INDIAN HEART JOURNAL 64 (2012) 397–401

Available online at www.sciencedirect.com

SciVerse ScienceDirect

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

Review article

Depression and the heart

R.K. Saran [a,*], Aniket Puri [b], Manu Agarwal [c]

[a] Professor and Head, Department of Cardiology, CSM Medical University (Erst. King George Medical University), Lucknow, India
[b] Associate Professor, Department of Cardiology, CSM Medical University (Erst. King George Medical University), Lucknow, India
[c] Lecturer, Department of Psychiatry, CSM Medical University (Erst. King George Medical University), Lucknow, India

ARTICLE INFO

Article history:
Received 10 April 2012
Accepted 15 June 2012
Available online 21 June 2012

Keywords:
Depression
Coronary artery disease
Heart failure

ABSTRACT

Cardio Vascular disease (CVD) as well as depression are both highly prevalent disorders and both of them cause a significant decrease in quality of life and increase the economic burden for the patient. Depressed individuals are more likely to develop angina, fatal or non-fatal myocardial infarction, than those who are not depressed. Over the past decade, evidence has accumulated to suggest that depression may be a risk factor for cardiac mortality in patients with established coronary artery disease (CAD). The 'vicious cycle' linking CVD to major depression and depression to CVD, deserves greater attention from both cardio-vascular and psychiatric investigators.[1]

1. Introduction

Cardio Vascular disease (CVD) as well as depression are both highly prevalent disorders and both of them cause a significant decrease in quality of life and increase the economic burden for the patient. Depressed individuals are more likely to develop angina, fatal or non-fatal myocardial infarction, than those who are not depressed. Over the past decade, evidence has accumulated to suggest that depression may be a risk factor for cardiac mortality in patients with established coronary artery disease (CAD). The 'vicious cycle' linking CVD to major depression and depression to CVD, deserves greater attention from both cardio-vascular and psychiatric investigators.[1] The apparent failure of current pharmacological therapy of depression with Selective Serotonin Receptor Inhibitors (SSRIs) and Tricyclic Antidepressants (TCAs) in improving mortality of such patients, emphasizes the importance of newer approaches.

2. Depression leading to CV disease

Diverse series of prospective studies show that depression in asymptomatic and apparently healthy subjects is a strong and independent predictor of Myocardial Infarction (MI). A recent meta-analysis[2] identified 10 prospective studies, in which the relative risk for CV events with depression was found to be 1.64 which was intermediate between passive smoking (1.25) and active smoking (2.5). Although depression need to be major depression to result in CV events later in life, some studies show a dose–response effect, in which a greater exposure to depression leads to a higher incidence of a coronary event; for example, a four year follow-up of the Amsterdam longitudinal ageing study reported a relative risk of cardiac mortality of 1.6 for individuals with depressive symptoms, and 3.8 for those with clinically diagnosed depression, after adjustment for age, sex, education, smoking, alcohol, hypertension, body mass index, diabetes, stroke, and cancer.[3] The Johns Hopkin's precursors study[4] followed 1190 medical students for a median

* Corresponding author.
E-mail addresses: rksaran@sify.com (R.K. Saran), aniketpuri@hotmail.com (A. Puri), drmanuagarwal7@gmail.com (M. Agarwal).
0019-4832/$ – see front matter
http://dx.doi.org/10.1016/j.ihj.2012.06.004

of 37 years and found a median interval of 15 years between the first episode of depression and the first coronary event. This suggests a chronic underlying link, with depression pre-dating the development of clinical CAD.

Very recently the effects of depressive symptoms and Coronary Heart Disease (CHD) and their interactive associations on mortality in middle-aged adults were studied in the Whitehall II cohort study which found that the age-adjusted and sex-adjusted hazard ratios for death from all causes were 1.67 ($p < 0.05$) for participants with only CVD, 2.10 ($p < 0.001$) for those with only depressive symptoms and 4.99 ($p < 0.001$) for those with both CVD and depressive symptoms when compared to participants without either condition. The relative excess risk due to the interaction between depressive symptoms and CVD for all-cause mortality was 3.58 (95% CI 0.09–7.26), showing evidence of an additive interaction. This study provides evidence that depressive symptoms are associated with an increased risk of all-cause and cardiovascular death and that this risk is particularly marked in depressive participants with co-morbid CHD.[5]

3. How prevalent is depression in CHD patients?

A review of 24 studies involving 14,326 patients of myocardial infraction was done recently.[6] Eight of these studies used a standardized interview for the diagnosis of depression .In these 8 studies, the prevalence of depression ranged form 16–45%. The largest of these studies, the Enhancing Recovery in CHD Patients (ENRICHD) examined 9279 patients and reported a prevalence of 20%. The weighted prevalence for all 8 studies was 20.5%. The remaining 16 studies used a validated questionnaire or rating scale. In these 16 studies 10–45% of patients had clinically significant symptoms of depression. The weighted prevalence was 31.1%.

