Clinical Depression
ISSN: 2572-0791

Pelletier et al., Clin Depress 2017, 3:3
DOI: 10.4172/2572-0791.1000127

Research Article Open Access

Sex Differences in Depression Treatment and Impact on Outcomes Following Premature Acute Coronary Syndrome

Roxanne Pelletier[1], Blaine Ditto[2], Kim L Lavoie[3], Igor Karp[4], Simon L Bacon[5], Jafna L Cox[6], Mark J Eisenberg[7], Stella S Daskalopoulou[8], Nadia A Khan[9], Karin H Humphries[10], Hassan Behlouli[11] and Louise Pilote[1,8*]

[1]*Division of Clinical Epidemiology, The Research Institute of the McGill University Health Centre, Montreal, Quebec, Canada*
[2]*Department of Psychology, McGill University, Montreal, Canada*
[3]*Department of Psychology, University of Quebec in Montreal, Montreal, Quebec, Canada*
[4]*Department of Epidemiology and Biostatistics, Schulich School of Medicine and Dentistry, University of Western Ontario, London, Ontario, Canada*
[5]*Department of Exercise Science, Concordia University, Montreal, Quebec, Canada*
[6]*Department of Medicine and Department of Community Health and Epidemiology, Division of Cardiology, Dalhousie University, Halifax, Nova Scotia, Canada*
[7]*Department of Medicine, Divisions of Cardiology and Clinical Epidemiology, McGill University Health Centre, Montreal, Quebec, Canada*
[8]*Department of Medicine, Division of General Internal Medicine, McGill University, McGill University Health Centre, Montreal, Quebec, Canada*
[9]*Department of Medicine, Center for Health Evaluation and Outcomes Science, University of British Columbia, Vancouver, British Columbia, Canada*
[10]*Division of Cardiology, University of British Columbia, Vancouver, British Columbia, Canada*
[11]*Division of Clinical Epidemiology, McGill University Health Centre, Montreal, Quebec, Canada*

Abstract

Aims: Access to anti-depressants, and prognosis in younger depressed men and women with acute coronary syndrome (ACS) requires further investigation. We assessed the prevalence of depression, antidepressant prescription, and the association of depression with major adverse cardiovascular events (MACE) in men and women with premature ACS.

Methods and results: 1071 ACS men and women (≤ 55 years) were recruited between January 2009 and April 2013 into GENESIS PRAXY, a multicentre prospective observational cohort study, from 24 hospitals in Canada, one in the US and one in Switzerland. Depression was measured by self-report using the Diagnostic and Statistical Manual of Mental Disorders criteria. Prescription of antidepressants at baseline and 12 months, and MACE over 12 months, were assessed using medical chart review and self-report. Depression was present in 20% of men and 32% of women. Only 1% of men and women with no antidepressants at hospital admission were prescribed antidepressants at hospital discharge. Depressed men were 3 times less likely than depressed women to be prescribed antidepressants. The determinants of antidepressants at 12 months included the presence of cardiovascular risk factors in men, and the presence of depression in women. In sex-specific Cox regressions, depressed men had a 2.57 times greater risk of MACE compared with non-depressed men (95% CI: 1.53-4.32), which difference was not seen in women (HR=0.71, 95% CI=0.28-1.81).

Conclusion: Despite a decade of sensitization, depression still needs to be better treated after ACS, especially in young men, given that depression is a potent risk factor for adverse outcomes.

Keywords: Acute coronary syndrome; Depression; Treatment disparities; Sex-specific

Introduction

Depression is the most commonly diagnosed psychiatric disorder among patients with acute coronary syndrome (ACS), with over 20% of ACS patients meeting the Diagnostic and Statistical Manual of Mental Disorders (DSM) criteria for major depression, and over 40% reporting depressive symptoms [1-4]. Recognition of the adverse role of depression on prognosis in ACS patients, as well as availability of low cardiac toxicity antidepressants medications such as selective serotonin reuptake inhibitors (SSRIs), highlights the importance of screening and treating depression in ACS patients [5-7].

However, whether depression is treated in patients with premature acute coronary syndrome (ACS) is unknown. The rate of hospitalization for ACS has actually increased in adults 20-55 years of age since 2009, thus this specific population of young to middle-aged men and women are an important group to assess. The active lifestyle of this population and the relatively greater number of years in their life that will be lived with a chronic disease make these younger patients particularly vulnerable to the adverse effects of depression following ACS. Furthermore, because sex differences have been reported with regard to the prevalence of depression, as well as with access to care and outcomes in patients with premature ACS, an evaluation of sex differences in the association between depression and ACS is required [8-13].

