Published in final edited form as:

Anesth Analg. 2008 July ; 107(1): 21–28. doi:10.1213/ane.0b013e3181606a65.

The Role of Postoperative Neurocognitive Dysfunction on Quality of Life for Postmenopausal Women 6 Months After Cardiac Surgery

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Abstract

BACKGROUND—Women are prone to neurological complications after cardiac surgery. We have previously reported that treatment perioperatively with the neuroprotectant steroid 17 β -estradiol did not improve neurocognitive end-points 4 to 6 wk after surgery for elderly women. In this study, we evaluated the influence of early postoperative neurocognitive dysfunction on quality of life in postmenopausal women undergoing cardiac surgery and whether it is impacted by perioperative 17 β -estradiol treatment.

METHODS—One hundred seventy-four postmenopausal women randomly received 17 β -estradiol or placebo in a double-blind manner beginning the day before surgery and continued until the fifth postoperative day. The patients underwent psychometric testing using a standard battery before surgery and again 4 to 6 wk and 6 mo postoperatively. Quality of life was assessed at baseline and 6 mo after surgery with the SF-36 questionnaire and the Lawton instrumental activities of daily living scale.

RESULTS—Complete data were available from 108 women of whom 13% demonstrated postoperative neurocognitive dysfunction. Based on multiple logistic regression analysis, a neurocognitive deficit 4 to 6 wk after surgery was an independent predictor of a lower SF-36 physical component score ($P=0.004$) and lower Lawton instrumental activities of daily living scale 6 mo postoperatively ($P=0.026$). Treatment with 17 β -estradiol ($P=0.003$) and smoking

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Clinical Trial Registration: <http://clinicaltrials.gov/show/NCT00123539>.

Reprints will not be available from the author.

status ($P=0.015$) were predictors of worse SF-36 mental health component rating. Preoperative lower scores were independently associated with low quality of life postoperatively for all measurements.

CONCLUSIONS—Postoperative neurocognitive dysfunction is associated with impaired quality of life in women after cardiac surgery. Perioperative treatment with 17β -estradiol provides no benefits to postoperative quality of life. The relationship between low preoperative and postoperative self-rated health status suggests that some aspects of quality of life in postmenopausal women are not amenable to improvements with cardiac surgery.

Women are a growing proportion of patients who present for cardiac surgery and at a more advanced age and with more comorbid medical conditions than men.^{1–4} It is, thus, not surprising that operative morbidity and mortality are consistently reported to be higher for women than for men.^{1–4} In addition to enhancing survival and relieving symptoms, improving quality of life is an important goal of cardiac surgery, particularly in an aging surgical population.⁵ Improvements in health status after cardiac surgery have been consistently demonstrated, although, in most of these investigations, men were the majority of the studied patients.^{6–16} Whether women experience similar improvements in quality of life after surgery as men is controversial, with some studies suggesting less improvement for women.^{7–14}

In a series of investigations, we have found that women are at higher risk than men for neurological complications after cardiac surgery and that these events explain a large portion of the excessive operative mortality experienced by women.^{2–4} Based on extensive experimental findings that estrogens limit the extent of ischemic neuronal injury, we conducted a prospectively randomized, double-blind, placebocontrolled trial to evaluate whether the perioperative use of 17β -estradiol would provide neuroprotection in postmenopausal women undergoing cardiac surgery.^{17,18} The study was stopped by the independent data and safety monitoring board after the second interim data analysis. Our findings were that treatment perioperatively with 17β -estradiol did not improve neurocognitive end-points 4 to 6 wk after surgery for elderly women compared with placebo (primary end-point). The study's monitoring board considered the likelihood of finding benefit from 17β -estradiol was low. The board also had some concerns about safety because women in the 17β -estradiol group had poorer performance on tests of attention and mental flexibility and more postoperative neurological deficits, as detected by an increase from baseline in the National Institutes of Health (NIH) Stroke Scale.

