

A New Start with HAART: Evaluating Breast Reconstruction in the Era of Highly Active Antiretroviral Therapy

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Background: As HIV-positive individuals utilizing highly active antiretroviral therapy live longer, the burden of breast cancer increases in the population. Breast reconstruction is an integral aspect of surgical treatment for many patients after a breast cancer diagnosis, prompting this examination of the characteristics and outcomes of breast reconstruction in this growing patient population.

Methods: Using Merative MarketScan Research Databases, a large multipayer database, HIV-positive adult patients who underwent autologous or implant-based breast reconstruction between 2007 and 2021 were identified using International Classification of Disease codes and Common Procedural Terminology codes. In both HIV-positive and -negative cohorts, patient demographics, procedure-related complications, and postoperative revisions were recorded. Shapiro-Wilk, chi-square, Wilcoxon-Mann-Whitney, and multivariable logistic regression tests were used for statistical analysis.

Results: Of 173,421 patients who underwent breast reconstruction, 1816 had an HIV diagnosis. HIV-positive patients were younger ($P < 0.001$), underwent surgery more recently ($P < 0.001$), more often underwent immediate breast reconstruction ($P < 0.001$), and had higher comorbidity levels ($P < 0.001$). There was a regional variation in which the patient cohorts underwent breast reconstruction. There was no significant difference in overall complication rates between patient groups, but HIV-negative patients more often underwent revision procedures ($P = 0.009$).

Conclusions: When compared to their HIV-negative counterparts, breast reconstruction can be considered safe and efficacious in patients living with HIV. HIV-positive patients are a growing demographic who seek breast reconstruction, and surgeons must continue to further understand the unique implications of breast reconstruction in this population. (*Plast Reconstr Surg Glob Open* 2024; 12:e6040; doi: 10.1097/GOX.0000000000006040; Published online 7 August 2024.)

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INTRODUCTION

Breast reconstruction in the setting of a positive HIV status in the era of highly active antiretroviral therapy (HAART) remains a poorly understood topic.¹ The advent of HAART has shifted the landscape of HIV-related illness from being invariably fatal to a chronic, survivable condition.² Progress in life expectancy for those living with HIV has been made with the introduction of HAART, and this medication regimen has significantly decreased the incidence of acquired immunodeficiency syndrome (AIDS)-defining malignancies.³ Furthermore, HAART

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has allowed for improved outcomes after the diagnosis of AIDS-defining malignancies.^{4,5}

Likely due to immune reconstitution and better viral suppression, the era of HAART has led to a reduction in rates of AIDS-defining malignancies in those living with HIV. The relationship between HAART and non-AIDS-defining malignancies, however, differs.⁶

Multiple studies have demonstrated that the burden of non-AIDS-defining malignancies has increased in people living with HIV, comprising the majority of cancers impacting this population in the era of HAART.⁶⁻⁹ Breast cancer is one such non-AIDS-defining malignancy that has shown a rising incidence in the HIV-positive population in the era of HAART. As the risk of breast cancer increases with age, it is hypothesized that the increased longevity of patients with HIV taking HAART is associated with the increased occurrence of neoplastic breast conditions.⁹⁻¹¹ Work from Pantanowitz et al¹² suggests that people living with HIV and being treated with HAART should be expected to encounter breast malignancy at higher rates. Thus, it is necessary and relevant to question what should be considered appropriate management of breast cancer in the population of people living with HIV.

Previous research has speculated about the impact of HIV and HAART on postoperative complication rates, although the evidence remains inconclusive. Elevated rates of postoperative complications, especially surgical site infection and wound healing challenges, are commonly corroborated in patients with HIV and may be inversely correlated with CD4 counts at the time of surgery. These higher complication rates are often attributed to the progressive immunological compromise associated with unmitigated HIV infection.^{13,14} However, this elevated risk of complications may, amid mixed evidence, be greatly reduced in patients on HAART with adequate CD4 counts.¹⁵⁻¹⁷

As the incidence of breast cancer increases for patients living with HIV, the safety and efficacy of breast reconstruction in this population must be explored as it is an important aspect of surgical management for many patients diagnosed with breast cancer.¹⁸⁻²⁰ The population of patients diagnosed with cancer and not living with HIV has previously demonstrated an increased utilization of breast reconstruction, and this trend continues in the HIV-positive population.^{14,21} This reality and the nuances of HAART, including the fact that immune restoration after HAART can lead to acute inflammatory responses that may complicate breast reconstruction outcomes, necessitates an evaluation of breast reconstruction and outcomes in this understudied population.^{22,23} Our study leverages national data to depict breast reconstruction in HIV-positive patients and investigate the ways in which breast reconstruction differs between HIV-positive and HIV-negative individuals.

