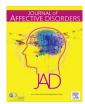
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#### Research paper

## Suicide in males and females with cardiovascular disease and comorbid depression



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#### ABSTRACT

Background: Myocardial infarction (MI) has been associated with an increased risk of suicide, further increased among individuals with a comorbid psychiatric illness. A paucity of studies have examined details of suicide among individuals with cardiovascular disease (CVD) and comorbid depression. We aimed to compare demographic, clinical and suicide-specific characteristics between suicide victims with CVD with depression (CVD+D) and without comorbid depression (CVD-D).

Methods: Coroner data on suicide decedents with CVD (n=413) occurring in Toronto, Canada from 1998 to 2012 were collected. Characteristics were compared between the CVD+D and CVD-D groups. Regression analysis examined for gender differences in these groups.

Results: CVD+D subjects compared to CVD-D were more likely to have had a past suicide attempt (p=0.008), and to have experienced a bereavement (p=0.008) or financial stressor (p=0.005) in the past year. Each of these variables remained significantly associated with the presence of depression after the regression analysis. Within the CVD+D group, females were more likely to die from suicide by self-poisoning (p<0.0001) and males by shooting (p=0.001).

*Limitations:* Psychological autopsies were not available. The definition of CVD was broad and the accuracy of its diagnosis could not be confirmed.

Conclusion: Individuals with CVD+D who died from suicide had significant differences in clinical characteristics and specific stressors compared to those without depression. These data may help to better characterize suicide risk and prevention in this vulnerable population.

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#### 1. Introduction

Suicide and CVD accounted for 1.4% (WHO, 2014) and 31.2% (WHO, 2015) of all deaths worldwide in 2012, making it the 1st and 15th leading cause of death respectively. In Canada, suicide

Abbreviations: CVD, Cardiovascular Disease; CAD, Coronary Artery Disease; CHD, Coronary Heart Disease; CVD+D, CVD and Depression; CVD-D, CVD without Depression; HF, Heart Failure; MI, Myocardial Infarction; OCC, Office of the Chief Coroner; RR, Rate Ratio; SD, Standard Deviation

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and diseases of the heart including, hypertensive heart disease, ischemic heart disease, and heart failure (HF) were the 9th and 2nd most common causes of death in 2011 (Canada, 2009).

Medical illness is an important contributor to suicide risk, being a significant factor in about 50% of suicides in people older than 50 (Hendin, 1999). Juurlink et al. (2004) found that people 66 or older with multiple medical illnesses had an increased risk of suicide compared to a control group having no identified illness. Furthermore, many studies have shown that patients with cancer, diabetes mellitus, stroke and neurological conditions among other chronic illnesses have an increased risk of suicide (Christensen et al., 2007; Harris and Barraclough, 1994; Hawton and van Heeringen, 2009; Hietanen and Lonnqvist, 1991; Kyvik et al., 1994). Other recognized factors that could contribute to suicide risk include substance use (Schneider, 2009; Wilcox et al., 2004) and

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hopelessness (Beck et al., 1990; Beevers and Miller, 2004; Minkoff et al., 1973; Nimeus et al., 1997). Furthermore, the CVD literature suggests that individuals with heart disease have a higher prevalence of psychological distress compared to those without heart disease (Ferketich and Binkley, 2005).

MI is a major medical and life event that comes with a substantial risk for depression. Following an acute MI, 16-27% of patients experience major depression (Carney et al., 1997; Rudisch and Nemeroff, 2003; Thombs et al., 2006; Zellweger et al., 2004); and up to 87% have at least sub-syndromal symptoms of depression (Moller-Leimkuhler, 2007). The risk of depression post-MI has been shown to be higher in women (Drory et al., 2003; Frasure-Smith et al., 1999; Mallik et al., 2006). It is well recognized that depression is more common in women compared to men (Weissman et al., 1993; Marcus et al., 2008). However, depression as well as the association between depression and CVD in men may be underestimated. Men may present with externalizing symptoms including irritability, aggressiveness, and alcohol misuse masking depression (Innamorati et al., 2011; Moller-Leimkuhler, 2007). On the other hand, multiple studies have found that externalizing features of depression do not differentiate depression between men and women (Innamorati et al., 2011; Moller-Leimkuhler et al., 2004). However, externalizing symptoms may help differentiate individuals at higher risk of self-inflicted aggressive behaviors (Innamorati et al., 2011). Depression is also common in individuals with HF and stroke, with rates ranging from 13% to 77.5% (Moudgil and Haddad, 2013) and 6-79%, respectively (Lokk and Delbari, 2010). Depression can have negative effects on adherence and completion in cardiac rehabilitation in individuals with coronary artery disease (Swardfager et al., 2011). In addition, depression increases the risk of suicide in individuals with history of stroke (Pompili et al., 2012).

