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Prognosis of critically ill patients with multiple organ failure

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Abstract: The purpose of this study was to determine the mortality rate in 527 critically ill patients with multiple organ failure (MOF), treated in our ICU between August, 1986 and January, 1992, and to compare it with the results obtained in a group of patients studied who had been treated between October, 1978 and July, 1986. The relationship between the mortality rate and each type of organ failure and the extent of organ system involvement was also investigated. The overall mortality rate was 25%, and the rate increased with the number of failed organs. Sepsis and disseminated intravascular coagulation were closely associated with the development of MOF. The mortality rate of patients with the failure of two organs in the present study was significantly lower than that found in those in the previous study. Although artificial organ mechanical life support technology other than that for patients with renal failure is still unsatisfactory, these results suggest that the prognosis of patients with MOF is improving.

Key words: Multiple organ failure, Mechanical life support, Renal failure, DIC, Sepsis

Introduction

Multiple organ failure (MOF) is one of the leading causes of death in patients in intensive care units (ICUs) [1,2]. Previous studies have established that the prognosis worsens as the number of failed organs increases [1,3], and that sepsis and disseminated intravascular coagulation (DIC) are consistently associated with MOF [1,3].

Although our understanding of the pathophysiology of MOF is still incomplete [4,5], the management of critically ill patients has markedly improved in recent years, and sepsis and DIC are now diagnosed and treated earlier [1]. In addition, advances have been made in artificial organ support technology to maintain adequate tissue oxygenation and to provide adequate nutrition [6,7]. However, it is not clear whether these therapeutic advances have substantially decreased the incidence of death in critically ill patients with MOF. In addition, the frequency and prognostic value of MOF in patients with failure of specific organs is not well understood.

The purpose of this study was to examine the mortality rate of critically ill patients with MOF and whether the results differed from those of a group of patients previously studied [1] who had been treated in our ICU between October, 1978 and July, 1986. The relationship of mortality rate to the failure of each organ and to the extent of organ system involvement was also investigated.

Patients and methods

The subjects of the study were 527 patients with life-threatening organ impairment who were urgently admitted to the multidisciplinary ICU of Kumamoto University Hospital during the 5-year, 6-month period between August, 1986 and January, 1992. The mean age of the 221 females and 306 males was 47 years (range, 0 to 93 years). Of the total of 559 patients of this description, 32 were excluded from the study because they were dead on arrival at ICU or had been discharged within a short period of time (<24 h).

Of the 527 patients, 74 were admitted to the ICU due to respiratory failure from pneumonia, pulmonary edema or asthma, 69 due to severe burns, 53 due to ischemic heart disease, 28 due to severe systemic infections, 26 due to thoracic and/or abdominal aneurysm, 25 due to intoxication, 20 due to neurological disease, 15 due to fulminant hepatitis, and 217 due to other disease.

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The definitions of failure of individual organs or organ systems were the same as those used in the previous study [1]. Briefly, organ failure was classified as respiratory, renal, liver, circulatory, gastrointestinal, or central nervous system failure. Respiratory failure was defined as the presence of one or more of the following findings under mechanical ventilation: $A\text{-}aDo_2 > 450$ mmHg with FIo_2 1.0 and 5–15 cmH_2O positive end-expiratory pressure (PEEP); $Pao_2 < 100$ mmHg with $FIo_2 > 0.6$ and 5–15 cmH_2O PEEP; and extracorporeal life support (ECLS) required. Renal failure was defined as the presence of one or more of the following findings: serum creatinine >5 $mg \cdot dl^{-1}$; creatinine clearance <10 $ml \cdot min^{-1}$; and the need for hemodialysis or hemofiltration. Hepatic failure was defined as the presence of one or more of the following findings: total bilirubin >10 $mg \cdot dl^{-1}$ with serum ammonia >100 $\mu g \cdot dl^{-1}$ or with prothrombin time <40% in the absence of systemic anticoagulation; and the need for blood purification including plasma exchange. Circulatory failure was defined as the presence of one or more of the following findings: dopamine or dobutamine >20 $\mu g \cdot kg^{-1}$ min; or the need for intra-aortic balloon pumping or ECLS required. Gastrointestinal failure was defined as the presence of gastrointestinal necrosis and/or gastrointestinal bleeding requiring blood replacement. Central nervous system (CNS) failure was defined as a diminished level of consciousness with a Japan Coma Scale Score ≧200 in the absence of sedative medication for at least 24 h. A patient with one or more of the above-mentioned organ failures during a 24-h period was defined as having organ failure on that day. MOF was defined as the failure of two or more organs in the same period.

