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Mortality, Revascularization, and Cardioprotective Pharmacotherapy After Acute Coronary Syndrome in Patients With Psychotic Disorders: A Population-Based Cohort Study

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Ischemic heart disease is the leading cause of mortality in psychotic disorders. There is a paucity of research comprehensively evaluating short-term mortality, cardiovascular complications, and treatment inequality after cardiac events in patients with psychotic disorders. This population-based cohort study examined 30-day and 1-year all-cause mortality, cardiovascular complication rates, 30-day and 1-year receipt of invasive cardiac procedures, and 90-day post-discharge cardioprotective medication treatment following admission for first-recorded acute coronary syndrome (ACS) among patients with psychotic disorders (*n* = 703) compared with patients without psychotic disorders (*n* = 66 989) between January 2006 and December 2016 in Hong Kong (HK). Study data were retrieved from territory-wide medical record database of public healthcare services to 7.5 million HK residents. Multivariate regression analyses (ORs and 95% CIs), adjusting for demographics and medical comorbidities, were conducted to evaluate associations between psychotic disorders and post-ACS outcomes. Our results showed that patients with psychotic disorders had higher 30-day (OR: 1.99 [95% CI: 1.65–2.39]) and 1-year (2.13 [1.79–2.54]) mortality, and cardiovascular complication rates (1.20 [1.02–1.41]), lower receipt of cardiac catheterization (30-d: 0.54 [0.43–0.68]; 1-y: 0.46 [0.38–0.56]), percutaneous coronary intervention (30-d: 0.55 [0.44–0.70]; 1-y: 0.52 [0.42–0.63]) and reduced β-blockers (0.81 [0.68–0.97]), statins (0.54 [0.44–0.66]), and clopidogrel prescriptions (0.66 [0.55–0.80]). Associations between psychotic disorder and increased mortality remained significant even after complications and treatment receipt were additionally adjusted. Our findings indicate that psychotic disorders are associated with increased risks of short-term post-ACS mortality, cardiovascular complications, and inferior treatment. Excess mortality is not substantially explained by treatment inequality. Further investigation is warranted to clarify factors for suboptimal cardiac-care and elevated mortality in psychotic disorders to enhance post-ACS outcome.

Key words: acute coronary syndrome/mortality/revascularization/cardioprotective medications/treatment inequality/psychotic disorders/schizophrenia/

Introduction

People with psychotic disorders including schizophrenia have markedly elevated risk of premature mortality,[1–4] contributing to 15–20 years of reduction in life expectancy compared with the general population.[5–8] It is well established that the vast majority of excess deaths associated with psychotic disorders are due to physical diseases.[1,2,4,6] Cardiovascular disease (CVD), especially ischemic heart disease (IHD) which is the leading cause of CVD-related health lost globally,[9,10] has been consistently shown to be a major contributor to mortality in psychotic disorders.[6,11–13] Recent data have indicated the widening mortality gap between people with psychotic disorders and the general population.[14–16] In particular, contrary to a significant decline in cardiac death in developed countries during the past decades,[17,18] the rates of CVD mortality were found to remain stably high or decrease to a much lesser degree than those of the general population.[19–23]

It is acknowledged that a multitude of factors may contribute to raised IHD mortality associated with psychotic disorders, including socioeconomic disadvantage, unhealthy lifestyle such as physical inactivity, poor dietary patterns, smoking, and alcohol use,[22,24–26] and antipsychotic-induced

metabolic side effects.[27,28] However, there is increasing concern regarding the possible contribution of suboptimal medical care for IHD to heightened mortality among people with psychotic disorders.[29–31] Most earlier studies have demonstrated that schizophrenia patients were significantly less likely to undergo revascularization interventions after acute coronary syndrome (ACS) relative to the general population,[21,32–38] while some,[39,40] but not all,[41,42] more recent reports have shown no treatment inequality in this respect. Similarly, literature generally revealed lower post-ACS prescription rates of secondary preventive medications in individuals with schizophrenia than those without the disorder.[33,34,39–41,43,44] Of note, the majority of prior studies either grouped patients into a broadly-defined category of severe mental illness for investigation or focused narrowly on schizophrenia without taking into consideration individuals with other non-affective psychoses. Although previous reports consistently indicated that schizophrenia patients displayed reduced long-term survival rate following cardiac events compared to the general population,[21,37,41,43,45–49] mixed findings were observed in short-term mortality, particularly 30-day mortality after ACS.[34,43,47,50,51] Until now, research that comprehensively evaluate mortality, cardiovascular complications, and receipt of invasive cardiac procedures and cardioprotective medications following ACS in a single cohort is very limited. Whether excess mortality among patients with psychotic disorders could be explained by disparity in quality of cardiovascular treatment remains to be clarified.

