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Journal of Affective Disorders 113 (2009) 255–262

Journal of Affective Disorders

www.elsevier.com/locate/jad

Research report

Risk of mortality among depressed younger patients: A five-year follow-up study

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Received 7 April 2008; received in revised form 29 May 2008; accepted 29 May 2008
Available online 21 July 2008

Abstract

Background: Young adults aged from 18 to 44 years comprise a large portion of the population suffering from depression. Yet few studies have compared the likelihood of dying of natural causes or by suicide among depressed patients. This study uses a case–control approach to compare the likelihood of dying of natural causes and by suicide for depressed and non-depressed patients based on a representative national sample in Taiwan.
Method: A retrospective case–control study design was used to analyze two nationwide population-based datasets: the National Health Insurance Research Database (NHIRD) and the official Cause of Death data file in Taiwan. The study cohort consisted of 827 patients from 18 to 44 years old who were hospitalized with a primary diagnosis of depressive disorder from 1998–2003. A comparison cohort of patients hospitalized for appendectomies was matched with the study sample in terms of age and gender (N=2481).
Results: After adjusting for the age and comorbid medical disorders, the hazard of dying during the five-year follow-up period was 1.72 times greater for depressed patients than for appendectomy patients. Depressed patients were more likely to die by suicide during the follow-up period, as no significant difference in odds of dying from natural causes was observed between these two cohorts.
Conclusion: Further studies should be initiated to identify specific risk factors for suicide among younger adults, while prevention strategies might focus on stresses associated with particular life stages, taking age and gender patterns into account.

Keywords: Completed suicide; Depression; Mortality

1. Introduction

Depression is a widespread mental disorder in adults, with more than 19 million adults in the U.S. alone suffering from depression (National Institute of Mental Health, 1999). Despite more than 50 studies published

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doi:10.1016/j.jad.2008.05.025

over the past three decades coming to the common conclusion that the risk of early death increases with depression, recently published well-designed controlled studies have revealed mixed results (Wulsin et al., 1999). Among mental disorders, researchers have found that risk of unnatural death is particularly high among patients with functional disorders, especially major depression and schizophrenia (Harris and Barraclough, 1998) and recurrent major depressive episodes (Schneider et al., 2001). A recent study exploring the long-term course of severe depression has found an increasing mortality rate over time (Brådvik and Berglund, 2001). The high mortality can largely be explained by the risk of suicide (Angst et al., 2002; Schneider et al., 2001; Zonda and Gróza, 2000). A recent psychological autopsy study in China investigated the risk factors for suicide using accidental deaths as a control group, finding that depressive symptoms increased substantially in the two weeks preceding suicide (Phillips et al., 2002). Studies reporting rates of suicide among depressed patients have revealed a range from 0% to 64% with a mean of 10.8% (Goodwin and Jamison, 2007; Lönnqvist, 2000; Wulsin et al., 1999).

Depressed adults are less physically healthy, less socially active and less satisfied with life, as well as more likely to be absent from work, compared to adults who are not depressed. Studies comparing demographic characteristics between adult populations with and without depression have found that the depressed population includes larger proportions of young adults aged 18 to 44 (61%), compared to the population without depression (57%). Also, the depressed population included a larger proportion of low-income individuals (51%) compared to their non-depressed counterparts (28%) (National Academy on an Aging Society, 2000).

In Taiwan, the suicide rate has been steadily increasing over the past ten years, with suicide among younger adults very common. Suicide was ranked as the second and the third leading cause of death among youths aged 15 to 24 and adults aged 25 to 44, respectively (Department of Health, 2007). According to Erikson (1963), the most important developmental tasks during adulthood are intimacy and generativity. A highly complicated relationship network and stress from occupational competition in Taiwan may coincide with increased rates of chronic illness during this stage of life, including depression.

