Effect of Functional Health-Related Quality of Life on Long-Term Survival After Cardiac Surgery

Colleen Gorman Koch, MD, MS; Liang Li, PhD; Michael Lauer, MD; Joseph Sabik, MD; Norman J. Starr, MD; Eugene H. Blackstone, MD

Background—Health-related quality-of-life instruments have become important measures of early health outcomes after cardiac surgery. The relationship between quality of life after recovery from surgery and subsequent long-term survival has not previously been explored. Our objective was to determine whether the Duke Activity Status Index (DASI) was predictive of subsequent time-related survival after recovery from cardiac surgery.

Methods and Results—We examined survival status among 6305 patients who underwent isolated coronary artery bypass grafting with or without valve procedures or isolated valve procedure between May 1995 and June 1998 who had a preoperative baseline and follow-up DASI. The postoperative DASI was administered nominally at 6 and 12 months. Baseline and perioperative variables and postoperative morbid events were prospectively collected concurrently with patient care. The end point was all-cause mortality. The Social Security Death Index was queried for survival status. Cox proportional-hazards analysis was used to study the associations between DASI, a number of traditional risk factors, and survival. Median follow-up was 8.6 years. The “dose-response” relationship between baseline and follow-up DASI and risk of long-term death was established. Follow-up DASI was associated with risk-adjusted long-term survival hazard ratio of 0.98 per unit increase (confidence limits, 0.97 to 0.98; \( P<0.0001 \)). Achieving maximum baseline DASI was associated with better risk-adjusted long-term survival (hazard ratio, 0.64; confidence limits, 0.50 to 0.83; \( P=0.0005 \)).

Conclusions—Poor health-related quality of life after recovery from cardiac surgery identifies patients who are at risk for reduced long-term survival. (Circulation. 2007;115:692-699.)

Key Words: mortality • quality of life • surgery • survival

Risk factors for long-term survival after cardiac surgery have traditionally involved clinical variables such as demographics, comorbidity, and operative factors.1–6 Health-related quality-of-life instruments represent another dimension of health status that summarizes the patient’s outlook regarding the impact of disease on overall health status.7,8 Increasingly, patient-reported health status has become important as a predictor of early morbid outcomes after cardiac surgery.2,7,9

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Our objective was to determine whether functional health-related quality of life as measured by the Duke Activity Status Index (DASI)10,11 was predictive of long-term survival after recovery from cardiac surgery. The relationship between follow-up quality of life and survival after recovery from cardiac surgery has not previously been explored.

Methods

Patient Population

The initial study population included 12,130 consecutive patients who underwent on-pump cardiac surgical procedures between May 1, 1995, and December 31, 1998. The exclusion criteria as shown in the Consolidated Standards of Reporting Trials (CONSORT)–style diagram in Figure 1 were applied and resulted in a working data set of 6305 patients who underwent isolated coronary artery bypass grafting (CABG) with or without valve procedures or an isolated valve procedure. All patients had a baseline and at least 1 follow-up DASI survey. Baseline and perioperative variables were prospectively collected concurrently with patient care and entered into the Cleveland Clinic Department of Cardiothoracic Anesthesia Registry and Cardiovascular Information Registry. These databases have been approved for research by the Institutional Review Board. Characteristics of the patient population are described in Table 1.

Duke Activity Status Index

The DASI is a disease-specific quality-of-life questionnaire that has been validated for patients with cardiovascular disease.5,11 The 12-item instrument measures activities of daily living for which each item is weighted by its known metabolic cost, and weights of positive terms are summed to form the individual patient DASI score. Higher scores represent better physical functioning10,11 (Table 2). The baseline DASI instrument was self-administered to patients in the preoperative period. If a patient was unable to complete the DASI independently, a trained research assistant read the exact wording of the survey. The follow-up DASI was completed via a telephone interview at nominally 6 and 12 months postoperatively.
Outcome

The end point was all-cause mortality. Vital status was obtained from the US Social Security Death Index. Registry records were linked to the death data on the basis of key identifiers such as patient name, date of birth, social security number, and gender, as well as date last known alive and state of last known residence. The Social Security Death Index data were pulled on January 31, 2006. Because our institution is a large international referral center, 947 patients did not have social security numbers and were excluded.

Statistical Analyses

Preliminary Analysis

Before modeling, summary statistics for the patient population were examined. There were <4% missing values for albumin, bilirubin, and distribution of coronary artery disease for left main trunk, left anterior descending, left circumflex, and right coronary arteries. Because missing values were sporadic, we replaced them with the average of the nonmissing values.

