Impact of Chronic Kidney Disease on Health-Related Quality-of-Life Improvement After Coronary Artery Bypass Surgery

Chirag R. Parikh, MD, PhD; Steven G. Coca, DO; Grace L. Smith, MD; Viola Vaccarino, MD, PhD; Harlan M. Krumholz, MD

Background: Little is known about the impact of chronic kidney disease (CKD) on health-related quality-of-life outcomes after coronary artery bypass grafting (CABG).

Methods: Our objective was to examine the changes in physical function (PF) and mental health (MH) 6 months after CABG in 1055 patients with and without CKD. The primary end points were mean change in score and status of “improved” or “worsened” in both PF and MH subscales of the Medical Outcomes Trust Short Form 36-Item Health Survey from baseline to 6 months after CABG, stratified by CKD stage (0-5).

Results: Absolute PF and MH scores at baseline and at 6 months varied by renal impairment level. Patients with severe CKD (stages 4-5) had a mean (SD) decrease in PF score at 6 months of 3 (3) compared with increases in the rest of the cohort ($P<.001$). After adjustment for baseline score, 21% of patients with advanced CKD experienced worsened PF scores, compared with 0% of patients with stages 0 to 2 and stage 3 CKD ($P<.001$). In contrast to PF scores, patients with and without CKD had similar improvements in mean MH scores at 6 months, and patients with stages 4 to 5 CKD had the highest frequency of those with improved MH scores (77%). After adjustment, no patients experienced worsened MH scores.

Conclusions: After 6 months, patients with severe CKD who underwent CABG had improvement in MH but not improvement in PF and may have had worsened PF compared with those without severe CKD. Comparable evidence regarding quality-of-life outcomes in the absence of CABG is needed to more fully inform decision making regarding patients with severe CKD and coronary artery disease.


More than 500,000 coronary artery bypass grafting (CABG) surgical procedures are performed annually in the United States, and chronic kidney disease (CKD) is present in 25% of these patients. Even mild to moderate degrees of CKD have an adverse effect on in-hospital mortality, perioperative bleeding, rehospitalization, and long-term mortality after CABG surgery. These risks may be offset by a marginal survival benefit in patients with CKD who undergo CABG; however, there are no randomized controlled trials of the net benefit of CABG in patients with CKD.

Although, on average, elective CABG surgery provides a significant improvement in patients’ quality of life (QOL), certain subgroups, such as elderly individuals, women, obese patients, and those with a good preoperative health status, are less likely to derive a substantial benefit. To our knowledge, no previous studies have investigated whether CKD alters the benefits derived in health-related QOL after CABG surgery. On one hand, because of the higher disease burden of coronary artery disease in patients with CKD, preoperative health status may be worse for patients with CKD, thus providing a greater opportunity for benefit. On the other hand, patients with CKD have higher in-hospital complication rates that may lead to worsening of QOL. In addition, patients with CKD have other problems, such as anemia, protein malnutrition and uremia, deranged mineral metabolism, and other comorbidities, such as diabetes mellitus, all of which may additionally limit the beneficial impact of surgery on their health-related QOL.

Because the survival benefits are unclear in most cases of CABG in patients with CKD, the decision to undergo this surgery should incorporate potential improvement in postoperative health-related QOL. However, information on this is lacking. To address this issue, we ex-
examined changes in physical function (PF) and mental health (MH) scores over a 6-month period in a cohort of patients with various degrees of CKD who underwent CABG surgery.

**METHODS**

**STUDY POPULATION AND DATA COLLECTION**

The study design for the Approaches to Recovery after Coronary Surgery Cohort has been described previously. Briefly, from February 1999 to February 2001, all patients admitted for CABG surgery at Yale–New Haven Hospital, New Haven, Conn, were screened for this study. Patients younger than 30 years, those with a previous CABG or undergoing concomitant operations, and those with barriers to the interview, such as those with impaired mental status or those who were non–English speaking, were excluded.

After surgery, patients completed a baseline interview while still in the hospital. To evaluate PF, we used 2 of the 8 subscales of the Medical Outcomes Trust Short Form 36-Item Health Survey (SF-36, version 1.0), the PF and MH subscales. The SF-36 has been validated in patients with coronary heart disease and has recognized validity in patients who have undergone CABG. The abstraction of other clinical variables was based on definitions consistent with the Society of Thoracic Surgery National Cardiac Database. This database contains 217 core fields with internal quality controls for out-of-range, inconsistent, contradictory, and missing data, making it a reliable database with high-quality data.

