Preoperative Cognitive Impairment as a Perioperative Risk Factor in Patients Undergoing Total Knee Arthroplasty

Sindhu Krishnan, MD1, Ethan Y. Brovman, MD2,3, and Richard D. Urman, MD, MBA1,2

Abstract

Background: The study assessed whether pre-existing cognitive impairment (CI) prior to elective total knee arthroplasty (TKA) is associated with worse postoperative outcomes such as delirium, in-hospital medical complications, 30-day mortality, hospital length of stay and non-home discharge. Methods: A retrospective database analysis from the NSQIP Geriatric Surgery Pilot Project was used. There was an initial cohort of 6350 patients undergoing elective TKA, 104 patients with CI were propensity score matched to 104 patients without CI. Results: Analysis demonstrated a significantly increased incidence of post-operative delirium (POD) in the cohort with pre-op CI (p < .001), a worsened functional status (p < .001) and increased nonhome discharge postoperatively compared to the group without CI (p = 0.029). Other post-operative outcomes included 30-day mortality of 0% in both groups, and low rate of complications such as infection (2.88% vs 0.96%), pneumonia (1.92% vs 0%), failure to wean (0.96% vs 0%), and reintubation (0.96% vs 0%). Some other differences between the CI group and non-CI group, although not statistically significant, included increased rate of transfusion (10.58% vs 6.73%), and sepsis (1.92% vs 0%). The length of stay was increased in the non-CI group (4.28% vs 2.32%, p = 0.122). Conclusion: CI in patients undergoing TKA is associated with an increased risk of POD, worsened postoperative functional status, and discharge to non-home facility.

Keywords
cognitive impairment, postoperative, delirium; functional status, discharge destination, cognitive dysfunction

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Introduction

Total knee arthroplasty (TKA) is a commonly performed surgery, with a projected increase by 143% calculating to 725 procedures/1000,000 from 425 procedures/100,000 in the United States by 2050 due to the expanding population of older adults of the age 65 and above.1 With studies showing an increased quality of life after TKA in older adults,2 it is expected there will be a higher demand for TKAs in the future.3 This population undergoing TKA tend to have a higher likelihood of comorbidities and have an increased incidence of pre-existing cognitive impairment (CI) prior to surgery relative to a younger population. To date, the impact of preexisting CI in older adults undergoing TKA remains unclear, with few robust studies assessing the association between preoperative CI and key postoperative outcomes after TKA.

Multiple studies have shown increased postoperative mortality in patients who are cognitively impaired in other surgical procedures.4-6 It has also been shown that there is a significantly decreased functional capacity at baseline in patients with preoperative CI. Mukka et al showed that patients with CI exhibited less mobility vs the control group after hemiarthroplasty for femoral neck fracture7 Culley et al that showed that patients with a Mini-Cog score less than or equal to 2 were likely to be discharged to a place other than home after lower

1 Department of Anesthesiology, Perioperative and Pain Medicine, Brigham and Women’s Hospital, Harvard Medical School, Boston, MA, USA
2 Center for Perioperative Research, Brigham and Women’s Hospital, Boston, MA, USA
3 Department of Anesthesiology and Perioperative Medicine, Tufts University School of Medicine, Boston, MA, USA

Corresponding Author:
Richard D. Urman, Department of Anesthesiology, Perioperative and Pain Medicine, Brigham and Women’s Hospital/Harvard Medical School, Boston, MA 02115, USA.
Email: rurman@bwh.harvard.edu
extremity orthopedic surgery.8 A study in Finland suggested that patients with low preoperative cognitive test scores were more likely to experience postoperative delirium (POD) after arthroplasty or need for follow up care in a healthcare facility.9 The study did not specify the type of follow up care that was required for these patients.

