Published in final edited form as:
Pain Med. 2013 August ; 14(8): . doi:10.1111/pme.12153.

Medical Comorbidity is Associated with Persistent Index Hip Pain after Primary THA

Jasvinder A. Singh, MBBS, MPH[1,2,3] and **David G. Lewallen, MD**[3]

[1]Medicine Service and Center for Surgical Medical Acute care Research and Transitions (C-SMART), Birmingham VA Medical Center, Birmingham, AL

[2]Department of Medicine at School of Medicine, and Division of Epidemiology at School of Public Health, University of Alabama, Birmingham, AL

[3]Department of Orthopedic Surgery, Mayo Clinic College of Medicine, Rochester, MN

Abstract

Objective—To characterize whether medical comorbidity predicts persistent moderate-severe pain after total hip arthroplasty (THA)

Methods—We analyzed the prospectively collected data from the Mayo Clinic Total Joint Registry for patients who underwent primary or revision THA between 1993–2005. Using multivariable-adjusted logistic regression analyses, we examined whether certain medical comorbidities were associated with persistent moderate-severe hip pain 2- or 5-years after primary or revision THA. Odds ratios (OR), along with 95% confidence intervals (CI) and p-value are presented.

Results—The primary THA cohort consisted of 5,707 THAs and 3,289 THAs at 2- and 5-years, and revision THA, 2,687 and 1,627 THAs, respectively. In multivariable-adjusted logistic regression models, in the primary THA cohort, renal disease was associated with lower odds of moderate-severe hip pain (OR, 0.6; 95% CI, 0.3, 1.0) at 2-years. None of the comorbidities were significantly associated at 5-years. In the revision THA cohort, heart disease was significantly associated with higher risk (OR, 1.7; 95% CI, 1.1, 2.6) at 2-years and connective tissue disease with lower risk (OR, 0.5; 95% CI, 0.3, 0.9) of moderate-severe hip pain at 5-years follow-up.

Correspondence: Jasvinder A. Singh, MBBS, MPH, University of Alabama, Faculty Office Tower 805B, 510 20th Street S, Birmingham, AL 35294. Phone: 205-934-8158 Jasvinder.md@gmail.com.

Financial Conflict: There are no financial conflicts related directly to this study. J.A.S. has received research and travel grants from Takeda and Savient; and consultant fees from URL pharmaceuticals, Savient, Takeda, Ardea, Regeneron, Allergan and Novartis. D.G.L. has received royalties/speaker fees from Zimmer, Orthosonic and Osteotech, has been a paid consultant and owns stock in Pipeline Biomedical and his institution has received research funds from DePuy, Stryker, Biomet and Zimmer.

IRB approval: This study was approved by the Mayo Clinic Institutional Review Board and all investigations were conducted in conformity with ethical principles of research.

Disclaimer: "The views expressed in this article are those of the authors and do not necessarily reflect the position or policy of the Department of Veterans Affairs or the United States government."

AUTHOR CONTRIBUTIONS
Study design and protocol: JAS
Review of study design: JAS, DGL
Data analyses: JAS
Review of analyses and results: JAS, DGL
Manuscript draft: JAS
Manuscript revision: JAS, DGL
Submission: JAS

Conclusion—This study identified new correlates of moderate-severe hip pain after primary or revision THA, a much-feared outcome of hip arthroplasty. Patients with these comorbidities should be informed regarding the increased risk or moderate-severe index hip pain, so that they can have a fully informed consent and realistic expectations.

Keywords

Pain; Function; functional limitation; Total hip replacement; primary; arthroplasty; joint replacement; outcomes; Patient-Reported Outcomes

Introduction

Total Hip Arthroplasty (THA) is a commonly performed joint arthroplasty in the U.S. and the annual volume was projected to double by 2030 (1). The annual estimated volume for primary THA was 427,000 in 2009 from a population-based study (2). While most of the THAs are successful in improving index hip joint pain (3–5), 8% patients with primary THAs (6) and 18% with revision THAs (7) reported moderate-severe index hip pain 2-years after THA. Thus, a significant proportion of patients report refractory index hip pain after THA.