METHODS

We conducted a retrospective analysis of the Merative MarketScan Research Databases, a large multipayer database, to evaluate demographic characteristics and postoperative outcomes in HIV-positive and HIV-negative adult

Takeaways

Question: How do breast reconstruction and subsequent outcomes compare between HIV-positive and HIV-negative individuals?

Findings: Using IBM MarketScan Research Databases, HIV-positive adult patients who underwent autologous or implant-based breast reconstruction between 2007 and 2021 were identified using International Classification of Disease codes and Common Procedural Terminology codes. HIV-positive patients were younger, underwent surgery more recently, and more often underwent immediate breast reconstruction. Although HIV-positive individuals had higher comorbidity levels, they did not have increased odds of experiencing complications.

Meaning: Breast reconstruction is safe to perform after surgical breast cancer management in patients living with HIV utilizing highly active antiretroviral therapy.

patients who underwent breast reconstruction between 2007 and 2021.²⁴ The Merative MarketScan Research Databases contain inpatient claims, outpatient claims, and prescription data for 182,915,708 unique patients with capacity for longitudinal assessment. Those who underwent implant-based or autologous breast reconstruction were identified using Common Procedural Terminology (CPT) codes and Healthcare Common Procedural Coding System codes. CPT codes were also used to identify patients who underwent mastectomy procedures on the same day as the index breast reconstruction procedure; these patients were considered to have undergone immediate breast reconstruction. HIV-positive individuals were defined as those who had an HIV diagnosis [International Classification of Disease, ninth (ICD-9) and tenth (ICD-10) edition] code. The authors assumed that any patients with HIV undergoing reconstructive surgery were taking HAART, as surgeons would be unlikely to perform an elective procedure in the setting of uncontrolled HIV.

Procedure-related complications [seroma, hematoma, dehiscence, acquired breast deformity, infection, fat necrosis, tissue necrosis, deep vein thrombosis (DVT) or other vascular complication, nonspecified complications of surgical care, and surgical complications (drainage and/or secondary closures)] within 90 days of the index breast reconstruction were recorded. Revision procedures (removal of intact breast implant, removal of ruptured breast implant, revision of capsule or breast, peri-implant capsulectomy, and revision of reconstructed breast) within 90 days of the index breast reconstruction were likewise recorded. Procedure and diagnosis codes can be found in the supplemental materials. (See table, Supplemental Digital Content 1, which displays the CPT and Healthcare Common Procedural Coding System codes used to identify patients in the Merative MarketScan Research Databases undergoing implant-based or autologous breast reconstruction. <http://links.lww.com/PRSGO/D405>.) (See table, Supplemental Digital Content 2, which displays the ICD-9 and ICD-10 codes used to identify patients

in the Merative MarketScan Research Databases with HIV and those who experienced complications after the index reconstruction procedure. <http://links.lww.com/PRSGO/D406>.)

Among this study population, demographic, operative characteristics, complication rates, and revision surgery rates were compared among HIV-positive and HIV-negative individuals. Multivariable logistic regression produced adjusted odds ratios (ORs) for experiencing one or more complications or for undergoing revision surgery following the index breast reconstruction for each of the following covariates: (1) age; (2) year of the index breast reconstruction; (3) HIV status; (4) reconstruction type; (5) immediate or delayed breast reconstruction; and (6) comorbidities, as measured by the Elixhauser index, an index that allows for the categorization of comorbidities based on ICD codes for a wide range of diseases.²⁵

Shapiro-Wilk testing was used to determine whether continuous variables were normally distributed. Chi-square, Wilcoxon-Mann-Whitney, and multivariable regression tests were used for statistical analysis. *P* values of less than 0.05 were considered statistically significant. All analyses were completed using Stata, version 16.1 (Stata Corp LLC).

