AAFP Guideline for the Detection and Management of Post–Myocardial Infarction Depression

Post–Myocardial Infarction Depression Clinical Practice Guideline Panel

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EVIDENCE-BASED RECOMMENDATIONS

The American Academy of Family Physicians (AAFP) Commission on Science convened a panel to review the evidence on the effect of depression on persons after myocardial infarction. The evidence report on this topic was published in May 2005 by the Agency for Healthcare Research and Quality (AHRQ) and is used as the basis for this review.[1] The AAFP Post–Myocardial Infarction Depression Clinical Practice Guideline Panel (Post-MI Guideline Panel) was charged with examining the evidence and developing an evidence-based clinical practice guideline for the detection and management of persons with postmyocardial infarction (post-MI) depression.

The following recommendations are provided only as assistance for physicians making clinical decisions regarding the care of their patients. As such, they cannot substitute for the individual judgment brought to each clinical situation by the patient's family physician. As with all clinical reference resources, they reflect the best understanding of the science of medicine at the time of publication, but they should be used with the clear understanding that continued research may result in new knowledge and recommendations.

Recommendations

Recommendation 1: Patients having a myocardial infarction should be screened for depression using a standardized depression symptom checklist at regular intervals during the postmyocardial infarction (post-MI) period, including during hospitalization (**Level A**).

Insufficient data are available to support a recommendation of one particular symptom checklist over another.

Recommendation 2: Post-MI patients with a diagnosis of depression should be treated to improve their depression symptoms, with systems in place to ensure regular follow-up and monitoring of their treatment response and adherence to treatment (**Level A**).

The recommendation to screen for and treat depression in patients with myocardial infarction is based on randomized controlled trials showing improvement in outcomes for depression. Treatment of depression has not been found to improve cardiac outcomes per se, though the evidence does not yet exclude the possibility of a small benefit. The literature does not provide guidance regarding the effects of treatment of depression on adherence to tertiary prevention[1] measures for coronary disease, such as diet, β-blocker, or aspirin use. The diagnosis of depression will be informed, not determined, by the screening instrument results from Recommendation 1. Definitive diagnosis is ultimately the treating clinician's responsibility.*

*In the cardiology literature, tertiary prevention is often referred to as secondary prevention.

Recommendation 3: Selective serotonin reuptake inhibitors (SSRIs) are preferred to tricyclic antidepressants for treatment of depression in post-MI patients **(Level A).**

Randomized controlled trials using SSRIs have shown improvement in measures of depression among post-MI patients. The evidence base for treatment with SSRIs is large enough and follow-up has been long enough to show that SSRIs are safe in the post-MI setting and do not share the adverse cardiac effects of tricyclic antidepressants. Insufficient evidence is available about other classes of antidepressants to make recommendations for or against their use in post-MI patients.

Recommendation 4: Psychotherapy may be beneficial for treatment of depression in post-MI patients. The existing evidence base does not establish what form of psychotherapy is preferred **(Level B).**

Trials of psychotherapy have used a variety of types of interventions. Taken as a whole, the body of evidence supports benefit in reducing depression symptoms, but not all studies supported this conclusion. Additionally, the heterogeneous nature of the interventions studied precludes direct comparisons.

INTRODUCTION

Cardiovascular disease remains the leading cause of death and disability among both men and women of all ethnic groups in the United States. Depression is an important predictor of morbidity and mortality in patients with coronary heart disease, particularly after a myocardial infarction, independent of previous cardiac history, coronary artery disease severity, or residual left ventricular function.[2] As many as 65% of patients with acute myocardial infarction report experiencing symptoms of depression, and major depression is present in 15% to 22% of these patients.[3] In 2003, the AAFP Commission on Clinical Policies and Research (now Commission on Science) decided there was a need for an evidence review on the effect of depression on post-MI patients and successfully nominated the topic to AHRQ. In May 2005, after publication of the AHRQ Evidence Report Number 123,[1] the AAFP established the Post-MI Guideline Panel, which was composed of family physicians who were well versed in practice guideline development and the care of post-MI patients with depression. The Post-MI Guideline Panel was charged with examining the evidence and developing an evidence-based clinical practice guideline for detection and treatment of depression post-MI. The guideline was peer-reviewed before being reviewed and approved by the AAFP Commission on Science and by the AAFP Board of Directors. The post-MI depression guideline describes the historical context, the methods used to review the literature, the results of the review, the evidence-based recommendations, and recommendations for future research in this area.