In this study, we assessed: (1) The prevalence of depression in men and women hospitalized for premature ACS; (2) The prevalence and determinants of antidepressants prescriptions in men and women; and (3) The association between baseline depression and adverse cardiovascular outcomes over 12 months post-ACS, as well as sex differences in this association.

***Corresponding author:** Louise Pilote, Division of Clinical Epidemiology, Research Institute of McGill University Health Centre, 5252 Boulevard de Maisonneuve O. Office 2B.39, Montreal, Quebec, H4A 3S5, Canada, Tel: (514)-934-1934 ext 44722; E-mail: louise.pilote@mcgill.ca

Received: November 29, 2017; **Accepted:** December 05, 2017; **Published:** December 13, 2017

Citation: Pelletier R, Ditto B, Lavoie KL, Karp I, Bacon SL, et al. (2017) Sex Differences in Depression Treatment and Impact on Outcomes Following Premature Acute Coronary Syndrome. Clin Depress 3: 127. doi:10.4172/2572-0791.1000127

Methods

Study design

GENESIS-PRAXY (GENdEr and Sex determInantS of cardiovascular disease: from bench to beyond - Premature Acute Coronary SYndrome) is a prospective observational cohort study including 24 participating centres across Canada, one in the United States and one in Switzerland. Men and women aged ≤ 55 years hospitalized for ACS between January 2009 and April 2013 was enrolled in the study. Detailed methods of the GENESIS-PRAXY study have been described previously [14]. The reporting of the present analyses follows the STROBE guidelines for observational studies [15].

Ethical considerations

Institutional ethics approval has been obtained from all participating centres, and written informed consent was obtained for each study participant.

Study population and data sources

Patients who were eligible to participate in the study were 18-55 years of age, presenting with ACS to one of the 26 recruiting centres, fluent in English and/or French, and able to provide informed consent. A research nurse approached eligible patients in the Coronary Care Unit at the earliest possible time after their admission. A total of 1213 patients were enrolled in GENESIS-PRAXY and, for the present study, 1071 patients with complete baseline and follow-up data were included (Appendix A).

At baseline, each participant completed a self-administered questionnaire on their demographic, psychosocial, and medical characteristics, and the research nurse collected anthropometric measurements. Medical chart reviews were carried out by the research nurse to collect participants' medical history, medication prescriptions, and current ACS characteristics.

One year following the index ACS, surviving patients were asked to complete a second self-report questionnaire (similar to the baseline questionnaire), and the research nurse conducted a phone interview and reviews of medical charts.

Assessment of depression

We assessed the presence of major depression symptoms using the DSM-IV criteria [3]. Specifically, as part of the self-reported questionnaire completed at baseline and 12 months, participants answered nine questions addressing DSM-IV criteria for major depression. Depression was identified when patients answered "yes" to at least five of the nine questions, with one of the reported symptoms being either loss of interest in daily activities, or feeling blue, sad, or depressed most days of the week for two consecutive weeks [3].

Outcome measures

The study outcomes were antidepressant prescription at hospital discharge and over the 12 months following discharge, as well as major adverse cardiovascular events (MACE: non-fatal recurrent ACS, cardiovascular death, percutaneous intervention, or coronary artery bypass graft, whichever happened first) over 12 months. Antidepressants prescription at hospital discharge was determined using medical chart review, while prescription over 12 months was determined using a combination of self-report and medical chart review data. MACE over 12 months was determined by a phone interview with patients (or relatives in cases of death), and a medical chart review was conducted for all surviving patients to confirm or complement data obtained through the interview.

Statistical analysis

Distribution of baseline demographic, psychosocial and medical characteristics, were compared between men and women with and without depression at baseline using *t* tests and χ^2 tests. Frequencies of antidepressants prescription and 12 months depression were further compared between men and women with and without depression at baseline. Patients' baseline demographic, psychosocial and medical characteristics were then compared a second time, but between men and women with and without antidepressant prescriptions at 12 months.

