Predictors of Cognitive Recovery After Cardiac Surgery

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Abstract

Background—Postoperative neurocognitive decline occurs frequently. Although predictors of cognitive injury have been well examined, factors that modulate recovery have not. We sought to determine the predictors of cognitive recovery after initial injury following cardiac surgery.

Methods—Two hundred eighty-one patients previously enrolled in cognitive studies who experienced cognitive decline 6 weeks after cardiac surgery were retrospectively evaluated. Eligible patients completed a battery of neurocognitive measures and quality-of-life assessments at baseline, 6 weeks, and 1 year after surgery. Factor analysis was conducted to calculate the cognitive index (CI), a unified, continuous measure of cognitive function. Cognitive recovery was defined as 1-year CI   baseline CI. Potential predictors of cognitive recovery including patient characteristics, quality-of-life factors, comorbidities, medications, and intraoperative variables were assessed with multivariable regression modeling; p<0.05 was considered significant.

Results—Of the 229 patients in our final dataset, 103 (45%) demonstrated cognitive recovery after initial decline in CI at 6 weeks. Multivariable analyses revealed that more education (OR 1. 332 [1. 131-1. 569], p<0. 001), baseline CI (OR 0. 987 [0. 976–0. 998], p=0. 02), less decline in CI at 6 weeks (OR 1. 044 [1. 014–1. 075], p=0. 004), and greater activities of daily living at 6 weeks (OR 0. 891 [0. 810–0. 981], p=0. 02) were significant predictors of cognitive recovery.

Conclusion—Cognitive recovery occurred in approximately one-half of the cardiac surgical patients experiencing early decline. The association between cognitive recovery and Instrumental Activities of Daily Living scores at 6 weeks merits further investigation as it is the only potentially modifiable predictor of recovery.

Introduction

Postoperative cognitive injury is characterized by decline of such mental functions as perception, memory, and information processing after a surgical procedure. [1,2] The occurrence of cognitive dysfunction after coronary artery bypass graft (CABG) surgery is frequent and persistent with 30 to 65% of patients showing cognitive injury at 6 weeks after surgery. [2–5] Despite surgical advancements reducing the once high mortality and morbidity rates associated with CABG, only a few strategies[6, 7] have been proposed to moderate postoperative cognitive decline and the associated reduction in quality of life. [8] Preoperative risk factors for cognitive injury after surgical intervention include age, level of education, baseline cognition and genetic predisposition.[2, 3, 9, 10] The hypothesized surgical risks for cognitive decline include cerebral embolism, cell salvage, valve surgery, hypoperfusion, systemic inflammatory responses, hemodilution, hyperglycemia, and hyperthermia. [3, 10–13]

Preoperative and perioperative factors associated with dysfunction have been well documented; nonetheless, there is much uncertainty and controversy surrounding the underlying pathophysiology, clinical sequelae, and chronicity of the phenomenon. It remains unclear in the literature whether short-term changes in cognitive performance lead to long-term postoperative declines. In a longitudinal study assessing neurocognitive function after

CABG, Newman et al. reported that impairment at discharge was associated with a decline from baseline function 5 years after surgery. [2] Other evidence suggests that postoperative cognitive dysfunction (POCD)is transient in nature, with no relationship between immediate and delayed cognitive injury. [5, 14] With the inclusion of a control group and adjustment for the variability of within-subject score changes, Selnes et al. found that while some cognitive dysfunction occurred directly after CABG, there were no significant differences in long-term cognitive decline between patients who had undergone CABG surgery and nonsurgical controls with diagnosed coronary artery disease. [14] Although these observations are of empirical importance to the phenomenon of cognitive decline, they have not identified factors that influence recovery from cognitive injury after cardiac surgery. Understanding the unique factors that contribute to recovery after postoperative cognitive injury may expedite overall recovery, inform risk stratification allowing for improved patient-family education, advance prevention models, and generate implications for treatment, thereby increasing the quality of life for cardiac surgical patients. We therefore sought to identify predictors associated with a return to baseline levels of cognitive performance after initial postoperative injury.