SCOPE

This guideline pertains directly only to patients who have sustained ST-elevation MI (STEMI) or non–ST-elevation MI (NSTEMI). Patients with unstable angina and those with acute coronary syndrome relieved by revascularization (thrombolysis, angioplasty, or bypass surgery) have not been included in studies to date. The studies available do not generally distinguish between STEMI and NSTEMI.

Full discussion of the details and comparison of the available screening tools is beyond the scope of this guideline. The user is referred to the US Preventive Services Task Force guideline on depression screening for further information. This guideline is intended to assist the primary care physician who is knowledgeable about depression management to improve practice; it does not replace training in depression management. Management of subsyndromal depression, dysthymia, suicidality, and details of psychopharmacology are beyond the scope of this document.

BACKGROUND

Depression is a common occurrence after an MI, and many studies (summarized below) have shown it to be associated with an increase in subsequent coronary events and with coronary-related mortality. The correlation of depression with adverse cardiac outcomes has led to trials examining the effect of depression treatment on coronary outcomes as well as depression outcomes.

METHODS

The AAFP strength of recommendation taxonomy (SORT)[4] framework was used to grade the recommendations for this guideline (see http://www.aafp.org/online/en/home/publications/journals/afp/afpsort.html for details). The recommendations were developed by discussion among the Post-MI Guideline Panel members after review of the AHRQ Evidence Report No. 123,[1] completed by the Johns Hopkins University Evidence-based Practice Center (EPC), and subsequent evidence. Decisions were by unanimous agreement; there was no voting, and the data were not amenable to formal methods such as meta-analysis. The evidence reviewed is summarized below.

AHRQ Evidence Report

The Post-MI Guideline Panel used the AHRQ Evidence Report No. 123 as the basis for constructing

this post-MI depression clinical practice guideline. The report provides a full description of the methods used in the AHRQ systematic review.[1] Conclusions are based on high-quality randomized controlled trials unless otherwise stated. Each key question in this guideline is one of the questions of evidence addressed in that report as nominated by the AAFP. Recommendations derive from the findings of the evidence report, as well as additional relevant evidence published in English language peer-reviewed literature subsequent to the date the EPC review was in final form.

Updated Evidence Review

Because 2 years had elapsed since the original evidence review, the Post-MI Guideline Panel conducted a systematic update of the evidence by reviewing studies published since the AHRQ EPC report. An updated literature search, addressing the same key questions as in the AHRQ EPC report, was performed covering the time period from April 2004 to November 15, 2006. Unlike the original evidence report, the updated report included only information from electronic searches (ie, hand searches were excluded); however, the databases searched were the same as in the original AHRQ EPC report. Identical search terms were used for the MEDLINE and Cochrane databases.[1] The search terms were slightly modified for the remaining 3 databases (ie, EMBASE, CINAHL, and PsycINFO) because of high rates of overlap with the results from MEDLINE (see the Supplemental Appendix, available online at http://www.annfammed.org/cgi/content/full/7/1/71/DC1).

The literature search resulted in 809 articles. After duplicates were eliminated, 2 reviewers independently scanned the titles and made a determination regarding relevance. The exclusion criteria used in the original evidence report were also used in the updated literature review. Specifically, articles were eliminated if (1) they were not in English, (2) they had no human data, (3) they had no original data, or (4) there was no full-text article to review (ie, it was a meeting abstract).[1] If both reviewers agreed that an article was irrelevant, it was excluded from further review. Any discrepancies were discussed and resolved by the reviewers.

All remaining articles were examined for relevance based upon their abstracts. Each of the 2 reviewers examined the abstracts independently. The reviewers again had to agree to the relevance of the article for inclusion or exclusion in the updated evidence review. All discrepancies were discussed by the reviewers and agreement was reached. If a citation did not have an abstract or the reviewers could not agree on the relevance, the full-text article was obtained. Consistent with the AHRQ EPC report, abstracts were marked for relevance to a key question, and those eliminated were given a reason for elimination. This resulted in 71 articles being examined for full-text review.

Each full-text article was then examined for relevance to the research questions. Consistent with the original evidence report, information was also gathered related to the methods and quality of the study. Articles that were unrelated to the study questions were again eliminated resulting in a total of 31 articles for the updated evidence review (Table 1). The AAFP Post-MI Guideline Panel made the determination that this new body of evidence did not contribute any substantive changes to the original evidence report but added more support to it; therefore, both the new evidence as well as the original report were used as the evidence sources for this guideline.

