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Prognostic Significance of Markers of Endothelial Dysfunction in Case of Severe Combined Blunt Abdominal Trauma

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INTRODUCTION In case of polytrauma, an imbalance occurs between substances produced by the endothelium, the rheological properties of the blood are disrupted, the content of procoagulants increases, the permeability of the vascular wall increases, which contributes to thrombus formation and increased tissue hypoxia, and subsequently to the development of multiple organ failure, and, of course, affects the course of traumatic disease, the development of complications and mortality. However, specific markers of endothelial dysfunction and their levels, by which it is possible to reliably predict the course of traumatic disease in severe combined closed abdominal trauma for the appropriate pathogenetic treatment have not yet been determined.

AIM OF THE STUDY To determine the significance of some markers of endothelial dysfunction (C-reactive protein, von Willebrand factor, the number of desquamated endothelial cells in the blood) in combined blunt abdominal trauma to predict the likelihood of complications and adverse outcomes.

MATERIAL AND METHODS The main group consisted of 31 patients with severe combined blunt abdominal trauma, the comparison group consisted of 5 patients operated on for large ventral hernias. All patients underwent blood tests for C-reactive protein, von Willebrand factor, the number of desquamated endothelial cells.

RESULTS The level of all three considered markers of endothelial dysfunction in severe abdominal trauma significantly differs from that in operated non-traumatized patients, which allows differential diagnostics to be made between abdominal wall contusion and damage to internal organs; extremely high values suggest an unfavorable course of traumatic disease and a high probability of a fatal outcome.

CONCLUSION Taking into account that the development of traumatic disease is based on damage to the vascular endothelium, it is necessary to consider as prognostic indicators changes in the level of activity of C-reactive protein, von Willebrand factor, desquamated endothelial cells in patients with severe combined blunt abdominal trauma.

Keywords: endothelium, endothelial markers, endothelial dysfunction, combined blunt abdominal trauma, fatal outcome, postoperative complications, multiple organ failure

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CRP — *C*-reactive protein
DEC — desquamated (circulating) endothelial cells
ED — endothelial dysfunction
MFS-AS — military field surgery — condition upon admission — scale for assessing the severity of the condition of a victim with multiple injuries on admission
MFS-MT — military field surgery-mechanical trauma — scale for assessing the severity of the condition of a victim with mechanical trauma
MOF — multiple organ failure
SCBAT — severe combined blunt abdominal trauma
SIR — systemic inflammatory response
TBI — traumatic brain injury
vWF — von Willebrand factor

INTRODUCTION

The endothelium is the largest endocrine organ in the body [1], diffusely scattered together with the vessels throughout all tissues. Histologically, it consists of a single layer of cells at the border of the circulating blood and the vascular wall [1] with a total weight of 1.5 to 1.8 kg and an area of 4,000 to 7,000 m^2 [2, 3]. The endothelium performs its main functions due to biologically active substances produced by endothelial cells, which normally ensure the regulation of hemodynamic parameters, thromboresistance, participate in hemostasis processes, inflammation and angiogenesis [4]. "Maestro of blood circulation" is how the Nobel laureate British pharmacologist J. Vane called the endothelium [2].

When the function or structure of the endothelium is disrupted, the spectrum of biologically active substances secreted by it changes dramatically [1], endothelial dysfunction (ED) occurs, an imbalance between the production of vasodilating, antithrombogenic, antiproliferative factors on the one hand and vasoconstrictor, prothrombotic, proliferative producers of the endothelium on the other [1, 5], and increased secretion of aggregants, coagulants, vasoconstrictors begins [1]. Endothelial dysfunction underlies the formation of the syndrome of multiple organ dysfunction in critical conditions, including injuries [3, 6, 7].

Increased activity of the sympathoadrenal system, proportional to the severity of injury and traumatic shock, leads to activation and damage of the endothelium. This process is realized by exocytosis of catecholamines (primarily norepinephrine) and enzymatically active tissue plasminogen activator from *the nervi vasorum*, both into the vascular wall and directly into the microcirculatory bed [1, 3, 6, 7].

The release of catecholamines (in particular, the vasoconstrictor effect of norepinephrine) causes endothelial damage, glycocalyx cleavage, and deendothelialization of perfused vessels. Activated/damaged endothelium promotes thrombosis, causing occlusion of the microcirculatory bed. Together with increased capillary permeability, perivascular edema, and vasoconstriction, these vascular reactions provoke progressive tissue hypoperfusion, hypovolemia, hypoxic organ damage, and, in a vicious circle, increased sympathoadrenal activation. Increased hypothalamic-pituitary-adrenal axis tone also increases the level of circulating catecholamines in plasma [2, 3, 6, 7].

The corresponding endothelial and hemostatic changes depend on the severity of the injury and traumatic shock: from physiological hemostasis to hypercoagulation in mild injury, to hypocoagulation in moderate injury, and finally to hyperfibrinolysis in severe injury [3, 6, 7].

Biologically active substances produced by the endothelium serve as diagnostic criteria for various diseases [6, 8]. However, there are no clear biomarkers of ED that would allow identifying endothelial damage in the early stages of traumatic disease. We considered it appropriate to study the level of *C*-reactive protein (*CRP*), *von Willebrand factor (vWF*), the number of desquamated (circulating) endothelial

cells (DEC) in the blood as markers of ED in severe combined blunt abdominal trauma (SCBT), to determine its role in the outcome of the combined trauma and to identify the diagnostic and prognostic significance of the above markers. The choice of these markers was dictated by their high information content and the possibility of their study in almost any medical institution [5, 6, 9–12].

The aim of the study is to determine the significance of some markers of ED (*CRP*, *vWF*, DEC in the blood) in SCBT to predict the likelihood of complications and unfavorable outcome.

MATERIAL AND METHODS

A total of 31 patients admitted to hospital with SCBT were examined. The male to female ratio was 2.1:1. The average age of the victims was 36.2±2.06 years.

Mechanism of injury: road traffic accident 71%, catatrauma 13%, domestic 9.6%, compression by a heavy object in 6.4%.

All patients underwent blood testing for *CRP, vWF,* and DE. Blood was collected from the central or peripheral vein in the anti-shock operating room upon patient admission, and in operated patients before surgery, then on the 3rd and 5th days of hospital stay at 8 a.m. on an empty stomach. They formed the main group. The choice of such study periods was explained by the fact that, according to the concept of traumatic disease, the time interval of up to 6 days (the period of traumatic shock, the period of relative stabilization of vital functions, the period of maximum probability of complications) is the most dangerous in terms of the risk of complications and death [7]. According to the concept of E.K. Gumanenko et al. (2008): "...In the dynamics of development, traumatic disease is characterized by a consistent change in the leading role of certain typical pathological processes, which include both adaptive and pathological reactions. This is what determines its periodization, as well as the possible outcome" [7].

The comparison group consisted of patients who had undergone elective surgery for large ventral hernias of various locations (n = 5). The choice of such patients was determined by minimal microbial contamination (class I — clean surgery), which suggests a mild inflammatory response to surgical trauma and minor ED in the postoperative period. The groups were comparable in age. Blood was collected from a peripheral vein before surgery at 8 a.m. on an empty stomach, and on the 3rd and 5th days after surgery at the same time.

The severity of the inflammatory reaction was determined by the level *of CRP* using the quantitative solid-phase enzyme-linked immunosorbent assay using the Vector-Best test system (Vector-Best; Novosibirsk) [4, 6].

The content of von Willebrand factor (calculated as a percentage of the standard sample using a calibration curve; the amount contained in a 1:100 dilution of the plasma standard was taken as 100% of the *vWF content) was assessed using an indirect solid-phase enzyme-linked immunosorbent assay using the Technoclone* test system [4, 8].

In order to identify necrobiotic processes in the vascular endothelium, the amount of DEC circulating in the blood was determined using the method of *J. Hladovec* as modified by N.N. Petrishchev using phase-contrast microscopy, taking into account the ratio between the number of cells in the grid and the volume of the Goryaev chamber; when counting the number of endothelial cells, the result was multiplied by 10^4/l [6, 8].

