Endothelial Glycocalyx Degradation Is Associated With Early Organ Impairment in Multiple Trauma Patients

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Research article

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Abstract

Background

Endothelial glycocalyx (EG) abnormal degradation were widely found in critical illness. However, data of EG degradation in multiple traumas is limited. We performed a study to assess the EG degradation and the correlation between the degradation and organ functions in multiple trauma patients.

Methods

A prospective observational study was conducted to enroll health participants (control group) and multiple traumas patients (trauma group) at a University affiliated hospital between Feb 2020 and Oct 2020. Syndecan1 (SDC1) and heparin sulfate (HS) were detected in serum sample of both groups. In trauma group, injury severity scores (ISS) and sequential organ failure assessments (SOFA) were calculated. Occurrences of acute kidney injury (AKI), trauma-induced coagulopathy (TIC) within 48 hours and 28-day all-cause mortality in trauma group were recorded. Serum SDC1 and HS levels were compared between two groups. Correlations between SDC1/HS and the indicators of organ systems in the trauma group were analyzed. ROC analyses were performed to assess the predictive value of SDC1 and HS for AKI, TIC within 48 hours, and 28-day mortality in trauma group.

Results

There were 45 multiple trauma patients and 15 healthy participants were collected, totally. SDC1 and HS were significantly higher in trauma group than in control group (69.39 [54.18–130.80] *vs*. 24.15 [13.89–32.36], 38.92 [30.47–67.96] *vs*. 15.55 [11.89–23.24], $P<0.001$, respectively). SDC1 and HS were both positively correlated with prothrombin time, activated partial thromboplastin time, EVLW, N-terminal pro-B-type natriuretic peptide, myoglobin, creatinine, lactic acid, interleukin-6, and tumor necrosis factor-α ($P<0.05$, respectively). SDC1 and HS were both negatively correlated with Ca^{2+}, anti-thrombin-III, PaO_2/FiO_2 ratio, pH and albumin ($P<0.05$, respectively). Trauma group was divided into high degradation group and low degradation group according to SDC1 median. High degradation group had more severe ISS, SOFA scores, worse organ functions (respiratory, kidney, coagulation and metabolic system), and higher incidence of hypothermia, acidosis and shock. ROC curve analyses demonstrated SDC1 can predict the occurrence risk of AKI, TIC within 48h, and 28-day mortality.

Conclusions

EG degradation was elevated significantly in multiple trauma patients, and the degradation was correlated with impaired respiratory, kidney, coagulation and metabolic systems. Serum SDC1 is a valuable predictive indicator of early TIC, AKI risk, and 28-day mortality in multiple trauma patients.

1. Background

Trauma remains a leading cause of morbidity and mortality worldwide and in China mainland[1,2]. Organ function impairments are common in trauma, especially in multiple traumas[3]. Endothelial glycocalyx (EG) is a layer of gel-like macromolecules widely distributed on the surface of vascular endothelium, mainly composed of proteoglycans (PGs) and glycosaminoglycans (GAGs). PGs, as the core proteins, are anchored on the surface of vascular endothelium, and the side chains of GAGs are covalently connected to it[4]. Highly sulfated GAGs side-chains are negatively charged and have electrical effects on plasma protein components such as albumin, fibrinogen, fibronectin, thrombomodulin, antithrombin-Ⅲ, peroxidase, and cell adhesion molecules[5].

EG maintains vascular homeostasis by regulating vascular tension and permeability, inhibiting thrombosis in microvessels and regulating leukocyte adhesion on endothelial cell surface[6–8].Currently, EG abnormal degradations were widely detected in sepsis, tumor and other critical illness[9,10]. However, data of EG degradation in multiple trauma patients, and the association with early organ function impairment are obscure. PGs include SDC1, phosphatidylinositol PG, basal membrane PG, among which SDC1 is the main component[11]. GAGs include HS, hyaluronic acid (HA) and dermatan sulfates, HS accounts for more than 50% of GAGs[12].

We selected SDC1 and HS as the representation of EG degradation, and conducted this study to detect EG degradation in multiple trauma patients, to fathom the correlation between EG degradation and early organ function impairment, and to demonstrate the predictive value of SDC1 and HS.

