



BIOCHEMICAL CORRELATIONS IN POLYTRAUMA PATIENTS WITH UNSTABLE PELVIC FRACTURES

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Abstract. Polytrauma represents an association of multiple injuries capable of inducing a systemic response and resulting in a life-threatening condition. Regardless of the different approaches and definitions, the severity of this association, determined by a specific pathophysiology, requires special therapeutic protocols, adapted to the status of the patient. One of the most challenging situations for the trauma specialists is represented by polytrauma with unstable pelvic fractures - the stabilization of these fractures is considered a resuscitative measure, but this must be done while avoiding the "second hit" phenomenon. These can be achieved by adapting the treatment to the patient's systemic response to aggression, which has to be evaluated by objective means. The authors perform a retrospective study in a Level 1 Trauma Centre in order to analyse the possibility of using biochemical markers to assess the status of the polytrauma patients with unstable pelvic fractures and to establish their treatment.

Keywords: biochemical markers, pelvic fractures

Introduction

Pelvic fractures in polytrauma patients represent a problem of great importance for modern traumatology for several reasons, including high incidence and high mortality. Their incidence in polytrauma patients has been reported to be around 23% by several authors. [1],[2] The mortality of unstable pelvic fractures in patients with haemodynamic instability is 40-80% compared to 30% mortality after myocardial infarction. [3, 4, 5, 6]

Remembering that "pelvic fractures" include injuries not only of the bones but of all the capsulo-ligamentous structures which assure the stability of the pelvic girdle, it must be underlined that the main phenomenon by which these fractures influence the outcome of polytrauma patients is bleeding. In pelvic fractures, bleeding can have many sources, both arterial and venous, and the blood loss is usually consistent with the extent of displacement; since the pelvic ring has no intrinsic stability, the possibility of displacement is quite common, especially in high-energy trauma. [7], [8] Although the volume of the pelvis is only 1.5 litres, the intact retroperitoneal space can accumulate 5L

of fluid with a pressure rise of only 30 mmHg, with a very low capacity to limit the bleeding, which worsens further when the fracture is displaced.[9], [10]

The main goal of pelvic fracture treatment, especially in polytrauma, is achieving stability:

- The haemodynamic stability of the patient, and
- The mechanical stability of the fracture, as they are closely connected, as presented before.[11]

The stability of the fractures is assessed in connection with their site, thus the following have been described:

- Stable fractures, affecting only the anterior arch,
- Partially stable fractures with an incomplete disruption of the posterior arch, and
- Unstable, with complete disruption of the posterior arch, the most severe of all, almost always associated with severe alteration of the haemodynamics of the patient.[12, 13]

Based on this classification regarding stability, surgery is indicated in unstable fractures both to reconstruct the pelvic girdle and to stop the bleeding.

Since the general consequences of any fracture are influenced by bleeding, it is obvious that unstable pelvic fractures have a considerably higher impact upon the overall outcome of the patient, so their stabilization is mandatory not only for local but especially for general reasons. [14], [15] This fact is particularly important in polytrauma due to the biological effects of the associated injuries, some of them life threatening. Therefore, in polytrauma, in order to avoid the "second

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hit” phenomenon, the chosen method of stabilization must be the least invasive possible, adapted to each patient’s condition. [16, 17]

In order to standardise the approach in the polytraumatised patient, several criteria are being used to classify the patient as: stable, borderline, unstable, or in extremis (Table I). [18, 19]

	Parameter	Stable (grade I)	Borderline (grade II)	Unstable (grade III)	In extremis (grade IV)
Shock	BP (mmHg)	≥ 100	80-100	60-90	<50-60
	Blood units (2 h)	0-2	2-8	5-15	>15
	Lactate levels	Normal range	Approx 2.5	>2.5	Severe acidosis
	Base deficit (mmol/L)	Normal range	No data	No data	>6-18
	ATLS classification	I	II-III	III-IV	IV
	UO (mL/h)	>150	50-150	<100	<50
Coagulation	Platelet count (µg/mL)	>110000	90000-110000	<70000-90000	<70000
	Factor II and V (%)	90-100	70-80	50-70	<50
	Fibrinogen (g/dL)	>1	Approx 1	<1	DIC
	D-Dimer	Normal range	Abnormal	Abnormal	DIC
Temperature		>35°C	33-35°C	30-32°C	30°C or less
Soft tissue injuries	Lung function, PaO ₂ /FiO ₂	>350	300	200-300	<200
	Chest trauma scores, AIS	AIS I or II	AIS ≥ 2	AIS ≥ 2	AIS ≥ 3
	TSS	0	I-II	II-III	IV
	Abdominal trauma (moore)	≤ II	≤ III	III	≥ III
	Pelvic trauma (AO classification)	A	B or C	C	C (crush, rollover with abd trauma)
	Extremities	AIS I or II	AIS II-III	AIS III-IV	Crush, rollover, extremities

