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The contribution of underlying systemic rheumatic diseases to the mortality in patients admitted for intensive care: A matched cohort study

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ABSTRACT

Objective. *The aim of this study was to determine the outcome of patients with systemic rheumatic diseases admitted to our medical-intensive care unit (ICU) in comparison to the outcome of patients with non-rheumatic diseases in the same ICU.*

Methods. *The hospital files of 50 patients with systemic rheumatic diseases who were treated in the medical-ICU of Hacettepe University Hospital, Ankara between 1995 and 2001 were retrospectively evaluated. 50 patients without any underlying systemic rheumatic diseases admitted to the medical-ICU in the same time period and matched for age, gender and acute physiology and chronic health evaluation scores were included in the control group. ICU outcome was compared between the two groups.*

Results. *The acute physiology score of the study group was lower than that of the control group (13.4 ± 5.7 [SD] vs. 17.3±7.2, p=0.04). Moreover, the study group received more immunosuppressive treatment but less invasive procedures (i.e. mechanical ventilation and central venous catheterization). Mortality rates (56% vs. 54%, respectively, p = 0.5), lengths of stay in the ICU and in the hospital, the infection rates were similar between the rheumatic disease group and the control group.*

Conclusion. *The presence of a systemic rheumatic disease seems to negatively affect the outcome in patients under intensive care.*

Introduction

Systemic rheumatic diseases include a group of diffuse inflammatory autoimmune disorders which are commonly treated with systemic immunosuppressive drugs. These disorders can cause immunosuppression because of the nature of the disorder itself and the use of cytotoxic therapies (1, 2). These patients occasionally need to be admitted to an intensive care unit (ICU) for infectious complications and/or organ dysfunction due to the primary "immunocompromising" disease (1-3). There are very few studies focusing on the prognosis of such patients however (1-3). Moreover it is difficult to confirm whether it is the underlying disease itself or the severity of the condition requiring admission to the ICU that influences most the ICU outcome of these patients. Therefore, we sought to compare the outcome of patients with underlying systemic rheumatic diseases who were treated in our medical-ICU with the outcome of patients without systemic rheumatic diseases.

Patients and methods

Hospital records of 50 patients with underlying systemic rheumatic diseases who were treated in the medical-ICU of Hacettepe University Hospital between 1995 and 2001 were retrospectively evaluated. The diagnoses of systemic rheumatic diseases were made according to the criteria defined by the American College of Rheumatology (4). The control group was structured from the database of the medical-ICU between the years 1995-2001. The factors that could affect the outcome of the patients were determined such as age, sex and disease severity. Disease severity was measured using the APACHE II score. The worst physiologic values in the first 24 hours were used to calculate the APACHE II scores (5).

To make a comparison with the results of the patients in the study group, patients without systemic rheumatic diseases were selected from the medical-ICU database by the method of age ± 5 years for each patient in the study group. A second elimination was made from the age-matched patients according to gender. From the gender- and age-matched patients a third elimination was carried out using the APACHE II score ± 3. After selection was completed, 50 age-, gender-and the disease severity-matched patients without any underlying systemic rheumatic diseases admitted to the medical-ICU in the same time period were included in the control group ($p > 0.05$ for age, sex, APACHE II scores)

The underlying diseases, admission diagnoses, administration of corticosteroids and/or cytotoxic drugs for more than 3 months prior to the admission, application of central venous catheterization and mechanical ventilation, infections acquired in the medical-ICU,

and length of stay (LOS) in the medical-ICU and in the hospital were recorded. The Glasgow coma score (GCS) and the acute physiologic scores (APS) were calculated using the worst values in the first 24 hours of admission (5).

Causes of admission to the medical-ICU were grouped as follows: (1) respiratory causes were defined as acute deterioration in gas exchange or ventilation and the need for an increased inspired oxygen concentration or mechanical ventilation; (2) cardiovascular causes were defined as acute coronary syndromes, cardiogenic shock/pulmonary oedema, severe arrhythmias necessitating emergent therapy; (3) gastrointestinal/hepatic causes were defined as severe gastrointestinal bleeding or impairment of hepatic functions sufficient to result in encephalopathy; (4) metabolic causes were defined as acute renal failure, severe fluid and electrolyte disturbances and endocrinologic emergencies such as diabetic ketoacidosis, hyperosmolar non-ketotic coma; (5) neurological causes include cerebrovascular accidents, seizures or coma; and (6) infectious causes were defined as the infections that cause sepsis and/or multiple organ failure.

The primary outcome was mortality in the medical-ICU. Secondary outcomes were LOS in the hospital and LOS in the medical-ICU.

Statistical analyses were performed using SPSS for Windows (version 10.0). Continuous variables were compared by using the paired t-test; categorical variables were compared using the chi-square test. A p value < 0.05 was considered statistically significant. Data are reported as the mean ± SD unless stated otherwise.

Results

The underlying diseases of the patients and the admission diagnoses are given in Table I and Table II, respectively. Pulmonary conditions were the main cause of admission to the ICU in both groups. Gastrointestinal/hepatic causes were more frequent in the control group ($p = 0.04$), whereas neurological causes as the admission diagnoses were more frequent in the study group ($p = 0.04$). The distribution of the demographical and general characteristics of the patients are presented in Table III.