RESULTS

The Post-MI Guideline Panel used the original key questions as they were written in the AHRQ EPC

Table 1. Articles Related to Key Questions

Abbreviated Citation	Key Question(s)
Akhtar et al,[5] 2004	1
Blumentha et al,[6] 2004	3
Carney et al,[7] 2004	3, 4
de Jonge et al,[8] 2006	1, 3
de Jonge et al,[9] 2006	3
Dias et al,[10] 2004	1
Dickens et al,[11] 2006	1, 3
Dickens et al,[12] 2004	1
Drago et al,[13] 2006	1, 3
Fauerbach et al,[14] 2005	1, 3
Ginzburg,[15] 2006	1
Grace et al,[16] 2005	4
Grunau et al,[17] 2006	3
Huffman et al,[18] 2006	1, 5
Huffman et al,[19] 2006	1
Jaffe et al,[20] 2006	3
Kaptein et al,[21] 2006	1, 3
Lacey et al,[22] 2004	1, 4
Mallik et al,[23] 2006	1
McGowan et al,[24] 2004	1
Mohapatra et al,[25] 2005	1, 4
Parashar et al,[26] 2006	1, 2, 3
Parker et al,[27] 2006	1
Schrader et al,[28] 2004	1
Sorensen et al,[29] 2006	1, 3
Spijkerman et al,[30] 2005	1
Spijkerman et al,[31] 2006	1
Spijkerman et al,[32] 2005	1
Taylor et al,[33] 2005	4
Van Melle et al,[34] 2006	1
Ziegelstein et al,[35] 2005	1

report[1] to guide the evidence panel in collecting the relevant research studies to best inform the report. The questions as they are written below are rephrased to be more relevant to practicing professionals but are not changed in substance.

Evidence Summary

Evidence Question 1: What Is the Prevalence of Depression During Initial Hospitalization for MI?

In the original AHRQ EPC report, prevalences varied by type of measure used. For example, use of the Structured Clinical Interview for the Diagnostic and Statistical Manual (SCID) yielded prevalences ranging from 17% to 27%. Including the ENRICHD trial at 20%[36] and validated depression scales, such as the Beck Depression Inventory (BDI), yielded prevalences ranging from 10% to 47%, depending on the cut points used.[37-43] The EPC report noted that there was a medium quantity of evidence of reasonable quality to address this question.

The updated evidence review continued to show a wide range of prevalences (7.2% to 41.2%) depending on the method used to assess depression. Structured interviews tended to produce lower prevalence estimates, and ratings scales, such as the BDI, produced higher prevalence estimates.* In general, across the studies, about 1 of every 5 patients with an MI has depression during an initial hospitalization.

Evidence Question 2: What Is the Prevalence of Continued Depression >1 Month Postdischarge and Beyond?

It is important to distinguish among the time courses of depression that may be identified, ie, prevalent depression that existed before the MI event and continues afterward, incident depression that begins after an MI, recurrent depression that was in remission but recurs after an MI, and incident depression immediately post-MI that remits spontaneously. Patients identified as depressed at 1 month or longer after discharge include patients with the first 3 of these depression time courses. Incident depression seems most relevant to this guideline, as it is most closely related to the MI event in its time course. In the EPC report 19 studies reported 1-month post-MI depression prevalence data; however, only 3 studies specifically addressed patients for whom depression was initially diagnosed immediately post-MI, incident depression, and who were observed for up to 1 month or longer. In these patients, 1-month or greater prevalences ranged from 36.7% to 60%.[38,44,45] Studies were rated as having a medium quantity of evidence with reasonable quality. The updated review of the literature found only 1 new study that again reported a 1-month 35.4% prevalence of depression in patients originally given a post-MI diagnosis of depression.[26]

Evidence Question 3: What Is the Independent Association of Measures of Depression With Post-MI Outcomes?

The AHRQ EPC report identified 11 independent studies meeting inclusion criteria that provided data on the association of depression with post-MI mortality.[36,46-55] All 11 studies related depression, as assessed 1 time shortly after MI, to survival at times varying from 4 months to 10 years. Studies were judged to be generally of high quality. Eight found a statistically and clinically significant association between depression and mortality, whereas 3 did not.[56-58] The sex of the patient did not appear to affect the relation between MI and depression, nor did correction for other cardiac risk factors. Subsequent to the AHRQ EPC report, several additional publications meeting criteria addressed the same issue.† All supported the association between post-MI depression and cardiac-related mortality, with a direct relation between severity of depression symptoms and probability of death.[40]

The AHRQ EPC report identified 6 independent studies meeting inclusion criteria that reported cardiac event rates among depressed patients.[50,59-63] Studies were judged to be of moderate quality. One study[50] found that the association between cardiac events and depression disappeared with adjustment for fatigue symptoms, and 2 others found the same when adjusting for a measure of anxiety.[61,62] Another[60] found that the association was significant for older (older than 65 years) but marginal for younger patients. Studies of similar methodological quality published since the EPC report have shown relations between post-MI depression symptoms and hospital readmission[21,26,29] and nonfatal cardiac events or symptoms.[8,13] Two adequately powered studies[26,29] did not support the relation between depression and nonfatal events.