2. Materials And Methods

2.1. Study Design

A prospective observational study was designed to enroll multiple trauma patients (trauma group) and healthy participants (control group) in a university affiliated hospital between February 2020 and October 2020. Trauma group inclusion criteria were: ①two or more severe injuries caused by single reason in at least two areas of the body, ②admitted to hospital after trauma less than 24 hours. Exclusion criteria were: ①age < 16 years, or >75 years, ②malignant tumor, ③chronic hepatic or kidney diseases, ④undrained pneumothorax.

The study was approved by the Ethics Committee of the 2nd Affiliated Hospital of Nantong University (No.20190612), Jiangsu, China.
The written informed consent was obtained from individual, patient or patient's guardian.

2.2. Data Collection

Gender, age and body mass index (BMI) of both groups were documented. In trauma group, the reasons of injury were recorded, injury severity scores (ISS), sequential organ failure assessment scores (SOFA) were graded, occurrences of hypothermia (T < 35℃), shock, acidosis, mechanical ventilation (MV), and

traumatic brain injury (TBI) on admission were recorded, incidences of acute kidney injury (AKI), trauma induced coagulopathy (TIC) within 48 hours, and 28-day mortality were documented.

2.3. Laboratory Methods

Blood samples of both groups were centrifuged (2500g for 15 minutes at room temperature) and stored at −80℃. Double antibody sandwich ELISA tests were conducted by Enzyme calibration equipment (Thermo scientific Inc., Waltham, MA, USA), to detect SDC1 (EK1339, BOSTER Biological Tech., Wuhan, China), HS (E-EL-H2364c, Elabscience Biotechnology Co., Ltd., Wuhan, China), interleukin-6 (IL-6) (KE00139, Proteintech Group Inc., Rosemont, IL, USA), and tumor necrosis factor-α (TNF-α) (KE00068, Proteintech Group Inc., Rosemont, IL, USA), respectively. The tests were processed using unthawed samples within 6 months, and according to the manufacturer's directions. All samples and standards were assayed in duplicate. Standard laboratory tests were measured on admission in the clinical laboratory of the hospital as the following :Blood routine (leukocyte count [WBC], hemoglobin [Hb], and platelet count [PLT]), Liver and kidney function (total bilirubin [TBIL], albumin [ALB], urea nitrogen[BUN], and serum creatinine[Cr], coagulation function(fibrinogen[Fib], prothrombin time[PT], activated partial thromboplastin time[APTT], anti-thrombin - [AT-III], and D-dimer), cardiovascular indicators(troponin I[Tn I], myoglobin [Mb], and N-terminal pro-B-type natriuretic peptide[NT-pro BNP]), and infection index (procalcitonin [PCT]), Blood gas analysis (pH, PaO_2 ,PaO_2/FiO_2 ratio, HCO_3^-, Ca^{2+} ,and lactic acid[Lac]).

2.4. Definitions of AKI and TIC

AKI definition: Serum Cr level increased ≥ 26.4μmol/L compared with baseline, or increased over 1.5-times above baseline, or urine output < 0.5ml/kg/h for at least 6 hours[13].

TIC definition: Trauma induced prolonged coagulation time, PT > 18s or APTT > 60s[14].

2.5. Semi-quantitative measurements of extravascular lung water (EVLW)

Lung ultrasound were performed using convex array (frequency 3.5–4.5MHz, 2D mode, LOGIQ V1, GE Healthcare, Marlborough, MA, USA) to semi-quantitatively assess EVLW. Bilateral lungs were divided into eight regions[15] ,and the ultrasound clips were recorded. Each patient's clips were independently graded and calculated average according lung ultrasound score (LUSS)[16] by two physicians with certifications of Chinese Critical Ultrasound Study Group (CCUSG). Regions scored according to the worst sign in the region (A lines or ≤2 B lines, score 0; ≥3 well-spaced B lines, score 1; coalescent B lines, score 2; tissue-like pattern, score 3).

2.6. Statistical Analyses

Statistical analyses were performed with SPSS 19.0 (IBM Inc., Chicago, IL, USA). Normality of continuous variables were detected by Shapiro-Wilk test. Normal distributed variable was presented as mean± standard deviation (mean±SD), and non-normal distributed variable as median (interquartile range) (median [IQR]), and categorical variable as number (percentage), respectively. Mann-Whitney *U* tests were

performed for continuous variables comparisons between two groups. Categorical variables were compared by Fisher's exact test. The correlation between the two variables was analyzed by Spearman's correlation. The receiver operating characteristic (ROC) curves were graphed and area under the curve (AUC) were calculated to investigate the accuracy of indicators for predicting AKI, TIC within 48 hours, and 28-day mortality in trauma group. All statistical tests were two-tailed, and $P < 0.05$ was considered statistically significant.

