Previous History of Breast Cancer Increases Rates of Pulmonary Embolism and Costs after Total Knee Arthroplasty: An Evaluation of 185,114 Matched Patients

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Abstract

Risk factors for adverse events after total knee arthroplasty (TKA) relating to malignancy have not been well studied. Thus, the purpose of this study was to conduct a retrospective case–control outcome and cost analysis after TKA in this population. Patients with a history of breast cancer (BrCa) were identified based on the International Classification of Disease 9th revision codes. An age- and sex-matched cohort was also identified of patients without a history of BrCa. Complications, length of stay, comorbidity burden, and reimbursements were tracked at 90 days. Each cohort comprised 92,557 patients. Length of stay was similar between cohorts ($p = 0.627$). Comorbidity status and incidence of pulmonary embolism (PE), lower extremity ultrasound, and chest computed tomography (CT) use were higher in patients with a history of BrCa ($p < 0.05$ for all). Control patients had a lower incidence of acute myocardial infarction (0.14 vs. 0.21%; $p < 0.001$). Surgical complications were similar. The 90-day reimbursements were greater in patients with a history of BrCa (US $13,990 vs. US$13,033 for controls; $p = 0.021$). Surgeons should be aware of the increased risk of PE after TKA in patients with a history of BrCa as well as increased 90-day costs, which warrant great attention.

Keywords

total knee arthroplasty; cancer; breast; outcomes; cost

Total knee arthroplasty (TKA) is one of the most common orthopaedic procedures performed in the United States.[1–3] TKA has demonstrated significant benefits to patients by decreasing pain, improving function, and allowing return to work and sports.[4] Adverse postoperative events, however, can have tremendous detrimental health effects.[5] Recent research efforts have been aimed to evaluate risk factors for poor outcomes. A particular population of interest is patients with a previous history of malignancy.

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Recent literature has highlighted the relationship between cancer and its effects on postoperative outcomes.[6] Epidemiological research has demonstrated that the number of patients living with cancer is expected to increase in the coming years due to the improving efficacy of anticancer therapies and management options.[7] This increased survivorship translates into an enlarging population of aging patients with a history of cancer who develop knee osteoarthritis.[8] Deviations from normal physiology during and after the treatment for malignancy in this patient population are well-noted.[9,10] These changes lead to an increased risk of thromboembolic events such as deep vein thrombosis (DVT), pulmonary embolism (PE), and changes in bone quality after radiation therapy and/or antineoplastic management,[11–14] potentially putting these patients at increased risk of poor outcomes after major joint reconstructions.

Breast cancer is the most common form of cancer in the United States.[15] The American Cancer Society estimated that in 2017, more than 250,000 new cases of breast cancer would develop.[16] Furthermore, the mortality of this disease has been declining at a mean of 1.8% per year with a 5-year survival rate of 91.3%, highlighting the fact that most patients survive. [15] With such a great survival rate, it is expected that these patients will suffer age-related diseases as they become older. Given the magnitude of patients currently living with a history of breast cancer, we aimed at studying this question in its relationship to TKA. Thus, the purpose of this study was to evaluate outcomes of patients with a previous history of breast cancer who underwent TKA. We hypothesized that these patients would have similar outcomes to age-matched controls, as tumor control is greatly successful.

Materials and Methods

This was a retrospective, matched case–control study using data extracted from a comprehensive Medicare database (PearlDiver Supercomputer, Warsaw, IN). This server holds the entire Medicare Standard Analytical Files and allows researchers to query the data through the International Classification of Disease (ICD) 9th revision codes as well as Current Procedural Terminology codes. It is a commercially and publicly available database that is compliant with the Health Insurance Portability and Accountability Act. The ICD codes used were similar to those used in previous literature.[17–20] The query was performed to include patients who underwent TKA from 2005 to 2014. Following initial identification of patients who underwent TKA, patients with a previous history of breast cancer were identified. A random cohort of patients without a previous history of breast cancer who underwent TKA was also extracted to serve as the control. A 1:1 matching was then performed to ensure that the control group had the same age and sex distributions as the group of breast cancer patients to diminish the potential of confounding based on demographical variables. Of note, this type of coding allowed us to identify only patients with a history of the disease, and given the standard billing coding practices, patients on any medication for active breast cancer are not coded as having a history and therefore no confounding with patients with active disease occurs.