Most studies exploring mortality outcomes relating to depression do not consider different age groups or take developmental considerations into account. Also, few studies have used a nationwide case–control study design to explore the risk of mortality associated with depression. The purpose of this study was therefore to explore the risk of mortality from natural causes and suicide among depressed younger patients, using a representative national sample of adults aged from 18–44 years. Specifically, Cox proportional hazard regression was used to compute the adjusted five-year survival rates after adjusting for socio-demographic variables and comorbid medical illnesses. Results from this study provide a basis for developing a comprehensive suicide prevention strategy for younger adults.

2. Methods

2.1. Database

This study used two nationwide population-based datasets. First, we used the National Health Insurance Research Database (NHIRD) records for the years 1998–2003, published by the National Health Research Institute in Taiwan. The dataset includes all inpatient claims, ambulatory care claims, details of inpatient orders, and details of ambulatory care orders from Taiwan's National Health Insurance (NHI) program, a single-payer payment system which finances healthcare for all Taiwanese citizens (around 23 million), offering unrestricted access to any healthcare provider of the patient's choice. The second database used in this study is the "cause of death" data file published by the Department of Health (DOH) in Taiwan. This dataset provides data on all deceased persons in Taiwan, including marital status, employment status, place of legal residence, date of birth and death, and the cause of death (ICD-9-CM code). Since registration of all deaths is mandatory in Taiwan, the data are considered to be very accurate and comprehensive. With the assistance of the DOH in Taiwan, the NHIRD data was linked to the "cause of death" data file through patients' identification numbers. Since the NHIRD consists of de-identified secondary data released to the public for research purposes, this study was exempted from full review by the Internal Review Board.

2.2. Study sample

Our study design consists of a study cohort and a comparison cohort; the study cohort included all patients in Taiwan aged between 18 and 44 years who were hospitalized with a principal diagnosis of depressive disorder (ICD-9-CM codes 296.2, 300.4, or 311) from January 1, 1998 to December 31 1998. The legal definition of adulthood varies in different countries. In Taiwan, adulthood is defined by civil law as beginning at 20 years old, while it can also be defined as beginning

at 18 years old in criminal law. Developmentally, a person 18 years old really experiences a challenging stage, such as entering college, university, or the workplace. Our study therefore adopted a wider definition of adult, starting at 18 years old, in order to differentiate our study subjects from adolescents.

Initially, 1093 patients aged from 18 to 44 years were selected from the datasets. We excluded those who had been hospitalized for depressive disorder during the preceding two-year period (1996–1997) (N=132) to assure that the selected patients were diagnosed with depressive disorder for the first time. However, since the NHIRD only provides data starting from 1996, we cannot trace the medical histories of sampled patients back further. To ensure the validity of the diagnosis of depressive disorder, we excluded patients diagnosed with bipolar disorder during the follow-up period after the index hospitalization (N=134). Ultimately, our study sample included 827 patients with depressive disorder.

Our comparison cohort included all patients aged between 18 and 44 years who were hospitalized for an appendectomy during 1998, with a principal operative code of 47.0. Patients undergoing an appendectomy were excluded if they had been diagnosed as having any type of mental disorder (ICD-9-CM codes 290–319) during the period from 1996 to 2003. The reason we selected appendectomy patients as a comparison group was that patients undergoing appendectomies were relatively indistinguishable from the general population. Our prior studies have found no statistically significant differences in gender and age between this comparison population and the general population in Taiwan. Moreover, the procedures involved in an appendectomy have no known long-term impact on risk of mortality or depressive disorder. We further refined our comparison cohort criteria by randomly selecting 2481 appendectomy patients (three for every patient with depressive disorder) matched with the study group in terms of age (18–29 and 30–44) and gender. Each patient was tracked for five years from index hospitalization in 1998 until 2003 in order to identify all patients who died.

