

Impact of Frailty on Outcomes of Total Joint Replacement and Differentiating the Impaction of Comorbidity and Frailty

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Abstract

Background: Frailty is a reduced capacity to recover from a physiologically stressful event. It is well established that preoperative frailty is associated with poor postoperative outcomes. Comorbidity often overlap with frailty in the patients and the known risk factors for frailty. No large-scale studies have explored the extent to which frailty impacts outcomes among TJA and it is also unclear the contributions of frailty and its interactions with comorbidity following anesthesia and TJA.

Methods: Discharge data of 2,029,843 patients who underwent TJA between 2005 and 2014 from the National Inpatient Sample (NIS) database was analyzed using cross-tabulations and multivariate regression modeling. Frailty was defined based on frailty-defining diagnosis clusters from the Johns Hopkins Adjusted Clinical Groups frailty-defining diagnosis indicator.

Results: Among patients who underwent total joint replacement surgery, 50,385 (2.5%) were identified as frail. Frailty was highly associated with older age, especially those over the age of 80 years, female, black race, a high Charlson comorbidity index (CCI) of ≥ 3 , emergency/urgent admission and teaching hospital. Frailty had a better predictive effect on in-hospital death and acute surgical complications, while comorbidity was associated with greater odds of acute medical complications. Notably, frailty did not show an enhancement of the predictive power of the Charlson comorbidity score for postoperative complications or in-hospital death. Furthermore, frailty was a good predictor for increased LOS and increased hospitalization costs. There was a synergistic interaction effect between frailty and Charlson comorbidity score on the OR for LOS and hospitalization costs.

Conclusion: Frailty independently predicted postoperative surgical and medical complications. Frailty also had a synergistic interaction with comorbidity for patients who are preparing to undergo TJA.

Introduction

Total joint arthroplasty (TJA) continues to be one of the most successful surgeries performed in orthopedics. As average lifespans increase, the need for joint replacement is growing in orthopedics, especially among the older adult. The demand for total hip arthroplasty is expected to increase by 174% to 572,000 procedures per year, and total knee arthroplasty is expected to increase by 673%, to 3.48 million procedures performed annually by 2030[1].

Frailty, a preventable geriatric syndrome, is a non-specific state of decreased ability to respond to acute stress, and an increased vulnerability to stressors resulting from an organism's decline in physiological reserves[2]. Frailty has been recognized as a predictor for adverse events in patients undergoing non-orthopedic surgery[3][4][5]. These surgeons also have an increased awareness of frailty. There are multiple instruments that are used to assess frailty, including the Clinical Frailty Scale, FRAIL questionnaire, and modified frailty index (mFI)[6][7][8]. However, relatively few large-scale studies have explored the extent to which frailty impacts outcomes among TJA [9] [10] [11]. Comorbidity is defined as the concurrent presence of two or more medically diagnosed diseases in the same individual in which an

index disease occurs first. The comorbidity is also one of the known risk factors for frailty, and multimorbidity significantly overlaps with the frailty, especially in older adults[5]. Wong et al reported that among community dwelling seniors who are frail 82% have comorbidities[5]. Although the close relationship existed between frailty and comorbidity, there are no large-scale studies to differentiate the effects of frailty and comorbidity and among patients who undergo TJA. Due to the different prevention strategies and treatments for patients with frailty and comorbidities, a preoperative medical evaluation of frailty is of great importance for the older patients who undergo joint replacement today [12].

We hypothesized that frailty would have a significant influence on both surgical and medical complications of TJA. Additionally, the integration of frailty and comorbidity would be significant for joint replacement surgery.

Methods

Data Source

The National (Nationwide) Inpatient Sample (NIS) database was used to identify the information of patients who underwent total joint replacement that was performed between 2005 and 2014 based on the International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) procedure codes. The NIS database is one of the largest all-payer inpatient care databases in the United States, and includes data on millions of hospital stays. It includes inpatient access, charges, operations, and outcomes.

Data Collection

The data was extracted from the NIS database from 2005 to 2014. Patients were identified by ICD-9-CM program code for TJA (81.51 and 81.54). The definition of frailty was based on 10 sets of frailty-defined diagnoses including the Hopkins Adjusted Clinical Groups (ACG) frailty indicator (a binary variable), using the ICD-9 codes assigned at the time of admission (Supplemental Table 1). Frailty-defined diagnoses were different from the diagnosis of comorbidities. Except for dementia, the ICD-9 code 290.0-290.3 that defines dementia in the frailty index was also part of the definition of dementia in the comorbidity code, but it only accounted for 1.5% of the cases of dementia defined by the comorbidity.