Cognitive impairment is associated with low quality of life in patients with cardiac disease.¹⁹ There are little data regarding the importance of postoperative cognitive decline for quality of life, particularly in women.^{14,15,20} Measuring the patient's self-perceived health status can provide information for judging the risks and effectiveness of interventions for cardiac disease beyond that provided by usual clinical variables.⁶ The purpose of this study was to evaluate a secondary aim of our trial, to assess whether postoperative neurocognitive dysfunction influences quality of life 6 mo after cardiac surgery in postmenopausal women, and whether it is impacted by the perioperative administration of 17β -estradiol.

METHODS

After receiving IRB approval, 174 postmenopausal women age 55 yr undergoing coronary artery bypass graft (CABG) and/or cardiac valve replacement surgery gave written informed consent and were enrolled in the trial. The protocol of the study has been described in detail.^{18,21} The patients were prospectively randomized to receive either identical 25 cm² transdermal patches containing 17 β -estradiol (Climara, Berlex Laboratories, Wayne, NJ) or placebo (blank patches) in a double-blind manner beginning the day before surgery until the fifth postoperative day. Supplemental IV 17 β -estradiol or placebo was given during cardiopulmonary bypass.

Cognitive Assessments

A standard neuropsychological testing battery was performed 1 to 2 days before surgery as well as 4 to 6 wk and 6 mo after surgery. The selected battery was in accordance with Consensus Statement guidelines.²² The battery included the Rey Auditory Verbal Learning Test on which patients are asked to recall after 30 min a previously presented 15-word-list; the Digit Symbol subtest of the Wechsler Adult Intelligence Scale, a measure of psychomotor speed, in which number-symbol pairs are transcribed under timed conditions; Trail Making Tests A and B, tests of attention and mental flexibility in which numbered and then alternately numbered and lettered dots are connected in order, under timed conditions; the Grooved Peg Board Test, a test of fine motor dexterity which involves placing notched pegs into fitted holes on a shallow box; and the Benton Visual Form Discrimination Test, a test of visuoperception which involves visually matching target shapes.^{23–29} Patients were evaluated before and after surgery with the NIH Stroke Scale, a standardized, validated neurological examination that quantifies neurological deficits in 11 categories on a 42-point scale.³⁰

Quality of Life Measurements

Quality of life was assessed during the preoperative and 6 mo postoperative psychometric testing session by the same trained study personnel. Health-related quality of life was measured with The SF-36 short form of the RAND Medical Outcomes Study questionnaire.^{31,32} This questionnaire is a multi-item scale that measures eight health-related subscales that are grouped into physical and emotional health component summaries (Fig. 1). The health-related concepts include assessments of self-perceived emotional and mental problems. The standardized scores for each of the eight domains range from 0 (worst) to 100 (best). Other instruments used included the Lawton instrumental activities of daily living (IADL) scale, an instrument measuring the well being of patients that is particularly suited for elderly populations.³³ The Lawton IADL scale assesses broad domains of activities required for independent function including ability to use the telephone, shop, prepare food, basic housekeeping chores, and personal responsibilities such as paying bills. The self-rated version consists of a series of questions scored on a 2 to 3 point scale. Mood status was assessed with The Beck Depression Inventory and The Beck Anxiety Inventory. The Beck Depression Inventory is a 21-item measure of the self-reported severity of depression symptoms.^{34,35} It is one of the most widely used instruments both for depression screening and for measuring the severity of depression in research and clinical settings. For descriptive

purposes only, the sample was characterized as being nondepressed (score = 9), mildly depressed (score between 10 and 15), moderately depressed (score between 16 and 23), and severely depressed (score >23). The Beck Anxiety Inventory is a widely used 21-item measure of the self-reported severity of anxiety symptoms.³⁶ Like the Depression Inventory, it assesses the presence and severity of clinically significant symptoms over the past 7 days.