The regression modeling also adjusted for socio-demographic characteristics such as age, gender, level of urbanization, the geographic location of the community in which the patient resided (Northern, Central, Eastern and Southern Taiwan), and monthly income (0, NT$1–NT15,840, NT15,841–NT25,000, ≥NT25,001). The reason we selected NT$15,840 as the first cutoff point for defining income levels was that this is the government-stipulated minimum wage for full-time employees in Taiwan. We used the criteria published by the Taiwanese National Health Research Institute on urbanization levels in Taiwan, which includes seven strata, with level 1 indicating the 'most urbanized' communities and level 7 referring to the 'least urbanized' communities (Liu et al. 2008). All 359 cities/towns in Taiwan were stratified into seven groups. These standards include the population density (people/km^2), the proportion of people with college education levels or above, the proportion of elderly people over 65 years of age, the proportion of agricultural workers and the number of physicians per 100,000 people. Detailed descriptions of each level of urbanization are presented in the Appendix. Given that there were only very small numbers of study subjects in levels 5, 6 and 7, these three levels were combined into one single group, which was thereafter referred to as level 5. In addition, we adjusted for select comorbid medical disorders, including hypertension and diabetes at the time of the index discharge.

Table 1
Demographic characteristics and comorbid medical disorders for depression patients and appendectomy patients in Taiwan, 1998 (n=3308)

Variable	Depression patients n=827		Appendectomy patients n=2481		p value
	Total no.	Column %	Total no.	Column %	
Gender					1.000
Male	362	43.8	1086	43.8	
Female	465	56.2	1395	56.2	
Age (years)					1.000
18–29	257	31.1	771	31.1	
30–44	570	68.9	1710	68.9	
Hypertension					0.038
Yes	9	1.1	11	0.4	
No	818	98.9	2470	99.6	
Diabetes					0.009
Yes	13	1.6	15	0.6	
No	814	98.4	2466	99.4	
Monthly income					<0.001
0	156	18.9	501	20.2	
NT$1–15,840	248	32.0	496	20.0	
NT$15,841–25,000	322	38.9	980	39.5	
≥NT$25,001	101	12.2	504	20.3	
Urbanization level					0.008
1	326	39.4	902	36.4	
2	261	31.6	711	28.7	
3	108	13.1	445	17.9	
4	104	12.6	314	12.3	
5	28	3.4	109	4.4	
Geographic region					<0.001
Northern	508	61.4	1238	49.8	
Central	119	14.4	527	21.2	
Southern	172	20.8	657	26.5	
Eastern	28	3.4	62	2.5	

Table 2
Mortality among depression patients and appendectomy patients in Taiwan during the five-year follow-up period (n=3308)

Variable	Mortality		
	Yes, row n (%)	No, row n (%)	p value
Cohort			<0.001
Depression	51 (6.2)	776 (93.8)	
Appendectomy	84 (3.4)	2397 (96.6)	
Gender			<0.001
Male	88 (6.1)	1360 (93.9)	
Female	47 (2.5)	1813 (97.5)	
Age (years)			<0.001
18–29	22 (2.1)	1006 (97.9)	
30–44	113 (5.0)	2167 (95.0)	
Hypertension			0.006
Yes	4 (20.0)	16 (80.0)	
No	131 (4.0)	3157 (96.0)	
Diabetes			<0.001
Yes	4 (14.3)	24 (85.7)	
No	131 (4.0)	3149 (96.0)	
Monthly income			<0.001
0	6 (0.9)	651 (99.1)	
NT$1–15,840	38 (5.1)	706 (94.9)	
NT$15,841–25,000	70 (5.4)	1232 (94.6)	
≥NT$25,001	21 (3.5)	584 (96.5)	
Urbanization level			0.375
1	41 (3.3)	1187 (96.7)	
2	40 (4.1)	932 (95.6)	
3	29 (5.2)	524 (94.8)	
4	20 (4.8)	398 (95.2)	
5	5 (3.7)	132 (96.4)	
Geographic region			0.349
Northern	73 (4.2)	1670 (95.8)	
Central	31 (4.8)	615 (95.2)	
Southern	26 (3.1)	803 (96.9)	
Eastern	5 (5.6)	85 (94.4)	

2.3. Statistical analysis

The SAS statistical package (SAS System for Windows, Version 8.2) was used to perform the analyses. Pearson χ^2 tests were performed to examine the differences between the two cohorts in terms of socio-demographic characteristics, select comorbid medical disorders and the risk of mortality. The five-year survival rate was then estimated using the log-rank test to examine the differences in the risk of mortality between the two cohorts. Cox proportional hazard regressions were also carried out to compute the adjusted five-year survival rate, after adjusting for the variables that were significantly related to mortality from the χ^2 analyses. We present hazard ratios (HR) along with the 95 percent confidence intervals (95% CI) adopting a significance level of 0.05.