We graded comorbidity using the the Charlson comorbidity index(CCI). The CCI incorporates the number of pre-existing conditions and their severity. In this index, each condition is assigned a score depending on the risk of death associated with that condition. Postoperative complications were divided into medical and surgical complications. The medical complications included acute cardiac events, severe pulmonary edema, acute renal failure, acute hepatic failure, acute cerebrovascular events, sepsis, pneumonia, and urinary tract infections. The surgical complications included postoperative infections; non-healing surgical wounds; accidental perforation or laceration of a blood vessel, nerve, or organ; a mechanical complication of prosthetic joint; and deep vein thrombosis/pulmonary embolism (DVT/PE)

(Supplemental Table 2). All complications had occurred in the hospital and were assigned a corresponding code before discharge.

Statistical Analysis:

We conducted a cross-sectional analysis utilizing discharge data from the Nationwide Inpatient Sample (NIS). The analytic cohort consisted of patients with a diagnosis of TJA. Frailty, in-hospital death, postoperative complications, length of hospitalization, and costs was examined as dependent variables. Interactions between frailty and comorbidity were investigated. Where independent, frailty was also examined as an independent variable. Other independent variables included were age, sex, comorbidity, nature of admission (emergent/urgent, or other), hospital bed size, hospital location (rural or urban), hospital teaching status[13] [14]. The non-significant interactions identified in some regression models were removed from the model. The hospital bed sizes were divided into three levels: low (<15), intermediate (15–65), and high (>65) number of beds. Odds ratios (ORs) and 95% confidence intervals (CIs) were reported for univariate and multivariate analyses.

Stata software, R version 3.5.3 (The R Foundation Inc) was used for data analysis. A P value<0.05 with OR and 95% CI was used to determine the statistical significance of the independent variables.

Results

Of the 2029843 patients who underwent hip and knee replacement in the NIS database from 2005 to 2014, there were 50385 patients with frailty (Table 1). The overall incidence rate for frailty was 2.5%. The incidence rate of TJA patients over the age of 80 years was two to three times with frailty than that of non-frail. Most preoperative frail patients were white, female, with an average age of 74 years and were older than those who were not frail. Patients with frailty accounted for 92.4% of those with a CCI ≥ 3 points. The mortality rate of patients with frailty was much higher than that of non-frail patients. The cost of hospitalization was higher for patients with frailty than that for non-frail patients (Table 1). Further, in Table 2, multiple logistic regression analysis shows that the patients with frailty were significantly associated with being over the age of 80 years, black race, female, having a CCI ≥ 3 , being treated in hospitals with medium or large bed sizes, teaching hospitals, and urban hospitals. Frailty was associated with a decreased odds of emergency/urgent admission and a CCI score of 2.

Table 1
Patient Characteristics with frail and Outcomes After THA (2005-2014)

Parameter	Non-Frail	Frail	P Value
Total(n=count)	1979458	50385	-
Total incidence	2.5%		
Age (mean±standard deviation, yrs.)	67.14±0.03	74.31±0.28	<0.0001
Age group (years)			<0.0001
≤40	1.4%	0.82%	
40–64	39.3%	20.3%	
65–80	45.7%	42.6%	
≥80	13.6%	36.28%	
Sex			<0.0001
Male	38.5%	33.6%	
Female	61.5%	66.4%	
Race			<0.0001
White	71%	74.6%	
Black	5.8%	5.7%	
Hispanic	3.9%	3.9%	
Asian or Pacific Islander	1%	1.1%	
Native American	0.4%	0.36%	
Other	1.8%	1.6%	
Nature of admission			<0.0001
Emergency/Urgent	14.7%	45%	
Elective	85.1%	54.8%	
Comorbidity			<0.0001
0	0.93%	4.5%	
1	4.4%	1.7%	
2	14.8%	5.4%	
≥3	79.8%	92.5%	
Medical complications			

