Liver Transplantation Does Not Increase Morbidity or Mortality in Women Undergoing Surgery for Breast Cancer

Gregory Veillette  
Westchester Medical Center

Maria Castaldi (Maria.Castaldi@wmchealth.org)  
Westchester Medical Center  https://orcid.org/0000-0002-2019-3802

Sacha Roberts  
Westchester Medical Center

Afshin Parsikia  
Albert Einstein Healthcare Network

Ankur Choubey  
The University of Toledo Medical Center

Kenji Okumura  
Westchester Medical Center

Rifat Latifi  
Westchester Medical Center

Jorge Ortiz  
Albany Medical Center

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Abstract

Purpose

The incidence of breast cancer (BC) in solid organ transplant recipients is comparable to the age-matched general population. The rate of reported de novo breast cancer following liver transplantation (LT) varies. Further, there is limited information on the management and outcomes of breast cancer in liver transplant recipients (LTR). We aim to evaluate the impact of LT on breast cancer surgery outcomes. Further we compare the outcomes after breast cancer surgery in LTR in transplant versus non-transplant centers.

Methods

National Inpatient Sample (NIS) database was accessed to identify LTR with BC. Mortality, complications, hospital charges and total length of stay (LOS) were evaluated with multivariate logistic regression testing. Weighted multivariate regression models were employed to compare outcomes at transplant and non-transplant centers.

Results

Ninety-nine women met inclusion criteria for LT + BC and were compared against a cohort of women with BC without LT (n=736,527). LT + BC had lower performance status as confirmed via higher Elixhauser Comorbidity Index (20.5% vs.10.2%, p < 0001). There were significantly more complications in the LT cohort when compared to the non-LTR (15.0% vs. 8.2%, p=0.012). However, on multivariate analysis, LT was not an independent risk factor for post-operative complications following breast cancer surgery (OR 1.223, p=0.480). Cost associated with breast cancer care was significantly higher in those with LT (2.621, p<0.001). Breast conservation surgery in LT had shorter LOS as compared to BC alone (OR 0.568, p 0.027) in all hospitals.

Conclusion

LT does not increase short-term mortality when undergoing breast cancer surgery. Although there were significantly more complications in the LT cohort when compared to the non-LTR (15.0% vs. 8.2%, p=0.012), on multivariate analysis, LT was not an independent risk factor for postoperative complications following breast cancer surgery. Additionally, breast cancer treatment is more costly in LTR. Breast cancer management in LTR at non-transplant centers incurred higher charges but no difference in complication rate, nor LOS when compared to breast cancer management in LTR at transplant centers.

Introduction:
Liver transplantation (LT) is the standard treatment for those with acute and chronic liver disease, as well as those with various types of liver neoplasms. Livers are the second most commonly transplanted organ in the United States. The number of liver transplants performed in the United States has steadily increased over the past twenty years. Almost 9,000 liver transplants were performed in 2020. The one, three, and five-year survival rate for women over the age of 40 following liver transplantation is 88.2%, 81.4%, 76.7%, respectively.

Chronic immunosuppressive therapy, essential for allograft survival, remains the most important long-term risk factor contributing to morbidity following LT. Both infectious and neoplastic complications are much more common in the immunosuppressed host. Malignancies in transplant recipients often have a more rapid progression, an unfavorable prognosis, and a poor response to standard treatment. Therefore, as both the number of liver transplants performed and survival increases, identification and management of complications in these patients is paramount.

Breast carcinoma (BC) is the leading cause of new cancer diagnosis in women. Approximately 13% of women in the United States will develop breast cancer during their lifetime. Treatment for breast cancer is individualized. However, the current mainstay of curative BC treatment is breast surgery. While the outcomes of those undergoing breast surgery are well documented in the general population, little is known regarding how patients fare if they have previously undergone a liver transplant.