Table I. Status of polytrauma patients

As can be seen, the criteria refer to different systems and organs, thus clearly indicating that the polytrauma patient needs a multidisciplinary assessment. Regarding the treatment of different injuries in polytrauma, several types of treatment have been described so far:

Early Total Care (ETC)- the definitive method of treatment is used from the beginning

Damage Control (DC) – a less invasive temporary method is used to improve the status of the patient until he/she can withstand the definitive method. [20, 21]

Considering the data in Fig. 2, ETC is indicated in stable patients, while in borderline and unstable patients DC is considered to minimize the potentially negative impact of surgery upon the fragile balance of the patient. When we refer to the pelvic fractures, ETC is usually represented by Open Reduction Internal Fixation (ORIF), while DC is performed usually by external fixation.

If DC is the method of choice, after the initial stabilization of the fracture, the complex systemic disturbances must be monitored and treated; their evolution can be:

- Favourable - the systemic response decreases and definitive treatment can be performed, or
- Negative - the Systemic Inflammatory Response Syndrome (SIRS) persists and overwhelms the healing mechanisms, inducing MSOF (Multiple System and Organ Failure) and probably death.

For the multidisciplinary team involved in treating these patients it is very important to have some criteria for monitoring them, so as to evaluate the outcome. If the outcome is negative, it is important to detect complications as early as possible and take the

appropriate measures; if the outcome is positive, the proper moment to perform definitive treatment must be chosen very carefully.

In both of the previously described situations, it is mandatory for these criteria to be objective, and several biochemical markers have been evaluated as guiding tools for polytrauma patients. As described in literature, inflammatory syndrome can be monitored using standard markers, like ESR, CRP, or the signal molecules, like IL-1 and IL-6. [22], [23], [24]

The authors present the experience of a Level 1 Trauma Centre in using such markers to establish therapeutic options for polytrauma patients with unstable pelvic fractures.

Material and Methods

This study retrospectively analysed 28 polytrauma patients with unstable pelvic fractures treated in our hospital (Clinical University Hospital Bucharest) between 01.01.2012- 01.01.2015 for which complete medical records were available.

The following criteria were used to analyse the study group:

- demography,
- haemodynamic stability of the patients,
- associated injuries,
- type of pelvic stabilisation,
- biochemical markers (ESR, C Reactive Protein, IL-1, IL-6) related to the outcome of the patients

Results

The demographic characteristics of the study group consisting of 28 patients are represented in Fig. 1,

underlining the importance of the problem of pelvic fractures in polytrauma for trauma surgeons: the mean age of the patients was 36 years old with only 1 patient over 60 years of age, thus demonstrating the social implications of the morbidity and mortality associated with these injuries.

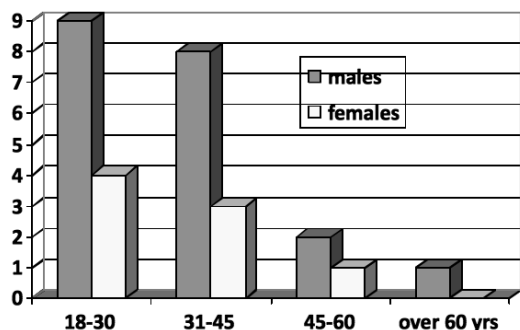


Fig.1. Age and gender of the study group

Regarding the associated injuries, as presented in Fig. 3, the most frequent were lung and head trauma, with several other types of abdominal injuries.