Parameter	Non-Frail	Frail	P Value
Acute cardiac event	4.1%	12.8%	<0.0001
Acute pulmonary edema/failure	0.57%	4.3%	<0.0001
Acute cerebrovascular event	0.1%	0.3%	<0.0001
Acute renal failure	2.2%	9.0%	<0.0001
Acute hepatic failure	0.03%	0.3%	<0.0001
Pneumonia	0.9%	5.4%	<0.0001
Urinary tract infection	0.4%	0.6%	<0.0001
Surgical complications			
Postoperative infection	0.1%	0.2%	<0.0001
Accidental perforation or laceration of blood vessel, nerve, or organ	0.1%	0.1%	<0.0001
mechanical complication of prosthetic joint	0.6%	1.9%	<0.0001
DVT/PE ^a	0.7%	1.7%	<0.0001
Average cost of hospitalization	49402\$(47731,47831)	69113\$	<0.0001
Death rate	0.3%	2.4%	<0.0001

^aDVT/PE: Deep vein thrombosis/pulmonary embolism

Table 2
Multivariate Logistic Regression Analysis of Variables Significantly Associated with Frailty.

Variable	OR ^a	95% CI ^b	P Value
Age group≥80 years	1.922	[1.88001–1.96560]	<0.0001
Female	1.0407	[1.01964–1.06216]	0.00013
Black race	1.1063	[1.06376–1.15062]	<0.0001
Emergency/urgent admission	0.2965	[0.29026–0.30295]	<0.0001
Charlson comorbidity index 2	0.8129	[0.70114–0.94254]	0.00607
Charlson comorbidity index ≥3	1.6231	[1.40687–1.87263]	<0.0001
Medium bed size	1.3109	[1.27074–1.35230]	<0.0001
Large bed size	1.2832	[1.24731–1.32016]	<0.0001
Teaching hospital	1.1	[1.04748–1.09068]	<0.0001
Urban hospital location	1.1	[1.05354–1.12313]	<0.0001

^aOR =Odds Ratio^bCI: Confidence Interval

Multiple logistic regression analysis comparing the effect of frailty and preoperative comorbidity on mortality, medical, and surgical complications is shown in Table 3. After controlling for the effects of all variables, patients with frailty, over the age of 80 years, in hospitals with a medium or large bed size, and teaching hospitals were the independent factors significantly associated with an increased risk of in-hospital death; however, emergency/urgent admission, and urban hospital location were significantly associated with decreased odds of mortality. Further, the comorbidity score was not significantly associated with in-hospital death. The odds of postoperative surgical complications were significantly higher in the hospitals with a medium or large bed size, urban hospital locations, and patients with frailty, whereas older age, female, and emergency/urgent admission were associated with lower odds of acute surgical complications. The comorbidity score was not significantly associated with surgical complications. Acute medical complications were significantly associated with older age, medium or large-volume hospital care, urban hospital location, teaching hospitals, frailty, and comorbidity. The odds of postoperative medical complications were lower for female patients and emergency/urgent admission. Frailty was associated with lower odds of acute medical complications than that for comorbidity.

Table 3
Multivariate Logistic Regression Analysis of Variables Significantly Associated with Risk of In-Hospital Death and Postoperative Complications.

Variable	OR ^a	95% CI ^b	P Value
In-hospital death			
Age group≥80 years	2.97051	[2.22332,3.9688]	<0.0001
Female	0.58008	[0.55220–0.6094]	<0.0001
Emergency/urgent admission	0.11309	[0.10627–0.1203]	<0.0001
Medium bed size	1.13505	[1.04606–1.2316]	0.00236
Large bed size	1.20576	[1.11979–1.2983]	<0.0001
Teaching hospital	1.12946	[1.07281–1.1891]	<0.0001
Urban hospital location	0.91320	[0.85014–0.9809]	0.01288
Frail	5.09046	[3.9917–6.44707]	<0.0001
Charlson comorbidity index=1	1.16483	[0.1909–7.10789]	0.86867
Charlson comorbidity index=2	1.01096	[0.1607–6.35993]	0.99073
Charlson comorbidity index≥3	1.88958	[0.3041–11.74262]	0.49478
Surgical complications			
40 to 64 years	0.17026	[0.13909–0.20842]	<0.0001
65 to 80 years	0.07460	[0.05996–0.09281]	<0.0001
>80 years	0.05248	[0.04036–0.06826]	<0.0001
Female	0.57444	[0.50722–0.65057]	<0.0001
Emergency/urgent admission	0.19200	[0.16757–0.21999]	<0.0001
Medium bed size	1.13505	[1.04606–1.2316]	0.00236
Large bed size	1.20576	[1.11979–1.2983]	<0.0001
Teaching hospital	2.11839	[1.85358–2.42104]	<0.0001
Urban hospital location	1.63107	[1.25291–2.12337]	0.00028
Frail	4.43661	[1.60858–12.23655]	0.00400
Charlson comorbidity index=1	0.37590	[0.03719–3.79894]	0.40707
Charlson comorbidity index=2	0.34613	[0.03080–3.88964]	0.39004
Charlson comorbidity index≥3	0.76419	[0.07303–7.99691]	0.82237