The rate of reported de novo breast cancer following liver transplantation varies. There is a general consensus that the risk of BC does not appear to be increased in those having undergone solid organ transplant. Nonetheless, once cancer develops in transplant recipients, the post-treatment outcomes may be worse than expected in the general population. Despite this, little is known regarding the outcomes of breast surgery in LTR. Koonce et al reported no significant complications following reconstructive surgery in those who previously underwent a solid organ transplant. However, this cohort consisted of only 17 women, two of whom underwent a LT. Similarly, in a case report by Nakakimura et al., no severe adverse events were observed in one woman who underwent breast surgery and chemotherapy following a LT. Others observed higher mortality when diagnosed with higher stage breast cancer after liver transplantation.

Breast cancer surgery outcomes data following solid organ transplantation has largely focused on those with kidney transplantation. Consequently, little attention has been afforded to LTR subsequently treated for BC. Since liver transplantation has become a common procedure and recipients live with allografts, it is imperative to develop a greater understanding of the outcomes of breast cancer surgery in this cohort. Our purpose is to evaluate the influence of LT on the short-term outcomes of breast cancer surgery in women at transplant and non-transplant centers.

Methods:

Data from the National Inpatient Sample (NIS), between 2005 to 2014 on Breast Lumpectomy and Mastectomy were isolated. The NIS is the largest publicly available all-payer inpatient healthcare
A database designed to produce U.S. regional and national estimates of inpatient utilization, access, charges, quality, and outcomes[21]. A history of liver transplant was determined within this subset. As such, the cohort was breast surgery patients that had a history of prior liver transplant. Exclusion criteria included concomitant history of prior organ transplant, complications related to prior organ transplants, benign breast tumor, age younger than 18, and male gender. Hospital and patient-level characteristics between breast cancer with and without liver transplant were compared with t-test, Mann-Whitney test and chi-squared test.

The Elixhauser Comorbidity Index (1988) categorized and scored comorbidities. The Elixhauser Comorbidity Index is a method of categorizing comorbidities of patients based on the International Classification of Diseases (ICD) diagnosis codes found in administrative data[22]. A greater score is associated with worse prognosis[23]. The influence of LT on mortality and morbidity was evaluated with logistic regression testing. Total hospital charge and length of stay were converted to a binary variable based on their median. The role of LT on the total hospital charge and length of stay was evaluated with logistic regression testing, where the dependent variable was length of stay or total hospital charge below or above median. Similarly, the effect of LT on total hospital charge and length of stay (LOS) was measured with linear regression. Total charges were adjusted based on consumer price index (CPI) 2020. Since there was no mortality in the LT cohort, only three of the outcomes were assessed in a multivariate fashion.

Multivariate logistic regressions were performed to compare outcomes sorted by transplant center (TC), teaching centers, and patients who underwent reconstruction following breast cancer surgery. The selected co-variates were standard patient and hospital characteristics in NIS which were statistically significant between LT and no LT. These include race, co-morbidity, primary expected payer, zip code income quartile, hospital ownership, location/teaching status, and region. Missing values are reported in Table I and Table II and were coded for the covariates. There was no exclusion in the result of multivariate logistic regression. We identified TC as hospitals with at least one liver transplant performed during the timeframe. All results were calculated after applying the sampling weight built in NIS.

**Results:**

A total of 736,626 women underwent surgery for breast cancer. Of these, 99 received liver transplantation. There was no statistical difference in terms of age at the time of diagnosis of breast cancer. The majority of women in each cohort were white, with a significantly higher percentage of women in the LT group being white (65.3% vs. 62.1%, p <0.001). Of the 99 LTR, 69.7% had an Elixhauser comorbidity score of 3 or greater (median score of 4), while only 21.5% of non-LT patients had a score of 3 or greater (median score of 0) (p<0.001, Table I). Socioeconomic status for the LTR cohort was higher than the non-LTR cohort, as these women belonged mostly to the higher income quartile (third quartile 35.8% vs. 24.3%, p 0.017). There was no statistical difference in the frequency or type of surgical procedure, lumpectomy or mastectomy (Table I).
The dominant payment method was private insurance (50.8%). However, Medicare was a more common method of payment for the LTR group compared to the non-LTR group (65.0 vs. 36.6%, p<0.001). Most centers were public hospitals, with large bed size, and urban teaching affiliates. Although there were some statistical differences in the components of these variables, overall, these hospitals were comparable (Table II).