However, these studies did not specifically differentiate TKA from total hip arthroplasty (THA) outcomes. There is also no data available on post-operative length of stay in TKA or an association between CI and postoperative outcomes. Given the lack of data specific to TKA and the large number of these procedures performed in older adults, we sought to examine the impact of pre-operative CI on post-operative outcomes after elective TKA. We hypothesized that patients undergoing an elective TKA who have co-existing CI will have an increased incidence of discharge to a rehabilitation facility rather than home, and show an increased incidence of delirium and other postoperative complications. With this data, we want to emphasize the importance of a multidisciplinary approach to caring for patients pre-operative CI and with the older population’s increased need for TKA, understand the long-term effects it could have on a patient’s recovery and overall health.

Methods
Data Source
This manuscript adheres to the appropriate STROBE guidelines. The study was approved by the Institutional Review Board and exempted from the consent requirement due to the deidentified nature of the data. All data were derived from the American College of Surgeons National Safety Quality Improvement Program (ACS-NSQIP) Geriatric Surgery Pilot Program.10 This pilot program contains information on individual surgeries retrospectively compiled from 25 participating clinical settings between January 1, 2014 and December 31, 2018 that collected data on patients aged 65 and older.11 We retrospectively examined patients who underwent total knee arthroplasty and had pre-existing cognitive impairment which was identified by NSQIP via preoperative documentation that the patient had dementia or listed predefined descriptors consistent with dementia.11

Patient Selection
The NSQIP Geriatric Surgery Research files for years 2014 through 2018 were compiled into a single data file containing 52,894 surgical cases. The cases were matched using their unique identifier codes to case information from the NSQIP participant user file for the same years, resulting in a total of 298 variables for each unique case. The combined data file was then queried for patients undergoing TKA as defined by CPT code 27447, “Arthroplasty, knee, condyle and plateau; medial and lateral compartments with or without patella resurfacing (total knee arthroplasty)”. Exclusion criteria included patients under age 65 years at the time of operation, trauma cases, transplant surgeries, cases failing to report the procedure CPT code or the variable defining pre-existing cognitive impairment and all cases where the patient was listed as an ASA physical status class 6, representing a brain-dead organ donor.

CI is defined in NSQIP to capture whether the patient has some degree of pre-existing dementia, with the following description: “Dementia is a chronic or persistent disorder of the mental processes caused by brain disease or injury and marked by memory disorders, personality changes, and impaired reasoning. Dementia may be recorded as: Dementia, Alzheimer’s disease, Vascular dementia, Parkinson’s dementia, Lewy Body Dementia, small vessel dementia, mild cognitive impairment (MCI), long term cognitive impairment, long term memory impairment, small vessel disease or white matter changes in the brain, memory disorder, cognitive disorder, chronic organic brain syndrome or chronic organic mental disorder”.12

Demographic and Baseline Variables
The present investigation compared the characteristics of patients undergoing TKA, grouped by whether the patient had pre-existing cognitive impairment. Baseline demographic variables included age, gender, ethnicity, American Society of Anesthesiologists (ASA) physical status (PS) classification, and body mass index (BMI). Co-morbid conditions included for the analysis were diabetes, smoking history with number of pack years, chronic obstructive pulmonary disease (COPD), congestive heart failure (CHF), chronic kidney disease (CKD), steroid dependence, presence of wound infection, bleeding disorders, sepsis and weight loss. Functional status in NSQIP is divided into 3 categories: independent, partially dependent, and totally dependent. Independent is defined as having no assistance from another person required for any ADLs, including patients who function independently with prosthetics, equipment or other supportive devices. Partially dependent is requiring some assistance from another person for ADLs and totally dependent is requiring total assistance for ADLs.11

Outcomes of Interest
The primary outcome was 30-day mortality. Secondary outcomes included rates of post-operative complications, including returning to the operating room, reintubation, failure to wean from ventilation, surgical site infections, dehiscence, pneumonia, acute kidney injury, renal failure, stroke, cardiac arrest, acute myocardial infarction, transfusion requirements, sepsis, urinary tract infections, venous thromboembolisms, total number of complications for each patient, and hospital length of stay. Post-operative delirium in patients was identified via chart audits. ACS NSQIP data abstractors routinely examined the entire medical record and assigned delirium if words characterized an acute confused state such as “mental status change, confusion, disorientation, agitation, delirium, inappropriate behavior, inattention, hallucination, combative”.12
**Statistical Analysis**