3. Results

Table 1 presents the distribution of demographic characteristics and select comorbid medical disorders for the study and control cohorts. It shows that depressed patients were more likely to have comorbidities such as hypertension (p=0.038) and diabetes (p=0.009) at the time of the index hospitalization, when compared to appendectomy patients. Table 1 also shows that depressed patients tended to have monthly incomes between NT$1 and NT$15,840 (p<0.001)—the lowest income category, to reside in more urbanized areas (p=0.008) and in the northern part of Taiwan (p<0.001).

Of the total sample of 3308 patients, 4.08% (135 total) died during the five-year follow-up period, including 6.17% of depressed patients (51 from the study cohort) and 3.39% of appendectomy patients (84 from the control cohort). Of the total deaths, 111 patients died of natural causes, and the other 24 by suicide. Among the suicidal deaths, 8 were from the study cohort (1.93% of the study cohort), and the other 16 were from the control cohort (0.32% of that cohort). The study cohort showed as much as a six-fold increase in risk of suicide compared with the control cohort. The log-rank test indicated that depressed patients had significantly lower five-year survival rates than appendectomy patients (p<0.001).

Table 2 describes the relationship between mortality, demographic characteristics and selected comorbid medical disorders. The Pearson χ^2 tests reveal that mortality from natural causes and suicide combined was related to patient age (p=0.006), gender (p<0.001), monthly income (p<0.001) as well as the presence of hypertension (p<0.001) and diabetes (p<0.001).

Table 3 presents the adjusted hazard ratios for mortality by cohort. After adjusting for the patients' age and comorbid medical disorders, the hazard of dying from natural causes or suicide during the five-year follow-up period was 1.72 times greater (95% CI=1.19–2.49, p<0.001) for depressed patients than for appendectomy patients. Furthermore, depressed patients were more likely to die of suicide during the follow-up period (HR=5.59, 95% CI=2.34–13.36, p<0.001). However, no significant difference in the hazard of dying from natural causes was observed between the two cohorts (HR=1.37, 95% CI=0.91–2.06, p>0.05).

4. Discussion

The purpose of this study was to explore the risk of mortality among depressed patients in Taiwan based

Table 3
Adjusted hazard ratio for mortality during the five-year follow-up period for depression patients and appendectomy patients in Taiwan (n=3308)

Variables	Mortality		
	Total	Natural	Suicide
	HR, 95%CI	HR, 95%CI	HR, 95%CI
Cohort			
Depression	1.72 (1.19–2.49)	1.37 (0.91–2.06)	5.59 (2.34–13.36)
Appendectomy (reference group)	1.00	1.00	1.00
Gender			
Male	2.33 (1.61–3.37)	2.49 (1.67–3.70)	2.01 (0.85–4.75)
Female (reference group)	1.00	1.00	1.00
Age (years)			
18–29 (reference group)	1.00	1.00	1.00
30–44	1.69 (1.04–2.77)	1.55 (0.93–2.58)	3.34 (0.74–15.15)
Hypertension			
Yes	3.56 (1.12–11.38)	2.11 (0.46–9.74)	6.84 (1.27–36.69)
No (reference group)	1.00	1.00	1.00
Diabetes			
Yes	1.89 (0.62–5.79)	2.57 (0.84–7.84)	1.37 (0.15–12.55)
No (reference group)	1.00	1.00	1.00
Monthly income			
0 (reference group)	1.00	1.00	1.00
NT$1–15,840	3.93 (1.62–9.56)	3.79 (1.15)	1.66 (0.78–15.78)
NT$15,841–25,000	4.25 (1.78–10.18)	3.57 (1.47–8.65)	4.24 (0.52–34.68)
≥NT$25,001	2.32 (0.89–6.04)	2.27 (0.86–5.96)	1.05 (0.09–12.79)

on a representative national sample of adults aged 18–44. We found that after adjusting for other factors, the hazard of dying from natural causes or suicide during the five-year follow-up period was 1.72 times greater for depressed patients than for appendectomy patients. Depressed patients were more likely to die by suicide; no significant difference in the hazard of dying from natural causes was observed between the two cohorts.