Patients were contacted by telephone 6 months after undergoing CABG and asked about their PF and MH by use of the same instruments as at baseline. The Yale University School of Medicine institutional review board approved the study, and all patients provided informed consent.

Renal function was measured based on estimated glomerular filtration rate (eGFR), calculated on the basis of the Modification of Diet in Renal Disease abbreviated equation:

\[
eGFR = \left( \frac{186}{S_{\text{cr}}} \right) \times (0.74 \text{ if Female}) \times (1.21 \text{ if Black}),
\]

where “S_{\text{cr}}” indicates serum creatinine. The preoperative creatinine level recorded in the medical record was included for this analysis. The CKD status was then classified based on the National Kidney Foundation guidelines and grouped into 3 categories: stages 0 to 2 CKD (eGFR=60 mL/min per m²), stage 3 CKD (eGFR 30–39 mL/min per 1.73 m²), and stages 4 to 5 CKD (eGFR<30 mL/min per 1.73 m²).

**PRIMARY OUTCOMES: PF AND MH**

At baseline and at the 6-month follow-up, PF and MH were assessed as follows. A PF score was calculated based on the PF subscale of the SF-36. For each question, patients were asked if various activities, such as running, vacuuming, lifting groceries, climbing stairs, walking, bathing, and dressing, had been limited a lot, a little, or not at all in the prior month. Consistent with prior validation of this instrument, each item was scored as 100 points (not at all), 50 points (a little), and 0 points (a lot), and scores were averaged across the 10 total items for a final score ranging from 0 to 100, indicating the best PF.

An MH score was calculated on the MH subscale of the SF-36. For each question, patients were asked to rank the frequency within the past month (ranging from all of the time to none of the time on a 6-point scale) with which they had experienced anxious moments, calm and peaceful moments, and cheerful or depressed moods. Scores were averaged across the 5 total items for a final score ranging from 0 to 100, with 100 indicating the best MH.

The main outcomes for this study were based on the change in PF and MH scores at 6 months compared with baseline scores. Each follow-up score subtracted the baseline score for a PF improvement score ranging from −100 to 100 at each follow-up time point, with 100 indicating the best improvement in functioning.

Patients were considered improved if they showed a positive change of at least 5 units in the scale scores. Patients were considered worsened if their PF or MH score declined by 10 units from baseline. A more prominent decrease was chosen a priori because we sought to determine a substantial worsening, and these changes have been deemed clinically relevant in previous studies. The other patients were classified as unchanged.

**SECONDARY OUTCOMES**

At baseline and at 6-month follow-up, other important variables were analyzed. These included bodily pain scores (from the SF-36) and depression scores (via the Abbreviated 15-item Geriatric Depression Scale). Potential confounders were selected based on previous literature that demonstrated certain patient and clinical characteristics that can influence the outcome after CABG surgery. The variables abstracted specifically for our study from the Society of Thoracic Surgery National Cardiac Database and chart abstraction are listed in Table 1.

**DATA ANALYSIS**

We used the Wilcoxon rank sum method to analyze differences in baseline and 6-month scores because these values were not normally distributed. Analysis of variance models were used to calculate mean changes in PF scores from preoperative values to follow-up values and analysis of variance models after adjustment of baseline factors. For calculating differences in rates of improvement or worsening and odds ratios by CKD subgroup, we used x² analyses and Cochran Mantel-Haenszel statistics. We used linear regression models that incorporated the covariates to obtain adjusted changes in scores and logistic regression models to calculate adjusted odds ratios. All tests for statistical significance were 2-tailed, with an α level of .05. All analyses were conducted with SAS statistical software (version 9.1; SAS Institute, Cary, NC).

**RESULTS**

**STUDY POPULATION AND BASELINE CHARACTERISTICS**

Of the 1164 patients in the original cohort, 14 were excluded who had no preoperative measure of renal function, and 95 were excluded owing to lack of completion of the 6-month PF survey, including 29 who died, 18 who refused the follow-up interview, and 11 who were too sick; the rest were lost to follow-up. In addition, 44 patients were excluded from the analyses of changes in MH owing to absence of completion of the MH survey. The final study sample included 1055 patients. There were no statistically significant differences in the percentage of patients with any of the clinical characteristics listed in Table 1 between the included and excluded patients except for a slightly higher percentage of subjects with an ejection fraction smaller than 40% (23% vs 15%; P=.03)
and with a medical history of myocardial infarction (65% vs 56%; \(P = .03\)) in the cohort of excluded subjects. Thirteen percent of the subjects had stages 4 to 5 CKD, but this difference was not statistically significant (\(P = .29\)) compared with the final analyzed cohort.