To estimate the association between baseline depression and the occurrence of MACE over 12 months, multivariable Cox proportional hazards regressions were estimated, including sex, age and ethnicity as covariates. An interaction term between depression and sex was further added in a second model. We did not initially include traditional cardiovascular risk factors as covariates in any of the models, as we consider these variables to be in the causal pathway of the association between depression and MACE. However, we conducted a sensitivity analysis including these risk factors, in order to assess whether this addition would modify the association between depression and MACE. Patients with missing data were excluded from the analyses.

All statistical analyses were performed using SAS version 9.2. Statistical tests were 2-sided; p≤.05 was considered statistically significant.

Results

Baseline characteristics

Our sample included 738 men and 333 women with a mean age of 48 years (SD=6 years). In our cohort, 20% of men and 32% of women had depression at baseline. Overall, there were more differences between men than between women with and without depression. For example, depressed men were less likely to be married and to have post-secondary education, and more likely to report poor health behaviors (i.e., smoking, increased alcohol and coffee intake, cocaine and other recreational drugs utilization) than non-depressed men; these differences were not observed between depressed and non-depressed women (Table 1).

Sex differences in antidepressant prescriptions

Among both patients with and without depression at baseline, men were less likely than women to have been prescribed antidepressants before hospital admission (10% and 6% in men with and without depression, vs. 27% and 16% in women with and without depression). Among depressed patients not on antidepressants on arrival, a new prescription for antidepressants was given to only 1% of both men and women at discharge.

Among depressed patients with no antidepressant prescriptions at hospital discharge, men were almost 3 times less likely than women (5% vs. 14%) to be prescribed antidepressants over the following 12 months, irrespective of depression at baseline (Table 2).

Sex differences in depression at 12 months

Among patients with depression at baseline, and equivalent proportion of men and women were still reporting depression at 12 months. Differently, among patients with no depression at baseline,

	Women			Men		
n (%)	**Depression n=107**	**No Depression n=226**	**p**	**Depression n=146**	**No Depression n=592**	**p**
Demographic						
Age, mean (SD)	49 (6)	48 (6)	0.72	48 (6)	48 (6)	0.68
Caucasian	105 (88)	219 (89)	0.82	140 (89)	521 (86)	0.39
Married or common law	72 (61)	158 (64)	0.50	98 (62)	430 (71)	0.03
No post-secondary education	56 (47)	107 (44)	0.52	67 (42)	195 (32)	0.02
Risk factors						
Diabetes	41 (34)	44 (18)	<0.001	30 (19)	79 (13)	0.06
Dyslipidemia	78 (66)	118 (48)	0.001	96 (61)	335 (55)	0.22
Family history of CVD	36 (30)	65 (26)	0.44	42 (27)	109 (18)	0.02
Hypertension	72 (61)	127 (52)	0.11	88 (56)	260 (53)	<0.01
Obesity (BMI≥ 30 kg/m2)	62 (52)	94 (38)	0.01	64 (41)	237 (39)	0.75
Poor health behaviors						
Smoking	54 (45)	104 (42)	0.58	82 (52)	212 (35)	<0.0001
Alcohol (≥2 /day)	28 (24)	54 (22)	0.73	74 (47)	232 (38)	0.04
Coffee (≥2 /day)	50 (42)	94 (38)	0.49	77 (49)	248 (40)	0.05
Cocaine use (ever)	21 (18)	21 (9)	0.01	38 (24)	85 (14)	<0.01
Recreational drugs use (ever)	48 (40)	86 (35)	0.32	80 (51)	229 (38)	<0.01
Disease severity markers						
GRACE score, mean (SD)	72 (18)	71 (17)	0.88	70 (17)	71 (16)	0.51
STEMI	50 (42)	126 (51)	0.10	82 (52)	398 (66)	0.001
NSTEMI	51 (43)	89 (36)	0.22	60 (38)	166 (27)	0.01
Unstable angina	17 (14)	24 (10)	0.20	10 (6)	32 (5)	0.61

Abbreviations: CABG, coronary artery bypass graft; PCI, percutaneous coronary intervention; STEMI, ST-elevation MACE, major adverse cardiovascular event; SD, standard deviation; CVD, cardiovascular disease; BMI, body mass index, kg, kilogram; m, meter; vWF-AG, vonWillebrand factor antigen; PAI-1, plasminogen activator inhibitor-1; hs-CRP, high-sensitivity C-Reactive Protein; mg, milligram; L, liter; nmol, nanomol; STEMI, ST-elevation myocardial infarction; NSTEMI, non-ST-elevation myocardial infarction

Table 1: Patients' baseline characteristics according to sex and major depression symptoms status.

