Long-term Outcomes of Patients Discharged from the ICU after Recovery

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Long-term Outcomes of Patients Discharged from the ICU after Recovery

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ABSTRACT

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Objective: To determine the long-term mortality of patients discharged from the ICU and identify predictive factors of mortality in these patients.

Methods: All patients admitted to the ICU between 2006 and 2011 who were discharged after recovery were followed up until December 1, 2012 (n = 3699). We examined the associations among gender, age, APACHE II score, type and cause of admission and mortality.

Results: The 1-year and 5-year mortalities were 13.6% and 30.0%, respectively. The mortalities in the first year after ICU discharge were higher than the mortalities in the other periods. Risk factors for mortality were age (hazard ratio range = 1.43 - 4.26), APACHE II score (1.26 - 1.89), type of admission (1.29 - 2.08) and cause of admission (1.74 - 9.21).

Conclusion: Thirty percent of patients discharged from the ICU died in five years. The risk of mortality was dominant in the first year. Age, APACHE II score, type and cause of admission were the factors associated with long-term survival.

Key words: APACHE II score, intensive care unit, mortality, prognosis

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I. INTRODUCTION

An intensive care unit (ICU) is a 24 hour ready unit that resuscitates and monitors patients. Thus, many patients are admitted to the ICU when hemodynamically unstable, or facing a life-threatening condition. For critically ill patients, survival is the outcome of greatest interest.[1,2] Survival in the ICU is only a short-term goal though. Garland *et al.*[3] mentioned that half of Americans spent their last year in an ICU and 20% died in ICUs. Sacanella *et al.*[4] reported 35% of discharged patients who were treated well in an ICU expired in 3 years when above 65 years of age. Although survival is the primary goal of treatment in the ICU, quality of life (QOL) after discharge is also an important issue for patients. This means long-term outcomes are necessary to appreciate the effectiveness of intensive treatment.[2,5] QOL can decrease even though severe diseases are cured because of complications from the diseases and long admission days.[6] Most patients treated in an ICU have a hard time getting back to life like before their hospitalization and some patients continue to die gradually and slowly following discharge. There are many reports on the relationships of short-term outcomes between mortalities and multifactors.[7,8]

However, the reports on long-term outcomes of patients discharged from an ICU are scarce because it is too difficult to follow up with patients, although many researchers have investigated ICUs and in-hospital mortality. We can say that patients are cured of a disease when they are discharged but they cannot live a normal life such because of muscle loss or posttraumatic stress disorder and impaired recognition during their ICU stay. Most people do not to struggle with such quality of life after discharge from the ICU.[9] An ICU stay can be a prognostic factor of mortality.[2] Some kind of indicators that can be measured are needed to understand the patterns of mortality and health care resource use during the time that follows critical illness to allow better targeting of follow-up care. Our study is the first report in Korea of a long-term follow up of patients discharged from the ICU. The aim of this single retrospective cohort study was to determine the long-term mortality of patients discharged from ICU and identify predictive factors of mortality in these patients.

II. MATERIALS AND METHODS

This study was conducted at a tertiary care hospital which had 23 ICU beds at the time of the study. This retrospective study was approved by the Institutional Review Board (IRB). The study cohort consisted of patients admitted between March 1, 2006 and November 30, 2011. During the 68 months of the study, all patients discharged from the ICU with recovery were enrolled. Patients less than 20 years old were excluded from the study. When patients were readmitted to the ICU, the data from their last admission were used. Data were recorded in a database with the following variables for every patient admitted to the ICU: (1) on ICU admission: patient's age, gender, on-admission severity of illness, as measured by the Acute Physiologic and Chronic Health Evaluation (APACHE) II score[10], type of admission (emergency surgery, elective surgery and medical),

cause of admission (multiple trauma, cardiovascular, gastrointestinal, hematologic, metabolic/endocrine, neurologic, renal, and respiratory); (2) during the ICU stay: mechanical ventilator day. The following data were collected at the time of the patient's admission but analyzed retrospectively: (3) after discharge from the ICU: Hospital length of stay (LOS), ICU LOS, survival time, and status on discharge (alive or expired). The severity of illness was estimated using the APACHE II score and recorded within 24 hours after ICU admission. Survival time was measured from the ICU discharge day surveyed on December 1, 2012 using the National Health Insurance Service (NHIS) database. We divided the demographic data into two groups: survivor and nonsurvivor. We made some groups to estimate survival probability: Age (20-49, 50-59, 60-69, 70-79 and 80 or higher), APACHE II score (0-9, 10-19 and 20 or higher), type of admission, and cause of admission. All patients were followed up for a minimum of 12 months and a maximum of 80 months. The expected mortality of the general population of Korea used statistics from the National Statistical Office that are published each year for the period up to December 1, 2012.