The surgical cohort was stratified by the presence or absence of CI. Initial comparison of the cohort with and without CI was performed utilizing Student’s t-test for continuous variables and chi-squared test for categorical variables along with conditional univariable logistic regression. Risk adjustment between the 2 cohorts was performed using propensity score matching. To develop the matched cohort, we analyzed this initial data set, shown in Appendix, for statistically significant associations, which were defined as a p value < 0.05 on a Student’s t or chi-square testing or a 95% confidence interval not containing 1.0 on logistic regression. We incorporated these variables into a propensity score model. To perform matching, we used a 1:1, greedy, nearest neighbor matching strategy, with a caliper set to 0.1, which resulted in the matching of 104 cases in patients with CI to 104 patients without CI. We then assessed the adequacy of this matching using Student’s t test for continuous variables and Pearson’s chi-square test for categorical variables along with univariable logistic regression as well as calculation of the absolute standardized differences for each variable, demonstrating adequate matching between cohorts. We then analyzed the association between CI and patient outcomes in this propensity-matched cohort using univariable logistic regression. In order to understand the effect of CI on individual patient outcomes, we calculated the total number of complications per patient as the sum incidence of all reported postoperative outcomes for each patient. For the multiple comparisons required to perform the outcomes analysis, we applied a Bonferroni correction with a selected omnibus criterion of significance of 0.05, yielding an adjusted p-value of significance of 0.0028 to maintain the familywise error rate at 0.05. All outcomes reported as significant in this manuscript were significant after application of this correction. Sample size was prespecified by the availability of TKA cases in the dataset. We performed all analyses using R Studio Version 1.1.463 (Boston, MA) and R Project for Statistical Computing, v.3.6.3 (Vienna, Austria).

**Results**

**Baseline Patient Characteristics**

**Before Propensity Matching**

Descriptive information about the patients included in this cohort is shown in Appendix. The ACS NSQIP Geriatric Pilot Program contained a total of 52,894 patients between 2014-2018 (Figure 1). 6,350 corresponded to CPT code 27447 (TKA), which included 126 patients with preoperative CI and 6,224 patients without CI. Baseline characteristics were divided into 2 groups, 1 with preoperative CI and 1 without. The primary age group was between 70-80 years old (50%), majority being white females, with an average body mass index (BMI) of 29-31. Most patients were categorized as ASA physical status (PS) 1 or 2 in the non-CI group, and ASA 3 in the CI group. The ASA PS classification system is to assess and communicate a patient’s pre-anesthesia medical co-morbidities. The classification does not predict perioperative risks, but used with other factors (e.g., type of surgery, frailty, level of deconditioning), it can be helpful in predicting perioperative risks ASA PS is classified 1-6, with 1 being a normal healthy patient, 2 is a patient with mild systemic disease, 3 is a patient with severe systemic disease, 4 is a patient with severe systemic disease that is. Constant threat to life, 5 is a moribound patient who is
Our study offers some novel insights into increased postoperative
risk in patients with existing CI and provides important data for
risk stratification and prevention strategies.

Postoperative Delirium

Although the mechanism of POD has not been clearly
described, there are multiple risk factors that are associated
with its development. Previously reported common preoperative
risk factors include age > 70, pre-existing CI, use of benzo-
diazepines, and previous history of POD. Interestingly,
opioid utilization at higher dose levels is also associated with
significantly reduced POD. This reflects the notion, supported
by existing data, that inadequate pain management is known to
precipitate POD. Ravi et al showed that prolonged surgical
duration in hip fractures was associated with POD. Wang et al also found that orthopedic surgery lasting longer than 3 hours was a risk factor for POD.

