ORIGINAL RESEARCH

Acute Care Hospital Mortality of Schizophrenic Patients

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BACKGROUND: Although schizophrenic patients have higher mortality than the general nonschizophrenic population, few studies have investigated acute care hospital mortality of schizophrenic patients.

METHODS: To assess acute care hospital mortality of schizophrenic patients, we analyzed hospital mortality, the risk factors for hospital mortality, and the causes of death of schizophrenic patients admitted to an acute care hospital in Japan over an 18-year period.

RESULTS: We identified 55 deaths among 1108 schizophrenic patients, for a mortality rate of 5.0%. The overall standardized mortality ratio was 1.29 (95% CI, 0.98-1.68) compared with nonschizophrenic hospitalized patients. Significant risk factors for mortality were malignant neoplasm, cardiovascular disease, and admission through the emergency department. The leading causes of death in acute care hospitalizations were suicide (14.5%), malignant lymphoma or leukemia (10.9%), stroke (9.0%), and sepsis (7.3%).

CONCLUSIONS: There was a nearly significant trend toward increased mortality of schizophrenic patients receiving acute hospital care compared with that of nonschizophrenic patients. Because suicide was the most frequent cause of death, a focus on suicide prevention is needed in this population. *Journal of Hospital Medicine* **2008;3:110–116.** © *2008 Society of Hospital Medicine.*

KEYWORDS: continuity of care transition and discharge planning, disease prevention, health promotion, multidisciplinary care.

Previous studies have found that the total mortality of schizophrenic patients was higher than that of the general population.[1–4] The all-cause mortality for schizophrenic patients was 2 to 4 times that of the general population.[5–7] Further, not only was the mortality of schizophrenic patients from suicide and traumatic causes higher than that of the general population, but mortality from natural causes was higher as well.[8,9] Of the specific causes of death of schizophrenic patients, suicide was the most important.[10] In one study, suicidal mortality was approximately 20 times that of the general population.[1] For natural causes, the most common cause of death was diseases of the circulatory system, followed by diseases of the respiratory system, the digestive system, and malignant neoplasm.[2,11] Overall, schizophrenic patients had a life expectancy about 20% shorter than that of the general population.[1]

However, few studies have investigated mortality among schizophrenic patients who were admitted to acute care hospitals. Studies involving large samples of inpatients with schizophrenia in general (nonpsychiatric) hospitals have also been scarce. The specific causes of death of hospitalized schizophrenic patients

have not been investigated thoroughly. In addition, little is known about risk factors associated with the mortality of schizophrenic patients during acute care hospitalization. In this study, we analyzed hospital mortality of schizophrenic patients admitted to an acute care community teaching hospital and compared mortality between schizophrenic and nonschizophrenic patients. Our mortality data included patients presenting with suicidal attempts who died during their admission. We also determined significant factors associated with this increased mortality and the specific causes of death of these patients.

METHODS

Study Patients

We studied all patients admitted to Okinawa Chubu Hospital from January 1, 1987, to December 31, 2004. Okinawa Chubu is a community teaching hospital that provides primary to tertiary care to a population of approximately 400,000 in Okinawa, Japan. Nearly all patients admitted during the study period were Japanese (more than 99.5%).

We identified all schizophrenic patients through the computerized inpatient registry. This registry includes the hospital discharge summary electronic database, which is updated and reviewed by certified hospital record technicians using the ICD-9 coding scheme (*International Classification of Diseases, 9th Revision, and Clinical Modification*). The diagnosis of schizophrenia was documented by staff psychiatrists, who provided basic psychiatric care for these patients in inpatient or outpatient settings. The study was approved by the Institutional Review Board of Okinawa Chubu Hospital.

Data Collection

We obtained basic demographic data on all patients admitted during the study period using the computerized inpatient registry. Data were extracted on demographics, discharge outcome (survival or nonsurvival), route of admission, direct transfer from psychiatric hospitals, admitting department, intensive care unit admission, liaison psychiatrist consultation, length of hospital stay (days), and diagnostic classifications based on the ICD-9. Routes of admission included the emergency department (ED) and outpatient clinic. From the computerized record, we also determined causes of death of schizophrenic as well as nonschizophrenic patients. We performed a manual chart review to determine specific causes of death of schizophrenic

patients because the administrative data included the ICD-9 coding scheme for admitting diagnosis but did not include information on specific causes of death.