The rate of complication was significantly higher in the LTR group compared to the non-LTR group (15.0 vs. 8.2%, p=0.012); the most common complication was acute renal failure in the LTR group (9.9 vs. 0.6%, p<0.001). Other complications were comparable (Table III).

Liver transplant recipients underwent breast cancer surgery predominantly in transplant centers when compared to non-LTR (35.0% vs. 23.2%, p=0.004). There were no deaths in the 99 liver transplant recipients. There were significantly more complications in the LT cohort when compared to the non-LTR (15.0% vs. 8.2%, p=0.012). However, on multivariate analysis, undergoing LT was not an independent risk factor for post-operative complications followed breast cancer surgery (OR 1.223 p 0.480) (Table IV). Total hospital charges for breast cancer surgery were higher in the liver transplant group ($63,724 vs. $43,003, p<0.001). (Table III) LOS for breast cancer surgery in the reconstructed group was significantly shorter in the liver transplant group (LOS> 2 days OR 0.170, p 0.002) (Table IV).

**Discussion:**

Organ transplantation has significant survival and quality of life benefits compared to best medical (non-transplant) management. One of the most important factors that has allowed for prolonged allograft survival has been the advances in immunosuppressive regimens. Although de novo malignancies are known long-term complications of organ transplantation, breast cancer is not increased in the transplant population when compared against age-matched SEER general population data. Incidencrates in published literature show age-specific breast cancer incidence after 50 years old in those with liver transplantation similar to that of the general population. Our sample size is small when compared to the overall incidence in the literature of de novo breast cancers in those with liver transplants. Nonetheless, after weighting, our results reflect a realistic appraisal of patients with breast cancer and liver transplantation.

The care of the liver transplant recipient requires a lifelong multidisciplinary effort by a wide range of specialists. Clinicians must not only consider all of the transplant-related complications, but also typical age-related comorbidities. Moreover, chronic immunosuppressive therapy can induce or accelerate some conditions that the non-transplant patient may not be routinely monitored for, specifically malignancy.

Centralized and specialized management of breast cancer in the liver transplant recipient is paramount. On univariate analysis, the complication rate, especially in acute renal failure was higher in LTR group. Currently most of breast surgery was performed in the outpatient setting. LTR might show the elevation of creatinine in perioperative workup since LTR require immunosuppression drugs and adjustment of the doses frequently according to serum creatinine levels. However, after adjustment and on multivariate
analysis, LTR was not an independent risk factor for developing a post-operative complication (OR 1.223 p 0.480) (Table IV). This suggests that factors other than liver transplantation are associated with development of post-operative complications.

A significantly higher proportion of LTR had an Elixhauser comorbidity score of ≥ 3 (69.7% vs.21.5%, p<0.001, Table I), indicating that LT patients suffered from a higher degree of co-morbidity. However, our data shows that despite the LTR having significantly more comorbidities, there were no differences in mortality, complication rate, total charge, or length of stay when these patients were managed at a transplant center (Table IV). Breast cancer management in LTR at non-transplant centers incurred higher charges but no difference in complication rate nor LOS when compared to breast cancer management in LTR at transplant centers.

Of women who received a liver transplant, length of stay following breast cancer surgery was significantly shorter in the group which underwent breast reconstruction. (OR <1, p 0.002) (Table IV). This may be due to the fact that, in general, immediate breast reconstruction is performed by careful selection of those patients who are possibly overall healthier. We do not have knowledge of pre- and posttransplant performance status, immunosuppressive regimens, or pretransplant health that may overall lend to healthier LTR and thus ability to withstand an immediate breast reconstruction with acceptable outcomes and LOS. We have found a significantly shorter LOS after reconstruction in the liver transplant cohort compared to the non-liver transplant cohort most likely explained by better selection of appropriate candidates. The liver transplant patients underwent probably simpler implant-based reconstruction as opposed to non-liver transplant patients who underwent autologous tissue based reconstructions usually associated with more than double the LOS.

