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Respiratory distress following major trauma

Predictive value of blood coagulation tests

We have evaluated the use of laboratory parameters to predict the risk of adult respiratory distress syndrome (ARDS) at an early stage after major trauma. Patients with lungcontusion were excluded. Five of 29 patients fulfilled our criteria of ARDS, i.e. $PaO_2/FiO_2 \leq 38$. They showed lower platelet counts and antiplasmin as well as a tendency to lower antithrombin III, fibrinogen, and plasminogen. These changes indicated activation of the coagulation and fibrinolytic systems by trauma. The most sensitive indicator of ARDS seemed to be the platelet count, although it was also related to blood loss and amount of blood transfused. Hence the platelet count should be considered in relation to blood replacement in the patient with major trauma. Tentative laboratory values are suggested to indicate risk levels of developing ARDS.

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The adult respiratory distress syndrome (ARDS), a major problem in the multitrauma patient, is a multifactorial disorder (Shoemaker et al. 1980), characterized by interstitial and alveolar edema leading to reduced PaO_2. It has been shown that the formation and deposition of circulating fibrin and aggregated platelets in the lung capillaries in ARDS is a result of proteolytic activation of the coagulation system (Busch et al. 1971, Saldeen 1979).

The aim of our study was to evaluate the possibility of establishing early diagnosis of ARDS with laboratory parameters.

Patients and Methods

Twenty-nine patients, 19 men and 10 women, with high energy major trauma were studied. Their median age was 64 (49–79) years. The causes of trauma were car accident in 10 patients, motor cycle or pedestrian accident in 17 patients, and accidental fall from a great height in two patients. One case, a patient with a severe head injury, was fatal. Patients with fractures of the femur or at least two other diaphyseal fractures, and serious pelvic fractures were included. The distribution of injuries in the patients is shown in Figure 1. Sixteen patients with pulmonary infiltrates in chest roentgenograms on admission, which were consistant with pulmonary contusion or aspiration were excluded.

Diagnosis of ARDS

ARDS was diagnosed from clinical symptoms, respiratory rate, and hypoxemia and was defined as PaO_2 less than 8 kPa on air breathing or $PaO_2/FiO_2 \leq 38$. Chest roentgenograms were obtained during at least 3 days.

Volume resuscitation consisted of crystalloid infusions, whole blood, and Reomacrodex R, 500 ml per 24 hours, which was given for 3 days. Great care was taken not to give the patients a too heavy load of fluid. All patients were kept in the intensive care unit for at least 24 hours.

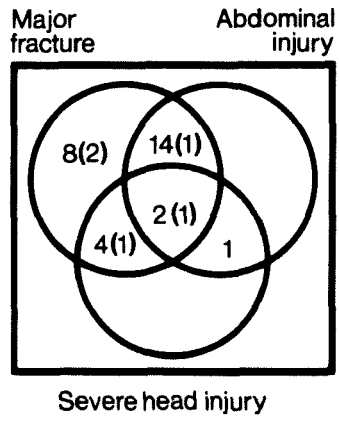


Figure 1. Distribution of injuries. Numbers in parentheses indicate ARDS patients.

Laboratory studies

For coagulation analyses blood was drawn into vacutainer tubes with 0.12 m sodium citrate (1 part venous blood + 9 parts citrate) containing EDTA. The coagulation analyses were performed 1–2 times in 24 hours starting immediately after admission and continuing for 8 days. Hemoglobin concentration, hematocrit, and platelet count were determined up to six times per 24 hours during the patient's stay in the intensive care unit.

Plasma-fibrinogen was measured as fibrin polymerization time by use of a commercial kit (Bio-Merieux). Clotting assays were carried out by use of Fibrometers® (Bio-Merieux). *Plasma-Prothrombin complex* (Simplastin A) was analyzed according to instructions from the manufacturer (General Diagnostics). *Plasma-APTT* was measured with Activated Thrombofax (Ortho Diagnostic Systems). *Serum-FDP* was determined with Wellcotest® (Wellcome Reagents Ltd). *Plasma-antithrombin III activity* was measured with amidolytic methods using chromogenic peptide substrates S-2222 and S-2238 (Kabi Diagnostica) (Odegård et al. 1975). *Plasma-plasminogen* was measured with chromogenic peptide substrate S-2251 (Kabi Diagnostica) as plasmin activity after activation with streptokinase (Friberger & Knöös 1979). *Plasma-alpha-2-Antiplasmin activity* was measured using chromogenic peptide substrate S-2251 (Kabi Diagnostica) (Teger-Nilsson et al. 1977).

Statistical methods. Analys of variance (one factor analysis) was used and 95 per cent confidence intervals for median values were calculated according to Dixon & Massey (1969).