Few studies have investigated predictors of persistent index hip joint pain after THA. In our previous studies, we reported that obesity and depression predicted moderate-severe pain after primary THA (6) and younger age, female gender, obesity and depression predicted moderate-severe pain after revision THA (7). In a recent study, Lubekke et al. reported that medical comorbidities and age partially explained the difference in pain and function outcomes between primary and revision THA (8). Two other studies reported that comorbidity was associated with perioperative adverse events and longer patient hospital stay after THA (9) and with major complications after revision THA (10). While evidence exists for association of comorbidities with poorer function after primary THA (11–15), to our knowledge, there are no well-designed studies investigating whether, and which medical comorbidities predict poor pain outcomes after THA. This knowledge would allow more informed patient-surgeon discussion for patients with comorbidities that are risk factors for poor pain outcomes.

In this study, we used data prospectively collected as part of an institutional total joint registry to investigate whether certain medical comorbidities were associated with the risk of moderate-severe index hip pain 2- and 5-years after primary or revision THA.

Methods

Data Sources and Study Cohort

We used prospectively collected data from the Mayo Clinic Total Joint Registry. The total joint registry collects data prospectively on every patient who undergoes hip arthroplasty at the Mayo Clinic, Rochester. At 2- and 5-years validated pain and function surveys are administered to patients at the clinic visit, by mail or on the telephone, by trained, registry staff. The Mayo Hip questionnaire has been validated (16–18). Several papers using these data have been published (6, 7).

Patients were included in this study if they underwent primary or revision THA between 1993 and 2005 and completed either a 2- or 5-year patient survey. We chose this period since electronic data capture began in 1993, and to allow 5-year follow-up for most of the cohort.

Study Outcome

The outcome of interest was moderate-severe pain in index hip at 2- or 5-years after primary or revision THA. Pain was assessed with the question "How much pain do you have in your operated hip?" Patients could respond- 'none', 'mild', 'moderate', 'severe'. None/mild was the reference category and moderate and severe categories were combined into moderate-severe pain, an a priori decision made long before data analyses, also used in previous studies (6, 7). Most importantly, this decision was based on an orthropedic surgeon's recommendation (D.G.), since moderate or severe index THA pain is considered a highly undesirable outcome of THA. Use of all four categories of pain would require the use of a multinomial logistic regression, leading to 3 odds ratios for each comorbidity, making the result very difficult to interpret, especially when not consistent. The pain question in the Mayo Hip questionnaire that we used in this paper (16–18) is similar to the pain question in Harris Hip Score, the most commonly used outcome instrument in patients with THA that is valid, reliable and sensitive to change (19–21).

Predictors of Interest

Medical comorbidities prior to THA were the main predictors of interest. Comorbidity was assessed with by Deyo-Charlson index, a validated comorbidity measure (22), consisting of 17 comorbidities (23, 24). Comorbidities were identified by the presence of International Classification of Diseases- ninth revision (ICD)-9 codes for these select comorbidities in the medical records of patients. We assessed whether the six preoperative comorbidities of interest (determined a priori) were associated with moderate-severe pain after THA: heart disease (myocardial infarction or congestive heart failure), peripheral Vascular Disease, renal disease, chronic obstructive pulmonary disease (COPD), diabetes (with or without organ damage) and connective tissue Disease (including rheumatoid arthritis, systemic lupus erythematosus, systemic sclerosis, polymyalgia rheumatica etc.).

Covariates and Confounders

Since several clinical, demographic and implant related factors have been previously shown to be associated with outcomes after THA, they were included in the analyses as covariates and potential confounders (6) (7) (8). These included: (1) demographic - age and gender; and (2) clinical – body mass index (BMI) (25), underlying diagnosis, American Society of Anesthesiologists (ASA) class (26, 27), depression and anxiety; (3) implant fixation-cemented/hybrid or uncemented (for primary THA only); and (4) distance from the medical center. As previously, age was categorized into ≤60, 61–70, 71–80 and >80, BMI into ≤25, 25.1–29.9, 30–34.9, 35–39.9 and ≥40, distance from the medical center into 0–100 miles, >100–500 miles, >500 miles (28–30) and ASA class into I–II vs. III–IV (6, 7). The reason to collapse categories for some covariates was that very small % were in last categories, e.g., only 0,7% and 0.4% of primary THA 2- and 5-year cohorts, respectively, had ASA class IV at surgery. Depression and anxiety were assessed by the presence of ICD-9 codes in medical records before the THA.

