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Effect of Delirium on Physical Function in Noncardiac Thoracic Surgery Patients

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Abstract

Background—The effect of delirium on physical function in patients undergoing noncardiac thoracic surgery has not been well described and may differ from that in other surgical populations.

Objective—To determine the effects of delirium on muscle strength and functional independence. The primary end point was change in Medical Research Council sum score (MRC-SS) by delirium status.

Methods—A secondary analysis of data from a clinical trial involving English-speaking adults aged 18 years or older who were undergoing major noncardiac thoracic surgery. Exclusion criteria were history of schizophrenia, Parkinson disease, dementia, alcohol abuse, or neuroleptic malignant syndrome; haloperidol allergy; being pregnant or nursing; QT prolongation; and taking

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levodopa or cholinesterase inhibitors. Delirium was assessed twice daily using the Confusion Assessment Method for the Intensive Care Unit. Preoperatively and postoperatively, muscle strength was assessed using the modified MRC-SS and functional independence was assessed using the Katz scale of activities of daily living. Changes in MRC-SS and Katz score by delirium status were analyzed using the Fisher exact test.

Results—Seventy-three patients were included in the analysis. Median (interquartile range) MRC-SS and Katz score before surgery did not differ significantly between patients without and with delirium (MRC-SS: 30 [30-30] vs 30 [30-30], $P > .99$; Katz score: 6 [6-6] vs 6 [6-6], $P = .63$). The percentage of patients with a change in MRC-SS was similar in patients without and with delirium (17% vs 13%, respectively; $P > .99$). More patients in the delirium group had a change in Katz score (13% vs 0%, $P = .04$).

Conclusions—Postoperative delirium was not associated with change in muscle strength. Follow-up studies using other muscle measures may be needed.

Delirium occurs in nearly 50% of patients undergoing noncardiac thoracic surgery.[1-3] In cardiac surgery patients, delirium is associated with decreased physical function, increasing the risk of institutionalization.[4] Patients experiencing postoperative delirium after transcatheter or surgical aortic valve replacement had decreased physical function at 1 month.[5] In cardiac surgery, long periods of cardiopulmonary bypass, arterial hypotension, and low cardiac output may increase the risk of postoperative delirium.[6] The effect of delirium on muscle strength and physical function in noncardiac thoracic surgery patients, however, has not been well described. We hypothesized that this effect might differ from that in cardiac surgery patients because of differences in anesthesia and surgical technique (eg, lack of cardiopulmonary bypass).[7]

Objective

The objective of this study was to determine the effect of delirium on muscle strength and functional independence in patients undergoing noncardiac major thoracic surgery. The primary endpoint was change in Medical Research Council sum score (MRC-SS) by delirium status. A secondary endpoint was change in score on the Katz scale of activities of daily living (ADLs) by delirium status.

Methods

Study Design

We conducted a secondary analysis of data from a previously reported randomized controlled trial comparing scheduled low-dose haloperidol versus placebo for prevention of delirium in patients who had undergone major noncardiac thoracic surgery.[2] The study was conducted at a tertiary care center from September 2013 to December 2015 and was approved by the Indiana University institutional review board.

Eligibility Criteria

The parent trial involved English-speaking adults aged 18 years or older who were undergoing major noncardiac thoracic surgery. Patients were excluded from the parent trial

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if they had a history of schizophrenia, Parkinson disease, dementia, alcohol abuse, or neuroleptic malignant syndrome or had an allergy to haloperidol. Patients who were pregnant or nursing, had QT prolongation of over 500 milliseconds, or were taking levodopa or cholinesterase inhibitors were also excluded. For the current analysis, we excluded patients who did not have both preoperative and postoperative MRC and Katz assessments completed.

Outcome Measures

The primary outcome of this analysis was change in MRC-SS by delirium status. We also examined change in Katz score by delirium status.

Medical Research Council Sum Score.—Global muscle strength was assessed by using a modified MRC-SS both preoperatively and postoperatively.[8] The MRC-SS has high interrater reliability (κ = 0.77-0.88) and intrarater reliability (Spearman r_s = 0.78).[9]

The MRC-SS was used to grade muscle strength from 0 to 5 (with 0 indicating paralysis, 3 indicating movement against gravity over near-full range of motion, and 5 indicating normal power) in the following muscle groups: shoulder abduction, elbow flexion, wrist extension, hip flexion, knee extension, and ankle dorsiflexion. We used a modified MRC-SS with strength assessed on one-half of the body, with a maximum possible score of 30 (the nonmodified MRC-SS maximum is 60). These assessments were repeated at the time of hospital discharge. A modified MRC-SS was used because all patients were high functioning and ambulatory at baseline, and the baseline assessments occurred in the time-constrained preoperative period.