It is important to identify patients at risk for POD as it has
been shown to increase in-hospital (and long-term) mortality
rates. POD is also associated with increased postoperative
complications, longer length of hospital stay, and higher rates
of discharge to an outside facility. A substantial portion
(approximately 20%) of elective surgical patients in the geri-
atric population without dementia have CI at baseline before
surgery. Studies have shown that preoperative cognitive
screening of older surgical patients may be valuable for risk
assessment and risk stratification, especially for identification
and possible prevention of POD. A Mini-Cog examination
can be performed prior to surgery and the patient may need a
referral for further evaluation by primary care physician, or
geriatrician. A 2020 recommendations statement from the
Society of Perioperative Assessment and Quality Improve-
ment (SPAQI) makes recommendations about the use of vari-
sous screening instruments for CI. Many of these tests, such
as the Clock drawing test command and copy (CDT),
Mini-Cog, and the mini mental status exam (MMSE) show
effective pharmacological techniques for the preven-
tion of POD are still being studied, and there have not been
different between the groups, included increased rate of trans-
fusion (10.58% vs 6.73%), and sepsis (1.92% vs 0%). Interest-
ingly, the length of stay was increased in the non-CI group
(4.28% vs 2.32%, p = 0.122).

Discussion

In this retrospective chart review, we studied post-operative
outcomes associated with pre-existing cognitive impairment
in geriatric patients who underwent an elective TKA. Using
the NSQIP Geriatric Surgery Pilot, we report a significant
increase in POD in patients with pre-existing CI (OR 40.15;
95% confidence interval 5.3-304.13). Additionally, patients
with CI were more likely to be discharged to a facility rather
than home (OR 1.89; 95% confidence interval 1.07 – 3.35), and
were less likely to be independent with ADLs compared to the
no CI cohort (OR 4.26; 95% confidence interval 2.24 – 8.1).
Our study offers some novel insights into increased postoperative
controlled trials on this topic. However, theoretically several groups of drugs targeting the cholinergic, dopaminergic, serotonergic or noradrenergic system could be used to prevent delirium. It has been suggested that intraoperative neuraxial anesthesia may decrease postoperative cognitive dysfunction when compared with general anesthesia, but this issue remains controversial, and there are ongoing, randomized trials to answer this important question. Unfortunately, we did not have enough data to show whether the choice of anesthesia (general versus regional) has any effect on POD.

**Post-Operative Decline in Independence**

Our study showed a significant difference in reduction in functional status in patients with pre-operative CI (from 94% of patients being independent in the baseline cohort to only

| Variable | Cognitive impairment | No cognitive impairment | p-value |
|----------|----------------------|-------------------------|---------|
| Age      | 75.75 6.27           | 75.32 6.17              | 1.01 (0.97 - 1.06) 0.617 |
| Age Groups | n %  | N %                   | OR (95% CI)    | p-value |
| 65-70    | 21 20.19          | 20 19.23               | Reference     | 0.979 |
| 70-80    | 55 52.88          | 55 52.88              | 0.95 (0.46 - 1.95) |
| >80      | 28 26.92          | 29 27.88               | 0.92 (0.41 - 2.05) |
| Sex      | Male 32 30.77      | Female 72 69.23        | Reference     | 0.88 |
| Demographics | White 88 84.62 | Black 7 6.73 | Not Reported 9 8.65 | Reference | 0.652 |
| BMI      | 29.53 5.91         | 29.23 5.45             | 1.01 (0.96 - 1.06) 0.706 |
| BMI Groups | n %  | n %                   | OR (95% CI)    | p-value |
| <18.5    | 1 0.96            | 0 0                    | 2394446.32 (0 - Inf) |
| 18.5-24.9 | 23 22.12        | 26 25                  | Reference     | 0.727 |
| 25-29.9  | 41 39.42          | 38 36.54               | 1.22 (0.6 - 2.49) |
| >30      | 39 37.5           | 40 38.46               | 1.1 (0.54 - 2.25) |