3. Results

3.1. Demographics

The trauma group had a median ISS of 24 (17–29). Main causes of trauma were traffic injuries and falling injuries (53.3% and 31.1%, respectively). There were 16 incidences of AKI, 13 incidences of TIC within 48 hours, and 8 death cases within 28 days in trauma group, totally. Fifteen healthy participants were recruited as control group. There were none significant differences in age, gender and BMI between two groups ($P>0.05$, respectively). The serum SDC1and HS in trauma group were significantly higher compared with control group (69.39 [54.18–130.80] *vs*. 24.15 [13.89–32.36]; 38.92 [30.47–67.96] *vs*. 15.55 [11.89–23.24]; $P < 0.001$, respectively) (Table 1, Fig. 1).

3.2. Correlation between EG degradation and organ function indicators

Spearman's correlation analyses were conducted for EG degradation indicators (SDC1 and HS, respectively) with organ function indicators in trauma group, and found that serum SDC1 and HS were both positively correlated with PT, APTT, EVLW, Cr, NT-pro BNP, Mb, Lac, IL-6 and TNF-α, both negatively correlated with PaO_2/FiO_2 ratio, Ca^{2+}, AT-III, pH and ALB (Table 2). Besides, SDC1 was significantly positively correlated with HS (r=0.639, P<0.001).

3.3. Comparison within trauma group by different degree of degradation

Trauma group was divided into high degradation groups (SDC1 ≥ median) and low degradation groups (SDC1 < medians) by SDC1 median (69.39 ng/ml), comparing the differences between the two sets. The differences in general conditions and injury mechanisms were not statistically significant, and the high degradation group had higher ISS, SOFA scores, higher hypothermia, acidosis ratio, and higher inflammation indicators (IL-6, TNF-α), while respiratory (oxygen index, EVLW), liver (ALB), kidneys (BUN, Cr), bleeding and coagulation (Hb, PLT, Ca^{2+}, PT, APTT, AT-III) and metabolic indicators (pH, HCO_3^-, Lac) were worse than the low degradation group ($P < 0.05$, respectively, Table 3).

3.4. Predictive values of EG degradation indictors

The ROC curve analyses indicated SDC1 was a valuable predicter to AKI (AUC of 0.838, cutoff of 94.12 ng/ml, sensitivity of 75%, and specificity of 79.3%), TIC (AUC of 0.700, cutoff of 92.66 ng/ml, sensitivity of 76.9%, and specificity of 71.9%) within 48 hours, and 28-day mortality (AUC of 0.764, cutoff of 123.63 ng/ml, sensitivity of 75.0%, and specificity of 81.1%) ($P < 0.05$, respectively, Table 4).

4. Discussion

Under physiological conditions, the synthesis and degradation of EG are in dynamic balance[5,17]. At present, studies on abnormal EG degradation and impaired endothelial barrier have become an important direction of critical diseases[18,19].EG abnormal degradation was found in sepsis[20], tumor[21], burns[22] and major surgery[23] patients. Our study demonstrated that serum SDC1 and HS were significantly higher in trauma group patients than those in the control group, indicating that multiple trauma patients also had significant elevated EG degradation.

AKI has high morbidity and mortality in hospitalized patients, and various factors such as traumatic bleeding, fluid imbalance and inflammatory mediators are considered to be the potential pathogenesis of AKI[24]. In our study, SDC1 and HS were significantly correlated with renal function and metabolic indicators in trauma group patients, and the EG high degradation group had a higher incidence of AKI, indicating that abnormal EG degradation after trauma is a risk factor for early occurrence of AKI.

Post-traumatic bleeding is the primary cause of death for trauma patients, and about one-third of trauma patients combined TIC, which significantly increased the risk of death[25]. EG has the effects of inhibiting platelet adhesion on the endothelial surface, anti-microthrombosis and maintaining coagulation-anticoagulant balance. Post-traumatic bleeding, inflammation and other factors lead to abnormal degradation of EG, which may participate in the TIC mechanism[26]. This study revealed SDC1 and HS were both correlated with blood loss and coagulation indexes including Hb, PLT, PT, APTT, AT-III and Ca^{2+}. The high degradation group had significantly worse blood loss and coagulation indexes, and a higher incidence of TIC. SDC1 was a risk factor and predictive index for early TIC. Abnormal EG degradation may be involved in the pathophysiological process of TIC.