The outcomes of interest in this study were medical and surgical complications within the 90-day global period after surgery and length of stay (LOS).[21] Costs, as reflected by reimbursements, were also tracked and analyzed based on the day of surgery (DOS) and 90-

day episode of care reimbursements. The 90-day postoperative period was the period of interest evaluated as it represents the most common pay period used in the Comprehensive Care for Joint Reconstruction payment model. The Charlson Comorbidity Index (CCI) score was also extracted and compared for both groups.

Statistical Analysis

Data analysis was performed on SPSS Software Version 20 (SPSS Inc., Armonk, NY) using Student's t-test for parametric data and Mann–Whitney U test for nonparametric data. The Kolmogorov–Smirnov test was used to assess normality. Chisquare analysis was also used for categorical variables. Odds ratios (OR) with the respective 95% confidence intervals (CIs) were reported. An α value of <0.05 was deemed as significant. For the CCI analysis, a weighted score was obtained from each cohort of patients.

Results

Our initial query identified a total of 2,369,594 TKAs from 2005 to 2014. After match-pairing, 92,557 patients were included in the cohort of patients with a history of breast cancer and in the cohort of patients without such a history. Table 1 demonstrates the demographic characteristics of the studied patients.

Medical Complications

Patients with a previous history of breast cancer had a higher incidence of PE (0.65 vs. 0.56%; OR: 1.147; 95% CI: 1.019– 1.290) (Table 2). This was associated with a greater use of diagnostic ultrasound (0.22 vs. 0.17%; OR 1.274; 95% CI: 1.034–1.571) and chest computed tomography (CT) (1.67 vs. 1.36%; OR: 1.233; 95% CI: 1.144–1.329). Interestingly, patients without a history of breast cancer demonstrated significantly higher incidences of acute myocardial infarction (AMI), pneumonia, and intubation ($p < 0.05$ for all).

Surgical Complications

The majority of reported surgical complications occurred at approximately the same rate in both groups (Table 3). Prosthetic joint dislocations were more common in patients with a history of breast cancer (OR: 1.522; 95% CI: 1.049– 2.208). The incidence of nonspecific osteomyelitis was greater in the control group, but the 90-day incidence of this complication was less than 1% in both groups.

Length-of-Stay Analysis

Patients with a personal history of breast cancer had a mean LOS of 3.269 ± 0.287 days, which was not statistically different compared with the controlgroup (3.375 0.325 days; $p = 0.627$) (Fig. 1).

Charlson Comorbidity Analysis

At the time of the operation, both cohorts were found to have nonnormally distributed CCI scores ($p < 0.001$ for both). The median CCI score was 6 ± 2.97 for patients with a history of breast cancer and 4 ± 2.14 for those without a breast cancer history ($p < 0.001$) (Fig. 2).

Reimbursement Analysis

Mean DOS reimbursements were US$12,525 ± US$1,957 and US$11,633 ± US$1,446 for the breast cancer and control groups, respectively ($p = 0.261$). In contrast, 90-day reimbursements were significantly greater in patients with a history of breast cancer compared with controls, that is, US $13,990 ± US$1,020 versus US$13,033 ± US$625, respectively ($p = 0.021$) (Fig. 3).

Discussion

The purpose of this study was to examine the effects of a personal history of breast cancer on the outcomes of TKA among Medicare beneficiaries. We conducted a retrospective case–control study with matching of demographics at a 1:1 ratio. This study demonstrated that patients with a history of breast cancer were more likely to sustain pulmonary emboli and prosthetic joint dislocations than age- and sex-matched controls. This supports our hypothesis that these patients are at a heightened risk of certain complications. The increased rate of PE in patients with a history of breast cancer resulted in greater use of vascular ultrasound and chest CT. Shahi et al[22] previously evaluated the economic burden of inhospital venous thromboembolism (VTE) in the United States using the National Inpatient Sample and found that a VTE was associated with a significantly longer LOS and greater hospital charges when compared with patients who did not sustain a VTE. The authors found that the median charges increased significantly from US$38,791 to US$53,307, which is in line with our findings. Dasta et al,[23] using a database of more than 45 million inpatient discharges within the United States, further demonstrated that the daily hospital costs of patients who sustain a DVT or PE were substantial, with means of US$1,594 (range: US $1,263–US$2,321) and US$1,735 (range: US$1,276–US$2,602). These data display the important association between VTE-related events and increased 90-day costs. Previous research efforts by van Erkel et al[24] demonstrated that the cost of chest CT for the investigation of PE was on average US$143 dollars. These factors associated with the likelihood of greater medical attention are likely the culprit of increased 90-day reimbursements.