1. Statistical analysis

The effects of gender, age, APACHE II score, and type and cause of admission on mortality were studied. Categorical variables were expressed as percentages. Chi-squared test was used for gender. Independent T test was used for age, APACHE II score, ICU length of stay (LOS), hospital LOS, and number of days on a mechanical ventilator. Continuous variables were expressed as means and standard deviations. Cox's proportional analysis was used for expression of hazard ratio (HR) among the cause of admission in connection with mortality. Univariate analysis was used for single values and multivariate for age, APACHE II score, type of admission, and cause of admission. Cox's proportional analysis was used for mortality. Statistical significance was set at p

< 0.05. All statistical analyses were performed using IBM SPSS Statistics 20 (IBM Inc., Armonk, NY).

III. RESULTS

In the 68 month study period, there were 4,975 admitted patients. One hundred seventy-two who were less than 20 years of age were excluded from any further analysis. Three hundred thirty-nine who were readmitted to ICU and 66 who had no laboratory results were excluded from the study. In addition, 699 patients who expired in the hospital, had do-not-resuscitate (DNR) orders or had a hopeless discharge were excluded from the study. Figure 1 shows the exclusion criteria of patients. A total of 3,699 patients were finally included in the study cohort.

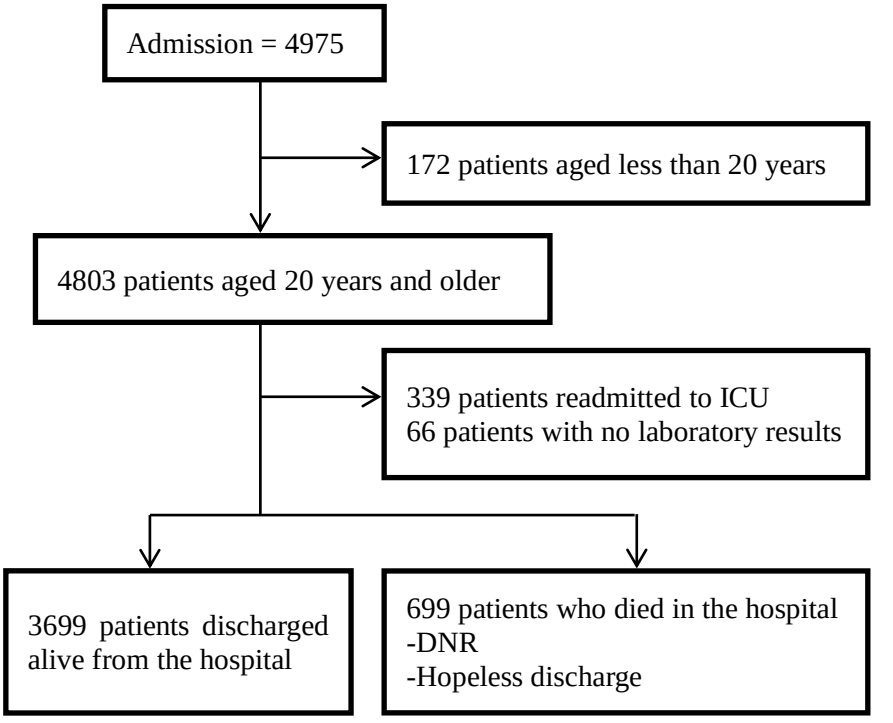

Figure. 1 Flow diagram of the patients screened and included in this study. The schematic shows the selection criteria of patients admitted to the ICU from 2006 to 2011 that were included in the study cohort.

Table 1. Demographic and clinical characteristics

Characteristics	Total (n=3699)	Survivors (n=2781)	Nonsurvivors (n=942)	P-value
Gender (M/F)	2170/1529	1617/1144	553/385	0.834
Age (years)	60.0 ± 16.3	57.6 ± 16.5	66.9 ± 13.8	<0.001
APACHE II	12.3 ± 6.7	11.8 ± 6.5	13.8 ± 7.0	<0.001
ICU LOS[a]	4.4 ± 8.3	4.0 ± 7.9	5.4 ± 9.5	<0.001
Hospital LOS[a]	27.4 ± 27.5	26.3 ± 27.5	30.6 ± 27.0	<0.001
Number of days on a Ventilator[b]	2.9 ± 8.7	2.4 ± 7.7	4.1 ± 11.2	<0.001

[a]LOS: length of stays (days)

[b] Unit: days

Data are shown as the mean ± standard deviation (SD).