Prior studies have proposed a variety of explanations for the association between depression and increased risk of mortality. Ösby et al. (2001) compared excess mortality between patients with bipolar and unipolar disorders using a population-based sample and found that the standardized mortality ratios for suicide were higher in subjects with unipolar disorder compared to their bipolar counterparts. Wulsin et al. (1999) proposed that patients with depression have a higher likelihood of death for the following reasons: poor self-care during medical illness, increased smoking and consumption of alcohol and suicidal behavior. Our study found no difference in the rate of death from natural causes between depressed and non-depressed patients, suggesting that poor self-care may *not* be one of the contributing causes to the higher mortality for depressed patients. However, it is possible that our findings do not support this aspect of Wulsin et al.'s hypothesis because of greater acceptance of dependence in Taiwan's culture as compared with western societies; in other words, different patterns of family support for sick family members could conceivably counter the effects of poor self-care during medical illness. However, our study does confirm higher rates of death by suicide for depressed younger adult patients.

Our analysis revealed that patients with depression had a greater likelihood of dying of unnatural, rather than natural causes, during the follow-up period. Little evidence exists to compare the likelihood between dying of unnatural or natural causes for depressed younger patients. Many studies only report rates of suicide as a percentage of deaths among depressed patients. For example, Wulsin et al. (1999) reviewed the mortality associated with depression and found that rates of suicide among the depressed people ranged from 0% to 64%, with a mean of 10.8%. Among the studies that used psychiatric samples, suicide rates ranged from 0%–64% with a mean of 16%. When taking study design into account, data from better studies (indicated by stronger evidence)

showed suicide rates ranged from 0 to 31% with a mean of 7.3%. One recent study (Schneider et al., 2001) found that rate of unnatural death was relatively high for patients with recurrent major depressive episodes (SMR, 46.7) compared with other subtypes of affective disorders from a sample of psychiatric inpatients aged 18–80. Our study found that the rate of suicide among depressed patients was 1.93% and the hazard of dying from suicide during the five-year follow-up period was 5.59 times greater for depressed patients than for appendectomy patients. The lower rate of suicide among the depressed compared to other studies might be due to our relatively homogeneous and nationally representative sample, while other studies used study subjects with a wider range of ages and some of them included all psychiatric inpatients who are a high suicide risk group. Our study has provided a good reference for suicide mortality among younger depressed patients in an Asian country.

Rates of suicide among depressed patients vary greatly according to different study designs, but suggest the occurrence of suicide among depressed patients is common. Social-demographic factors strongly associated with major depressive disorder include gender, marital status, and migration (Barraclough and Pallis, 1975; Roy, 1983). Completed suicide has been linked to psychopathological factors such as anxiety symptoms (Fawcett et al., 1990), psychotic features, delusions of sin, guilt, and hypochondria (Roose et al., 1983; Wolfersdorf, 1987; Schneider et al., 2001), current alcohol or drug abuse/dependence, cluster B personality disorders, and higher levels of impulsivity and aggression (Dumais et al., 2005). Some studies have found completed suicide to be associated with a previous history of suicide attempts (Diekstra, 1989; Fawcett et al., 1987; Suominen et al., 2004), feelings of hopelessness (Beck et al., 1990, 1985), and discharge from psychiatric care (Goldacre et al., 1993). More specifically, Dumais et al. (2005) found that risk factors known to be associated with suicide completion for depressed men (namely, alcohol and drug abuse/dependence and cluster B personality disorders) were more common among men aged 18–40. When comparing younger men (18–44), older men (45–75), younger women (18–44) and older women (45–75), younger men are the segment of the population most at risk of completing suicide (not shown in the tables) and therefore more attention should be paid to warning signs and contributing causes of suicide in this group.