Variable	OR ^a	95% CI ^b	P Value
Medical complications			
40 to 64 years	1.64373	[1.53057–1.76525]	<0.0001
65 to 80 years	2.09409	[1.95107–2.24759]	<0.0001
>80 years	4.15499	[3.86966–4.46135]	<0.0001
Female	0.79571	[0.78688–0.80465]	<0.0001
Emergency/urgent admission	0.33972	[0.33555–0.34393]	<0.0001
Medium bed size	1.18791	[1.16748–1.20869]	<0.0001
Large bed size	1.22394	[1.20499–1.24318]	<0.0001
Teaching hospital	1.14781	[1.13486–1.16091]	<0.0001
Urban hospital location	1.04192	[1.02415–1.06001]	<0.0001
Frail	2.00216	[1.81372–1.90562]	<0.0001
Charlson comorbidity index=1	3.09695	[1.58599–2.21624]	<0.0001
Charlson comorbidity index=2	4.79525	[2.46746 ,3.43978]	<0.0001
Charlson comorbidity index≥3	18.30816	[9.44622, 13.15078]	<0.0001

^aOR =Odds Ratio^bCI: Confidence Interval

Compared with comorbidities, the correlation between frailty and hospital mortality or surgical complications had a greater significance (Figure 1a&1c). In contrast, fragility was less relevant for medical complications than it was for comorbidities (Figure 1b). The interaction between frailty and comorbidity was not substantial regarding mortality, internal, or surgical complications.

Linear multiple regression analysis of the independent variables associated with hospitalization time or costs are shown in Table 4. The result showed that patients who were older than 80 years, female, in hospitals with a large bed size, teaching hospitals, and urban hospital locations were significantly associated with longer hospitalization time. The interaction between frailty and comorbidities was significant for the length of hospital stay (Figure 2a). Hospital costs were significantly associated with hospitals with medium and large bed sizes, and urban hospitals. The interaction between frailty and comorbidities was significant for the cost of hospitalization (Figure 2b). Furthermore, frailty was a good predictor for increased LOS and increased hospitalization costs (Supplemental Table 3).

Table 4
Generalized Linear Regression Analysis of Length of Stay and Hospital Costs

Variable	OR^a	95% CI^b	P Value
Length of stay (days)			
40 to 64 years	-0.17228	[-0.20180– -0.14275]	<0.0001
65 to 80 years	-0.07707	[-0.10659– -0.04755]	<0.0001
>80 years	0.45668	[0.42602–0.48733]	<0.0001
Female	-1.95904	[-1.96905– -1.94903]	<0.0001
Emergency/urgent admission	0.03105	[0.02409–0.03801]	<0.0001
Medium bed size	0.10855	[0.09828–0.11881]	<0.0001
Large bed size	0.22233	[0.21324–0.23142]	<0.0001
Teaching hospital	0.12199	[0.11495–0.12904]	<0.0001
Urban hospital location	0.00993	[-0.00096–0.02082]	<0.0001
Non-Frail, CCI ^c =1	0.18586	[0.11042–0.26129]	<0.0001
Non-Frail, CCI =2	0.24974	[0.17365–0.32584]	<0.0001
Non-Frail, CCI \geq 3	0.44118	[0.36514– 0.51723]	<0.0001
Frail, CCI =0	1.53533	[1.09748–1.97318]	<0.0001
Frail, CCI =1	0.57325	[0.38423–0.76227]	<0.0001
Frail, CCI =2	0.58512	[0.46956–0.70068]	<0.0001
Frail, CCI \geq 3	1.31211	[1.23151–1.39271]	<0.0001
Cost of hospitalization (Dollars)			
40 to 64 years	\$-5122.97	[-5509.2– -4736.8]	<0.0001
65 to 80 years	\$-6494.01	[-6880.1– -6107.9]	<0.0001
>80 years	\$-6415.72	[-6816.7– -6014.7]	<0.0001
Female	\$-7194.00	[-7325.0– -7063.0]	<0.0001
Emergency/urgent admission	\$-1626.37	[-1717.7– -1535.0]	<0.0001
Medium bed size	\$2816.81	[2681.8–2951.8]	<0.0001
Large bed size	\$3434.61	[3315.5–3553.7]	<0.0001
Teaching hospital	\$-1701.21	[-1793.7--1608.7]	<0.0001