Perioperative Care

Patient management during and after surgery has been previously reported.^{18,21} The patients received midazolam, opioids, and volatile anesthetics and underwent nonpulsatile cardiopulmonary bypass with a membrane oxygenator and a 40 μ m in-line arterial filter at a body temperature between 32°C and 34°C. Epiaortic ultrasound scanning of the ascending aorta was used in all patients and the images recorded for off-line assessment of atherosclerosis of the ascending aorta. These images were available to the operating team at the time of surgery.

Statistical Analysis

The primary outcome measures reported are the physical and mental health scale summary scores of the SF-36. Because these were the primary outcome measures, subjects included in this analysis were the 108 who had both complete baseline and 6 mo data. We also used the Lawton IADL score as an outcome measure.

Pearson correlation coefficients were used to evaluate the association among the three quality of life outcomes and continuous demographic measures, and the Beck depression and anxiety indices. After confirming that normality and equal variance assumptions were satisfied, *t*-tests provided comparisons of the outcome measures according to whether neurocognitive dysfunction was present at 4 to 6 wk after surgery. Neurocognitive dysfunction was defined as: (a) postoperative decline by >1 SD on 2 or more of the psychometric tests, and/or (b) an increase from baseline in the NIH Stroke Scale by >2 points postoperatively.¹⁸ Partial correlation coefficients were used to evaluate the association between continuous predictor variables and the 6-mo value of each primary outcome measure after adjusting for the baseline value of the outcome measure. Analyses of covariance that adjusted for the baseline value of the outcome measure assessed the relationship between the 6 mo value of the outcome and all categorical predictors. These analyses were performed using the GLM procedure in SAS which provided least square (adjusted) means that quantified 6 mo outcome variable values by category of the predictor variables. After beginning with the set of variables that were significantly associated with the physical and mental health summary scores and IADL, stepwise multiple linear regression was used to identify an independent set of predictors of these two primary outcome measures. The only variables that were entered or retained in the stepwise regression model were those that had a *P* value of <0.1. Variables included as potential predictors in these models were all parameters that were significantly associated with the relevant outcome measure. The baseline value of the outcome measure was always included in the multivariate models. Analyses involving days in the intensive care unit or days in the hospital were performed after a log transform because of the lognormal distribution of these variables. All analyses were performed using version 9.1 of SAS (SAS Institute, Cary, NC).

RESULTS

We enrolled 174 of a projected 334 patients. Of the 174 enrolled patients, at 6 mo, 15 patients had died and 31 patients were unavailable for follow-up. One hundred twenty-eight patients completed the 6 mo postoperative testing session. Of this group, complete quality of life data were available from 108 patients. Patients not completing all of the postoperative testing had lower scores before surgery on several psychometric scales including the Digit Symbol ($P=0.003$), Trails A ($P=0.003$), Trails B ($P=0.09$), and Benton Visual Form ($P=0.009$) tests. They had a higher score on the Beck Anxiety Index and they were more likely to have had a prior transient ischemic attack ($P=0.016$), congestive heart failure ($P=0.017$), previous myocardial infarction ($P=0.071$), and to have been randomized to 17β -estradiol treatment ($P=0.021$). Other variables did not differ according to the availability of 6 mo quality of life data. The 108 patients providing baseline and follow-up data included 46 women who received 17β -estradiol treatment and 62 women receiving placebo. Demographic information for this group is listed in Table 1. There were no differences in the psychometric test scores between treatment groups. Neurological outcomes for the patients in the present study are listed in Table 2. The rates of neurocognitive dysfunction in this cohort at 4 to 6 wk and 6 mo after surgery (13%) are lower than that observed in the entire cohort (21.4%–22.4%).¹⁸ Thirty-one percent of women reported some symptoms of depression before surgery whereas 24% reported depressive symptoms 6 mo after surgery. Twenty-two percent, 5%, and 2% of the patients reported mild, moderate, or severe depressive symptoms, respectively, before surgery. Six months after surgery 15%, 8%, and 2% reported mild, moderate, or severe depressive symptoms, respectively. These differences were not significant.