Survival Analysis

The objective was to examine the predictive ability of follow-up DASI on survival for patients who were considered recovered from the surgical procedure. Survival was right censored by using July 31, 2005, as the closing date for Social Security Death Index (6 months before the date of data pull to adjust for the reporting lag of the Social Security Death Index). Time from surgery to follow-up DASI ranged from 3 to 15 months. If a patient had 2 follow-ups, only the second DASI score was used. Because patients were included in this study only when they had a follow-up DASI score, survival was considered left truncated by the time of follow-up DASI assessment.

Cox proportional-hazards survival analysis with left truncation was used to study the association between survival and a number of traditional risk variables. We considered preoperative and intraoperative variables and postoperative morbid events as potential prognostic factors for survival (Table 1). Variable selection for the final model was done by stepwise model selection. Baseline and follow-up DASI scores are semicontinuous variables with data clustered at its maximum value, representing a ceiling effect. Figure 2 displays the distribution of DASI scores that illustrates this ceiling effect.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Summary Statistics* (N=6305)</th>
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<tbody>
<tr>
<td>Demographics</td>
<td>Age, y 66 (57.73)</td>
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<tr>
<td></td>
<td>Male, n (%) 4335 (68.75)</td>
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<tr>
<td></td>
<td>BMI, kg/m² 27.17 (24.39, 30.46)</td>
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<tr>
<td>Preoperative laboratory values</td>
<td>Hematocrit, % 40 (37.43)</td>
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<tr>
<td></td>
<td>Albumin, mg/dL 4.2 (3.8, 4.4)</td>
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<td></td>
<td>Creatinine, mg/dL 1.0 (0.9, 1.2)</td>
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<td></td>
<td>Bilirubin, mg/dL 0.7 (0.5, 0.9)</td>
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<tr>
<td>Cardiac morbidity, n (%)</td>
<td>Abnormal LVF 2951 (47)</td>
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<tr>
<td></td>
<td>Heart failure 1519 (24)</td>
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<tr>
<td></td>
<td>NYHA class I 861 (14)</td>
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<td></td>
<td>NYHA class II 2999 (48)</td>
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<td></td>
<td>NYHA class III 999 (16)</td>
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<td></td>
<td>NYHA class IV 1446 (23)</td>
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<td></td>
<td>Prior myocardial infarction 2408 (38)</td>
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<tr>
<td>Clinical presentation, n (%)</td>
<td>Cardiogenic shock 15 (0.24)</td>
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<td></td>
<td>Preoperative IABP 130 (2.1)</td>
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<td></td>
<td>Emergency surgery 108 (1.71)</td>
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<td>Comorbidity, n (%)</td>
<td>Hypertension 3651 (58)</td>
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<td></td>
<td>COPD 450 (7.1)</td>
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<tr>
<td></td>
<td>Smoking 3727 (59)</td>
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<td>Diabetes mellitus 572 (9.1)</td>
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<td></td>
<td>Stroke 380 (6)</td>
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<td></td>
<td>PVD 635 (10)</td>
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<td>Perioperative factors</td>
<td>Aortic clamp time, min 75 (56, 96)</td>
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<td></td>
<td>RBC in OR, n (%) 2047 (32)</td>
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<td>RBC in ICU, n (%) 1776 (28)</td>
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<td>FFP transfusion, n (%) 209 (3.3)</td>
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<td>Platelet transfusion, n (%) 807 (13)</td>
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<td></td>
<td>Reoperation, n (%) 1393 (22)</td>
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<tr>
<td>Coronary disease, &gt;70% stenosis, n (%)</td>
<td>Left main trunk 533 (8.4)</td>
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<tr>
<td></td>
<td>Left anterior descending 3759 (60)</td>
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<tr>
<td></td>
<td>Left circumflex 3133 (50)</td>
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<tr>
<td></td>
<td>Right coronary artery 3429 (54)</td>
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<td>Operative procedure, n (%)</td>
<td>CABG 4680 (74)</td>
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<td>Valve procedure 2577 (41)</td>
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<td></td>
<td>LITA 3202 (51)</td>
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<td></td>
<td>RITA 721 (11)</td>
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<td>Postoperative morbid events, n (%)</td>
<td>Infection 108 (1.7)</td>
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<td></td>
<td>Neurological 82 (1.3)</td>
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<td></td>
<td>Cardiac 56 (0.89)</td>
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<td></td>
<td>Renal 21 (0.33)</td>
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</table>

LVF indicates left ventricular function; NYHA, New York Heart Association; IABP, intra-aortic balloon pump; COPD, chronic obstructive pulmonary disease; PVD, peripheral vascular disease; RBC, red blood cell; OR, operating room; ICU, intensive care unit; FFP, fresh frozen plasma; CABG, coronary artery bypass graft; LITA, left internal thoracic artery; and RITA, right internal thoracic artery.