Sepsis was diagnosed in the presence of three or more of the following findings: rectal temperature >39°C; total leukocyte count >12 000 ml with many immature forms; a blood culture positive for a recognized pathogen; and positivity for endotoxemia by an endospecific test. The criteria used for the diagnosis of disseminated intravascular coagulation (DIC) were based on the 1987 criteria for DIC of the Ministry of Health and Welfare of Japan [8]. Statistical analysis was performed using a chi-square test with a 2×2 or 2×6 contingency table. Probability values of 0.05 or less were considered significant.

Results

Figure 1 shows the mortality rates of patients classified according to the number of failed organs. The overall mortality rate was 25%, and that of the 214 patients (41%) who did not have organ failure was 0%. The mortality rate increased with the number of failed organs; it was 13% in patients with single organ failure ($n = 142$), and 65% in those with MOF ($n = 171$).

The mortality rate in the 110 patients who had sepsis on or after admission was 60%. Of these, 14% (15 patients) had no organ failure and their mortality rate was 0%; 15% (16 patients) had single organ failure and their mortality rate was 19%; 72% (79 patients) had MOF and their overall mortality rate was 80%. Sepsis was highly associated with MOF; as the number of organ failures increased with the rate of sepsis (Fig. 2).

The mortality rate in the 161 patients who had DIC on or after admission was 59%. Of these, 7% (12 pa-

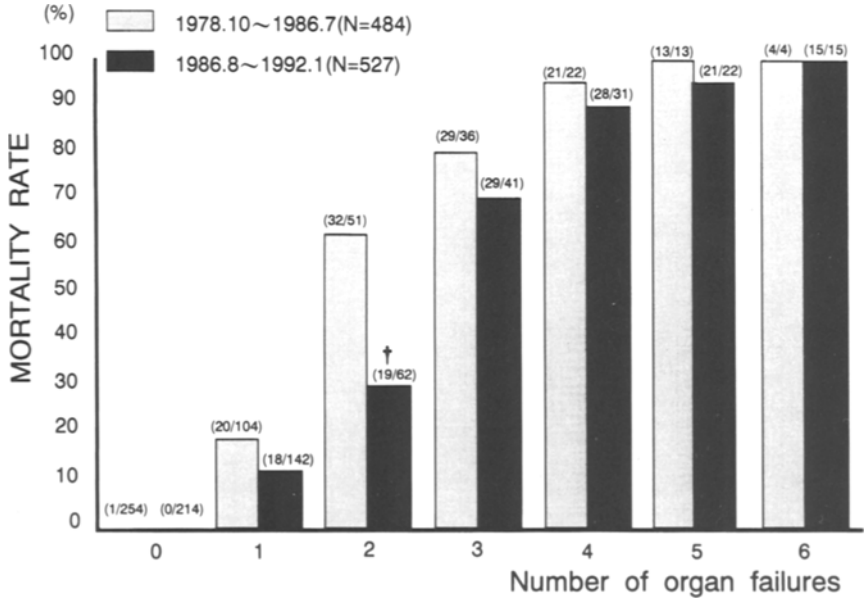

Fig. 1. Mortality rates of patients classified according to the number of patients with organ failure admitted during the period of the present study (August, 1986 to January, 1992) and of our previous study (October, 1978 to July, 1986). There is a linear relationship between mortality rate and the number of organ failures in both groups ($P < 0.001$).
† $P < 0.01$, compared with mortality rate found in the previous study