Statistical processing was performed using the *Statistica v* 10.0 (*StatSoft,* USA) statistical software package. The data were expressed as *M±m,* where *M* is the mean value and *m* is the standard error of the mean. The statistical significance of differences was determined using the Mann – *Whitney U-test.* The criterion for statistical significance of the statistical difference in mean values was p <0.05.

RESULTS

The severity of injury in 54.8% of patients (n = 17) was 3.46±0.32 points on the MFS-MT scale (MFS-MT — military field surgery — mechanical trauma — a scale for assessing the severity of the victim's condition in mechanical trauma) with a possible fatal outcome of less than 25%; in 25.8% (n = 8) it was 8.41±0.51 points with a possible fatal outcome of less than 60%, and in 19.4% (n = 6) it was 18.19±2.03 points with a possible fatality of more than 70% (Table 1).

Table 1

Distribution of patients by severity of injuries according to the supplemented MFS-MT scale (M±m)

Supplemented MFS-MT scale, points, predicted mortality		Severity of damage in the examined patients (n = 31)	
		n	score ($M±m$)
1.2–6.2	severe, <25%	17	3.46±0.32
6.3–12.2	severe, <60%	8	8.41±0.51
12.3–30.2	extremely severe >70%	6	18.19±2.03

Note: MFS-MT – military field surgery-mechanical trauma – scale for assessing the severity of a victim's condition with mechanical trauma

All victims had injuries to several areas of the body: 2 areas – 8 patients, 3 areas – 12, and 4 areas – 11 (Table 2).

In cases of damage to 2 areas of the body, abdominal trauma was combined with traumatic brain injury (TBI) in 4 cases, with trauma to the musculoskeletal system in 2 cases, and with trauma to the chest in 2 cases.

Table 2

Distribution of patients by injury severity according to the supplemented MFS-MT scale depending on the number of damaged areas of the body

Severity of injury in examined patients, points	Severity of injury in examined patients depending on the number of damaged body areas, points		
	2 areas	3 areas	4 areas
3.46±0.32 (*n*=17)	2.99±0.39 (*n*=5)	3.45±0.48 (*n*=8)	4.14±0.62 (*n*=4)
8.41±0.51 (*n*=8)	7.80±0.20 (*n*=3)	8.10±1.10 (*n*=3)	10.50±0.53 (*n*=2)
18.19±2.03 (*n*=6)	–	16 (*n*=1)	18.63±2.52 (*n*=5)

Note: MFS-MT — military field surgery-mechanical trauma — scale for assessing the severity of a victim's condition with mechanical trauma

In cases of damage to 3 areas of the body, abdominal trauma was combined in 6 cases with trauma to the musculoskeletal system and chest; in 4 cases - with trauma to the musculoskeletal system and TBI, and in 2 cases - with trauma to the chest and TBI.

Injuries to 4 body regions occurred in 11 patients, abdominal trauma was combined with trauma to the musculoskeletal system, chest, and TBI.

The severity of the patients' condition upon admission was assessed using the supplemented MFS- scale [7] (military field surgery-state upon admission - a scale for assessing the severity of the condition of a victim with multiple trauma, developed by E.K. Gumanenko et al., 1997) (Table 3).

The condition upon admission was assessed as severe in 61.3% of patients (*n* = 19) and amounted to 26.47±0.62 points, extremely severe in 35.5% (*n*=11), which corresponded to 36.9±0.74 points, and critical in 3.2% (1 patient) - 47 points.

Table 3

Distribution of patients by severity of condition upon admission according to the supplemented MFS-AS scale (M±m)

Supplemented MFS-SA scale, points, severity of condition, incidence of complications and predicted mortality		Severity of damage in the examined patients	
		n	points (*M±m*)
22–32	severe, mortality up to 38%, complications up to 66%	19	26.47±0.62
33–46	extremely severe, mortality up to 84%, complications up to 90%	11	36.9±0.74
>46	critical, mortality 99-100%, complications 100%	1	47

Note: MFS-AS — military field surgery — state upon admission — scale for assessing the severity of the condition of a victim with multiple injuries upon admission

27 patients (87.1%) had abdominal organ injuries, 25 of whom were operated on. Spleen hematomas were detected in 2 patients, and conservative treatment was performed. In 4 patients, abdominal organ injuries were excluded during examination, and abdominal wall contusion was diagnosed.

We analyzed the dynamics of endothelial disfunction depending on the severity of the injuries (Table 4); the presence of damage to the abdominal organs or abdominal wall contusion and depending on the outcome of the injury.

An analysis of the dynamics of CRP, vWF, DE was carried out in patients with varying degrees of injury severity.

In trauma, the triggers of the systemic inflammatory response (SIR) are direct damage and subsequent tissue ischemia. Endo(auto)toxicosis begins 15–20 minutes after severe mechanical trauma. Damaged tissues are the source of hyperantigenemia, which growth, in addition to natural histohematic barriers, is prevented by humoral factors, to a greater extent by CRP and phagocytic cells [7].

C-reactive protein has the greatest neutralizing and opsonizing ability with respect to antigens, activates the complement system via the classical pathway. Its concentration in the systemic circulation increases many times during the implementation of a generalized inflammatory reaction [7]. In addition, CRP neutralizes bacterial toxins, inhibits phospholipases, binds the chemokine IL-8 and neutralizes its biological activity as a chemoattractant. Thus, CRP can regulate the severity of the inflammatory response, as well as limit nonspecific regulatory immunosuppression [7].

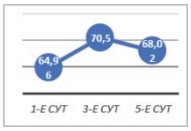
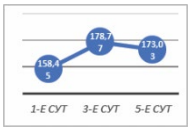
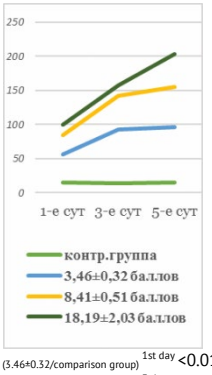
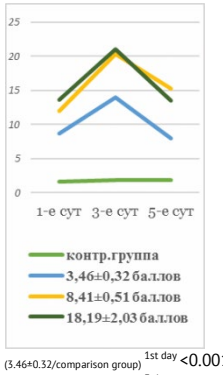
Our study determined the dynamics of changes in the level of the proinflammatory factor - CRP depending on the severity of the damage received as a non-specific protective mechanism in SCBAT.

In patients with injury severity of 3.46±0.32 points on the MFS-MT scale, an increase in the CRP level by 3.7 times was noted *already* on day 1 after injury, by days 3 and 5 the CRP level *continued* to grow, exceeded the values in the comparison group patients by 6.4 and 6.7 times and amounted to 55.81±8.98 mg/ml; 92.29±8.79 mg/ml; 96.6±12.73 mg/ml (p <0.05 compared to the comparison group), respectively. On day 3 after injury, the increase *in CRP* was 65.3%, on the 5th day - 73.1% in relation to the first day (p <0.05). The increase *in* CRB on the 5th day relative to the 3rd day was insignificant and statistically insignificant – by 4.7% (p >0.05).

With the injury severity of 8.41±0.51 points, the CRP level *was* 5.7; 9.9; 10.7 times higher than in the comparison group on the 1st, 3rd and 5th days, respectively, and was 84.94±11.21 mg/ml; 142.24±10.54 mg/ml; 154.78±28.27 mg/ml (p <0.05 compared to the comparison group). The increase in the CRP level *by* the 3rd day relative to the first in this category of patients was 67.45%, by the 5th day — 82.2% (p <0.05). On the 5th day of observation, the CRP level *remained* virtually unchanged compared to the 3rd day, being only 8.8% higher (p>0.05).