| Functional status | Cognitive impairment | No cognitive impairment | OR (95% CI) p-value |
|-------------------|----------------------|-------------------------|---------------------|
| No Dyspnea        | 100 96.15            | 101 97.12               | Reference           | 0.605 |
| Dyspnea with moderate exertion | 3 2.88          | 3 2.88             | 1.01 (0.52 - 1.31) |
| Dyspnea at rest   | 1 0.96              | 0 0                    | 2139361.78 (0 - Inf) |
| Independent       | 102 98.08           | 102 98.08              | Reference           | 0.98 |
| Partially/Totaly Dependent in ADLs | 2 1.92          | 2 1.92              | 1 (0.14 - 7.24) |
| ASA class         | 1/2 39 37.5         | 33 31.73               | Reference           | 0.14 |
| 3                 | 60 57.69            | 70 67.31               | 0.73 (0.41 - 1.29) |
| 4                 | 5 4.81             | 1 0.96                 | 4.23 (0.47 - 38.05) |

| Comorbidities | Cognitive impairment | No cognitive impairment | p-value |
|---------------|----------------------|-------------------------|---------|
| Smoking       | 4 3.85               | 5 4.81                  | 0.79 (0.21 3.04) 0.733 |
| Hypertension  | 71 68.27             | 82 78.85                | 0.58 (0.31 - 1.08) 0.084 |
| Diabetes      | 20 19.23             | 20 19.23                | 1.00 (0.50 - 1.99) 1 |
| COPD          | 5 4.81               | 1 0.96                  | 5.20 (0.60 - 45.32) 0.098 |
| Steroid use   | 5 4.81               | 5 4.81                  | 1.00 (0.28 - 3.56) 1 |
| Bleeding disorder | 6 5.77            | 8 7.69                  | 0.73 (0.25 - 2.20) 0.58 |
| Sepsis        | 0 0                  | 0 0                     | Reference           | 0.6 |

| Labs | Cognitive impairment | No cognitive impairment | p-value |
|------|----------------------|-------------------------|---------|
| Creatinine | 0.94 0.30       | 0.96 0.33               | 0.83 (0.35 - 1.97) 0.67 |
| Hematocrit | 39.7 5.00        | 40.1 4.50               | 0.86 (0.48 - 1.52) 0.596 |
| Platelets  | 238 68            | 243 74                  | 0.9 (0.61 - 1.33) 0.6 |

| Anesthesia | Cognitive impairment | No cognitive impairment | p-value |
|------------|----------------------|-------------------------|---------|
| Spinal     | 87 83.65             | 76 73.08                | Reference | 0.036 |
| General    | 15 14.42             | 28 26.92                | 0.47 (0.23 - 0.94) |
| Epidural   | 2 1.92               | 0 0                     | Inf (0 - Inf) | 0.6 |

**Abbreviations: BMI, body mass index; ASA, American Society of Anesthesiologists; ADLs, activities of daily living; COPD, chronic obstructive pulmonary disease.**
17% post-operatively). Poor functional status correlates with increased morbidity and mortality; patients needing assistance are likely to develop post-operative complications including pneumonia, infections, and reintubations. Thorough pre-operative evaluation of CI and possible intervention, or rehabilitation could improve outcomes for functional status post operatively. A study performed in Norway showed patients who underwent preoperative and postoperative rehabilitation at a sports medicine clinic showed superior patient-reported outcomes 2 years postoperatively compared to patients who received usual care. The prehabilitation program was 5 weeks long and included heavy resistance strength training. Another study showed that co-management of hip fracture patients by geriatricians and orthopedic surgeons had shorter length of stays, fewer cardiac complications, and decreased incidence of delirium and infection. Prehabilitation has also been shown to reduce total healthcare expenditure, although there needs to be further research in whether this is helpful in patients with preoperative CI undergoing a TKA.

Having a more multidisciplinary team consisting of anesthesiologists, geriatricians, orthopedic surgeons, nurses and other clinical staff could improve patient outcomes with integration of prehabilitation. Additionally, physical therapists are critical members of the team in optimization of post-operative recovery. One study has shown that just a one-time session with a physical therapist to learn and practice postoperative precautions, exercises, bed mobility preoperatively achieved readiness to discharge from PT faster than the control group. Recent SPAQI recommendations for the preoperative management of frailty as well those on launching a dedicated geriatric surgery center have outlined specific steps and considerations in vulnerable populations undergoing elective surgery. This includes active screening for frailty as well as developing clinical pathways, and incorporating geriatric co-management, shared decision-making, and multimodal prehabilitation to improve postoperative outcomes. In fact, frailty assessment can facilitate preoperative counseling regarding post-operative disposition and discharge planning.