Katz Scale of Activities of Daily Living.—Activities of daily living were assessed by using the Katz scale both preoperatively and postoperatively. The Katz scale is a widely used 6-item self-report tool to assess functional capacity and independence in performing ADLs.[10] The scale assesses independence in bathing, dressing, toileting, transferring, continence, and feeding, with higher scores indicating better function. Scores range from 0 (very dependent) to 6 (fully independent). The Katz scale has high content validity even in patients with neurologic decline, and lower Katz scores were predictive of adverse events in cardiovascular patients undergoing transcatheter valve replacements.[11,12]

Delirium Measures

Level of sedation was assessed twice daily using the Richmond Agitation-Sedation Scale (RASS), and delirium was assessed using the Confusion Assessment Method for the Intensive Care Unit (CAM-ICU).[13] The RASS has excellent interrater reliability (interclass correlation coefficient=0.956, κ = 0.73, 95% CI = 0.71-0.75).[13] The CAM-ICU is a highly sensitive and specific instrument that has been validated in the hospital setting (sensitivity = 97%, specificity = 98%, accuracy = 98.4%). The CAM-ICU also has high interrater reliability (κ = 0.96, 95% CI = 0.92-0.99).[14] Delirium was defined as any positive assessment using the CAM-ICU.

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Other Data Collection

Participant demographic and clinical data were collected from the electronic medical records. Information was collected on demographic characteristics, chronic comorbidities as determined with the Charlson Comorbidity Index, and American Society of Anesthesiologists classification of fitness before surgery.[15]

Statistical Analysis

The outcomes of interest were change in MRC-SS and change in Katz score by delirium status. Descriptive statistics were analyzed as mean and SD or median and interquartile range (IQR), as appropriate, for continuous variables and proportions for categorical variables. The *t* test or the Wilcoxon rank sum test was used to assess differences for continuous variables between groups, whereas the χ^2 test or the Fisher exact test was used to assess differences for categorical variables. We imputed missing MRC-SS and Katz subscales from the person-specific mean of nonmissing items if 50% or fewer of the items were missing. Changes in MRC-SS and Katz score by delirium status were analyzed by using the Fisher exact test. All data analyses were performed using SAS version 9.4.

Results

A total of 73 patients were included in the analysis. Baseline characteristics are shown in the Table. Mean (SD) age in the sample population was 61.1 (12.7) years, 99% of participants were white, and 27% were female. Fifteen patients (21%) experienced delirium. The delirium group had significantly longer median (IQR) stays (in days) in the hospital (10 [9-10] vs 7 [6-10], $P = .04$) and the ICU (3 [2-6] vs 2 [1-3], $P = .01$). Patients in the delirium group had a longer mean (SD) duration of surgery in minutes (272.1 [86.9] vs 211.9 [92.3], $P = .03$).

Patients had high muscle strength and functional independence preoperatively. No significant differences were found at baseline between those without and with delirium in median (IQR) MRC-SS (30 [30-30] vs 30 [30-30], respectively; $P > .99$) or Katz score (6 [6-6] vs 6 [6-6], respectively; $P = .63$). There was no significant difference between patients without and with delirium in percentage of patients with a change in MRC-SS (17% vs 13%, respectively; $P > .99$). A subgroup analysis of the esophagectomy patients did not alter the findings. As shown in the Table, there was a significant difference between patients without and with delirium in mean (SD) postoperative Katz score (6 [0] vs 5.3 [1.8], respectively, $P = .005$). A larger percentage of patients in the delirium group had a change in Katz score (13% vs 0%, $P = .04$).

Discussion

In this study, we did not find a significant difference between groups in the percentage of patients with a change in MRC-SS after major noncardiac thoracic surgery, despite a high incidence of delirium in esophagectomy patients. These results may have been due to participants' good muscle strength and functional independence at baseline and their candidacy for surgery. We did, however, find postoperative delirium to be associated with a

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change in Katz score for ADLs, consistent with previous studies involving other surgical populations.

In studies of patients after aortic valve surgery and older nonsurgical patients admitted to the hospital, delirium was associated with increased risk of institutionalization after hospital discharge and the need for rehabilitation.[4,5] These findings may be due to the patients with delirium having a higher likelihood of treatment with antipsychotics or psychotropic medications, increased use of restraints resulting in immobility, or greater metabolic derangements hindering their recovery.[16] We hypothesized that delirium's negative effects on muscle strength could be the driver of loss of functional independence, but our study results do not confirm this hypothesis.