Table 4

Dynamics of endothelial dysfunction markers depending on the severity of injury according to the supplemented MFS-MT scale

MFS-MT, scorenumber of patients	*CRP*, mg/ml			*vWF*, %			ED, number of cells ×10 ^{4}/l		
	1st day	3rd day	Day 5	1st day	3rd day	Day 5	1st day	3rd day	Day 5
Group comparisons *n* =5	15.03±0.8	14.37±0.9	14.47±1.01	64.96±3.3	70.5±2.6	68.02±5.2	1.6±0.2	1.8±0.4	1.8±0.5
									
3.46±0.32 *n* = 17	55.81±8.98*	92.29±8.79*, **	96.6±12.73*, ***	158.45±4.7*	178.77±4.9*, **	173.03±6.03*, ***	8.7±0.72*	13.94±1.29*, **	7.94±0.96*, ****
									
8.41±0.51 *n* = 8	84.94±11.21*	142.24±10.54*, **	154.78±28.27*, ***	173.37±5.58*	204.8±13.03*, **	228.45±21.16*, ***	12±1.75*	20.37±2.25*, **	15.25±2.8*
									
18.19±2.03 *n* =6	99.36±9.95*	157.61±11.69*, **	203.67±21.15*,***,****	190.58±14.3*	214.4±16.1*	229.43±18.75*	13.66±2.2*	21±0.93*, **	13.5±2.3*, ****
									
Dynamics of endothelial dysfunction markers depending on the severity of injury according to the supplemented VPK-MT scale in the form of a diagram, *p* is the level of statistical significance	 $p_{(3.46\pm0.32/\text{comparison group})}^{1\text{st day}}$ <0.01 $p_{(3.46\pm0.32/\text{comparison group})}^{3\text{ days}}$ <0.001 $p_{(3.46\pm0.32/\text{comparison group})}^{5\text{th day}}$ <0.001 $p_{(8.41\pm0.51/3.46\pm0.32)}^{1\text{st day}}$ =0.055 $p_{(8.41\pm0.51/3.46\pm0.32)}^{3\text{ days}}$ <0.05 $p_{(8.41\pm0.51/3.46\pm0.32)}^{5\text{th day}}$ =0.074 $p_{(18.19\pm2.03/8.41\pm0.51)}^{1\text{st day}}$ =0.357 $p_{(18.19\pm2.03/8.41\pm0.51)}^{3\text{ days}}$ = 0.350 $p_{(18.19\pm2.03/8.41\pm0.51)}^{5\text{th day}}$ =0.194			 $p_{(3.46\pm0.32/\text{comparison group})}^{1\text{st day}}$ <0.001 $p_{(3.46\pm0.32/\text{comparison group})}^{3\text{ days}}$ <0.001 $p_{(3.46\pm0.32/\text{comparison group})}^{5\text{th day}}$ < 0.001 $p_{(8.41\pm0.51/3.46\pm0.32)}^{1\text{st day}}$ =0.053 $p_{(8.41\pm0.51/3.46\pm0.32)}^{3\text{ days}}$ = 0.075 $p_{(8.41\pm0.51/3.46\pm0.32)}^{5\text{th day}}$ <0.05 $p_{(18.19\pm2.03/8.41\pm0.51)}^{1\text{st day}}$ =0.287 $p_{(18.19\pm2.03/8.41\pm0.51)}^{3\text{rd day}}$ = 0.652 $p_{(18.19\pm2.03/8.41\pm0.51)}^{5\text{th day}}$ =0.973			 $p_{(3.46\pm0.32/\text{comparison group})}^{1\text{st day}}$ <0.001 $p_{(3.46\pm0.32/\text{comparison group})}^{3\text{ days}}$ <0.001 $p_{(3.46\pm0.32/\text{comparison group})}^{5\text{th day}}$ <0.001 $p_{(8.41\pm0.51/3.46\pm0.32)}^{1\text{st day}}$ =0.095 $p_{(8.41\pm0.51/3.46\pm0.32)}^{3\text{ days}}$ <0.05 $p_{(8.41\pm0.51/3.46\pm0.32)}^{5\text{th day}}$ <0.05 $p_{(18.19\pm2.03/8.41\pm0.51)}^{1\text{st day}}$ =0.567 $p_{(18.19\pm2.03/8.41\pm0.51)}^{3\text{ days}}$ = 0.800 $p_{(18.19\pm2.03/8.41\pm0.51)}^{5\text{th day}}$ =0.638		

Notes: * — statistically significant in relation to the comparison group; **—differences with data on days 1 and 3, ***—differences with data on days 1 and 5, ****—differences with data on days 3 and 5 p <0.05. MFS–MT — military field surgery–mechanical trauma — a scale for assessing the severity of a victim's condition with mechanical trauma; DE - desquamated (circulating) endothelial cells; CRP—C-reactive protein; vWF - von Willebrand factor

CRP level was 18.19±2.03 points higher than in the comparison group by 6.6; 11; 14 times on the 1st, 3rd and 5th days, respectively, and was 99.36±9.95 mg/ml, 157.61±11.69 mg/ml, 203.67±21.15 mg/ml (p <0.05 compared to the comparison group). The increase in the CRP level *by* the 3rd day relative to the 1st in this category of patients was 58.6%, by the 5th - 105% (p <0.05). On the 5th day, the CRP level *increased* by 29.2% relative to the 3rd day (p <0.05).

The endothelium, producing biologically active substances, normally participates in the processes of hemostasis, which is carried out with the involvement of three main components: blood cells, plasma enzymatic systems and the endothelium of the vascular wall itself. Damaged endothelium has the ability to change its antithrombogenic potential to thrombogenic in combination with the depression of antithrombogenic mechanisms [7].

Severe combined trauma is characterized by the simultaneous activation of the blood coagulation system and a decrease in the antithrombin potential of the vascular wall, which is the main pathogenetic mechanism of disruption of the physiological balance between the coagulation and anticoagulation systems of the blood with activation of the first, depletion and depression of the second [7].

When the vascular wall is damaged, the endothelial cells activate the processes of synthesis and release of substances into the vascular bed that activate the processes of hemocoagulation. Von Willebrand factor (*vWF*) is a glycoprotein that plays a major role in the process of platelet adhesion to the vascular wall. When endothelial cells die, the subendothelium is exposed, containing a large amount of collagen, in contact with which platelet adhesion and aggregation occurs, while *vWF* forms a kind of bridge between collagen and platelet receptors in the presence of Ca^{2+} ions . Systemic damage to the vascular endothelium, the acquisition of thrombogenic properties by it triggers the coagulation cascade along the external and internal pathways. The consequence of these processes is the block of the microcirculatory bed by cellular aggregates, fibrin threads and microthrombi, which, given the systemic damage to the vascular endothelium and the reduction of its antithrombogenic properties, underlies the disruption of microcirculation and the formation of multiple organ failure syndrome [7].

In patients with injury severity of 3.46±0.32 points, the *vWF level* was increased by 2.43; 2.52; 2.54 times (p <0.05) on the 1st, 3rd and 5th days, respectively, compared with the comparison group indicator and was 158.45±4.7%, 178.77±4.9% and 173.03±6.03%. The increase in *vWF concentration* by the 3rd day relative to the 1st in this category of patients was 12.82%, by the 5th - 9.2% (p <0.05). On the 5th day of observation, the *vWF level* remained virtually unchanged relative to the 3rd day.

With the injury severity of 8.41±0.51 points, the *vWF level,* compared to that of the comparison group patients, was increased by 2.67; 2.9; 3.36 times (p <0.05) on the 1st, 3rd and 5th days, respectively, and amounted to 173.37±5.58%, 204.8±13.03% and 228.45±21.16%. The increase in *vWF concentration* by the 3rd day relative to the 1st in this category of patients was 18.12%, by the 5th day — 31.77% (p <0.05). On the 5th day of observation, no significant increase in the *vWF level was noted* relative to the value obtained on the 3rd day.

In extremely severe trauma of 18.19±2.03 points, the *vWF level,* compared to that of the comparison group patients, was increased by 2.93; 3.04; 3.37 times (p<0.05) on the 1st, 3rd and 5th days, respectively, and amounted to 190.58±14.3%, 214.4±16.01% and 229.43±18.76%. The increase in *vWF concentration* by the 3rd day relative to the 1st in this category of patients was 12.49%, by the 5th day — 20.38% (p >0.05). On the 5th day of observation, the *vWF level* remained virtually unchanged relative to the 3rd day.

Damage to the vascular endothelium in combined trauma is nonspecific and manifests itself in the form of reactive, dystrophic and necrobiotic changes in endothelial cells. The changes are accompanied by focal or total destruction of cells, which significantly complicates microcirculation and promotes aggregation of blood cells [7].