Due to the electrochemical properties of highly sulfated GAG side chain complex of EG, the permeability of EG to solute molecules is dependent on molecular size and its negative charge, which plays a role in isolating water and maintain the gel-like structure of EG, maintaining the low permeability of albumin and preventing the extravasation of intravascular liquid[12]. The increase of EVLW is the basic pathophysiological change in the early stage of lung injury. studies of isolated animal lungs and isolated human donor lungs indicated that LUSS[27] can accurately reflect the degree of extravascular lung water[28,29], and more clinical evidence supported the application of lung ultrasound in critical diseases[30]. This study found that SDC1 and HS were both positively correlated with EVLW and negatively correlated with oxygenation index. Compared with the low degradation group, high degradation group had higher EVLW and lower oxygenation index, suggesting that EG degradation was related to early lung injury after

trauma. The integrity of EG barrier structure and function is of great significance for the study of lung injury mechanism and lung protection after trauma[31].

This study showed that SDC1 and HS were significantly positively correlated with NT-pro BNP and Mb, but cardiac function after trauma was not evaluated, so the significance was not analyzed.

Studies have shown that abnormal expressions of IL-6, IL-8 and TNF-α may be involved in EG degradation[19,23]. We observed serum IL-6 and TNF-α levels were significantly elevated in trauma group, and the levels were both positively correlated with SDC1 and HS levels, suggesting that post-traumatic inflammatory responses may be involved in the abnormal EG degradation mechanism, although various pathways could be associated with EG degradation, theoretically.

It should be noted that there were also some limitations in our study. First, the selected cases were patients with multiple traumas admitted to EICU, which may have selection bias and information bias. Second, sample size was small, and the statistical results may not be robust enough. In consideration of the complexity of multiple traumas, meanwhile, transfusion and emergency surgery further increase the heterogeneity of the research objects, enhancing sample size and observing longer periods would be more meaningful to demonstrate the mechanism and influence of EG degradation in multiple trauma patients.

5. Conclusions

In summary, we demonstrated significant elevated EG degradation in multiple trauma patients, and the association between EG degradation indicators and multiple organ function impairment, including coagulation, kidney, metabolism and respiratory system. Our study indicated SDC1 is a valuable predicter of early TIC, AKI and 28-day mortality in multiple trauma patients.

Abbreviations

APTT	activated partial thromboplastin
AKI	acute kidney injury
ALB	albumin
AT-III	anti-thrombin-III
AUC	area under the curve
BUN	blood urea nitrogen
BMI	body mass index
CCUSG	Chinese Critical Ultrasound Study Group
Cr	creatinine
EG	endothelial glycocalyx
ELISA	Enzyme-linked immunosorbent assay
EVLW	extravascular lung water
Fib	fibrinogen
GCS	Glasgow coma score
GAG	glycosaminoglycan
Hb	hemoglobin
HS	heparan sulfate
ISS	injury severity score
IL-6	Interleukin-6
IQR	interquartile range
Lac	lactic acid
WBC	leukocyte count
LUSS	lung ultrasound score
MV	mechanical ventilation
Mb	myoglobin
NT-pro BNP	N-terminal pro-B-type natriuretic
PLT	platelet
PCT	procalcitonin
PG	proteoglycan

PT	prothrombin time
ROC	receiver operating characteristic
SOFA	sequential organ failure assessment
SD	standard deviation
SDC1	syndecan-1
TBIL	total bilirubin
TIC	trauma induced coagulopathy
TBI	traumatic brain injury
Tn I	troponin I
TNF-α	tumor necrosis factor-α

Declarations

Ethics approval and consent to participate

The study was approved by the Ethics Committee of the 2nd Affiliated Hospital of Nantong University (No.20190612), Jiangsu, China. The written informed consent was obtained from individual, patient or patient's guardian.

Consent for publication

Not applicable

Availability of data and material

All data generated or analyzed during this study are including in this article.

Competing interests

The authors declare no completing interests.

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Authors' contributions

F.Li and F. Qi contributed to the conception and design of the study; F. Qi, H. Zhou, and P. Gu performed the experiment, F. Qi and F. Li performed the data analyses and drafted the manuscript. BF. Zhu, JR. Chen,

and JS. Zhang contributed to manuscript revision. All authors commented on and approved the final manuscript.