Based on the National Kidney Foundation classification system, 29% of the study sample had stage 3 CKD. Five percent had stages 4 to 5 CKD, and of these, 1.6% (17 patients) were undergoing long-term hemodialysis (Table 1). Patients with stages 0 to 2 CKD were more likely to be male and younger. Patients with stages 3 and 4 to 5 CKD had significantly more comorbidities and were more likely to have a low ejection fraction, anemia, hypertension, and diabetes mellitus (Table 1).

### RENAL IMPAIRMENT AND PF SCORES

Absolute PF scores at baseline and at 6-month follow-up varied by renal impairment level, were significantly lower at both time points in the group with stage 3 CKD, and were lowest in the group with stages 4 to 5 CKD (Table 2). At 6-month follow-up, the change in the mean PF increased the most in the group with stages 0 to 2 CKD followed by the group with stage 3 CKD. Patients with advanced CKD (stages 4-5) had a mean decrease in their PF scores after adjusting for baseline score. This graduated relationship of decreasing change in PF score with worsening CKD persisted after adjusting for other demographic and clinical variables.

### PROPORTION AND RELATIVE RISK OF IMPROVEMENT AND WORSENING

The percentage of patients whose PF scores improved at 6 months exceeded 50% in all strata of GFR (Table 2). The odds of improved PF scores were not different among the stages of CKD after adjusting for a comprehensive set of demographic and clinical variables.

The percentage of patients whose PF scores worsened at 6 months increased as GFR declined. After adjusting for baseline scores, patients with stages 4 to 5 CKD experienced a worsened PF score at 6 months at a frequency of 21% compared with 0% of patients with stages 0 to 2 and stage 3 CKD (\(P < .001\)).

### RENAL IMPAIRMENT AND MH SCORES

Absolute MH scores at baseline also varied by renal impairment level, with those with stages 4 to 5 CKD having the lowest scores (Table 2). However, at 6 months, MH scores improved equally among all 3 strata of CKD, which persisted after adjusting for baseline score and other covariates.

### PERCENTAGE AND RELATIVE RISK OF IMPROVEMENT AND WORSENING

The percentage of patients whose MH scores were improved at 6 months exceeded 50% in all strata of CKD and

### Table 1. Baseline Characteristics of the 1055 Patients in the Study*

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Patients per CKD Stage</th>
<th>(P) Value†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients, No.</td>
<td>700 (66)</td>
<td>304 (29)</td>
</tr>
<tr>
<td>Male</td>
<td>557 (80)</td>
<td>175 (58)</td>
</tr>
<tr>
<td>Age, mean, y</td>
<td>64</td>
<td>71</td>
</tr>
<tr>
<td>Race</td>
<td>665 (95)</td>
<td>284 (93)</td>
</tr>
<tr>
<td>White</td>
<td>665 (95)</td>
<td>284 (93)</td>
</tr>
<tr>
<td>Black</td>
<td>17 (2)</td>
<td>16 (5)</td>
</tr>
<tr>
<td>Other</td>
<td>18 (3)</td>
<td>4 (1)</td>
</tr>
<tr>
<td>Diseased coronary vessels, No.</td>
<td>23 (3)</td>
<td>8 (3)</td>
</tr>
<tr>
<td>1</td>
<td>111 (16)</td>
<td>32 (11)</td>
</tr>
<tr>
<td>2</td>
<td>562 (81)</td>
<td>263 (87)</td>
</tr>
<tr>
<td>EF &lt; 40%</td>
<td>87 (13)</td>
<td>55 (19)</td>
</tr>
<tr>
<td>Anemia, HCT &lt; 34, %</td>
<td>103 (15)</td>
<td>84 (28)</td>
</tr>
<tr>
<td>Cardiac history</td>
<td>Angina</td>
<td>637 (91)</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>377 (54)</td>
<td>180 (59)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>515 (74)</td>
<td>252 (83)</td>
</tr>
<tr>
<td>Hypercholesterolemia</td>
<td>533 (76)</td>
<td>229 (76)</td>
</tr>
<tr>
<td>Smoking</td>
<td>140 (24)</td>
<td>46 (18)</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>233 (33)</td>
<td>115 (38)</td>
</tr>
<tr>
<td>Stroke</td>
<td>43 (6)</td>
<td>25 (8)</td>
</tr>
<tr>
<td>Preadmission medications</td>
<td>Aspirin</td>
<td>638 (91)</td>
</tr>
<tr>
<td>(\beta)-Blocker</td>
<td>582 (83)</td>
<td>256 (84)</td>
</tr>
<tr>
<td>Diuretics</td>
<td>163 (23)</td>
<td>123 (40)</td>
</tr>
</tbody>
</table>