The demographic details and clinical characteristics are shown in Table 1. There were significant differences between the survivors and nonsurvivors in age, APACHE II score, ICU LOS, hospital LOS and number of days on a ventilator ($P < 0.001$). Gender had no significant correlation with mortality ($p = 0.834$).

Table 2. Types and causes of admission for the study population

	All	Survivors		Nonsurvivors	
	n	n	%	n	%
Types of admission					
Emergency surgery	459	387	84.3	72	15.7
Elective surgery	2055	1578	76.8	477	23.2
Medical	1185	796	67.2	389	32.8
Causes of admission					
Multiple trauma	95	89	93.7	6	6.3
Cardiovascular	650	499	76.8	151	23.2
Gastrointestinal	1191	844	70.9	347	29.1
Hematologic	18	9	50.0	9	50.0
Metabolic/endocrine	84	69	82.1	15	17.9
Neurologic	737	592	80.3	145	19.7
Renal	164	113	68.9	51	31.1
Respiratory	764	546	71.5	214	28.5

Table 2 shows the numbers and percentages of the types and causes of admission for the ICU patients.

Table 3. Mortality among patients discharged from the ICU compared with gender, age and era-matched general population of Korea

Mortality	One year mortality (%)	General population (%)
Age (year)		
20 – 49	6.5	0.11
50 – 59	9.9	0.38
60 – 69	13.7	0.85
70 – 79	18.5	2.50
≥ 80	28.9	8.85

Table 3 shows the one year mortality after ICU care compared with general population of Korea. The mortality of post-ICU patients was surveyed on December 1, 2012 and the mortality data of the general population of Korea used the statistics from the National Statistical Office retrieved on December 1, 2012 with a gender, age and era-matched population.

Table 4. One and five year mortalities categorized by age, APAPCHE II score, type of admission and cause of admission. Results of Cox proportional analysis of survival after hospital discharge: univariate, multivariate (the risk factors adjusted)

	One year mortality (%)	Five year mortality (%)	Univariate		P-value	Multivariate		P-value
			HR[a]	95% CI[b]		HR[a]	95% CI[b]	
Age (years)								
20 - 49	6.5	15.5	Reference			Reference		
50 - 59	9.9	23.7	1.61	1.26-2.01	<0.001	1.43	1.11-1.83	0.006
60 - 69	13.7	30.6	2.17	1.74-2.71	<0.001	1.92	1.50-2.35	<0.001
70 - 79	18.5	39.5	3.00	2.41-3.73	<0.001	2.52	2.02-3.14	<0.001
≧ 80	28.9	56.9	5.02	4.00-6.34	<0.001	4.26	3.35-5.41	<0.001
APACHE II score								
0 - 9	9.9	22.9	Reference			Reference		
10 - 19	14.7	32.1	1.50	1.29-1.74	<0.001	1.26	1.09-1.47	0.003
≧ 20	21.8	45.5	2.34	1.95-2.82	<0.001	1.89	1.56-2.28	<0.001
Type of admission								
Emergency surgery	8.6	20.1	Reference			Reference		
Elective surgery	12.1	27.0	1.41	1.10-1.80	0.007	1.29	1.01-1.67	0.045
Medical	18.6	38.9	2.19	1.70-2.82	<0.001	2.08	1.61-2.70	<0.001
Cause of admission								
Multiple trauma	3.1	7.2	Reference			Reference		
Cardiovascular	12.4	28.0	4.38	1.94-9.91	<0.001	2.39	1.05-5.43	0.038
Gastrointestinal	15.9	34.5	5.69	2.54-12.74	<0.001	3.65	1.62-8.22	0.002
Hematologic	38.4	69.2	15.83	5.63-44.50	<0.001	9.21	3.26-26.08	<0.001
Renal	18.3	38.9	6.57	2.82-15.21	<0.001	2.92	1.24-6.87	0.014
Respiratory	15.0	33.3	5.39	2.40-12.14	<0.001	3.37	1.49-7.65	0.004
Metabolic/endocrine	8.9	21.0	3.13	1.21-8.06	0.018	1.74	0.67-4.52	0.257
Neurologic	10.5	23.6	3.61	1.60-8.31	0.002	2.25	0.99-5.13	0.053

[a]HR: Hazard ratio

[b]CI: confidence interval

Table 4 presents the one and five year mortalities categorized by age, APACHE II score, type of admission, and cause of admission, and the results of the Cox proportional analysis of survival probability after hospital discharge with univariate and multivariate analysis. The variables at ICU admission associated with ICU mortality were age, APACHE II score, type of admission and cause of admission. The average and corresponding confidence interval of the hazard ratios for determinants are listed above. The most important determinants based on the hazard ratios were age, APACHE II score, type of admission and cause of admission, especially hematologic patients which will be explained below in the discussion.