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Tables

Table 1
Comparison of characteristics between trauma group and control group

Characteristic	Trauma group (*n*=45)	Control group (*n*=15)	*P* value
Demographic			
Age, mean±SD, year	56.07±15.20	51.73±14.41	0.278
Male, n (%)	25 (73.3%)	9 (60.0%)	0.296
BMI, mean±SD, kg/m^2	25.28±1.99	25.83±2.02	0.407
EG degradation			
SDC1, median (IQR), ng/ml	69.39 (54.18–130.80)	24.15 (13.89–32.36)	< 0.001
HS, median (IQR), ng/ml	38.92 (30.47–67.96)	15.55 (11.89–23.24)	< 0.001
Abbreviation: BMI, body mass index; EG, endothelial glycocalyx; SDC1, syndecan-1; HS, heparan sulfate.			
SD denotes standard deviation.			
IQR denotes interquartile range.			

Table 2
Correlation between EG degradation indicators and organ function in trauma group on admission

Characteristic	Serum SDC1		Serum HS	
	r	*P* value	*r*	*P* value
Demographic				
Age	0.209	0.169	-0.009	0.956
BMI	-0.141	0.356	-0.024	0.875
Score system				
GCS	0.020	0.897	-0.312	0.037
ISS	0.380	0.010	0.320	0.032
SOFA	0.267	0.076	0.296	0.048
Liver function				
TBIL	-0.089	0.562	0.065	0.670
ALB	-0.652	< 0.001	-0.373	0.012
Kidney function				
BUN	0.558	< 0.001	0.262	0.082
Cr	0.603	< 0.001	0.388	0.009
Respiratory function				
PaO_2	-0.318	0.033	-0.232	0.125
PaO_2/FiO_2 ratio	-0.458	0.006	-0.396	0.007
EVLW	0.515	< 0.001	0.344	0.021
Metabolism system				
pH	-0.513	< 0.001	-0.367	0.014
HCO_3^-	-0.471	0.001	-0.209	0.169
Lac	0.507	< 0.001	0.377	0.011

Abbreviations: EG, endothelial glycocalyx; SDC1, syndecan-1; HS, heparan sulfate; BMI, body mass index; GCS, Glasgow coma score; ISS, injury severity score; SOFA, sequential organ failure assessment; TBIL, total bilirubin; ALB, albumin; BUN, blood urea nitrogen; Cr, creatinine; EVLW, extravascular lung water; Lac, lactic acid; NT-pro BNP, N-terminal pro-B-type natriuretic peptide; Tn I, troponin I; Mb, myoglobin; Hb, hemoglobin; PLT, platelet; Fib, fibrinogen; PT, prothrombin time; APTT, activated partial thromboplastin time; AT-III, anti-thrombin; WBC, white blood cell; PCT, procalcitonin; IL-6, interleukin-6; TNF-α, tumor necrosis factor.

Characteristic	Serum SDC1		Serum HS	
	r	*P* value	*r*	*P* value
Cardiovascular				
NT-pro BNP	0.379	0.010	0.296	0.049
Tn I	0.289	0.054	0.289	0.054
Mb	0.481	0.001	0.455	0.002
Coagulation				
Hb	-0.468	0.001	-0.263	0.080
PLT	-0.314	0.036	-0.272	0.071
Ca^{2+}	-0.545	< 0.001	-0.398	0.007
Fib	-0.006	0.970	0.037	0.809
PT	0.502	< 0.001	0.511	< 0.001
APTT	0.592	< 0.001	0.600	< 0.001
AT-III	-0.752	< 0.001	-0.522	< 0.001
D-dimer	-0.063	0.683	0.122	0.424
Inflammation				
WBC	-0.059	0.700	0.148	0.331
PCT	0.437	0.003	0.285	0.057
IL-6	0.384	0.009	0.326	0.029
TNF-α	0.531	< 0.001	0.390	0.008

Abbreviations: EG, endothelial glycocalyx; SDC1, syndecan-1; HS, heparan sulfate; BMI, body mass index; GCS, Glasgow coma score; ISS, injury severity score; SOFA, sequential organ failure assessment; TBIL, total bilirubin; ALB, albumin; BUN, blood urea nitrogen; Cr, creatinine; EVLW, extravascular lung water; Lac, lactic acid; NT-pro BNP, N-terminal pro-B-type natriuretic peptide; Tn I, troponin I; Mb, myoglobin; Hb, hemoglobin; PLT, platelet; Fib, fibrinogen; PT, prothrombin time; APTT, activated partial thromboplastin time; AT-III, anti-thrombin; WBC, white blood cell; PCT, procalcitonin; IL-6, interleukin-6; TNF-α, tumor necrosis factor.