### Discharge Destinations

Non-home discharge adds $1.82 billion annually to postoperative rehabilitation costs. There are several factors that could predict being discharged to acute rehabilitation facilities such as living status, age, preoperative systemic health and medical insurance. The ARISE (Arthroplasty Rehabilitation Initial Screening Evaluation) trial which investigated patient characteristics associated with postoperative disposition, incorporated psychological, functional, and socio-demographic factors to determine discharge destination. It showed that pre-operative patient beliefs regarding rehabilitation and future home social support are highly predictive of discharge destination after primary TKA. The only demographic variable that is predictive is increasing age, and in particular, age 75 years and over. Our study showed increased likelihood of discharge to a facility other than home in a patient with preoperative CI.

### Table 2. 30-Day Patient Outcomes.

| Outcomes                        | Cognitive impairment | No cognitive impairment | OR (95% CI) | p-value |
|---------------------------------|----------------------|-------------------------|------------|---------|
|                                 | n         | %     | N      | %  |          |           |
| Death                           | 0         | 0     | 0      | 0  | –        | –         |
| Return to the OR                | 5         | 4.81  | 0      | 0  | –        | 0.994     |
| Failure to wean                 | 1         | 0.96  | 0      | 0  | –        | 0.997     |
| Reintubation                    | 1         | 0.96  | 0      | 0  | –        | 0.997     |
| Surgical site infection         | 3         | 2.88  | 1      | 0.96| 4.17 (0.4 - 42.99) | 0.231 |
| Pneumonia                       | 2         | 1.92  | 0      | 0  | –        | 0.997     |
| Renal insufficiency             | 1         | 0.96  | 0      | 0  | –        | 0.998     |
| Acute MI                        | 0         | 0     | 1      | 0.96| 0 (0 - ∞) | 0.997     |
| Transfusion                     | 11        | 10.58 | 7      | 6.73| 1.72 (0.63 - 4.68) | 0.291 |
| VTE                             | 3         | 2.88  | 2      | 1.92| 1.32 (0.21 - 8.13) | 0.764 |
| UTI                             | 3         | 2.88  | 2      | 1.92| 1.83 (0.29 - 11.66) | 0.521 |
| Sepsis                          | 2         | 1.92  | 0      | 0  | –        | 0.998     |
| Readmission                     | 9         | 8.65  | 7      | 6.73| 1.57 (0.54 - 4.51) | 0.405 |
| Post-operative Delirium         | 28        | 26.92 | 1      | 0.96| 40.15 (5.3 - 304.13) | <0.001 |
| Length of stay                  | 3.62      | 3.35  | 4.28   |    | 1.12 (0.97 - 1.3) | 0.122 |
| Number of complications         | 1.26      | 0.72  | 1.11   | 1  | 1.15 (0.89 - 1.49) | 0.272 |
| Post op Functional Status       |           |       |        |    |          |           |
| Independent                     | 18        | 17.31 | 50     | 48.08| Reference |           |
| Partial/Totally Dependent       | 86        | 82.69 | 54     | 51.92| 4.26 (2.24 - 8.1) | <0.001 |
| Discharge Location              |           |       |        |    |          |           |
| Home                            | 52        | 50    | 67     | 64.42| Reference |           |
| Not Home                        | 52        | 50    | 37     | 35.58| 1.89 (1.07 - 3.35) | 0.029 |

Abbreviations: OR, operating room; MI, myocardial ischemia; VTE, venous thromboembolism; UTI, urinary tract infection.
A recently published study on non-home discharge (NHD) in the general surgical population showed that it is indeed multifactorial and includes risk factors such as advanced age, high risk surgeries (orthopedic, cardiac, and neurosurgery), prior use of mobility aid, fall within 3 months, and body mass index > 30. Other associated factors include access to home services, addressing patient’s pre-surgical beliefs about perceived challenges of rehabilitation at home, as well as multimodal pain management and early mobilization. Another interesting finding in our study was that the non-CI group had increased length of stay. One possible explanation could be that patients destined for non-home discharge (such as rehabilitation) would be able to leave the hospital sooner and therefore have decreased length of stay in the CI group.