Statistical Analyses

Univariate and multivariable models were used to assess the association of medical comorbidities with the odds of moderate-severe pain at both 2- and 5-years post-primary and post-revision THA. The multivariable model included gender, age, BMI, ASA score, distance from the medical center, operative diagnosis, depression, anxiety, six medical comorbidities and implant fixation (for primary only). Odds ratios (ORs) with 95% confidence intervals (CIs), and p-values are reported. A p-value ≤ 0.05 was considered statistically significant. We performed all analyses using logistic regression using a generalized estimating equations (GEE) approach to adjust the standard errors for the

correlation between observations on the same subject due to both hips having been replaced and/or multiple operations on the same hip.

Results

Clinical and Demographic Characteristics

The mean age of the primary THA cohort was 65 years, 51% were female, 76% were overweight or obese, and 38% has ASA class III or IV (Table 1). The underlying diagnosis was osteoarthritis in 87% and 65% implants were cemented or hybrid. Medical comorbidities were common - 7% had heart disease, 4% peripheral vascular disease, 5% mild-moderate renal disease, 9% chronic obstructive pulmonary disease (COPD), 6% diabetes and 6% connective tissue disease (Table 1).

In the revision THA cohort, the mean age was 65 years, 53% were female, 71% were overweight or obese and 43% had ASA class III or IV (Table 1). The underlying diagnosis was loosening, wear or osteolysis in 73%. Medical comorbidities were common in these patients, ranging 4% to 8% (Table 1).

Comorbidity Correlates of Hip Pain after Primary THA

Unadjusted analyses showed that peripheral vascular disease was associated with higher odds of moderate-severe pain 2-years after primary THA (Table 2). No significant associations were seen at 5-years after primary THA.

Multivariable-adjusted model showed that peripheral vascular disease had a non-significant association with moderate-severe pain 2-years after primary THA (p=0.06), while renal disease seemed protective (Table 3). None of the other comorbidities were associated with moderate-severe pain at 5-years after primary THA (Table 3).

Comorbidity Correlates of Hip Pain after Revision THA

In unadjusted analyses, we found that heart disease increased the odds at 2-years, while connective tissue disease, reduced the odds of moderate-severe pain 5-years after revision THA (Table 4).

Multivariable-adjusted models confirmed both findings from univariate models. Heart disease was associated with 1.7 times higher odds at 2-years, while connective tissue disease was associated with 0.5-times odds of moderate-severe index hip pain 5-years after revision THA (Table 5).

Discussion

In this study in a large sample of patients who underwent primary or revision THA, some medical comorbidities were significantly associated with pain outcome at 2- or 5-years post-THA. To our knowledge, no prior studies have examined the impact of specific medical comorbidities on pain outcome after THA, provided data up to 5-year follow-up and performed in a multivariable-adjusted analyses accounting for important covariates and confounders. Thus, these results add to the knowledge in this area of pain outcomes. Presence of connective tissue disease (rheumatoid arthritis etc.) and renal disease were associated with a lower risk of moderate-severe pain. On the other hand, heart disease was associated with significantly higher and peripheral vascular disease with borderline non-significantly higher risk of moderate- severe pain after THA. Several common conditions such as diabetes and COPD were not significantly associated with moderate-severe pain in adjusted analyses.

Several study findings merit discussion. In the primary THA cohort, peripheral vascular disease had a non-significant association with moderate-severe pain 2-years after primary THA (p=0.06), while renal disease seemed protective. The finding of revere relationship of renal disease was surprising and is somewhat counter-intuitive. We are unaware of any other study that has evaluated impact of renal disease on pain outcomes after hip arthroplasty. One study that compared patients with various degrees of chronic kidney disease and normal controls found no significant differences in pain scores between groups (31); interestingly pain scores were numerically, but not statistically significantly, lower for stage 4 kidney failure compared to stage 1–3. Another study reported less pain with more chronic kidney disease stages 3–5 compared with stages 1–2 (32). These studies seem to indicate that pain severity or duration seemed to be lower with more advanced renal disease. Renal failure is also associated with neuropathy (35) secondary to renal failure itself, but may also due to associated diabetes, one of the two commonest causes, which might contribute to favorable outcome. The negative association between renal failure and moderate-severe pain that we observed is a bit counterintuitive and the reasons are not entirely clear to us. Whether that explains this finding in our study is unclear. It is possible that severe renal disease impacts peripheral nervous system and may reduce the pain perception. This finding needs confirmation in future studies. We believe this finding needs confirmation in future studies. The finding of borderline association of peripheral vascular disease with moderate-severe pain is not unexpected, due to associated claudication symptoms. While many chronic pain conditions are associated with increased sensitization, it is not known whether claudication is associated with this phenomenon leading to more hip pain.