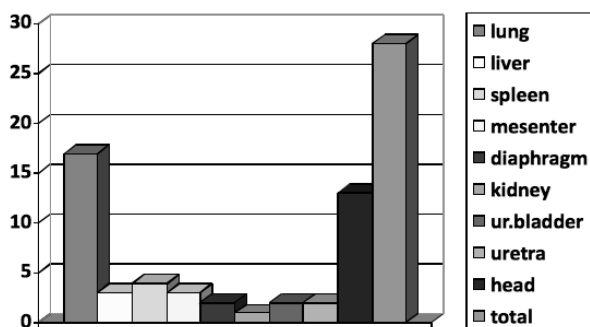


Fig.2. Injuries associated with pelvic fractures in polytrauma

According to the medical records, the patients were classified as:

- unstable - 8 patients
- borderline - 8 patients
- stable - 12 patients

After the initial evaluation, the treatment for the unstable pelvic injuries was the pelvic binder, which was applied to the patient and kept on while the life threatening injuries were managed; after that, the patient was re-evaluated and, according to the clinical and paraclinical parameters, the decision was made regarding pelvic fracture stabilization: ETC with internal stabilization was performed in 8 patients (anterior plates in all 8 cases, along with posterior sacral bars in 4 cases and iliosacral screws in 3 cases), while external fixation (DC) was used for the remaining 20 patients.

Since the purpose of this research is not to discuss the type of fixation, the medical data of the patients were examined regarding the biochemical profile in connection with the following elements:

- the initial fixation,
- the outcome of the patients, and
- the moment of definitive fixation.

Regarding the biochemical markers, some of them are routinely measured to assess the stability of the patient, but

this is only performed during the initial evaluation, whereas we believe that the monitoring of these patients should be continuous, especially in those cases where treatment requires sequential surgical interventions.

For this purpose, we chose to monitor the following inflammatory markers in the study group:

- ESR
- C Reactive Protein
- IL-1
- IL-6

These markers were evaluated by looking at the medical records of the patients and they were found to be considerably modified in unstable and borderline patients, for whom Damage Control is currently recommended. Aside from the 16 cases (8 unstable + 8 borderline) with predictable indication for primary external stabilization, four patients, although considered stable, had their pelvic fractures fixed in the same manner. In these cases, a significant inflammatory syndrome was detected, so the choice had to be made between an extensive type of surgery (ORIF) and a temporary, much less invasive method; as described in the medical documents, external fixation was considered appropriate for these patients.

Table II presents the general complications in relation to the initial status of the patients; as can be expected, the rate of complications is higher for initially unstable patients:

	ARDS	MSOF	Death	Total
Unstable patients	4	3	2	8
Borderline patients	3	2	1	8
Stable patients-ExFix	0	0	0	4
Stable patients-ETC	0	0	1	8

Table II- General complications within the study group

The inflammatory markers were thus analysed comparatively within the following groups of patients:

- Those who did not develop general complications (Fig. 3)
- Those who developed general complications but lived (Fig. 4)
- Those who developed general complications and died (Fig. 5)

Note that the actual values obtained are compared to the normal level, so what is shown on the graphs is not the absolute value, but the ratio between the value in study group and the mean normal value. Therefore, level 1 on the vertical axis of the graph means that the value in the study group matched the mean normal value, 2 on the vertical axis means that levels obtained were twice as high as the normal value, 3 means three times as high, and so on.

As can be seen by analysing the 24 patients who survived without complications (Fig. 4), the following are to be underlined:

- There is an initial increase in the levels of all the inflammatory markers up to day 7, then they decrease to normal values; this corresponds to the well known period of acute inflammation.
- The most rapid increase and decrease can be found in IL-1 and especially IL-6, thus suggesting that they can be considered more valuable for assessing the intensity of the post-aggressive systemic reaction.
- Comparing to ESR and CRP, which reached the maximal value in D6, both IL-1 and IL-6 increased until

D7, thus showing the persistence of the inflammatory response beyond the limit of D5, routinely considered as to be the end of the acute inflammatory phase.