Methods

Study Population and Procedure

After IRB approval, 281 patients undergoing elective cardiac surgery (CABG, Valve, or CABG + Valve) with cardiopulmonary bypass from February 2000 to August 2009 who demonstrated cognitive decline 6 weeks after surgery in prospective cognitive trials[4, 10, 12, 15, 16] and had complete data at baseline, 6-weeks, and 1-year assessments were retrospectively evaluated. The requirement for written informed consent was waived by the IRB. Patients were excluded from the parent trials if they presented with characteristics known to have confounding effects on cognition including a history of symptomatic cerebrovascular disease with residual deficit, psychiatric illness (any clinical diagnoses requiring therapy), hepatic insufficiency (liver function tests > 1. 5 times the upper limit of normal), and renal insufficiency (creatinine levels > 2 mg/dL), and who were unable to read and thus unable to complete the cognitive testing or who scored < 24 on a baseline Mini Mental State examination. Patients who experienced an adverse postoperative event, such as a subsequent cardiac event were also excluded in order to create a more homogenous population and to isolate the effect of baseline characteristics on 1-year cognitive functioning. Of note, patients suffering from depression after surgery were not excluded.

Measures

Neurocognitive Assessment—To evaluate cognitive function, trained psychometricians administered a neurocognitive test battery at baseline (1. 61 ± 1. 74 days before surgery), 6 weeks, and 1 year after surgery including the Short story module of the Randt Memory Test, a reliable measurement of discourse memory (immediate and delayed) and oral language comprehension;[17] the Modified Visual Reproduction Test from the Wechsler Memory Scale on which patients are required to reproduce from memory several geometric shapes both immediately and after a 30-minute delay, testing for short- and long-term figural memory;[18] the Digit Span subtest of the Wechsler Adult Intelligence Scale-Revised (WAIS-R) examination, a measure of short-term auditory memory and attention that calls on subjects to repeat a series of digits that have been orally presented to them both forward and, in an independent test, in reverse order;[18] the Digit Symbol subtest of the WAIS-R, an evaluation of psychomotor processing speed, in which number-symbol pairs are transcribed under timed conditions;[18] and the Trail Making Test Part B, a timed test in which patients connect alternately letters and numbers in order to assess processing speed, attention, and mental flexibility. [19]

Quality of Life Testing—To identify quality-of-life outcomes, the following assessments were also administered at baseline, 6 weeks, and 1 year after surgery:

1. The Duke Activity Status Index (DASI). [20] A 12-item instrument designed specifically to evaluate functional status and physical capabilities in cardiovascular populations. Limitations experienced by the patients during household tasks, personal care, leisure activities, sexual function, and ambulation were reported on a 4-point Likert scale.

2. The Duke Older Americans Resources and Services Procedures- Instrumental Activities of Daily Living (OARS-IADL). [21] Six IADL items from the OARS are used to measure patients' ability to perform important daily self-care activities (e. g. "Could you prepare your own meals?" "Could you do errands, such as shopping for groceries or household necessities?"). Higher scores indicate increasing difficulty in engaging in daily activities.

3. The Medical Outcomes Study 36-item Short Form Health Survey (SF-36). A survey of health-related limitations and general health conditions used to assess overall health status. [22] Two scales were used: General Health (one item) and Work Activities (four items). Higher Work Activities scores indicate more health-related difficulties.

4. A social activities measure that indicates degree of social interaction (e. g. "About how often do you visit with friends and relatives?"), with lower scores indicating more social activity.

5. A symptoms limitations checklist on which patients were asked how often various symptoms (e. g. angina, shortness of breath, arthritis, etc.) restricted daily activities. [23] Higher scores signified greater limitations.

6. The Center for Epidemiological Studies Depression Scale. [24] Clinically significant depression is indicated by a score of 16 or higher.

7. The State-Trait Anxiety Inventory. [25] A 20-item instrument used to measure anxiety on which patients are asked how frequently they experienced a particular symptom (e. g. "I feel worried" "I feel nervous"), on a 4-point Likert scale ranging from "not at all" to "very much so."

8. The Perceived Social Support Scale. An assessment of global social support on which patients are asked how often various types of support are available to them. [26]

9. The Cognitive Difficulties Scale. An instrument (based on a 5-point Likert scale) of self-perceived cognitive deficits in memory, concentration, attention, and psychomotor coordination. [27]

Statistical Analysis

To account for the correlation among cognitive test scores, baseline raw test scores were subjected to a factor analysis as previously described[2]. To maintain consistent factor definitions across time, follow-up scores were calculated using weights resulting from this baseline analysis. Analysis yielded independent scores representing 4 cognitive domains: 1) verbal memory and language comprehension; 2) attention, psychomotor processing speed, and concentration; 3) abstraction and visuospatial orientation; and 4) figural memory.