The increased risk of prosthetic joint dislocation in patients with a history of breast cancer is most likely multifactorial. Lebel and Lewallen[25] evaluated all the TKA performed at their institution since 1970 and found only 58 cases of dislocations, with a described incidence of 0.93% for primary TKAs. The authors concluded that associated factors were a history of ligament laxity, extensor mechanism deficiency, and prosthetic joint infection (PJI). In our study, PJI rates were similar in both cohorts, leading us to believe that the dislocations were more likely due to other reasons. Jethanandani et al[26] evaluated 14 patients who presented to their clinic with tibiofemoral dislocations.[26] Of the 14, 10 (71%) had instability (either flexion instability or posterior/ medial cruciate ligament instability). High levels of estrogen have been related to increase in anterior cruciate ligament laxity, and thus a high level of this hormone may predispose TKA patients to lax joints that may change with antineoplastic therapy including estrogen decreasing agents,[27,28] but focused studied on this topic are required to understand this difference.

Contrary to our hypothesis, we demonstrated that patients with a history of breast cancer presented with lower rates of AMI and pneumonia compared with controls. These findings may correlate with a likelihood of greater postoperative multispecialty monitoring of patients with a history of breast cancer and/or differences in other confounding variables such as obesity or obstructive sleep apnea.[29] Furthermore, it is possible that some patients who have a history of breast cancer and had adverse events during treatment or may not have been candidates for a TKA, thus self-selecting patients who later received the surgery. In addition, many treatment regimens for breast cancer include docetaxel, cyclophosphamide, doxorubicin, and 5-fluorouracil.[21,30] Some of these treatments, most notably doxorubicin, can cause cardiac abnormalities including heart failure, leading to these patients receiving cardiac ultrasound more often and to an increased likelihood of protective self-selection from a cardiac health standpoint and the risk of receiving a TKA.[31] Patient-specific factors are mostly related to these adverse events, which may be more predictive of outcome instead of a personal history of breast cancer. A retrospective study of the Danish national registries identified that AMI rates are increased in patients who undergo TKA, especially for the first 2 weeks after surgery.[32] The authors described that age played a strong effect modification and that patients younger than 60 years did not have any difference in AMI rates based on receiving a TKA or not. This later finding demonstrates how multiple confounders play a role in such adverse events, which should increase awareness for their occurrence and draw greater research efforts.

LOS did not differ between the two groups. This finding could be expected as we did not examine patients with a current breast cancer diagnosis and, as such, would expect similar postoperative protocols for both groups. This comparable LOS may have also helped diminish the possible differences in 90-day costs as a wider variation in LOS would have had a greater effect on overall costs.[33] Nonetheless, patient-specific factors usually play a major role in deciding the optimal time to send a patient home, and thus a previous history of breast cancer would not have an impact on this measure.

Our analysis of the CCI aids in demonstrating that patients who have a history of breast cancer may also be at increased risk of complication even during remission. The significantly higher comorbidity status in patients with a history of breast cancer may aid surgeons in risk-stratifying these patients as comorbidities other than cancer may play a confounding role.

Limitations

This study is subject to similar limitations to those seen in all investigations using large databases. First, the information extracted from the database directly relies on the quality of the information put into the database. Thus, coding errors by physicians would lead to incorrect data and analysis. Second, several characteristics that may affect outcomes are not captured in this type of investigation, for example, hospital volume, operative time, and anesthetic technique. Moreover, the use of a large database of Medicare beneficiaries introduces selection bias because it precludes the inclusion of patients with private insurers. Additionally, the retrospective nature of this study introduced an inherent limitation because postoperative protocols could not be standardized. However, the use of a large sample size

from this database provides the necessary number of patients to investigate postoperative complications associated with less commonly researched conditions in arthroplasty, such as breast cancer. An additional limitation of our study is the different comorbidity status between cohorts. Nonetheless, this demonstrates that patients with a history of breast cancer have a greater overall CCI, thus further explaining the cost differences in the 90-day global period. Despite these limitations, the large sample sizes afforded by the database allows for the determination of cost impact on a relevant population, which is of high interest in the currently evolving health care system.

Conclusion

Surgeons should be aware of the increased risk of PE after TKA in patients with a personal history of breast cancer. It appears that this complication and the increased use of diagnostic studies have an effect on increasing 90-day costs after TKA.