Several studies have examined the interaction between CVD and suicidal ideation and/or attempts. Shemesh et al. (2009) demonstrated that suicidal ideation was present in 12% of patients with coronary artery disease (CAD) and HF in an outpatient Cardiology clinic. Furthermore, depression seems to be the key mediator of suicidal ideation in individuals with CVD although this finding has not been consistent in all studies. Kishi et al. (2001) found that suicidal ideation among patients with CVD occurred mostly among patients with major depression and sometimes in those with minor depression while another study found that suicidal ideation and attempts remained statistically significant in individuals with heart disease or heart attack after adjusting for mental disorders (Scott et al., 2010).

Recent evidence shows that patients with MI have a higher risk of suicide independent of stroke, diabetes mellitus, socioeconomic factors, or psychiatric illness. Larsen et al., found that 4.3% of individuals that died by suicide had a history of MI and the adjusted incidence rate ratio (RR) for suicide death was 1.24 (95% CI, 1.14–1.35) for those with MI compared to those without MI. The study found that MI was associated with increased suicide risk in both those with and without a history of psychiatric illness, although more strongly for the former (adjusted rate ratio 64.05 vs. 3.25). The suicide risk was higher among individuals with a mood disorder and, in this group, was strongest for the year following the MI (RR=32.13, CI, 10.20–101.23) (Larsen et al., 2010). On the other hand, Pompili et al. (2007) found individuals with coronary heart disease (CHD) without previous psychopathology not to have an increased suicide risk.

Of note, while Larsen et al., found the risk of suicide in CVD to be similar between men and women (RR, 1.24 vs. 1.32, respectively), a large case control study in English primary care patients found a 2-fold increased risk of suicide in women with CAD compared to men, independent of depression (Webb et al., 2012). Overall, there are limited data describing the relationship between

sex, CVD, comorbid depression, and details of the suicide.

This study seeks to compare demographic, personal and suicide-specific characteristics of suicide victims with CVD with comorbid depression (CVD+D) and without comorbid depression (CVD-D) in order to understand what factors may distinguish these two groups. We also aim to identify any sex differences between these groups.

#### 2. Method

#### 2.1. Study design

The Office of the Chief Coroner (OCC) of Ontario granted us access to its records for the purposes of this research. Data were collected from the OCC charts for all deaths occurring in the city of Toronto from 1998 to 2012, inclusive, that were ruled as suicides.

Each chart contained a coroner's investigation report and a pathology report as part of the determination of the cause of death and the particulars of the death. Additional information was collected by the OCC from transcripts of interviews with family members, acquaintances, and physicians; letters from family members; police reports; hospital records; and copies of suicide notes when available. This methodology is well established in previous similar studies and is distinct from psychological autopsies. Sociodemographic and clinical data, as well as suicide relevant details were present in > 99% of coroner's records. Specific data extracted from the charts included, (i) Demographics: age, sex, marital status and living circumstances (living with others or alone); (ii) Clinical variables: the presence of cardiovascular disease (any mention of heart attack (history of or recent event), 'heart condition', or more specifically if cardiovascular disease, atherosclerosis, or congenital heart condition were noted), depression (as indicated by a prior history and/or treatment of depression, or any collateral (family/friend/other) statement indicating that the decedent appeared to be 'depressed' in the days leading up to their death), substance abuse history (including alcohol, drugs, or both), known past suicide attempts, contact with psychiatric or emergency services in the week prior to death; (iii) Recent stressors for the previous year to the suicide: employment/financial, interpersonal stressor (conflict or relationship breakup), medical/ health, police/legal, bereavement; (iv) Details of suicide: method (hanging, other asphyxia, drowning/hypothermia, self-poisoning, jump/fall from height or subway/train/motor vehicle collision, cutting/stabbing, or shooting) location of death and presence of a suicide note.

#### 3. Statistical analysis

Univariate and multivariate analyses comparing the CVD+D and CVD-D suicide groups were conducted on demographic, clinical, stressor, and suicide-specific variables described above. We used t-tests for continuous variables, and chi-square tests for categorical variables at a threshold for significance of 0.05. Multivariate regression was completed for all significant differences between CVD+D and CVD-D groups, with the gender variable entered a priori. All analytical analyses were performed using INM SPSS Statistics 23 (SPSS Inc, Chicago, IL.)

#### 4. Results

Of the 3317 suicide deaths in the city of Toronto from 1998 to 2012, CVD was recorded in 12.4% (413/3317) and of those 69.7% were male. Depression was recorded as comorbid in 59.8% (247/

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