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Venous Thromboembolism after Joint Replacement in Older Male Veterans with Comorbidity

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Abstract

Objectives—Identifying older adults with comorbidities or poor functional status at high risk for postoperative venous thromboembolism

Design—Retrospective cohort study

Setting—Veterans Affairs Medical Center

Participants—Older adults who underwent total hip and knee replacement (THR and TKR) from 2002–2009

Measurements—Using multivariate logistic regression, we analyzed the independent effect of cardiopulmonary comorbidities and diabetes on VTE. Secondarily, we analyzed functional status expressed in a summary physical component score (PCS) in a subset of patients for whom it was available.

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Competing Interests
None of the authors have any financial or non-financial competing interests to declare as related to the contents of this manuscript.

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Author's Contributions
Alok Kapoor was responsible for the study design, analysis, interpretation, and manuscript write up. Priscilla Chew, Rebecca A. Silliman, Elaine M. Hylek, Jeffrey N. Katz, Howard Cabral, and Dan Berlowitz were responsible for the study design, interpretation, and manuscript write-up. All authors read and approved the final manuscript.

Results—There were 23,326 THR and TKR surgeries performed at the VA during the study period. COPD predicted a 25% increase in VTE (OR=1.25, 95% CI 1.06–1.48) CAD, CHF, CVD did not predict increased VTE. Diabetes predicted decreased VTE (OR=0.77 95% CI 0.64–0.92). Very low values of PCS, which was available for 3,169 patients, demonstrated a 62% increase in risk although the effect did not reach statistical significance (lowest versus highest quartile OR =1.62, 95% CI 0.93–2.80).

Conclusion—COPD predicted a small increase in VTE whereas very low functional status had a larger effect which did not reach statistical significance. More definitive conclusions about the role of these comorbidities and functional status are limited by the constraints of administrative data analysis and sample size available for PCS.

Keywords

Preoperative evaluation; thromboembolism; functional assessment

INTRODUCTION

Venous thromboembolism (VTE) is a common, costly and often fatal complication of major surgery in older adults particularly after total hip and knee replacement (THR and TKR). Fear of excessive hemorrhage induced by aggressive prophylaxis regimens factors into physician selection of an effective prophylaxis regimen. The trade-off between VTE prevention and excess hemorrhage has also created challenges in developing a consensus in the guidelines of major professional societies.[1,2] The ability to identify a high-risk cohort among older adults undergoing THR and TKR, who would potentially benefit from high potency prophylaxis, would help resolve this controversy and improve the selection of prophylaxis by preoperative consultants and surgical teams.

The link between comorbidities and venous thromboembolism has been demonstrated before.[3] Translating these findings from multiple settings into an understanding of the role of comorbidities in the postoperative time has been more limited. Comorbidities such as congestive heart failure (CHF) and chronic obstructive pulmonary disease (COPD) have been associated with increased postoperative VTE risk in some studies[4–7] but not in others.[8,9] Recent studies in both surgical[4,5,8,9] and non-surgical settings[10] suggest that atherosclerotic conditions are on a continuum with VTE such that coronary artery disease (CAD) and cerebrovascular disease (CVD) will likely predict an increased risk of postoperative VTE. Diabetes Mellitus (DM) has paradoxically predicted decreased postoperative VTE although the mechanism is uncertain.[8] Prior studies did not focus on discrete surgical procedures and also had small numbers, limiting their informativeness.

Our prior work[11] examined more than 300,000 surgical admission records in the Nationwide Inpatient Sample (NIS). That data contained administrative records of utilization from non-federal hospital inpatient stays from most states. Women accounted for 63 to 65% of the population. Our analysis indicated that CHF, and to a lesser extent COPD, predicts increased VTE. That analysis was limited by the absence of preoperative information about comorbidities, post discharge follow-up, medication records, and physical functional status. Physical functional status may prove to be a better representation of disease burden than presence of diagnosis and therefore a more powerful predictor of postoperative complications.

Veterans Affairs data (VA data) stored in Austin, TX is a national database which has extensive inpatient, outpatient, and pharmacy records which enhance the study of health outcomes such as postoperative VTE. Investigators can link information from encounters (inand outpatient) preceding surgical admission to improve the accuracy of comorbidity

information. Further, the VA data includes post discharge utilization, extending follow-up time to capture all postoperative VTE events. In 2002, the Veteran Affairs Hospital system embarked on an innovative path of systematically measuring functional status using the VR-12 (an enhanced version of the Short Form-12)[12] in 440,000 veterans annually as part of its Survey of Healthcare Experiences of Patients consumer satisfaction survey.[13] Thus, functional status is available for a subset of patients undergoing surgery.

We analyzed VA data to test our hypothesis that presence of CAD, CHF, COPD, and CVD and absence of DM would increase the risk of VTE. This analysis builds on our prior work which only examined the hospital period outcomes and did not have the benefit of preoperative information to define comorbid diseases. Also in distinction with our prior work, we tested a secondary hypothesis that low functional status as expressed in VR-12 instrument would predict increased VTE in the subset of veterans for whom this information was available.