Statistical Analysis

We obtained the standardized mortality ratio of schizophrenic patients compared with general patient population during each admission year and calculated the 95% confidence interval (95% CI) using sex-stratified 5-year bands and the exact Poisson distribution method. We also analyzed risk factors associated with hospital mortality. In unadjusted logistic regression analyses, we calculated the odds ratios (ORs) and 95% CIs of the demographic and clinical variables for hospital mortality among all schizophrenic patients. We then performed multivariable-adjusted logistic regression analysis to identify significant risk factors associated with increased hospital mortality, adjusted for demographic and clinical variables. A 2-sided *P* value < .05 was considered statistically significant. All statistical analyses were performed using Stata Software Version 8.2 (StataCorp LP, College Station, TX).

RESULTS

We identified a total of 189,049 general nonschizophrenic patients admitted to Okinawa Chubu Hospital during the 18-year period (Table 1). Of these, 7528 patients died during hospitalization, with an overall hospital mortality rate of 4.0% (95% CI, 3.9%-4.1%). There were 55 deaths among 1108 schizophrenic patients admitted to Okinawa Chubu Hospital during the same period. Schizophrenic patients had an overall hospital mortality rate of 5.0% (95% CI, 3.8%-6.4%). The hospital mortality rate was 4.4% (95% CI, 2.9%-6.5%) for schizophrenic women and 5.5% (95% CI, 3.8%-7.7%) for schizophrenic men.

Comparing the schizophrenic patients and general patients admitted to Okinawa Chubu Hospital during the same period showed no significant differences in acute hospital mortality, with an overall standardized mortality ratio of 1.294 (95% CI, 0.975-1.684) based on sex-stratified 5-year bands using the exact Poisson distribution method. However, there were no deaths among schizophrenics in 2004, which we considered an outlier. Thus, when excluding data on mortality in 2004 from the analysis, we obtained a significant standardized mortal-

TABLE 1
Clinical Characteristics of Schizophrenic and Non-schizophrenic Patients

Clinical characteristic	Schizophrenics n = 1108	Non-schizophrenics n = 189049	p-value**
Age, mean (SD)	48.7 (14.2)	40.0 (28.8)	<0.001
Women, n (%)	543 (49.0)	101218 (53.5)	0.0026
Transferred from psychiatric hospital, n (%)	254 (22.9)	N/A	
Admission through ED, n (%)	853 (77.0)	111109 (58.8)	<0.001
Admitted department, n (%)			
Internal medicine	643 (58.0)	65657 (34.7)	
General surgery	222 (20.0)	43036 (22.8)	
Other departments	243 (21.9)	80356 (42.5)	
Intensive care unit admission, n (%)	157 (14.2)	9900 (5.2)	<0.001
Liaison psychiatrist consultation, n (%)	239 (21.6)	N/A	
Length of hospital stay (days), mean (SD)	25.2 (44.1)	18.0 (42.1)	<0.001
Admission diagnosis, n (%)			
Infectious diseases without organ involvement	13 (1.2)	8009 (4.2)	
Malignant neoplasms	92 (8.3)	18481 (9.8)	
Endocrine, nutritional and metabolic diseases	63 (5.7)	3389 (1.8)	
Hematologic diseases	11 (1.0)	1364 (0.7)	
Mental diseases except schizophrenia	32 (2.9)	673 (0.4)	
Diseases of the nervous system	28 (2.5)	8433 (4.5)	
Diseases of the circulatory system	108 (9.8)	23163 (12.3)	
Diseases of the respiratory system	133 (12.0)	31212 (16.5)	
Diseases of the digestive system	120 (10.8)	15570 (8.2)	
Diseases of the genitourinary system	44 (4.0)	13816 (7.3)	
Complications of pregnancy	46 (4.2)	17132 (9.1)	
Diseases of the skin	23 (2.1)	2582 (1.4)	
Diseases of the musculoskeletal system	20 (1.8)	4221 (2.2)	
Congenital anomalies	1 (0.1)	3496 (1.8)	
Complications in the perinatal period	1 (0.1)	4178 (2.2)	
Ill-defined conditions	40 (3.6)	4677 (2.5)	
Injury and poisoning	190 (17.1)	16083 (8.5)	
Social reasons	5 (0.5)	66 (0.0)	
Indeterminate	138 (12.5)	12504 (6.6)	

*Malignant neoplasms are categorized together rather than included in individual organ systems.