Our analyses revealed no statistical difference when comparing the overall survival of the two cohorts. This mirrors previous reports. Jeong et al. compared the prognosis of post-transplant breast cancer patients receiving immunosuppressants to general breast cancer survivors. All individuals had previously undergone either a liver or kidney transplant. They discovered that after matching by tumor size, lymph node metastasis, and age, disease-free survival, breast-cancer specific survival, and overall survival were not significantly different between the two cohorts[24].

A final, notable point is the fact that total hospital charges for breast cancer surgery were higher in the liver transplant group, even after controlling for other variables (OR 2.621, p <0.001) (Table IV). This may be explained by LTR suffer from a higher degree of co-morbidity. An analysis of 126,664 individuals with breast cancer, revealed the average medical cost per patient with comorbidity was higher compared to the average medical cost per person without comorbidity (p<0.05)[25]. We hypothesize that increased comorbidities in the LT cohort may have played a role in these women incurring higher costs for breast cancer surgery.

This analysis is not without limitations, as there is inherent weakness of large database analysis. Time between liver transplantation and breast cancer surgery was not known. Prolonged periods of immunosuppressive treatment may induce DNA damage and inhibit immune surveillance mechanisms,
thus increasing risk of lymph node metastases which would require more extensive BC surgery, possibly axillary node dissection, with locally advanced disease at presentation\textsuperscript{24}. Additionally, immunosuppressive medications are unknown. This prevented us from stratifying outcomes based on type of immunosuppressive agent. Further, information on the breast cancer stage and neoadjuvant chemotherapy treatment prior to surgery is unknown. Thus, we were unable to assess outcomes on early versus advanced disease. Similarly, long term patient outcomes are not available due to database limitations, and could not be assessed, and may differ from the reported short-term outcomes in our analyses. Further, there is no data available on cancer stage distribution or method of breast cancer detection or screening rates in those with liver transplantation.

Additional research is needed to more comprehensively understand the difficulties that post-livertransplant breast cancer survivors face following breast cancer surgery compared to the general breast cancer population. Future analyses should consider factors such as breast cancer stage, type of immunosuppressive therapy, and time since LT.

The strengths of this manuscript are reflected in this being the largest and first reported analysis that determines that prior liver transplantation does not increase morbidity nor mortality in women undergoing surgery for breast cancer. However, we found total hospital charges for breast surgery were significantly higher in LTR. These results may be used to guide clinical practice when treating women for breast cancer who have undergone a liver transplant.

**Declarations**

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**Availability of data and material:** Data from the National Inpatient Sample (NIS), between 2005 to 2014 on Breast Lumpectomy and Mastectomy were isolated (ICD 9 code: 85.20-85.23 and 85.33-85.36 and 85.41 – 85.48).