Age and APACHE II score, type of admission and cause of admission continued to be strongly associated with survival ($p < 0.05$) after the univariate analysis.

Multivariable Cox regression analysis selected four variables associated with ICU mortality: age, sex, APACHE II score, type of admission, and cause of admission. No interaction among these four factors was demonstrated and a nonsignificant Hosmer-Lemeshow test confirmed the model's goodness-of-fit. The factors strongly and independently associated with survival from this multivariate analysis were age, APACHE II score and type of admission. The total mortalities were 13.6% (one year) and 30.0% (five year). Mortality in the first year after ICU discharge was higher than the mortalities in the other periods.

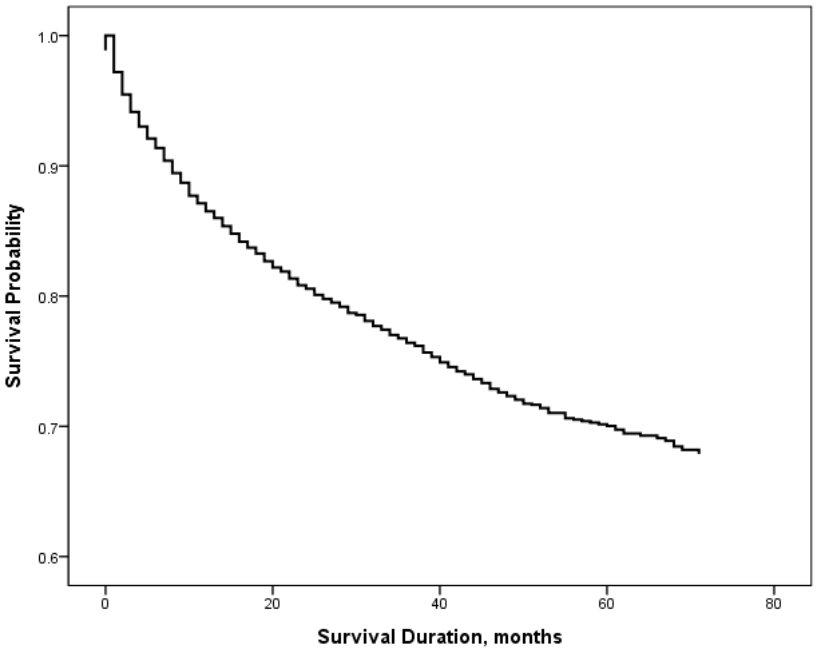

Figure 2. Survival curve of total post-ICU patients. The one year mortality was 13.6% and the five year mortality was 30.0%.

The results of the Cox regression analysis for survival probability are shown in Figure 3. The younger groups have better survival probability than the older groups.