Heart disease (myocardial infarction or congestive heart failure) was associated with 1.7 times higher odds at 2-years, while connective tissue disease was associated with 0.5-times odds of moderate-severe index hip pain 5-years after revision THA. Connective tissue diseases such as rheumatoid arthritis (RA) are associated with better implant survival after THA (33, 34), compared to osteoarthritis as the underlying diagnosis. Our finding of a lower risk of refractory hip pain in THA patients with connective tissue disease is in concert with these previous findings, since among the connective tissue diseases leading to THA, RA is the most common underlying cause. In addition, patients with underlying conditions other than connective tissue diseases (in this case rheumatoid arthritis in most cases), such as osteoarthritis have higher prevalence of obesity, which we have shown to be a risk factor for poor pain outcomes in our previous THA study (6).

The association of heart disease with poor outcome extends the finding from a previous small study of a statistically non-significant trend towards lower improvement in pain scores in patients with congestive heart failure at 6-months after THA (36). Comorbidities have been linked to more peri-operative complications, adverse events and longer hospital stay after primary THA (9, 10). These may impact the risk of pain at short- and intermediate-term follow-up. A much larger sample in our study allowed us the ability to examine this association, which may not have been statistically significant in the previous study due to a small sample size. These findings add to this growing body of literature linking medical comorbidity to arthroplasty outcomes.

Another interesting observation in our study was that several significant associations at 2-years were not significant at 5-years. This might be due to several potential reasons: (1) different source/etiology of pain at 2-years post-surgery compared to that at 5-years post-surgery; (2) temporality of association of comorbidity and pain; and (3) smaller sample size at 5- compared to 2-years. An important exception to this was that connective tissue disease was associated with significantly more moderate-severe hip pain at 5-, but not at 2-years. This implied that factors other than sample size were contributing to somewhat discrepant findings between 2- and 5-years.

Our study has important implications for patients undergoing THA, namely, that patients with heart disease, peripheral vascular disease and connective tissue disease can be better informed regarding pain outcomes after THA that allows them to have realistic expectations. Our study does not provide data to support whether optimization of medical comorbidities will improve short- and intermediate-term arthroplasty outcomes, including pain and function; this remains to be seen.

Our study has important limitations and strengths. Survey non-response biased our findings towards null, therefore these are likely conservative estimates. Non-response rate was higher at 5-year follow-up making these estimates potentially more biased. Despite our attempts and success at controlling for several important factors, residual confounding is possible in this cohort study, since we did not measure factors such as patient engagement, patient coping skills and pain catastrophizing, rehabilitation regimens used and compliance with them, social support etc. Our study was designed to investigate which of the specific comorbidities are associated with the outcome and not why or how a given comorbidity is associated. Future studies should now use pharmacy data related to comorbidities to examine whether the differences in pain outcomes related to comorbidities are due to disease itself, its treatment or both. A large study sample with availability of enough outcome events, analysis of prospectively collected data (collected as part of total joint registry), adjustment for a large number of important confounding factors and covariates and analysis of both 2- and 5-year follow-up data are study strengths.

In summary, in this study of prospectively collected data as part of a total joint registry, we found that specific medical comorbidities were associated with moderate-severe pain at 2- and 5-years post-THA. We studied both primary and revision THA cohorts. These study findings can be used to educate patients with these conditions, so that they have realistic expectations regarding post-operative pain and function outcomes. Future studies should examine if optimization of medical conditions pre- and peri-operatively can improve short- and long-term pain and function outcomes.

Acknowledgments

Grant support: This material is the result of work supported with research grants from the Mayo Clinic Orthopedic Surgery research funds, National Institutes of Health (NIH) Clinical Translational Science Award 1 KL2 RR024151-01 (Mayo Clinic Center for Clinical and Translational Research) and the resources and use of facilities at the Birmingham VA Medical Center, Alabama, USA. J.A.S. is also supported by grants from the Agency for Health Quality and Research Center for Education and Research on Therapeutics (CERTs), National Institute of Aging and National Cancer Institute.