Our findings may be explained by the brief duration of delirium in the study sample, the occurrence of muscle strength assessment before hospital discharge, and the small sample size. In addition, whereas the MRC-SS is objectively measured, the Katz score is self-reported. The subjective decrement in Katz score among delirious patients could be driven by the delirium experience or the longer ICU or hospital stay. Our study also highlights the value of selection of highly functional candidates for surgery, as high baseline strength and functional independence may prevent a decrease in muscle strength despite postoperative delirium.

Strengths of our study include analysis of a noncardiac surgical population, robust methodological design with use of a well-validated measure of muscle strength, and twice-daily delirium assessments. Our study has several limitations. First, the sample size was small. As this was a secondary analysis of a randomized controlled trial, the sample size was not based on prespecified changes in MRC-SS. Second, time points for postoperative assessments were limited to the hospital stay. With a median hospital stay of 8 days, the Katz score may not have been sensitive to small changes in functional status. Third, the Katz scale may have limited sensitivity in patients with good baseline function.[17] Finally, compared with an analog scale, the MRC-SS may be less accurate in detecting weakness in strong, bulky muscles.[18]

Our findings add to the existing evidence on the relationship among delirium, reduced muscle strength, and increased risk of institutionalization after discharge. Further studies are needed to better describe effects of delirium on muscle function and return to independence.

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FINANCIAL DISCLOSURES

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Table

Baseline, clinical, and functional characteristics of study participants

Variable	All patients (N = 73)	No delirium (n = 58)	Delirium (n = 15)	*P*
Baseline characteristics				
Age, mean (SD), y	61.1 (12.7)	60.0 (13.3)	65.1 (9.1)	.17
Female, No. (%)	20 (27)	17 (29)	3 (20)	.75[a]
White, No. (%)	72 (99)	57 (98)	15 (100)	>.99[a]
Education greater than high school,[b] No. (%)	40 (56)	31 (54)	9 (60)	>.99[a]
Charlson Comorbidity Index, median (IQR)	2 (2-3)	2 (2-3)	3 (2-4)	.40
ASA III, No. (%)	71 (97)	57 (98)	14 (93)	.37[a]
Chemotherapy before surgery,[c] No. (%)	39 (55)	28 (49)	11 (79)	.07[a]
Clinical characteristics				
ICU LOS, median (IQR), d	2.5 (2-3)	2 (1-3)	3 (2-6)	.01
Hospital LOS, median (IQR), d	8 (6-10)	7 (6-10)	10 (9-10)	.04
Operative characteristics				
Surgery type, No. (%)				.32[a]
Esophagectomy	45 (62)	33 (57)	12 (80)	
Pneumonectomy	4 (5)	4 (7)	0 (0)	
Thoracotomy	24 (33)	21 (36)	3 (20)	
Surgery duration, mean (SD), min	224.3 (93.9)	211.9 (92.3)	272.1 (86.9)	.03
Benzodiazepine equivalent doses,[d] mean (SD)	27.1 (23.9)	25.0 (23.2)	34.8 (25.6)	.16
Opioid equivalent doses,[e] mean (SD)	34.5 (13.4)	34.1 (13.1)	35.8 (14.9)	.67
Muscle strength and functional independence				
MRC-SS, mean (SD)				
Preoperative	30.0 (0.0)	30.0 (0.0)	30.0 (0.0)	NA
Postoperative	29.7 (0.8)	29.7 (0.7)	29.6 (1.1)	.59
Change in MRC-SS, No. (%)	12 (16)	10 (17)	2 (13)	>.99[a]
Katz score, mean (SD)				

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Variable	All patients (N = 73)	No delirium (n = 58)	Delirium (n = 15)	*P*
Preoperative[f]	6.0 (0.1)	6 (0.1)	6 (0.0)	.61
Postoperative	5.9 (0.8)	6 (0)	5.3 (1.8)	.005
Change in Katz score, No. (%)	2 (3)	0 (0)	2 (13)	.04[a]

Abbreviations: ASA, American Society of Anesthesiologists classification (fitness before surgery); ICU, intensive care unit; IQR, interquartile range LOS, length of stay; MRC-SS, Medical Research Council sum score; NA, not applicable.

[a]Fisher exact test.

[b]Data were missing for 1 patient in the no delirium group.

[c]Data were missing for 1 patient in the no delirium group and 1 patient in the delirium group.

[d]Benzodiazepines presented as lorazepam equivalents.

[e]Opioids presented as morphine equivalents.

[f]Data were missing for 1 patient in the no delirium group.

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