These prevalence rates of depression in MI population are higher than the possibly conservative rate of major depression in the general population, which is about 5% as reported by the National Co-morbidity Study,[7] 5–10% in primary care, or in 6–14% in other inpatient medical settings. It is closer to the prevalence rates of 20–30% reported among patients with a stroke.[8]

These high prevalence rates of depression are not restricted to patients of CHD with acute MI only. In stable CHD patients with angiographically proven CAD, the prevalence of depression was approximately 18% in one study.[9] There is scarcity of data on this topic in Indian Population. Agarwal et al[10] from our institution reported depression in 23.7% of patients 4–6 weeks after Acute MI. Depressive symptoms not amounting to a disorder (Sub-syndromal depression) was seen in 20.7% patients. The psychiatric Co-morbidity in this study was independent of the clinical profile including the site of MI, severity of the infarction, intervention done or complications.

4. Is depression in post MI phase adverse prognostic factor?

The evidence that depression affects prognosis in patients with CAD, especially in patients with MI is growing. Reported relative risks for adverse outcome ranges from 2.5 to 5.7.[11–14] In a meta-analysis, post-myocardial infarction patients with a clinical diagnosed depressive disorder or self reported depressive symptoms had a 2.0–2.5 fold increased risk of new cardiovascular events and cardiac mortality.[15] Lane et al[16] raised a controversy that depression in MI patients has predicted mortality almost exclusively in studies in which it correlated with CHD severity at base line. Agarwal et al,[10] however reported that depression or depressive symptoms were not related to severity of MI.

It is interesting to note that not only major depression accounted for worse outcome but a multivariate analysis demonstrated that depressive symptoms, anxiety, and history of major depression each had an impact on outcome independent of each other.[17]

Impact of major depression on prognosis was as relevant as left ventricular dysfunction and history of previous myocardial infarction[18] and proved to be a significant predictor of 1-year cardiac mortality independent of sex or other post-myocardial infarction risk.[19] A higher prevalence of ventricular tachycardia during 24 h Holter monitoring was found among patients with CAD and depression, which may explain the increased risk for cardiac mortality in such patients.[20]

In patients with coronary artery bypass surgery, depression diagnosed before surgery was found to be related to higher hospital re-admission rates and was an independent risk factor for cardiac events after surgery.[14,21] Thus there is considerable evidence suggesting that depression and co-morbid CAD may lead to an increased risk of death, regardless of which illness occurred first and this is more so in patients with depression after MI.

5. Heart failure and depression

Depression has been shown to be a risk factor for poor outcomes among CAD patients. However, little is known about the influence of depression on development of Heart Failure in CAD patients. In a study of 1377 patients, 10.0% had a post-CAD clinical depression diagnosis. The incidence of Heart Failure among those without a post-CAD depression diagnosis was 3.6 per 100 compared with 16.4 per 100 for those with a post-CAD depression diagnosis. Diagnosis of depression was shown to be associated with an increased incidence of Heart Failure after CAD diagnosis, regardless of treatment.[22] Another study showed that elevated depressive symptoms predicted long term cardiovascular mortality in patients with atrial fibrillation and heart failure.[23]

In the Heart Failure Adherence and Retention Trial (HART), depression was found to be a strong predictor of repeated hospitalizations for HF.[24] In the trial, depressed individuals, in comparison with non-depressed, were hospitalized for HF 1.45 times more often, even after controlling for patient adherence to HF drug therapy and salt restrictions, physician adherence to evidence-based medications and illness severity, suggesting screening for depression early in the course of HF management.

6. Link between depression & CAD – common behavioural and physiological factors

A number of similar behavioural and physiological risks are associated with both depression and CAD. These

include smoking, hypertension, diabetes, and obesity etc. Depressed individuals are less likely to practice healthy habits, so they generally have more of these risk factors compared to those without depression. Non-adherence, which includes the improper use of drugs, not following a prescribed diet or exercise programme, or not visiting doctor on scheduled appointment may be behavioural risks that may lead to the development and worsening of CAD. Depression has been shown to be a risk factor for poor medication adherence and CV outcomes with poor adherence have worst prognosis.