To quantify overall neurocognitive function a composite cognitive index score (CI) was calculated as a mean of the four domain scores. This unified index score has been shown to be a stronger correlate of quality-of-life outcomes than the individual domain scores. [8]

Patients who showed any decline in CI score from baseline to 6 weeks were considered "decliners" and comprised the analysis dataset. The outcome variable cognitive recovery was then defined dichotomously as 1-year CI ≥ baseline CI. The association between cognitive recovery at 1 year and potential predictors including patient characteristics, quality-of-life factors, comorbidities, medications, and intra operative variables was assessed with chi-square tests for categorical variables and t-tests for continuous variables, followed by multivariable logistic regression modeling. Based on previous findings demonstrating significant associations with neurocognitive outcomes, three variables (age, years of education, and baseline cognition) were prespecified for inclusion in the model. [2, 9] To avoid model overfitting, based on the number of outcomes in our sample we selected the 7 additional variables with the lowest univariate p-values to incorporate into the multivariable modeling. Nonsignificant variables were individually dropped from the multivariable models until only significant variables remained; $p < 0.05$ was considered significant. Model fit and discrimination were evaluated using the Hosmer-Lemeshow goodness-of-fit test and the area under the receiver operating characteristic curve (c-index).

In secondary analysis, continuous change between 6 weeks and 1 year (rather than the dichotomous variable based on a return to baseline) was assessed using multivariable linear regression. Similarly, we assessed cognitive decline at 6 weeks as a 1 standard deviation or more decline in at least 1 of the 4 cognitive domains with cognitive recovery defined as a return to baseline at 1 year.

Results

Of the 281 patients who had demonstrated a decline in CI from baseline to 6 weeks after surgery, 52 patients were excluded due to 54 major cardiac events in the first year (10 cardiac surgeries and 44 deaths). Of the 229 "decliners" in our final analysis dataset, 178 underwent CABG surgery, 32 had CABG + valve surgery, and 19 had valve surgery alone. Forty-five percent (95% CI: 38.5 – 51.5) of the patients (103/229) experienced cognitive recovery while 55% (126/229; 95% CI: 48.5 – 61.5) remained below baseline at 1 year assessments. With regard to age, gender, comorbidities, surgical characteristics, statin use, depression, anxiety, marital status, and level of social support, no significant differences were observed between those patients who showed cognitive recovery and those who did not (Table 1).

Predictors of Change in Neurocognitive Function

Patients who demonstrated cognitive recovery one year after surgery were more likely to be Caucasian (89% vs. 79%; p = 0.04) and declined less between baseline and 6 weeks than those who did not recover at one year (−0.16±0.15 vs. −0.23±0.23; p = 0.01). In addition, cognitive improvement at 1-year post surgery was related to lower IADL scores (higher IADL scores reflect worse daily functioning) 6 weeks after surgery (8.7±3.8 vs. 10.8±5.3, p = 0.006) (Table 1). Multivariable logistic regression revealed four independent predictors of cognitive recovery: years of education (p < 0.001), baseline CI (p = 0.02), amount of cognitive decline between assessments at baseline and 6 weeks after surgery (p = 0.004), and greater functional performance (lower IADL scores) at 6 weeks postoperatively (p=0.02) (Table 2). The c-index for this model was 0.77, indicating moderately good discrimination of subjects. The Hosmer-Lemeshow test chi-square value was 11.73, p=0.16, indicating that the observed event rates match the expected event rates. By examining the influence diagnostic plots, we found that there are 3 data points which are not well accounted for by the model, and which may exert a large effect on goodness of fit. To determine if our significant association was affected by these data points, we conducted a follow-up analysis excluding these data points. The model c-index improved to 0.79 and the

p-value for IADL to p=0. 002. The association between IADL and probability of recovery is depicted in Figure 1.