Results

The results of blood coagulation tests and hematologic data showed varying patterns. Platelet number and plasminogen activity decreased until days 2–4 and increased later (Figure 2, 3). Fibrinogen and alpha-2-antiplasmin increased at varying rates from initially subnormal to elevated values (Figure 3, 4). AT III activity showed a similar increase, although less in the ARDS patients (Figure 4). APTT values showed a slight progressive decrease. A high proportion of FDP values on days 1–3 were elevated but gradually decreased after that, but the range was wide (Table 1).

Five patients fulfilled the criteria of ARDS

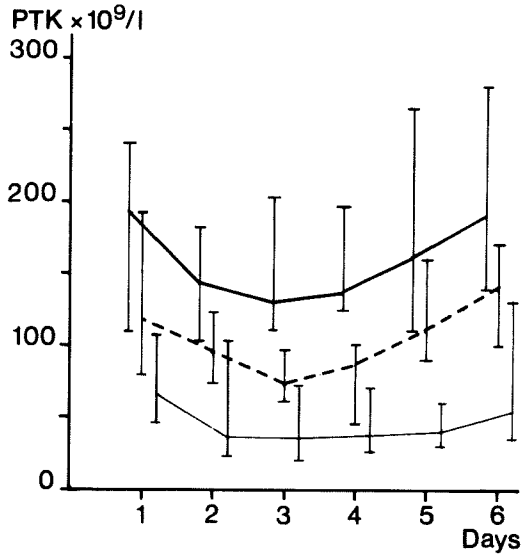
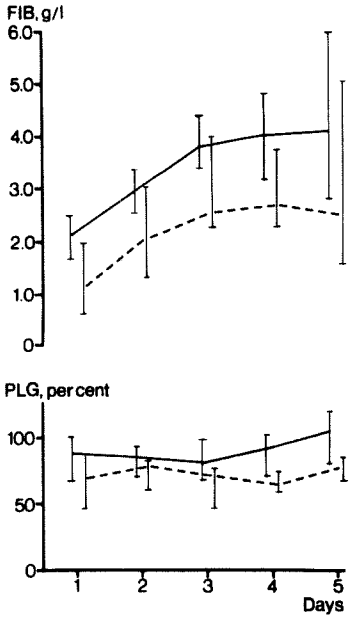


Figure 2. Platelet number (B-TPK). Median values with 95% confidence limits.
— non-ARDS patients with loss of less than 50% of blood volume.
--- non-ARDS patients with loss of more than 50% of blood volume.
— ARDS patients.

(Figure 1). The clinical picture of ARDS developed in these patients 36–72 hours after the trauma. Varying degrees of respiratory impairment, pyrexia, tachycardia, irritability, and restlessness occurred. Three of these patients were put on a mechanical ventilator to prevent severe brain injury. Of the remaining two ARDS patients, one had respiratory failure that necessitated artifical ventilation, and one managed on spontaneous respiration. On chest roentgenograms, varying findings of unilateral localized infiltrates were recorded in 10 patients without ARDS and in three patients with ARDS. None of the patients developed diffuse bilateral infiltrates involving all lung fields.

The ARDS patients had more pronunced changes in blood coagulation parameters than the non-ARDS patients. The platelet counts of the ARDS patients remained low (Figure 2). Mean values for individual patients during the first 6 days differed between non-ARDS and ARDS patients ($p < 0.001$).

The platelet number was influenced by the amount of blood transfused, which in turn was related to the degree and typ of trauma (Figure



◀ Figure 3. Fibrinogen (FIB) and plasminogen (PLG) concentration. Median values and 95% confidence limits. —— ARDS patients, -- non-ARDS patients.

Figure 4. Antithrombin (AT III) and alpha-2-antiplasmin (APL) activity. Median values with 95% confidence limits. —— ARDS patients, -- non-ARDS patients. ▶

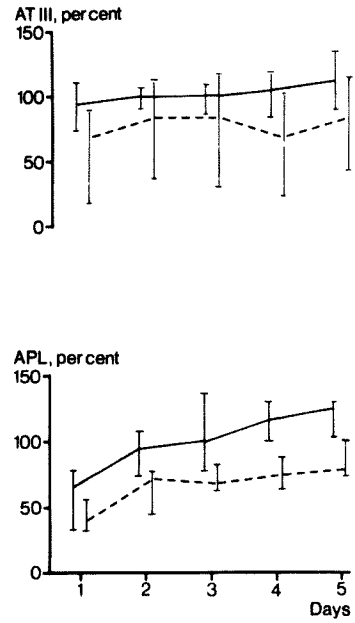


Table 1. Changes in fibrinolytic response in trauma patients in relation to development of ARDS

Days after accident	ARDS		Serum-FDP mg/l				
	+	−	>160	160–80	80–40	40–10	<10
1	5		4	1	0	0	0
		17	2	2	1	8	4
2	5		2	0	2	1	0
		22	0	0	3	11	8
3	5		0	2	0	3	0
		19	0	0	2	8	9
4	3		0	0	1	2	0
		18	0	1	1	10	6
5	4		0	1	1	2	0
		14	0	1	0	7	6
6	4		0	1	2	1	0
		14	0	0	2	7	5

2). When only patients transfused with similar amounts of blood were compared, there was still a difference between ARDS and non-ARDS patients ($p < 0.01$).