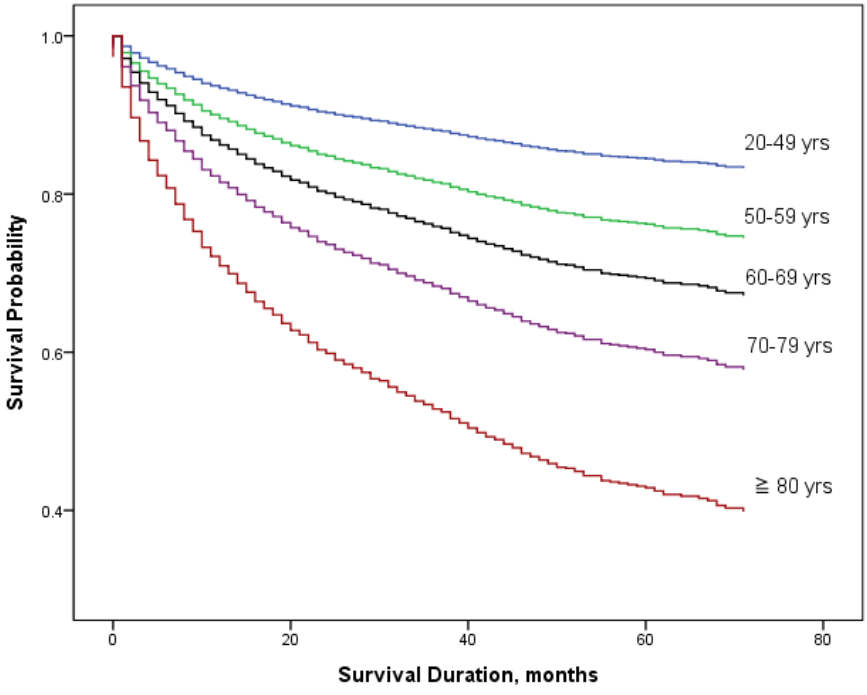

Figure 3. Survival curves showing survival stratified by age. The younger groups have better survival probability than the older groups.

Figure 4 shows the results of the Cox regression analysis of the survival probability for different groups of APACHE II scores. Patients with an APACHE II score of 9 or lower survived longer than patients with an APACHE II score of 10 to 19 or higher than 20.

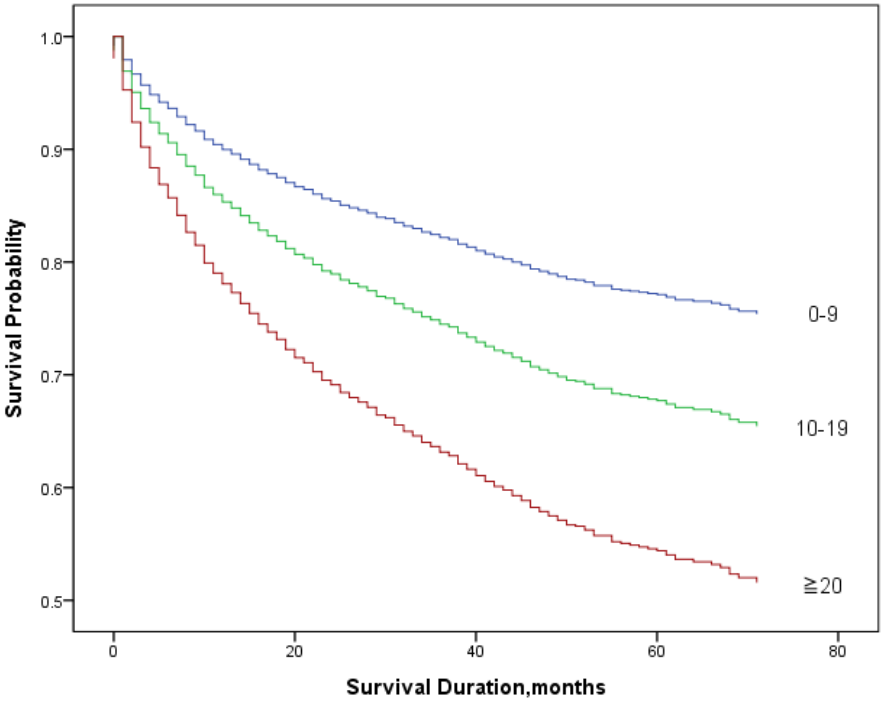

Figure 4. Survival curves showing survival stratified by APACHE II score. If the APAHCE II score is high, the survival probability is expected to be low.

Figure 5 shows the survival probability for the type of admission to the ICU. Patients with emergency surgery survived longer than that of elective surgery and medical reasons.