With an injury severity of 3.46±0.32 points, the amount of DE in relation to the indicator of patients in the comparison group on the 1st, 3rd and 5th days was increased by 5.4; 7.7; 4.4 times (p <0.05), respectively. On the 1st day, the amount of DE was $8.7±0.72×10^4$/l. The increase by the 3rd day was 60.2% (p<0.05) ($13.9±1.29×10^4$/l), by the 5th day in relation to the 1st day their amount decreased by 8.7% (p>0.05) ($7.94±0.96×10^4$/l). On the 5th day, the amount of DE decreased by 43% (p <0.05) in comparison with the indicator obtained on the 3rd day.

In patients with an injury severity score of 8.41±0.51 points, the amount of DE compared to the values in the comparison group on the 1st, 3rd and 5th days was 7.5; 11.3; 8.47 times higher, respectively (p<0.05). On the 1st day, the amount of DE increased to $12±1.75×10^4$/l. The increase by the 3rd day in relation to the first was 69.75%, which was $20.37±2.25×10^4$/l (p <0.05), on the 5th day - 27.08% (p>0.05) ($15.25±2.8×10^4$/l). On the 5th day, the number of DE relative to 3 decreased by 25.2% (p>0.05), but remained higher than the indicators on the 1st day.

In extremely severe trauma of 18.19±2.03 points, the number of DE in relation to the indicators of the comparison group on the 1st, 3rd and 5th days was 8.5; 11.7; 7.5 times higher (p <0.05). On the 1st day

after the injury, the number of DE in this category of patients was 13.66±2.2×10 ^{4}/l, on the 3rd it increased to 21±0.93×10 ^{4}/l, the increase was 53.73% *(p* <0.05), by the 5th day the indicator did not differ from the values obtained on the 1st day (13.5±2.3×10 ^{4}/l), but was significantly higher than those of the physiological norm. On the 5th day, the number of DE in comparison with the 3rd day decreased by 35.71% *(p*<0.05).

In case of combined trauma, abdominal organ damage was diagnosed in 27 victims. Isolated abdominal organ damage was observed in 19 patients: liver, spleen, mesentery ruptures, and in 1 case, rectal rupture. Of these, 7 patients had intra-abdominal bleeding: 1000 ml in 3 patients, 1500 ml in 1, 2000 ml in 3. Multiple damage to parenchymatous organs and mesentery was detected in 8 patients, of which 1 had a small intestine rupture, and in one case, a diaphragm and liver rupture. Bleeding of more than 1000 ml was observed in 1 case.

In patients with combined trauma and abdominal wall contusion, the increase in the CRP level *on* the first day after trauma relative to the comparison group was not statistically significant and amounted to 40.1±15.11 mg/ml *(p*>0.05) (Table 5). By the 3rd and 5th days, the CRP level *increased,* exceeding the values in the comparison group patients by 5 and 6.4 times and amounted to 71.8±18.17 mg/ml and 93.3±26.03 mg/ml (*p*<0.05), respectively. The increase *in* CRP on the 3rd and 5th days relative to the first was statistically insignificant.

In patients with combined trauma and abdominal wall contusion, the vWF level was increased by 2.37; 2.5; 2.58 times (p<0.05) on the 1st, 3rd and 5th days, respectively, compared with the comparison group and was 153.95±10.91%, 176.45±3.38%, 175.85±10.14%. On the 3rd and 5th days of observation, the vWF level did not change statistically significantly compared to the 1st day.

In patients with combined trauma and abdominal wall contusion, the amount of DE in relation to the comparison group on the 1st, 3rd and 5th days was increased by 6.0; 9.1; 4.4 times (p<0.05), respectively, and was 9.75±1.18×10^4/l; 16.5±1.84×10^4/l; 8.0±1.47×10 4 /l. The increase by the 3rd day was 69.2% (*p*<0.05), by the 5th day in relation to the 1st their amount decreased by 18% (*p*>0.05). On the 5th day, the amount of DE decreased by 51.5% *(p*<0.05) compared to the 3rd day.

In patients with combined trauma and damage to abdominal organs, a 5-fold increase in the CRP level was noted already on the 1st day after injury; by the 3rd and 5th days, the CRP level continued to grow and exceeded the values in the comparison group of patients by 8.7 and 9.89 times and amounted to 76.19 ± 7.8 mg / ml; 125.5 ± 7.8 mg / ml; 143.1 ± 15.6 mg / ml (p < 0.05). On the 3rd day after injury, the increase in CRP was 64.9%, on the 5th day - 88% in relation to the 1st day (p < 0.05). The increase in CRP on the 5th day relative to the 3rd was insignificant and statistically insignificant - by 14% (p > 0.05).

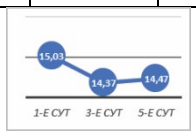
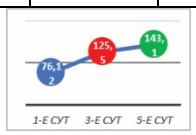
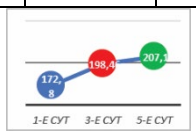
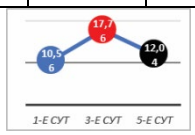
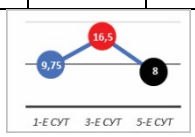
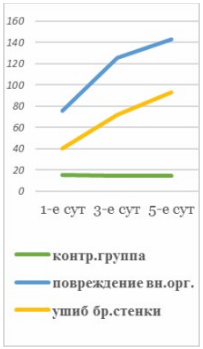
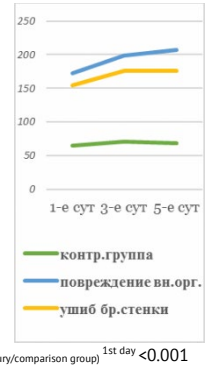
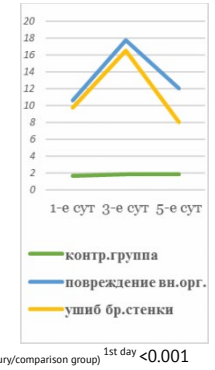
In patients with combined trauma and damage to abdominal organs, the *vWF level* was increased by 2.66; 2.8; 3.04 times (*p*<0.05) on the 1st, 3rd and 5th days, respectively, compared with the comparison group indicator and was 172.8±5.0%, 198.46±6.8% and 207.11±10.3%. The increase in *vWF concentration* by the 3rd day relative to the first in this category of patients was 14.85%, by the 5th - 19.85% (*p* <0.05). On the 5th day of observation, the *vWF level* remained virtually unchanged compared to the 3rd day.

In patients with combined trauma and damage to abdominal organs, the amount of DE in relation to the indicator of patients in the comparison group on the 1st, 3rd and 5th days was increased by 6.6; 9.9; 6.7 times (*p* <0.05), respectively. On the 1st day, the amount of DE was 10.96±0.98×10 ^{4}/l. The increase by the 3rd day was 68.2% (*p* <0.05) (17.76±1.3×10 ^{4}/l), by the 5th day in relation to the 1st their amount remained virtually unchanged (*p*>0.05) and was 12.04±1.4×10 ^{4}/l. On the 5th day, the amount of DE decreased by 32.31% (*p*<0.05) compared to the indicator obtained on the 3rd day. Uncomplicated course of traumatic disease in patients with damage to abdominal organs was observed in 14 patients. Three had multiple injuries to abdominal organs: liver + small intestine; spleen + mesentery of the small intestine; diaphragm + liver; nine had isolated injuries: liver - 4, spleen - 4, mesentery of the small intestine - 1; abdominal wall contusion - 2. The volume of intra-abdominal bleeding ranged from 0.3 to 1.0 l. Blood reinfusion was performed in 3 cases.