Antithrombin III, fibrinogen, and plasminogen were lower in the ARDS patients ($p<0.05$), as well as antiplasmin activity ($p<0.01$) (Figures 3 and 4). The results of FDP were difficult to evaluate due to the large variation, but levels exceeding 160 mg/l on the second and third day were only encountered in ARDS patients (Table 1). FDP was abnormal in all ARDS patients during the observation period. APTT values were higher ($p<0.01$) in ARDS patients, but prothrombin complex and ethanol gelatin test did not show significant differences between ARDS and non-ARDS patients.

Discussion

The recognition of subclinical forms of ARDS and early diagnosis are essential in order to prevent secondary injuries from hypoxia (Bradford et al. 1970, Kierulf et al. 1982, Shoemaker et al. 1980, String et al. 1971). It may be assumed that early blood fluid replacement and stabilization of respiration reduces the morbidity and mortality after severe trauma (Apple & Shoemaker 1981, Shoemaker et al. 1980). Secure and early fracture fixation is also of great importance to prevent ARDS (Goris et al. 1982).

Fully developed ARDS is characterized by hypoxia, new diffuse bilateral infiltrates involving all lung fields in chest roentgenograms, pulmonary capillary wedge pressure less than 10 mm Hg, and hypoxia (Pepe et al. 1982).

However, hypoxia is present in ARDS patients at an early stage before the development of diffuse pulmonary infiltrates (Blaisdell & Schlobohm 1973). If treatment is initiated early, pulmonary roentgenographic findings would be reduced. Definition of ARDS based on $PaO_2 < 8$ kPa on air breating or $PaO_2/FiO_2 \leqq 38$ as used by Ogawa et al. (1977) and on clinical signs is valid only if other reasons of hypoxia can be excluded.

ARDS in connection with sepsis usually occurs the second or third week after trauma. Our study was focused on the events during the first week after trauma when infectious complications as a cause of respiratory failure is unusual.

There was a predominance of older people in our series. It can partly be explained by the high mean age of the inhabitants in the admittance area and partly be exclusion of severe thoracic injury, which was common among younger patients.

Our results indicate that early changes in blood coagulation parameters might separate ARDS from non-ARDS in high-energy trauma patients. During the first 48 hours after admission, significant differences between ARDS and non-ARDS patients were found in platelets, fibrinogen, FDP, antiplasmin, and APTT reflecting an activation of the coagulation and fibrinolytic systems in 23 of 29 patients. The changes in antithrombin were not as striking as in other reports (Kierulf et al. 1982, Risberg et al. 1982). Judging from the mean values of the individual patients during the first 6 days, the platelet count showed the greatest difference between ARDS and non-ARDS patients. The platelet number, however, was also influenced by the amount of blood transfused to the patients to replace blood losses. A possible explanation of this is a short survival of transfused platelets. When patients transfused with a similar amount of blood were compared the difference was still significant, indicating consumption of platelets caused by the trauma. The observed changes in hemostatic parameters suggest disseminated intravascular coagulation (DIC).

However, ARDS does not seem to correspond completely to DIC (Ogawa et al. 1977). Some of our patients had changes in coagulation tests as in DIC, but a diagnosis of ARDS or DIC could not be established.

Laboratory values to suggest risk levels for developing ARDS were obtained from the confidence limits of the values recorded in non-ARDS patients (Table 2) with similar blood losses as the ARDS patients.

We conclude that in multiple trauma patients blood coagulation studies showed activation of the coagulation and fibrinolytic systems. These changes were most pronounced in the patients who developed ARDS (5 of 29 patients). The most sensitive laboratory indicator of ARDS was the platelet count, if related to the amount of blood transfused to the patients.

Acknowledgements

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Table 2. Proposed limits of some coagulation factors for prediction of ARDS risk

Day	Bood-TPK ×10(9)/l Blood loss >50%	<50%	Plasma-Fib g/l	Serum-FDP mg/l	Plasma-ATIII %	Plasma-PLG %	Plasma-APL %
1	<80	<110	≦1.7	>80	≦75	≦80	≦40
2	<70	<100	<2.6	>10	<90	<70	<75
3	<60	<110	<3.4	>10	<90	<70	<75

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