METHODS

Data Sources and Study Sample

We used VA data from fiscal years (FY) 2002–2009 for our analysis. Multiple years of data were necessary in order to identify associations between comorbidities and relatively infrequent but serious outcome of postoperative VTE. VA data comprise several individual data sources. The Patient Treatment File, the inpatient file, includes primary and secondary diagnosis codes, procedures, admission and discharge status, and patient demographics (sex, age, race, median income, and residence zip code); it also contains surgical variables such as the route of anesthesia administration. The Outpatient file contains diagnosis codes relevant to outpatient encounters. The Decision Support System contains pharmacy records for both inpatient and outpatient prescriptions.

We identified a cohort of patients (age 65 or older) who underwent primary or revision THR or TKR (ICD-9-CM procedure codes 81.51, 81.53, 81.54, and 81.55). We did not include hemi-arthroplasty cases (81.52) because this group of patients typically has sustained a hip fracture and represents a distinct population with different risks for VTE.[14,15] We also excluded patients with any VTE code in the two years prior to surgery so as not to confuse new VTE events from prior ones which may have been addressed during the surgical admission or otherwise appeared in the roster of codes listed at the time of discharge. We permitted more than one surgical record from the same patient as long as no less than 90 days separated each admission.

Outcome

We determined VTE to have occurred if any one of thirteen ICD-9-CM DVT or PE codes were present within 90 days of surgery in the initial admission record or subsequent ED, outpatient, or inpatient encounter records in any of the diagnosis code positions - primary or secondary. (Appendix I for specific codes) We also followed the following algorithm for determining the date of outcome. For the initial surgical admission, we assumed a patient developed VTE on the date of discharge given that hospital records in the VA do not specify on which day of the hospitalization a complication occurred. For subsequent outpatient or inpatient utilization, we used the date of visit or date of admission respectively.

Predictor variables

Independent variables—We included specific comorbidities based on evidence of associations with VTE documented in the literature or for which a biological link has been proposed. These included CAD, CHF, COPD, CVD, and DM. Comorbidities were coded by

the ICD-9-CM codes elaborated by Elixhauser et al.[16] (Appendix II) Because CAD is not part of the Elixhauser inventory, our clinical team determined a consensus set of codes following our prior work.[11] To be counted as having a comorbidity, we required two eligible ICD-9-CM codes in the two years preceding surgery consistent with prior work.[17] We also examined the effect of co-occurring comorbidities if their co-occurrence was a statistically significant interaction. To ensure adequate power, we limited analysis of combinations to those with a prevalence of greater than 2%.

Functional status—In a subset of patients, we were also able to analyze functional status information as expressed in the Physical Component Score (PCS) of the VR-12 mentioned earlier. Like the SF-12[12], the VR-12 measures self-reported health related quality of life.[13] Differences with SF-12 exist in the response format for role physical and role emotional from a two item yes/no to a five point Likert scale. The second modification is the use of two items to assess health change, one focusing on physical health and one on emotional problems. PCS is a summary score of questions about general health, physical functioning, activity level, ability to accomplish goals, and interference in function by pain. Inquiries about pain and role limitations capture the degree to which physical health contributes to function. The VR-12 has been normed to a median of 50 representing the median value for adult Americans, similar to the SF-12. We included this PCS if it was available in the six months preceding the surgical admission.

Potential Confounders—We analyzed several potential confounders following the example of relevant publications in the literature.[14,15,18] This included age, sex, race, income (as measured through median household Zip code data from the 2000 Census[19]), hospital surgical volume (grouped into quartiles based on annual volume for the age 65+ population at each facility in which surgery occurred), surgery type (primary vs. revision and multi-joint / bilateral surgery), other medical conditions (chronic kidney disease, obesity, hypertension and cancer) defined by Elixhauser codes (Appendix II), and post-operative medications. We determined a patient's VTE prophylaxis regimen based on a presence of pharmacy records for one of five commonly used medications: fondaparinux, low molecular weight heparin (LMWH), warfarin, unfractionated heparin, and aspirin. If we identified more than one eligible medication, we followed the following hierarchy to identify the prophylaxis regimen: fondaparinux, LMWH, warfarin, heparin, and aspirin. For example, for a patient prescribed fondaparinux and aspirin, we assigned fondaparinux as the VTE prophylaxis regimen.

Analysis

We calculated descriptive statistics and cross-tabular frequencies for each comorbidity with the outcome to determine the shape of distributions, the extent of missing data, and the presence of small frequencies. Then, we examined whether prevalent combinations of comorbidities (as defined above) resulted in statistically significant positive interaction with VTE in multivariate models. Finally, we built multivariate logistic regression models to assess the independent effects of comorbidities. These models accounted for potential clustering by facility using generalized estimating equations (GEE) with an exchangeable working correlation structure implemented in PROC GENMOD in SAS.