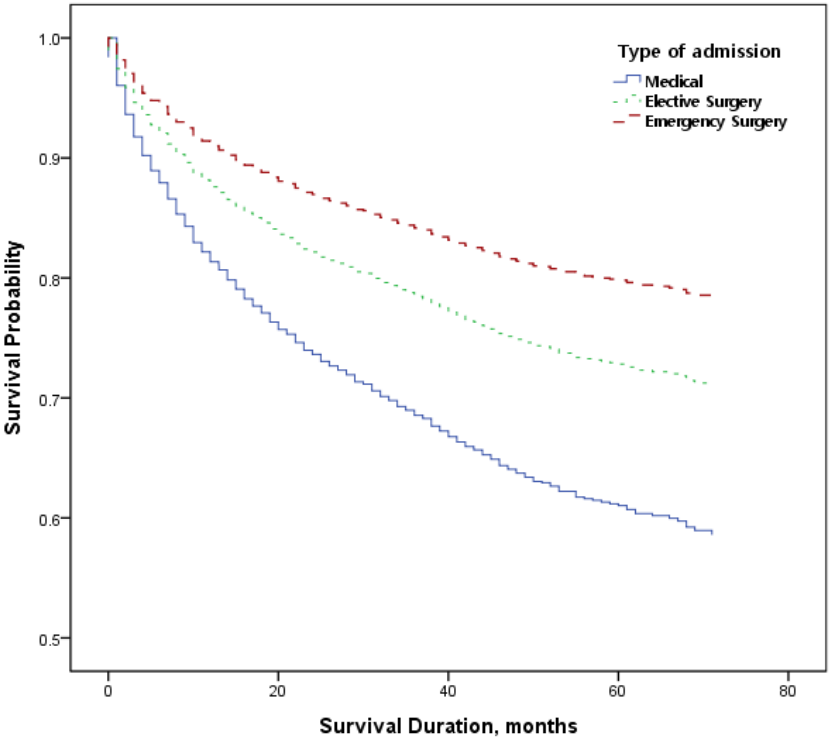

Figure 5. Survival curves showing survival stratified by type of admission. Patients admitted because of emergency surgery has the highest survival probabilityfollowed by patients with elective surgery. The medical group is expected to have the lowerest probability of all.

Figure 6 shows the survival probability for the cause of admission. The causes of admission in order of higer survival probability were multiple trauma, metabolic/endocrine, neurologic, cardiovascular, respiratory, gastrointestinal, renal and hematologic. Patients with hematological disease had particularly poor outcomes.

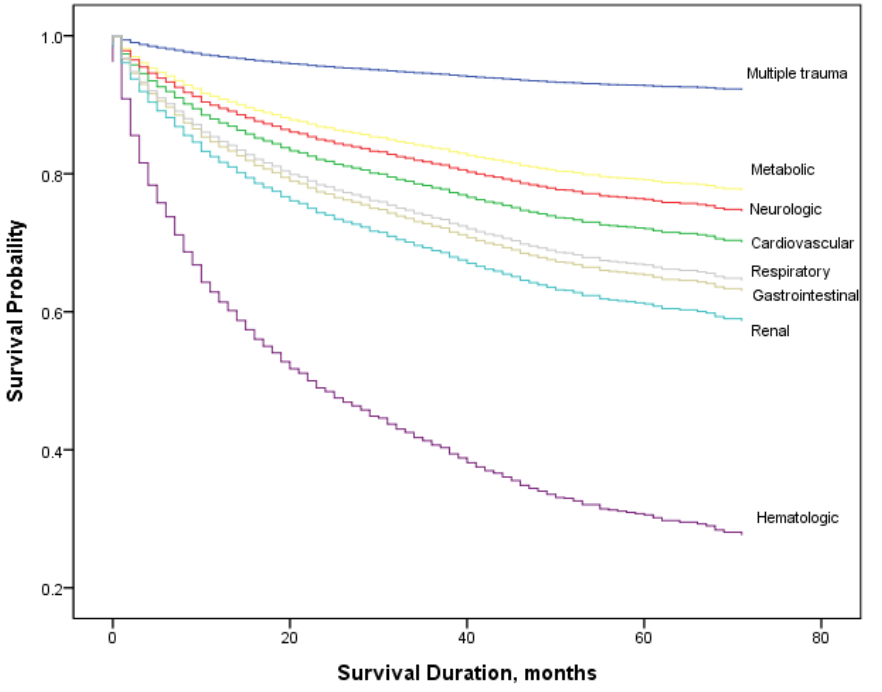

Figure 6. Survival curves showing survival stratified by cause of admission.

IV. DISCUSSION

This study showed that, although patients treated in ICU were discharged because they were fully or moderately recovered, their mortality within the first year after discharge was 13.6% and within five years was 30.0% (about 43% of the patients who died within five years after discharge died within the first year). In particular, it was found that the greatest number of patients died within the first year and the mortality decreased as time passed. The risk factors for long-term mortality after discharge were age, severity of disease (APACHE II score), and type and cause of admission.