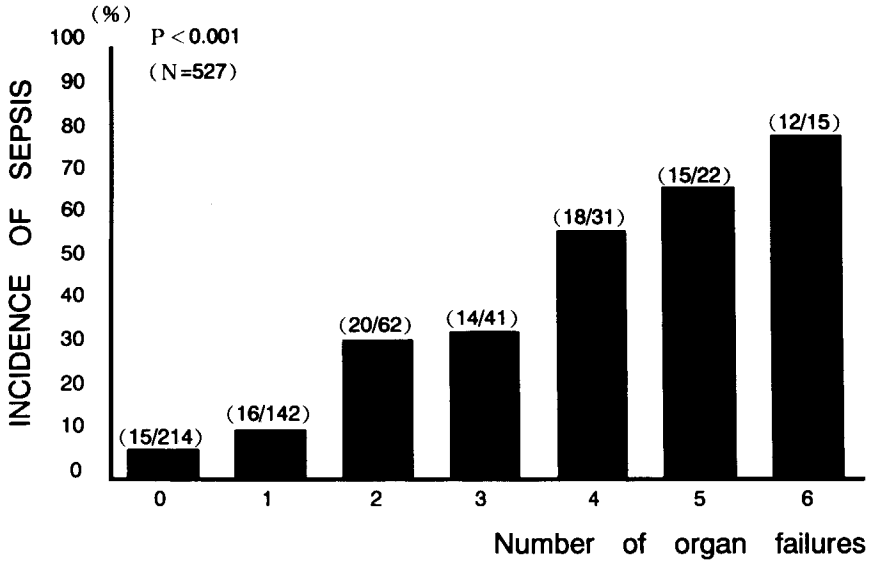

Fig. 2. Relationship between the incidence of sepsis and the number of organ failures

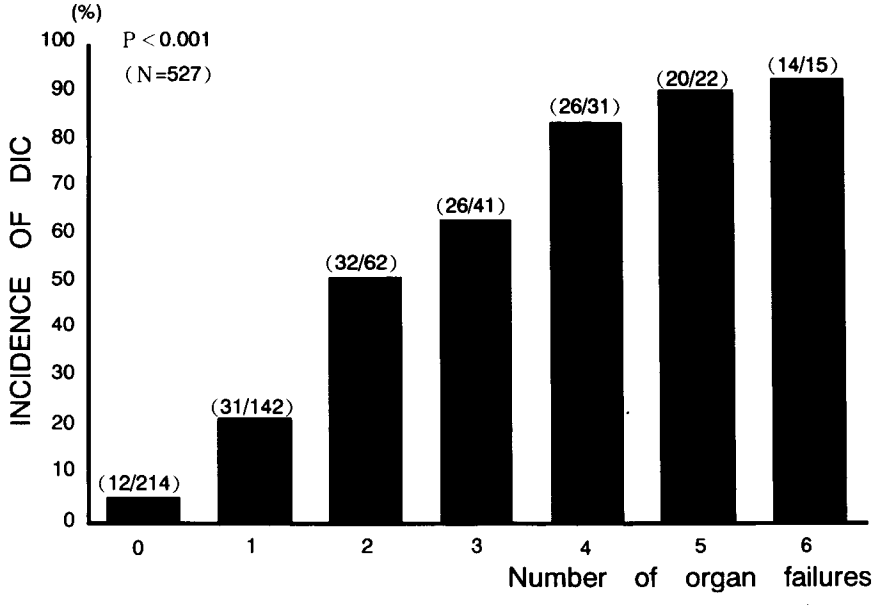

Fig. 3. Relationship between the incidence of disseminated intravascular coagulation (*DIC*) and the number of organ failures

tients) had no organ failure and their mortality rate was 0%. The mortality rate of the 31 patients (19%) with single organ failure was 26%; 73% (118 patients) had MOF and their mortality rate was 74%. As the number of organ failures increased, the rate of DIC increased (Fig. 3).

Table 1 shows the relationship of mortality rate to specific organ failure and the extent of organ system involvement. No patients with single renal failure died. However, 9%–24% of the patients with single respiratory, liver, circulatory, gastrointestinal, or CNS failure died. In every organ failure group, the mortality rate increased with the number of failed organs, and that in patients with sepsis and with DIC was significantly higher than in those without.

Discussion

While advances in the management of critically ill ICU patients are widely believed to have improved the mortality rate in these patients [9], there have been few studies of whether recent therapeutic advances have actually decreased the mortality rate of critically ill patients with MOF [1]. In our previous study, we found no difference in the survival rates of critically ill patients between the first half of the study period and the second half. The overall mortality rate in the previous study, 25% [1], was identical to that found in the present study.

