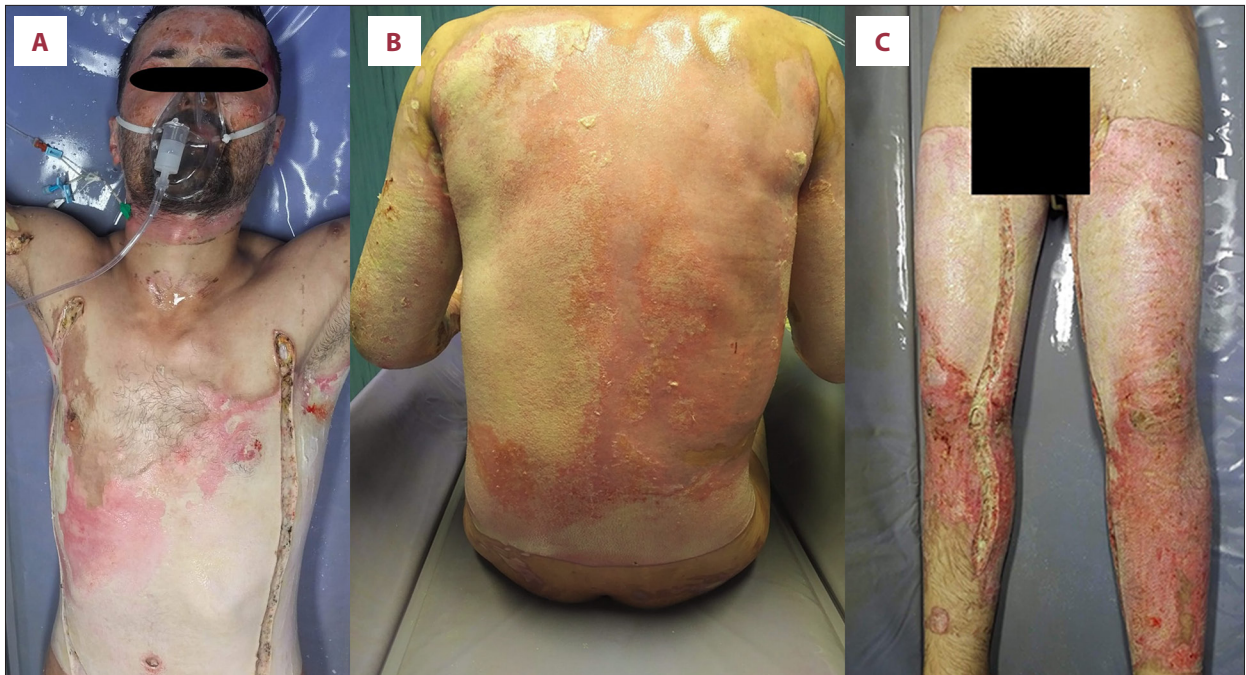
Another feature of burns is the potential for septic complications, due to loss of the skin barrier coupled with depressed immune function.

At the root of these systemic reactions are certain cytokines, especially  $TNF\alpha$  and  $IL-1\beta$ , which produce tissue lesions, as well as secretion of some biomarkers, such as procalcitonin. Although procalcitonin is a validated sepsis marker, it is induced by the same cytokines in both inflammatory reactions and septic ones. Procalcitonin has proven to be a good, specific marker for bacterial infection, with no relevance to viral infection (due to  $IFN\gamma$  inhibition of  $IL-1\beta$  secretion) or fungal infection (similarly due to  $IFN\gamma$  inhibition of  $IL-1\beta$  secretion) [2-5]. Moreover, there are some reports describing elevated procalcitonin levels in non-septic conditions such as pancreatitis or trauma, as well as burns [6]. Procalcitonin has a rapid kinetic course, with an early increase within the first few hours after sepsis onset, reaching a maximum at 24-48 h after the injury [7,8].

In septic burn patients, procalcitonin has a cut-off value ranging from 0.5-1.5 ng/ml [7,9,10] although some debate still



**Figure 1.** The main mechanisms of systemic injuries (heart, lungs, capillaries, kidneys, gastrointestinal tract, immune cells, metabolic response) induced by burn lesions. CO – cardiac output; SIRS – systemic inflammatory response syndrome; Pi – interstitial fluid pressure; RBF – renal blood flow; GFR – glomerular filtration rate.



**Figure 2.** (A) Superficial and deep partial-thickness burns (grade IIA, IIB) due to circular burns on the upper extremities, chest, and abdomen. (B) Mixed-type second-degree burns (superficial and deep partial-thickness burns grade IIA, IIB) evolving on the posterior trunk. (C) Superficial and deep partial-thickness burns (grade IIA, IIB) due to circular burns on the lower extremities.

exists about the utility of procalcitonin in diagnosing septic complications in burns [11]. Early high values of procalcitonin in non-septic conditions seem to be associated with an unfavorable outcome, possibly related to future sepsis occurrence in these patients. A solid correlation between early procalcitonin value and sepsis occurrence has been observed [7,12-14].