Abbreviations: CKD, chronic kidney disease; EF, ejection fraction; HCT, hematocrit.
*Data are given as number (percentage) unless otherwise indicated.
†\(P\) values obtained from results of \(\chi^2\) test.
was 77% in the group with stages 4 to 5 CKD (P = .02) (Table 2). Unadjusted MH scores worsened in 10% at 6 months in all strata of CKD (P = .35). However, when the follow-up scores were adjusted for baseline score, no subjects worsened in any of the 3 groups of CKD (Table 2). The odds of improved or worsened MH scores were not different among the stages of CKD after adjusting for a comprehensive set of demographic and clinical variables.

CORRELATION BETWEEN PF AND MH SCORES

Changes in PF and MH scores were significantly correlated in the groups with stages 0 to 2 and stage 3 CKD (r = 0.43, P < .001 and r = 0.38, P < .001, respectively). Changes in PF and MH scores did not correlate in the group with stages 4 to 5 CKD (r = 0.23; P = .11).

SECONDARY OUTCOMES

To ensure internal validity of the MH assessment, changes in MH scores were compared with changes in the abbreviated 15-item Geriatric Depression Scale. There was a strong correlation between the change in the 2 scores (r = 0.49, P < .001). Bodily pain, measured by the bodily pain subscale of SF-36, improved equally among the 3 groups.

Table 2. Physical Function and Mental Health Scores at 6 Months After CABG Stratified by CKD Stage

<table>
<thead>
<tr>
<th>Score, Mean (SD)</th>
<th>Stages 0-2 (n = 780)</th>
<th>Stages 3 (n = 394)</th>
<th>Stages 4-5 (n = 51)</th>
<th>P Value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physical Function Scores</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline score</td>
<td>73 (1)</td>
<td>64 (2)</td>
<td>56 (4)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>6-mo Postsurgery score</td>
<td>85 (1)</td>
<td>78 (1)</td>
<td>63 (4)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Change in score†</td>
<td>14 (1)</td>
<td>9 (1)</td>
<td>−3 (3)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Change in score, adjusted for covariates‡</td>
<td>13 (1)</td>
<td>12 (1)</td>
<td>2 (4)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Improved score, %†</td>
<td>51</td>
<td>59</td>
<td>51</td>
<td>.04</td>
</tr>
<tr>
<td>Worse score, %†</td>
<td>0</td>
<td>0</td>
<td>21</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Mental Function Scores</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline score</td>
<td>72 (1)</td>
<td>72 (1)</td>
<td>62 (3)</td>
<td>.02</td>
</tr>
<tr>
<td>6-mo Postsurgery score</td>
<td>82 (1)</td>
<td>83 (1)</td>
<td>80 (3)</td>
<td>.45</td>
</tr>
<tr>
<td>Change in score†</td>
<td>11 (1)</td>
<td>12 (1)</td>
<td>11 (2)</td>
<td>.76</td>
</tr>
<tr>
<td>Change in score, adjusted for covariates‡</td>
<td>11 (1)</td>
<td>13 (1)</td>
<td>14 (3)</td>
<td>.44</td>
</tr>
<tr>
<td>Improved score, %†</td>
<td>58</td>
<td>56</td>
<td>77</td>
<td>.02</td>
</tr>
<tr>
<td>Worse score, %†</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>ND</td>
</tr>
</tbody>
</table>

Abbreviations: CABG, coronary artery bypass grafting; CKD, chronic kidney disease; ND, no data.

*P values for differences in baseline scores and 6-month postsurgery scores were obtained from results of Wilcoxon rank sum test. P values for differences in changes in score from baseline were obtained from results of analysis of covariance. P values for adjusted changes in scores were obtained from results of analysis of covariance. P values for differences in percentages were obtained from results of χ² test.