To this end, we conducted a population-based cohort study with an aim to examine short-term mortality (30-d and 1-y mortality), occurrence of cardiovascular complications, and quality of medical care as indexed by receipt of revascularization interventions and prescription of cardiac medications after admission for incident ACS in patients with psychotic disorders (schizophrenia and other non-affective psychoses) compared to those without psychotic disorders. The current investigation utilized clinical data retrieved from a territory-wide medical record database of public healthcare services in Hong Kong (HK). Based on prior literature, we hypothesized that patients with psychotic disorders would have higher rates of mortality and cardiovascular complications, as well as decreased likelihood of receiving cardiac procedures and cardioprotective medications relative to those without psychotic disorders. Given these a priori predictions, we further explored whether differential rates of cardiovascular complications and treatment receipt played a role in explaining the associations between increased mortality and psychotic disorders.

Methods

Data Source

This study was conducted using Clinical Data Analysis and Reporting System (CDARS),[52] a territory-wide electronic health-record database developed by the Hospital Authority (HA) which is a statutory body delivering government-subsidized, universal health coverage to 7.5 million HK residents by managing all public hospitals, specialist and general outpatient clinics in HK. In particular, HA provides >95% of hospital admission services in HK.[53] Detailed description of CDARS has been reported elsewhere.[54,55] Briefly, CDARS is an integrated, longitudinal patient electronic record system capturing clinical data across all healthcare settings of HA facilities since 1995.[52] The database contains information on patients' demographics and details of their diagnoses, operations, prescriptions, visits to emergency departments and outpatient clinics, and hospital admissions. It also contains data on deaths through its internal linkage to regional death registry from the Immigration Department. Clinical data are collected and entered into the computerized clinical management system by treating clinicians and other healthcare professionals and are then transferred to CDARS for audit and research purposes. CDARS generates unique, anonymized patient identifiers to protect patient confidentiality and to link all medical records. This database has been used to conduct high-quality population-based epidemiological studies on various physical (including ACS and other cardiovascular outcomes, with CDARS-derived diagnoses validated)[56] and psychiatric outcomes.[57–60]

Study Population and Patient Identification

We identified all individuals aged ≥18 years who had a hospital admission for first-recorded ACS in HK during a period between January 1, 2006 and December 31, 2016 as the study cohort. Principal diagnosis of ACS was identified by ICD9-CM (a diagnostic system used to record physical diseases and procedures in CDARS) codes for acute myocardial infarction (MI, 410.x) or unstable angina (411.1). Patients with past record of ACS diagnosis or other chronic IHD is (ICD9-CM codes 410–412 and 414) before an index admission were excluded. From the incident ACS cohort, we derived a group of patients who were diagnosed to have psychotic disorders, which included schizophrenia, schizoaffective disorder, persistent delusional disorder, acute and transient psychotic disorders, and unspecified non-organic psychosis, preceding an index admission for ACS. Diagnoses of psychotic disorders (F20, F22-23, F25, and F28-29) were verified by ICD10 (a diagnostic system used to record psychiatric disorders in CDARS) codes. Diagnostic algorithm was adopted to enhance diagnostic validity for psychotic disorders. First, as diagnostic assignment of psychotic disorders is based on longitudinal approach taking into consideration cumulative clinical information documented over an individual patient's course of illness, the last-recorded principal diagnosis of psychotic disorder per patient before an index admission was thus

ascertained as the final diagnosis. Additionally, inpatient discharge diagnosis took precedence over outpatient diagnosis in determining patients' final diagnosis. CDARS-derived diagnostic ascertainment has been used for patient-sample identification in previous retrospective studies for psychotic disorders and bipolar disorder.[60–63] To evaluate the impact of psychotic disorder on mortality and receipt of cardiovascular treatments, the remaining patients in the incident ACS cohort were served as a "reference group" for comparison. Patients with mania or bipolar disorder (ICD10 codes F30-31) recorded as the last principal psychiatric diagnosis or without later recorded diagnoses of psychotic disorders before an index admission were excluded. The study was approved by the Institutional Review Board of the University of Hong Kong/Hospital Authority Hong Kong West Cluster. The study data were anonymized and individual patient records were completely unidentifiable during the analysis. Since our study was based on medical record database, the requirement for informed consent was waived.