*Continuous variables are expressed as median (25th quintile, 75th quintile); categorical variables are summarized by count (percentage).
†There are missing data for left main trunk in 19 patients; for left anterior descending in 16 patients; for left circumflex in 16 patients; and for right coronary artery in 16 patients.
effect value. Therefore, a variable was created to indicate that a patient had reached this ceiling value. This ceiling effect variable was analyzed, along with the continuously recorded DASI scores. For better illustration of the “dose-response” relationship between DASI and long-term risk of death, we represented DASI by 7 groups of increasing functional capacity (1/H11005 to 10, 2/H11005 to 20, 3/H11005 to 30, 4/H11005 to 40, 5/H11005 to 50, 6/H11005 to 58.2, and 7/H11005). Adjusted risk and unadjusted risk of survival were compared among groups and are illustrated graphically.

Model diagnostics demonstrated that body mass index (BMI) may have a bowl-shaped relationship with long-term survival, with its middle range corresponding to the lowest risk of mortality. Hence, a conventional linear-type model would fail to capture this nonlinear relationship. This is modeled parsimoniously by a segmented regression approach. The 2 linear segments model the risk associated with BMI within the range of BMI <30 kg/m² and BMI >30 kg/m², respectively, with different slopes and a joint at BMI =30 kg/m². Interactions between the key predictors (baseline and follow-up DASI scores) were tested; none were found to be significantly related to survival.

All authors had full access to the data and take responsibility for their integrity. All authors have read and agree to the manuscript as written. The Cardiothoracic Anesthesia Registry and the Cardiovascular Information Registry have been approved by the Institutional Review Board for research purposes, and individual patient consent was waived. All results were obtained with SAS 8.2 software, SAS Institute (Cary, NC).

**Results**

**Duke Activity Status Index**

Most patients reported improvement in functional quality of life after surgery (Figure 2). Seventeen percent of patients had a preoperative baseline DASI score at the ceiling value (58.2), whereas 43% of them achieved this value when tested 3 to 15 months after surgery.

**Survival**

Median follow-up was 8.6 years for the 6305 patients. Twenty-seven percent of patients (n=1687) died during the follow-up interval; their median time to death was 5.1 years. Survival at 1, 2, 4, 6, and 8 years after surgery was 99.4%, 96.7%, 90.6%, 83.4%, and 75.4%, respectively.
DASI and Survival

Figure 3 illustrates the dose-response relationship between DASI and survival, univariately and in conjunction with other variables (Table 3). The risk-unadjusted association between baseline (Figure 3a) or follow-up DASI (Figure 3b) and log mortality hazard ratio (HR) appeared to be linear, although there is a little curvature in baseline DASI. When both baseline and follow-up DASI scores are considered together (Figure 3c), the range of log HRs both shrink from −2.0 to 0.0 to −1.5 to 0.0. The reason is that the 2 DASI scores are correlated, and the effect of one is partially explained by the other. With the addition of other covariates in Table 3 (Figure 3d), further shrinkage in the log hazard is seen, particularly for the curve for baseline DASI, and there is more shrinkage for lower values of baseline DASI than near the ceiling value. The more correlated these other covariates are with DASI, the more likely its effect is partially explained by those covariates and the more its log HR shrinks. What has been illustrated in Figure 3d using DASI groups is represented in Table 3 by the pair of entries for baseline and follow-up DASI on the continuous scale, where the slump in log HR at group 7 is represented by the indicator variable for reaching the ceiling value. Another manifestation of the dose-response relationship between DASI and risk of death for selected groups is presented in the survival curves for baseline and follow-up DASI in Figure 4.

The other covariates in Table 3 are mostly preoperative, which naturally correlate more with the baseline DASI score. Almost all covariates in Table 3 measure morbidity or degree of illness. None measure the degree of patient health. However, the DASI score contains information about good health (an important aspect of quality-of-life measures). Therefore, the confounders are more likely correlated with DASI among patients with a ceiling value <58.2 than among patients with the ceiling value. As a result, they more likely enroach the effect of baseline DASI in the range of <58.2 than for the 58.2 group. That causes different shrinkage as described above and leads to the results in Figure 3 and Table 3.