Table I. The underlying diseases of the patients in both groups.

Study group	(n = 50)	Control group	(n = 50)
Systemic lupus erythematosus	25	Malignancy	1
Rheumatoid arthritis	8	Pulmonary diseases	11
Churge-Strauss syndrome	1	Haematological diseases	10
Systemic sclerosis	5	Metabolic diseases	11
Behçet's disease	4	Gastrointestinal diseases	8
Wegener's granulomatosis	2	Cardiovascular diseases	4
Polymyalgia rheumatica	1	Infectious diseases	1
Familial Mediterranean fever	2	Others	4
Polyarteritis nodosa	1		
Juvenile rheumatoid arthritis	1		

Table II. The reasons for admission to the intensive care unit.

	Study group (n = 50)	Control group (n = 50)	p
Pulmonary causes	18 (36%)	20 (40%)	0.189
Cardiovascular causes	4 (8%)	5 (10%)	0.120
Gastrointestinal/hepatic causes	4 (8%)	9 (18%)	**0.04**
Metabolic causes	9 (18%)	8 (16%)	0.8
Neurologic causes	7 (14%)	2 (4%)	**0.04**
Infectious causes	8 (16%)	6 (12%)	0.6

Patients with systemic rheumatic diseases received more immunosuppressive agents and steroids than the patients in the control group ($p = 0.02$ for each). However, invasive procedures (i.e., central venous catheterization and mechanical ventilation) were applied more frequently in the control group than in the study group ($p < 0.01$ for each). The frequency of infections acquired in the ICU were similar between the two groups ($p = 0.46$).

The first 24 hour acute physiology score (APS) was higher in the control group (17.3± 7.2) than in the study group (13.4 ± 5.7) ($p = 0.04$). GCS were comparable between the two groups ($p = 0.4$). Fifteen patients in the control group did not have an underlying systemic chronic disease. Five patients had been hospitalized due to infections of the lower respiratory tract, 2 had acute renal failure, 3 had acute cardiovascular problems, 4 had impaired general health status and electrolyte imbalance, and 1 was hospitalized due to fever of unknown origin.

Mortality rates in the ICU were similar in the study and the control groups (56% vs. 54%, respectively; $p = 0.05$). LOS in the ICU were 8.3±11.4 days vs. 9.6±11.1 days for the study and control groups ($p = 0.73$), and LOS in the hospital were 21.5 ± 26.6 days vs. 26.2 ± 25.2 days for the study and control groups ($p = 0.64$).

Discussion

In our study we demonstrated that the observed mortality and hospital outcome of the patients admitted to our ICU with underlying systemic rheumatic diseases was similar to that of age, sex and APACHE-matched patients with non-rheumatic diseases. The APSs of the patients in the systemic rheumatic disease group in the first 24 hours of admission were better than the scores of the patients in non-rheumatic disease group. Therefore we concluded that the underlying systemic rheumatologic disease negatively influenced the outcome in the ICU because after the elimination of age and sex factors that could influence the outcome, the APACHE II score was the main quantity that could show the patient's health status on admission in ICU.

Table III. The distribution of the demographics and general characteristics of the patients.

	Study group (n = 50)	Control group (n = 50)	p
Age (years)	45.6 ± 16.1	47.4 ± 14.6	0.99
Male/female	15/35	15/35	0.99
APACHE II score	20.1 ± 7.0	20.9 ± 7.0	0.85
Acute physiology score	13.4 ± 5.7	17.3 ± 7.2	**0.04**
GCS	9.3 ± 6.6	10.1 ± 4.5	0.4
LOS in the medical-ICU (days)	8.3 ± 11.4	9.6 ± 11.1	0.725
LOS in the hospital (days)	21.5 ± 26.6	26.2 ± 25.2	0.643
Immunosuppressive therapy	24 (48%)	18 (36%)	**0.019**
Steroid treatment	38 (76%)	16 (32%)	**0.019**
Central venous catheterization	14 (28%)	30 (60%)	**0.001**
Mechanical ventilation	19 (38%)	36 (72%)	**0.001**
Infections acquired in the ICU	9 (18%)	12 (24%)	0.461

APACHE: Acute physiology and chronic health evaluation; GCS: Glascow coma score; LOS: Length of stay; ICU: Intensive care unit.

The APACHE score is a summation of APS, age and chronic health status. Age was eliminated by matching, the maximum chronic health status score was given to all patients in the systemic rheumatologic disease group because of the immunosuppresion of the diseases themselves and the given medications. However, in the non-rheumatologic disease group some patients had accompanying organ insufficiency or an immunocompromised state that could affect their previous health status but some did not. Overall, APS shows the health status of patients in the ICU during the first 24 hours. APS is a summation of the worst values of the vital signs, blood partial oxygen and pH, white blood cell count, hematocrit, blood electrolytes (sodium, potassium), blood creatinine, and the Glascow coma score (GCS) during the first 24 hours after admission. GCS were comparable between the two groups ($p > 0.05$).