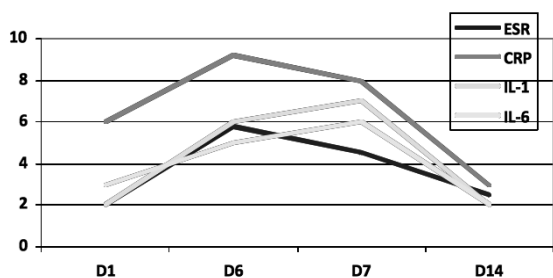


Fig.3. Patients with favourable outcomes without complications

Regarding the polytrauma patients who developed general complications (ARDS and/or MOSF) but survived (Fig. 5), the values of the inflammatory markers rose during the whole period of established acute inflammation, but after reaching a peak value they started to decrease and after 3 weeks from initial trauma they had reached values close to the initial ones.

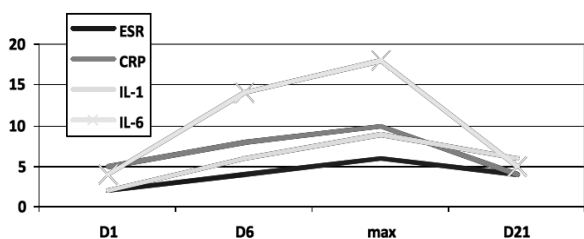


Fig.4. Inflammatory markers in patients who developed general complications but survived

If we compare Fig. 4 and Fig. 5, we can see a similar initial trend with values rising up to day 6/7, but in Fig. 4 after this moment the levels clearly decrease and this can be correlated with the remission of post-traumatic disturbances and with stronger healing mechanisms, while in Fig. 5 the values continue to increase due to a persistent catabolic phase until the imbalance is so severe that it generates systemic complications. It must be underlined that the peak values of the markers in this situation are considerably higher than in the previous group. Because the treatment (started from the beginning) was finally able to surpass the pathologic processes, the patients survived and the outcome was favourable in the end, but the healing process took much longer – as we can see, it took 3 weeks (mean value) for the inflammatory parameters to get back to normal.

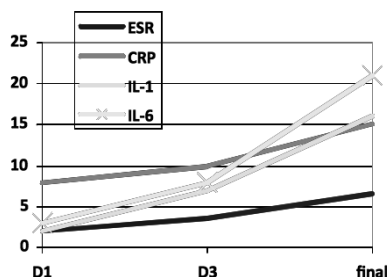


Fig.5. Inflammatory markers in patients who developed MSOF and died

When considering the patients who died due to general complications (Fig. 6), the inflammatory markers showed the same initial tendency of increasing up to day 3, but after that they continued to increase up to the death of the patient. Regardless of the moment when the fatal complications occurred, the increase was again much more brutal for IL-1 and IL-6, which have proven to reflect the intensity of the systemic consequences much better than ESR and CRP.

The above mentioned data are of outstanding relevance to clinical practice: during this research, the retrospective analysis showed that no definitive stabilization of the pelvic fracture was performed until after the total remission of the inflammatory syndrome, proving that adapting the treatment to the status of the patient is the most appropriate attitude especially in this very fragile type of patients.

The same data were then analysed regarding each type of inflammatory marker in each of the following groups of patients:

- Polytrauma patients who survived without developing any general complications (group I);
- Polytrauma patients who survived after having developed general complications (group II);
- Patients who died (group III).

Figure 6 presents the graphics for ESR (a) and CRP (b), and Figure 7 for IL-1 (Fig.7.a) and IL-6 (Fig.7.b). The graphs all show the same types of evolution curves for all the markers within each of the groups previously described.

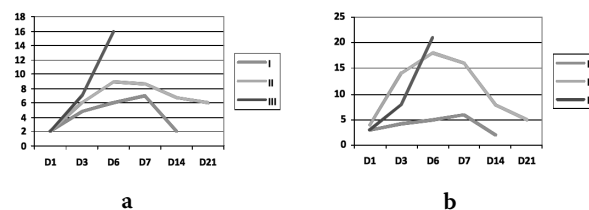


Fig.6. The values of ESR (a) and CRP (b) related to the outcome of the polytrauma patients