**p-values are calculated using chi-square test for proportions and t-test for continuous variables

SD=standard deviation; ED=emergency department; N/A=data not available

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ity ratio of 1.421 (95% CI, 1.090-1.884) for the schizophrenic patients.

Table 1 also shows the clinical characteristics of schizophrenic and nonschizophrenic patients admitted to the hospital. Admissions of schizophrenic patients showed that 643 patients (58%) were admitted to the department of internal medicine, 222 patients (20%) to the department of surgery, and 243 patients (22%) to other departments. The most common admission diagnoses of schizophrenics were: 190 patients (17%) diagnosed with injury and poisoning, 133 (12%) with diseases of the respiratory system, and 120 (11%) with diseases of the digestive system. Patients with an admitting diagnosis of injury and poisoning included those who had attempted suicide, although the exact number

of patients with suicidal tendencies was unclear in this registry data. Comparison of the clinical characteristics of schizophrenic and nonschizophrenic patients indicated that schizophrenics were more likely to be older, have a longer hospital stay, be male, be admitted through the emergency department, and be admitted to the intensive care unit.

Table 2 presents the specific causes of death of hospitalized schizophrenic and nonschizophrenic patients based on ICD-9 coding. Forty-five schizophrenic patients (81.8%; 95% CI, 69.1%-90.9%) died from natural causes (all deaths excluding injury and poisoning). The most frequent of all causes of death (>2 total cases) were suicide (n = 8; 14.5%), malignant lymphoma or leukemia (6; 10.9%), stroke (5; 9.0%), and sepsis (4; 7.3%). Suicide was the cause of

TABLE 2
Leading Causes of Hospital Mortality in Schizophrenic and Non-schizophrenic Patients

	Schizophrenic patients			Non-schizophrenic patients	
Rank	Cause	No. (%)	Rank	Cause	No. (%)
1	Suicide	8 (14.5)	1	Malignant neoplasms	2646 (35.1)
2	Malignant lymphoma or leukemia	6 (10.9)	2	Diseases of the circulatory system	1769 (23.5)
3	Stroke	5 (9.0)	3	Diseases of the respiratory system	787 (10.5)
4	Sepsis	4 (7.3)	4	Diseases of the digestive system	427 (5.7)
5	Lung cancer	2 (3.6)	5	Injury and poisoning	407 (5.4)
6	Acute myocardial infarction	2 (3.6)	6	Sepsis	262 (3.5)
7	Pneumonia	2 (3.6)	7	Diseases of the genitourinary system	150 (2.0)
8	Uterine cancer	2 (3.6)	8	Diseases of the nervous system	119 (1.6)
9	Neuroleptic malignant syndrome	2 (3.6)	9	Endocrine, nutritional, and metabolic diseases	86 (1.1)
10	Other causes	22 (40.0)	10	Others	875 (11.6)
	Total	55 (100)		Total	7528 (100)

*Specific Causes are shown in schizophrenic patients and ICD-9 classification is used in non-schizophrenic patients.

**Other causes include all causes with single case of hospital mortality in schizophrenic patients

TABLE 3
Risk Factors Associated with Hospital Mortality among Schizophrenic Patients

Clinical characteristic	Unadjusted analysis odds ratio (95% CI)	Multivariable analysis odds ratio (95% CI)
Malignant neoplasms	5.83 (3.14 - 10.83)	12.93 (5.67 - 29.51)
Admission through ED	1.29 (0.62 - 2.68)	3.30 (1.33 - 8.20)
Diseases of the circulatory system	2.17 (1.06 - 4.43)	2.63 (1.20 - 5.77)
Intensive care unit admission	1.37 (0.68 - 2.78)	1.43 (0.65 - 3.11)
Male gender	1.26 (0.73 - 2.17)	1.39 (0.77 - 2.50)
Older age	1.02 (1.00 - 1.04)	1.01 (0.99 - 1.03)
Longer hospital stay	1.00 (0.99 - 1.01)	1.00 (0.99 - 1.01)
Liaison psychiatrist consultation	0.43 (0.18 - 1.02)	0.45 (0.18 - 1.11)
Transferred from psychiatric hospital	0.48 (0.21 - 1.07)	0.37 (0.16 - 0.87)

*Logistic regression analyses are used for each of the clinical characteristics.