The AHRQ EPC report[1] identified 11 independent studies meeting inclusion criteria that addressed quality of life among post-MI patients with depression.‡ A variety of effects on physical, psychological, and social health and function have been shown for post-MI patients with depression, some sex-specific and some not, with a moderate degree of inconsistency among the studies. These effects were seen across a range of follow-up duration, from 3 months to 5 years. The body of evidence was judged to be of low quality. Most studies of quality-of-life measures since the EPC report[8,14,26] have similar findings. One found no relation

* References 5,8,10-15,18,19,21-32,34,35.

† References 6,7,9,13,17,20,21,26,29.

‡ References 39,41,43,48,56,57,64-68.

between depression at baseline (immediately post-MI) and quality of life, though it did find that a 6-month post-MI measure of depression was associated with reduced quality of life.

Three studies reviewed in the EPC report[69-71] provided data on surrogate markers for risk of recurrent MI. The studies, judged to be of high quality, found consistent associations between post-MI depression and abnormalities in the frequency spectrum of the cardiac beat-to-beat intervals, increased platelet activity, and inflammatory markers. No new studies meeting inclusion criteria have added information since the EPC report.

No studies attempted to address potential harms from screening. Harm might result, for example, from treating patients whose depression would spontaneously resolve or from using unnecessary resources.

Evidence Question 4: Does Treatment of Post-MI Depression Improve Outcomes?

The AHRQ EPC report identified 6 randomized clinical trials (RCTs)[36,72-76] and 1 prospective cohort study[77] that evaluated the general impact of psychosocial intervention on cardiac outcomes, and 5 RCTs[78-82] that specifically evaluated antidepressant medication treatment (typically with SSRIs). The quality of the studies varied widely, with larger trials generally of higher quality. The nature of the studies was heterogeneous: some included only post-MI patients, whereas others included post-MI patients and patients with unstable angina, and still others included patients hospitalized for coronary care with or without an acute coronary syndrome. Psychosocial interventions resulted in consistent improvement in depression outcomes but not in cardiac end points. The nature of the interventions was heterogeneous. Antidepressant medications also improved depression outcomes. A trend toward improved cardiac outcomes in the largest and best-designed of the medication studies did not reach statistical significance.[78]

Three additional publications since the EPC report have addressed medication treatment. A post hoc subgroup analysis[33] of the ENRICHD trial,[36] a 2,481-patient study of psychosocial intervention, found a 43% reduction in death, nonfatal MI, and all-cause mortality among those patients taking SSRIs. Assignment was not randomized, and selection bias could have been substantial. A study from India[25] found both significantly reduced rates of depression and cardiac events among depressed post-MI patients taking antidepressant medication, but the sample size was only 50 patients. The CREATE trial[83] randomized 284 patients with moderate to severe depression of at least 4 weeks' duration and coronary heart disease (approximately two-thirds of whom had had previous MIs) to citalopram vs placebo and independently to interpersonal psychotherapy or usual clinical care. Citalopram was found to have a clinically and statistically significant benefit on depression symptoms during the 12-week follow-up. The CREATE trial was neither sufficiently powered nor of long-enough duration to detect differences in mortality.

Three additional publications since the EPC report addressed psychosocial interventions. One was a new study[22] finding that self-help intervention reduced anxiety and depression scores. Another post hoc subgroup analysis of ENRICHD[7] supported that patients receiving cognitive behavioral therapy (some of whom also received SSRIs) and whose depression scores improved had lower mortality. The CREATE trial cited above compared interpersonal therapy to usual clinical care and did not find a benefit for interpersonal therapy.

SSRIs appear to be safe from a cardiac standpoint and effective in reducing depression symptoms. SSRIs are preferred over tricyclic antidepressants because of the heart rate and conduction effects of tricyclic antidepressants.[7] The effects of psychotherapy are difficult to interpret because of the heterogeneity of the modalities used; however, at least cognitive behavioral therapy appears to improve depression symptoms. Subgroup analyses of several studies suggest that benefit accrues to patients with preexisting depression or previous episodes of depression, whereas patients whose initial symptoms appear after an MI have a very high placebo response rate and generally improve regardless of therapy.[16]

Evidence Question 5: What Are the Performance Characteristics of Depression Measures Post-MI?

