Comorbid Psychiatric Disorders in Patients Hospitalized for Pulmonary Embolism and Acute Myocardial Infarction:
A Japanese Nationwide Database Study

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ABSTRACT

Objective: While the most common cause of sudden cardiac arrest (SCA) in the general population is ischemic cardiac disease including acute myocardial infarction (AMI), previous preliminary data highlighted pulmonary embolism (PE) as a common cause of SCA among psychiatric patients. The aim of this study was to examine the proportion of patients with comorbid psychiatric disorders among patients hospitalized for either AMI or PE using a Japanese nationwide database.

Methods: This study used Diagnosis Procedure Combination (DPC) data between April 2013 and March 2018 provided by the Ministry of Health, Labor, and Welfare. The DPC data included information on the causes of hospitalization and comorbidities of psychiatric diseases among inpatients in all acute care hospitals in Japan. The proportions of patients with schizophrenia (*ICD-10* code F20), mood disorders (F31 or F32), and no psychiatric disorders were analyzed among patients who were hospitalized for AMI and PE.

Results: The data from 351,159 AMI patients (mean age = 70.3 years) and 52,036 PE patients (mean age = 69.2 years) were used. Mortality rates were 8.0%–14.4% in AMI patients and 4.3%–9.8% in PE patients. The AMI group was predominantly male. The proportions of patients with schizophrenia and mood disorder were significantly higher in the PE group than in the AMI group (schizophrenia: 2.53% [1,314/52,036] vs 0.55% [1,922/351,159], $P < .001$; mood disorder: 2.94% [1,532/52,036] vs 0.60% [2,099/351,159], $P < .001$).

Conclusions: The results highlight the importance of PE as a major cause of SCA in this specific population and the need for preventive measures to mitigate the mortality gap among patients with psychiatric disorders.

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Sudden cardiac arrest (SCA) is known to occur more frequently among patients with psychiatric disorders than in the general population.[1,2] More than half of SCA in the general population is caused by ischemic cardiac disease.[3] However, this proportion may not be the same among psychiatric patients. In fact, our previous data[4,5] have suggested that pulmonary embolism (PE) is a relatively common cause of SCA in this specific population. Among patients who were resuscitated after out-of-hospital cardiac arrest (OHCA) and hospitalized in the Tertiary Emergency Medical Center of Tokyo Metropolitan Bokutoh Hospital in Japan, a cardiac cause of OHCA was less common in psychiatric patients than in non-psychiatric patients (26.5% vs 58.5%, respectively), while PE was more common in the former than in the latter (12.2% vs 1.5%, respectively).[4] Moreover, another study from the same institution[5] suggested that the proportion of psychiatric disorders was significantly higher in patients with PE than in patients with acute myocardial infarction (AMI) (18.1% vs 4.0%, respectively). However, the interpretation of these data was somewhat limited because of the relatively small sample size and single-center source of data.

In Japan, all citizens are enrolled in a health insurance plan under the Japanese health care system, which is characterized by universal health insurance coverage. The Diagnosis Procedure Combination (DPC) is a classification based on the *International Statistical Classification of Diseases and Related Health Problems, Tenth Revision* (*ICD-10*), which covers every inpatient under the health insurance system. Approximately 91.5% of acute hospital beds are included in the DPC database,[6] and previous studies[7–9] have shown that the validity of the DPC data is high. The DPC data included information on the causes of hospitalization and comorbidities of psychiatric diseases among patients hospitalized in all acute care hospitals throughout Japan. Taking advantage of this large-scale database, we aimed to examine the proportion of patients with comorbid psychiatric disorders among patients hospitalized for either AMI or PE. Our hypothesis was that the proportion of patients with psychiatric disorders among those with PE would be higher than that among patients with AMI. Moreover, we hypothesized that the mortality rate would be higher in patients with psychiatric disorders than in those without. The aim of this study was to investigate the generalizability of the findings of the previous single-center studies by using national data in Japan.

Clinical Points

- Pulmonary embolism, compared to myocardial infarction, has not garnered sufficient attention as a cause of sudden cardiac arrest in psychiatric patients.
- Clinicians should seriously consider prophylaxis of not only myocardial infarction but also pulmonary embolism to reduce the risk of sudden cardiac arrest for psychiatric patients.