Brinkman *et al*.[11] published in 2013 a review article regarding the long-term mortality of ICU patients. They reported that the median value of mortality one year after admission to the ICU was 24% (16-44%).[11] When compared to the result of this study, the mortality was higher because the data included the mortality of patients who died in the ICU as well as in the ward.[11] Williams *et al*.[12] compared the mortality of patients who were treated in the ICU, survived death and discharged between 1987 and 2002 and that of general patients who were not treated in the ICU. As in this study, the mortality of the patients who experienced treatment in the ICU was higher in the first year following discharge than in the other periods (5.4%) and the survival rate was lower than that of the general patients until at least 15 years.[12] Niskanen *et al*.[13] observed the five year survival rate of 12,180 patients who were admitted to 25 ICUs in Finland in 1987 and reported that the mortality was the highest in the first three months following discharge from the ICUs and that it was parallel with the survival rate of the general population from the second year on after discharge.[14] Wright *et al*.[15] compared the mortality of patients admitted to an ICU between 1985 and 1992 and their long-term follow-up mortality after discharge with those of the general population. As in the results of Niskanen *et al*.,[13] the highest mortality was found within the first year and the mortality decreased from the

second year on similar to that of the general population.[15] The first year mortality reported by Niskanen *et al*.[13] and Wright *et al*.[15] was higher than that of this study (27.9%, 36.7% vs. 13.6%). The difference in mortality may be because the follow-up starting point was admission to the ICU in the two previous studies, while this study was conducted with patients who had already been treated in the ICU and discharged, and thus, death in hospitals was excluded when calculating mortality. On the contrary, the mortality within the first year after discharge reported by Williams *et al*.[12] was lower than that of this study (7.4 vs. 13.6%). The difference may be because of the difference in the treatment circumstances after the ICU patients were discharged among the different countries.

The major factors of the long-term survival rate for patients whose health conditions first required ICU treatment but improved later to allow discharge from the ICU were age, severity of disease (APACHE II score), type and cause of admission, and length of hospital stay (LOS). Various factors were found in many studies to be related to long-term mortality but the common and most important factors were severity of illness (APACHE II score) and age at the time of admission.[12,14,16,17] In this study, mortality after discharge was higher when the severity of illness at the time of admission was worse. In the case of critically ill patients, as the severity of illness worsens, hormonal and immune system imbalances increase more than that of general patients. Hence, it is presumed that muscle loss due to a disease and continued immobilization could be associated with the long-term survival rate. Williams *et al*.[12] reported through the Charlson Co-morbidity Index that the severity of an accompanied illness before admission and the onset of a cancer affect the long-term survival rate. In other words, a chronic disease which a patient has had beside the cause of the ICU admission, for example, an accompanied disease such as a hematologic disease or cancer, may affect the APACHE II score at the time of admission and increase the long-term mortality even though the patient is discharged after an

acute illness is treated. In this study also, patients with a hematologic illness showed high mortality, which could be explained by the correlation between co-morbidity and long-term mortality, although this study is limited in that a small number of patients were included in the analysis due to the high mortality of the patient group in the hospital.

Mortality generally increases as age increases. In this study, however, there was a great difference between the first year mortality of the general population and that of the discharged patients. The patients were divided into five age groups, 20-49, 50-59, 60-69, 70-79, and 80 or higher and the morality of the general population was investigated by using the statistical data of 2012 provided by the National Statistical Office. The mortality of each age group was 0.1%, 0.4%, 0.9%, 2.5%, and 8.9%, respectively, suggesting that the mortality increased as age increased.[18] According to Meynaar *et al*.[19] the first year mortality was 3.4% among patients aged 50 or under, 26.6% aged between 80 and 89, and 44.7% aged 90 or over. Although this study was conducted with patients aged 16 or higher and cardiac surgery cases were excluded, the mortality pattern of the general population was similar to that of this study. One particular point of this study is that, when the first year mortality, which was high, was compared with that of the general population for each age group, the mortality of the young patients was high. In the case of the patients whose age was between 20 and 49, the mortality of the patients who were treated in the ICU was 6.5%, which was 59 times higher than that of the general population with the same age group. Although the difference decreased as the age increased, the mortality of the patients aged 80 or over who were treated in the ICU was 28.9%, which was higher than 8.95, which is the mortality of the general population of the same age group. The result contrasts the general expectation with respect to the recovery of patients after discharge that young patients may recover better than that of old patients who are given much concern. Moreover, this result suggests that young patients also need to be particularly concerned about their recovery

after discharge.