The determination of clinically significant levels of depression in the AHRQ EPC report differed across studies depending largely on the method or instrument used to determine the level of depression symptoms. Even studies using the same instrument often set different scores as representing clinically significant depression. Rates also varied according to the type of symptoms included in determining the level of depression. It seems evident that structured interviews, such as the SCID, tend to produce lower prevalence estimates than rating scales, such as the BDI, that include symptoms of general distress. The AHRQ EPC report cited insufficient data to allow an adequate assessment of the performance characteristics of instruments.

In general, this remains the case. One study[19] did assess performance characteristics of BDI-II questions against the SCID. Unfortunately, it was focused on developing a brief, 1- to 2-item screen, and therefore they did not evaluate the overall operating character-

istics of the BDI-II. For these 1- to 2-question screens using BDI-II questions, they found relatively low positive predictive values (32 to 48.3) and high negative predictive values (97.1 to 98.9), compared with published characteristics for the Patient Health Questionnaire-9 in the general population, for which a positive predictive value of 55% is noted.[84]

Evidence Question 6: Does Depression Affect Cardiac Health Care Utilization Post-MI?

The EPC report found evidence that physicians' prescribing behavior for patients was conflicting, with some suggestion that β-blockers might be underprescribed for depressed patients in North America, but that prescribing for other important tertiary prevention interventions was not affected by depression status. The evidence was similarly unclear for the relationship between depression and use of invasive procedures post-MI. The evidence base was consistent in showing that depression was associated with reduced medication adherence and reduced adherence to lifestyle modification behaviors by patients. The report writers cited a low quantity of medium- to low-quality evidence addressing this question.

The literature search performed by the Post-MI Guideline Panel discovered no new information relevant to this question. No trials exist on the important question in primary care: whether or how depression treatment affects adherence to post-MI recommendations that improve outcomes. Hence, it is currently not possible to formulate a recommendation.

LIMITATIONS

This guideline has several limitations, largely reflecting limitations in the available evidence base. Few studies separate incident from prevalent depression. The literature does not contain any studies that directly compare of screened with unscreened groups after an MI, so conclusions in that area are based on intermediate outcomes and observational studies. Advances in the treatment of acute coronary ischemia have resulted in a population labeled as having "acute coronary syndrome," which includes those who, through emergency medical intervention, have been spared myocardial damage. It is not known whether this subgroup suffers the same incidence of and outcomes from depression as the confirmed infarction patients in the existing studies.

The AHRQ EPC panel included a range of specialties, but the evidence update and formulation of the guideline presented here were conducted entirely by family physicians. Both the AHRQ EPC panel and the present authors found that the studies available were methodologically too heterogeneous to permit formal meta-analyses. The available literature is focused on efficacy rather than effectiveness trials, and no good data on external validity exist as yet.

FUTURE RESEARCH RECOMMENDATIONS

Depression Measures

A number of instruments have been used by the various studies and trials To identify and monitor post-MI patients with depression. Unfortunately, very little information exists on the operating characteristics of these instruments in this population. This lack of information is of particular concern in post-MI patients, for whom symptoms of fatigue and other somatic symptoms may be elevated in the post-MI state independent of the presence of depression. There is a need for epidemiologic studies that assess post-MI patients for depression using a reference standard measure, such as the SCID, along with such instruments as the BDI, Hospital Anxiety and Depression Scale, and Patient Health Questionnaire-9. This work should be done in the immediate post-MI patient population, as well as in those patients who are further removed from their cardiac event, for patients with resolved acute coronary syndromes as well as MI, and for those who have and have not undergone perfusion (either by angioplasty or bypass). Similar issues have arisen in studies of patients who have diabetes and depression, and recent studies have indicated that disease-related distress may be tied more to the diabetes outcomes than the depression itself.[85] Further studies aimed at distinguishing the symptoms and issues that are most related to post-MI outcomes would be helpful.

Subpopulations of Patients

There are several subpopulations of post-MI patients who have persistent depression: those who were depressed before the MI and stayed depressed, those who were not depressed before the MI but became depressed soon after the MI, and those who were not previously depressed but became depressed at a later time after the MI. The depression could have a different impact on the cardiac outcomes and disease course in each of these situations, and the treatment implications may be different. This also applies to those who were spared myocardial damage by way of medical interventions but who had transiently blocked coronary arteries and ischemia. Further studies investigating outcomes and treatment for the specific subpopulations are needed.

Adherence to Treatment

Depression does appear to affect patients' adherence to post-MI lifestyle change and medication

recommendations. The lack of trials exploring and attempting to improve adherence among patients with post-MI depression is a major deficit in the evidence base needed by primary care physicians. The Post-MI Guideline Panel recommends that this issue should be addressed further.

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