Abnormal platelet function, including increased platelet reactivity, increased levels of platelet factor-4 and beta-thromboglobulin, increased platelet reactivity to serotonin and decreased platelet reactivity to adenosine diphosphate have been demonstrated in depressed patients.[24–26]

Moreover, endothelial dysfunction has been reported in depressive patients. In a study 15 patients with major depressive disorder without conventional risk factors for CAD were compared to matched control with respect to brachial artery flow-mediated vasodilation. It was found that the only independent predictor of the amount of reactive hyperaemia was presence or absence of depression indicating that major depression in the absence of other conventional risk factors may be associated with endothelial dysfunction.[27]

There is growing evidence for atherosclerosis as an inflammatory process. Depression is also associated with an acute phase response as evidenced by a higher C reactive protein and raised concentrations of pro-inflammatory cytokines such as interleukin-6 (IL-6), Interleukin-1 beta (1L-1 beta), tumour necrosis factor alpha (TNF-alpha) as well as interleukin-1 receptor antagonist (IL-1Ra).[28] These pro-inflammatory cytokines can produce symptoms of depression, anorexia, weight loss, malaise, and sleep disturbances. Raised levels of intercellular adhesion molecule-1 (ICAM-1), E-selectin, and monocyte chemoattractant protein-1 (MCP-1) are present in depressed individuals,[27] and may play a role in the cellular infiltration associated with atherosclerotic disease. Despite robust association with depression, inflammatory biomarkers explain only a small portion of the association between depression and CVD incidence.[29]

In patients of recent MI with evidence of depression, indices of heart rate variability were significantly reduced compared to patients without depression indicating that greater autonomic dysfunction as reflected by decreased heart rate variability might be a plausible mechanism linking depression to increased cardiac mortality in post-myocardial infarction patients.[30]

Thus, abnormal platelet function raised pro-inflammatory cytokines, endothelial dysfunction and reduced heart rate variability have been implicated as possible inter relationships between depression and CAD. However, more research is needed to confirm these links.

7. Treatment of depression with coronary artery disease

Treatment of depression has been shown to improve quality of life of patients with CAD. Patients treated for their depression might better adhere to risk factor modifications, prescribed medications and rehabilitation programmes. Therefore, patients with known CAD with evidence of depression should be evaluated for antidepressive therapy such as cognitive behavioural therapy, cardiac rehabilitation programmes and pharmacologic treatment.

Behavioural activation intervention, to improve affect has been recently suggested by Davidson et al.[31] These include perusal of hobbies or enjoyable activities on daily basis to increase quality of life. They may have a beneficial effect on CV risk in patients with depression. Strong societal support increases happiness and sense of well being.[32] Activities such as expressing gratitude, acts of kindness, regularly visualizing one's best possible self, forgiveness therapy may all be helpful in increasing subjective well being. Regular exercise, sexual activity and good sleep have been shown to improve self-reported happiness.[33,34] Currently RCT's of intervention to increase positive affect in patients with CVD are underway.

Regarding pharmacological treatment, SSRI's may be preferred for their good tolerability and absence of significant cardiovascular side effects over TCA's. Aminoketone antidepressants (Buproprion) modulate dopaminergic and noradrenergic activity and improve affect better than SSRI's. Buproprion has added benefits of causing reduction in weight and smoking cessation.

However, treatment with antidepressants (SSRI's & TCA's) does not appear to improve survival in CAD patients associated with depression despite correcting some of the pharmacological abnormalities linking CVD to depression.[27,35,36] Even combination of omega-3 fatty acid with SSRI's in CAD patients have shown no further benefit in a randomized trial.[37] Table 1 shows 3 randomized trials[38–40] in which SSRI's and Mirtazepine have been compared with usual care over long term, in patients of MI and acute coronary syndromes with depression. These drugs improve symptoms of depression and quality of life but none of them improved survival. Apparent failure of SSRI's and TCA's to improve survival in such patients, emphasize the importance of new approaches to deal with such situations as suggested by Davidson et al.[31]

8. Treatment resistant depression and mortality after acute coronary syndrome

Although SSRI's & TCA's do not improve survival, it is important to note that treatment resistant depression to one or more of these drugs may be associated with a particularly high risk of mortality or cardiac morbidity in patients of acute coronary syndromes with depression.