RESULTS

Among the 173,421 patients meeting inclusion criteria, 1816 (1.0%) were categorized as HIV positive (Table 1). Most patients were middle-aged at the time of the index breast reconstruction (average age 49.47 ± 8.96 y), underwent surgery before 2017, and had low comorbidity levels (59% had Elixhauser index scores of 0 or 1). Implant-based reconstruction was prevalent (77%), and the majority of patients (57%) underwent immediate breast reconstruction. Thirty percent of patients experienced at least one complication as a result of the index procedure, and 13% of patients underwent revision surgery. Breast reconstruction most often occurred in the South US region (43%), followed by North Central (20%), Northeast (18%), and West (17%).

When compared with HIV-negative patients, HIV-positive patients, on average, were younger ($P < 0.001$), underwent surgery more recently ($P < 0.001$), more often underwent immediate breast reconstruction ($P < 0.001$), had higher comorbidity levels ($P < 0.001$), and more frequently underwent breast reconstruction in the Northeast ($P < 0.001$) (Table 2). Notably, HIV-positive patients underwent revision surgery less often than HIV-negative patients (11% versus 13%; $P = 0.009$). There were no significant differences in reconstruction type ($P = 0.059$) or complication rates ($P = 0.435$) between the two groups.

Table 3 outlines rates of Elixhauser comorbidities between HIV-positive and HIV-negative cohorts, excluding cohort-defining (HIV and malignancy) diagnoses. Rates of all assessed comorbidities were significantly higher in the HIV-positive cohort than in the HIV-negative cohort ($P \leq 0.003$). Additional analyses involving a modified Elixhauser comorbidity index that omits

Table 1. Characteristics of the Study Cohort (n = 173,421)

Characteristic	No. (%)
Age, y	
18–35	12,403 (7)
36–45	42,443 (24)
46–55	68,830 (40)
56+	49,745 (29)
Age	
Mean (± SD)	49.47 (±8.96)
Year of reconstruction procedure	
2007–2011	67,680 (39)
2012–2016	67,123 (39)
2017–2021	38,618 (22)
HIV positive	
No	171,605 (99)
Yes	1816 (1)
Reconstruction type	
Implant-based	133,750 (77)
Autologous	39,670 (23)
Immediate reconstruction	
No	74,624 (43)
Yes	98,797 (57)
Elixhauser index	
0 or 1	102,256 (59)
2	15,623 (9)
3	14,665 (8)
4+	40,877 (24)
Experienced 1+ complication	
No	122,032 (70)
Yes	51,389 (30)
Underwent revision	
No	150,429 (87)
Yes	22,992 (13)
Region	
Northeast	31,476 (18)
North Central	34,801 (20)
South	73,667 (43)
West	30,166 (17)
Unknown	3311 (2)

Entries are frequency (percentage) unless otherwise specified.

cohort-defining diagnoses can be found in Supplemental Digital Contents 3 and 4. [See table, Supplemental Digital Content 3, which displays the patient factors associated with experiencing one or more complications after the index procedure in the study cohort (n = 173,421) in a multivariable logistic regression, utilizing a modified Elixhauser comorbidity index score that omits the contributions of HIV and cancer diagnoses. A total of 51,389 (29.6%) patients experienced at least one complication due to the index procedure. <http://links.lww.com/PRSGO/D407>.] [See table, Supplemental Digital Content 4, which displays the patient factors associated with undergoing a revision after the index procedure in the study cohort (n = 173,421) in a multivariable logistic regression. A total of 22,992 (13.3%) patients underwent revision surgery after the index procedure, utilizing a modified Elixhauser comorbidity index score that omits the contributions of HIV and cancer diagnoses. <http://links.lww.com/PRSGO/D408>.]