This association between IADL scores and cognitive recovery remained significantin the secondary analysis, in which cognitive improvement was assessed as a continuous outcome. IADL also remained a predictor of return to baseline at 1 year when cognitive decline was defined as a 1 standard deviation or more decline in at least 1 of the 4 cognitive domains at 6 weeks. Cognitive recovery at one year (return to baseline) using this 1 standard deviation definition was seen in 40% (95% CI: 31. 1 – 48. 6). Post hoc analysis incorporating the patients who had been excluded for a subsequent cardiac event showed that the adverse event itself was not a significant predictor of cognitive recovery and did not alter the predictive capacity of the other variables in the model.

Discussion

To our knowledge, this is the first study to identify factors associated with cognitive improvement after early cognitive decline in patients undergoing cardiac surgery. We found that almost one-half of the patients who exhibited cognitive decline 6 weeks after cardiac surgery demonstrated cognitive recovery by 1 year. We also identified four predictors that were associated with one-year recovery including higher education level, baseline cognitive performance, less cognitive decline between baseline and 6 weeks, and lower IADL scores at 6 weeks (i. e. better functional performance).

In support of previous studies which showed an association between level of education and cognitive performance, [28–39] we found a relationship between level of education and cognitive recovery after an initial decline. Possible explanations for this effect may lie in education's influence over important environmental and neurological factors. Less educational attainment may put one at greater risk for cognitive deterioration, decreasing the likelihood of cognitive recovery through its association with other potential risk factors such as nutritional deficiencies, less health care access, psychiatric illness, or exposure to increased occupational hazards. [29,30] Education may also directly influence brain structures early in development, resulting in increased synapses or vascularization and leading to improved lifetime cognitive function and brain plasticity. [28, 30], [31, 34] Alternatively, education may lead to a reserve of cognitive capacity that does not alter vulnerability to decline, but delays the appearance of clinical symptoms and/or compensates for early cognitive injury.[40]

Cognitive performance at 6 weeks also was a significant predictor of cognitive recovery at 1 year. Similar to quantity of education, heightened cognitive function can result in increased neuronal count and network capacity, efficiency, or compensation that may decrease risk for future cognitive impairment and increase ability to recover from cognitive damage. [31, 38, 40] Additionally, increases in cognitive function reflect lifestyle patterns that promote stimulation and recovery, thereby preventing or delaying cognitive decline. Epidemiologic studies have found slower rates of decline among those who routinely engage in more cognitively demanding tasks such as reading books and newspapers, playing cards, watching television, and solving puzzles than those who lead less cognitively engaged lifestyles. [31, 40]

Our finding that heightened IADL performance 6 weeks after surgery is associated with the likelihood of cognitive recovery at 1year after initial decline supports the previous findings of an association between functional status and cognition. [41–48] IADL are complex, adaptive behaviors that facilitate independent living, reflect on one's functional capacity, and include the following activities: meal preparation, telephone use, medication management, transportation, financial management, housekeeping duties, and shopping. [42, 46, 48]

Functional impairment is first expressed among instrumental activities[44, 46, 49] and is an essential feature for the diagnosis of dementia. [44] In other words, functional disability as shown by poor performance on IADL items separates individuals with severe cognitive dysfunction from those with moderate to no cognitive deficit. The functional changes associated with such cognitive decline have repercussions expanding from the individual (e. g. decreased quality of life, increased dysphoria and low self-efficacy) to the communal level (e. g. premature institutionalization, increased caregiver burden, and higher health care costs). [50] The association between increased functional status in the early postoperative period and the likelihood of cognitive recovery in the later postoperative stages suggests that interventions which encourage the performance of instrumental activities immediately after surgery may result in improved cognitive performance.

The DASI, also a measure of functional status, was not found to significantly predict cognitive recovery. Unlike the IADL, which focuses on daily activities that involve planning or increased cognitive control (e. g. can you handle your own money, pay bills, write checks, balance checkbook?), the DASI concentrates more on the completion of more physically demanding or mechanical activities (e. g. can you climb a flight of stairs or walk up a hill?). [51] Both instruments assess functional status and assess ability to perform routine activities; however, the IADL approaches functional capacity from a cognitive framework, and IADL impairment reflects difficulty in organizing, initiating, and performing actions, whereas DASI impairment suggests increased physical limitations, possibly as a result of poor cardiac function. Because the IADL inherently addresses functional capacity with a cognitive component, this distinction may help explain why IADL scores predict future cognitive recovery while DASI scores do not.