Acute physiological scores were better in the study group than in the control group. This means 24-hour vital signs and the physiological status of the patients in the study group was better than those in the control group. The length of stay in the ICU and in the hospital, and the rate of acquired infections in the ICU were similar between the two groups. However, patients with underlying systemic rheumatic disease had a worse ICU outcome even though their acute physiologic score was less than the control group. This might be due to the presence of ongoing systemic inflammation in the rheumatic disease patients causing an immunocompromised state. Our results were similar to previous observations of Godeau *et al*. (1), who demonstrated that baseline chronic systemic diseases, when the effect of age was eliminated, seemed to be the only significant factor affecting the short-term outcome in the medical intensive care unit. However the French study previously demonstrated a comparable intensive care mortality rate for the patients with or without systemic rheumatologic diseases with a similar simplified APS, and the authors concluded that systemic rheumatic diseases did not negatively influence the outcome in the intensive care unit (3).

Recent efforts to measure the quality and the efficiency of hospital care have focused on the patients'survival, duration of the hospitalization period, duration of stay in the ICU, and infections acquired in the ICU (1-3). In our study hospital mortality rates were similar in both groups. LOS in the medical-ICU and LOS in hospital were also comparable in the two groups and not longer than in previous reports (6,7). Infectious complications were the most common cause of death, and hence appear to be important as a prognostic factor of the short-term outcome and mortality (1,2). Hellman *et al.* suggested that mortality often results from the interplay of multiple processes and that infection can be a major contributor to the patient mortality in ICU (8).

In the present study, despite the previous use of steroids and immunosuppressive drugs, the occurrence of infections during the hospitalization period in the ICU was comparable in both groups. The more frequent need for a venous catheter and/or mechanical ventilation in the control group could have caused this finding. Therefore, infectious complications do not seem to contribute to the observed mortality rates of the study and the control groups. One more important result was the prevalence of systemic lupus erythematosus (SLE) in the study group (50% of the patients). However, the overall patient population in the study group was not large enough to speculate on the effects of SLE itself on the ICU outcome. Respiratory insufficiency is another leading cause of ICU admission. Recent trials demonstrated that respiratory failure could be a more common indication for ICU than infectious causes (7, 9, 10). Similarly the main cause of ICU admission was acute respiratory failure in our study. However, since the rates of respiratory failure were comparable in both groups (36% and 40% for the study group and the control group, respectively, $p = 0.189$), respiratory problems could not be expected to affect our results.

In conclusion, despite the better physiological status, progress in the management of the underlying systemic diseases, and novel technologies for the follow-up of patients in the ICU, the mortality rate of patients with systemic rheumatic diseases was similar to the APACHE II-matched patients without systemic rheumatic diseases. However, the relatively small sample size of the study and control groups does not allow us to draw a definitive conclusion. Therefore, future prospective trials with larger disease-specific patient groups with longer follow-up periods will help to make more dependable conclusions.

References

1. GODEAU B, MORTIER E, ROY PE *et al*.:

Short and long term outcome for patients with systemic rheumatic diseases admitted to intensive care units: a prognostic study of 181 patients. *J Rheumatol* 1997; 24: 1317-23.

2. GODEAU B, BOUDJADJA A, DHAINAUT JF *et al*.: Outcome of patients with systemic rheumatic disease admitted to medical intensive care units. *Ann Rheum Dis* 1992; 51: 627-31.
3. ROSENTHAL G: Potential for bias in severity adjusted hospital outcomes data analysis of patients with rheumatic disease. *J Rheumatol* 1994; 21: 721-7.
4. KOOPMAN WJ: *Arthritis and Allied Conditions. A Textbook of Rheumatology*. 14th ed., Vol. 1 and 2. Philadelphia, 2001; chapters 5-7.
5. KNAUS WA, DRAPER EA, WAGNER DP, ZIMMERMAN JE: APACHE II: A severity of disease classification system. *Crit Care Med* 1985; 13: 818-28.
6. KOLLEF M, ENZENAUR R: Predicting outcome from intensive care for patients with rheumatologic diseases. *J Rheumatol* 1992; 19: 1260-2.
7. NAJWA KB, SHENNAK M, SHUKRI A *et al*.: Nasocomial infections in the intensive care units at a university hospital in a developing country: comparison with national nasocomial infections surveillance intensive care unit rates. *Am J Infect Control* 1999; 27: 547-52.
8. HELLMAN D, PETRI M, WHITTING-O'KEEFE Q: Fatal infections in systemic lupus erythematosus: The role of opportunistic organisms. *Medicine(Baltimore)* 1987; 66: 341-8.
9. THONG BY, TAI DY, GOH SK, JOHAN A: An audit of patients with rheumatic diseases requiring medical intensive care. *Ann Acad Med Singapore* 2001; 30: 254-9.
10. POURRAT O, BUREAU JM, HIRA M, MARTIN-BARBAZ F, DESCAMPS JM, ROBERT R: Outcome of patients with systemic rheumatic diseases admitted to intensive care units: A retrospective study of 39 cases. *Rev Med Interne* 2000; 21: 147-51 (abstract).