	Depression			No Depression		
n (%)	**Men n=146**	**Women n=107**	**p**	**Men n=592**	**Women n=226**	**p**
Antidepressant before admission	14 (10)	29 (27)	0.0002	33 (6)	36 (16)	<0.0001
Antidepressant at discharge	15 (10)	27 (25)	0.0016	25 (4)	25 (11)	0.0003
Among patients with no antidepressant at admission	2 (2)	1 (1)	0.89	4 (1)	2 (1)	0.65
Antidepressant over 12 months*	9/87 (10)	24/70 (34)	0.0003	31/414 (7)	24/162 (15)	0.007
Among patients with no antidepressant at baseline*	4/77 (5)	7/49 (14)	0.08	17/394 (4)	15/139 (11)	0.005
Major depression at 12 months*	39/87 (45)	36/70 (51)	0.41	48/414 (12)	37/162 (23)	0.0006

Abbreviation: ACS, acute coronary syndrome
*Includes patients with self-report questionnaire data available at 12 months

Table 2: Antidepressant prescriptions at baseline and 12 months.

men were less likely than women to have developed depression at 12 months (Table 2).

Determinants of 12 months antidepressant prescriptions in men and women

Men who received a new prescription of antidepressants during the 12 months following discharge were more likely to be unemployed, have a low household income, have hypertension, and be obese than men who were not prescribed antidepressants over 12 months. Women who were prescribed antidepressants over 12 months were more likely to be unemployed, have a low level of education, and have depression than women with no antidepressant prescriptions over the 12 months following hospital discharge (Table 3).

Sex differences in the association between depression and MACE

Multivariable analyses adjusted for sex, age, and ethnicity revealed that depression was associated with a 1.67-fold increased risk of MACE over 12 months (95% Confidence Interval [CI]=1.07-2.64). The inclusion of traditional CVD risk factors (i.e., hypertension, diabetes, dyslipidemia, obesity, and smoking) as covariates did not modify the association between depression and MACE.

The addition of an interaction term between sex and depression in the model yielded a statistically significant interaction (p for interaction 0.01). Specifically, 16% vs. 6% of the men with and without depression had sustained a MACE over 12 months (p<0.001), compared to 6% vs.

n (%)	Women			Men		
	Antidepressants	No Antidepressants	p	Antidepressants	No Antidepressants	p
Demographics						
Age, mean (SD)	49 (4.1)	48 (5.6)	0.39	47 (6.2)	48 (6.1)	0.57
Caucasian	40 (83.3)	169 (91.8)	0.08	36 (90.0)	385 (83.5)	0.28
Married or common Law	30 (62.5)	118 (64.1)	0.83	29 (72.5)	337 (73.1)	0.93
Risk factors						
Diabetes	8 (16.7)	41 (22.3)	0.39	7 (17.5)	48 (10.4)	0.16
Dyslipidemia	26 (54.2)	95 (51.6)	0.75	24 (60.0)	262 (56.8)	0.69
Family history of CVD	15 (31.3)	44 (23.9)	0.29	8 (20.0)	91 (19.7)	0.96
Hypertension	28 (58.3)	101 (54.9)	0.66	24 (60.0)	199 (43.2)	0.04
Obesity (BMI ≥ 30 kg/m^2)	22 (45.8)	66 (35.9)	0.2	24 (60.0)	162 (35.1)	0.002
No post-secondary education	29 (60.4)	76 (41.3)	0.02	13 (32.5)	144 (31.2)	0.86
Low household income (<$50,000)	19 (45.2)	71 (45.8)	0.94	16 (44.4)	89 (23.4)	0.005
Poor Health Behaviors						
Current smoking	18 (37.5)	79 (42.9)	0.49	13 (32.5)	153 (33.2)	0.92
Ever smoked	17 (35.4)	82 (44.6)	0.25	13 (32.5)	181 (39.3)	0.39
Cocaine use	8 (16.7)	16 (8.7)	0.1	3 (7.5)	63 (13.6)	0.26
Alcohol (≥ 2 /day)	18 (37.5)	39 (21.2)	0.02	12 (30.0)	187 (40.6)	0.19
Recreational drugs	16 (34.8)	62 (36.3)	0.85	18 (51.4)	170 (40.2)	0.19
Coffee (≥ 2 /day)	21 (43.7)	67 (36.4)	0.35	10 (25.0)	188 (40.8)	0.05
Disease severity markers						
STEMI vs. NSTEMI/UA	19 (39.6)	88 (48.4)	0.27	23 (57.5)	283 (61.6)	0.6
GRACE score (SD)	74.9 (18.2)	70.4 (17.6)	0.12	65.4 (16.7)	70.5 (16.5)	0.06

Table 3: Patients' baseline characteristics according to sex and antidepressants prescription at 12 months.

