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Jan Hambrecht, Philipp Vetter, Cédric Niggli, Hans-Christoph Pape, Ladislav Mica*

Abstract

Sepsis presents a challenge in polytrauma patients care, where timing of procedures is crucial. The University Hospital of Zurich and IBM developed *IBM Watson Trauma Pathway Explorer* for predicting polytrauma complications such as SIRS, Sepsis, and early death within 72 hours. We intended to investigate the association of surgical treatment (Damage Control, DCS and Early Total Care, ETC) and injury severity (Injury Severity Score, ISS) with the development of sepsis. Data from 3653 patients was included. Patients were divided into two groups based on the type of surgical management (DCS, ETC) and injury severity (ISS \leq 30, ISS $>$ 30). The groups were assessed for the development of sepsis. Totally, 1242 patients had an ISS $>$ 30 (34.6%), while 2374 had an ISS \leq 30 (65.4%). DCS was conducted in 66.3% of cases versus 33.7% for ETC. DCS was performed in 73.5% of patients with an ISS $>$ 30 and in 62.5% of patients with an ISS \leq 30. ETC was performed in 26.5% for ISS $>$ 30 and 37.5% for ISS \leq 30. Sepsis was detected in 15% of the patients. 50.8% of sepsis cases had an initial ISS $>$ 30. Regarding ETC, sepsis occurred in 9.6% of cases with ISS \leq 30 and in 18.5% of cases with an ISS $>$ 30. Regarding DCS, sepsis was detected in 12.3% with ISS \leq 30 and in 23.4% with ISS $>$ 30. Development of sepsis was associated with ISS $>$ 30 (OR 2.21, $p < 0.001$) and DCS treatment (OR 1.45, $p < 0.001$). The findings confirm the association of sepsis development in polytrauma patients with a higher injury severity (ISS $>$ 30). On the other hand, DCS does not generally imply a lower risk for this complication.

Keywords: Damage Control; Early Total Care; Sepsis; Polytrauma; Injury Severity Score; IBM Watson

Abbreviations

DCS = Damage control

ETC = Early total care

ISS = Injury severity score

OR = Odds ratio

SD = Standard deviation

ASA = American society of anesthesiology

Introduction

Sepsis continues to be a significant cause of mortality and morbidity in polytrauma patients, posing a challenge to healthcare providers. Polytrauma often necessitates immediate medical intervention [1]. Two contrasting treatment strategies have emerged in recent years for polytrauma patients: Damage Control (DCS) and Early Total Care (ETC), each offering distinct

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approaches to manage the interplay between maximum treatment and minimal risk of complications such as sepsis. DCS adopts a staged approach in the management of polytrauma patients. It involves immediate addressing of life-threatening injuries by interim measures to minimize surgical load and thereby risk of sepsis. Definitive surgical interventions are then performed at a later stage once physiological stability of the patient is achieved. On the other hand, ETC represents the early implementation of definitive surgical interventions, although associated with a higher surgical load. While both DCS and ETC have been employed in clinical practice, a clear consensus on the optimal management strategy for sepsis in polytrauma patients is yet to be established [2,3]. To quantify the injury severity, the ISS was established, providing insights into the patient's physiological response and predicting outcomes [4]. Understanding the relationship between ISS and the choice of treatment strategy is of utmost importance in optimizing patient outcomes including a minimum risk of complications such as sepsis [3,5]. The *Watson Trauma Pathway Explorer*® is an outcome prediction tool invented by the University Hospital of Zurich in collaboration with IBM®, representing an artificial intelligence application to predict the most adverse outcome scenarios in polytrauma patients: Systemic Inflammatory Respiratory Syndrome (SIRS), sepsis within 21 days and death within 72 h. We intended to investigate the association of surgical treatment (DCS, ETC) and injury severity (ISS) with the development of sepsis.

Material and Methods

Patient collective sample

Data from 3653 patients in an internal database, with ongoing implementation (2022), served for analysis (*Watson Trauma Pathway Explorer*®). All prospectively enrolled polytrauma patients aged ≥ 16 years with an ISS ≥ 16 were included retrospectively into the data sample. Complete datasets were required. We excluded non-survivors prior to admission and patients referred from external hospitals. Patients were split in two groups according to the type of surgical management (ETC, DCS) and injury severity (ISS $<$ 30 vs. ISS $>$ 30). Differences between groups were analyzed. The presence of sepsis was evaluated.

Definition of Sepsis

Using the most extreme readings of parameters including leucocyte count, respiratory rate, heart rate, the SIRS score was computed daily (6). This calculation was performed throughout the duration of the patient's hospital stays. Sepsis was characterized as a SIRS score ≥ 2 with a specific infection focus, and it needed to manifest within the observation period of 21 days (7).

Laboratory analysis

Measurements were conducted using a standardized latex-enhanced immune turbidimetry at the laboratory institute of the University of Zurich.