In patients with concomitant abdominal trauma without complications during traumatic disease, the CRP level *was* 3.6; 6.6; 4.8 times higher on the 1st, 3rd and 5th days compared to the comparison group patients and was 54.77±10.2 mg/ml, 94.33±8.92 mg/ml, 69.78±11.29 mg/ml (*p* <0.05 compared to the comparison group), respectively (Table 6). The increase *in* CRP by the 3rd day relative to the 1st in this category of victims was 72% (*p* <0.05), on the 5th day of observation, the CRP level *relative* to the 1st (by 27%) and 3rd (by 26%) did not change statistically significantly (*p* >0.05).In patients with concomitant abdominal trauma in the absence of complications, the *vWF level* was increased by 2.44; 2.48; 2.38 times (*p* <0.05) on the 1st, 3rd and 5th days, respectively, compared with the comparison group indicators and was 158.56±5.85%, 175.0±5.85% and 162.52±3.49%, respectively. The increase in *vWF concentration* by the 3rd day relative to the first in this category of patients was 10.37% (*p<0.05). On the 5th day of observation, the vWF* level relative to the 1st remained virtually unchanged. By the 5th day relative to the 3rd, the *vWF level* decreased by 7.14% (*p* <0.05).

Table 5

Dynamics of markers of endothelial dysfunction depending on the presence of damage abdominal organs or abdominal wall contusion and in the comparison group

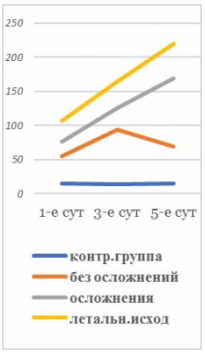
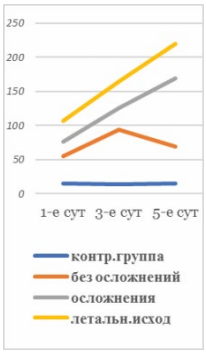
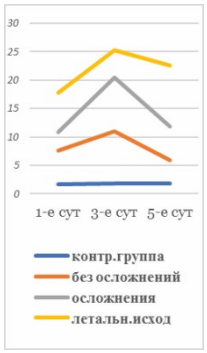
Nature of injuries, groups and number of patients	*CRP*, mg/ml			*vWF*, %			DE, number of cells ×10 ^{4}/l		
	1st day	3rd day	5th day	1st day	3rd day	5th day	1st day	3rd day	5th day
Comparison group *n* =5	15.03±0.8	14.37±0.9	14.47±1.08	64.96±3.3	70.5±2.58	68.02±5.15	1.6±0.22	1.8±0.44	1.8±0.53
									
Damage to abdominal organs *n* =27	76.12±7.8*	125.5±7.8*, **	143.1±15.6*, ***	172.8±5.0*	198.46±6.8*, **	207.11±10.3*, ***	10.56±0.98*	17.76±1.3*, **	12.04±1.4*, ****
									
Abdominal wall contusion *n* =4	40.1±15.11	71.8±18.17*	93.3±26.03*	153.95±10.91*	176.45±3.38*	175.85±10.14*	9.75±1.18*	16.5±1.84*, **	8±1.47*, ****
									
Dynamics of endothelial dysfunction markers depending on the presence of abdominal organ damage or abdominal wall contusion and in the comparison group in the form of a diagram, *p* is the level of statistical significance	 $p_{(injury/comparison\ group)}^{1st\ day} = 0.149$ $p_{(injury/comparison\ group)}^{3\ days} < 0.05$ $p_{(injury/,\ comparison\ group)}^{5th\ day} < 0.05$ $p_{(damage\ to\ internal\ organs/comparison\ group)}^{1st\ day} < 0.001$ $p_{(damage\ to\ internal\ organs/comparison\ group)}^{3\ days} < 0.001$ $p_{(damage\ to\ internal\ organs/comparison\ group)}^{5th\ day} < 0.001$ $p_{(damage\ to\ internal\ organs/contusion)}^{1st\ day} < 0.05$ $p_{(damage\ to\ internal\ organs/contusion)}^{3\ days} < 0.05$ $p_{(damage\ to\ internal\ organs/contusion)}^{5th\ day} = 0.112$			 $p_{(injury/comparison\ group)}^{1st\ day} < 0.001$ $p_{(injury/comparison\ group)}^{3\ days} < 0.001$ $p_{(injury/comparison\ group)}^{5th\ day} < 0.01$ $p_{(damage\ to\ internal\ organs/comparison\ group)}^{1st\ day} < 0.001$ $p_{(damage\ to\ internal\ organs/comparison\ group)}^{3\ days} < 0.001$ $p_{(damage\ to\ internal\ organs/comparison\ group)}^{5th\ day} < 0.001$ $p_{(damage\ to\ internal\ organs/contusion)}^{1st\ day} = 0.127$ $p_{(damage\ to\ internal\ organs/contusion)}^{3\ days} < 0.01$ $p_{(damage\ to\ internal\ organs/contusion)}^{5th\ day} < 0.05$			 $p_{(injury/comparison\ group)}^{1st\ day} < 0.001$ $p_{(injury/comparison\ group)}^{3\ days} < 0.001$ $p_{(injury/comparison\ group)}^{5th\ day} < 0.001$ $p_{(damage\ to\ internal\ organs/comparison\ group)}^{1st\ day} < 0.001$ $p_{(damage\ to\ internal\ organs/comparison\ group)}^{3\ days} < 0.001$ $p_{(damage\ to\ internal\ organs/comparison\ group)}^{5th\ day} < 0.001$ $p_{(damage\ to\ internal\ organs/contusion)}^{1st\ day} = 0.602$ $p_{(damage\ to\ internal\ organs/contusion)}^{3\ days} = 0.580$ $p_{(damage\ to\ internal\ organs/contusion)}^{5th\ day} = 0.056$		

Notes: * — statistically significant in relation to the comparison group; ** — differences with the data of the 1st and 3rd days (red on the diagram), *** — differences with the data of the 1st and 5th days (green on the diagram), **** — differences with the data of the 3rd and 5th days (black on the diagram); p <0.05. DE - desquamated (circulating) endothelial cells; CRP—C-reactive protein; vWF - von Willebrand factor

In patients with concomitant abdominal trauma in the absence of complications, the amount of DE in relation to the indicator of patients in the comparison group on the 1st, 3rd and 5th days was increased by 4.7; 6.1; 3.25 times (p<0.05), respectively. On the 1st day, the amount of DE was 7.57±0.36×10 ^{4}/l. The increase by the 3rd day was 45.3% (p <0.05) (11.0±0.58×10 ^{4}/l), by the 5th day in relation to the 1st day, their amount decreased by 22.6% (p <0.05) and was 5.86±0.2×10 ^{4}/l. On the 5th day, the amount of DE decreased by 46.73% (p<0.05) compared to the indicator obtained on the 3rd day.

Table 6

Dynamics of markers of endothelial dysfunction depending on the outcome of the traumatic disease