Variable	OR ^a	95% CI ^b	P Value
Urban hospital location	\$11664.11	[11522.2–11806.0]	<0.0001
Non-Frail, CCI =1	\$3151.7	[1899.9–4403.4]	<0.0001
Non-Frail, CCI =2	\$3630.6	[2367.9–4893.4]	<0.0001
Non-Frail, CCI≥3	\$5443.3	[4181.4–6705.2]	<0.0001
Frail, CCI =0	\$26426.7	[19202.9–33650.6]	<0.0001
Frail, CCI =1	\$13345.7	[10213.9–16477.5]	<0.0001
Frail, CCI =2	\$13885.7	[11966.2–15805.1]	<0.0001
Frail, CCI≥3	\$16748.2	[15409.8–18086.6]	<0.0001

^aOR =Odds Ratio^bCI: Confidence Interval^c CCI= Charlson comorbidity index

Discussion

This study shows that frailty rate of joint replacement was only 2.5%, which is consistent with the results of McIsaac et al.. However, the incidence rate is also far lower than that for other surgical operations, which range from 8–28%, possible because the high rates of frailty comprised only older adults[3].

Our study found that frailty was significantly associated with advanced comorbidity (CCI ≥3). This reflects that among patients undergoing TJA, those who are frail before surgery do easily have combined with comorbidities. This may also be related to the comorbidity being a major cause of frailty. We further found that frailty was significantly associated with in-hospital death, and surgical complications, while comorbidity was not an independent predictor for in-hospital death and surgical complications, the interaction between frailty and comorbidity was not significant, suggesting that comorbidity did not affect the state of frailty during the short term perioperative period. This means that in the preoperative assessment of patients who are frail before surgery, there is no need to afraid that whether the comorbidities may increase the risk of frailty postoperative in-hospital death and postoperative surgical complications. Although both frailty and comorbidity could independently predict medical complications, comorbidities have a greater impact on medical complications. The interaction between frailty and comorbidity was also not significant, Therefore, When considering postoperative medical complication, more attention should be paid to comorbidity.

There was a synergistic interaction between frailty and comorbidity for length of stay and hospitalization costs. Generally speaking, costs and LOS of the patient with non-frailty is far less than that of frailty (figure 2a and 2b). Interestingly, the combined predictor, frailty, CCI=0, had a greater influence on the length of stay and hospitalization costs than the other predictor that CCI≠0, This suggests that for people

without comorbidities, frailty is easy to be neglect by doctors, which will made patient cost more in hospital.

This study has some limitations. Due to the limitations of the NIS database, the study could not fully examine the effect of frailty on patients who underwent TJA. For example, the long-term complications or re-admission indicators were not included in the database. Moreover, the specific mechanism of the effect of frailty on particular difficulties associated with TJA requires further investigation. Frailty did not stratify according to different severities such as the Clinical Frailty Scale because of the limitations of the database.

Nevertheless, this study demonstrates the importance of frailty in joint replacement surgery.

Frailty and comorbidities are often present in patients concurrently; however, frailty is independent of comorbidities and has an impact on the postoperative complications associated with joint replacement. From the perspective of the synergistic interaction between frailty and comorbidities in hospitalization costs and length of stay, frailty is a factor that requires consideration for joint replacement.