METHODS

Data Source

The Japanese health care system is characterized by universal health insurance coverage and was established by the government in 1961. Under this system, all citizens in Japan are enrolled in the single health insurance plan and have universal access to any clinic/hospital or primary/specialty care as a general rule. We used the DPC data provided by the Ministry of Health, Labor, and Welfare (MHLW). The DPC is a classification based on the *ICD-10* that covers all inpatients and is usually used for reimbursement of hospitalization costs with data on diagnosis, severity, age, operations, procedures, and complications. The DPC data are strictly managed by the MHLW and provided upon reasonable request.[10] The MHLW provided us with the number of patients who were hospitalized due to AMI and PE from April 2013 to March 2018. The data also included the mean age, proportion of male patients, number of patients with a diagnosis of schizophrenia (F20) or with depression (F31) or bipolar disorder (F32) (mood disorders), mean length of hospital stay, and in-hospital mortality during this time window, while the data on mortality in PE patients with schizophrenia and mood disorders were available for the period from April 2014 to March 2018. Since this was a post hoc analysis of deidentified data processed by the MHLW, the approval by an institutional review board was waived according to the regulations of the MHLW and Keio University School of Medicine.

Statistical Analysis

Statistical analyses were performed using IBM SPSS version 25.0 (IBM; New York, New York). The χ^2 test was used for all comparisons. The proportions of patients with schizophrenia, mood disorders, and no psychiatric disorders were compared between patients who were hospitalized for AMI and PE. In-hospital mortality rates were compared between patients with schizophrenia and those without psychiatric disorders and between those with mood disorders and those without psychiatric disorders in the AMI and PE groups, respectively. The comorbidity rates of diabetes, hypertension, or dyslipidemia with AMI and the comorbidity rate of cancer with PE were compared between patients with schizophrenia and those without psychiatric disorders and between those with mood disorders and those without psychiatric disorders, respectively. All tests were 2-tailed, and a P value < .05 was considered statistically significant.

RESULTS

Table 1 summarizes the demographic and clinical characteristics of the patients who were hospitalized for either AMI or PE from April 2013 to March 2018. The proportion of men was significantly higher in the AMI group than that in the PE group (71.9% vs 40.3%, respectively; P < .001). The proportions of patients with schizophrenia and mood disorders (ie, depression and bipolar disorder) were significantly higher in the PE group than those in the AMI group (2.53% vs 0.55%, P < .001 for schizophrenia; 2.94% vs 0.60%, P < .001 for mood disorder, respectively). There was no significant difference in the in-hospital mortality rates of patients with AMI between the patients with schizophrenia and those without psychiatric disorders, whereas the in-hospital mortality rate was significantly lower in those with mood disorders than in those without psychiatric disorders. In addition, the in-hospital mortality rates of patients with PE were significantly lower in those with mood disorders and those with schizophrenia than in those without psychiatric disorders.

In the AMI group, patients with schizophrenia had lower likelihood of comorbid diabetes, hypertension, or dyslipidemia than patients without psychiatric disorders, and patients with mood disorders had higher likelihood of these comorbidities. In the PE group, both patients with schizophrenia and those with mood disorders had a lower risk of comorbid cancer.

DISCUSSION

To our knowledge, this study is the first to compare the proportion of patients with psychiatric disorders between AMI and PE patients. As we hypothesized, the proportion of patients with psychiatric disorders among PE patients was substantially higher than that among AMI patients, which suggests that PE is more commonly encountered among psychiatric patients. Contrary to the other hypothesis, however, the mortality rates from AMI and PE were generally lower in patients with psychiatric disorders than in those without.

Considering that the DPC data cover all patients hospitalized in acute care hospitals, the incidence captured in the present study is reasonably representative of Japan. From this point of view, the incidence of PE is approximately 70% of that of AMI in patients with schizophrenia and mood disorders (1,314/1,922 and 1,532/2,099) (Table 1). On the other hand, the incidence of PE in comparison with AMI in non-psychiatric control patients was found to be much lower (49,305/347,228; 14.2%). There are some specific risk factors for thromboembolism among psychiatric patients. For example, psychotropic drugs are a well-known risk factor for PE. In fact, the use of antipsychotic drugs and

Table 1. Demographic and Clinical Characteristics of Patients Hospitalized for Either Acute Myocardial Infarction or Pulmonary Embolism (April 2013–March 2017)

Patient Group	Patients	Age, Mean, y	Male, %	Complications, %		Mortality, %[a]
				Diabetes, hypertension, or dyslipidemia	Cancer	
Acute myocardial infarction total, n	351,159	70.3	71.9[b]	73.4	NA	14.4
Schizophrenia, n (%)	1,922 (0.55)[c]	73.7	63.1	67.7[d]	NA	12.9
Mood disorders, n (%)	2,099 (0.60)[e]	69.1	60.9	76.2[f]	NA	8.0[g]
No psychiatric disorders, n (%)	347,228 (98.88)	70.3	72.0	73.4	NA	14.4
Pulmonary embolism total, n	52,036	69.2	40.3	NA	14.4	9.6
Schizophrenia, n (%)	1,314 (2.53)	61.7	31.7	NA	5.9[h]	5.8[i]
Mood disorders, n (%)	1,532 (2.94)	65.3	26.4	NA	8.9[j]	4.3[k]
No psychiatric disorders, n (%)	49,305 (94.75)	69.6	40.9	NA	14.8	9.8