Table 2. Characteristics of the Study Cohort (n = 173,421) among Those Categorized as HIV Positive (n = 1816) and HIV Negative (n = 171,605)

Characteristic	HIV Negative (n = 171,605), N (%)	HIV Positive (n = 1816), N (%)	P
Age, y			
18–35	12,120 (7)	283 (15)	<0.001
36–45	41,895 (24)	548 (30)	
46–55	68,201 (40)	629 (35)	
56+	49,389 (29)	356 (20)	
Age			
Mean (±SD)	49.51 (±8.95)	46.16 (±9.62)	<0.001
Year of reconstruction procedure			<0.001
2007–2011	67,446 (39)	234 (13)	
2012–2016	66,504 (39)	619 (34)	
2017–2021	37,655 (22)	963 (53)	
Reconstruction type			
Implant-based	132,383 (77)	1367 (75)	0.059
Autologous	39,221 (23)	449 (25)	
Immediate reconstruction			
No	73,936 (43)	688 (38)	<0.001
Yes	97,669 (57)	1128 (62)	
Elixhauser index			
0 or 1	101,936 (60)	320 (18)	<0.001
2	15,384 (9)	239 (13)	
3	14,369 (8)	296 (16)	
4+	39,916 (23)	961 (53)	
Experienced 1+ complication			0.435
No	120,739 (70)	1293 (71)	
Yes	50,866 (30)	523 (29)	
Underwent revision			
No	148,816 (87)	1613 (89)	0.009
Yes	22,789 (13)	203 (11)	
Region			
Northeast	31,087 (18)	389 (21)	<0.001
North central	34,458 (20)	343 (19)	
South	72,893 (43)	774 (43)	
West	29,868 (17)	298 (16)	
Unknown	3299 (2)	12 (1)	

Entries are frequency (percentage) unless otherwise specified. Statistical analyses conducted included chi-square, Shapiro-Wilk, and Wilcoxon-Mann-Whitney tests. Values in boldface indicate significance of a $P < 0.05$.

Table 4 compares complication and revision surgery rates between the HIV-positive and HIV-negative cohorts. Interestingly, HIV-positive patients incurred fewer postoperative infections (4% versus 5%) and more nonspecified complications of surgical care (15% versus 14%) than their HIV-negative counterparts ($P \leq 0.046$). There were no significant differences between the two groups in rates of hematoma or hemorrhage, seroma, DVT or vascular complications, wound dehiscence, acquired breast deformities, fat necrosis, tissue necrosis, or other surgical complications (requiring drainage and/or secondary closure). HIV-negative patients more often underwent removal of intact breast implant (4% versus 3%; $P = 0.009$) and revision of reconstructed breast (7% versus 5%; $P = 0.010$) than HIV-positive patients, although rates of other revision procedures did not vary significantly between the two groups.

Table 5 describes patient characteristics associated with experiencing one or more complications following the index breast reconstruction procedure. Older age ($P < 0.001$), undergoing surgery more recently ($P \leq 0.042$), undergoing autologous reconstruction (OR 1.799; $P < 0.001$), undergoing immediate breast reconstruction (OR

1.202; $P < 0.001$), and Elixhauser index scores of four or higher (OR 1.139; $P < 0.001$) were associated with increased odds of experiencing one or more complications, whereas Elixhauser scores of 2 or 3 (relative to scores of 0 or 1) were linked to lower odds of complications ($P \leq 0.005$). HIV status did not have a significant impact on the odds of experiencing one or more complications ($P = 0.120$).

Table 6 displays patient characteristics associated with undergoing revision surgery after the index breast reconstruction procedure. Older age ($P \leq 0.014$), undergoing surgery before 2012 ($P < 0.001$), undergoing autologous reconstruction (OR 1.296; $P < 0.001$), undergoing immediate reconstruction (OR 1.637; $P < 0.001$), and Elixhauser index scores greater than 1 ($P \leq 0.009$) were associated with increased odds of undergoing revision surgery. Notably, patients with an HIV diagnosis had reduced odds of undergoing a revision procedure (OR 0.829; $P = 0.013$).

