General Hospital Psychiatry 50 (2018) 45–50

Contents lists available at ScienceDirect

General Hospital Psychiatry

journal homepage: www.elsevier.com/locate/genhospsych

Diseases of the pancreas and suicide mortality: A nationwide nested case-control study among patients with mental health disorders in Taiwan

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ARTICLE INFO

Keywords:
Diseases of the pancreas
Pancreatitis
Suicide
Mental disorders

ABSTRACT

Objective: Diseases of the pancreas, especially pancreatitis, have been implicated as possible risk factors for psychiatric illnesses, such as depression and anxiety disorder. This nested case-control study aimed to investigate the association between diseases of the pancreas and completed suicide in a psychiatric population-based study.
Methods: The case group comprised 6568 completed suicides (ICD-9: E950-E959, E980-989) patients from the national mortality database between January 1, 2002 and December 1, 2010. These cases were compared with 6568 gender-, age-, residence-, and insurance premium-matched controls. Both suicide and non-suicide study patients were drawn from a group with previous psychiatric diagnoses. The risk of suicide among patients with diseases of the pancreas was analyzed using a conditional logistic regression model that controlled for alcohol-related disorder, drug dependence, schizophrenia, depressive disorder, bipolar disorder, anxiety disorder, Charlson comorbidity score, and outpatient visits.
Results: Disease of the pancreas was an independent risk factor for psychiatric patients who had completed suicide when adjusted for clinical and other comorbid factors. Among these covariates, alcohol-related disorders partially mediate the suicide risk among patients with disease of the pancreas, and mental disorders may not mediate this suicide risk.
Conclusions: Diseases of the pancreas were associated with increased risk of completed suicide after controlling for potential confounding factors.

1. Introduction

Diseases of the pancreas, primarily acute and chronic pancreatitis, are common gastrointestinal causes of hospital admission [1]. Besides the financial cost of admission, chronic pancreatitis also reduces patient quality of life [2]. There are multiple causes for pancreatitis, including alcohol intake, hyperlipidemia, obstruction of pancreatic duct, trauma, medication use, and autoimmune disease. Acute pancreatitis is an acute abdominal disorder which usually needs hospital admission and has an overall mortality rate of 2–5% [3]. Chronic pancreatitis, a consequence of repeated acute pancreatitis or injury of the pancreas, is a progressive and debilitating disease, which usually needs further pain control.

Current studies indicate that patients with pancreatitis, no matter whether acute or chronic, might have poor mental health. One review which included 16 studies showed that quality of life declined after acute pancreatitis [4]. In patients with chronic pancreatitis, quality of life also declined, with especially the problem of pain [5]; they also suffered from depression, anxiety, or addiction that needed to be managed [6]. In addition, mental disorders may also interact with pancreatic disorders and worsen them. A report indicated that concomitant mental disorder predicted hospital readmissions of patients with acute and chronic pancreatitis [7]. Comorbid psychological

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http://dx.doi.org/10.1016/j.genhosppsych.2017.09.008
Received 29 May 2017; Received in revised form 28 September 2017; Accepted 28 September 2017

problem or psychiatric disorder should be also part of the treatment target for diseases of the pancreas.

Mental disorders, especially depressive disorders, have been known to be associated with risk of suicide [8–10]. Thus, we hypothesized that diseases of the pancreas, especially pancreatitis with known consequences for mental health, had higher risk of suicide too. The rate of suicide in pancreatic cancer increased significantly [11], but knowledge about the suicide risk of diseases of the pancreas is limited. A 5-year nationwide study in Denmark reported mortality and the causes of death for patients with chronic pancreatitis [12]. They indicated that patients with chronic pancreatitis, compared with controls, have a significantly higher mortality rate, more cancer incidence, more cancer-associated death, and a higher suicide rate. However, no further covariates were analyzed in that study.

The present study aimed to investigate the association between diseases of the pancreas and suicide mortality among a population with mental disorders through a nationwide database study. We hypothesized that patients with diseases of the pancreas have a higher risk of completed suicide. We also explored various covariates that were associated with diseases of the pancreas and suicide, such as mood disorders and alcohol use disorders [13,14] to clarify if they can affect this association.