Other Factors and Survival

Additional variables significantly related to the risk of long-term mortality after recovery from surgery include older age, higher preoperative creatinine, abnormal left ventricular function, preoperative heart failure, reoperation, and comorbidities such as chronic obstructive pulmonary disease, smoking, hypertension, diabetes, and peripheral vascular disease (see Table 3). Operative factors such as fresh frozen plasma transfusion and increasing aortic clamp time also increased the hazard for mortality during the follow-up period. High preoperative hematocrit and albumin values and right internal thoracic artery grafting were associated with improved survival after recovery from surgery. BMI also is a related factor, but its effect appears to have a U-shaped relationship. For example, we found that in the range of <30 kg/m², increasing BMI is associated with reduced risk of death (HR=0.98; P=0.03), whereas in the range of >30 kg/m², increasing BMI is associated with increased risk of death (HR=1.035; P=0.0007). In other words, the lowest risk corresponds to the middle range of BMI, whereas being too lean or too obese is associated with worse survival. Of course, the actual relationship between BMI and survival is likely continuous and does not have a sharp changing point at 30 kg/m². But, our model is a parsimonious representation of this nonlinear relationship.

Responders Versus Nonresponders

The 1094 patients who failed to respond to the follow-up DASI survey were similar for most demographic variables,
comorbidities, and operative procedures to the responders. The 2 groups had similar median baseline DASI scores (responders, 30; nonresponders, 32; \( P = 0.17 \)). Responders were older, with a median age of 66.5 years compared with 65 years for the nonresponders (\( P < 0.001 \)). There was higher red blood cell transfusion in the nonresponder group (red blood cell transfusion in the operating room: 32% for responders, 34% for nonresponders, \( P = 0.007 \); red blood cell transfusion in the intensive care unit: 28% for responders, 34% for nonresponders, \( P = 0.012 \); and platelet usage (yes/no): 13% for responders, 15% for nonresponders, \( P = 0.043 \)).

**Discussion**

**Principal Findings**
Overall functional health-related quality of life improves after recovery from cardiac surgery. Lower functional health-related quality of life beyond the posthospital recovery phase after cardiac surgery is predictive of reduced long-term survival even after adjustment for known risk factors associated with survival after cardiac surgery. The degree of functional recovery is directly related to subsequent survival.

What can be analogous to a dose-response curve between DASI and risk of death is illustrated in Figure 3, which
depicts the reduction in risk of long-term mortality and increasing DASI scores.

In the noncardiac surgical populations, health-related quality-of-life information has offered important prognostic information. A recent investigation by Rodriguez-Artalejo and colleagues reported that the Short Form-36 yielded important prognostic information regarding hospital readmission and death among patients with heart failure. Similarly, Soto and colleagues found that health status, as measured with the Kansas City Cardiomyopathy Questionnaire, was associated with 1-year cardiovascular mortality and hospitalization in patients with heart failure after acute myocardial infarction. Spertus and colleagues reported that quality of life as measured with the Seattle Angina Questionnaire further identified patients at high risk for 1-year mortality in patients with coronary disease. The authors suggested that identification of these high-risk patients could lead to implementation of interventions to possibly improve patient outcomes.

The DASI health-related quality-of-life questionnaire is a disease-specific instrument that accurately accesses functional capacity on the basis of peak oxygen uptake associated with aspects of quality of life. Although we were unable to find prior studies examining the relationship between quality of life beyond the postsurgical recovery phase and survival, a number of investigations relate low peak oxygen uptake to reduced survival. In heart failure patients, Myers and colleagues reported that, in contrast to a number of demographics, hemodynamic variables, and right-heart catheterization data, peak oxygen uptake was a significant predictor for death among patients referred for heart failure evaluation. This measure of functional impairment has become an important indicator for selection of heart failure patients for cardiac transplantation because low values have been associated with reduced survival.

Unlike this study, some investigations have related quality of life to short-term morbid outcomes after cardiac surgical procedures. However, none of these investigated an effect of quality-of-life status on long-term survival after recovery from surgery.