DISCUSSION

As demonstrated by the results in this study, the rate of breast reconstruction in the patient population of those

Table 3. Frequencies of Comorbidities Included in the Elixhauser Comorbidity Index within the Study Cohort (n = 173,421) among Those Categorized as HIV Positive (n = 1816) and HIV Negative (n = 171,605)

Elixhauser Comorbidity Index	HIV Negative (n = 171,605), N (%)	HIV Positive (n = 1816), N (%)	P
Congestive heart failure	3833 (2)	93 (5)	<0.001
Cardiac arrhythmias	15,279 (9)	373 (21)	<0.001
Valvular disease	10,529 (6)	259 (14)	<0.001
Hypertension	33,043 (19)	665 (37)	<0.001
Anemia	11,558 (7)	332 (18)	<0.001
Diabetes	11,805 (7)	240 (13)	<0.001
Pulmonary circulatory disorders	2130 (1)	48 (3)	<0.001
Peripheral vascular disorders	5451 (3)	134 (7)	<0.001
Paralysis	569 (0.3)	14 (0.8)	0.001
Other neurological disorders	3930 (2)	96 (5)	<0.001
Chronic pulmonary disease	17,402 (10)	393 (22)	<0.001
Hypothyroidism	19,272 (11)	367 (20)	<0.001
Renal failure	2709 (2)	80 (4)	<0.001
Liver disease	12,373 (7)	310 (17)	<0.001
Peptic ulcer disease (excluding bleeding)	1295 (1)	36 (2)	<0.001
Lymphoma	1172 (1)	23 (1)	0.003
Rheumatoid arthritis/collagen vascular	6698 (4)	138 (8)	<0.001
Coagulopathy	4854 (3)	120 (7)	<0.001
Obesity	22,869 (13)	570 (31)	<0.001
Weight loss	3502 (2)	99 (5)	<0.001
Fluid and electrolyte disorders	13,428 (8)	345 (19)	<0.001
Alcohol use disorder	1854 (1)	61 (3)	<0.001
Drug use disorder	2227 (1)	81 (4)	<0.001
Psychoses	403 (0.2)	13 (1)	<0.001
Depression	27,092 (16)	707 (39)	<0.001

Table 4. Rates of Nonsurgical and Surgical Complications and Revision Procedures in the Study Cohort (n = 173,421) among Those Categorized as HIV Positive (n = 1816) and HIV Negative (n = 171,605)

	HIV Negative (n = 171,605), N (%)	HIV Positive (n = 1816), N (%)	P
Complication			
Hematoma or hemorrhage	4057 (2)	42 (2)	0.886
Seroma	6628 (4)	54 (3)	0.050
DVT or vascular complication	2235 (1)	20 (1)	0.452
Wound dehiscence	10,214 (6)	119 (7)	0.282
Postoperative infection	8141 (5)	68 (4)	0.046
Acquired breast deformity	2239 (1)	21 (1)	0.579
Fat necrosis	6287 (4)	78 (4)	0.155
Tissue necrosis	6182 (4)	59 (3)	0.421
Nonspecified complication of surgical care	23,174 (14)	276 (15)	0.036
Other surgical complication (drainage and/or secondary closure)	2368 (1)	23 (1)	0.680
Revision surgery			
Removal of intact breast implant	6879 (4)	51 (3)	0.009
Removal of ruptured breast implant	1040 (0.6)	N < 11	—
Revision of capsule or breast	4583 (3)	39 (2)	0.169
Peri-implant capsulectomy	5478 (3)	52 (3)	0.428
Revision of reconstructed breast	12,029 (7)	99 (5)	0.010

A total of 51,389 (29.6%) patients experienced at least one complication after the index procedure. A total of 22,992 (13.3%) patients underwent revision surgery after the index procedure. Chi-square tests were used for statistical analysis.

living with HIV has continued to increase in recent years. The safety and efficacy of this aspect of breast cancer surgical management in these patients, however, are understudied. Viral suppression with HAART is a part of surgical optimization for patients living with HIV undergoing elective surgical procedures, and it should be presumed that all patients were utilizing an HAART regimen to suppress

viral load at the time of operation. In the cohort of patients included in this study, there was no significant difference between the overall number of complications experienced by those living with HIV utilizing HAART and their HIV-negative counterparts after breast reconstruction. As the presentation of breast cancer in patients living with HIV utilizing HAART is still a topic under investigation, these