We also performed several sensitivity analyses. Specifically, we examined changes in the main effects if we excluded patients with no documented post-discharge follow-up (compared to the main analysis where they were counted as not having VTE). Because we did not have cause of death available, we recalculated main effects using contrasting assumptions: excluding all patients who died from the analysis and then later counting all deaths as VTE events.

For the subset of patients with PCS information, we repeated our calculations to measure the effects of comorbidities on risk of VTE while controlling for functional status. Because PCS has not been studied before in this context, we divided PCS into quartiles of function and then compared each of the lower three quartiles against the highest functioning quartile. As a sensitivity analysis, we also compared those with PCS ≤ 29 (which some[20] have reported as a rough correlate of frailty) and those with PCS between 29 and 44 against the average value for adults over the age of 65.

We performed all analyses using Statistical Analytic Software version 9.2.[21]

RESULTS

Descriptive Statistics

We identified 23,326 THR and TKR surgeries. Overall, age distributed evenly into the following age categories: 65–69, 70–74, 75–79, and 80 or older. (Table 1) Black and Hispanic minorities accounted for 8.4% of the sample and patients of other races or for whom race data was not available accounted for another 30.8% of patients. Single comorbidity prevalence ranged from 4.3% (CVD) to 26.5% (DM). Prevalence of co-occurring comorbidities ranged from 1.5% (CHF with DM) to 5.8% (CAD with DM).

PCS was available for 3,169 patients. The mean score was 31.8 (± 10.4). We divided patients into four quartiles, 2–24, 25–32, 33–39, 40–64 and found no differences in the demographic, comorbid disease prevalence, preoperative utilization, or facility level characteristics for patients for whom PCS was available compared to the population without this information. Mortality was higher in the group without PCS. (Appendix III)

Dividing patients into quartiles of volume based on yearly counts of THR and TKR, we noted that most patients had surgery within low or medium volume centers according to thresholds established using data from non-federal hospitals.[15,22] Ninety-one percent of patients had primary hip or knee surgery with 8.4% undergoing revision procedures. Most patients (73.3%) received general anesthesia with the remainder receiving regional anesthesia (spinal/epidural). LMWH administered both in the hospital and as the prophylaxis choice beyond hospitalization was the most common choice of prophylaxis.

During the 90 days following surgery, VTE occurred in 3.8% (n= 896) of patients, although no follow-up was available for 16% of patients. One point eight percent of patients died during this period.

Multivariate modeling

Compared to a group without COPD, older adults with COPD had a 25% increase in the risk of postoperative VTE (OR=1.25, 95% CI 1.06–1.48) and DM was associated with a 23% decrease (OR=0.77, 95% CI 0.64–0.92) in the risk of postoperative VTE. There was no significant association with the other comorbidities. We did not find evidence for confounding by age, race, income, other health conditions including cancer, prophylaxis regimen, preoperative medications, or surgical and anesthesia variables tested. (Table 2) There was also no evidence of an interaction between comorbidities and therefore we did not measure the effect of cooccurring comorbidities.

Our results were stable across different modeling assumptions. When we excluded patients with no follow-up visits (instead of assuming absence of VTE), our main effects remained the same. Apart from CHF, main effects were also stable if we assumed that deaths were alternatively all related or all not related to VTE. When we assumed that deaths were all

related to VTE, the effect of CHF increased from 1.16 (95% CI 0.89–1.52) to 1.52 (95% CI 1.22–1.89).

Multivariate modeling in the population with PCS available—When we repeated the same model described above for the patients with PCS available, we did not observe the previously measured effects of COPD and DM. (Table 2) When we included PCS, there was no change in the measured effects for any comorbidity. The lowest quartile of function was associated with a 62% increase in VTE although the effect was not statistically significant (OR =1.62, 95% CI 0.93–2.80) compared with the highest functioning group; the other two quartiles showed a steady decrease in risk with increasing PCS. Comparison of a PCS value ≤ 29 (correlating with frailty) with a value of 44 or higher was associated with a 76% increase in risk of VTE although the effect was not statistically significant (OR= 1.76, 95% CI 0.87–3.59).

DISCUSSION

We examined the association of comorbidities and co-occurring comorbidities and VTE in a population of older male veterans undergoing total hip and knee replacement, high risk surgeries for VTE. These patients had a substantial comorbidity burden and high rates of VTE and death. COPD predicted a small increase in VTE, and very low functional status demonstrated a moderate sized association with VTE which did not reach statistical significance.

Comparison of our results with our previous analysis of the NIS[11] is limited by the differences in follow-up time, how we modeled comorbidity, and the availability of PCS. (Table 3) Although our findings do not align with the prior analysis that suggested a substantial effect of CHF and COPD on risk of VTE (Table 3), the absence of post discharge information in the previous data set significantly limited our ability to accurately measure the effects of comorbidity. Because patients with comorbidities likely stayed longer in the hospital for issues related to their cardiopulmonary status (pulmonary edema, myocardial ischemia), their VTE events were more likely to occur during the initial, index hospitalization. Alternatively patients with comorbidities may develop VTE earlier than patients without them. Future research should examine this issue in data where the exact date of VTE events is available.