Injury outcome, patient groups and numbers	*CRP*, mg/ml			*vWF*, %			DE, number of cells ×10 ^{4}/l		
	1st day,	3rd day	Day 5	1st day	3rd day	5th day	1st day	3rd day	Day 5
Comparison group *n* =5	15,027±0,81	14.37±0.85	14.47±1.08	64.96±3.3	70.5±2.58	68.02±5.15	1.6±0.22	1.8±0.44	1.8±0.53
Without complications *n* = 14	54.77±10.2*	94.33±8.92*,**	69.78±11.29*	158.56±5.85*	175.0±5.85*,**	162.52±3.49*,****	7.57±0.36*	11±0.58*,**	5.86±0.2*,***,****
Complications n=12	76.75±8.48*	125.93±12.98*,**	168.9±12.26*,***,****	168.46±3.35*	188.69±4.32*,**	200.95±3.99*,***,****	10.91±1.09*	20.5±0.62*,**	11.91±0.95*,****
Fatalities *n* =5	107.26±12.51*	164.21±6.1*,**	219.98±17.92*,***,****	196.54±16.99*	249.9±12.06*,**	291±13.1*,***,****	17.8±1.02*	25.2±0.66*,**	22.6±0.87*,***,****
Dynamics of endothelial dysfunction markers depending on the outcome of traumatic disease in the form of diagrams, *p* is the level of statistical significance	 $p_{(donkey/no\ donkey)}^{1\ day} = 0.111$ $p_{(donkey/no\ donkey)}^{3\ days} = 0.056$ $p_{(donkey/no\ donkey)}^{5\ days} < 0.001$ $p_{(years,\ outg/without\ donkey)}^{1\ day} < 0.01$ $p_{(years,\ outg/without\ donkey)}^{3\ days} < 0.001$ $p_{(years,\ outg/without\ donkey)}^{5\ days} < 0.001$ $p_{(years,\ original/deficit)}^{1\ day} = 0.063$ $p_{(years,\ in/d)}^{3\ days} < 0.05$ $p_{(years,\ in/d)}^{5\ days} < 0.05$	 $p_{(donkey/no\ donkey)}^{1\ day} = 0.155$ $p_{(donkey/no\ donkey)}^{3\ days} = 0.072$ $p_{(donkey/no\ donkey)}^{5\ days} < 0.001$ $p_{(years,\ outgoing/without\ donkey)}^{1\ day} = 0.050$ $p_{(years,\ outg/without\ donkey)}^{3\ days} < 0.001$ $p_{(years,\ outg/without\ donkey)}^{5\ days} < 0.001$ $p_{(years,\ outg/d)}^{1\ day} = 0.127$ $p_{(years,\ in/d)}^{3\ days} < 0.001$ $p_{(years,\ int/d)}^{5\ days} < 0.001$	 $p_{(osl/no\ osl)}^{1\ day} < 0.01$ $p_{(donkey/no\ donkey)}^{3\ days} < 0.001$ $p_{(donkey/no\ donkey)}^{5\ days} < 0.001$ $p_{(years,\ outg/without\ donkey)}^{1\ day} < 0.001$ $p_{(years,\ outg/without\ donkey)}^{3\ days} < 0.001$ $p_{(years,\ outg/without\ donkey)}^{5\ days} < 0.001$ $p_{(years,\ in/d)}^{1\ day} < 0.001$ $p_{(years,\ in/d)}^{3\ days} < 0.001$ $p_{(years,\ int/d)}^{5\ days} < 0.001$

Notes: * — statistically significant in relation to the comparison group; ** — differences with data on days 1 and 3; *** — differences with data on days 1 and 5; **** — differences with data on days 3 and 5 p <0.05. DE - desquamated (circulating) endothelial cells; CRP—C-reactive protein; vWF - von Willebrand factor

Twelve patients had complicated course of traumatic disease. They had the following intra-abdominal injuries: 2 — diaphragm rupture, 1 — spleen rupture, 3 — liver rupture, 2 — abdominal wall contusion, 4 — multiple injuries — liver + small intestine; liver + spleen; liver + mesentery; liver + pancreas. In 2 patients, the hemoperitoneum volume was 1.5 and 2.0 l. On the 5-6th day, pulmonary complications developed in 9 people: purulent endobronchitis — in 4, pneumonia — in 4 and in 1 — respiratory distress syndrome; chest injuries occurred in 7 cases. Reactive hepatitis developed in one patient on the 5th day after injury; one had acute adhesive small intestinal obstruction on the 6th day and one had a liver abscess detected on the 10th day of the postoperative period with subsequent formation of a biliary fistula.

In the group of patients with complicated traumatic disease, the CRP level *was* 5.1; 8.76; 11.67 times higher than in the comparison group on the 1st, 3rd and 5th days, respectively, and was 76.75±8.48 mg/ml; 125.93±12.98 mg/ml; 168.9±12.26 mg/ml (p <0.05). The increase in the CRP level *by* the 3rd day relative to the 1st in this category of patients was 64%, and by the 5th day — 120% (p<0.05). On the 5th day of observation, an increase in the CRP level by 34.1% was also noted *relative* to the 3rd day (p < 0.05).

In patients with complicated traumatic disease, the *vWF level* was increased by 2.59; 2.67; 2.95 times (p <0.05) on the 1st, 3rd and 5th days, respectively, compared with the comparison group indicator and was 168.46±3.35%, 188.69±4.32% and 200.95±3.99%. The increase in *vWF concentration* by the 3rd day relative to the 1st in this category of patients was 12.0% (p <0.05), by the 5th relative to the first 19.28% (p <0.05) and by the 5th relative to the 3rd 6.49% (p <0.05).

In patients with complicated traumatic disease, the amount of DE in relation to the comparison group indicator on the 1st, 3rd and 5th days was increased by 6.8; 11.38; 6.6 times (p <0.05), respectively, and was 10.91±1.09×10⁴/l, 20.5±0.62×10 ^{4} /l, 11.91±0.95×10 ^{4} /l. The increase by the 3rd day was 87.9% (p <0.05), by the 5th day in relation to the 1st their number practically did not change (p >0.05). On the 5th day, the amount of DE decreased by 41.9% (p <0.05) in comparison with the indicator obtained on the 3rd day.

In 5 patients, the course of traumatic disease ended fatally. They had the following intra-abdominal injuries: two had a rupture of the mesentery of the small intestine, one had a rupture of the rectum + subcutaneous hematomas of 2 liters, one had a rupture of the spleen + hemoperitoneum of 2 liters, one had a rupture of the liver + hemoperitoneum of 1.5 liters. Two patients had injuries to three areas of the body, three had injuries to four areas. Death occurred on the 7th, 12th, 15th, 24th, and 90th days. The cause of death was multiple organ failure (MOF).

In the group of patients with fatal outcomes, the highest values of CRP, vWF, and DE on the day of admission were noted: the *CRP* level, compared with the values in the comparison group, was 7.14; 11.43; 15.2 times higher on the 1st, 3rd, and 5th days, respectively, and was 107.26±12.51 mg/ml; 164.21±6.1 mg/ml; 219.98±17.92 mg/ml (p <0.05). The increase in the CRP level *by* day 3 relative to day 1 in this category of patients was 53.09%, by day 5 — 105% (p <0.05), by day 5 relative to day 3 — 33.9% *(*p<0.05).

In patients with a fatal outcome, the concentration of vWF was increased by 3.02; 3.54; 4.28 times (p <0.05) on the 1st, 3rd and 5th days, respectively, compared with the indicator of the comparison group (196.54±16.99%, 249.9±12.06% and 291.0±13.1%). The increase in the concentration of *vWF* by the 3rd day relative to the 1st in this category of patients was 27.14% *(*p<0.05), by the 5th relative to the 1st x - 48.0% *(*p <0.05), to 5 relative to 3 - 16.4% (p <0.05).

In patients with a fatal outcome, the amount of DE in relation to the indicator of patients in the comparison group on the 1st, 3rd and 5th day was increased by 11.1; 14.0; 12.55 times (p<0.05), respectively. In the 1st On day 3, the amount of DE was 17.8±1.02×10 ^{4} /l. The increase by day 3 was 41.57% (p <0.05) (25.2±0.66×10 ^{4} /l); by day 5, compared to day 1, the increase was 26.96% (p <0.05), the amount of DE was 22.6±0.87×10 ^{4} /l. By day 5, compared to day 3, the amount of DE decreased by 10.32% (p <0.05).

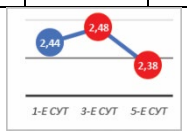
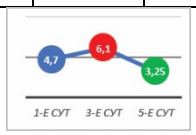
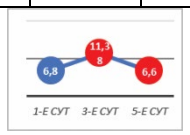
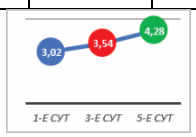
Thus, with a favorable course of traumatic disease, the level *of CRP* in the first day after injury increases by 3.6 times compared to the comparison group (Table 7), reaching maximum figures by the 3rd day (p < 0.05), by the 5th day its level decreases, not reaching statistical significance compared to previous measurements. The level of *vWF* in the first day after injury increases by 2.44 times compared to the comparison group, increases by the 3rd day compared to the 1st day (p < 0.05) and decreases by the 5th compared to the 3rd day (p < 0.05). The amount of DE in the 1st day after injury increases by 4.7 times compared to the comparison group, increases by the 3rd day (p < 0.05) and decreases by the 5th day (p < 0.05).

In complicated traumatic disease, the CRP level *on* the first day after injury increases by 5.1 times compared to the comparison group and maintains an upward trend: by the 5th day, relative to the 1st day, the CRP level *increases* by 2.3 times (p<0.05). The *vWF concentration* on the first day after injury increases by 2.59 times compared to the comparison group, by the 5th day, relative to the 1st day, *the vWF level* increases by 1.14 times (p<0.05). The amount of DE on the first day after injury increases by 6.8 times compared to the comparison group, increases by the 3rd day (p <0.05) and decreases by the 5th day (p <0.05).