When doctors understand the contributions and interactions of frailty and comorbidity, they can optimize the patient's status before surgery. Regarding the patients with multiple comorbidities, the doctor should consider multi-drug therapy to prevent acute medical complications or balance the advantages and disadvantages of the risk of comorbidities and the benefits after TJA. Yet, for patients with frailty who undergo TJA, interventions to treat frailty should be a priority. Most importantly, it is vital to strengthen nutritional reserves to improve the patient's ability to respond to surgery. For instance, similar to nutrient-dense fluids, oral nutritional supplements can be provided to patients with frailty. Administration of oral nutritional supplements shows a decrease in the mortality rate for hip fractures[14].Second, early treatment with vitamin D in the range of 200–1000 IU could reduce falls, and improve muscle and nerve function^[14] Finally, exercise is an essential part of the treatment for frailty. Progressive strength training before surgery has been deemed the key exercise for patients with frailty[15].

Conclusion

Frailty is an independent risk factor for postoperative complications, in-hospital death, length of stay, and hospitalization costs in TJA patients. Further, frailty did not show the significance synergistic interaction with the advance comorbidity for postoperative complications or in-hospital death. Compared with comorbidity, frailty had a greater influence on surgical complications, which might be the reason to increase the in-hospital death rate for patients with frailty who undergo TJA. Above all, the frailty need to be pay more attention to the patient following anesthesia and undergo the joint replacement, especially for the acute postoperative surgical complication and the in-hospital death.

Abbreviations

TJA= total joint replacement; NIS= National Inpatient Sample; ICD-9-CM= International Classification of Diseases, Ninth Revision, Clinical Modification ; CCI= Charlson comorbidity index.

Declarations

Ethics approval and consent to participate

Not applicable. Administrative permissions were required to access the raw data used in this study and the corresponding author's (Zhang yang) work unit (Division of Orthopaedic Surgery, Department of Orthopaedics, Nanfang Hospital, Southern Medical University, Guangzhou, Guangdong, 510515, China.) has already granted permission from Agency for Healthcare Research and Quality (AHRQ) to access Healthcare Cost and Utilization Project (HCUP) Nationwide Databases. However, this observational study used deidentified publicly available data, hence there was no requirement for consent to participate and it was deemed exempt by the ethics committee. So there are no need to grant permission in the Ethics approval and consent to participate section. What is more, the data used in this study were no need anonymized before its use. All methods are carried out in accordance with relevant guidelines and regulations. the data used in this study were no need anonymized before its use.

The datasets generated during and analyzed during the current study are not publicly available due to Data Use Agreement and more information can be found in AHRQ HCUP (www.hcup-us.ahrq.gov). They are available from the corresponding author on reasonable request.

The Nationwide Inpatient Sample (NIS) database, conducted by the Healthcare Cost and Utilization Project, and sponsored by the Agency for Healthcare Research and Quality, was the data source of this study. In the United States, NIS represents the largest all-payer database of hospital admissions. NIS collects a stratified sample from more than 1000 hospitals, of approximately 20% of the hospitalizations in the United States each year.

Consent for publication

Not applicable.

Availability of data and materials

Due to the data usage agreement, the data set generated and analyzed during the current study is not publicly available. More information can be found in AHRQ HCUP (www.hcup-us.ahrq.gov). They can be obtained from the corresponding author upon reasonable request.

Competing interests

The authors declare that they have no competing interests funding.

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None.

Authors' contributions

Qiang Lian performed the research design and wrote the manuscript with revision, guidance, and feedback from Yang Zhang. The acquisition of data and proofreading of this manuscript was performed by Jian Wang. Data analysis and interpretation was performed by Yun Lian, Qinfeng Yang, Mingchen Zhao. All authors have read and approved the final submitted manuscript.

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Figures

Figure 1

a. Differences of the Charlson Comorbidity Index and the Frailty
on surgical complications of Total Joint Replacement from 2005 to 2014

- b. Differences of the Charlson Comorbidity Index and the Frailty
on medical complications of Total Joint Replacement from 2005 to 2014**
- c. Differences of the Charlson Comorbidity Index and the Frailty
on the in-hospital death of Total Joint Replacement from 2005 to 2014**

Figure 2

- a. comparing with the combined indictor (Non-frail, CCI=0), the increased days of LOS of patients undergoing TJA**
- b. comparing with the combined indictor (Non-frail, CCI=0), the increased days of LOS of patients undergoing TJA**

Supplementary Files

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