The population we studied in the current study differs from other published studies.[11] Our study using the NIS Sample included women who constituted 63 to 65% of the population. The death rate was high in our VA sample (1.8%) compared with reports[15,22] based on Medicare samples (0.9–1.0%). It is unclear what the significance of this elevated mortality has on the relationship we measured for COPD using ICD-9-CM diagnostic codes. Patients with COPD in our sample may have had more severe form of disease and therefore developed more VTE than would be expected in other populations with COPD undergoing surgery. Diagnostic billing codes do not differentiate severe from less severe COPD. In a subsequent paragraph we discuss further the limitation of using diagnostic codes for the construction of comorbid disease information.

In addition, we reported the effects of comorbidities as single conditions in our prior work compared with individuals without any of our chosen comorbidities. Individuals with CHF alone, for example, may be different from those with CHF in combination with CAD or DM. When we modeled CHF the way we had in our prior publication, the effect rose but was not statistically significant (OR=1.60 95% CI 0.88–2.91). The effect of COPD was largely unchanged (OR=1.46 95% CI 0.92–2.32).

Several other studies have analyzed the role of comorbid conditions and postoperative VTE. (Table 3) Our current findings agree with two studies[8,9] which did not find an effect of cardiopulmonary comorbidities. The authors of the latter study surmised that hip and knee surgery were already quite high risk settings and that the effects of other predictors may be mitigated in that context. Our findings differed with two studies[4,5] which each found substantial effects of CAD or CHF. Differences may be explained by the heterogeneity of surgical patients and relatively smaller sample sizes in the latter two studies. In addition, Kikura et al.[4] examined history of acute myocardial infarctions, but not all CAD, which may reflect a more disabled population. Pederson and colleagues did not analyze outpatient visits and so it is possible that they missed less severe forms of VTE which did not require hospitalization.

Prior studies provide some support for our finding on the role of functional status. Mahid and colleagues[23] noted an association between impaired functional status and increased postoperative morbidity and mortality (VTE was not specifically considered). Sasaki et al.[24] found a significant difference in baseline Get Up and Go test[25,26] times between groups with elevated post-operative d-dimer levels, a proxy for VTE. We did not find any study that specifically analyzed PCS and postoperative VTE.

The effects of comorbidities and very low functional status that we measured have important implications and point to several potential future directions for research. For one, our findings suggest that clinicians should not factor the comorbidities that we studied into decisions about choice of prophylaxis. Although COPD predicted a 25% increase in the risk of VTE, on an absolute scale, this amounts to less than a 1% increase in VTE. The amount of excess risk which should trigger a change in medication prescription has not been established. Decision analysis or other modeling studies may suggest the appropriate threshold. Knowing a patient's individualized risk better may also guide choosing from among an array of new preventive strategies including new oral anticoagulants[27] and portable mechanical compression.[28] Measuring observed performance is another potential direction informed by our work. Slow 5 meter walk speed predicted more than threefold increase in major morbidity and mortality after cardiac surgery.[29] Future research may suggest other simple performance tests which may predict the risk of postoperative outcomes.

There are multiple limitations to the work we presented. ICD-9-CM diagnosis codes available in discharge data may not detect all eligible cases of VTE.[18] In addition, like other administrative information, we also did not have information about disease severity or clinical exam findings such as edema. Selecting Veterans Affairs data limited our ability to understand the role of our independent variables in women. We did not analyze the duration of prophylaxis given that there was a high proportion of patients who did not receive medications at the VA in the post discharge phase.

We also did not analyze postoperative variables. Complications such as urinary tract infection or pneumonia may have predisposed individuals to VTE. The inpatient data source we used did not permit distinguishing which postoperative events preceded VTE from those that followed it. We also do not have information about postoperative immobility. Our primary focus was risk profiling in the preoperative setting. Further study of data sets with postoperative variables would clarify the role these variables play. We selected the most extensive data set available to us given sample size needed to measure the effect of comorbidities and physical function. Our analysis improves upon prior work by adding preoperative comorbidity information derived from both inpatient and outpatient sources, post-discharge utilization to identify 90 day outcomes, and medication including prophylaxis regimen.

We also only had complete functional status information on 3,169 of 23,326 the patients we studied. Demographic and comorbidity profiles were comparable between patients with and without PCS but a small sample size with PCS limited our ability to compare its effect in the two cohorts. As PCS did not confound the relationship between COPD and VTE, we believe that the effects we measured in the larger population without PCS are still valid even though the effect estimate was different in the PCS model. Our study distinguishes itself as the first to integrate administrative data with self-reported physical function for the purpose of predicting postoperative VTE.