It is generally accepted that the severity and prognosis depend on the burn surface area, the patient's age, the preexistence of coexisting diseases, and the presence or absence of airway burns. However, procalcitonin, a sepsis-dedicated biomarker with a rapid kinetic profile (onset at 24-48 h), might play a role in prognosis prediction even in non-septic condition, such as burns. Consequently, we have chosen an extensive burn case to illustrate this observation.

## Case Report

The Ethics Committee of the Clinical Emergency Hospital of Plastic Surgery and Burns approved the publication of this case (Notice 3/19.06.2020) after informed consent was obtained.

A 28-year-old man experienced a thermal burn due to improper handling of a gasoline can within a house outbuilding. The patient was initially transported to Bacau Emergency Hospital with superficial, deep partial-thickness burns (grade IIA, IIB) and full-thickness burns (grade III on approximately 3% total

body surface area), resulting in a total of approximately 80% body surface area lesions (Figure 2A-2C). He was treated with chest and abdominal debridement and decompression incisions. The patient also underwent protective tracheal intubation in the context of suspicion of airway burns. Initial blood tests revealed increased C-reactive protein (CRP) (312.38 mg/L), moderately elevated procalcitonin (1.9 ng/ml), and severe hypoproteinemia (total protein=29.1 g/L; albumin=18 g/L). The severity scores amounted to the following values: ABSI=12 points, Baux=108 points, R-Baux=85 points.

Upon being transferred to the Clinical Hospital of Plastic, Reparatory, and Burn Surgery (48 h after the fire incident), local conservative nonsurgical treatment for superficial burns was performed. This treatment consisted of lavage and dressing with silver-containing products, followed by admission of the patient to the Intensive Care Unit where respiratory support using mechanical ventilation was continued. The patient presented with signs of an extremely aggressive burn-induced inflammatory reaction, reflected in the values for CRP (679 mg/L), albumin (25 g/L), presepsin (642 ng/L), and serum iron (Fe; 15 µg/dL) on admission to our department. In our department, sepsis was monitored via presepsin as opposed to procalcitonin levels.

The patient's respiratory function was stabilized, and because the patient showed no signs of inhalation injury (judging by the oxygenation index, ventilator parameters, and chest X-ray image), he was extubated the next day.

**Table 1.** Values of albumin, procalcitonin, C-reactive protein (CRP), presepsin, and iron (Fe) during hospitalization.

	Day 1	Day 4	Day 10	Day 13	Day 17	Day 23
Albumin (g/L)	18	25	26	28	31.5	36.3
Procalcitonin (ng/ml)	1.9	NA	NA	NA	NA	NA
CRP (mg/L)	312.38	679	158	166	189	91
Presepsin (ng/L)	NA	642	1498	1429	1143	NA
Fe (µg/dL)	NA	15	14	NA	23	49

The standard procedure for the management of large mixed-type second-degree burns includes conservative local treatment methods (removing devitalized tissue and application of special topical antimicrobial agents). Superficial and deep partial-thickness burns were treated conservatively by use of silver-containing products and full-thickness burns were excised and grafted with expanded meshed autografts. An unfavorable evolution of the burn lesions would require a more complex approach, such as allogenic grafts, xenografts, or synthetic skin.

The patient received burn-protocol treatment consisting of: proton-pump inhibitor (pantoprazole 40 mg), thromboprophylaxis with enoxaparin (40 mg per day), analgesics (paracetamol 4 g/day, morphine on request), antioxidants (acetylcysteine), oligoelements, and enteral and parenteral nutrition followed by normal feeding (to provide adequate nutrition in accordance with the Toronto formula estimation for caloric intake) [15]. Adequate tissue perfusion was achieved with the help of crystalloid solutions, maintaining MAP >65 mmHg and diuresis >0.5 ml/bw/h, lactate <2 mmol/L, and ScVO<sub>2</sub> >70% (in the absence of anemia or desaturation) [16].

From the 8<sup>th</sup> day of hospitalization and after colonization of the wound with *Pseudomonas aeruginosa* leading to an increase in presepsin value to 1498 pg/ml, the patient was prescribed additional antibiotic therapy (chosen taking into account bacterial sensitivity) with colistin (3 million IU every 8 h) and cefoperazone/sulbactam (1000 mg each; 2 g every 12 h). Antibiotic therapy continued for 2 weeks until swab cultures became negative and presepsin decreased to the cut-off value for sepsis (Table 1). Swab cultures were sampled twice per week, on Monday and Thursday, according to our hospital protocol. Iron level is also recognized as a good marker of inflammation and is associated with mortality, so its values were also tracked [17].

The evolution of the intermediary burn injuries was favorable and resulted in complete recovery. On the 21<sup>st</sup> day, the patient was transferred to the burn unit where he stayed for another 3 weeks. On the 35<sup>th</sup> day the full-thickness burn was excised and grafted with expanded meshed (3: 1) autograft harvested from the right forearm and the anterior side of the thigh. In the case of our patient, during the recovery process,

the second-degree (IIA/IIB) lesions, treated conservatively, did not deepen, and had a favorable evolution towards spontaneous epithelialization. After healing of the second-degree lesions (more precisely, on the 35<sup>th</sup> day after the accident), we excised and grafted the deep lesions that remained unhealed and that covered 3% TBSA. The patient was discharged on the 44<sup>th</sup> day from the initial injury.