Table 3
Comparison within trauma group deviated by degradation degree

Characteristic	Trauma group (n=45)	EG degradation degree		*P* value §
		High degradation group (n=23)	Low degradation group (n=22)	
SDC1, median (IQR), ng/ml	69.39 (54.18–130.80)	128.74(95.50–163.96)	54.17(46.34–59.21)	< 0.001
HS, median (IQR), ng/ml	38.92 (30.47–67.96)	67.39(48.90–89.58)	31.22(27.07–36.44)	< 0.001
Demographic				
Age, mean±SD, year	56.0±15.20	57.26±16.21	54.82±14.33	0.510
Male, n (%)	25 (55.56%)	12(52.17%)	13(59.09%)	0.641
BMI, mean±SD, kg/m^2	25.27±1.99	24.94±2.06	25.61±1.91	0.212
Cause of injury				
Traffic, n (%)	22(48.89%)	12(52.17%)	10(45.46%)	0.768
Falling, n (%)	14(31.11%)	7(30.43%)	7(31.82%)	1.000
Score system				
GCS, median (IQR)	12.0(6.0–15.0)	12.0(5.0–15.0)	12.5(6.0–15.0)	0.982
ISS, median (IQR)	24.0(17.0–29.0)	26.0(22.0–29.0)	17.0(12.0–27.0)	0.011
SOFA, mean±SD	6.91±2.55	7.78±2.58	6.00±2.23	0.019
TBI, n (%)	21(46.67%)	8(34.78%)	13(59.09%)	0.139
Hypothermia, n (%)	14(31.11%)	12(52.17%)	2(9.09%)	0.003
Acidosis, n (%)	25(55.56%)	18(78.26%)	7(31.82%)	0.003
Shock, n (%)	28(62.22%)	18(78.26%)	10(45.45%)	0.033
MV, n (%)	36(80.00%)	21(91.30%)	15(68.18%)	0.071
AKI, n (%)	16(35.56%)	12(52.17%)	4(18.18%)	0.029
TIC, n (%)	13(28.89%)	10(43.48%)	3(13.64%)	0.047
28-d mortality, n (%)	8(17.78%)	6(26.09%)	2(9.09%)	0.243
Organ function				
TBIL, median (IQR), μmol/L	14.2(11.2–22.3)	14.2(10.9–22.1)	14.85(11.35–22.55)	1.00

Characteristic	Trauma group (n=45)	EG degradation degree		*P* value [§]
		High degradation group (n=23)	Low degradation group (n=22)	
ALB, median (IQR), g/L	30.6(21.9–37.3)	22.8(19.3–32.5)	34.6(30.58–41.33)	< 0.001
BUN, median (IQR), mmol/L	6.10(5.05–9.00)	8.80(5.70–11.20)	5.30(4.55–6.30)	0.002
Cr, median (IQR), μmol/L	72.1(52.3–103.3)	89.9(62.5–144.0)	55.0(46.73–75.85)	0.001
PaO_2, median (IQR), mmHg	112.8(89.5–155.1)	101.2(86.7–134.4)	131.7(92.1–168.7)	0.102
PaO_2/FiO_2 ratio, mean±SD	289.2±107.1	243.3±87.4	337.1±106.4	0.005
EVLW, median (IQR)	6.00(4.25–9.50)	9.00(6.00–10.50)	4.75(2.88v6.63)	0.001
Metabolism				
pH, mean±SD	7.30±0.12	7.25±0.13	7.36±0.07	0.003
HCO_3^-, median (IQR), mmol/L	20.3(15.8–22.4)	18.4(14.2–20.7)	21.75(19.65–23.10)	0.009
Lac, median (IQR), mmol/L	4.43(2.65–7.99)	6.60(4.21–9.60)	3.39(2.26–4.57)	0.003
Cardiovascular				
NT-pro BNP, median (IQR),	265.3(130.4–839.0)	723.6(163.1–1136.0)	209.8(119.1–430.2)	0.063
Tn I, median (IQR), μg/L	0.09(0.03–0.26)	0.22(0.01–1.14)	0.05(0.03–0.17)	0.108
Mb, median (IQR), μg/L	652.0(302.8–1141.0)	945.7(631.2–1890.0)	466.0(249.4–758.3)	0.010
Bleeding and coagulation				
Hb, mean±SD, g/L	105.22±20.36	95.61±18.98	115.27±16.86	0.001
PLT, mean±SD, $\times10^9$/L	151.09±51.93	132.52±53.18	170.50±43.75	0.021
Ca^{2+}, median (IQR), mmol/L	1.09(1.04–1.15)	1.06(0.99–1.11)	1.12(1.09–1.19)	0.001
Fib, median (IQR), g/L	1.50(1.13–1.89)	1.52(0.90–2.12)	1.48(1.28–1.81)	0.910