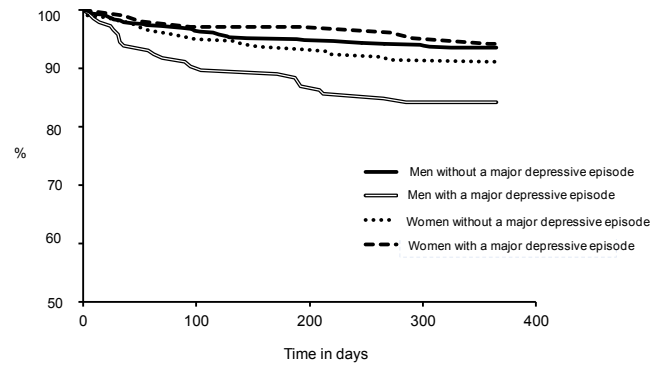

Figure 1: Proportions of patients free of MACE at 12 months according to sex and major depression symptoms status.

9% of the women with and without depression (p=0.30). Additional subgroup Cox regression analyses provided further evidence that depression were associated with MACE in men (adjusted Hazard Ratio [HR]=2.57, 95% CI=1.53-4.32) but that in women, the association was not statistically significant (adjusted HR=0.71, 95% CI=0.28-1.81) (Figure 1).

Discussion

We observed that one in four patients hospitalized with premature ACS reported symptoms consistent with a diagnosis of major depression, with men being less likely than women to report such symptoms. We also observed that depressed men at baseline were 3 times less likely than depressed women to be prescribed antidepressants over the following 12 months, despite the fact that an equivalent proportion of men and women remained depressed at 12 months. Yet, depression conferred an increased risk of MACE to men, while the association in women was not statistically significant.

The proportion of patients with depression in our sample is consistent with previous studies of patients with myocardial infarction (MI), which ranges between 20-25% [2,3]. Studies of sex differences in the association between depression and ACS are scarce and as such, the comparison of our results with previous literature is limited. In a study by Frasure-Smith et al. 5% of men and 27% of women with ACS reported symptoms of major depression assessed using a structured interview, while 25% of men and 35% of women had elevated depressive symptoms assessed using a self-report questionnaire [16]. However, it is noteworthy that our study population is younger than participants from Frasure-Smith's study and as such, the high prevalence of major depression symptoms in young to middle-age ACS patients should be highlighted.

It is noteworthy that only 1% of men and women with depression and no antidepressants at hospital arrival were prescribed antidepressants at discharge. This result is alarming and suggests that depression is not addressed in these younger adults with ACS. What we observed is consistent with previously published results, which indicated that depressed post-MI patients were consistently less likely than depressed non-MI subjects to receive an antidepressant between 1993 and 2002 [17]. Unfortunately, our data suggests that a decade later, much work still remains to be done in order to improve the care ACS patients with depression receive.

Several reasons may explain why depression is not addressed post-ACS; the belief that depression is "normal" and constitutes an aspect of coping with heart disease; the difficulty of distinguishing between symptoms of heart disease and depression; and patients' reluctance in reporting symptoms and taking antidepressants [9]. Most of these reasons have been previously discussed by other researchers in attempts to sensitize the medical personnel about the importance of screening and treating depression in ACS patients. For example, medical personnel can refer to a review by Lespérance and Frasure-Smith to learn about tools to screen for depression in ACS patients, as well as how to distinguish between ACS and depressive symptoms [9]. Depression is a psychiatric disease that deserves its own treatment, at the least to relieve patients' distress and improve daily functioning, irrespective of heart disease treatment [18-20].