CONCLUSION

COPD predicted a small increase in VTE whereas very low functional status had larger effect on risk of VTE which did not reach statistical significance. Our findings suggest that clinicians should not factor CAD, COPD, CHF, CVD and DM into decisions about thromboprophylaxis but may want to consider functional status. More definitive decisions about the role of these comorbidities and functional status await verification in data which contain radiologic outcome confirmation, disease severity information, and temporal sequence of postoperative events.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Sponsor's Role: N/A

Appendix

Appendix I

ICD-9-CM Diagnosis Codes* VTE Codes

ICD-9-CM Pulmonary Embolism Diagnosis Codes

Codes	Diagnosis
4151	Pulmonary Embolism and infarction
41511	Iatrogenic pulmonary embolism and infarction
41519	Iatrogenic pulmonary embolism and infarction

ICD-9-CM Deep Vein Thrombosis Diagnosis codes:

Codes	Diagnosis
45111	Phlebitis and thrombosis of femoral vein (deep) (superficial)
45119	Phlebitis and thrombophlebitis of deep vessel of lower extremities – other
4512	Phlebitis and thrombophlebitis of deep vessel of lower extremities - unspecified
45181	Phlebitis and thrombophlebitis of iliac vein
4519	Phlebitis and thrombophlebitis of other sites – of unspecified sites
45340	DVT-embolism lower ext NOS (OCT 04)
45341	DVT-EMB proximal lower ext (OCT 04)

ICD-9-CM Deep Vein Thrombosis Diagnosis codes:

Codes	Diagnosis
45342	DVT-EMB distal lower ext (OCT 04)
4538	Other venous embolism and thrombosis of other specified veins
4539	Other venous embolism and thrombosis of unspecified site

*Agency for Health Care Research and Quality. Patient Safety Indicators Technical Specifications. 2006; http://www.qualityindicators.ahrq.gov/downloads/modules/psi/v32/psi_technical_specs_v32.pdf. Accessed July 13, 2008.

Appendix

Appendix II

Elixhauser Comorbidities**

	ICD9 CM Diagnosis	Discharge does not	Discharge does not
1. Congestive Heart Failure	398.91, 402.01, 402.11, 402.91, 404.01, 404.03,	Cardiac: 103–112, 115–118, 121–127,	Cardiac: 001–002, 215–238,242–251,
Changes from 3.2 to 3.3	None	Delete 524	New
2. Valvular disease	093.20–093.24, 394.0–397.1,	Cardiac: 103–112, 115–118, 121-	001–002, 215–238,
Changes from 3.2 to 3.3	None	Delete 524	New
3. Pulmonary Circulation disorders	415.11–415.19, 416.0–416.9, 417.9	Cardiac: 103–112, 115–118, 121–127,	Cardiac: 001–002, 215–238, 242–251,
Changes from 3.2 to 3.3	Add 415.11-	Delete 524	New
4. Peripheral vascular disease	440–440.9, 441.00-	Peripheral vascular:	Peripheral vascular:
Changes from 3.2 to 3.3	Added 444.21-	None	New
5. Hypertension (combine uncomplicated	Hypertension, uncomplicated:	Hypertension: 22, 134	Hypertension: 077-
	Hypertension, complicated: 401.0,	Cardiac: 103–122, 115–118, 121–127,	Cardiac: 001–002, 215–238, 242–251,
Changes from 3.2 to 3.3	None	Delete 524	New
6. Paralysis	342.0–344.9,	Cerebrovascular:	Cerebrovascular:
Changes from 3.2 to 3.3	None	None	New
7. Other neurological disorders	330.1–331.9, 332.0, 333.4, 333.5, 333.71–333.79, 333.85,	Nervous system: 1–35, 524, 528–534, 543, 559–564, 577	Nervous system: 020–042, 052–103
Changes from 3.2 to 3.3	None	None	New
8. Chronic pulmonary disease	490–492.8,	COPD asthma:	COPD asthma:
Changes from 3.2 to 3.3	None	None	New
9. Diabetes without chronic	250.00–250.33,	Diabetes: 294,	Diabetes: 637–639
Changes from 3.2 to 3.3	None	None	New
10. Diabetes with chronic	250.40–250.93,	Diabetes: 294,	Diabetes: 637–639
Changes from 3.2 to 3.3	None	None	New
11. Hypothyroidism	243–244.2, 244.8,	Thyroid	Thyroid