Statistical analysis

Continuous data are presented with mean and standard deviation (SD), and categorical variables are presented with numbers and percentages. The ggplot2-package was used for data-visualization. Data was visually tested for normality using Kolmogorov-Smirnov. Unpaired student T-tests were used for parametric data. Non-parametric data was tested using Wilcoxon-Mann-Whitney tests. Binary categorical data was assessed using Fisher's exact test, and non-binary categorical data using chi-squared test with Yates' correction for continuity. Odds ratios (OR) were calculated using a logistic regression model. Statistical analysis was performed in R (R Core Team (2018). R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. URL: <https://www.R-project.org/>). The threshold for statistical significance was determined as a p-value of <0.05 .

Ethical approval

This study was conducted according to the guidelines for good clinical practice and the Helsinki guidelines. Research was based on the TRIPOD statement, representing a guideline for multivariable prediction model. Ethical approval for analysis of patient data was granted by the ethical committee of the University Hospital Zurich and the government of Zurich upon the development of the database (Nr. StV: 1–2008) and reapproved for development of the *Watson Trauma Pathway Explorer*® (BASEC 2021–00391).

Results

In total, 3653 patients were included, with a mean age of 45 ± 20.2 year, 73.4% of patients were male. Patients developing sepsis had higher values for the (*New*) *Injury Severity Score* (NISS/ISS) and the *Acute Physiology and Chronic Health Evaluation* (APACHE)-II-Score than patients without sepsis development (Figure 1). Sepsis occurred in 15% of all included cases.

Overall, 1242 patients presented with an ISS > 30 (34.6%), while 2374 patients showed an ISS of ≤ 30 (65.4%). DCS was performed in 66.3% of cases and ETC was carried out in 33.7%. According to ISS, DCS was performed in 73.5% of the patients with an ISS > 30 and in 62.5% of the patients with an ISS ≤ 30 . ETC was performed in 26.5% of the patients with an ISS > 30 and in 37.5% with an ISS ≤ 30 . 50.8% of the patients with sepsis showed an initial ISS > 30 . An ISS of 30 or lower was detected in 49.2% of the patients. Overall, ETC was performed in 26.9% of all patients who

Table 1: Patient sample characteristics

	Patient Sample	Sepsis	No Sepsis	p-Value
n	N = 3653	N = 547	N = 3106	
Demographics				
Age (mean (SD))	45.8 ± (20.2)	42.8 (± 18.1)	46.3 (± 20.5)	0.0002
Sex = Male (%)	2681 (73.4%)	430 (78.6%)	2251 (72.4%)	
Baseline characteristics				
Blunt trauma	3336 (91.3%)	518 (94.7%)	2818 (90.7%)	
Head trauma	1400 (38.3%)	245 (44.8%)	1155 (37.2%)	
Early death (within 72 hours)	708 (19.3%)	8 (1.48%)	700 (22.5%)	
BMI	25 ± 4.4	25.9 ± 4.4	24.8 ± 4.3	< 0.001
ISS (median, IQR)	25 (17–34)	30 (25–41)	25 (17–34)	< 0.001
NISS (median, IQR)	34 (25–50)	41 (33–50)	34 (24–48)	< 0.001
APACHE II (median, IQR)	14 (7–21)	17 (11–21)	13 (6–21)	< 0.001
GCS (median, IQR)	10 (3–15)	3 (3–14)	11 (3–15)	< 0.001
Systolic blood pressure (mean ± SD)	130.7 ± 27.6	128.5 ± 27.7	131.2 ± 27.5	0.0715
Hemoglobin (mean ± SD)	11.4 ± 4	11 ± 2.8	11.5 ± 4.2	0.005
CRP (mean ± SD)	13.74 ± 41.21	23.15 ± 62.96	11.94 ± 35.32	< 0.001
pH (mean ± SD)	7.31 ± 0.13	7.30 ± 0.15	7.32 ± 0.13	0.00632
PCT (mean ± SD)	1.23 ± 4.3	0.48 ± 0.56	1.15 ± 4.86	0.559
Lactate (mean, SD)	2.94 +- 2.53	2.94 +- 2.27	2.94 +- 2.58	0.943

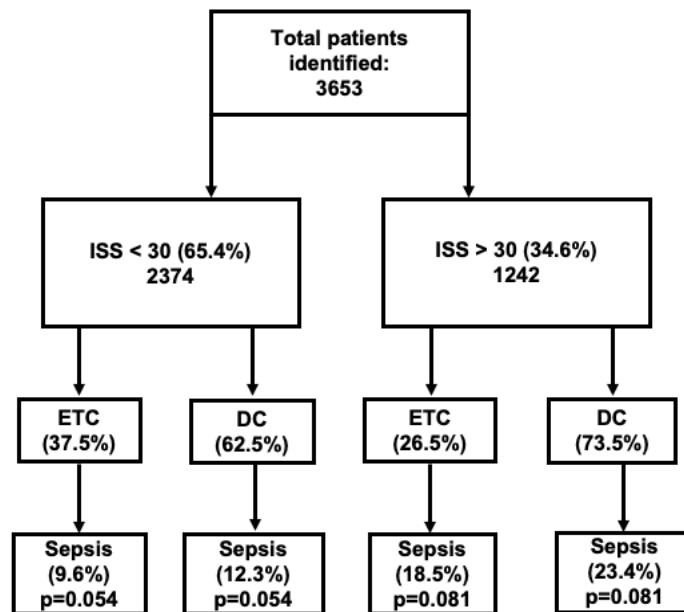


Figure 1: Appearance of sepsis depending on Injury Severity Score and trauma strategy

developed sepsis. In patients with an initial ISS < 30, sepsis tended to be more common in the DCS group (p = 0.054) (Table 2). In patients with an ISS > 30, there was the same tendency (p = 0.081).