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Summary

In this study of a large institutional U.S. Joint Registry, we found that several medical comorbidities were associated with the risk of moderate-severe pain 2- and 5-years after total hip arthroplasty (THA). Renal disease decreased the odds (0.6-times) of moderate-severe pain after primary THA. Heart disease was associated with 1.7 times higher odds at 2-years, while connective tissue disease was associated with 0.5-times odds of moderate-severe index hip pain 5-years after revision THA.

Pain Med. Author manuscript; available in PMC 2014 August 01.

Table 1

Demographic features of primary and revision THA cohorts

	Primary THA		**Revision THA**	
	2-year (n = 5,707)	**5-year (n = 3,289)**	**2-year (n=2,687)**	**5-year (n=1,627)**
Mean Age (±SD)	65.0 ± 13.3	64.7 ± 12.9	65.7 ± 13.1	64.6 ± 13
Men/Women (%)	49%/51%	47%/53%	47%/53%	46%/54%
Age groups n (%)				
≤60 yrs	30%	30%	30%	32%
>60–70 yrs	31%	32%	27%	29%
>70–80 yrs	30%	31%	34%	32%
>80 yrs	9%	6%	10%	7%
Body Mass index (in kg/m^2)				
≤24.9	24%	24%	29%	29%
25–29.9	39%	40%	38%	40%
30–34.9	24%	23%	21%	21%
35–39.9	8%	8%	7%	6%
≥40	4%	4%	3%	3%
American Society of Anesthesiologists				
Class I–II	62%	64%	52%	56%
Class III–IV	38%	36%	48%	43%
Deyo-Charlson Comorbidities				
Heart Disease	7%	6%	6%	4%
Peripheral Vascular Disease	4%	3%	4%	3%
Renal Disease	5%	4%	4%	3%
Chronic Obstructive Pulmonary Disease	9%	9%	7%	7%
Diabetes (with or without organ damage)	6%	5%	7%	7%
Connective tissue disease	6%	6%	8%	8%

Table 2

Univariate association of comorbidities with Moderate-severe pain after Primary Total Hip Replacement (THA)

	2-year Moderate severe pain			5-year Moderate-severe pain		
Variable	**n/N (%)**	**Odds ratio (95 % CI)**	**p-value**	**n/N (%)**	**Odds ratio (95 % CI)**	**p-value**
Heart Disease (MI, CHF)						
No	401/5,033=8%	1.0 (Ref)		321/2,953=10.9%	1.0	
Yes	33/351=9.4%	1.2 (0.8, 1.8)	0.35	18/175=10.3%	0.9 (0.6, 1.6)	0.81
Peripheral Vascular Disease						
No	406/5,150=7.9%	1.0 (Ref)		329/3,028=10.9%	1.0	
Yes	28/234=12%	**1.6 (1.1, 2.4)**	**0.03**	10/100=10%	0.9 (0.5, 1.8)	0.79
Renal Disease						
No	418/5,134=8.1%	1.0 (Ref)		324/3,004=10.8%	1.0	
Yes	16/250=6.4%	0.8 (0.5, 1.3)	0.33	15/124=12.1%	1.1 (0.6, 2.0)	0.66
Chronic Obstructive Pulmonary Disease						
No	386/4,886=7.9%	1.0 (Ref)		318/2,854=11.1%	1.0	
Yes	48/498=9.6%	1.2 (0.9, 1.7)	0.18	21/274=7.7%	0.7 (0.4, 1.1)	0.08
Diabetes (with or without organ damage)						
No	401/5,053=7.9%	1.0 (Ref)		320/2,968=10.8%	1.0	
Yes	33/331=10%	1.3 (0.9, 1.9)	0.19	19/160=11.9%	1.1 (0.7, 1.9)	0.68
Connective tissue Disease						
No	413/5,087=8.1%	1.0 (Ref)		318/2,948=10.8%	1.0	
Yes	21/297=7.1%	0.9 (0.5, 1.4)	0.52	21/180=11.7%	1.1 (0.7, 1.8)	0.73

Ref, reference category

Moderate-severe index THA pain was reported by 435/5,390 at 2-years and by 339/3,128 at 5-years; At 2-years, numbers don’t add up to 435 due to missing data on comorbidities in one case