**Multivariable-adjusted logistic regression is used including all variables analyzed in the unadjusted analyses.

ED=emergency department; CI=confidence interval.

14.5% (95% CI, 6.5%-26.7%) of all deaths of schizophrenic patients. The initial hospital presentations of patients with schizophrenia whose suicide attempts were successful included burns (3), brain injury (1), drug overdose (1), organophosphate pesticide ingestion (1), hanging (1), and drowning (1). Although 2 of the patients had attempted suicide while hospitalized at a psychiatric hospital, we did not identify any patients who succeeded in killing themselves while hospitalized at the acute care general hospital. There were 2 deaths of schizophrenic patients with neuroleptic malignant syndrome in the study period. Nonschizophrenic patients who died from injury and poisoning (n = 407; 5.4%) included patients who had committed suicide, al-though the exact number of nonschizophrenic patients were successful suicides was unclear in these registry data.

Table 3 shows the logistic regression analyses for variables associated with acute hospital mortality of schizophrenic patients. In unadjusted analysis, the significant variables associated with the increased mortality included malignant neoplasm, diseases of the circulatory system, and older age. There was no significant difference in mortality between female and male schizophrenic patients. Unadjusted analysis showed that the mortality of schizophrenic patients directly transferred from a psychiatric hospital was not increased.

In multivariable-adjusted analysis (Table 3), the

significant variables associated with increased mortality included malignant neoplasm (OR 12.93; 95% CI, 5.67-29.51), diseases of the circulatory system (OR 2.63; 95% CI, 1.20-5.77), and admission through an emergency department (OR 3.30; 95% CI, 1.33-8.20). Further, a significant variable associated with decreased mortality was direct transfer from a psychiatric hospital (OR 0.37; 95% CI, 0.16-0.87). Consultation with a liaison psychiatrist in our hospital was not associated with decreased mortality.

DISCUSSION

The results of our study suggest that schizophrenic and nonschizophrenic patients were admitted with similar levels of medical pathology to an acute care hospital and that they responded comparably to inpatient medical care. The crude hospital mortality rate of schizophrenic patients admitted to our acute care hospital in Japan was 5.0%, whereas the crude mortality rate of nonschizophrenic patients during the same period was 4.0%. There was a nearly significant trend toward an increase in the overall standardized mortality ratio of schizophrenic patients compared with nonschizophrenic patients. Significant risk factors for the increased mortality of the schizophrenic patients were malignant neoplasm, cardiovascular disease, admission through an emergency department, and not transferred directly from a psychiatric hospital.

Although the overall standardized mortality ratio between schizophrenic and nonschizophrenic patients was not statistically significant in this study population, our reanalysis excluding the probable outlier data for 2004 did show a significant increase in the mortality of schizophrenic patients. Previous community-based cohort studies, including a Japanese study, have consistently shown that the mortality of patients with schizophrenia was higher than that of the general population.[12,13] A meta-analysis also suggested that schizophrenic patients had a significantly higher mortality from suicide and traumatic death as well as natural causes.[14] In a recent study in Sweden, natural cause of death was found to be the main cause of excess deaths.[15] Natural causes were also likely to be important in our study, because deaths from natural causes were 82% of all deaths of schizophrenic patients in settings of acute care hospitalization in Okinawa, Japan.

Suicide was the most important cause of death among our reported schizophrenic patients (14.5% of all deaths). In another survey, suicide was also the most frequent cause of death (36%).[16] We may need improved and vigilant suicide prevention programs and better control of the psychiatric symptoms of these patients. In addition, there may be subgroups of schizophrenic patients at higher risk for suicide who should be targeted for suicide prevention. For instance, previous studies have suggested that the need for psychosedative medication at discharge from a psychiatric hospital and multiple previous hospitalizations increased the risk of suicide.[17,18] Suicide risk may also be increased in the first year after discharge from a psychiatric hospital.[10,17,18]