Limitations

This analysis was based on data acquired through the NSQIP dataset and is therefore limited by the study’s retrospective nature and limitations of data collection as have been described previously. However, a large and diverse group of hospitals with different practice models submit their noncontrolled data to the NSQIP, therefore we still believe that this study’s findings are broadly generalizable to current practice. The incidence of delirium was based off a manual chart review by NSQIP trained clinical reviewers, looking for keywords that are suggestive of delirium. These data could potentially be underreported if the healthcare provider failed to document characteristics of delirium. Literature suggests that the incidence of postoperative delirium depends on the type of surgery, with hip fracture being the highest followed by cardiac surgery, however, there is variation in this data as well due to the different methods used to report incidence of delirium. CI was identified in patients through documentation by a nurse or doctor stated that the patient had dementia or listed predefined descriptors consistent with dementia. This could limit the sensitivity of the variable to capture early CI and therefore it may have been underestimated. Another confounding factor which could change outcomes post-TKA is the lack of standardization or data available regarding frequency of physical therapy and occupational therapy. Considering how much of an impact pre-op CI had on functional status, it would’ve been important to know the amount of physical therapy these patients had post operatively. Additionally, due to the incidence of cognitive impairment in our cohort, we are unable to comment on the impact of anesthesia type, such as spinal versus general anesthesia, on outcomes in patients undergoing TKA.

Conclusions

Post-operative outcomes such as delirium and reduction in ADLs are associated with an increase in morbidity and mortality. Our study showed that preoperative CI is a predictor for post-operative delirium, non-home discharge and functional decline in patients undergoing TKA. These outcomes could affect patients’ quality of life and also increase burden on the healthcare system. Early identification of patients with CI and preemptive interventions such as multidisciplinary care involving geriatricians and/or neurocognitive specialists may decrease adverse outcomes for these high-risk patients.

Appendix. Baseline Characteristics and Comorbidities in Unmatched Cohort.

| Variable          | Cognitive impairment | No cognitive impairment | OR (95% CI) p-value |
|-------------------|----------------------|-------------------------|---------------------|
| **Age**           | Mean 75.48 ± 6.21    | Mean 73.14 ± 5.92       | 1.06 (1.03 - 1.09) p-value <0.001 |
| Age Groups        | n 25 %               | n 2075 %                |                     |
| 65-70             |                      | 2075.98 ± 19.84         | 1.81 (1.14 - 2.87) 0.001 |
| 70-80             | 68.53 ± 53.97        | 3124.51 ± 50.19         | 1.81 (1.14 - 2.87) 0.001 |
| >80               | 33.52 ± 26.19        | 1025.51 ± 16.47         | 2.67 (1.58 - 4.52) 0.001 |
| **Sex**           | Male 38.19 ± 30.16   | Male 2307.80 ± 37.07    | Reference 0.112     |
| Female            | 88.51 ± 69.84        | 3917.62 ± 62.93         | 1.36 (0.93 - 2) 0.222 |
| **Demographics**  |                      |                         |                     |
| White             | 103.81 ± 81.75       | 5049.82 ± 82.23         | Reference 0.222     |
| Black             | 13.10 ± 10.32        | 425.69 ± 6.92           | 1.5 (0.84 - 2.69) 0.009 |
| Not Reported      | 10.79 ± 7.94         | 666.80 ± 10.85          | 0.74 (0.38 - 1.42) 0.001 |
| **BMI**           | Mean 29.7 ± 5.89     | Mean 31.11 ± 6.01       | 0.96 (0.93 - 0.99) p-value 0.009 |
| BMI Groups        | n 1 %                | N 14 %                  | OR (95% CI) p-value 0.016 |
| <18.5             |                      | 0.79 ± 0.23             | 2.31 (0.29 - 18.23) 0.016 |

