



The Pre-Existing Depressive Disorders, Substance Use Disorders Predicted the Suicidal Death of the Patients with Eating Disorders – A Preliminary Result of National Health Insurance Research Databases in a Chinese Population

Chiu-Lan Yan^{1,2,3}, Jung-Chen Chang^{4,5}, Shu-Chuan Weng⁶, Ming-Kung Yeh^{3,*}, Chin-Bin Yeh^{1,7,*†}

ABSTRACT

Objective

Recent evidence suggests that additional psychiatric disorders in patients with eating disorders (ED) may contribute to suicide risk. The aim of our study was to investigate the association between eating disorders, its comorbidity and suicidal deaths by the analyzing the data from National Health Insurance Research Databases (NHIRD) and statistical reports on the causes of death.

Methods

We identified 19,648 patients with ED diagnoses from the Taiwan National Health Insurance Database between 2001 and 2012. The patients who had been diagnosed eating disorders ≥ 4 times at outpatient visits, or had ≥ 1 time of hospitalization were recruited as the group of ED (N=9974). The outcome of measurements was defined as the death of the group of eating disorders either by suicide (N=113), accidental death (N=35) or others (N=97). Cox regression was applied to investigate the relationship between psychiatry comorbidities and the suicidal death of the patients with ED.

Results

Age of onset with Anorexia Nervosa (AN) was significantly younger than Bulimia Nervosa (BN) or Eating disorders, NOS (EDNOS) in patients with ED. The risk of suicide had 2.4-fold higher of pre-existing (aHR=2.4; 95% CI=1.6-3.7) but not concurrent (aHR=1.0; 95% CI=0.7-1.5) or subsequent (aHR=0.8; 95% CI=0.4-1.3) any psychiatric comorbidity with ED patients than without psychiatric comorbidity. The risk of suicide was 1.8-fold higher in patients with previous major depressive disorder (aHR=1.8; 95% CI=1.2-2.7), and 2.6-fold higher in patients with prior substance use disorder (aHR=2.6; 95% CI=1.5-4.5). Patients with four or more psychiatric comorbidities had a 6.3-fold increased risk of suicide (aHR=6.3; 95% CI=3.1–12.8; $p < 0.05$).

¹Graduate Institute of Medical Sciences, National Defense Medical Center, Taipei, Taiwan

²Department of Pharmacy Practice, Tri-Service General Hospital, National Defense Medical Center, Taipei, Taiwan

³School of Pharmacy, National Defense Medical Center, Taipei, Taiwan.

⁴School of Nursing, College of Medicine, National Taiwan University, Taipei, Taiwan

⁵Department of Nursing, National Taiwan University Hospital, Taipei, Taiwan

⁶Bachelor's Degree Program of Golden-Age Well-being Management, Yuanpei University of Medical Technology, Hsinchu, Taiwan

⁷Department of Psychiatry, Tri-Service General Hospital, School of Medicine, National Defense Medical Center, Taipei, Taiwan

[†]Author for correspondence: Chin-Bin Yeh, PhD, Department of Psychiatry, Tri-Service General Hospital, National Defense Medical Center, 325, Sec. 2, Cheng-Gong Road, Nei-Hu District, Taipei 114, Taiwan, Republic of China, Tel: +886-915-376-404; Fax: +886-2-87927154; e-mail: chinbinyeh@gmail.com

*These authors contributed equally to the research work.

Conclusion

The previous psychiatric comorbidities including major depressive disorder and substance use disorder were associated with the suicidal death in patients with ED. The patients with more psychiatric comorbidities had a higher risk of suicide.

Keywords

Suicide, Mood disorder, Eating disorders, Anorexia nervosa, Bulimia nervosa, Health insurance database.

Introduction

Eating disorders (ED) are complex chronic mental disorders, accompanied abnormal eating habits and weight control behavior. ED are relatively rare among the general population, but its affect adolescent in many developed countries [1]. In the 20th century, ED attitudes and behaviors increased dramatically across Asia's high-income populations of young females [2], and psychiatric disorders associated with risk for the development of ED [3]. Previous studies have individuals with ED report histories of anxiety [4], depression [5], substance abuse [6], and personality disorders [7] maybe play an essential role in the development of eating disorders.