Results of randomized control trials (RCTs) assessing whether depression treatment also improves medical outcomes in patients with heart disease and depression have been controversial. Although randomization of patients to treatment versus usual care is generally not associated with a difference in medical outcomes, in the MIND IT (Multiple INterventions in type 2 Diabetes. Italy), ENRICHD (ENhancing Recovery in Coronary Heart Disease), and SADHART (Sertraline AntiDepressant Heart Attack Trial) trials, short-term improvement in depression was associated with longer-term reduction in later adverse medical outcomes, regardless of treatment arm [6,21-27]. These results therefore suggest that a treatment with antidepressants that leads to reducing depression symptoms in ACS patients is likely to improve their daily functioning as well as their medical prognosis. Thus, efforts must be made in order to improve antidepressants prescription practices in patients with premature ACS.

Similar to baseline results, the rate of antidepressants prescription over the 12 months following ACS was very low among men and women with depression at baseline. Indeed, 90% of men and 66% of women with depression at baseline remained untreated in the following 12 months. We cannot be sure whether this is inappropriate or not, given that we do not have data on the evolution of depressive symptoms from baseline to 12 months. Nonetheless, half of both men and women with depression at baseline were still meeting the criteria for major depression at 12 months, suggesting that a considerable proportion of depressed patients at 12 months, especially men, remained untreated. We further observed that both sexes with lower SES were more likely to receive prescriptions for antidepressants, which may be appropriate given the association between low SES and depression. More concerning was that depression was associated with prescription in women but not in men, while CVD risk factors were associated with prescription in men but not in women. These results may suggest that depression is more often screened for in women, which may influence antidepressants prescription in women. Differently, in men, a worse medical condition may more often be relied upon to decide whether an antidepressant should be prescribed, irrespective of depression which may remain unassessed. Overall, these results suggest that awareness with regards to screening and treating depression in men after premature ACS must be increased.

Aside from the physician perspective, it is likely that patients' self-representation of depression influences the reporting of depressive symptoms and as such, prescription of antidepressants. For example, results of a recent review suggest that "[...] *conformity to dominant masculine gender norms ("boys don't cry") leads to self-stigmatization in depressed men who feel that they should be able to cope with their illness without professional help*" [28]. In this same review, it is reported that a genuine connection between depressed men and a health care professional may help these men overcome the inhibitory effect of traditional masculine gender norms on help-seeking for emotional distress. Based on these data, further studies may need to assess whether in-depth depression assessment over multiple meetings with the same health care professional help men disclose depressive symptoms and accept therapy after ACS.

The previous results are of fundamental importance in light of the adverse effects of depression on the risk of MACE in men of our cohort. Indeed, the reason why we observed adverse effects in men only may be due to a lower probability of depressive symptoms disclosure and the tendency in men, especially younger men, to deny depression, which may leave depression untreated more often in men compared to women [29]. Because of the very low rate of antidepressant prescriptions in our cohort, we could not assess whether antidepressants modify the association between depression and MACE. On a different note, it is noteworthy that in the present study, the comparison between men and women with and without depression yielded important differences. Depressed men were less likely to be married and to have post-secondary education, and they were more likely to report poor health behaviors than non-depressed men, which were differences not observed between depressed and non-depressed women. It is possible that depressed men with no antidepressants self-medicated through cigarette smoking and alcohol/drug consumption, which may also help to explain the adverse effect of depression in men. This hypothesis is somewhat supported by the consistent trend we observed in the association between antidepressant prescription and lower levels of poor health behaviors in men but not in women.

Our results differ from previous studies that suggested an adverse effect of depression in women but not in men, or in both women and men, in CVD-free populations. Interestingly, our results are concordant with those of the only other study to our knowledge that has assessed sex differences in the relationship between depression and adverse cardiovascular outcomes in older post-ACS patients [16,30-33]. The fact that our results and those of Frasure-Smith differ from the results of studies conducted in CVD-free populations may suggests that patient's coping style and disease management in the specific context of an ACS influence responses to major depression differently in men and women.

Our study includes some limitations. First, patients who died early after hospital arrival could not be approached and included in the study, which may have introduced a selection bias. Symptoms of depression were self-reported, which method of assessment may not be as sensitive and specific as an interview, and which may have biased the prevalence of depression we observed. However, the rate of depression in men and women of our cohort is representative of what has been reported in previous studies having used a self-reported measure to assess depression in post-ACS patients. Third, the low rate of antidepressants prescription prevented us from conducting multivariate analyses, which limits the interpretation of our findings. Finally, we did not collect data regarding other types of therapy for depression, such as psychotherapy, which also limits the interpretation of our findings.