Similar to the DASI, the two SF-36 subscales were found to have no significant predictive relationship to cognitive recovery. The SF-36 and the IADL, both measures of quality of life, differ in test objective and agenda. The SF-36 was designed as a health economics tool to assess quality-adjusted life years, a pivotal variable in determining the cost effectiveness of treatment. The SF-36 is foremost a means of monitoring and comparing disease burden and not aptitude, which is the measured intent of the IADL. As with the DASI, poor performance on the SF-36 indicates functional limitation at the level of overall physical condition and not cognitive ability. The inability of both the DASI and the SF-36 to significantly predict cognitive recovery highlights the IADL as a distinct, cognitively focused quality-of-life measure important in assessing the course of postoperative cognitive rehabilitation.

Prior studies have shown depressive symptoms to be independently associated with cognitive decline. [48, 52] However, we were unable to demonstrate an association between depression and social support systems and cognitive recovery at 1 year. Depression and social support systems often occur as byproducts of functional status[52] and are therefore less robust predictors of enhanced cognition in comparison to functional status itself.

Our study is limited by the observational and exploratory design; thus our findings should be considered the first step in identifying the factors that may lead to recovered cognitive functioning after an initial postoperative decline. Our study could also be criticized for our definition of cognitive recovery as a return to baseline, which is a dichotomous variable. For this reason, in a secondary supportive analysis, we examined cognitive recovery as a continuous outcome and found that IADL score remains a significant predictor. Furthermore, from the point of view of the patient, a return to baseline functioning is an important landmark with numerous benefits and quality-of-life implications. Another consideration in the interpretation of our study is the inclusion of subjects with any decline from baseline to 6 weeks, rather than a prespecified unit of decline, such as a standard

deviation. Although there is little consensus in the literature about how to define POCD and a standard deviation-based definition of decline is often challenged as being arbitrary, we do acknowledge that this decision leaves us unable to fully discount the effects of measurement error or regression to the mean. To further address this concern, we assessed cognitive decline at 6 weeks as a 1 standard deviation or more decline in at least 1 of the 4 cognitive domains and found that 6-week IADL is still a predictor of return to baseline at 1 year. In addition to the inclusion of the IADL in the study battery, future studies should ideally include additional measures of functional status to provide a more comprehensive understanding of the components of functional aptitude and how they relate to cognitive recovery. Future studies should include also include control groups to elucidate the effect of surgery and coronary heart disease on this relationship.

To summarize, in this first study to examine factors predicting recovery from POCD, 45% of patients who experience cognitive decline at 6 weeks return to baseline cognitive function by 1 year. Higher educational levels, baseline cognitive performance, smaller cognitive decline at 6 weeks, and lower IADL scores (better functional performance) at 6 weeks are associated with cognitive recovery 1 year after cardiac surgery. Of note, age, depression, and social support systems do not appear to modulate this recovery. Whether increasing patients' functional capacity through increased occupational activity (e. g. acts of self-care, work, and leisure) before a surgical admission (as opposed to postoperatively) would allow the individual to retain a higher level of functional capacity over their entire perioperative experience with resulting increases in quality of life and cognitive recovery should be further examined.