	ICD9 CM Diagnosis	Discharge does not	Discharge does not
Changes from 3.2 to 3.3	None	None	New
12. Renal failure	403.01, 403.11, 403.91, 404.02, 404.03, 404.12,	Kidney transplant, Renal	Kidney transplant, Renal
Changes from 3.2 to 3.3	None	None	New
13. Liver disease	070.22, 070.23, 070.33, 070.44, 070.54, 456.0,	Liver: 199–202, 205– 208	Liver: 420–425, 432– 434, 441–446
Changes from 3.2 to 3.3	None	None	New
14. Chronic Peptic ulcer disease (includes bleeding only if obstruction is also present)	531.41, 531.51, 531.61, 531.70, 531.71, 531.91, 532.41, 532.51,	GI Hemorrhage or ulcer: 174–178	GI Hemorrhage or ulcer: 377–384
Changes from 3.2 to 3.3	None	None	New
15. HIV and AIDS (Acquired	042–044.9	HIV: 488, 489,	HIV: 969–970,
16. Lymphoma	200.00–202.38, 202.50–203.01,	Leukemia/lymphoma:	Leukemia/lymphoma:
Changes from 3.2 to 3.3	None	None	New
17. Metastatic cancer	196.0–199.1, 789.51	Cancer, Lymphoma: 10, 11, 64, 82,	Cancer, Lymphoma: 054, 055, 146-
Changes from 3.2 to 3.3	Added 789.51	None	New
18. Solid tumor without metastasis	140.0–172.9, 174.0-	Cancer, Lymphoma:	Cancer, Lymphoma:
		355, 357, 363,	715–716, 722-
Changes from 3.2 to 3.3	Added 258.01-	None	New
19. Rheumatoid arthritis/collagen	701.0, 710.0–710.9,	Connective tissue:	Connective tissue:
Changes from 3.2 to 3.3	None	None	New
20. Coagulation deficiency	286.0–286.9, 287.1,	Coagulation	Coagulation
Changes from 3.2 to 3.3	None	None	New
21. Obesity	278.0, 278.00, 278.01, 649.10-	Nutrition/metabolic:	Nutrition/metabolic:
Changes from 3.2 to 3.3	None	None	New
22. Weight loss	260–263.9, 783.21,	Nutrition/metabol	Nutrition/metabol
Changes from 3.2 to 3.3	None	None	New
23. Fluid and electrolyte disorders	276.0–276.9	Nutrition/metabol	Nutrition/metabol
Changes from 3.2 to 3.3	None	None	New
24. Blood loss anemia	280.0, 648.20-	Anemia: 395,	Anemia: 808–812
Changes from 3.2 to 3.3	None	None	New
25. Deficiency anemias	280.1–280.9,	Anemia: 395,	Anemia: 808–812
Changes from 3.2 to 3.3	None	None	New
26. Alcohol abuse	291.0–291.3, 291.5, 291.8, 291.81,	Alcohol or drug: 433-	Alcohol or drug: 894-
Changes from 3.2 to 3.3	None	None	New

	ICD9 CM Diagnosis	Discharge does not	Discharge does not
27. Drug abuse	292.0, 292.82–292.89, 292.9,	Alcohol or drug: 433-	Alcohol or drug: 894-
Changes from 3.2 to 3.3	None	None	New
28. Psychoses	295.00–298.9,	Psychoses: 430	Psychoses: 885
Changes from 3.2 to 3.3	None	None	New
29. Depression	300.4, 301.12,	Depressive	Depressive
Changes from 3.2 to 3.3	None	None	New
Comments: The following DRGs has been deleted prior to 2007 and renumbered to a different DRG;			

** Agency for Health Care Research and Quality. Clinical Classifications Software (CCS) for ICD-9-CM 2008; http://www.hcup-us.ahrq.gov/toolssoftware/ccs/ccs.jsp. Accessed July 10, 2008.

Appendix

Appendix III

Descriptive Statistics Stratified by PCS Status

Parameter	PCS missing N=20,157		PCS non missing N=3,169	
	N	%	N	%
Age, yr				
65–69	4,564	22.6	743	23.5
>69–74	5,590	27.7	895	28.2
>74–79	5,307	26.3	880	27.8
>79	4,696	23.3	651	20.5
Race				
White	12,027	59.7	1,929	60.9
Black	1,507	7.5	198	6.3
Hispanic	230	1.1	18	0.6
Other	196	1.0	50	1.6
Not known	6,197	30.7	974	30.7
Area level income quartile †				
Lowest <$30K	6,273	31.1	942	29.7
Second lowest $30–50K	5,569	27.6	883	27.9
Highest two>$50	7,495	37.2	1,207	38.1
Not Known	820	4.1	137	4.3
Comorbid diseases				
CAD	4,942	24.5	778	24.6
CHF	1,071	5.3	152	4.8
COPD	2,861	14.2	428	13.5
CVD	859	4.3	134	4.2

Parameter	PCS missing N=20,157		PCS non missing N=3,169	
	N	%	N	%
Diabetes	5,300	26.3	874	27.6
CAD + CHF	661	3.2	94	2.9
CAD + COPD	904	4.3	140	4.3
CAD + Diabetes	1,669	8.0	267	8.2
CHF + Diabetes	417	2.0	71	2.2
COPD + Diabetes	741	3.6	126	3.9
None of the above	1,360	6.5	211	6.5
Other health conditions				
CKD	261	1.3	44	1.4
Hypercoagulable state	2	0.0	0	0.0
Obesity	2,409	12.4	426	13.4
MALIGNANCY-active prior 6 months	1,371	6.8	192	6.1
HTN	8,559	42.5	1,395	44.0
Elixhauser				
0	2,324	11.5	358	11.3
1	6,198	30.8	998	31.5
2	5,902	29.3	896	28.3
3+	5,733	28.4	917	28.9
Preoperative Utilization				
Mean number of records *	25.5 (± 15.0)		25.1 (± 14.2)	
Surgery Type				
Multi-joint	68	0.3	6	0.2
Primary hip	5,744	28.5	824	26.0
Primary knee	12,584	62.4	2,138	67.5
Revision hip	773	3.8	63	2.0
Revision knee	988	4.9	138	4.4
Anesthesia				
General	14,840	73.6	2,230	70.4
Neuroaxial	4,667	23.2	821	25.9
Other	650	3.2	118	3.7
Not known	1	0.0	1	0.0
Facility Annual Volume for Veterans aged 65+ (divided into quartiles)				
71–170	5,094	25.3	800	25.2
44–70	4,853	24.1	819	25.8
29–43	5,070	25.2	887	28.0
1–28	5,140	25.5	663	20.9
Outcomes (90 day postop)				
VTE				