Conclusion

In conclusion, results of our study suggest that premature ACS men and women with depression do not receive the antidepressants prescription they may require. Furthermore, depression appears to confer a risk for adverse outcomes in men but not women after ACS. Overall, despite a decade of sensitization and the availability of safe and effective medications, depression still needs to be better screened for and treated after ACS, especially in young men.

Funding

This work was supported by the Canadian Institutes of Health Research (CIHR) (200804MOP-190260-GSH-CFAC-40513) and the Heart and Stroke Foundations of Quebec, Nova Scotia, Alberta, Ontario and Yukon and British Columbia, Canada. The study sponsors had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; and preparation, review, or approval of the manuscript. RP is supported by a Canadian Institute of Health Research Award (CFE-113622). KLL is supported by CIHR and Fonds de recherche du Québec– Santé (FRQS) investigator awards. SLB is supported by a FRQS Chercheur-Boursier Senior salary award. JLC holds the inaugural Heart and Stroke Foundation of Nova Scotia Endowed Chair in Cardiovascular Outcomes Research. SSD is a Chercheur-Boursier Clinicien, supported by an FRQS salary award. KHH holds the UBC- Heart and Stroke Foundation Professorship in Women's Cardiovascular Health. LP is supported by a FRQS award. LP holds a James McGill Chair in medicine.

Disclosures

For activities outside the scope of the study reported here, Kim Lavoie has received consultancy and/or presentation fees from Takeda, AbbVie, Boehringer Ingelheim and Merck, and Simon Bacon has received personal fees from Kataka Medical Communication. No other competing interest declared.