Functional health-related quality of life improves for most patients after cardiac surgery (see Figure 2). Our findings are similar to a number of other investigations that report improvements in health-related quality of life after cardiac surgical procedures as measured with a number of different quality-of-life instruments. Jarvinen and colleagues reported improvements in quality of life and functional capacity among CABG patients 1 year after surgery with the use of the RAND-36 Health Survey. Welke and colleagues reported improvements in physical functioning and mental function 6 months after isolated CABG with the Short Form-36. Similarly, using the Short Form-36 survey, Rumsfeld and colleagues demonstrated improvement in physical and mental health status after CABG.

Clinical Implications

Our results raise questions about whether our findings could be altered by postsurgical interventional measures such as participation in cardiac rehabilitation programs. For example, could participation in cardiac rehabilitation improve a patient’s functional status and risk factor profile to the extent that it could improve survival? Enrollment and participation in cardiac rehabilitation programs has traditionally been low. Pasquali and colleagues reported improved physical functioning and adoption of secondary preventive measures in patients with coronary disease who participated in cardiac rehabilitation. Lindsay and colleagues noted higher overall general Short Form-36 health scores in CABG patients who attended cardiac rehabilitation programs. Others have demonstrated that even short-term cardiac rehabilitation has a positive impact on quality-of-life scores. Perhaps increased physician referral would improve participation in these programs. Furthermore, could cardiac rehabilitation services be modified to meet the need of the subset of patients with low functional status scores? For example, should these high-risk patients remain in cardiac rehabilitation until a set of functional status measures are met? Certainly, investigation is needed to determine whether methods to improve functional health status such as cardiac rehabilitation translate into improved survival.
Other Risk Factors for Survival

Demographic variables such as increasing age and BMI >30 kg/m², laboratory values, and comorbidities such as chronic obstructive pulmonary disease, diabetes mellitus, hypertension, smoking, and peripheral vascular disease also were related to reduced survival in our investigation. Cardiac factors such as abnormal left ventricular function, heart failure, and reoperation, as well as operative variables such as aortic clamp time, valve procedures, lack of internal thoracic artery use, and administration of fresh frozen plasma, were associated with reductions in long-term survival. Others have reported similar traditional risk factors for reduced survival after cardiac surgery.1–3,6,33,34

Study Limitations

Our investigation was performed at a single-center tertiary referral center, which may limit the generalizability of the study findings. However, our study population represents a large number of patients with an extensive list of prospectively collected demographic, clinical, and operative factors related to patient care and data that include both a preoperative baseline and follow-up measures of functional quality of life.

Quality of life involves both physical and mental dimensions. Mental health status was not captured in our functional quality-of-life instrument. A number of investigations have reported that poor mental health status adversely affects outcome after cardiac surgery.35–37 Furthermore, the relationship between functional recovery and mental health appears to be interrelated. Mallik and colleagues38 reported that moderate to severe perioperative depression was associated with less improvement in physical functioning after CABG.

Conclusions

The unique feature of this investigation is that we have examined the effect of health-related quality of life on survival in the intervening years after cardiac surgery. Poor functional status beyond the postrecovery phase after cardiac surgery identifies patients at high risk for reduced long-term survival. The ability to identify these patients presents an opportunity for potentially improving survival through more aggressive referral to cardiac rehabilitation and by modifying and extending participation in rehabilitation for those patients most functionally impaired. Whether interventional measures would affect survival remains to be investigated.

Disclosures

None.

References

23. Mancini D, LeJemtel T, Aaronson K. Peak VO(2): a simple yet enduring health-related quality of life instrument. A number of investigations have reported that poor mental health status adversely affects outcome after cardiac surgery.35–37 Furthermore, the relationship between functional recovery and mental health appears to be interrelated. Mallik and colleagues38 reported that moderate to severe perioperative depression was associated with less improvement in physical functioning after CABG.
Health-related quality-of-life assessments have not always been at the forefront of risk assessment in patients with cardiac disease. Increasingly, these instruments have been predictive of a number of “hard” outcome measures after cardiac interventions. Using a validated functional health status measure, the Duke Activity Status Index, we examined the relationship between functional quality of life after recovery from cardiac surgery and subsequent long-term survival. We report that overall functional health-related quality of life improves after recovery from cardiac surgery. Poor functional status beyond the postrecovery phase identifies patients at risk for reduced long-term survival, even after adjustment for known risk factors associated with survival after cardiac surgery. Identification of subgroups of patients at high risk could perhaps allow for interventional measures such as participation in cardiac rehabilitation services to improve functional health status and possibly to improve survival.
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