Table 3

Multivariable-adjusted[a] Odds of Moderate-severe pain after Primary THA

Variable	Moderate-severe pain at 2 years Odds Ratio (95% CI)	p-value	Moderate-severe pain at 5 years Odds Ratio (95% CI)	p-value
Heart Disease (MI, CHF)	1.1 (0.7, 1.7)	0.67	1.0 (0.6, 1.7)	0.91
Peripheral Vascular Disease	1.5 (1.0, 2.4)	0.06	1.1 (0.6, 2.2)	0.73
Renal Disease	**0.6 (0.3, 1.0)**	**0.04**	1.2 (0.6, 2.2)	0.59
Chronic Obstructive Pulmonary Disease (COPD)	1.1 (0.8, 1.6)	0.54	0.7 (0.4, 1.1)	0.09
Diabetes (with or without organ damage)	1.0 (0.6, 1.5)	0.91	0.6 (0.3, 1.2)	0.15
Connective tissue Disease	0.8 (0.5, 1.4)	0.51	1.4 (0.8, 2.3)	0.26

[a]Multivariable model simultaneously adjusted for age, gender, BMI, ASA class, distance from medical center, operative diagnosis, implant fixation (cement status), six Deyo-Charlson comorbidity categories, anxiety and depression.

Table 4

Univariate association of comorbidities with Moderate-severe pain after Revision THA

	2-year Moderate severe pain			5-year Moderate-severe pain		
Variable	**n/N (%)**	**Odds ratio (95 % CI)**	**p-value**	**n/N (%)**	**Odds ratio (95 % CI)**	**p-value**
Heart Disease (MI, CHF)						
No	415/2397=17.3%	1.0 (Ref)		296/1482=20%	1.0	
Yes	36/151=23.8%	**1.5 (1.0, 2.3)**	**0.05**	9/69=13%	0.6 (0.3, 1.3)	0.20
Peripheral Vascular Disease						
No	430/2456=17.5%	1.0 (Ref)		294/1504=19.5%	1.0	
Yes	21/92=22.8%	1.4 (0.8, 2.4)	0.24	11/47=23.4%	1.3 (0.6, 2.7)	0.55
Renal Disease						
No	432/2451=17.6%	1.0 (Ref)		297/1497=19.8%	1.0	
Yes	19/97=19.6%	1.1 (0.7, 1.9)	0.62	8/54=14.8%	0.7 (0.3, 1.5)	0.36
Chronic Obstructive Pulmonary Disease						
No	418/2359=17.7%	1.0 (Ref)		279/1448=19.3%	1.0	
Yes	33/189=17.5%	1.0 (0.7, 1.4)	0.93	26/103=25.2%	1.4 (0.9, 2.2)	0.14
Diabetes (with or without organ damage)						
No	414/2368=17.5%	1.0 (Ref)		280/1444=19.4%	1.0	
Yes	37/180=20.6%	1.2 (0.8, 1.8)	0.28	25/107=23.4%	1.3 (0.8, 2.0)	0.31
Connective tissue Disease						
No	417/2337=17.8%	1.0 (Ref)		290/1426=20.3%	1.0	
Yes	34/211=16.1%	0.9 (0.6, 1.3)	0.53	15/125=12%	**0.5 (0.3, 0.9)**	**0.03**

1.0 (Ref), reference category

Moderate-severe index THA pain was reported by 451/2,548 at 2-years and 305/1,551 at 5-years

Table 5

Multivariable-adjusted[a] Odds of Moderate-severe pain after Revision THA

Variable	Moderate-severe pain at 2 years Odds Ratio (95% CI)	p-value	Moderate-severe pain at 5 years Odds Ratio (95% CI)	p-value
Heart Disease (MI, CHF)	**1.7 (1.1, 2.6)**	**0.03**	0.7 (0.3, 1.8)	0.48
Peripheral Vascular Disease	1.4 (0.8, 2.4)	0.28	1.8 (0.8, 4.1)	0.17
Renal Disease	1.0 (0.6, 1.8)	0.86	0.6 (0.2, 1.5)	0.29
Chronic Obstructive Pulmonary Disease (COPD)	0.8 (0.5, 1.3)	0.39	1.5 (0.9, 2.5)	0.14
Diabetes (with or without organ damage)	1.2 (0.8, 1.8)	0.30	1.4 (0.8, 2.3)	0.21
Connective tissue Disease	0.8 (0.5, 1.2)	0.34	**0.5 (0.3, 0.9)**	**0.02**

[a]Multivariable model simultaneously adjusted for age, gender, BMI, ASA class, distance from medical center, operative diagnosis, six Deyo-Charlson comorbidity categories, anxiety and depression.