†Adjusted for baseline scores.

‡Adjusted model included the following covariates: baseline score; age; sex; current smoking; history of hypertension; angina; diabetes mellitus; cerebrovascular accident and myocardial infarction; depressed left ventricular ejection fraction; anemia; number of diseased vessels; and medications including diuretics, β-blockers, and aspirin.

Our results show a mixed effect of CABG surgery on 2 health-related QOL measures 6 months after the procedure in patients with varying degrees of CKD. Although PF scores were improved in those with moderate (stage 3) CKD (GFR 30-60 mL/min per 1.73 m²), they were not improved in patients with severe (stages 4-5) CKD (GFR < 30 mL/min per 1.73 m²), regardless of the baseline functional status. Alternatively, patients with moderate (stage 3) CKD were able to achieve improvements in physical outcomes similar to those patients with normal or mildly depressed GFR. In contrast, patients from all strata of GFR garnered an improvement in MH scores 6 months after the procedure. Even patients with severe CKD had significant improvements in measures of MH, and these patients were the most likely to have an improvement in their MH score at 6 months.

To our knowledge, there are no previous reports specifically studying health-related QOL in patients with CKD who have undergone CABG. In 2 studies that examined predictors of health-related QOL after CABG, elevated serum creatinine was associated with a lower postoperative PF score in 1 study but not in the other.12,14 In regard to overall health, patients with CKD have a higher frequency of comorbidities such as diabetes mellitus, hypertension, anemia, low ejection fraction, increased clinical severity of CHF, increased frequency of left main and 3-vessel disease, and peripheral vascular disease.1-3 Patients with CKD have more postoperative complications, such as prolonged mechanical ventilation, stroke, bleeding, and longer length of stay.5 Patients with CKD are also more likely to be readmitted to the hospital after CABG surgery.20 Thus, it is plausible that patients with CKD, especially advanced CKD, may not have as great of a beneficial response in PF as the groups with normal or near-normal GFR. In addition, the group with the most
severe degree of CKD (stages 4-5) had no appreciable improvement in overall PF scores, before and after adjustment, which implies that it is not just the associated comorbidities of CKD that are limiting but also some additional factor that is intrinsic to advanced CKD (eg, uremic toxins, immune suppression, or malnutrition). In fact, the uremic milieu is known to impair pulmonary function, impair wound healing, and most relevant to this study, impair muscle function and strength. Indeed, several other studies have found that PF, when measured with validated instruments such as the SF-36, is negatively correlated with GFR. It is not clear why the changes in PF and MH were discordant in the severe CKD group in our study. However, previous data have revealed a discrepancy between PF and MH scores in patients with CKD. In one study, the SF-36 PF and MH scores were only very weakly correlated in patients with end-stage renal disease. In another study, although PF scores were lower in patients with CKD, MH scores in patients with GFR less than 60 mL/min per 1.73 m² were not different from those with preserved GFR. We did find lower MH scores at baseline in the group with stages 4 to 5 CKD, with this group having the largest improvement in MH scores 6 months after undergoing the procedure. Improvement in MH scores across the CKD subgroups could be related to a decrease in anxiety owing to alleviation of bodily pain with surgery. In our study, across all strata of CKD, bodily pain improved. In addition, the improvement in MH scores may also be related to improvement in symptoms of depression because the MH scores correlated well with an improvement in depression.

Although the present study is, to our knowledge, the first to evaluate the health-related QOL outcomes after CABG among patients with CKD, there are limitations that should be considered when interpreting the results of this study. A major limitation is that the group with severe (stages 4-5) CKD is small. Part of this may reflect a bias of surgeons toward performing less surgery in these patients because of the potential for worse postoperative outcomes. In addition, the patients with severe CKD who were selected for surgery were probably healthier than a general cohort of patients with severe CKD because this was not a randomized trial. Another major limitation is that the baseline PF and MH scores were retrospectively obtained at discharge. This may have led to biases in recall of preoperative status, particularly influenced by an individual’s postoperative course. However, previous studies suggest that recall of preadmission health status is valid and reliable. Other limitations include use of the SF-36, which is a general function measure, rather than instruments designed specifically for patients with coronary heart disease. However, the SF-36 has been validated extensively in patients with coronary heart disease and those undergoing CABG. Finally, we are limited by the fact that we do not have a control group of patients with CKD who did not receive CABG to assess what would have happened to QOL measures in the absence of surgery. Unfortunately, to our knowledge, there are no longitudinal studies of changes in health-related QOL in patients with CKD and coronary artery disease who do not undergo CABG.