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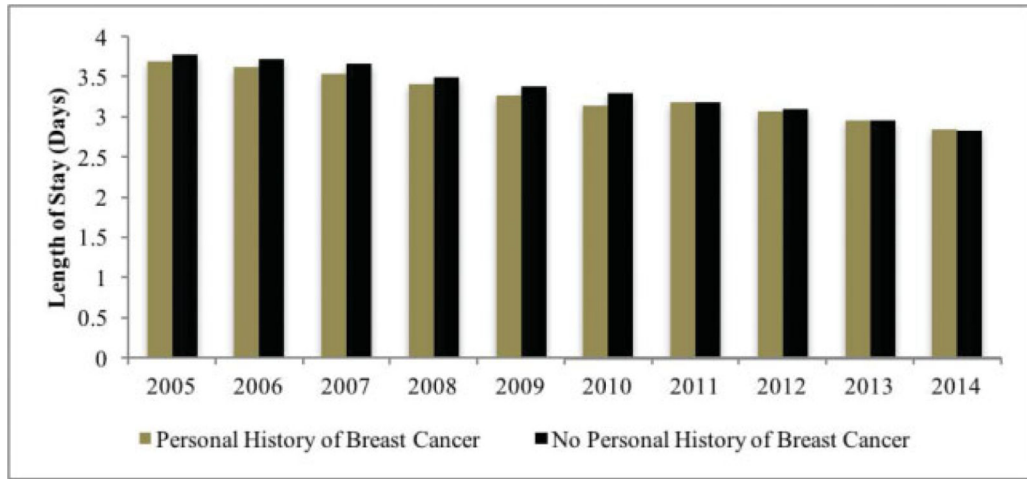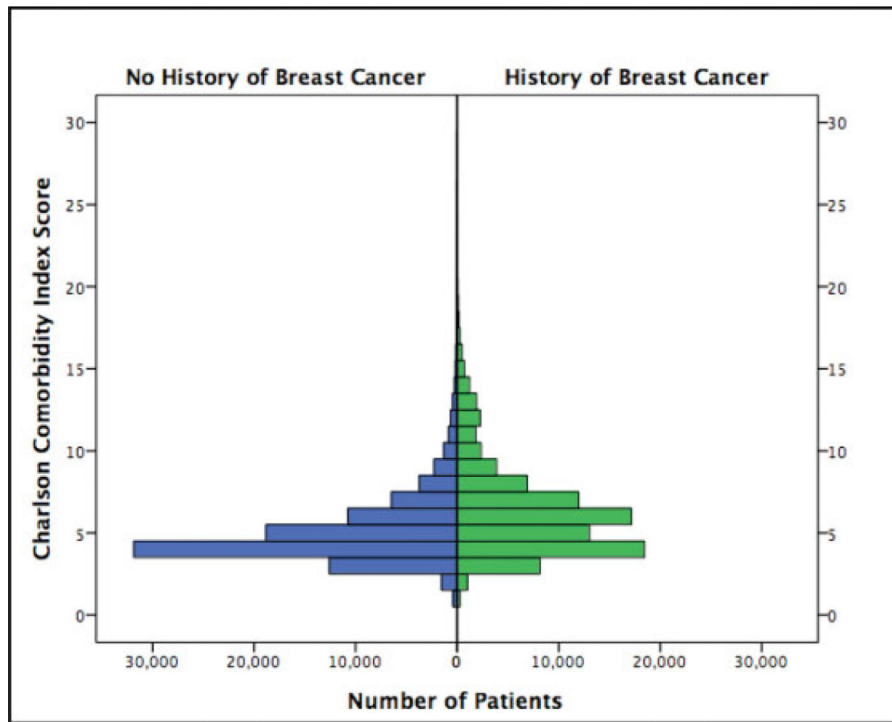
Fig. 1.
Length of stay over time.