Quality of life assessments obtained at baseline and 6 mo after surgery are listed in Table 3. Associations between predictor variables and each of the three primary outcome variables are listed in Table 4, with all results in that table being adjusted for the baseline value of the outcome measure. The 6 mo SF-36 physical health summary score was lower in subjects with peripheral vascular disease ($P=0.012$), type I diabetes ($P=0.097$), and a neurocognitive deficit 4 to 6 wk after surgery ($P=0.004$). The baseline adjusted 6 mo value of the SF-36 mental health summary score was lower in subjects randomized to receive 17β -estradiol ($P=0.002$) and in subjects who were current smokers or who never smoked ($P=0.017$). The mental health summary score was negatively correlated with the baseline Beck Depression Index ($P=0.026$). Adjusted 6 mo IADL scores were lower in subjects with a history of transient ischemic attack ($P=0.087$) and those with a neurocognitive deficit at 4 to 6 wk ($P=0.029$) and they were negatively correlated with days spent in the intensive care unit. Twelve patients' scores decreased by 10 points or more from baseline on the SF-36 physical component summary score. There were no patients' scores with decrement of 10 or more from baseline for the mental health component summary.

The results of the stepwise multiple linear regression analysis are listed in Table 5. In addition to the baseline value, the only variable that had a significant independent association with lower postoperative SF-36 physical health summary score was the presence of a neurocognitive deficit 4 to 6 wk after surgery ($P=0.004$). The R^2 value for the model involving the baseline value only was 0.398, a value that was increased to 0.471 when

neurocognitive deficit was added as a predictor. In addition to the baseline value, variables associated with a lower score on the SF-36 mental health summary score included randomization to the 17 β -estradiol group ($P=0.003$), smoking status ($P=0.015$), and increased depression at baseline as measured by the Beck Depression Index ($P=0.095$). The R^2 for the model involving the baseline value only was 0.125, a value that increased to 0.306 when all predictors were included in the model. In addition to the baseline value, the only variable that had a significant independent association with a lower IADL score was the presence of a neurocognitive deficit at 4 wk ($P=0.029$). R^2 for the model involving the baseline value only was 0.117, a value that was increased to 0.181 when neurocognitive deficit was added as a predictor.

DISCUSSION

Women are at higher risk than men for neurological complications after cardiac surgery independent of known stroke risk factors.^{2–4} Experimentally, 17 β -estradiol has been persuasively shown to reduce the extent of ischemic neuronal injury in a variety of *in vitro* and whole animal models via multiple mechanisms.¹⁷ In ovariectomized animals, for example, treatment with 17 β -estradiol reduces the volume of infarcted brain by >60% after middle cerebral artery ligation compared with controls.¹⁷ We, thus, hypothesized that perioperative estrogen replacement would reduce the frequency of neurological complications in postmenopausal women undergoing cardiac surgery. In a double-blind study we found, however, no differences in the frequency of neurocognitive dysfunction 1 mo after surgery (primary outcome) between postmenopausal women prospectively randomized to receive perioperatively 17 β -estradiol in physiological doses or placebo (17 β -estradiol, 22.4% vs placebo, 21.4%, $P=0.45$).¹⁸ We now report self-rated health status from this trial for women completing all questionnaires after surgery.

In the current study, we assessed quality of life using a broad array of measurements of physical, psychological, and social functioning using validated instruments suited for an elderly population. We performed the surveys 6 mo after surgery allowing time for patient recovery while minimizing the confounding effects of evolving cerebral vascular disease and aging that might influence the assessments after a longer testing interval. Preoperative scores on each quality of life measurement were independently associated with low postoperative scores. We further found that patients with neurocognitive dysfunction 4 to 6 wk after surgery had significantly worse self-perceived physical health and lower IADL 6 mo after surgery. Rather than having any beneficial effect, we found that perioperative treatment with 17 β -estradiol (along with smoking status) was independently associated with impairment on the mental health component of the SF-36.