In conclusion, to our knowledge, this is the first study to quantify the changes in health-related QOL in subjects with varying degrees of CKD. Current American College of Cardiology and American Heart Association guidelines indicate that improvement in QOL is a primary indication for CABG surgery. Patients with CKD typically have a more complicated postoperative course after CABG for several reasons (discussed in the second paragraph of the “Comment” section). It is imperative to include outcomes such as health-related QOL when performing risk-benefit analyses prior to making decisions to proceed with this surgery in certain individuals. The results from this study and future studies in this area with an appropriate control group (those without CABG) may assist in the decision process of whether to pursue CABG in patients with coronary artery disease in those with advanced CKD. Specifically, if our data, which indicate that there is a high likelihood of worsened PF in patients with CKD after CABG surgery, are confirmed by others, and if these new data reveal worsened PF after CABG in comparison with those who do not receive surgical intervention, it may deter some patients with CKD and their physicians from pursuing surgery and provide those who pursue such a strategy with realistic estimates of what they can expect in terms of health-related QOL.

Accepted for Publication: June 12, 2006.
Correspondence: Chirag R. Parikh, MD, PhD, Section of Nephrology, Yale University and VAMC, Clinical Epidemiology Research Center, 950 Campbell Ave, Mail Code 151B, Building 35A, Room 219, West Haven, CT 06516.

Author Contributions: Dr Parikh and Dr Coca had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis; they contributed equally to the study. Study concept and design: Parikh, Vaccarino, and Krumholz. Acquisition of data: Parikh, Vaccarino, and Krumholz. Analysis and interpretation of data: Parikh, Coca, and Smith. Drafting of the manuscript: Parikh and Coca. Critical revision of the manuscript for important intellectual content: Parikh, Smith, Vaccarino, and Krumholz. Statistical analysis: Parikh, Coca, and Smith. Obtained funding: Vaccarino. Administrative, technical, and material support: Parikh, Vaccarino, and Krumholz. Study supervision: Krumholz.

Financial Disclosure: None reported.

Funding/Support: This study was support by a career development award to Dr Parikh from the National Institutes of Health (NIH) and the National Institute of Diabetes and Digestive and Kidney Diseases (grant K23 DK064689); by grants K24 HL077506, R01 HL68630, and R01 AG026255 to Dr Vaccarino from the NIH; by the Ethel F. Donaghue Women’s Health Investigator Program, New Haven, Conn; and by a grant from the Quality Care Research Fund, Aetna Foundation, Hartford, Conn.

Role of the Sponsor: The funding and support organizations had no role in the design or conduct of the study; collection, management, analysis, or interpretation of the data; and preparation, review, or approval of the manuscript.
REFERENCES


11. Vaccarino V, Lin ZQ, Kasi SV, et al. Sex differences in health status after coro-


15. Ferguson TB Jr, Dzubiwa SW Jr, Edwards FH, et al; Committee to Establish a Na-


21. Johansson G, Bergtsson BA, Ahlmen J. Double-blind, placebo-controlled study of growth hormone treatment in elderly patients undergoing chronic hemodi-


24. Colin JF, Elliot P, Ellis H. The effect of uremia upon wound healing: an experi-


26. Chow FY, Briganti EM, Kerr PG, Chadban SJ, Zimmer P, Atkins RC. Health-


29. Knight EL, Ofsthun N, Teng M, Lazarus JM, Curhan GC. The association be-


32. Eagle KA, Guyton RA, Davidoff R, et al; American College of Cardiology; Ameri-


36. Eagle KA, Guyton RA, Davidoff R, et al; American College of Cardiology; Ameri-


40. Eagle KA, Guyton RA, Davidoff R, et al; American College of Cardiology; Ameri-


42. Eagle KA, Guyton RA, Davidoff R, et al; American College of Cardiology; Ameri-


44. Eagle KA, Guyton RA, Davidoff R, et al; American College of Cardiology; Ameri-


46. Eagle KA, Guyton RA, Davidoff R, et al; American College of Cardiology; Ameri-


48. Eagle KA, Guyton RA, Davidoff R, et al; American College of Cardiology; Ameri-


50. Eagle KA, Guyton RA, Davidoff R, et al; American College of Cardiology; Ameri-