However, Clinical studies also indicated that comorbid psychiatric disorders had been associated with suicide attempts in individuals who have an ED [8-12]. As such as the rate of suicide attempts is 3–20% and 25–35% in patients with anorexia nervosa and bulimia nervosa, respectively [9], but little is known about the risk factors associated with suicidal death among the patients with ED. In addition, although most studies have used community samples or enrolled patients at primary care clinics [13,14], even in Asia have been cross-sectional survey questionnaires with face-to face interviews or case reports in select population [15-18], the results of the studies were inconsistent due to the small sample sizes, racial differences, and the use of different assessment scales and changes in the sources of diagnostic criteria. Here we present an investigation with regards to the impact of the characteristics including the subtypes of ED, demography data, and psychiatric comorbidities in the relationship between ED and suicidal death with the analysis of Databases.

Methods

■ Data source

All data had been obtained from the Taiwan's Health and Welfare Data Science Center,

Ministry of Health and Welfare between 2011 and 2012. Data includes the National Health Insurance Database, statistics reports on the causes of death, and household information, regarding annual national marital status and level of education. The data transmissions were encrypted and linked with a personal ID between Databases. The Taiwan National Health Insurance scheme covers 99% of Taiwan's population and provides data on consultation, emergency consultation, and inpatient diagnoses of insured people. This database demonstrates the healthcare utilization of Taiwanese citizens [19].

■ Study population

We identified the ED group based on an International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) code 307.5X and 307.1 of the National Health Insurance Database (NHID) from 2001 to 2012. There were 19,648 patients were screened with the diagnosis of eating disorders by psychiatrists in NHID. The ED group was defined as either having been diagnosed ED equal to or more than four times at outpatient visits or had at least one time of hospitalization with the diagnosis of eating disorders (n=9,974). They were included in the current study and classified into the four following groups based on the diagnosis: AN (anorexia nervosa, ICD-9-CM code 307.1), BN (bulimia nervosa, ICD-9-CM code 307.51), AN+BN (the presence of both anorexia nervosa and bulimia nervosa, ICD-9-CM code 307.1 and 307.51), and EDNOS (eating disorders not otherwise specified, ICD-9-CM code 307.52–307.59). The follow-up period was defined from the time of first ED diagnosis until death or study termination. **Figure 1** outlines the process of sample inclusion.

■ Potential confounders

In this study we identified psychiatric comorbidities including anxiety disorders (ICD-9-CM code 300 except 300.4), major depressive disorders (ICD-9-CM code 296.2, 296.3, 296.82, 300.4), bipolar disorders (ICD-9-CM