Study Outcomes

The primary outcomes were 30-day and 1-year all-cause mortality rates after incident ACS. Two sets of secondary outcomes indicating quality of cardiac care were investigated. First, we measured receipt of invasive cardiac procedures within 30 days and 1 year of index admission, including cardiac catheterization, percutaneous coronary intervention (PCI), and coronary artery bypass grating (CABG). Second, prescription of secondary preventive cardiac medications within 90 days of discharge from index admission, including β-blockers, angiotensin-converting enzyme inhibitors (ACEIs)/angiotensin II receptor blockers (ARBs), statins, and antiplatelet agents (aspirin and clopidogrel) were examined. Cardiac procedures were identified using ICD9-CM codes (supplementary table S1).

Cardiovascular Complications and Covariates

We assessed occurrence of cardiovascular complications during index admission as proxy measures of ACS severity including congestive heart failure, cardiogenic shock, conduction problems, cardiac dysrhythmias, and acute/acute on chronic respiratory failure based on the method adopted by previous research.[38] Literature indicates that certain CVD risk factors (eg, hypertension, diabetes, and dyslipidemia), other physical morbidity and substance abuse are associated with worse post-ACS outcomes and are more frequently occurred in patients with psychotic disorders. Taking into consideration the availability of clinical information that were adequately recorded in and could be reliably retrieved from the database, we selected a priori an array of candidate covariates to address potential confounding effects on outcome analyses comprising demographics (age at index admission, sex), calendar year of index admission, catchment area where patients received cardiovascular treatment for incident ACS (for geographic and hospital-based variation), physical conditions that are known CVD risk factors including hypertension, diabetes and dyslipidemia, other physical comorbidities as quantified by Charlson-Deyo comorbidity index (a weighted summary score based on 1-y mortality risk),[64] and alcohol and substance use disorders. Those variables that were found to be significantly different between groups in bivariate analyses were then adjusted as covariates in multivariate regression analyses (please also refer to *Statistical Analysis*). Physical diseases (including cardiovascular complications) and alcohol/substance use disorders were identified by ICD9-CM and ICD10 codes, respectively (supplementary table S1).

Statistical Analysis

Demographic and baseline characteristics between patients with and without psychotic disorders were compared using chi-square test and independent-samples *t*-test for categorical and continuous variables, respectively. A series of multivariate logistic regression analyses (with ORs and 95% CIs calculated) adjusting for covariates were performed to investigate the effect of psychotic disorders on rates of mortality, receipt of invasive procedures, prescription of cardiac medications and cardiovascular complications. To assess whether associations between mortality and psychotic disorders were explained by differences in ACS severity and cardiac-care quality, we repeated multivariate regression analyses on mortality by additionally adjusting for the effects of cardiovascular complications, revascularization (PCI or CABG) and medication treatment. Furthermore, 3 sets of additional analyses were conducted. First, we repeated the analyses by comparing patients with schizophrenia to those without psychotic disorders on cardiac outcomes and treatment receipt. Second, we stratified the analyses by age (<65 y and ≥65 y) to examine whether the effect of psychotic disorders on adverse outcomes was more pronounced in younger age-group. Finally, the analyses were repeated for men and women separately to assess sex-specificity of the associations between psychotic disorders and study outcomes. The level of statistical significance was set at $P < .05$.

Results

Characteristics of the Study Cohort

The cohort comprised 67 692 patients, including 703 individuals with psychotic disorders (1.0%; 371 men [52.8%]; mean [SD] age: 69.3 [13.4] y) and 66 989 individuals without psychotic disorders (99.0%; 41 674 men [62.2%]; mean [SD] age: 71.2 [14.2] y). Demographic and baseline characteristics of the study cohort are summarized in table 1. Patients with psychotic disorders were

Table 1. Demographic, Clinical, and Service Characteristics of Patients Admitted for Acute Coronary Syndrome