Reasons for the high prevalence of depression and suicide among younger males in Taiwan may be due to multiple stressors experienced by this age group. According to Chuang and Huang (2007) Taiwan has experienced substantial changes economically, socially and environmentally during the past ten years. For example, a Richter scale 7.3 earthquake on Sep. 21, 1999 occurred, causing 2400 deaths and 11,000 injuries as well as property damage estimated to cost US$10 billion (Chuang and Huang, 2007). On the other hand, the unemployment rate in Taiwan had been lower than 2% for many years up to 1995, but then began increasing steadily, rising from 2.6% in 1996 to 5.2% in 2002. Chuang and Huang found that the earthquake and the unemployment rate significantly influenced the male suicide rate. In a sample of 150 people who committed suicide aged 15–59 years in Hong Kong, Chen et al. (2006) found that unemployment significantly impacted young people aged 20–24 years. A study conducted in Japan has also found that low income and unemployment significantly contributed to the suicide mortality rate among middle-aged men (Yamasaki et al., 2005). Relative poverty has a negative effect on life expectancy independent of absolute poverty levels; future research might focus on how lowered expectations or perceived changes in status relating to economic opportunity may affect particular subgroups of a population in ways reflected in the rate of depression and suicide. Further studies should be conducted to investigate the underlying determinants of suicide among younger males in Taiwan. Furthermore, strategies for suicide prevention in Taiwan might take specific age, gender and life stage patterns into account.

One advantage of this study estimating the risk of mortality for depressed patients is that it is based on a nationally representative sample of younger adults, so selection biases can be ruled out. Moreover, we used two comprehensive nationwide databases, allowing us to trace the medical history of every sampled patient. However three important caveats must be mentioned; the datasets do not provide information on the following possible risk factors for mortality: tobacco, alcohol or drug use, cluster B personality disorders or body mass index. Furthermore, our study used appendectomy patients as a proxy for the general population. Although our prior research has demonstrated no significant difference between appendectomy patients and the general population in terms of gender and age, there may be other differences between these two groups. Finally, although the “cause of death” data file is considered to be very accurate and comprehensive, the accuracy of the individual physicians is beyond this study’s control and could cause error.

In conclusion, this is the first study to specifically assess mortality risk from suicide for depressed younger adults. We found that after adjusting for other factors, depressed patients were more likely to die of suicide than non-depressed patients, while no significant difference in the hazard of dying from natural causes was observed between the two cohorts. Further studies should be initiated to identify specific risk factors for suicide among younger adults, while prevention strategies might focus on stresses associated with particular life stages in order to more effectively target high risk groups for intervention. One unique advantage of this study is that it estimates the risk of mortality for younger depressed patients on the basis of nationally representative data.

Role of funding source
Nothing declared.

Conflict of interest
No conflict declared.

Acknowledgements

This study is based in part on data from the *National Health Insurance Research Database* provided by the Bureau of National Health Insurance, Department of Health and managed by the National Health Research Institutes, Taiwan. The interpretations and conclusions contained herein do not represent those of the Bureau of National Health Insurance, Department of Health, or the National Health Research Institutes.

Appendix A

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Table 4
Description and criteria of the seven levels of urbanization in Taiwan

Criteria / Level	Population density (people/km^2)	Proportion of people with college educational levels or above (%)	Proportion of people over age 65 (%)	Proportion of agricultural workers (%)	Number of physicians per 100,000 people
1 (most urbanized)	1	1	5	7	1
2	2	2	6	6	2
3	3	3	7	5	4
4	4	4	3	4	3
5	6	5	1	2	7
6	7	7	2	1	5
7 (last urbanized)	5	6	4	3	6

This table was modified from a study by Lin et al. For each category, 1 represents the greatest and 7 represents the least.

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