[a]Data on in-hospital mortality rate among patients with pulmonary embolism were available from April 2014 to March 2017.
[b]$\chi^2_1 = 20736.5$, $P < .001$ vs those with pulmonary embolism.
[c]$\chi^2_1 = 22.9$, $P < .001$ vs those with pulmonary embolism who had a diagnosis of schizophrenia.
[d]$\chi^2_1 = 31.8$, $P < .001$ vs those without psychiatric disorders.
[e]$\chi^2_1 = 31.0$, $P < .001$ vs those with pulmonary embolism who had a diagnosis of depression or bipolar disorder.
[f]$\chi^2_1 = 8.4$, $P = .004$ vs those without psychiatric disorders.
[g]$\chi^2_1 = 69.5$, $P < .001$ vs those without psychiatric disorders.
[h]$\chi^2_1 = 81.5$, $P < .001$ vs those without psychiatric disorders.
[i]$\chi^2_1 = 20.5$, $P < .001$ vs those without psychiatric disorders.
[j]$\chi^2_1 = 41.4$, $P < .001$ vs those without psychiatric disorders.
[k]$\chi^2_1 = 44.7$, $P < .001$ vs those without psychiatric disorders.
Abbreviation: NA = not applicable.

antidepressant drugs is reported to increase the risk of venous thromboembolism by 30%[11] and 40%,[12] respectively. In addition, performing fewer physical activities as well as inadequate hydration could result in a greater chance of deep vein thrombosis (DVT) among psychiatric patients compared to that in the general population. In light of the potentially greater incidence and greater inherent risk for DVT and PE among psychiatric patients, active preventive measures should be considered in this population.

Previous studies have generally shown that the mortality rate due to comorbid physical conditions was higher among psychiatric patients than among the general population,[13] possibly because of insufficient knowledge of those physical conditions, suboptimal self-care ability, and insufficient and less aggressive treatment interventions.[14,15] However, in this study, the mortality rate was significantly lower among patients with mood disorders for both AMI and PE and among those with schizophrenia for PE than among non-psychiatric patients. Patients with mood disorders may have sought medical care at an earlier opportunity since they may be more concerned about somatic symptoms, potentially resulting in prompt treatment interventions.[16] Moreover, the antiplatelet effect of selective serotonin reuptake inhibitors may have contributed to lower the mortality rate in patients with AMI.[17,18] Our results need replication, though with regard to PE patients, fewer cancer-related complications[19] may have led to lower mortality due to PE among patients with mood disorders and schizophrenia since the mortality from PE is reportedly higher among patients with cancer than among those without.[20] Furthermore, younger age may be also associated with the low mortality among patients with schizophrenia who had PE compared to non-psychiatric patients. Alternatively, it is possible that the lower rates of comorbid diabetes, hypertension, and dyslipidemia as well as cancer among psychiatric patients in our sample may reflect underdiagnosis in this population. Such underdiagnosis is likely because psychiatric patients in general are considered to constitute a high-risk group for metabolic syndrome.[21]

There are several limitations to be noted in this study. First, the dataset that we obtained from the MHLW did not include patient-level DPC data but summary data. Therefore, we could not conduct multiple regression analysis adjusting for confounding factors, such as age, sex, and comorbidities. Furthermore, we were unable to present confidence intervals. Second, we had no information on the severity of physical diseases that are expected to be associated with mortality rate. This was also the case regarding the severity of psychiatric diseases. Additionally, data on psychotropic medications that psychiatric patients may have been taking were also unavailable. Third, only schizophrenia and mood disorders were examined in this study. Furthermore, depressive disorder and bipolar disorder were included in the same category since the dataset that was provided to us did not include the data separately for depressive disorder and bipolar disorder. Fourth, since we could not obtain the prevalence rate of schizophrenia or mood disorders, the incidence rates of PE or AMI could not be compared between the patients with and without psychiatric disorders. Fifth, information on the details of somatic treatment, which should influence the prognosis of AMI and PE, was unavailable. Sixth, we targeted only inpatients, although almost all AMI and PE patients are treated in hospital in Japan. Finally, the data were derived from Japanese medical institutions, limiting the generalizability of the data to other populations.

In conclusion, the proportion of patients with psychiatric disorders among PE patients was higher than that among AMI patients, which suggests that PE may be more common among psychiatric patients than among non-psychiatric patients. PE, in comparison to AMI, has thus far received less attention as a cause of SCA, possibly because of its much

lower prevalence in the general population. However, the results of this study highlight the importance of PE as a major cause of SCA in this specific population and the need for preventive measures, not only for cardiac diseases such as AMI, but also for DVT and PE, to reduce the risk of SCA among patients with psychiatric disorders. Furthermore, long-term longitudinal studies are needed to evaluate the effects of preventive measures on the risk of SCA among patients with psychiatric disorders.

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