However, analysis of the relationship between mortality rate and the number of failed organs revealed that the mortality rate of patients with two failed organs in

Table 1. Relationship of mortality rate to specific organ failure and the extent of organ system involvement

	No. of patients	No. who died	Mortality (%)
Respiratory failure (REF)	186	93	50
REF only	63	10	16
REF + 1 OF	40	12	30
REF + 2 or more OF	83	71	86
REF + sepsis	63	49	78*
REF + DIC	97	71	73**
Renal failure (RNF)	92	47	51
RNF only	16	0	0
RNF + 1 OF	19	0	0
RNF + 2 or more OF	57	47	82
RNF + sepsis	46	34	74*
RNF + DIC	54	39	72**
Liver failure (LIF)	107	69	64
LIF only	16	2	13
LIF + 1 OF	17	4	24
LIF + 2 or more OF	74	63	85
LIF + sepsis	62	51	83*
LIF + DIC	85	61	72**
Circulatory failure (CIF)	118	91	77
CIF only	17	4	24
CIF + 1 OF	18	10	56
CIF + 2 or more OF	83	77	93
CIF + sepsis	60	54	90*
CIF + DIC	73	66	90**
Gastrointestinal failure (GIF)	91	67	74
GIF only	11	1	9
GIF + 1 OF	8	2	25
GIF + 2 or more OF	71	64	90
GIF + sepsis	58	48	83*
GIF + DIC	68	59	87**
Central nervous system failure (CNF)	117	82	70
CNF only	21	3	14
CNF + 1 OF	19	7	37
CNF + 2 or more OF	77	72	94
CNF + sepsis	48	47	98*
CNF + DIC	73	63	86**

OF, organ failure; DIC, disseminated intravascular coagulation.
* $P < 0.01$ compared with that in patients without sepsis; ** $P < 0.01$ compared with that in patients without DIC.

the present study was significantly lower than in the previous study. In addition, the mortality rate of those with no organ failures and with 1, 3, 4, and 5 organ failures in the present study also showed a slight decrease compared with the previous results. These results suggests that the prognosis for patients with MOF is improving.

Although it is not known whether the slight decrease in mortality rate is attributable to recent technological advances and changes in protocol in our ICU, advances have been made in the following: (1) ventilatory management with low-volume pressure-limited ventilation with permissive hypercapnea in patients with acute respiratory failure introduced in 1985–1990 [10,11]; (2) more aggressive use of continuous hemodiafiltration (CHDF) in those with renal failure commencing in 1990 [12]; (3) combined use of plasmapheresis and CHDF in those with hepatic failure introduced in 1990 [13]; (4) more aggressive use of extracorporeal life support in those with respiratory and circulatory failure introduced in 1986 [14]; (5) aggressive use of enteral nutrition to prevent bacterial translocation commencing in 1990 [9]; and (6) earlier diagnosis of DIC as well as the use of gabexate mesilate or nafamostat mesilate rather than heparin commencing in 1983–1985 [1].

Our examination of the relationship of mortality rate to each type of organ failure and to extent of organ involvement revealed that none of the patients without

organ failure died, nor did any with renal failure alone. However, 9% to 24% of the patients with single respiratory, liver, circulatory, gastrointestinal, or CNS failure died. For example, seven patients died due to idiopathic interstitial pneumonia alone. These results indicate that artificial organ mechanical life support technology, other than that for renal failure, is still unsatisfactory. In addition, the mortality rate increased with the number of failed organs. Sepsis and DIC were strongly associated with sequential failure of multiple organs. These findings are consistent with those in other studies of the relation of acute respiratory failure [15,16], and suggest that, to improve the survival rate of critically ill patients, it is essential to prevent the development of sequential organ failure and to maintain the function of unaffected organs and organ systems, which are susceptible to exacerbation by sepsis or DIC.

Finally, our review of studies of organ failure revealed that the criteria used to define each type of organ failure vary widely from one study to another [1–5]. It is therefore not possible to evaluate the mortality rates by direct comparison. As we have stated previously [1], we consider that "organ failure" should be distinguished from "organ insufficiency". We define organ failure as the requirement or imminent requirement for some degree of mechanical life support. Thus, the criteria we used to define each type of organ failure in both our studies were more stringent than those used in the other studies [2–5]. MOF criteria should be standardized so that the mortality rates of patients with MOF reported in various clinical studies can be compared.

In conclusion, the present findings demonstrate that the mortality rate in critically ill patients increased with the number of failed organs, and that sepsis and DIC were consistently associated with MOF. In addition, although artificial organ mechanical life support technology, other than that for renal failure, is still unsatisfactory, we believe that the prognosis of patients with MOF is improving.

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