In the ENRICHD study[38] patients whose depression worsened by $\geq$ 10 BDI (Beck's Depression Inventory) points despite treatment were 1.6 times more likely to die in the ensuing months than were those who merely failed to improve (i.e. no or minimal change in BDI score), and 2.5 times as likely to die as those who improved by 10 or more points on the BDI. These effects were independent of the baseline BDI score, antidepressant use, and established predictors of mortality following myocardial infarction, including left ventricular ejection fraction, age, and prior history of myocardial infarction.[41]

Table 1 – Randomized clinical drug trials in patients of CAD with depression.

Trial	Patient	Intervention	Remarks
SADHART (2002)	3355 patients of Recent MI	Sertraline v/s usual care	Trends towards reduction in mortality at 6 months Caveat: was not intended or powered to study medical outcomes
ENRICHD (2003)	2481 patients of MI	Cognitive Behaviour Therapy± sertraline. v/s usual care	- Improvement in depression scores - No significant improvement in mortality and MI after 29 months of follow-up. Caveat: There was a small between group difference in depression scores.
MIND-IT (2007)	2140 patients of MI	Mirtazepine v/s usual care	No difference in mortality following 27 months of follow-up

Similarly in SADHART study, using the Clinical Global Impression (CGI) score to measure improvement in depression following treatment, it was found that the patients in both the placebo and sertraline groups with the most improvement ($N = 130$) had the lowest rate of mortality (11.5%). For those with moderate improvement ($N = 80$), 22.5% died, and for those whose depression minimally improved, worsened, or stayed the same following treatment ($N = 148$), 28.4% died during the follow-up interval ($p = 0.001$).[39]

It is not apparent, why depression, which is unresponsive to treatment, is associated with a greater risk for cardiac morbidity and mortality. However, a number of biological markers that predict poor response to depression treatment have also been identified as risk markers for cardiac events. If specific cardiac risk markers can be identified to predict treatment resistance in patients with CAD, it might be possible to improve depression and even survival in these patients by aggressive treatment of cardiovascular risk factors, or by choosing depression treatments that also modify these risk factors. If elevated inflammatory markers are associated with treatment resistance in coronary heart disease patients, then patients who do not respond to antidepressants could be tried on an anti-inflammatory drug or on specific cytokine antagonists along with standard depression treatment.

9. Should we routinely screen for depression in CVD patients?

Depression as an illness meets most criteria for screening. Depression is a common disorder with significant morbidity, low cost and low risk of screening and availability of effective drugs. The 2008 AHA Science Advisory[42] concluded that depression is commonly present in patients with CHD and is independently associated with increased cardiovascular morbidity and mortality. Therefore, screening tests for depressive symptoms should be applied to identify patients who may require further assessment and treatment. In view of adverse outcomes of depression associated with CVD and the availability of easy-to-administer and reasonably accurate screening methods, it is reasonable to screen for depression to improve outcomes.[43] Whooley[44] was of the opinion that until we are able to demonstrate that screening for depression improves cardiovascular outcomes, patient with CVD should be screened for depression by primary physicians in the context of a collaborative care intervention programme. This programme consists of a depression care manager (an allied health professional) to educate patients and a psychiatrist for supervision and giving advice to primary physicians. Others have suggested that routine screening may benefit patients but only if performed in the context of a collaborative care treatment, with the General practitioner being very successful in identifying depression.[45,46]

10. Conclusions

The prevalence of depression in CAD patients is high in western countries and ranges from 10–45% depending upon the method of diagnosing depression. There is scarcity of data on this subject in Indian population. Agarwal et al[10] have recently reported depression in 23% patients of Acute MI, 4–6 weeks after the event. Common behavioural and psychological factors seem to be the links between depression and CHD. Significantly increased risk of new cardiovascular events and mortality is a matter of great concern. In view of adverse outcomes and the availability of easy-to-administer and reasonably good screening methods, in 2008 the AHA advisory concluded that it is reasonable to screen for depression in CHD patients to improve outcomes. Three randomized trials on antidepressants in the last decade in these patients, although improved symptoms of depression and quality of life to variable degree, they failed to improve survival. The apparent failure of the current antidepressant therapy to improve mortality emphasizes the need for newer approaches in future.