Characteristic	Trauma group (n=45)	EG degradation degree		*P* value §
		High degradation group (n=23)	Low degradation group (n=22)	
PT, median (IQR), s	13.2(11.9–16.9)	14.2(13.2–19.5)	12.2(11.2–13.2)	< 0.001
APTT, median (IQR), s	31.7(27.0–42.8)	37.0(31.7–51.6)	28.0(25.4–31.4)	< 0.001
AT-III, mean±SD, %	100.91±19.16	87.24±13.02	115.21±13.15	< 0.001
D-dimer, median (IQR),	15645(6494–43654)	15645(5385–63978)	15977(8311–36585)	0.874
Inflammation				
WBC, mean±SD, $\times 10^9$/L	15.29±5.80	15.09±6.76	15.50±4.73	0.750
PCT, median (IQR), ng/ml	1.34(0.41–5.38)	2.45(0.52–10.20)	0.90(0.23–2.05)	0.027
IL-6, median (IQR), ng/ml	281.71(160.97–507.79)	351.49(227.93–762.31)	234.56(117.71–382.92)	0.023
TNF-α, median (IQR), ng/ml	70.23(54.03–106.93)	95.32(64.90–131.48)	61.88(48.01–79.85)	0.002

Abbreviations: SDC1, syndecan-1; HS, heparan sulfate; BMI, body mass index; GCS, Glasgow coma score; ISS, injury severity score; SOFA, sequential organ failure assessment; TBI, traumatic brain injury; MV, mechanical ventilation; AKI, acute kidney injury; TIC, trauma induced coagulopathy; TBIL, total bilirubin; ALB, albumin; BUN, blood urea nitrogen; Cr, creatinine; EVLW, extravascular lung water; Lac, lactic acid; NT-pro BNP, N-terminal pro-B-type natriuretic peptide; Tn I, troponin I; Mb, myoglobin; Hb, hemoglobin; PLT, platelet; Fib, fibrinogen; PT, prothrombin time; APTT, activated partial thromboplastin time; AT-III, anti-thrombin; WBC, white blood cell; PCT, procalcitonin; IL-6, interleukin-6; TNF-α, tumor necrosis factor.

§ denotes the comparison between high degradation group and low degradation group.

Indicates mortality rate for 28 days after admission

IQR denotes interquartile range.

SD denotes standard deviation.

Hypothermia denotes patient with temperature below 35 degree Celsius.

Shock denotes patient with blood pressure maintained via infusions of dopamine, norepinephrine, epinephrine.

Table 4
Comparison of the predict value of SDC1, HS, ISS and SOFA on early AKI, TIC, and 28-day mortality

	AKI within 48 hours			TIC within 48 hours			28-day mortality		
	AUC	95% *CI*	*P* value	AUC	95% *CI*	*P* value	AUC	95% *CI*	*P* value
SDC1	0.838	0.720–0.957	< 0.001	0.700	0.514–0.885	0.038	0.764	0.543–0.984	0.021
HS	0.671	0.488–0.854	0.059	0.786	0.650–0.922	0.003	0.721	0.506–0.937	0.052
ISS	0.697	0.541–0.854	0.030	0.642	0.464–0.819	0.140	0.662	0.444–0.880	0.154
SOFA	0.635	0.463–0.806	0.138	0.662	0.506–0.818	0.091	0.583	0.406–0.760	0.467

Abbreviations: AKI, acute kidney injury; TIC, trauma induced coagulopathy; SDC1, syndecan-1; HS, heparan sulfate; BMI, body mass index; ISS, injury severity score; SOFA, sequential organ failure assessment.

AUC denotes area under the curve.