## Discussion

The main concern in a patient with extensive burn lesions is the event of a cytokine storm, which induces multiple organ dysfunction syndrome, when the body becomes frail and more susceptible to infections due to impairment of the skin barrier and presence of immunosuppression [18-26]. This inflammatory reaction is induced by skin burn lesions and is aggravated by their unfavorable evolution (burn deepening). In our patient, CRP and total protein values (based on samples collected upon admission) suggested an extremely severe inflammatory disorder secondary to the burn injury. An ABSI score of 12 points (the score for our patient) is associated with an 80-90% mortality rate. Nonetheless, procalcitonin values lower than 1.9 ng/mL after 48 h signify a favorable prognosis [14,27].

In our case, we observed a discrepancy between CRP value (312.38 mg/L) and procalcitonin value (1.9 ng/ml) at 24 h. The CRP value of 312.38 is a high value that is theoretically associated with a high inflammatory response and should indicate a poor outcome. Nevertheless, the procalcitonin value was not similarly elevated, and both previous reports and our own experience led us to believe that procalcitonin could be a more reliable marker of inflammatory response and outcome. This may be due to the fact that CRP is induced by IL-6 and procalcitonin by TNF $\alpha$  and IL-1 $\beta$ . On the other hand, increased procalcitonin values in the initial days following a burn are reported to be associated with an increased risk for sepsis [3,8]. This was also the case for our patient, who started presenting signs of sepsis on the eighth day of hospitalization.

Aiming to prevent a poor outcome, our first intention was to combat deepening of the intermediate burn lesions, which



represented 77% of his body surface area [28]. To accomplish this, 3 principles should be complied with: proper blood flow for tissue perfusion of the burn lesions, adequate caloric intake, and the prevention of infection of the burn lesions. Adequate tissue perfusion was monitored using mean arterial pressure, diuresis, lactate, and central venous oxygen saturation values. Caloric intake was initially ensured by means of enteral and parenteral nutrition solution, followed by normal feeding in accordance with the Toronto formula for burns. Parenteral nutrition was added at the beginning, to supplement enteral nutrition to target the caloric requirement according to the Toronto formula. Parenteral nutrition was continued for no more than a week after the injury; until his gastric tolerance was ascertained. Although enteral nutrition using nasojejunal tube would have been preferred, unfortunately, such a device was not available at that time. Instead, gastric nutrition with prokinetics supplements was used.

In our present case, clinical monitoring (mean arterial pressure, urine output, and SCvO<sub>2</sub>) and a nutrition plan according to the Toronto formula proved to be sufficient for the patient's improvement despite the lack of calorimetry or invasive cardiac output monitoring.

Regarding the second-degree burn lesions, although recent studies suggest that silver can delay the wound-healing process and should not be used in a routine manner, we considered that in this case of a patient with extensive burns and treated under conditions of high risk of nosocomial infections, the efficacy of a local antimicrobial treatment should be of high priority in burn wound care. This is why we used silver-containing products for our patient during the healing process.

Regarding the management of the third-degree burns, we considered that later excisions and grafting were reasonable because we anticipated the possibility of burn wounds deepening during the wound evolution (a progression of a superficial partial-thickness burn to a deep partial-thickness or full-thickness burn), as well as the lack of homologous donor areas. In addition, there was a lack of other possibilities to cover the excised areas with homologous or temporary skin substitutes.

Burn lesion infection prevention was achieved by isolating the patient and performing daily wound dressing after debridement with bactericidal solutions [29]. Despite these measures, the patient presented signs of infection on the eighth

day after the accident (sixth day from admission to our hospital). Wound cultures detected colonization with *Pseudomonas aeruginosa* and laboratory tests revealed increased presepsin and CRP values. Targeted antibiotic therapy was administered and nursing management continued. Following these procedures, the infection was contained after 14 days and did not result in deepening of intermediate burn lesions, possibly due to initiation of healing.

Despite the poor severity score, other factors were encouraging: his age, low procalcitonin values within the first 48 h of the incident, and no vasopressor requirement [30-34]. As we have previously observed in our burn victims, young patients with vasopressor necessity and high levels of procalcitonin within 48 h after the injury are at risk of a poor outcome and increased mortality [27]. In their cases, procalcitonin levels were in accordance with the severity score, while low levels of procalcitonin correlated well with survival, as in our present case.

## Conclusions

Procalcitonin values within 48 h after burn injury (in non-septic patients) currently do not constitute a standardized marker for injury severity scores. However, the aforementioned observation in our patients, previous reports, and this particular case urge us to take procalcitonin into consideration as a credible severity outcome marker in connection with other severity predictors and vasopressor requirement. The correlation of early isolated procalcitonin values, as an endogenous marker of inflammatory response and outcome, should be investigated in future studies to be validated. For the moment, we can merely notice the association between low early values and favorable outcome.

## Acknowledgements

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## Declaration of Figures' Authenticity

All figures submitted have been created by the authors who confirm that the images are original with no duplication and have not been previously published in whole or in part.

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