Improvements in health-related quality of life after cardiac surgery have been reported by multiple investigations.^{6–16} These improvements include increases in physical function, decreased pain, less depression and anxiety, increased participation in social activities, return of sexual desire and pleasure, and return to work. In a study of 2480 patients undergoing CABG surgery at 14 Veterans Administration hospitals, Rumsfeld et al.⁶ found an independent association between quality of life assessed by the SF-36 and 6-mo mortality after surgery. In that study, a 10-point lower score on the physical component summary than

population normative data was associated with a 39% increased risk of mortality, a magnitude of risk greater than that associated with other known risk factors such as serum creatinine and smoking history. Other analyses suggested that preoperative self-reported health status is an independent predictor of 6-mo mortality after cardiac surgery in older (>65 yr), but not younger, patients.¹⁶ In our study, we only included patients who completed the 6 mo questionnaires, thus, excluding patients who died during the first postoperative months. Although only slightly higher than projected in our sample size calculations, the failure to capture data at the 6 mo testing session on all surviving patients (“drop-out”) is acknowledged as a limitation to this study. Our approach likely led to a selection bias and influenced the rates of neurocognitive dysfunction that we observed in this cohort and possibly contributes bias to our analysis.

Several investigations have reported that women have similar quality of life and functional outcome benefits from cardiac surgery as men, although there are discrepancies among studies.^{7–14} Differences in results might be accounted for, in part, by lower functional status, economic hardships, and reduced social support experienced by women before surgery.^{9–11} In many of these studies, only a minority of the patients were women, the average age was younger than in our study, mood status was not considered in the analysis, and detailed psychometric testing results were mostly not performed. In a study of 172 patients followed for 5 yr after cardiac surgery, Newman et al.²⁰ found correlations between neurocognitive dysfunction and quality of life. Significant covariate-adjusted correlations were found in the composite cognitive index and physical component scores on the SF-36, general health perceptions, and depression and anxiety measures. There were no significant correlations between cognitive scores and SF-36 mental component scores. The mean age of patients in that study was 60.8 ± 10.4 yr and only 49 of participants (28.4%) were women potentially biasing the results towards men and younger patients. Nonetheless, our findings support those of Newman et al.²⁰ suggesting that postoperative neurocognitive dysfunction more adversely impacts physical aspects of quality of life than self-perceived mental health components.

There are fewer data on the effects of neurocognitive dysfunction on sex-specific changes in quality of life after cardiac surgery. Phillips-Bute et al.¹⁴ examined quality of life before and 1 yr after CABG surgery in 96 women and 184 men. The mean age of women was 63.7 yr. Although the rates of neurocognitive dysfunction were similar between sexes, women scored significantly worse on several measures of quality of life than men. After adjusting for baseline differences, women were at increased risk for subjective cognitive difficulties, anxiety, inability to perform activities of daily living, reduced exercise capacity, and impaired work activities than men. When viewed as a whole, all patients experienced improvement in quality of life after surgery. Nonetheless, these benefits were not experienced equally by women and men. Even after adjusting for known risk factors for compromised quality of life in that study, women did not show the same long-term quality of life benefits after CABG surgery than men.

Women undergo fewer CABGs than men and they are less likely to receive a durable internal mammary artery as a bypass graft, both suggesting less complete revascularization, at least in some women.¹ Less symptom relief and higher rates of depression and anxiety in

women than men have been proposed as explanations for their poorer quality of life after surgery.¹⁴ After adjusting for baseline scores, measures of depression and anxiety were not significantly related to physical aspects of quality of life or IADL in our study, but there was a trend for a relation between depression and self-perceived mental health. As noted by others, postoperative quality of life in women might simply be less strongly related to cardiac disease as for men.¹⁴ Our findings that preoperative assessments independently predicted lower postoperative self-rated health status support the notion that many aspects of quality of life are not amenable to improvement from cardiac surgery in postmenopausal women. The results of our study support the possibility, though, that measures aimed at reducing the frequency of neurocognitive dysfunction might have quality of life benefits for women recovering from cardiac surgery.