Parameter	PCS missing N=20,157		PCS non missing N=3,169	
	N	%	N	%
Yes	779	3.9	117	3.7
No	16,019	79.5	2,689	84.9
Missing	3,359	16.7	363	11.5
Death				
Yes	407	2.0	14	0.4
No	19,750	98.0	3,155	99.6

Abbreviations: CAD= coronary artery disease, CHF=congestive heart failure, COPD= chronic obstructive pulmonary disease, CVD= cerebrovascular disease, CKD= chronic kidney disease, HTN= hypertension, VTE = venous thromboembolism

† Based on median income in 2000 U.S. Census for ZIP code of patient

* Tabulated as simple sum of inpatient or ambulatory care encounters

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Table 1

Demographic characteristics of the 23,312 male patients

Variable	Total Hip/Knee	
	N	%
Age, yr		
65.0–69.0	5303	22.8
>69.0–74.0	6481	27.8
>74.0–79.0	6183	26.5
>79.0	5345	22.9
Race		
White	13948	59.8
Black	1705	7.3
Hispanic	248	1.1
Other *	246	1.1
Unknown / Not reported	7412	30.8
Area level income quartile†		
Lowest <$30K	7215	30.9
Second lowest $30–50K	6452	27.7
Highest two>$50	8702	37.3
Not Known	957	4.1
Comorbid diseases		
CAD	5720	24.5
CHF	1223	5.24
COPD	3289	14.1
CVD	993	4.3
Diabetes	6174	26.5
CAD + CHF	311	1.3
CAD + COPD	688	3.0
CAD + Diabetes	1350	5.8
CHF + Diabetes	345	1.5
COPD + Diabetes	848	3.6
None of the above comorbidities	2371	10.1
Other health conditions		
CKD	305	1.3
Hypercoagulable state	2	0.01
Obesity	2916	12.5
MALIGNANCY-active prior 6 months	1563	6.7
HTN	9954	42.7
Elixhauser		
0	2682	11.5
1	7196	30.9
2	6798	29.1

Variable	Total Hip/Knee	
	N	%
3+	6650	28.5
PCS score within 6 months of surgery¥		
Present	3242	13.9
mean score among cohort with PCS available	31.8 (± 10.4)	
Not known	20084	86.1
Facility Volume		
71–170	5894	25.3
44–70	5672	24.3
29–43	5957	25.6
1–28	5803	24.9
Surgery Type		
Multi-joint	74	0.3
Primary hip	6568	28.2
Primary knee	14722	63.1
Revision hip	836	3.6
Revision knee	1126	4.8
Anesthesia		
General	17070	73.2
Neuroaxial	5488	23.5
Other	768	3.3
Not known	2	0
Preoperative medication		
LMWH	67	0.3
Aspirin	2656	11.4
ESA	74	0.3
Estrogen	2	0
Statin	8602	36.9
Warfarin	907	3.9
Other antiplatelet	666	2.9
VTE Prophylaxis Regimen		
Fondaparinux	466	2.0
LMWH	13435	57.6
Warfarin	3838	16.5
Heparin	504	2.2
Aspirin	1532	6.6
Unknown	3551	15.2
VTE – 90 days		
Yes	896	3.8
No	18708	80.2
Not known -- no follow up encounters within VA	3722	16
Death – 90 Days		

Variable	Total Hip/Knee	
	N	%
Yes	421	1.8
No	22905	98.2

Abbreviations: CAD= coronary artery disease, CHF=congestive heart failure, COPD= chronic obstructive pulmonary disease, CVD= cerebrovascular disease, CKD= chronic kidney disease, HTN= hypertension, ESA= erythropoiesis-stimulating agents, LM WH = low molecular weight heparin, VTE = venous thromboembolism

*Other includes Asian, other, and none reported.