Characteristic[a]	Psychotic Disorder (n = 703)	No Psychotic Disorder (n = 66 989)	P
Age, y	69.3 (13.4)	71.2 (14.2)	.007**
Sex			<.001***
Male	371 (52.8)	41 674 (62.2)	
Female	332 (47.2)	25 315 (37.8)	
Calendar-year period			.004**
2006–2011	360 (51.2)	37 895 (56.6)	
2012–2016	343 (48.8)	29 094 (43.4)	
Medical comorbidity			
Hypertension	360 (51.2)	32 987 (49.2)	<.001***
Diabetes	243 (34.6)	17 284 (25.8)	<.001***
Dyslipidemia	122 (17.4)	12 825 (19.1)	.231
Charlson-Deyo comorbidity index[b]	4.6 (2.4)	4.6 (2.3)	.724
Alcohol use disorder	10 (1.4)	104 (0.2)	<.01**
Substance use disorder	23 (3.3)	121 (0.2)	<.01**
Catchment areas of public healthcare service[c]			.076
Hong Kong East	56 (8.0)	6747 (10.1)	
Hong Kong West	53 (7.6)	4262 (6.4)	
Kowloon Central	118 (16.8)	12 567 (18.9)	
Kowloon East	110 (15.7)	9972 (15.0)	
Kowloon West	163 (23.3)	13 804 (20.7)	
New Territories East	95 (13.6)	10 290 (15.4)	
New Territories West	106 (15.1)	9008 (13.5)	

Note: [a]Potential group differences were examined using independent-samples t tests and chi-square tests for continuous and categorical variables, respectively. Data are presented in number (n) and percentage (%) for all variables, with the exception of age and Charlson-Deyo comorbidity index which are presented in mean (SD).
[b]Age-adjusted adapted Charlson-Deyo comorbidity index (CCI) was computed. As diabetes was already treated as a medical comorbidity for covariate analysis, it was thus excluded from CCI score calculation.
[c]In Hong Kong, the Hospital Authority manages public healthcare service delivery (inpatient and specialist/general outpatient services) which is organized into 7 clusters based on geographical locations (ie, catchment areas).
*P < .05. **P < .01, ***P < .001.

significantly younger, more often women, and had higher rates of hypertension, diabetes, alcohol, and substance use disorders than a control sample.

Mortality and Receipt of Cardiovascular Treatments

As presented in table 2, individuals with psychotic disorders had significantly higher 30-day (25.2% vs 16.8%) and 1-year (38.5% vs 27.3%) mortality rates than those without psychotic disorders (adjusted OR [95% CI]: 1.99 [1.65–2.39] for 30-day mortality; 2.13 [1.79–2.54] for 1-y mortality). Concerning cardiovascular treatments, receipt of cardiac catheterization within 30 days (13.1% vs 21.9%; adjusted OR [95% CI]: 0.54 [0.43–0.68]) and 1 year (21.9% vs 35.6%; adjusted OR [95% CI]: 0.46 [0.38–0.56]) of index admission were significantly lower among patients with psychotic disorders than those without psychotic disorders (table 3). Likewise, individuals with psychotic disorders had significantly lower rates of undergoing PCI within 30 days (12.8% vs 21.1%; adjusted OR [95% CI]: 0.55 [0.44–0.70]) and 1 year (20.6% vs 32.2%; adjusted OR [95% CI]: 0.52 [0.42–0.63]) of index admission than patients in a reference group. Regarding post-discharge cardiac medication treatment, patients with psychotic disorders were significantly less likely to receive β-blockers (62.6% vs 66.5%; adjusted OR [95% CI]: 0.81 [0.68–0.97]), statins (67.7% vs 76.1%; adjusted OR [95% CI]: 0.54 [0.44–0.66]), clopidogrel (54.3% vs 61.7%; adjusted OR [95% CI]: 0.66 [0.55–0.80]), dual-antiplatelet therapy (52.3% vs 60.0%; adjusted OR [95% CI]: 0.59 [0.50–0.70]) and combination therapy (67.5% vs 73.9%; adjusted OR [95% CI]: 0.67 [0.56–0.81]) than those without psychotic disorders (table 4).

Cardiovascular Complications

Compared with a reference group, patients with psychotic disorders had significantly higher likelihood of experiencing any cardiovascular complications (33.9% vs 30.9%; adjusted OR [95% CI]: 1.20 [1.02–1.41]) and several specific complications including cardiogenic shock (7.8% vs 6.0%; adjusted OR [95% CI]: 1.37 [1.04–1.81]) and conduction problems (3.1% vs 2.3%; adjusted OR [95% CI]: 1.56 [1.02–2.40]) during index admission (table 2).