Hormone replacement in postmenopausal women is anecdotally reported to provide benefits on general feelings of well-being and skin tone.³⁷ The effect of estrogen with or without progestin replacement on quality of life, though, has been inconsistent and influenced by a large placebo effect.^{38–41} Analysis of data from a subgroup of 1511 postmenopausal women enrolled in the Women's Health Initiative found that estrogen plus progestin treatment for 1 yr had no effect on general health, vitality, mental health, depressive symptoms, or general assessments of sexual satisfaction.³⁸ Clinically small but statistically significant benefits of hormone replacement on physical functioning, sleep disturbances, and body pain were observed at 1 yr but were not found after 3 yr of treatment. Hormone treatment in the current study was completed before the 6 mo testing session. In our previously reported trial, we noted worse adjusted performance on the Trails A test (psychomotor speed) for women in the 17 β -estradiol group compared with the placebo group.¹⁸ Whether these cognitive findings or other factors not considered in this analysis contributed to the observed association between 17 β -estradiol treatment and lower mental health ratings by our women is unknown.

In summary, postoperative neurocognitive dysfunction is significantly associated with impaired quality of life in women 6 mo after cardiac surgery. Low self-rated health status before surgery predicts poor postoperative quality of life suggesting that some aspects of quality of life in postmenopausal women are not amenable to improvements with cardiac surgery. Perioperative treatment with 17 β -estradiol provides no benefits on quality of life assessed 6 mo after surgery.

Acknowledgments

This work was funded by a grant from the National Institutes of Health, Bethesda, MD to Dr. Charles Hogue, MD (NHLBI RO1 64600).

We are grateful to all of the cardiac surgeons, anesthesiologists, cardiologists, and research staff at participating enrolling sites for their endorsement of this study.

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Figure 1. Physical and mental health concepts and summary components of the SF-36 short form health related quality of life questionnaire.

Table 1

Patient Demographic Characteristics, Medical and Surgical Data, and Postoperative Outcomes

Variable	Subjects (<i>n</i> = 108)
Age	70 ± 9 (48–90)
Race	
Caucasian	97 (90%)
African American	11 (10%)
History of CVA	11 (10%)
History of TIA	5 (5%)
COPD	12 (11%)
Congestive Heart Failure	19 (18%)
Left ventricular function	
Normal	58 (67%)
Mildly reduced	19 (19%)
Moderately reduced	8 (8%)
Severely reduced	6 (6%)
Hypertension	91 (84%)
Previous MI	39 (36%)
Peripheral Vascular Disease	17 (16%)
Insulin Dependent Diabetes	17 (16%)
Noninsulin Dependent Diabetes	30 (28%)
Carotid Bruit	4 (4%)
Smoking Status	
Never	61 (56%)
Current	17 (16%)
Prior	30 (28%)
Type of Surgery	
CABG only	69 (65%)
CABG/AVR	8 (8%)
CABG/MVR	6 (6%)
AVR	14 (14%)
MVR	8 (8%)
Postoperative atrial fibrillation	42 (39%)
Low cardiac output syndrome	2 (2%)
Postoperative MI	
Non Q-wave	11 (10%)
Q-wave	6 (6%)
Days in the ICU	2.6 ± 2.5 (1–12)
Days in the Hospital	8.1 ± 5.2 (4–48)

Listed are the number of subjects for discrete variables with percentages and ranges for continuous variables in parentheses.

CVA = cerebrovascular accident; TIA = Transient ischemic attack; CABG = coronary artery bypass graft; AVR = aortic valve replacement; MVR = mitral valve replacement; ICU = intensive care unit; COPD = chronic obstructive pulmonary disease; MI = myocardial infarction.