In case of combined injury with fatal outcome, the level *of* CRP on the 1st day increases by 7.14 times relative to the comparison group indicators and maintains an upward trend — by the 5th day, relative to the 1st day, the level *of CRP* increases by 2.13 times (p <0.05). The concentration of *vWF* on the 1st day after injury increases by 3 times relative to the comparison group indicators and continues to grow and by the 5th day exceeds the indicators of the 1st day by 1.41 times (p<0.05). The amount of DE increases on the 1st day by 11.1 times, by the 5th day — exceeds the indicators of the 1st day by 1.13 times.

Table 7

Prognostic value of the dynamics of markers of endothelial dysfunction (multiplicity increase in endothelial dysfunction indices / fold relative to the indicators groups comparisons)

Outcome of traumatic disease in the examined patients	*CRP*			*vWF*			DE		
	1st day	3rd day	Day 5	1st day	3rd day	Day 5	1st day	3rd day	Day 5
Favorable	3.6	6.6	4.8	2.44	2.48	2.38	4.7	6.1	3.25
									
Complicated course of traumatic disease	5.1	8.76	11.67	2.59	2.67	2.95	6.8	11.38	6.6
									
Fatal outcome	7.14	11.43	15.2	3.02	3.54	4.28	11.1	14.0	12.55
									

Notes: red fill of the corresponding indicator on the diagram indicates a reliable difference compared to the previous study (eg, day 5 to day 3 or day 3 to day 1); green fill indicates a reliable difference between the indicator on day 5 to day 3 and day 1. DE - desquamated (circulating) endothelial cells; CRP—C-reactive protein; vWF - von Willebrand factor

DISCUSSION

The key role of the endothelium is to regulate homeostasis and hemostasis, vascular tone, proliferation of their smooth muscles, participation in immune processes, etc. [1, 9]. Endothelial factors can be divided into:

1. Causing contraction and relaxation of the muscular layer of the vascular wall:

a) constrictors - endothelins, angiotensin-I, II (AT-I, II), thromboxane A 2 (*TxA* 2), prostaglandin H2 (*Pg* H2), etc. [4, 5, 9];

b) dilators - nitric oxide (*NO),* prostacyclin (prostaglandin *Pg* l2), endothelial depolarizing factor (*Endothelium-Derived Hyperpolarizing Factor*, *EDHF*), carbon monoxide (CO), angiotensin-I, adrenomedulin, etc. [1, 4, 5, 9].

2. Procoagulant and anticoagulant factors:

a) prothrombogenic - platelet -*derived growth factor (PDGF*), tissue plasminogen activator inhibitor, *TxA* 2, *vWF,* angiotensin -IV, endothelin-1, fibronectin, thrombospondin, platelet activating factor, etc. [3, 5, 9];

b) antithrombogenic - *NO,* tissue plasminogen activator (*tPA),* Pg *l2,* thrombomodulin, etc. [1, 5, 9].

3. Factors influencing the growth of blood vessels and smooth muscle cells:

a) stimulants - endothelin-1, AT-II, superoxide radicals, endothelial growth factor, etc. [5];

b) inhibitors - *Pg* l2, natriuretic peptide *C,* heparin-like growth inhibitors, etc. *NO* stimulates angiogenesis, but inhibits the proliferation of smooth muscles in vessels [1, 3].

4. Pro-inflammatory and anti-inflammatory factors:

a) pro-inflammatory - tumor necrosis factor ⟨ (TNF- ⟨), superoxide radicals, *C* RB, etc.;

b) anti-inflammatory – *NO,* etc. [1, 4, 7].

In various severe critical conditions, including trauma, dysfunction of the endothelium occurs, an imbalance between the substances produced by it, a violation of the rheological properties of the blood, an increase in the content of procoagulants, an increase in the permeability of the vascular wall, which contributes to thrombus formation and increased tissue hypoxia, and subsequently to PON [1, 6, 9].

According to the concept of E.K. Gumanenko et al., 2008 [7]: "...in the early stages after a severe injury, a critical state for the body is formed, in which the factors and mechanisms of natural resistance cannot ensure effective adaptation of the body to the damaging effects of injury and SIRS, and the adaptive immune system has not yet been included in the processes of immediate compensation... Of the indicators of an immune nature, probably the

greatest diagnostic value for predicting the risk of developing MOF during the first (acute) period of traumatic disease and the period of relative stabilization of vital functions is <...> the dynamics of increasing concentrations in the peripheral blood of <...> adaptogen proteins (*C* -reactive protein)". *CRP* is a pro-inflammatory factor, produced in the liver and refers to acute phase proteins of inflammation, stimulates protective reactions, activates immunity [7].

In uncomplicated postoperative periods in uninjured patients, the concentration of CRP decreases *from* the 1st to the 3rd day and then stabilizes.

In the main group, there is an increase in the average concentration *of* CRP with an increase in the time from the moment of injury, these differences are reliable compared to the comparison group in all studied time intervals (1st, 3rd and 5th days), the increase in concentration is statistically significant at any injury severity between the 1st and 3rd and 1st and 5th days in the corresponding subgroups, with extremely severe injury, the differences are statistically significant between the 3rd and 5th days. Despite the increase in average concentrations *of* CRP with increasing severity of injury, it should be noted that there are no reliable differences between them in most studies. That is, with SCBAT, there is an increase in the concentration *of CRP* from the 1st to the 5th day, but its concentrations do not statistically significantly correlate with the severity of the injury. Apparently, *CRP,* depending on the severity of damage, regulates the severity of the SIR to the injury. As a factor of natural resistance, *CRP* prevents the increase in hyperantigenemia, which occurs in response to damage to body tissues and is a factor of non-specific protection [7].

The level *of CRP* is statistically significantly higher in injured patients compared to non-injured patients.

In both abdominal organ injury and anterior abdominal wall contusion, with increasing time from the moment of injury, there is an increase in average CRP concentrations *;* these differences are statistically significant in comparison with uninjured patients, but in the case of internal organ injury, there are statistically significant differences between the 1st and 3rd days and the 1st and 5th days, which is not observed with anterior abdominal wall contusion. In patients with SCBT with average CRP values of *76.12* ±7.8, 125.5±7.8 mg/ml on the 1st and 3rd days, respectively, with difficulties in differential diagnosis with abdominal wall contusion, the presence of abdominal organ injury should be assumed.

In both complicated traumatic disease and unfavorable (fatal) outcome, there is a statistically significant increase in the CRP indices in relation to the comparison group and in time in the subgroups *;* in the latter case, the differences are also statistically significant with the group of patients with uncomplicated traumatic disease; with average *CRP values* of 107.26±12.51, 164.21±6.1, 219.98±17.92 mg/ml on the 1st, 3rd and 5th days, respectively, an extremely unfavorable course of traumatic disease and a high probability of developing a fatal outcome should be assumed. In uncomplicated traumatic disease in patients with TSZTZ, there is an increase in CRP indices *by* the 3rd day, and then a decrease by the 5th. The multiple increase in the level *of CRP in the blood produced by activated endothelial cells* revealed in our study indicates the implementation of a generalized inflammatory reaction, which predetermines the occurrence of organ dysfunction. Our results are consistent with the literature data [7].

According to E.K. Gumanenko et al., 2008 [7]: "At high shear rates in the blood flow, which are most typical in the microcirculatory bed, the activity of von Willebrand factor increases sharply ... The described processes develop simultaneously in various microcirculatory regions, represented in almost all organs, which predetermines the formation and deepening of multiple organ dysfunction." *vWF* is a prothrombogenic factor, synthesized in the endothelium and megakaryocytes; stimulates the onset of thrombus formation: promotes the attachment of platelet receptors to collagen and fibronectin of blood vessels, enhances their adhesion and aggregation [1, 4, 9].

vWF increases from the 1st to the 3rd day and then stabilizes.