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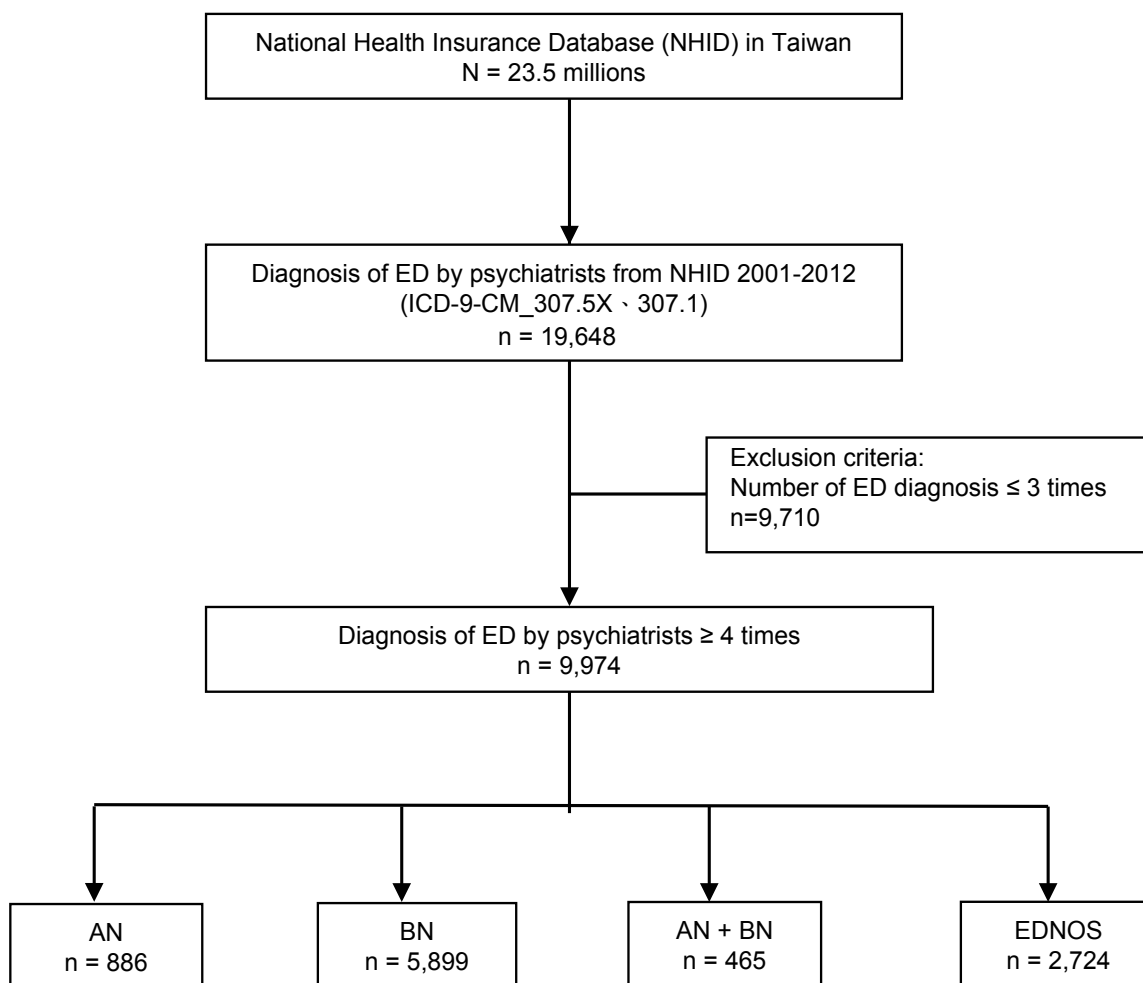


Figure 1: Flow chart of case enrollment from the National Health Insurance Database in Taiwan.

ED: Eating Disorder; AN: Anorexia Nervosa; BN: Bulimia Nervosa; AN+BN: Anorexia Nervosa and Bulimia Nervosa; EDNOS: Eating Disorder not Otherwise Specified.

code 296.0, 296.1, 296.4, 296.5, 296.6, 296.7, 296.80, 296.81, 296.89, 296.90), schizophrenia (ICD-9-CM code 295), substance-use disorders (ICD-9-CM code 291, 292, 303, 304, 305), and personality disorders (ICD-9-CM code 301) of the patients with ED. Information on the comorbidities mentioned above was obtained with the ICD-9-CM codes occurring at 4 or more times during medical visits.

We also used the following parameters included income group, treatment period (time of the first ED diagnosis and treatment, to the time of the last ED diagnosis), history of suicide (E950-959) and information regarding the marital status and educational level were collected from the connected household data. The status of death (including a cause of death/suicide/unnatural death) of all follow-up cases of ED was collected from mortality statistics. The occurrence sequence

of first diagnose psychiatric comorbidities were defined pre-existing (the period before ED), concurrent (in the same period with ED), and subsequent (the period after ED).

■ **Statistical analysis**

The data analyzed in this study included gender, marital status, educational level, comorbidity, which were presented as percentages, while age at the time of treatment, treatment period, length of the follow-up, were presented as mean ± standard deviation. The differences of all variables between the different types of ED were evaluated using Chi-squared tests or a single-factor analysis of variance (ANOVA). The Cox proportional hazard model was used to investigate the association of suicide risk and mental illness in patients with ED. Statistical significance was set at $P < 0.05$. All data were analyzed using the statistical software, SAS Version 9.3 (SAS Institute, Inc, 1995, Cary, NC).