Long-term mortality was dependent on the type of admission. In this study, the long-term mortality was the lowest among patients who underwent an emergency surgery and the survival rate was the lowest among patients who were admitted for a medical problem. Studies on the effect of the type of admission on the long-term prognosis of patients after discharge showed various results which are not in accordance with each other. Some studies showed that the type of admission is not correlated with long-term survival.[16,20] On the contrary, a study by Brinkman *et al*.[11] conducted with surgical and medical ICU patients showed the lowest mortality among patients who underwent an elective surgery and the highest mortality among medical patients. In this study, the mortality was the lowest among emergency surgery patients, and the hazard ratio of elective surgery patients and elective surgery patients with reference to the mortality of emergency surgery patients was 1.29 and 2.08, respectively, indicating a significant difference. However, another study reported that the mortality was higher among emergency surgery patients than elective surgery patients, showing an opposite result to that of this study. The cause for this difference may be that patients who underwent open heart surgery such as a coronary bypass surgery and valve replace surgery were admitted to a cardiac critical care unit and thus excluded from the subjects group and neurosurgical patients were also excluded from the subjects group for the same reason. According to Williams *et al*.,[12] the kind of surgery a patient underwent and the existence of sepsis and cardiac arrest had a greater effect on the survival rate than that of surgical type or the existence of an emergency. As in this study, many studies have shown a higher mortality among internal medicine patients than that of surgery patients. Internal medicine patients are more probable to have various chronic diseases beside an acute disease and the chronic diseases may be correlated with mortality.

Although many studies have been conducted on the survival of ICU patients

after discharge, they are limited making a direct comparison with this study difficult for various reasons. First, depending on the characteristics of the ICU at each institution, different patient groups were included in the subjects group. Some studies were conducted only with surgical patients or medical patients, while others were conducted with many cardiac surgery patients because of the characteristics of the institution. Second, mortality may include ICU mortality or hospital mortality depending on the follow-up starting point, which may be at the time of the ICU admission, ICU discharge or hospital discharge, and thus, the mortality after hospital discharge in this study might not be accurately compared.

Although this study was conducted with a large sample size, it still has several limitations. Because the accompanied illness that a patient had before ICU admission and its severity were not investigated, their effect on ICU admission and hospital discharge mortality could not be investigated. It should be taken into account that the subjects of this study did not include open heart surgery patients or neurosurgical patients due to the characteristics of the ICU. The number of neuromuscular patients was particularly great. With respect to the readmission patients, when a patient was admitted during the same hospitalization period, the data of the last admission was used in this study, which might have the effect of being bias.

Therapists for infant and neonatal ICU patients are concerned about the long-term prognosis of the infants and neonatal patients they have treated including the growth of the treated patients in addition to the short-term prognosis. On the contrary, therapists of adult ICU patients consider it a success if the patients survive the ICU and are discharged from the hospital. Therapists of adult ICU patients are interested in the short-term prognosis including ICU mortality, hospital mortality, and 28-day mortality but less interested in the survival of the patients after discharge. Considering that the objective of ICU patient treatment is to help a patient whose life is threatened to return to a

healthy life, attention should be paid to quality of life after discharge. Although having some limitations, it is hoped that this study may provide an opportunity to bring about further research on ICU patients so that ICU patients may return to a healthy life after discharge.

V. CONCLUSIONS

This study showed that the mortality of discharged ICU patients was the highest within the first year following discharge and 30.0% within the first five years. Factors which may affect the long-term prognosis of ICU treatment survival included age, severity of illness, and type and cause of admission. This study showed that ICU patients whose acute disease was treated continuously showed a higher mortality even after discharge. More concern should be given, appropriately so, to the long-term prognosis of ICU patients.

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ABSTRACT (IN KOREAN)

중환자실에서 질병 호전으로 퇴원한 환자의 장기적 예후

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목적: 질병의 호전으로 중환자실을 퇴실한 환자를 장기적으로 추적 관찰하여 사망률과 이에 미치는 요인을 알아본다.
방법: 2006년부터 2011년까지 중환자실에서 질병의 호전으로 퇴실한 환자를 2012년까지 추적 관찰하여 성별, 나이, APACHE II 점수, 입원사유, 입원원인과 사망률을 비교해보았다.
결과: 1년사망률은 13.6%, 5년사망률은 30.0%였다. 사망률에 대한 위험인자는 나이 (위험비구간 1.43-4.26), APACHE II 점수 (1.26-1.89), 입원형태 (1.29-2.08), 입원원인 (1.74-9.21)이다.
결론: 30.0%의 환자가 완치 후 퇴원하여도 5년 내에 사망한다. 1년사망률이 의미 있게 높다. 사망률에 대한 위험인자는 나이, APACHE II 점수, 입원사유, 입원원인을 통해 예측할 수 있다.

핵심 되는 말: APACHE II 점수, 중환자실, 사망률, 예후