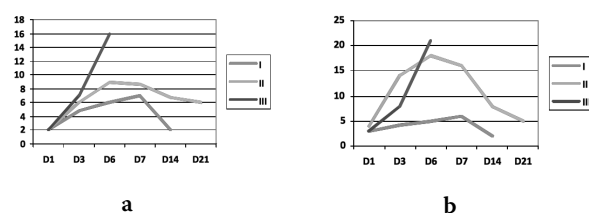


Fig.7. The values of IL-1 (a) and IL-6 (b) related to the outcome of the polytrauma patients

The curves had similar aspects, as follows:

- For group I (survival-without-complications) - ascending line followed by descending line.
- For group II (survival-after-MSOF) - initial ascending line, then supplementary ascending line, then a line that descended but more slowly than in group I.
- For group III (MSOF followed by death) - initial ascending line, followed by supplementary abruptly ascending line (similar to the graph of an exponential function).

Discussions

The incidence of general complications in the study group confirms the correlation between the outcome of the patients and the initial status of the patient as a direct result trauma. Due to the complex treatment performed in the ICU and the multidisciplinary involvement, not all the patients with ARDS or MSOF died. There is one case of an initially stable patient whose pelvic injury was managed with ETC and who died, but this happened 3 weeks after the initial trauma when the patient had already started physical rehabilitation and was due to a massive pulmonary embolism, with no previous ARDS or MSOF. Aside from this case, general complications occurred only in the groups of unstable and borderline patients.

The incidence of general complications, including death, is comparable to those described in literature, showing that the protocols followed during the management of the patients in this study group are compatible with the international ones.[25, 26, 27]

The values of the inflammatory markers “followed” the evolution of the patients: there was an initial inflammatory phase until day 6/7 when the values reached the first peak corresponding to the physiological response known as the “post-aggressive systemic reaction”. After that, the evolution of the inflammatory markers took two different directions:

When the healing mechanisms became stronger than the post-traumatic disturbances, the catabolic phase was replaced by the anabolic one; the markers decreased and the outcome was favourable, or

Due to a persistent systemic reaction, the markers continued to increase, reflecting the well-known SIRS (Systemic Inflammatory Response System), leading to general complications; depending on the balance between the aggression and the body’s compensatory mechanisms, either these complications were efficiently tackled by the organs and systems helped by the treatment, or they exhausted the healing resources and the patient died.

It must be underlined that, as described in literature, IL-1 and IL-6 more closely follow the positive or negative systemic reactions, proving to be more reliable than ESR and CRP when evaluating polytrauma patients.[28, 29, 30]

This is important especially from the point of view of the multidisciplinary team which must have objective criteria to be able to guide the patients’ treatment of. Since the inflammatory mechanisms are responsible for most of the complications in polytrauma patients, monitoring these processes might improve patient outcomes.

Conclusions

Based on the pathophysiology of polytrauma, this research analysed some of the markers of acute inflammation in a challenging group of patients - polytrauma patients with pelvic fractures. The impact of an unstable pelvic fracture becomes even more important when other severe injuries are associated, as in polytrauma. This is proven by the proportion of unstable patients in the study group, reflecting the haemodynamic impact of these types of fractures and underlining the importance of the basic idea of this research.

Among the inflammatory markers, both conventional ESR and CRP proved to reflect the response to trauma, but the most sensitive reaction is that of IL-1 and IL-6 especially, which were found to have more distinctive curves of variance depending on the pathological mechanisms triggered both by the trauma and by the treatment. The curves of both IL-1 and IL-6 had an aspect which can be considered predictive for either MSOF or favourable outcome, thus giving useful information regarding the extent of the surgical treatment that the patient can withstand in order to prevent the “second hit” phenomenon.

Since unstable pelvic fractures in polytrauma patients continue to have a high mortality even with all the progress of modern medicine, the interest in improving their treatment is considerable. Multidisciplinary teams are nowadays trained to treat these patients and research is looking for better protocols and algorithms, as well as for better methods to assess the patients and guide the treatment.

This research paper demonstrates that in polytrauma patients with unstable pelvic fractures inflammatory markers and especially Interleukins IL-1 and IL-6 represent valuable objective elements based on which the trauma team can establish a flexible, patient-adapted and thus efficient therapeutic protocol, able to ensure first of all the survival of the patients, followed by their healing.

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