Conflicts of interest

All authors have none to declare.

REFERENCES

1. Pitt B, Deldin PJ. Depression and cardiovascular disease: have a happy day–just smile!. *Eur Heart J*. 2010;31(9):1036–1037.
2. Nicholson A, Kuper H, Hemingway H. 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. *Eur Heart J*. 2006;27:2763–2774.
3. Penninx BW, Beekman AT, Honig A, et al. Depression and cardiac mortality: results from a community-based longitudinal study. *Arch Gen Psychiatry*. 2001;58:221–227.
4. Stansfeld S, Fuhrer R. *Depression and Coronary Heart Disease. Stress and the Heart*. London: BMJ Books; 2002;101–123.

5. Nabi H, Shipley MJ, Vahtera J, et al. Effects of depressive symptoms and coronary heart disease and their interactive associations on mortality in middle-aged adults: the Whitehall II cohort study. *Heart*. 2010;96(20):1645–1650.
6. Thombs BD, Bass EB, Ford DE, et al. Prevalence of depression in survivors of acute myocardial infarction and review of evidence. *J Gen Intern Med*. 2006;21:30–38.
7. Blazer DG, Kessler RC, Mcgonagle KA, et al. The prevalence and distribution of major depression in a national community sample. *Am J Psychiatry*. 1994;151:979–986.
8. Burill PW, Johnson GA, Tamozozak FD, et al. Prevalence of depression after stroke. *Br J Psych*. 1995;166:320–327.
9. Carney RM, Rich MW, Tevelde A, et al. Major depressive disorder in coronary artery disease. *Am J Cardiol*. 1987;60:1273–1275.
10. Agarwal M, Trivedi JK, Sinha PK, Dalal PK, Saran RK. Depression in patients of myocardial infarction –a cross sectional study in Northern India. *J Assoc Phys Ind*. Oct-2011;59:636–639.
11. Frasure-Smith N, Lesperance F, Gravel G, et al. Social support, depression, and mortality during the first year after myocardial infarction. *Circulation*. 2000;101:1919–1924.
12. Lesperance F, Frasure-Smith N, Juneau M, et al. Depressionand1-year prognosis in unstable angina. *Arch Intern Med*. 2000;160:1354–1360.
13. Lesperance F, Frasure-Smith N, Talajic M, et al. Five-year risk of cardiac mortality in relation to initial severity and one-year changes in depression symptoms after myocardial infarction. *Circulation*. 2002;105:1049–1053.
14. Denollet J, Sys SU, Stroobant N, et al. Personality as independent predictor of long-term mortality in patients with coronary heart disease. *Lancet*. 1996;347:417–421.
15. van Melle JP, de Jonge P, spijkerman TA, et al. Prognostic evaluation of depression following myocardial infarction with mortality and cardiovascular events: a meta analysis. *Psycho Som Med*. 2004;66:814–822.
16. Lane D, Carroll D, Lip GY. Anxiety, depression, and prognosis after myocardial infarction: is there a causal association? *J Am Coll Cardiol*. 2003 19;42(10):1808–1810.
17. Frasure-Smith N, Lesperance F, Talajic M. The impact of negative emotions on prognosis following myocardial infarction: is it more than depression? *Health Psychol*. 1995;14:388–398.
18. Frasure-Smith N, Lesperance F, Talajic M. Depression following myocardial infarction. Impact on 6-month survival. *JAMA*. 1993;270:1819–1825.
19. Frasure-Smith N, Lesperance F, Juneau M, et al. Gender, depression, and one-year prognosis after myocardial infarction. *Psychosom Med*. 1999;61:26–37.
20. Carney RM, Freedland KE, Rich MW, et al. Ventricular tachycardia and psychiatric depression in patients with coronary artery disease. *Am J Med*. 1993;95:23–28.
21. Connerney I, Shapiro PA, McLaughlin JS, et al. Relation between depression after coronary artery bypass surgery and 12-month outcome: a prospective study. *Lancet*. 2001;358: 1766–1771.
22. May HT, Horne BD, Carlquist JF, et al. Depression after coronary artery disease is associated with heart failure. *J Am Coll Cardiol*. 2009;53:1440–1447.
23. Frasure-Smith N, Lesperance F, Habra M, Talajic M. Elevated depression symptoms predict long-term cardiovascular mortality in patients with atrial fibrillation and heart failure. *Circulation*. 2009;120:134–140.