Acknowledgments

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Appendix 1

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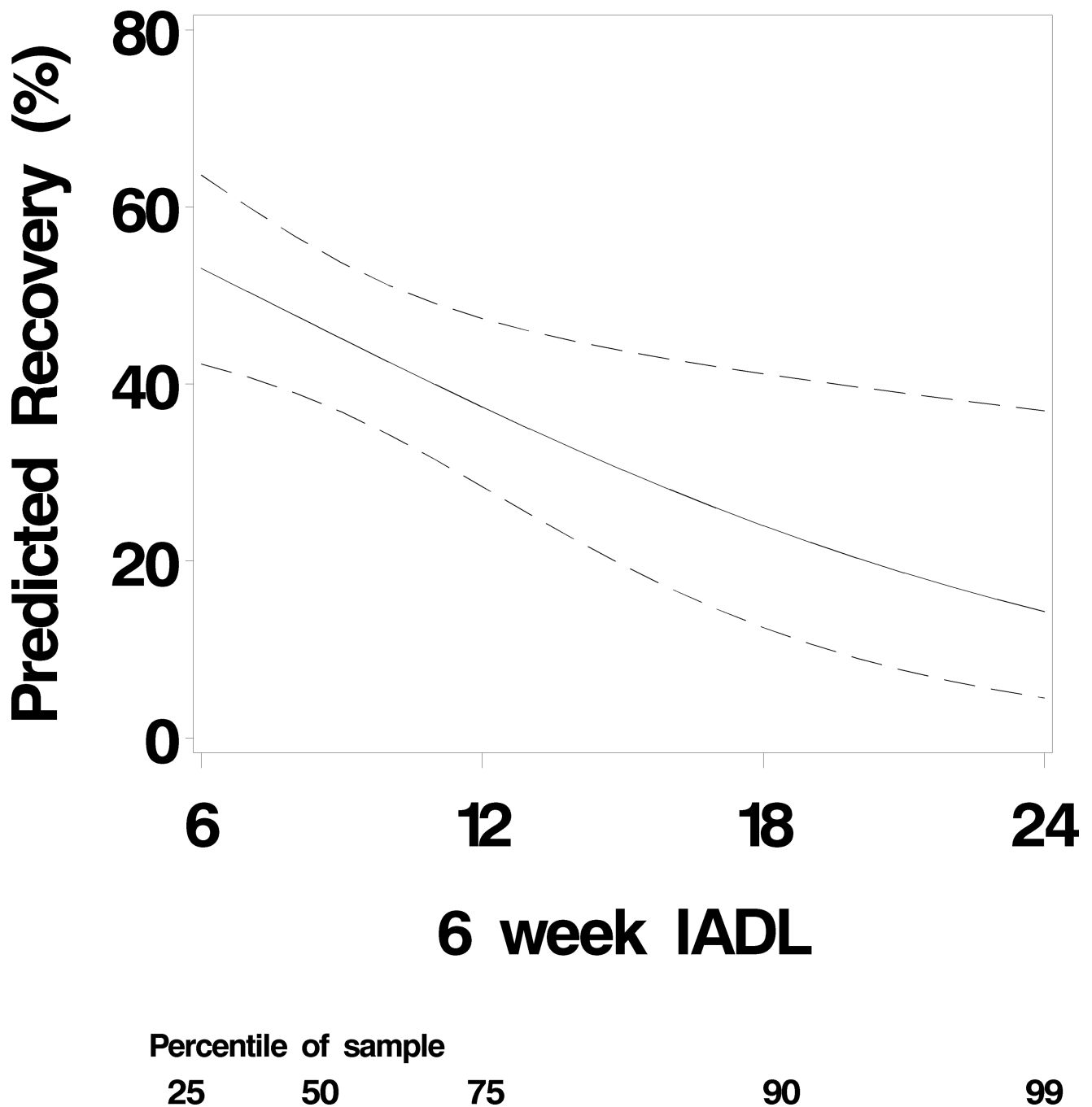
Figure 1.
The association between Instrumental Activities of Daily Living at 6 weeks and predicted probability of cognitive recovery. The predicted probability of recovery is derived from the multivariable logistic regression model, which estimates a greater likelihood of cognitive recovery with increasing IADL scores after adjusting for years of education, baseline function, and amount of decline at 6 weeks. That is, a patient with a higher IADL score is more likely to recover cognitive function than a patient with a lower IADL score, even if the two patients have the same baseline score, the same education level, and experienced the same amount of decline. Lower IADL scores indicate enhanced function and the dashed lines represent 95% confidence intervals. The figure footnote indicates the percentage of the

sample which had the corresponding IADL score or a lower score; for example, 75% of the sample scored 12 or lower.

Table 1

Patient Characteristics and Cognitive Improvement.