Table 2

Independent Effects of Single Comorbidities and Functional Status in a Multivariate Model for Predicting Postoperative VTE*

Exposure	Comorbidity Model N=24,051		Comorbidity Model *without* adjustment for PCS but within sample with PCS available N=3,242		Comorbidity Model *with* adjustment for PCS within sample with PCS available N=3,242	
	Odds Ratio	95% Cl	Odds Ratio	95% Cl	Odds Ratio	95% Cl
CAD (vs. no CAD)	0.98	0.84–1.14	1.07	0.65–1.77	1.05	0.64–1.72
CHF (vs. no CHF)	1.16	0.89–1.52	1.30	0.52–3.29	1.30	0.52–3.27
COPD (vs. no COPD)	1.25	1.06–1.48	0.99	0.59–1.65	0.95	0.57–1.59
CVD (vs. no CAD)	0.88	0.57–1.36	1.13	0.44–2.90	1.09	0.44–2.75
PCS 2–23 (vs. 39–64 ref)					1.62	0.93–2.80
PCS 24–31					1.52	0.87–2.67
PCS 32–38					1.29	0.66–2.53

Abbreviations: CAD= coronary artery disease, CHF= congestive heart failure, COPD= chronic obstructive disease, CVD= cerebrovascular disease, DM= diabetes mellitus, PCS= physical component score; Cl= confidence interval

*Adjusting for age, sex, race, surgery type (hip vs. knee and primary vs. revision), other health conditions (including chronic kidney disease, obesity, malignancy, hypertension, prophylaxis regimen, facility knee and hip surgery volume, anesthesia type, income); N.B. None of these adjustments significantly changed the above reported effects. Preoperative medications not included in Comorbidity with PCS Model due to problems with model convergence; in a sensitivity analysis on the results from the main Comorbidity Model, inclusion of preoperative medications did not change the effects reported.

Table 3

Comparisons of Studies Examining Effects of Comorbidities and Physical Function with Postoperative VTE

Studies Examining Effects of Comorbidities					
Study	**Population**	**Procedure**	**Comorbidity Data Source**	**Outcome Data Source**	**Significant findings***
Kapoor(current)	24,051 veterans aged 65+	THR, TKR	ICD-9-CM codes from inpatient and outpatient utilization in 2 years preop	Hospitalization and 90 days post-op in- or outpatient VA follow-up	COPD 1.24 (1.06–1.45)
Kapoor[11]	316,671 adults aged 65+	Primary THR, TKR	ICD-9-CM codes listed at time of discharge from index hospitalization	Initial hospitalization	CHF alone€ THR 3.08 (2.05–4.65) TKR 2.47 (1.95–3.14) COPD alone TKR 1.49 (1.31–1.70)
Kikura[3]	21,903 adults	Any elective surgery	Prospective preop evaluations	Hospitalization and 30 days post op	CAD 2.9 (1.8–4.8)
Jaffer[4]	269 female patients aged 50+ median age = 74	TKR	Retrospective manual chart review	Initial hospitalization and 45 days post op	CHF 6.55 (1.47–45.3)
Pedersen[6]	67,469 adults	Primary THR	ICD-8 and ICD-10 codes inpatient utilization in 15 years preop	Initial and subsequent hospitalizations	Cardiovascular diseases† 1.40(1.15–1.70) Other diseases‡ 1.45 (1.21–1.72)
Gangireddy[7]	118,258 adults mean age = 65	9 common surgeries including THR	Retrospective chart review	Hospitalization and 30 day post op	COPD 1.45 (1.23–1.70)
Schiff[8]	310 adults mean age =72	THR, TKR, HFS	Retrospective chart review	Initial + 1 year postop	CHF or recent MI¥ 1.12 (0.38–3.29)
Studies Examining Effects of Physical Functional Status					
Study	Population	Procedure	Functional Status Source	Outcome Data Source	Significant Findings *
Kapoor(current)	24,051 veterans aged 65+	THR, TKR	VR-12 PCS within 6 months of surgery	Hospitalization and 90 days postop in- or outpatient VA follow-up	PCS 2–23 1.65 (0.96–2.85) PCS 24–31 1.50 (0.85–2.64) PCS 31–38 1.28 (0.67–2.46)
Sasaki[24]	102 women mean age = 65	Total hip arthroplasty	Prospective timed Up and Go (TUG) measure	Initial hospitalization	Difference in average time to complete TUG was statistically significant (patients with vs. without VTE)

Abbreviations: preop = preoperative, postop=postoperative, THR= total hip replacement, TKR=total knee replacement, HFS = hip fracture surgery, COPD= chronic obstructive pulmonary disease, CHF= congestive heart failure, CAD= coronary artery disease, MI= myocardial infarction, VTE = venous thromboembolism, VR-12 PCS= Veteran Rand-12 Physical Component Score[13] which resembles closely the Short-Form 12[12] ICD-9-CM= international classification of diseases 9th edition clinical modification

*Findings include excess risk associated with individual comorbid conditions or functional status expressed as an odds ratio with 95% confidence interval contained within parentheses. In the case of functional status, reference category is PCS <38.

[€] Comorbidities and co-occurring comorbidities in this study were modeled as stand-alone conditions compared with individuals without any of the other analyzed conditions (CAD, CHF, COPD, CVD, DM)

[†] Included previous myocardial infarction, congestive heart failure, and / or stroke; comorbidity information only determined by prior hospitalizations.

[≠] Chronic pulmonary disease, connective tissue diseases, or peptic ulcers (as a combined group)

[¥] Only the risk ratio reported in this study

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