In the main group, there is an increase in the average concentration of *vWF* with an increase in the time from the moment of injury, with the exception of the subgroup with a predicted mortality of up to 25%, where there is an insignificant decrease from the 3rd to the 5th day, these differences are reliable compared to the comparison group in all studied time intervals (1st, 3rd and 5th days). Despite the increase in average concentrations *of vWF* with the severity of injury, it should be noted that there are no statistically significant differences between them in most studies. In SCBAT with a predicted mortality of more than 25%, there is an increase in the concentration of *vWF* from the 1st to the 5th day, but its concentrations do not reliably correlate with the severity of the injury.

vWF level is statistically significantly higher in injured patients compared to non-injured patients.

In both abdominal organ injury and anterior abdominal wall contusion, with increasing time from the moment of injury, there is an increase in average *vWF concentrations*; these differences are statistically significant in comparison with uninjured patients, but in the case of internal organ injury, there are statistically significant differences between the 1st and 3rd days and the 1st and 5th days, which is not observed in contusion. In patients with SCBT with

average *vWF values* of 198.46±6.8%, 207.11±10.3% on the 3rd and 5th days, respectively, with difficulties in differential diagnosis with contusion of the anterior abdominal wall, it is necessary to assume the presence of abdominal organ injury.

vWF values increase in relation to the comparison group and in time in subgroups, with average *vWF values* of 249.9±12.06%, 291±13.1% on the 3rd and 5th days, respectively, an extremely unfavorable course of traumatic disease and a high probability of developing a fatal outcome should be assumed. In uncomplicated traumatic disease in patients with combined closed abdominal trauma, *vWF* values increase by the 3rd day, and then decrease by the 5th, practically reaching the level of the 1st day.

Based on the study, it can be concluded that high *vWF concentrations in relation to the comparison group* from the 1st day of the post-traumatic period, persisting until the 3rd and 5th days, indicate systemic damage to the vascular endothelium in response to extremely severe trauma.

Cellular markers of ED include the amount of circulating DE, indicating damage to the vascular endothelium and impaired permeability of the vascular wall [6, 8].

In uncomplicated postoperative periods in uninjured patients, the concentration of DE increases from the 1st to the 3rd day and then the level stabilizes.

In the main group, there is an increase in the average concentration of DE from the 1st to the 3rd day from the moment of injury, and then a decrease on the 5th day, these differences are reliable compared to the comparison group in all studied time intervals (1st, 3rd and 5th days). Despite the higher values of DE concentrations with the severity of injury, the differences were statistically significant only when comparing subgroups with a predicted mortality of up to 25% and up to 60% on the 3rd and 5th days. That is, with TSZTZ, there is an increase in DE concentration from the 1st to the 3rd day, then a decrease by the 5th, but their concentrations do not always correlate with the severity of the injury.

The level of DE is statistically significantly higher in injured patients compared to non-injured ones.

In both abdominal organ damage and anterior abdominal wall contusion, from the 1st to the 3rd day from the moment of injury, there is an increase in average DE concentrations, and then a decrease on the 5th day. These differences are statistically significant in comparison with uninjured patients and in each subgroup over time, but we did not find any statistically significant differences in the DE level in abdominal wall contusion and abdominal organ damage.

In both complicated traumatic disease and unfavorable (fatal) outcomes, there is a statistically significant increase in DE values from the 1st to the 3rd day in relation to the comparison group and subgroups, then a decrease by the 5th day, with average DE values of $10.91±1.09×10^4$/l, $20.5±0.62×10^4$/l, $11.91±0.95×10^4$/l on the 1st, 3rd and 5th days, respectively, the development of complications should be expected, and with average DE values of $17.8±1.02×10^4$/l, $25.2±0.66×10^4$/l, $22.6±0.87×10^4$/l on the 1st, 3rd and 5th days, respectively, an extremely unfavorable course should be assumed. traumatic disease and a high probability of developing a fatal outcome. This indicator is the most reliable for diagnosing the risk of complications and fatal outcomes in all time intervals studied. In uncomplicated traumatic disease in patients with SCBAT, an increase in DE indicators was noted by the 3rd day, and then a decrease by the 5th, below the level of the 1st day.

It can be concluded that increased desquamation of endothelial cells in the blood indicates endothelial damage in response to injury. The number of endothelial cells circulating in the blood is directly dependent on the severity of injury when comparing subgroups with predicted mortality of up to 25% and up to 60% on the 3rd and 5th days.

High levels *of CRP, vWF,* DE in combined trauma with damage to abdominal organs on the 1st day indicate a systemic response of the body to trauma, significant damage to the vascular endothelium and the inclusion of non-specific protective mechanisms in response to existing damage. An increase in indicators indicates a deepening of ED in response to severe damage and the implementation of SIR. An increase in the levels *of* CRP, *vWF,* DE indicates the involvement of the vascular endothelium in the processes, while in response to trauma there is increased desquamation of damaged endothelial cells and excessive production of pro-inflammatory and prothrombotic factors, which is a non-specific protective mechanism that develops during trauma regardless of its severity and localization. With a favorable course, the levels *of CRP, vWF,* DE tend to decrease by the 5th day, which indicates regression of SIR and is a positive prognostic factor.

In complicated traumatic disease, in conditions of increasing antigenemia, the source of which is damaged tissues of the body, the level of *CRP* increases many times, since it has the greatest neutralizing ability in relation to antigens. Systemic damage to the vascular endothelium, the acquisition of thrombogenic properties by it is accompanied by an increase in the concentration of *vWF* and the amount of DE.

Such high levels of *CRP, vWF,* and DE indicate the implementation of a generalized inflammatory response of the body to trauma, the progression of ED with the development of MOF, which was the cause of death.

Based on our study, it is clear that the increase in ED indicators is a prognostic sign of the course and outcome of combined injury.

CONCLUSION

All three endothelial dysfunction markers under consideration have an important prognostic value in severe combined blunt abdominal trauma. Their level in severe abdominal trauma significantly differs from that in operated uninjured patients. The levels of *C* -reactive protein and von Willebrand factor allow differential diagnostics between abdominal wall contusion and damage to internal organs; their extremely high values suggest an unfavorable course of traumatic disease and a high probability of fatal outcome. The level of desquamated endotheliocytes turned out to be the most reliable in diagnosing the risk of complications and fatal outcome from the 1st to the 5th day after injury. Necrotic processes in the endothelium, reflected by the content of desquamated endotheliocytes in the blood, are leading in the pathogenesis of multiple organ failure.

1. Objective assessment of endothelial dysfunction in trauma surgery may have prognostic value. Taking into account that the development of traumatic disease is based on damage to the vascular endothelium, it is necessary to consider as prognostic indicators changes in the level of activity of *C*- reactive protein, von Willebrand factor, desquamated endothelial cells in patients with severe combined closed abdominal trauma.

2. In patients with SCBAT with mean values *of C*-reactive protein of 76.12±7.8, 125.5±7.8 mg/ml on the 1st and 3rd days, respectively ($p<0.05$) and mean values *of vWF* of 198.46±6.8%, 207.11±10.3% on the 3rd and 5th days, respectively *(*$p<0.05$), with difficulties in differential diagnosis with abdominal wall contusion, the presence of damage to abdominal organs should be assumed.

3. With average values of *C*-reactive protein of 107.26±12.51, 164.21±6.1, 219.98±17.92 mg/ml on the 1st, 3rd and 5th days, respectively ($p<0.01$) and average values *of vWF* of 249.9±12.06%, 291±13.1% on the 3rd and 5th days, respectively *(*$p<0.001$), one should assume an extremely unfavorable course of traumatic disease and a high probability of a fatal outcome.

4. With average DE values of $10.91±1.09×10^4$/l, $20.5±0.62×10^4$/l, $11.91±0.95×10^4$/l on the 1st, 3rd and 5th days, respectively ($p<0.01$), the development of complications should be expected, and with average DE values of $17.8±1.02×10^4$/l, $25.2±0.66×10^4$/l, $22.6±0.87×10^4$/l on the 1st, 3rd and 5th days, respectively ($p<0.001$), an extremely unfavorable course of traumatic disease and a high probability of a fatal outcome should be assumed.

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