(continued)
Appendix. (continued)

| Variable                        | Cognitive impairment | No cognitive impairment | OR (95% CI) | p-value |
|---------------------------------|----------------------|-------------------------|-------------|---------|
|                                  | Mean     | SD       | Mean     | SD       |          |           |
| 18.5-24.9                       | 27       | 21.43    | 874      | 14.07    | Reference|           |
| 25-29.9                         | 46       | 36.51    | 2023     | 32.56    | 0.74 (0.45 - 1.19) |           |
| >30                              | 52       | 41.27    | 3302     | 53.15    | 0.51 (0.32 - 0.82) |           |
| Functional status               |          |          |          |          |           |           |
| No Dyspnea                      | 122      | 96.83    | 6024     | 96.79    | Reference| 0.219     |
| Dyspnea with moderate exertion  | 3        | 2.38     | 190      | 3.05     | 0.78 (0.25 - 2.47) |           |
| Dyspnea at rest                 | 1        | 0.79     | 10       | 0.16     | 4.94 (0.63 - 38.88) |           |
| Independent                     | 119      | 94.44    | 6134     | 98.55    | Reference| <0.001    |
| Partially/Totally Dependent in ADLs | 7       | 5.65     | 90       | 1.45     | 3.44 (1.47 - 8.01) |           |
| ASA class                       |          |          |          |          |           |           |
| 1/2                             | 47       | 37.6     | 3290     | 52.93    | Reference| 0.001     |
| 3                               | 73       | 58.4     | 2814     | 45.27    | 1.82 (1.25 - 2.63) |           |
| 4                               | 5        | 4        | 112      | 1.8      | 3.12 (1.22 - 8.01) |           |
| Comorbidities                   |          |          |          |          |           |           |
| Smoking                         | 4        | 3.17     | 236      | 3.79     | 0.83 (0.3 - 2.27) | 0.719     |
| Hypertension                    | 86       | 68.25    | 4332     | 69.6     | 0.94 (0.64 - 1.37) | 0.745     |
| Diabetes                        | 25       | 19.84    | 1049     | 16.85    | 1.22 (0.78 - 1.9) | 0.376     |
| COPD                            | 5        | 3.97     | 232      | 3.73     | 1.07 (0.43 - 2.64) | 0.888     |
| Steroid use                     | 6        | 4.76     | 228      | 3.66     | 1.31 (0.57 - 3.02) | 0.517     |
| Bleeding disorder               | 7        | 5.56     | 149      | 2.39     | 2.4 (1.1 - 5.23) | 0.023     |
| Sepsis                          | 1        | 0.79     | 5        | 0.08     | 9.95 (1.15 - 85.8) | 0.01      |
| Labs                            |          |          |          |          |           |           |
| Creatinine                      | 0.95     | 0.31     | 0.92     | 0.4      | 1.14 (0.84 - 1.56) | 0.274     |
| Hematocrit                      | 39.9     | 4.90     | 41.3     | 4.10     | 0.48 (0.33 - 0.7) | 0.002     |
| Platelets                       | 234      | 67       | 243      | 66       | 0.8 (0.6 - 1.07) | 0.145     |
| Anesthesia                      |          |          |          |          |           |           |
| Spinal                          | 94       | 80.34    | 4194     | 75.26    | Reference| 0.025     |
| General                         | 21       | 17.95    | 1358     | 24.37    | 0.69 (0.43 - 1.11) |           |
| Epidural                        | 2        | 1.71     | 21       | 0.38     | 4.25 (0.98 - 18.38) |           |

Abbreviations: BMI, body mass index; ASA, American Society of Anesthesiologists; ADLs, activities of daily living; COPD, chronic obstructive pulmonary disease.

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ORCID iD

Sindhu Krishnan, MD @ https://orcid.org/0000-0002-9198-6260

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