Our study showed that malignant neoplasm and cardiovascular disease were significantly associated with increased hospital mortality of schizophrenic patients, although malignant lymphoma/leukemia was the most frequent specific cause of death from malignant neoplasm. One previous study showed that fatal smoking-related diseases were more prominent in schizophrenic patients than in the general population.[19,20] Attention to designing health educational programs specifically for schizophrenic patients, including healthy diet, smoking cessation, and physical exercise may be necessary. Smoking cessation may be important because a high percentage of schizophrenic patients in Japan are smokers.[13]

In our study survival of patients coming from psychiatric hospitals was greater than that of those coming from the community. In contrast, a study in Italy suggested that longer psychiatric hospitalization and chronic custodial care at psychiatric hospitals were risk factors for death of schizophrenic patients.[11] The Japanese psychiatric management system is usually based on a model in which half the schizophrenic patients are managed in psychiatric hospitals and half are managed in community outpatient psychiatric clinics. Schizophrenic patients who are followed as outpatients may not receive adequate preventive care for common medical illnesses in Japan. Psychiatric hospitalization may provide an opportunity for preventive medicine for these patients.

The suicide rate of 14.5% among all causes of death suggests the need to focus on suicide prevention in schizophrenic patients. Prevention efforts should focus on suicidal tendencies, smoking, and other cardiovascular risk factors. Because most schizophrenic patients are followed regularly by practicing psychiatrists on a long-term basis, we

encourage practicing psychiatrists to use preventive health programs as a regular part of their treatment plans.[21] However, we need to recognize that the psychiatric conditions could limit their ability to communicate symptoms of comorbid conditions. In addition, schizophrenic patients sometimes even refuse to undergo treatment for any illness they may have. These barriers that make it difficult to provide preventive care may be challenging issues for health care providers of psychiatric services.

Early recognition of comorbid medical conditions and the subsequent referral to acute care hospitals in a timely manner may be necessary for the improvement of care to reduce the mortality of schizophrenic patients. One review article suggested that schizophrenic patients suffered from more comorbid medical illnesses, which were largely undiagnosed and untreated and which may cause or exacerbate psychiatric symptoms.[22] However, there may be multiple barriers to optimal primary medical care for these patients. In patients with schizophrenia, atypical presentation may be common; schizophrenic patients may be less symptomatic for localized symptoms and signs.[23] There may be system-based and politically based disparities between psychiatric hospitals and general hospitals in the treatment of schizophrenic patients depending on the country and region.[22] Both political advocacy and development of primary care programs may be instituted to efficiently meet the health needs of these patients.

We did not find any significant differences in hospital mortality between patients with liaison psychiatrist consultation and those without. Liaison psychiatrists at our hospital received consultations from inpatient medical care teams and provided advice to 20% of admitted schizophrenic patients. Although their advice appears to be useful for controlling psychiatric symptoms, their consultations may not be significantly important for lowering hospital mortality.

Our study conducted in Japan may have implications for physicians working as general internists, especially hospitalists, in other countries. This may be the first study to comprehensively assess acute hospital care among schizophrenic patients. We determined common causes of and several risk factors associated with acute care mortality. These findings may help to identify schizophrenic patients at risk of dying when caring for these patients in acute care hospitals. In addition, the importance of pre-ventive programs focusing on suicide would also be applicable to other countries.

We interpreted our results according to whether they are clinically significant. First, we performed the study at a single institution in Okinawa, Japan. Thus, our findings would require external confirmation for their generalizability to other acute care hospital settings. Second, different systems of health care in different countries may influence not only overall mortality but also hospital mortality. Comparative studies of hospital mortality at acute care general hospitals in different countries would be helpful. Third, we analyzed inpatient hospital mortality rather than long-term mortality, including follow-up, after hospital discharge. Further studies are needed to determine whether there may be excess mortality after patients are discharged from acute care hospitals. Fourth, our study used administrative data. Possible misclassification in coding disease and clinical characteristics may limit the utility of administrative data for interpreting the results.

In summary, this study may be the first report on the mortality of schizophrenic patients in acute care hospitalization. There was a nearly significant trend towards an increase in the standardized mortality of schizophrenic patients compared with that of general patients. Malignant neoplasm and cardiovascular diseases were significant factors associated with increased mortality. Suicide was the most frequent cause of death in this patient population.

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