Effect of Psychotic Disorders on Mortality Adjusting for Complications and Treatment Receipt

To clarify whether the effect of psychotic disorders on elevated mortality was attributable to greater ACS severity

Table 2. Mortality and Cardiovascular Complications for Patients Admitted With Acute Coronary Syndrome

	Psychotic Disorder		No Psychotic Disorder				
	n	%	*n*	%	Unadjusted OR (95% CI)	Adjusted OR (95% CI)[a]	*P*
Mortality							
30-d mortality	177	25.2	11 252	16.8	1.67 (1.40–1.98)	1.99 (1.65–2.39)	<.001***
1-y mortality	271	38.5	18 259	27.3	1.67 (1.44–1.95)	2.13 (1.79–2.54)	<.001***
Cardiovascular complications							
Any cardiovascular complication	238	33.9	20 684	30.9	1.15 (0.98–1.34)	1.20 (1.02–1.41)	.028*
Congestive heart failure	121	17.2	11 311	16.9	1.02 (0.84–1.25)	1.08 (0.89–1.32)	.478
Cardiogenic shock	55	7.8	4026	6.0	1.33 (1.01–1.75)	1.37 (1.04–1.81)	.027*
Conduction problems	22	3.1	1525	2.3	1.39 (0.90–2.13)	1.56 (1.02–2.40)	.043*
Cardiac dysrhythmias	98	13.9	9081	13.6	1.03 (0.83–1.28)	1.06 (0.86–1.32)	.580
Respiratory failure[b]	29	4.1	2101	3.1	1.33 (0.91–1.93)	1.40 (0.96–2.04)	.083

Note: [a]Adjusted for age, sex, calendar-year period of index admission and medical comorbidity.
[b]Acute respiratory failure or acute on chronic respiratory failure.
*P < .05, **P < .01, ***P < .001.

Table 3. Invasive Cardiac Procedures for Patients Admitted With Acute Coronary Syndrome

	Psychotic Disorder		No Psychotic Disorder				
	n	%	*n*	%	Unadjusted OR (95% CI)	Adjusted OR (95% CI)[a]	*P*
Cardiac procedure done within 30 d of admission							
Cardiac catheterization	92	13.1	14 692	21.9	0.54 (0.43–0.67)	0.54 (0.43–0.68)	<.001***
Percutaneous coronary intervention	90	12.8	14 148	21.1	0.55 (0.44–0.69)	0.55 (0.44–0.70)	<.001***
Coronary artery bypass graft	5	0.7	636	0.9	0.75 (0.31–1.81)	0.81 (0.33–1.97)	.643
Cardiac procedure done within 1 y of admission							
Cardiac catheterization	154	21.9	23 829	35.6	0.51 (0.43–0.61)	0.46 (0.38–0.56)	<.001***
Percutaneous coronary intervention	145	20.6	21 586	32.2	0.55 (0.46–0.66)	0.52 (0.42–0.63)	<.001***
Coronary artery bypass graft	13	1.8	2120	3.2	0.58 (0.33–1.00)	0.60 (0.34–1.04)	.066

Note: [a]Adjusted for age, sex, calendar-year period of index admission and medical comorbidity.
*P < .05, **P < .01, ***P < .001.

and poorer cardiac-care quality, multivariate regression analyses for mortality adjusting for cardiovascular complications, revascularization, and post-discharge prescription of cardiac medications were conducted. As shown in table 5, associations of psychotic disorders with 30-day (reduced adjusted OR: 1.99 to 1.87 in model 2) and 1-year (reduced adjusted OR: 2.13 to 1.49 in model 3) mortality remained significant, albeit with small to modest attenuation.