**Code availability:** Data and coding available upon request.

**Ethics approval:** Not applicable

**Consent to participate:** Not applicable

**Consent for publication:** Not applicable

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Tables
| Table I: Patient Characteristics | No LT (n=736,527) | LT (n=99) | TOTAL (n=736,626) | p-value |
|---------------------------------|-------------------|-----------|-------------------|---------|
|                                 | Number            | %         | Number            | %       | Number            | %       |        |
| Age > 65 y                      | 273,841           | 37.2      | 34                | 34.7    | 273,876           | 37.2    | 0.559  |
| Age, mean (SD), year            | 59.8 (14.3)       | 59.7 (11.2)| 59.8 (14.3)       | 0.945   |
| Race                            |                   |           |                   |         |
| White                           | 457,621           | 62.1      | 65                | 65.3    | 457,685           | 62.1    | <0.001 |
| Black                           | 74,295            | 10.1      | 15                | 15.2    | 74,310            | 10.1    | <0.001 |
| Hispanic                        | 48,565            | 6.6       | 5                 | 5.0     | 48,570            | 6.6     | <0.001 |
| Asian or pacific islander       | 22,562            | 3.1       | 5                 | 4.6     | 22,567            | 3.1     | <0.001 |
| Native American                 | 2,882             | 0.4       | 0                 | 0.0     | 2,882             | 0.4     | <0.001 |
| Other                           | 17,956            | 2.4       | 10                | 9.9     | 17,966            | 2.4     | <0.001 |
| Race unknown                    | 112,645           | 15.3      | 0                 | 0.0     | 112,645           | 15.3    | N/A    |
| Elixhauser co-morbidity category|                   |           |                   |         |
| ≤-1                             | 258,101           | 35.0      | 20                | 20.2    | 258,121           | 35.0    | 0.002  |
| 0-2                             | 319,982           | 43.4      | 10                | 10.1    | 319,992           | 43.4    | <0.001 |
| 3-10                            | 83,208            | 11.3      | 49                | 49.2    | 83,256            | 11.3    | <0.001 |
| >10                             | 75,237            | 10.2      | 20                | 20.5    | 75,257            | 10.2    | 0.001  |
| Elixhauser co-morbidity index, median (IQR) | 0 (-1.0 – 1.0) | 4.0 (1.0 – 8.0) | 0 (-1.0 – 1.0) | <0.001 |
| Zip code income quartile        |                   |           |                   |         |
| First quartile                  | 154,371           | 21.0      | 10                | 10.6    | 154,381           | 21.0    | 0.008  |
| Second quartile                 | 165,913           | 22.5      | 19                | 19.4    | 165,932           | 22.5    | 0.235  |
| Third quartile                  | 178,762           | 24.3      | 35                | 35.8    | 178,798           | 24.3    | 0.017  |
| Forth quart                     | 222,375           | 30.2      | 34                | 34.2    | 222,409           | 30.2    | 0.264  |
| Zip code unknown                | 15,107            | 2.1       | 0                 | 0.0     | 15,107            | 2.1     | N/A    |
| Carcinoma insitu of breast      | 132850            | 18.0      | 21                | 21.0    | 132871            | 18.0    | 0.441  |
| Procedures                      |                   |           |                   |         |
| Unilateral mastectomy           | 494,188           | 67.1      | 69                | 69.7    | 494,257           | 67.1    | 0.582  |
|                          | Count | Rate | Age | 100 | Count | Rate | Age |
|--------------------------|-------|------|-----|-----|-------|------|-----|
| Bilateral mastectomy     | 161,699 | 22.0 | 15  | 15.2| 161,714 | 22.0 | 0.102 |
| Lumpectomy               | 91,137  | 12.4 | 15  | 15.2| 91,152  | 12.4 | 0.401 |
| Reconstruction           | 76,159  | 10.3 | 15  | 15.2| 76,174  | 10.3 | 0.116 |
| Immediate reconstruction | 64,343  | 97.1 | 15  | 100 | 64,358  | 97.1 | 0.501 |
Table II: Hospital Characteristics