References

1. American Psychiatric Association (2000) Diagnostic and statistical manual of mental disorders (4th edn.). APA, Washington, DC.
2. Glassman AH, Shapiro PA (1998) Depression and the course of coronary artery disease. Am J Psychiatry 155: 4-11.
3. Lespérance F, Frasure-Smith N (2000) Depression in patients with cardiac disease: A practical review. J Psychosom Res 48: 379-391.
4. Lauzon C, Beck CA, Huynh T, Dion D, Racine N, et al. (2003) Depression and prognosis following hospital admission because of acute myocardial infarction. Can Med Assoc J 168: 547-552.
5. Nicholson A, Kuper H, Hemingway H (2006) Depression as an aetiologic and prognostic factor in coronary heart disease: A meta-analysis of 6362 events among 146 538 participants in 54 observational studies. Euro Heart J 27: 2763-2774.
6. Glassman AH, O'Connor CM, Califf RM, Swedberg K, Schwartz P, et al. (2002) Sertraline treatment of major depression in patients with acute MI or unstable angina. JAMA 288: 701-709.
7. Lichtman JH, Froelicher ES, Blumenthal JA, Carney RM, Doering LV, et al. (2014) Depression as a risk factor for poor prognosis among patients with acute coronary syndrome: Systematic review and recommendations: A scientific statement from the american heart association. Circulation 129: 1350-1369.
8. Izadnegahdar M, Singer J, Lee MK, Gao M, Thompson CR, et al. (2014) Do younger women fare worse? Sex differences in acute myocardial infarction hospitalization and early mortality rates over ten years. J Women's Health 23: 10-17.
9. American Psychiatric Association (1994) Diagnostic and statistical manual of mental disorders (dsm-iv). American Psychiatric Press, Washington DC.
10. Choi J, Daskalopoulou SS, Thanassoulis G, Karp I, Pelletier R, et al. (2014) Sex- and gender-related risk factor burden in patients with premature acute coronary syndrome. Can J Cardiol 30: 109-117.
11. Jneid H, Fonarow GC, Cannon CP, Hernandez AF, Palacios IF, et al. (2008) Sex differences in medical care and early death after acute myocardial infarction. Circulation 118: 2803-2810.
12. Pancholy SB, Subash Shantha GP, Patel T, Cheskin LJ (2014) Sex differences in short-term and long-term all-cause mortality among patients with st-segment elevation myocardial infarction treated by primary percutaneous intervention. A meta-analysis. JAMA Intern Med 174: 1822-1830.
13. Claassen M, Sybrandy KC, Appelman YE, Asselbergs FW (2012) Gender gap in acute coronary heart disease: Myth or reality? World J Cardiol 4: 36-47.
14. Pilote L, Karp I (2012) Genesis-praxy (gender and sex determinants of cardiovascular disease: From bench to beyond-premature acute coronary syndrome). Am Heart J 163: 741-746.
15. von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, et al. (2007) The strengthening the reporting of observational studies in epidemiology (strobe) statement: Guidelines for reporting observational studies. Ann Intern Med 147: 573-577.
16. Frasure-Smith N, Lespérance F, Irwin MR, Sauvé C, Lespérance J, et al. (2007) Depression, c-reactive protein and two-year major adverse cardiac events in men after acute coronary syndromes. Biol Psychiatry 62: 302-308.
17. Benazon NR, Mamdani MM, Coyne JC (2005) Trends in the prescribing of antidepressants following acute myocardial infarction, 1993-2002. Psychosom Med 67: 916-920.
18. Strik J, Honig A, Lousberg R, Lousberg A, Cheriex E, et al. (2000) Efficacy and safety of fluoxetine in the treatment of patients with major depression after first myocardial infarction: Findings from a double-blind, placebo-controlled trial. Psychosom Med 62: 783-789.
19. Davidson KW, Rieckmann N, Clemow L, Schwartz JE, Shimbo D, et al. (2010) Enhanced depression care for patients with acute coronary syndrome and persistent depressive symptoms: Coronary psychosocial evaluation studies randomized controlled trial. Arch Intern Med 170: 600-608.
20. Lespérance F, Frasure-Smith N, Koszycki D, Laliberté MA, van Zyl LT, et al. (2007) Effects of citalopram and interpersonal psychotherapy on depression in patients with coronary artery disease: The canadian cardiac randomized evaluation of antidepressant and psychotherapy efficacy (create) trial. JAMA 297: 367-379.
21. Taylor C, Youngblood ME, Catellier D, Veith RC, Carney RM, et al. (2005) Effects of antidepressant medication on morbidity and mortality in depressed patients after myocardial infarction. Arch Gen Psychiatry 62: 792-798.
22. Shapiro PA (2013) Depression treatment and coronary artery disease outcomes: Time for reflection. J Psychosom Res 74: 4-5.
23. Zuidersma M, Conradi HJ, van Melle JP, Ormel J, de Jonge P (2013) Depression treatment after myocardial infarction and long-term risk of subsequent cardiovascular events and mortality: A randomized controlled trial. J Psychosom Res 74: 25-30.
24. de Jonge P, Honig A, van Melle JP, Schene AH, Kuyper AMG, et al. (2007) Nonresponse to treatment for depression following myocardial infarction: Association with subsequent cardiac events. Am J Psychiatry 164: 1371-1378.
25. Berkman LF, Blumenthal J, Burg M, Carney RM, Catellier D, et al. (2003) Effects of treating depression and low perceived social support on clinical events after myocardial infarction: The enhancing recovery in coronary heart disease patients (enrichd) randomized trial. JAMA 289: 3106-3116.
26. Carney RM, Freedland KE (2009) Treatment-resistant depression and mortality after acute coronary syndrome. Am J Psychiatry 166: 410-417.
27. Glassman AH, Bigger J, Gaffney M (2009) Psychiatric characteristics associated with long-term mortality among 361 patients having an acute coronary syndrome and major depression: Seven-year follow-up of sadhart participants. Arch Gen Psychiatry 66: 1022-1029.
28. Latalova K, Kamaradova D, Prasko J (2014) Perspectives on perceived stigma and self-stigma in adult male patients with depression. Neuropsychiatr Dis Treat 10: 1399-1405.
29. Ketterer MW, Denollet J, Chapp J, Thayer B, Keteyian S, et al. (2004) Men deny and women cry, but who dies? Do the wages of "denial" include early ischemic coronary heart disease? J Psychosom Res 56: 119-123.
30. Gilmour H (2008) Depression and risk of heart disease. Health Rep 19: 7-17.
31. Haukkala A, Konttinen H, Uutela A, Kawachi I, Laatikainen T (2009) Gender differences in the associations between depressive symptoms, cardiovascular diseases, and all-cause mortality. Ann Epidemiol 19: 623-629.
32. Ferketich AK, Schwartzbaum JA, Frid DJ, Moeschberger ML (2000) Depression as an antecedent to heart disease among women and men in the nhanes i study. Arch Intern Med 160: 1261-1268.
33. Mendes de Leon CF, Krumholz HM, Seeman TS, Vaccarino V, Williams CS, et al. (1998) Depression and risk of coronary heart disease in elderly men and women: New haven epese, 1982-1991. Arch Intern Med 158: 2341-2348.