Additional Analyses

When comparing patients with schizophrenia (n = 509) to a reference group, we observed patterns similar to the findings in the main analyses for psychotic disorders. Schizophrenia patients displayed significantly higher rates on mortality (30-d and 1-y) and any cardiovascular complications, as well as lower likelihood of receiving cardiac catheterization, PCI, and post-discharge cardiac medications (supplementary tables S2–S6). Overall, our age- (supplementary tables S7–S10) and sex-stratified (supplementary tables S11–S14) analyses revealed similar results as observed in the main analyses, with psychotic disorders being found to be associated with higher risks of mortality and cardiovascular complications, and lower rates of cardiac procedures and medication prescription. However, the effect of psychotic disorders on heightened mortality was more pronounced among younger (<65 y) (vs ≥65 y: adjusted OR [95% CI]: 3.33 [2.34–4.75] vs 1.71 [1.38–2.12] for 30-d mortality; 3.11 [2.26–4.27] vs 1.88 [1.53–2.30] for 1-y mortality) (supplementary table S8) and male (vs female: adjusted OR [95% CI]: 2.25 [1.73–2.93] vs 1.74 [1.34–2.25] for 30-d mortality; 2.42 [1.89–3.10] vs 1.86 [1.46–2.38] for 1-y mortality) patients (supplementary table S12).

Table 4. Prescription of Cardiovascular Medications for Patients Discharged With Acute Coronary Syndrome[a]

	Psychotic Disorder		No Psychotic Disorder				
	n	%	*n*	%	Unadjusted OR (95% CI)	Adjusted OR (95% CI)[b]	*P*
β-blockers	347	62.6	38 752	66.5	0.71 (0.61–0.82)	0.81 (0.68–0.97)	.020*
Statins	375	67.7	44 344	76.1	0.58 (0.50–0.68)	0.54 (0.44–0.66)	<.001***
ACEIs / ARBs	355	64.1	38 435	66.0	0.76 (0.65–0.88)	0.92 (0.77–1.10)	.380
Antiplatelets							
Aspirin	523	94.4	55 477	95.2	0.60 (0.51–0.72)	0.84 (0.58–1.22)	.359
Clopidogrel	301	54.3	35 978	61.7	0.65 (0.56–0.75)	0.66 (0.55–0.80)	<.001***
Dual therapy[c]	290	52.3	36 952	60.0	0.64 (0.55–0.75)	0.59 (0.50–0.70)	<.001***
Combination therapy[d]	374	67.5	43 092	73.9	0.73 (0.61–0.88)	0.67 (0.56–0.81)	<.001***

Note: ACEIs = Angiotensin-converting enzyme inhibitors; ARBs = Angiotensin II receptor blockers.
[a]Medications prescribed within 90 d of discharge from index admission for acute coronary syndrome. In medication analyses, 554 patients with psychotic disorder and 58 277 patients without psychotic disorders were included.
[b]Adjusted for age, sex, calendar-year period of index admission, and medical comorbidity.
[c]Dual therapy was defined as concomitant prescription of aspirin and clopidogrel.
[d]Combination therapy was defined as concomitant prescription of more than 2 of the 4 studied cardioprotective medications (β-blockers, statins, ACEIs/ARBs, and antiplatelet agent).
*$P < .05$, **$P < .01$, ***$P < .001$.

Table 5. Mortality Analyses Adjusting for Cardiovascular Complications, Revascularization, and Medications

	Psychotic Disorder		No Psychotic Disorder			
Model	*n*	%	*n*	%	Adjusted OR (95% CI)	*P*
30-d mortality	177	25.2	11 252	16.8	1.99 (1.65–2.39)[a]	<.001***
Model 1[b]					1.99 (1.65–2.40)	<.001***
Model 2[c]					1.87 (1.55–2.26)	<.001***
1-y mortality	271	38.5	18 259	27.3	2.13 (1.79–2.54)[a]	<.001***
Model 1[b]					2.13 (1.78–2.54)	<.001***
Model 2[d]					1.83 (1.53–2.20)	<.001***
Model 3[e]					1.49 (1.22–1.82)	<.001***

Note: [a]This was the original regression model adjusted for age, sex, calendar-year period of index admission and medical comorbidity.
[b]The regression model was further adjusted for any cardiovascular complications during index admission.
[c]The regression model was further adjusted for cardiovascular complications and revascularization intervention (ie, percutaneous coronary intervention or coronary artery bypass graft) within 30 d of index admission.
[d]The regression model was further adjusted for cardiovascular complications, and revascularization intervention within 1 y of index admission.
[e]The regression model was further adjusted for cardiovascular complications, revascularization intervention within 1 y of index admission, and medication prescription (β-blockers, statins, and clopidogrel) within 90 d after discharge from index admission.
*$P < .05$, **$P < .01$, ***$P < .001$.