24. Johnson TJ, Basu S, Pisani BA, et al. Depression predicts repeated heart failure hospitalizations. *J Card Fail*. 2012;18:246–252.
25. Shimbo D, Child J, Davidson K, et al. Exaggerated serotonin-mediated platelet reactivity as a possible link in depression and acute coronary syndromes. *Am J Cardiol*. 2002;89:331–333.
26. von Kanel R, Mills PJ, Fainman C, et al. Effects of psychological stress and psychiatric disorders on blood coagulation and fibrinolysis: a biobehavioral pathway to coronary artery disease? *Psychosom Med*. 2001;63:531–544.
27. Rajagopalan S, Brook R, Rubenfire M, et al. Abnormal brachial artery flow-mediated vasodilation in young adults with major depression. *Am J Cardiol*. 2001;88:196–198.
28. Appels A, Bar FW, Bar J, et al. Inflammation, depressive symptomtology, and coronary artery disease. *Psychosom Med*. 2000;62:601–605.
29. Vaccarino V, Johnson BD, Sheps DS, et al. Depression, inflammation, and incident cardiovascular disease in women with suspected coronary ischemia: The National Heart, Lung, and Blood Institute–Sponsored WISE Study. *J Am Coll Cardiol*. 2007;50:2044–2050.
30. Carney RM, Blumenthal JA, Stein PK, et al. Depression, heart rate variability, and acute myocardial infarction. *Circulation*. 2001;104:2024–2028.
31. Davidson KW, Mostofsky E, Whang W. Don't worry, be happy: positive affect and reduced 10-year incident coronary heart disease: the Canadian Nova Scotia Health Survey. *Eur Heart J*. 2010;31(9):1065–1070.
32. Berkman LF, Glass T, Brissette I, Seeman TE. From social integration to health: Durkheim in the new millennium. *Soc Sci Med*. 2000;51(6):843–857.
33. Mutrie N. Healthy body, healthy mind? *The Psychologist*. 2002;15:412–413.
34. Rosen R, Bachman G. Sexual wellbeing, happiness and satisfaction in women: the case for a new conceptual paradigm. *J Sex Marital Ther*. 2008;34:291–297.
35. Follath F. Depression, stress and coronary artery disease. *Rev Med Suisse*. 2009;5:515–519.
36. Dome P, Teleki Z, Rihmer Z, et al. Circulatory endothelial progenitor cells and depression, a possible novel link between heart and soul. *Mol Psychiatry*. 2009;14:523–531.
37. Carney RM, Freedland KE, Rubin EH, Rich MW, Steinmeyer BC. Harris WS.Omega-3 augmentation of sertraline in treatment of depression in patients with coronary heart disease: a randomized controlled trial. *JAMA*. 2009 21;302(15):1651–1657.
38. 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*. 2003;289(23):3106–3116.
39. Glassman AH, O'Connor CM, Califf RM, et al. Sertraline treatment of major depression in patients with acute MI or unstable angina. *JAMA*. 2002;288:701–709.
40. Van Melle JP, de Jonge P, Honig A, et al. MIND_IT investigators. *Br J Psych*. 2007;190:460–466.
41. Carney R, Freedlan KE. Depression as a riskfactor for post MI mortality. *J Am Coll Cardiol*. 2004;44:469–474.
42. Lichtman JH, Bigger JT Jr, Blumenthal JA, et al. Depression and coronary heart disease: recommendations for screening, referral, and treatment: a science advisory from the American Heart Association Prevention Committee of the Council on Cardiovascular Nursing, Council on Clinical Cardiology, Council on Epidemiology and Prevention, and Interdisciplinary Council on Quality of Care and Outcomes Research: endorsed by the American Psychiatric Association. *Circulation*. 2008;118:1768–1775.
43. Thombs BD, de Jonge P, Coyne JC, et al. Depression screening and outcomes in CV care. *JAMA*. 2008;300:2161–2171.
44. Whooley MA. To screen or not to screen?: Depression in patients with cardiovascular disease. *J Am Coll Cardiol*. 2009;54:891–893.
45. Christensen KS, Sokolowski I, Olesen F. Case-finding and risk-group screening for depression in primary care. *Scand J Prim Health Care*. 2011;29(2):80–84.
46. Ski CF, Thompson DR. Beyond the blues: the need for integrated care pathways. *Eur J Cardiovasc Prev Rehabil*. 2011;18(2):218–221.