Results

■ **Preliminary analyses**

In this study, we included 9,974 ED patients that were separated into four subtypes. The four subtypes were included as follows: 886 AN (8.9%), 5899 BN (59.1%), 465 AN+BN (4.7%) and 2724 EDNOS (27.3%) and the age of onset about 23.0±10.4 years, 29.1±10.4 years, 22.5±6.01 years and 30.4±10.9 years in AN, BN, AN+BN and EDNOS, respectively. While AN is the most common age was 11-20, another subtype is most common among aged 21-30. The average duration of treatment about two years, but AN+BN was longest treatment (4.4±3.3 years). 56.7% of the BN patients reported at death by suicidal was the highest in all group, while accidental deaths was the highest in the AN+BN patients (26.7% of all deaths in the group). The demographic characteristics of four subtype ED in **Table 1**.

■ **The risk factors associated with suicide**

The majority of ED patients were female (91.7%) and single (78.8%). As showed in **Table 2**, the risk of suicide in patients with AN was 2.2-fold higher than that in patients with other ED groups (aHR=2.2; 95% confidence interval [CI]=1.2–4.3). Patients with a history of suicide attempted had 6.1-fold higher suicidal risk (aHR=6.1; 95% CI=3.5–10.8) compared without such a history. The risk of suicide had 2.4-fold higher of pre-existing of any psychiatric comorbidity with ED patients than without psychiatric comorbidity (aHR=2.4; 95% CI=1.6-3.7). However,

concurrent (in the same period with ED) and subsequent (the period after ED) psychiatric comorbidities were not significantly associated with risk of suicide for ED patients. **Table 3** also reveals that the risk of suicide was 1.8-fold higher in patients with comorbid pre-existing depression (aHR=1.8; 95% CI=1.2-2.7), and 2.6-fold higher in patients with comorbid prior substance use disorder (aHR=2.6; 95% CI=1.5-4.5). In addition, we found that patients with 4 or more pre-existing psychiatric comorbidities had a 6.3-fold increased risk of suicide (aHR=6.3; 95% CI=3.1–12.8; p<0.05).

Discussion

Consistent with previous studies [20,21], our result indicated that more female patients than male patients with ED diagnose. Patients with AN were found to have an earlier onset of disease aged 11–20 years (n=429, 48.4%), while patients in the other three ED groups were mostly 21–30 years. Our finding is similar to the results of an early investigation of ED from United States National database of Health insurance [22,23], although gender and age did not influence risk factor of suicide with ED.

Our finding indicated that history of major depressive disorder, but not concurrent depressive disorders predicted suicide of the patients with ED. However, the concurrent rate with depression (9.4-21.2%) had been found to be higher than those who without (1-3%) of patients with BN in previous studies [24,25]. Godart et al. [26] also found the

Table 1: The demographic characteristics of four subtypes of eating disorders.

Sub-groups (n=9974)	AN (n=886)	BN (n=5899)	AN+BN (n=465)	EDNOS (n=2724)	
Variable	n (%) or mean ± S.D.				P value
Age of onset (years)	23.0 ± 10.4	29.1 ± 9.3	22.5 ± 6.01	30.4 ± 10.9	<0.001
≤ 10	15 (1.7)	7 (0.1)	0	44 (1.6)	<0.001
11-20	429 (48.4)	926 (15.7)	196 (42.2)	401 (14.7)	
21-30	291 (32.8)	2792 (47.3)	232 (49.9)	1088 (39.9)	
31-40	106 (12.0)	1423 (24.1)	27 (5.8)	716 (26.3)	
41-50	25 (2.8)	602 (10.2)	#	338 (12.4)	
>50	20 (2.3)	149 (2.5)	#	137 (5.0)	
Duration of treatment (years)	2.0 ± 2.4	2.3 ± 2.5	4.4 ± 3.3	1.7 ± 1.9	<0.001
Study Follow-up (years)	6.5 ± 3.8	6.1 ± 3.6	7.9 ± 3.7	5.5 ± 3.6	<0.001
All causes of death	42 (4.7)	127 (2.2)	15 (3.2)	61 (2.2)	<0.001
Suicide	13 (31.0)	72 (56.7)	6 (40)	22 (36.1)	0.004
Accidental death	4 (9.5)	19 (15.0)	4 (26.7)	8 (13.1)	
Other causes	25 (59.5)	36 (28.3)	5 (33.3)	31 (50.8)	

S.D., standard deviation

#Cells that have less than 2 patients are not permitted to appear in the table, to avoid their possible identification.