|                              | No LT (n=736,527) | LT (n=99) | TOTAL (n=736,626) | p-value |
|------------------------------|-------------------|-----------|-------------------|---------|
| Primary expected payer       |                   |           |                   |         |
| Medicare                     | 269,300           | 64        | 65.0              | 269,364 | 36.6 | <0.001 |
| Medicaid                     | 63,848            | 10        | 10.1              | 63,858  | 8.7  | 0.830  |
| Private insurance            | 373,971           | 25        | 24.9              | 373,995 | 50.8 | <0.001 |
| Self-pay                     | 10,957            | 0         | 0.0               | 10,957  | 1.5  | 0.445  |
| No charge                    | 2,542             | 0         | 0.0               | 2,542   | 0.3  | 0.0794 |
| Other                        | 15,027            | 2.0       | 2.0               | 15,027  | 2.0  | 0.335  |
| Payer unknown                | 883               | 0.1       | 0.1               | 883     | 0.1  | N/A    |
| Hospital ownership           |                   |           |                   |         |
| Government or private        | 205,257           | 27.9      | 27.9              | 205,282 | 27.9 | 0.637  |
| Public                       | 60,805            | 8.3       | 8.3               | 60,820  | 8.3  | 0.036  |
| Private, non for profit      | 384,870           | 52.3      | 52.3              | 384,919 | 52.3 | 0.640  |
| Private, investor owned      | 70,272            | 9.5       | 9.5               | 70,282  | 9.5  | 0.758  |
| Private                      | 11,439            | 1.6       | 1.6               | 11,439  | 1.6  | 0.349  |
| Ownership unknown            | 3,884             | 0.5       | 0.5               | 3,894   | 0.5  | N/A    |
| Hospital bed size            |                   |           |                   |         |
| Small                        | 99,611            | 13.5      | 13.5              | 99,626  | 13.5 | 0.694  |
| Medium                       | 174,011           | 23.6      | 23.6              | 174,026 | 23.6 | 0.061  |
| Large                        | 459,020           | 62.3      | 62.3              | 459,090 | 62.3 | 0.194  |
| Bed size unknown             | 3,884             | 0.5       | 0.5               | 3,894   | 0.5  | N/A    |
| Location/teaching status     |                   |           |                   |         |
| Rural                        | 64,412            | 8.7       | 8.7               | 64,412  | 8.7  | 0.006  |
| Urban, non-teaching          | 268,225           | 36.4      | 36.4              | 268,275 | 36.4 | 0.012  |
| Urban, teaching              | 400,005           | 54.3      | 54.3              | 400,055 | 54.3 | 0.456  |
| Teaching status unknown      | 3,884             | 0.5       | 0.5               | 3,894   | 0.5  | N/A    |
| Region                       |                   |           |                   |         |
|            | Acute adults |   |   |  | Acute adults |   |   |            | Acute adults |   |   |  | Acute adults |
|------------|--------------|---|---|---|--------------|---|---|------------|--------------|---|---|---|--------------|
| Northeast  | 180,178      | 24.5 | 11 | 10.6 | 180,189      | 24.5 | 0.002 |
| Midwest    | 151,372      | 20.6 | 20 | 20.6 | 151,393      | 20.6 | 0.931 |
| South      | 249,991      | 33.9 | 45 | 45.3 | 250,036      | 33.9 | 0.016 |
| West       | 154,986      | 21.0 | 23 | 23.5 | 155,009      | 21.0 | 0.593 |
| Transplant center | 99,260 | 13.5 | 30 | 35.3 | 99,290 | 13.5 | 0.004 |
### Table III: Outcomes