	Not improved (N =126)	Improved (N =103)	P value
Age in years (SD)	67.6 (10.3)	65.4 (9.30)	0.09
Gender (% female)	31	30	0.88
Race (% Caucasian)	79	89	0.04
Years of education (SD)	12.6 (3.3)	13.1 (2.1)	0.26
Weight in kg (SD)	81.5 (14.8)	83.3 (17.1)	0.40
BMI in kg/m^2(SD)	27.6 (4.5)	25.6 (5.6)	0.14
Euroscore (SD)	6.17 (3.26)	5.68 (3.03)	0.31
Hannan comorbidity score (SD)	0.01 (0.01)	0.02 (0.03)	0.47
Diabetes (%)	29.4	27.2	0.72
Hypertension (%)	72.2	67.0	0.39
Prior smoker (%)	61.9	60.0	0.78
COPD (%)	5.6	6.8	0.70
LVEF (SD)	52 (13)	53 (12)	0.69
CABG surgery	77.0	78.6	0.76
Valve surgery	14.3	13.6	0.88
CABG + valve surgery	8.7	7.8	0.79
Number of grafts (SD)	2.8 (1.3)	2.9 (1.3)	0.64
CPB time in minutes (SD)	129.6 (50.5)	143.7 (76.5)	0.10
Postopatrial fibrillation (%)	37.3	37.9	0.93
Working status (% employed)	11.1	16.5	0.24
Marital status (% married)	77	76	0.89
Living arrangement (not alone)	77	74	0.57
CES-D at baseline (SD)	11.9 (9.3)	11.0 (7.0)	0.56
CES-D at 6 weeks (SD)	13.3 (10.3)	13.0 (9.2)	0.83
Social support score at baseline (SD)	85.0 (13.1)	84.6 (13.0)	0.80
Social support score at 6 weeks (SD)	81.9 (14.8)	81.2 (16.8)	0.86
STAI at baseline (SD)	37.1 (12.5)	36.6 (12.4)	0.86
STAI at 6 weeks (SD)	34.7 (13.9)	34.2 (12.2)	0.82
Optimism at baseline (SD)	1.4 (0.6)	1.2 (0.4)	0.04
Optimism at 6 weeks (SD)	1.3 (0.6)	1.4 (0.6)	0.76
IADL at baseline (SD)	6.6 (1.6)	6.9 (1.9)	0.33
IADL at 6 weeks (SD)	10.8 (5.3)	8.7 (3.8)	0.006
DASI at baseline (SD)	19.6 (15.4)	18.1 (15.6)	0.61
DASI at 6 weeks (SD)	8.8 (10.6)	8.9 (8.9)	0.96
Symptom limitation at baseline (SD)	14.8 (4.4)	14.6 (4.8)	0.79
Symptom limitation at 6 weeks (SD)	14.8 (5.3)	14.2 (4.3)	0.43

	Not improved (N =126)	Improved (N =103)	P value
Cognitive difficulties score at baseline (SD)	77.0 (19.5)	76.9 (20.3)	0.97
Baseline cognitive score (SD)	0.11 (0.49)	0.06 (0.46)	0.36
Cognitive change at 6 weeks (SD)	−0.23 (0.23)	−0.16 (0.15)	0.01
Discharge statins (%)	47	42	0.44

*BMI, body mass index; COPD, chronic obstructive pulmonary disease; LVEF, left ventricular ejection fraction; CABG = coronary artery bypass graft surgery; CPB, cardiopulmonary bypass; CES-D, Center for Epidemiological Studies – depression Scale; STAI, Spielberger State Anxiety Inventory; IADL, Instrumental Activities of Daily Living; DASI, Duke Activity Status Index; SD, standard deviation. On the DASI and the Social support scores, a higher score is better, whereas for the IADL, CES-D, STAI, optimism, symptom limitations, and cognitive difficulties, a lower score is better. Univariate p values were calculated with chi-square tests of association for categorical variables and t-tests for continuous variables.

Table 2

Predictors of cognitive recovery after cardiac surgery. More years of education, lower baseline cognitive index, less decline in cognitive index at 6 weeks, and lower Instrumental Activities of Daily Living (IADL) scores (better performance) at 6 weeks predicts cognitive recovery at 1 year.

Variable	Odds Ratio	95% Confidence Interval	P-value
Years of education (per year)	1.332	1.131–1.569	< 0.001
Baseline cognitive index (per 0.01 change)	0.987	0.976–0.998	0.018
Decline in cognitive index at 6 weeks (per 0.01 change)	1.044	1.014–1.075	0.004
IADL score at 6 weeks (per 1 unit change)	0.891	0.810–0.981	0.018

*N=229; multivariable logistic regression modeling was developed to predict cognitive recovery. Based on a prior study demonstrating their significance in cognitive outcomes, three variables (age, years of education, and change in cognitive index at 6 weeks) were predetermined for inclusion in the model. To avoid model overfitting, only 7 additional variables with the lowest univariate p-values were incorporated into the multivariable modeling.