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Table 2: Risk factors associated with suicide in major eating disorders: Cox proportional hazards model.

Variable	ED patient (n = 9974)			
	n (%) or mean ± S.D.	HR (95% CI)	aHR (95% CI)	P value
ED Disorder				
Other ED	2724 (27.3)	1	1	
AN	886 (8.9)	1.8 (1.0-3.4)	2.2 (1.2-4.3)	0.01
BN	5899 (59.1)	1.4 (0.9-2.2)	1.4 (0.9-2.2)	0.15
AN+BN	465 (4.7)	1.1 (0.5-2.7)	1.2 (0.5-3.1)	0.66
Age (in y/o)	28.6 ± 10.0	1.0 (0.9-1.0)	1.0 (0.9-1.0)	0.4
Low-income	486 (4.9)	0.3 (0.1-1.4)	0.3 (0.8-1.1)	0.07
Female gender	9148 (91.7)	1.3 (0.6-2.6)	1.0 (0.5-2.1)	0.97
Marital status				
Married	2117 (21.2)	1	1	
Single	7857 (78.8)	0.9 (0.6-1.4)	1.2 (0.7-1.9)	0.58
Education				
≤senior	5950 (59.7)	1	1	
≥junior college	3204 (32.1)	0.6 (0.4-0.8)	0.6 (0.4-0.9)	0.01
unknown	820 (8.2)	0.4 (0.1-1.0)	0.5 (0.2-1.3)	0.15
Suicide attempt (E950-E959)	186 (1.9)	7.1 (4.1-12.3)	6.1 (3.5-10.8)	<0.001
No. of physical comorbidities*	2718 (27.3)	1.0 (0.6-1.4)	0.8 (0.5-1.2)	0.24
No. of pre-existing psychiatric comorbidities#	5664 (56.8)	2.5 (1.7-3.8)	2.4 (1.6-3.7)	<0.001
No. of concurrent psychiatric comorbidities#	4624 (46.4)	0.8 (0.6-1.2)	1.0 (0.7-1.5)	0.88
No. of subsequent psychiatric comorbidities#	1094 (11.0)	0.8 (0.5-1.4)	0.8 (0.4-1.3)	0.34

***including:** Diabetes mellitus: ICD9_250; Hypertensive Disease: ICD9_401-405; Lipoid metabolism: ICD9_272; Cancer: ICD9_140-208; Cardio Vascular Disease: ICD9_390-398, 410-414, 420-429; Cerebral Vascular Accident: ICD9_430-438.

#including: Anxiety: ICD9_300; Major Depressive Disorder: ICD9_296.20-296.26,296.30-296.36,296.82,300.4; Bipolar Disorder: ICD9_296.00-296.06,296.10-296.16,296.40-296.46,296.50-296.56,296.60-296.66,296.7,296.80,296.81,296.89,296.90; Schizophrenia: ICD9_295x; Substance use disorders: ICD9_291s, 292s, 303s, 304s, and 305s; Personality disorders: ICD9_301

Table 3: Number of six pre-existing psychiatric comorbidities with suicide risk.

Variable	ED patient (n=9974)			
	n (%)	HR (95% CI)	aHR (95% CI)	P value
No. of six pre-existing psychiatric comorbidities	5664 (56.8)	2.5 (1.7-3.8)	2.4 (1.6-3.7)	<0.001
Major depressive disorder	4285 (43.0)	2.5 (1.7-3.6)	1.8 (1.2-2.7)	0.005
Bipolar disorder	952 (9.5)	2.2 (1.3-3.5)	1.0 (0.6-1.8)	0.89
Schizophrenia	326 (3.3)	2.7 (1.4-5.2)	1.9 (1.0-1.8)	0.06
Substance use disorder	471 (4.7)	5.0 (3.1-8.1)	2.6 (1.5-4.5)	0.001
Anxiety	3488 (35.0)	2.1 (1.5-3.0)	1.5 (1.0-2.2)	0.06
Personality Disorder	422 (4.2)	3.0 (1.7-5.4)	1.2 (0.6-2.3)	0.57
Number of comorbidities	4310 (43.2)			
1 comorbidity	2767 (27.7)	1.6 (1.0-2.6)	1.7 (1.0-2.7)	0.05
2 comorbidities	1899 (19.0)	2.9 (1.8-4.7)	2.9 (1.7-4.8)	<0.001
3 comorbidities	697 (7.0)	3.7 (2.0-6.9)	3.6 (1.8-6.9)	<0.001
4 or more comorbidities	226 (2.3)	8.2 (4.3-15.6)	6.3 (3.1-12.8)	<0.001