Discussion

In the current analysis of a territory-wide, population-based cohort of 67 692 patients admitted for incident ACS in HK, we observed that individuals with psychotic disorders were significantly younger, more often women, and had higher prevalence of hypertension, diabetes, alcohol and substance use disorders than those without psychotic disorders. Importantly, our results showed that, compared with the remainder of the cohort, patients with psychotic disorders had elevated 30-day and 1-year mortality as well as higher occurrence of inpatient cardiovascular complications. This is consistent with a number of previous studies demonstrating increased short-term mortality among schizophrenia patients following cardiac events.[34,38–40,42,47] Moreover, our findings also suggested that patients with psychotic disorders may present with more advanced ACS upon admission relative to those without psychotic disorders. Intriguingly, our additional analyses further revealed that the effect of psychotic disorder on heightened mortality was even more pronounced among younger age group and men. In particular, although older age was linked to higher mortality irrespective of comorbid psychotic disorder, we found that psychotic disorder was associated with

approximately 3-fold increased odds of 30-day and 1-year mortality in those ACS patients aged under 65 years. This echoes widely replicated findings of markedly reduced life expectancy in patients with psychotic disorders compared with the general population.[5–8] It should, however, be noted that the less increased mortality rates in older patients might be due to survival bias. Alternatively, our observation of a higher proportion of women in psychotic disorder group relative to the reference comparison group might partly be explained by a significantly shorter average lifespan in males with psychotic disorders than their female counterparts.[8]

Many,[21,32–38,41–44] though not all,[39,40,51] prior studies reported that psychotic disorder was associated with decreased receipt of invasive cardiac procedures and cardioprotective medications. We confirmed these findings and found that patients with psychotic disorders had significantly lower likelihood of receiving cardiac catheterization and PCI as well as post-discharge prescription cardioprotective medications than those without psychotic disorders. Our results thus indicate deficits in quality of post-ACS treatment for patients with psychotic disorders. It is posited that the observed inequitable medical care is likely multifactorial, encompassing patient, physician and system factors.[65] Generally, accumulating evidence suggests that patients with psychotic disorders are less likely to receive standard levels of care for physical diseases. Literature showed that guideline-recommended screening and follow-up monitoring of cardiovascular risk factors and metabolic parameters were inadequately performed in patients with psychotic disorders.[66–68] Some past studies demonstrated that patients with psychotic disorders exhibited lower utilization of primary healthcare,[69,70] medical specialist[71] and cardiologist services[36] than the general population. A recent study further revealed under-diagnosis of CVD prior to CVD-related death among schizophrenia patients.[72] Moreover, previous research suggested that schizophrenia patients might be more likely to decline cardiovascular examination and revascularization following MI than those without schizophrenia.[73] We did not have additional information to identify barriers contributing to inferior post-ACS treatment associated with psychotic disorders. Further research is warranted to clarify differential roles of patient and provider factors in disparities in cardiac care so as to facilitate improvement in access to and provision of optimal cardiovascular treatment for patients with psychotic disorders.