|                             | No LT (n=736,527) | LT (n=99) | TOTAL (n=736,626) | \(p\)-value |
|-----------------------------|-------------------|-----------|-------------------|--------------|
| **Number**                  | 599               | 0         | 599               | 0.776        |
| **%**                       | 0.1%              | 0.0%      | 0.1%              |              |
| **Death**                   |                   |           |                   |              |
| **Disposition of patient**  |                   |           |                   |              |
| **Home Health Care**        | 148,568           | 16        | 148,584           | 0.747        |
| **(uniform)**               | 20.2%             | 16.0%     | 20.2%             |              |
| **Transfer to SNF, ICF, or**|                   |           |                   |              |
| **other**                   | 24,187            | 0         | 24,187            |              |
| **Transfer to short term**  |                   |           |                   |              |
| **hospital**                | 839               | 0         | 839               |              |
| **Routine**                 | 561,498           | 83        | 561,581           | 0.747        |
| **Unknown**                 | 66                | 0         | 66                |              |
| **Other**                   | 770               | 0         | 770               |              |
| **Any complication**        |                   |           |                   | 0.012        |
| **Cardiovascular**          | 3,567             | 0         | 3,567             | 0.488        |
| **Respiratory**             | 2,435             | 0         | 2,435             | 0.567        |
| **Peripheral vascular**     |                   |           |                   | 0.863        |
| **complication**            | 223               | 0         | 223               |              |
| **Central nervous system**  |                   |           |                   | 0.833        |
| **complication**            | 329               | 0         | 329               |              |
| **Hematomas**               | 23,670            | 5         | 23,675            | 0.300        |
| **Accidental cut, puncture**|                   |           |                   | 0.732        |
| **or hemorrhage during a**  | 871               | 0         | 871               |              |
| **procedure**               |                   |           |                   |              |
| **Complications of operative**|                |           |                   | 0.657        |
| **wound**                   | 1,467             | 0         | 1,467             |              |
| **Post-operative infection**|                   |           |                   | 0.507        |
| **Other**                   | 2,489             | 0         | 2,489             | 0.562        |
| **Acute renal failure**     |                   |           |                   | <0.001       |
| **Urinary complications**   |                   |           |                   | 0.664        |
| **Digestive system**        |                   |           |                   | 0.616        |

**Note:** The \(p\)-values are calculated using appropriate statistical tests to compare the outcomes between the No LT and LT groups.
| complications                          | 30 | 0  | 0  | 0  | 30 | 0  | 1.000 |
|---------------------------------------|----|----|----|----|----|----|-------|
| Acute vascular insufficiency-intestine |    |    |    |    |    |    |       |
| Platelet transfusion                  | 990| 0.1% | 0  | 0.0% | 990 | 0.1% | 0.715 |
| Fresh frozen plasma transfusion       | 1,458 | 0.2% | 0  | 0.0% | 1,458 | 0.2% | 0.658 |
| pRBC transfusion                      | 24,280 | 3.3% | 5  | 5.0% | 24,285 | 3.3% | 0.328 |
| SIRS                                  | 1,339 | 0.2% | 0  | 0.0% | 1,339 | 0.2% | 0.671 |
| Complication of graft                 | 3,263 | 0.4% | 0  | 0.0% | 3,263 | 0.4% | 0.507 |
| Length of stay, day, median (IQR)     | 2.0 (1.0-2.0) | 2.0 (1.0-2.0) | 2.0 (1.0-2.0) | 0.493 |
| Total charges associated with breast cancer surgery, $, median (IQR) | 43,002 (26,952-71,027) | 63,724 (33,068-91,809) | 43,003 (26,953-71,032) | <0.001 |

CPH: cut, puncture, hemorrhage, SNF: skilled nursing facility, ICF: intermediate care facility, pRBC: packed red blood cells, SIRS: systemic inflammatory response syndrome

IQR: interquartile range

Total charges were adjusted based on inflation price index 2020.
Table IV: Weighted Multivariate Adjusted Outcome for Liver Transplant Patients Based on Type of Center

|                                | All centers | Transplant Centers | Non-liver transplant center | Teaching centers | Reconstruction |
|--------------------------------|-------------|--------------------|-----------------------------|------------------|----------------|
|                                |             | P-value            | OR                          | P-value          | OR             | P-value          | OR |
| Any complication               | .480        | 1.223              |                             | .651             | 1.254          | .732             | 1.126 |
| Total charge>43,000 USD        | <0.001      | 2.621              |                             | .146             | 1.782          | <0.001           | 2.802 |
| Length of stay>2 days          | .027        | .568               |                             | .186             | .516           | .078             | .590 |

Note:
1. N/A, not applicable because of zero mortality and zero complications in only reconstructed patients
2. Total charges were adjusted based on consumer price index 2020.
3. The multivariable analyses were adjusted for race, co-morbidity, primary expected payer, zip code income quartile, hospital ownership, location/teaching status, region.