A significantly higher incidence of sepsis was detected in patients with an ISS >30 (OR 2.21, p <0.001) and when DCS was used (OR 1.45, p <0.001) (Table 2).

Table 2: Summary of statistical analyses. Odds ratios represent the likelihood of sepsis based on Injury Severity Score and trauma strategy. CI = confidence interval.

	Odds Ratio	Lower 95% CI	Higher 95% CI	p-value
Sepsis				
ISS > 30	2.21	1.82	2.69	< 0.001
ISS < 30	0.452	0.372	0.549	< 0.001
Damage control	1.45	1.18	1.81	< 0.001
Early total care	0.687	0.554	0.85	< 0.001
Sepsis in patient cohort ISS <30				
Damage control	1.32	0.994	1.77	0.054
Early total care	0.76	0.564	1.01	0.054
Sepsis in patient cohort ISS >30				
Damage control	1.35	0.968	1.91	0.081
Early total care	0.74	0.525	1.03	0.081

Discussion

Sepsis, a life-threatening condition resulting from a dysregulated host response to infection, poses a significant challenge in the management of polytrauma patients. There is still a controversial discussion in trauma surgery when it comes to the treatment strategies of polytraumatized patients. Appropriate surgical management can reduce the appearance of complications significantly [8]. The Watson Trauma Pathway Explorer[®] opened the relevance for sepsis in polytraumatized patients admitted to our trauma bay [9]. In this study, the Watson Trauma Pathway Explorer[®] allowed a risk stratification for the incidence of sepsis in polytrauma patients according to ISS and surgical treatment type. The development of sepsis in patients after polytrauma is normally associated with a higher injury severity. Prior studies have detected risk factors beside the initial ISS that can affect the development of sepsis like male gender, a preexisting medical condition, the Glasgow Coma Scale (GCS) ≤ 8 or number of surgeries [10]. Our outcomes are concordant with these results. Multicenter studies from South Africa and Germany detected the appearance of sepsis in 14.4% and 12.4% [11,12]. Our results of patients developing sepsis (15%) showing similar numbers. Only a few studies investigated

the connection between the development of sepsis and the ISS. Nevertheless, the ISS is described as a potential predictor of sepsis after trauma [13,14]. In our study, we saw the appearance of sepsis in patients with an ISS between 25 and 41. Other studies detected that Patients with sepsis after polytrauma were injured more severely as indicated by a higher ISS (33 vs 25) [15]. Nevertheless, we were able to show that sepsis can also occur in patients with less severe injuries. Osborn et al. investigated the appearance of sepsis with respect to the initial ISS. Patients with mild injuries (ISS < 15) and moderate injuries (ISS 15-29) developed sepsis in 61% the two groups combined. The appearance of sepsis in patients with ISS > 30 was detected in 39% [16]. The treatment strategy was not described in the mentioned literature. Prior studies investigated cofactors which potentially influence the development of sepsis like pre-existing diseases with a higher risk of respiratory failures, kidney-or liver diseases [17]. With DCS, the risk of complications and the survival rate was improved [18,19]. In our study the occurrence of sepsis was seen in DCS and ETC with a similar frequency. These findings are initially counterintuitive, and are interpreted in light of the general patient health status (e.g. pre-existing diseases as mentioned above) apart from trauma. Although, patient condition could not be specified in this regard, the current study implies that DCS does not generally imply a lower risk for sepsis development, urging clinicians not to underestimate the context this technically risk-minimizing surgical treatment strategy. Yet, since polytrauma and sepsis are heterogenic in their clinical presence and respective treatment, a holistic approach should be taken to maximize treatment effects while minimizing complication for better outcomes in polytrauma patients. There are limitations to be mentioned: During the years of data collection and building this database, preexisting diseases and the patient specific American Society of Anesthesiology-Score (ASA) were not registered. The appearance of sepsis is only documented in binary Information, the beginning or duration is not detected. Additionally, any alterations in treatment guidelines that occurred after the commencement of data collection were not taken to account.

Conclusion

Sepsis after trauma remains a substantial challenge and further efforts to reduce the occurrence of complications are necessary. The development of sepsis is significantly more likely in patients with ISS > 30 and the use of DCS. Nevertheless, sepsis can occur in patients with less severe injuries, a lower ISS but potential preexisting diseases. On the other hand, DCS does not generally imply a lower risk for this complication.

Remark: *Watson Trauma Pathway Explorer* © by Ladislav Mica and IBM

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