It is suggested that (increased) severity of ACS and inequitable cardiac care, in particular, may explain a substantial portion of excess mortality in psychotic disorders.[29] To our knowledge, the current analysis is among one of the very few studies comprehensively comparing between patients with and without psychotic disorders in short-term mortality, cardiovascular complications, specialized procedure receipt and prescription of secondary preventive medications after admission for incident ACS. Our results showed that cardiovascular complications, a proxy measure of ACS severity, did not exert significant effect on raised mortality associated with psychotic disorders. Critically, the associations between psychotic disorder and elevated mortality remained robust, albeit attenuated with a mild-to-moderate degree, even after revascularization receipt and medication treatment (both as indicators of cardiac-care quality) were additionally adjusted in multivariate regression models. Hence, our findings indicate that neither more advanced ACS presentation nor inequitable cardiac care could substantially account for increased mortality associated with psychotic disorders. This is contrary to one earlier study revealing that the association between schizophrenia and increased 1-year post-MI mortality became insignificant after revascularization and medication treatment were adjusted.[50] Nonetheless, this study was limited by focusing only on patients aged ≥65 years and small sample size (schizophrenia, n = 161).[50] In fact, our results are broadly concordant with 2 recent studies demonstrating that schizophrenia remained significantly associated with heightened 30-day[38,39] and 1-year mortality[39] with minimal attenuation even when rates of cardiovascular complications,[38,39] cardiac procedures[38,39] and prescription of cardioprotective medication[39] were controlled for. Of note, the lack of significant between-group differences in receipt of revascularization and medication treatment in one of these 2 studies[39] may render it less optimal in investigating the potential influence of treatment disparity on increased mortality associated with psychotic disorders. Conversely, a recent Danish nationwide cohort study revealed that schizophrenia patients who were not exposed to (or exposed to suboptimal) recommended medications following MI exhibited excess mortality over 20-year study period.[44] It is thus possible that mortality-reducing effect of cardioprotective medications might only become evident after longer follow-up duration. Alternatively, it is acknowledged that raised IHD-related mortality in psychotic disorders could be attributable to factors other than insufficiency in cardiac care, especially lifestyle behaviors including physical inactivity, unhealthy diet and smoking. In addition, recent data, which revealed that schizophrenia patients had higher mortality on all levels of multi-morbidity and across a broad range of physical diseases such as CVD, suggested clusters and trajectories of symptoms associated with schizophrenia as the main driver of excess mortality.[74] Future investigation is required to systematically delineate the impact of these potentially modifiable lifestyle factors and illness-related symptom profiles on post-ACS outcomes in patients with psychotic disorders.

Several limitations of the study should be noted. First, a number of cardiovascular risk factors, including lifestyle patterns, obesity, and family history of CVD were not adequately recorded in medical database and thus

were not included in the current analysis. Second, we did not have prescription data on psychotropic medications, including antipsychotics, which are associated with increased CVD risk.[28] Third, patients' adherence to prescribed cardioprotective medications could not be assessed in this study. Fourth, our lack of information on clinical characteristics of ACS, such as infarction type and left ventricular function precludes us from deriving more accurate estimation of ACS severity. This may also affect our evaluation of cardiac procedure rates as MI secondary to myocardial oxygen supply/demand mismatch without acute coronary thrombosis[75] does not indicate revascularization. Fifth, reduced likelihood of undergoing cardiac procedures in patients with psychotic disorders might also contribute to their increased risk of inpatient cardiovascular complications. This possibility, however, could not be adequately addressed in our study owing to the lack of information to delineate temporal sequence between occurrence of cardiovascular complications and receipt of cardiac interventions. Sixth, we only examined patients who were hospitalized for incident ACS. This may introduce bias by potentially underestimating post-ACS mortality risk in patients with psychotic disorders, who were associated with lower healthcare service utilization[36,69–71] and under-diagnosis of CVD relative to the general population.[72] Seventh, CDARS-derived diagnoses of psychotic disorders have not been systematically validated. We have employed a refined diagnostic algorithm to minimize diagnostic misclassification, and evidence has shown that clinical diagnosis of psychotic disorders routinely collected in health-record database is generally reliable for research (yielding high concordance rate with research diagnosis).[76] Nonetheless, future study evaluating validity of CDARS-derived diagnoses for psychosis disorders is required to facilitate estimation of diagnostic accuracy and potential impact of misdiagnosis bias on outcome analyses. Eighth, patients with bipolar disorder were excluded from our study cohort, and therefore we could not address and verify recent findings suggesting that bipolar disorder is associated with more favorable post-ACS outcomes, particularly short-term mortality, compared with schizophrenia.[38,42] Lastly, given the short follow-up period, we were not able to examine longer-term mortality and its relationship with treatment inequality in patients with psychotic disorders.

In conclusion, in a large, population-based cohort of patients admitted for incident ACS, our study indicates that psychotic disorder is associated with elevated short-term mortality, increased risk of cardiovascular complications, lower receipt of revascularization, and decreased prescription of cardioprotective medications. Our findings, nonetheless, suggest that excess mortality experienced by patients with psychotic disorders could not be fully explained by their greater ACS severity and inferior cardiac care. Given the significance of under-treatment and heightened mortality among ACS patients with psychotic disorders, more research is needed to better understand the impact of and interactions among various factors contributing to inequalities in cardiovascular treatment and poorer prognosis in this vulnerable population, which will, in turn, facilitate outcome improvement following cardiac events.

Supplementary Material

Supplementary material is available at *Schizophrenia Bulletin* online.

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