Fig. 2.
Charlson Comorbidity Index distribution.
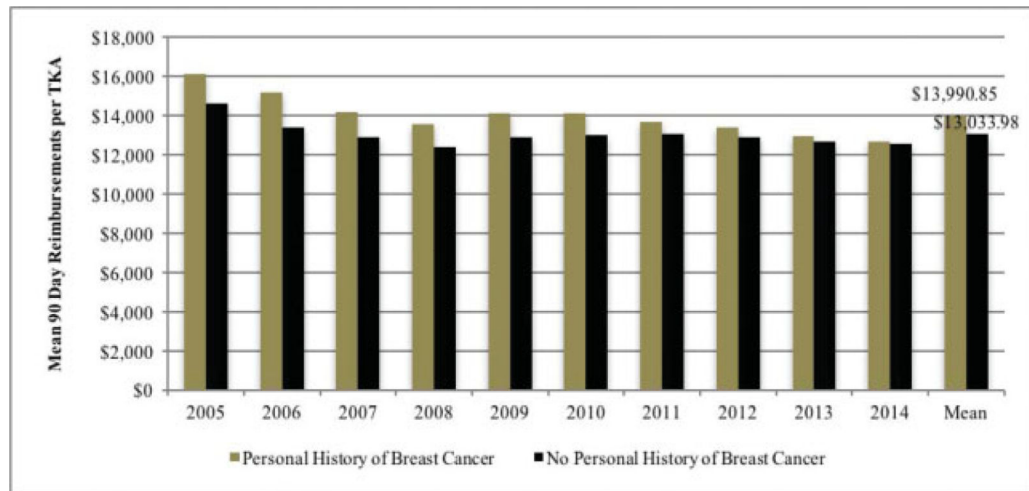
Fig. 3.
Ninety-day reimbursements over time.

Table 1

Demographical characteristics of both cohorts after matching

64 and under	4,625	5%
65–69	22,797	24.6%
70–74	23,572	25.5%
75–79	21,299	23%
80–84	13,735	14.8%
85 and over	5,459	5.9%
Unknown	1,070	1.2%
Total	92,557	
Female	90,913	98.2%
Males	574	0.6%
Unknown	1,070	1.2%
Total	92,557	

Table 2

Medical complication rates and comparison

Medical complications	ICD code	Breast cancer history (%)	No breast cancer history (%)	Odds ratio	95% confidence interval	P-Value
Acute postoperative anemia	285.1	2.60	2.50	1.04	0.982–1.102	0.184
Pulmonary embolism	415.1	0.65	0.56	1.147	1.019–1.290	**0.023**
Acute myocardial infarction	410	0.14	0.21	0.657	0.524–0.824	**<0.001**
Deep venous thrombosis	453.4	1.24	1.20	1.027	0.945–1.116	0.525
Pneumonia	480–486	0.46	0.54	0.852	0.749–0.970	**0.015**
Pulmonary insufficiency	518.5	0.04	0.04	1.088	0.683–1.734	0.722
Postoperative bleeding	998.11 998.12	0.23	0.22	1.049	0.866–1.272	0.624
Cardiac complication	997.1	0.06	0.06	1.076	0.740–1.563	0.703
Peripheral vascular complication	997.2	0.07	0.07	1	0.709–1.410	1
Urinary complication	997.5	0.03	0.03	1.192	0.708–2	0.508
Transfusion of blood	99.X	1.17	1.18	0.988	0.908–1.075	0.779
Diagnostic ultrasound of peripheral vascular system	88.77	0.22	0.17	1.274	1.034–1.571	**0.023**
Chest computed tomography	71,250, 71,260, 71,270, 71,275	1.67	1.36	1.233	1.144–1.329	**<0.001**

Abbreviation: ICD, International Classification of Disease.

Note: Statistically significant differences are presented in bold.

Table 3

Surgical complication rates and comparison

Surgical complications	ICD code	Breast cancer (%)	No cancer (%)	Odds ratio	95% confidence interval	p-Value
Osteomyelitis	730	0.02	0.04	0.424	0.227–0.793	0.006
Mechanical complication of the orthopaedic device	996.4	0.30	0.29	1.042	0.880–1.234	0.635
Unspecified mechanical complication of internal orthopaedic device, implant, and graft	996.40	0.03	0.04	0.889	0.552–1.431	0.628
Mechanical loosening of the prosthetic joint	996.41	0.02	0.02	0.636	0.326–1.244	0.182
Dislocation of the prosthetic joint	996.42	0.08	0.05	1.522	1.049–2.208	0.026
Broken prosthetic joint implant	996.43	0.01	0.0	0.706	0.337–1.478	0.353
Periprosthetic fracture around the prosthetic joint	996.44	0.06	0.05	1.17	0.793–1.728	0.428
Other mechanical complication of prosthetic joint implant	996.47	0.07	0.06	1.123	0.786–1.605	0.524
Other mechanical complication of other internal orthopaedic device, implant, and graft	996.49	0.03	0.03	1.167	0.676–2.013	0.579
Infection of orthopaedic device	996.66	0.32	0.32	1.01	0.860–1.186	0.902

Abbreviation: ICD, International Classification of Disease.

Note: Statistically significant differences are presented in bold.