Table 2

Neurological End-points for the Study Population

Type of Deficit	Percentage of Patients
Clinically detected stroke	3 (3%)
Neurocognitive dysfunction 4–6 wk after surgery	14 (13%)
Neurocognitive dysfunction 6 mo after surgery	14 (13%)

The data are presented as the number of patients with percentages in parenthesis.

Table 3

Baseline and 6 mo Values of Quality of Life Measures

Quality of Life Measurement	Baseline	6 mo After Surgery	P
Physical Health Component Summary	39 ± 11	44 ± 12	<0.0001
Bodily Pain	46 ± 11	48 ± 11	0.060
General Health	46 ± 12	47 ± 9	0.260
Physical Functioning	33 ± 11	38 ± 13	<0.0001
Role Physical Scale	38 ± 12	44 ± 12	<0.0001
Mental Health Component Summary	43 ± 2	44 ± 3	0.904
Mental Health Scale	36 ± 5	37 ± 6	0.686
Emotional Scale	49 ± 10	54 ± 7	<0.0001
Social Functioning	49 ± 8	47 ± 7	0.007
Vitality Scale	39 ± 7	38 ± 6	0.019
IADL	25 ± 3	25 ± 4	0.059
Beck Anxiety Scale	11 ± 9	8 ± 6	0.0006
Beck Depression Scale	7.71 ± 4.9	6.70 ± 5.6	0.220

IADL = Lawton instrumental activities of daily living scale.

Table 4

Univariate Associations Between Quality of Life End-points 6 mo After Surgery

Variable	Outcome Measure					
	Physical score			Mental score		
	Correlation or mean $\pm$ SE	P		Correlation or mean $\pm$ SE	P [R]	IADL Correlation or mean $\pm$ SE P [R]
Age	$r = -0.073$	0.471		$r = -0.122$	0.229	$r = -0.114$ 0.261
Group						
Placebo	44 $\pm$ 1.4	0.509		44 $\pm$ 0.3	0.002	25 $\pm$ 0.4 0.822
Estradiol	43 $\pm$ 1.6			43 $\pm$ 0.4		25 $\pm$ 0.4
Race						
Caucasian	44 $\pm$ 1.1	0.544		44 $\pm$ 0.3	0.886	25 $\pm$ 0.3 0.712
African American	39 $\pm$ 3.2			44 $\pm$ 0.7		24 $\pm$ 0.9
History CVA						
No	44 $\pm$ 1.1	0.273		44 $\pm$ 0.3	0.148	25 $\pm$ 0.3 0.314
Yes	40 $\pm$ 3.2			45 $\pm$ 0.7		24 $\pm$ 0.9
History TIA						
No	44 $\pm$ 1.1	0.645		44 $\pm$ 0.2	0.675	25 $\pm$ 0.3 0.087
Yes	41 $\pm$ 4.7			43 $\pm$ 1.1		23 $\pm$ 1.3
COPD						
No	43 $\pm$ 1.1	0.842		44 $\pm$ 0.3	0.376	25 $\pm$ 0.3 0.751
Yes	44 $\pm$ 3.1			43 $\pm$ 0.7		25 $\pm$ 0.8
CHF						
No	43 $\pm$ 1.1	0.612		43 $\pm$ 0.3	0.172	25 $\pm$ 0.3 0.870
Yes	45 $\pm$ 2.5			44 $\pm$ 0.6		25 $\pm$ 0.7
LV function						
Normal	44 $\pm$ 1.3	0.287		44 $\pm$ 0.3	0.104	25 $\pm$ 0.4 0.654
Mild reduced	41 $\pm$ 2.5			43 $\pm$ 0.6		24 $\pm$ 0.7
Moderately reduced	49 $\pm$ 3.8			42 $\pm$ 0.9		25 $\pm$ 1.1
Severely reduced	42 $\pm$ 4.4			45 $\pm$ 1.0		25 $\pm$ 1.2
Hypertension						