2. Method

2.1. Study subject and control definition

The government of Taiwan started a nationwide health insurance program on March 1, 1995. It also developed a National Health Insurance Research Database (NHIRD) for research usage [15]. By December 2010, 23.074 million people were enrolled nationwide, with a coverage rate of 99.6%. In this study, we enrolled patients who had a psychiatric diagnosis (International Classification of Diseases (ICD)-9: 290-319) during the period 2002–2010. A diagnosis was defined as having a medical claim with the relevant diagnostic code on one occasion through inpatient services or on multiple occasions spread over at least one year through outpatient services; 2,329,989 people were enrolled (Fig. 1). We designed a nationwide nested case-control study. The nationwide mortality database of those aged 15 years and above was provided by the Department of Health of the Executive Yuan of Taiwan for the years 2002–2010. Since suicide mortality statistics are usually underestimated, and the most commonly misclassified category is death from undetermined causes, suicide deaths were defined in this study as those coded E950-E959 and E980-E989 according to the ICD-9. Among people with a diagnosis of psychiatric illness, there were 6568 completed suicides during the period 2002–2010 in Taiwan, including 4156 male suicides and 2412 female suicides, with a male-to-female ratio of 1.9. These cases were compared with 6568 controls matched on sex-, age-, residence-, and insurance premium (a proxy indicator of economic status) also drawn from those with a diagnosis of psychiatric illness. Both suicide and non-suicide study patients were hence drawn from a group with previous psychiatric diagnoses.

2.2. Ethics statement

The Institutional Review Board (IRB) of the Chang Gung Memorial Hospital approved this study which was conducted in Taiwan. The patients were not required to give written consent for the study because the NHIRD and mortality database consists of de-identified secondary data used for research purposes, and the IRB gave a formal written waiver of the need for consent.

2.3. Statistical analysis

Diseases of the pancreas (ICD-9: 577.X) were analyzed using a conditional logistic regression model that controlled for mental disorders (schizophrenia (ICD-9: 295.XX), depressive disorders (ICD-9: 296.2X, 296.3X, 300.4, and 311), bipolar disorders (ICD-9: 296.0, 296.4, 296.5, 296.6, 296.7, 296.80 or 296.89), anxiety disorders (ICD-9: 300.0, 300.01, 300.02, 300.2, 300.21, 300.23, 300.3)), alcohol-related disorders (ICD-9: 291, 303.0, 303.9, 305.0, 571.0, 571.1, 571.2, or 571.3), drug dependence (substance apart from alcohol, ICD-9:304), and general health condition (Charlson comorbidity score and outpatient visits). All of the potential comorbid diseases and Charlson comorbidity score were defined using outpatient and inpatient diagnosis before the index date, and outpatient visits were calculated by one-year medical claims before the index date. The index date was defined as the date of suicide for the case and assigned to their matched control. The odds-ratio (OR), which indicates the association between diseases of the pancreas and suicide, was estimated. First, we performed univariate conditional logistic regression to reveal the unadjusted association between each covariate and suicide. Second, we performed multivariable regression, including all previous covariates except alcohol-related disorder (model 1). Finally, we included all study covariates including alcohol-related disorders for further adjustment to confirm if diseases of the pancreas contributed to risk of suicide independently (model 2). The model was tested using the total group of patients initially and then using subgroups according to gender and age (15–44, 45–64 and ≥ 65 years) (Table 3). Analyses were carried out using SAS version 9.4 (SAS Institute Inc., Cary, NC, USA).

3. Results

3.1. Clinical characteristic of suicide and non-suicide group

In total, 6568 suicide cases and 6568 non-suicide matched controls were included among psychiatric illness population. Table 1 shows the demographic and clinical characteristics of suicide cases and non-suicide controls. Because of the exact matching, there was no difference in gender, age, residence (rural, urban), and insurance premium (a proxy indicator of economic status). In suicide cases, there were more diseases of the pancreas, alcohol-related disorders, drug dependence, schizophrenic disorders, depressive disorders, bipolar disorders, and anxiety disorders (all $P < 0.001$). Compared with the control group, suicide cases had higher Charlson comorbidity score ≥ 4 (26.42% vs. 19.49%) and more frequent outpatient visits (≥ 31 times in one year before the index date, 45.37% vs. 26.33%).

3.2. Unadjusted (univariate) analysis

Diseases of the pancreas were associated with suicide risk (OR = 2.66, 95% CI = 2.08–3.38, $P < 0.001$). Among other study covariates, alcohol-related disorders, drug dependence, schizophrenic disorders, depressive disorders, bipolar disorders, anxiety disorders, Charlson comorbidity score, and outpatient visits were also associated with suicide risk (Table 2).

3.3. Adjusted analysis

We included all study covariates except alcohol-related disorders in model 1 (Table 2), and the strength of association between diseases of the pancreas and suicide risk (OR = 2.67) was similar to the unadjusted value (OR = 2.66). All of the other study covariates, drug dependence, schizophrenic disorders, depressive disorders, bipolar disorders, anxiety disorders, Charlson comorbidity score, and outpatient visits were also associated with suicide risk independently after adjustment (Table 2).

In model 2, we adjusted for all covariates including alcohol-related disorders (Table 2). The suicide risk of each covariate was similar to the result in model 1. However, the association of diseases of the pancreas to suicide risk decreased from OR = 2.67 to 1.60.