CI: Confidence Interval

lifetime prevalence at least one mood disorder varies considerably, from 24.1–90% with BN, while it was 31–88.9% for AN. Furthermore, patients with ED have a higher prevalence of concurrent mood disorders than the general population. Tseng et al. [27] also conducted a study on psychiatric patients and found that patients with ED had a high percentage of comorbid depressive symptoms (41.3–66.7%),

followed by bipolar disorders (16.7–49.3%). They demonstrated that patients with ED and comorbid bipolar disorders showed an increased risk of weight dysregulation, impulsive behavior, and suicides. Additionally, alcohol abuse, self-harm, and illicit drugs use were common in women with bulimia and binge eating disorders [28]. Novelty seeking, self-directedness and impulsivity were proposed to be associated with

both the pathology of substance use and bulimia [29]. Moreover, the prior substance use might complicate the treatment of eating disorders [30]. Those findings provided the evidence and were consistent with our finding that either history of major depression or prior substance use might also be associated with the suicidal death among the patients with ED.

Our investigation also found that ED with at least one pre-existing psychiatric comorbidity had higher risk of suicidal deaths, compared with patients without comorbidities. In addition, patients were more suicide risks as the number of pre-existing psychiatric comorbidities increased. In recent years, Bühren et al. [31] demonstrated the binge-purging subtype and the severity of eating disorder were associated with the presence of suicidal ideation. However, to our knowledge, our study was the first one showed that the pre-existing psychiatric comorbidities including major depressive disorders or substance use disorders but not concurrent or subsequent psychiatric comorbidities were associated with the suicidal death of patients with ED. Future studies were warranted to investigate the role of ED in the development of suicidal death of the patients with major depressive disorder and/or substance use disorder. Our results implicated that it is critical for the identification and intervention of the pre-existing psychiatric comorbidities among the patients with ED since there was addictive effect regarding the numbers of psychiatric comorbidities. On the other hand, we did not find the impact of comorbidities of anxiety disorders, personality disorders, schizophrenia in the suicidal death among the patient with ED although the impulsivity, and interpersonal deficits might explain the pathology of obsessive-compulsive disorder [32,33], personality disorders [34-36], schizophrenia [37,38] and eating disorders.

Some limitations of the study must be noted. First, to increase the specificity of the ED diagnosis, only patients with ≥ 4 diagnoses by psychiatrists was included in the study. Second, the data from the National Health Insurance Database lacked some clinical information, such as height, weight, family history, blood examination, and psychological behavioral therapy. This could have limited the comprehensive comparison of similarities and differences between patients with different types of ED. Third, data on the level of education of the patient cohort in the current study were obtained based on

the enrollment status. Since this data does not require mandatory recording, part of the data could be missing; thus, its accuracy requires further confirmation.

In fact, apart from psychiatric disorders affecting the risk of suicides, other factors such as genetics [39,40], society [41,42], family [43], and cognitive behavior [44,45] may have also increased the risk of suicidal thoughts and depressive symptoms. This study only carried out a preliminary investigation based on databases. Future studies focusing on one type of ED, including a collection of medical examinations and survey questionnaires, could be conducted to further validate our findings.

Conclusions

The risk of suicide was linked with psychiatric comorbidity in patients with ED, particularly those with pre-existing major depression and/or substance use disorders. Future longitudinal studies were warranted to validate the preliminary results from the investigation of databases.

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This study also approved by the Institutional Review Board of the Tri-Service General Hospital (reference number 1-104-05-048) and was conducted in accordance with the Helsinki Declaration. Informed consent from patients was not required for this study, as they were not asked to follow rules of behavior. Patient data were coded and anonymity of patients was guaranteed.

Conflicts of Interest

None of the authors report any conflicts of interest.

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