Variable	Outcome Measure					
	Physical score			Mental score		
	Correlation or mean $\pm$ SE	P		Correlation or mean $\pm$ SE	P [R]	IADL Correlation or mean $\pm$ SE P [R]
No	45 $\pm$ 2.6	0.547		44 $\pm$ 0.6	0.856	26 $\pm$ 0.7 0.319
Yes	43 $\pm$ 1.1			44 $\pm$ 0.3		25 $\pm$ 0.3
Previous MI						
No	44 $\pm$ 1.3	0.460		44 $\pm$ 0.3	0.752	25 $\pm$ 0.4 0.528
Yes	42 $\pm$ 1.7			44 $\pm$ 0.4		25 $\pm$ 0.5
PVD						
No	45 $\pm$ 1.1	0.012		44 $\pm$ 0.3	0.535	25 $\pm$ 0.3 0.272
Yes	37 $\pm$ 2.6			43 $\pm$ 0.6		24 $\pm$ 0.7
Type I Diabetes						
No	44 $\pm$ 1.1	0.097		43 $\pm$ 0.3	0.106	25 $\pm$ 0.3 0.755
Yes	40 $\pm$ 2.6			45 $\pm$ 0.6		25 $\pm$ 0.7
Type II Diabetes						
No	44 $\pm$ 1.2	0.166		44 $\pm$ 0.3	0.405	25 $\pm$ 0.3 0.122
Yes	41 $\pm$ 2.0			44 $\pm$ 0.5		24 $\pm$ 0.5
Smoking						
Never	44 $\pm$ 1.4	0.636		43 $\pm$ 0.3	0.017	25 $\pm$ 0.4 0.485
Current	41 $\pm$ 2.7			43 $\pm$ 0.6		24 $\pm$ 0.7
Prior	44 $\pm$ 2.0			45 $\pm$ 0.4		25 $\pm$ 0.5
Postoperative No	44 $\pm$ 1.1	0.448		44 $\pm$ 0.3	0.655	25 $\pm$ 0.3 0.896
Atrial Fibrillation Yes	42 $\pm$ 2.8			44 $\pm$ 0.6		24 $\pm$ 0.8
Neurocognitive No	47 $\pm$ 1.3	0.004		44 $\pm$ 0.4	0.936	26 $\pm$ 0.4 0.029
Deficit Yes	37 $\pm$ 3.3			44 $\pm$ 0.9		24 $\pm$ 1.1
Log days in hospital	$r = -0.041$	0.686		$r = 0.054$	0.598	$r = -0.118$ 0.245
Log days in ICU	$r = -0.106$	0.295		$r = 0.093$	0.358	$r = -0.200$ 0.047
Beck depression index	$r = -0.098$	0.336		$r = -0.223$	0.026	$r = -0.023$ 0.823
Beck anxiety index	$r = -0.041$	0.685		$r = -0.099$	0.332	$r = 0.113$ 0.264

All *P*-values are adjusted for the baseline value of the outcome measure. Entries are baseline-adjusted partial correlation coefficient between continuous predictors and outcomes and baseline-adjusted least square means $\pm$ SE of categorical predictors.

CVA = cerebrovascular accident; COPD = chronic obstructive pulmonary disease; CHF = congestive heart failure; LV = left ventricular; MI = myocardial infarction; PVD = peripheral vascular disease; ICU = intensive care unit; IADL = Lawton instrumental activities of daily living scale.

Table 5

Independent Predictors of the 6 mo Quality of Life Measures

Independent Predictors	<i>P</i>
Reduced 6-mo physical health summary score	
Baseline physical health score	<0.0001
Neurocognitive deficit at 4–6 wk	0.004
Reduced 6-mo mental health summary score	
Baseline mental health score	0.014
Perioperative 17 β -estradiol treatment	0.003
Smoking status	0.015
More depressive symptoms measured with the Beck Depression Inventory	0.095
Worse IADLs at 6 mo	
Baseline IADL score	0.026
Neurocognitive deficit at 4–6 wk	0.029

IADL = Lawton instrumental activities of daily living scale.