Table 5. Patient Factors Associated with Experiencing One or More Complications after the Index Procedure in the Study Cohort (n = 173,421) in a Multivariable Logistic Regression

Characteristic	Average OR of 1+ Complication (95% CI)	P
Age, y		
18–35	1	—
36–45	1.030 (0.984–1.078)	0.208
46–55	1.116 (1.068–1.166)	<0.001
56+	1.184 (1.132–1.238)	<0.001
Year of reconstruction procedure		
2007–2011	1	—
2012–2016	1.102 (1.075–1.130)	<0.001
2017–2021	1.036 (1.001–1.071)	0.042
HIV positive		
No	1	—
Yes	0.921 (0.830–1.022)	0.120
Reconstruction type		
Implant-based	1	—
Autologous	1.799 (1.757–1.842)	<0.001
Immediate reconstruction		
No	1	—
Yes	1.202 (1.177–1.228)	<0.001
Elixhauser index		
0 or 1	1	—
2	0.926 (0.900–0.963)	<0.001
3	0.943 (0.905–0.983)	0.005
4+	1.139 (1.106–1.173)	<0.001

A total of 51,389 (29.6%) patients experienced at least one complication due to the index procedure. CI, confidence interval. Values in boldface indicate significance of a $P < 0.05$.

findings contribute to a limited existing body of work in this patient population. The results of this study demonstrate that breast reconstruction is safe to perform after surgical breast cancer management in patients living with HIV utilizing HAART.

In this patient cohort, the characteristics of those living with HIV utilizing HAART differed significantly from their non-HIV-infected counterparts. Patients were significantly younger in the population of patients with HIV, had their reconstruction in more recent years, more often underwent immediate reconstruction, and had greater Elixhauser index scores.

Overall complication rates were relatively similar between HIV-positive (29%) and HIV-negative patients (30%; $P = 0.435$), although revision rates were higher in HIV-negative patients (13% versus 11%; $P = 0.009$). Prior evaluations demonstrating heightened odds of complications in HIV-positive individuals, notably wound healing failures and surgical site infections, may not account for disease progression and control. When comparing complication rates in HIV-negative patients and HIV-positive patients with well-controlled disease and modern HAART, postoperative complication rates are broadly found to be comparable, as in our study.^{15–17,26} Interestingly, HIV diagnoses were associated with lower odds of revision. This finding contradicts some prior analyses that demonstrate comparable or elevated revision rates in HIV-positive patients after some nonbreast operations, and warrants further study.²⁷

Table 6. Patient Factors Associated with Undergoing Revision Surgery after the Index Procedure in the Study Cohort (n = 173,421) in a Multivariable Logistic Regression

Characteristic	Average OR of Revision (95% CI)	P
Age, y		
18–35	1	—
36–45	1.082 (1.016–1.151)	0.014
46–55	1.146 (1.080–1.217)	<0.001
56+	1.110 (1.044–1.180)	0.001
Year of reconstruction procedure		
2007–2011	1	—
2012–2016	0.815 (0.788–0.842)	<0.001
2017–2021	0.651 (0.622–0.682)	<0.001
HIV positive		
No	1	—
Yes	0.829 (0.715–0.961)	0.013
Reconstruction type		
Implant-based	1	—
Autologous	1.296 (1.256–1.338)	<0.001
Immediate reconstruction		
No	1	—
Yes	1.637 (1.589–1.686)	<0.001
Elixhauser index		
0 or 1	1	—
2	1.075 (1.018–1.134)	0.009
3	1.080 (1.021–1.142)	0.007
4+	1.319 (1.268–1.371)	<0.001

A total of 22,992 (13.3%) patients underwent revision surgery after the index procedure. CI, confidence interval. Values in boldface indicate significance of a $P < 0.05$.

To properly account for the impact of HIV status and HAART utilization on surgical outcomes after breast reconstruction, a multivariable logistic regression was performed. Similar to data that exist in the current literature on the subject, patients 46 years of age and older, who had reconstruction after 2012, underwent autologous reconstruction, underwent immediate reconstruction, and had an Elixhauser score of 4 or greater all had greater odds of experiencing one or more complications after breast reconstruction.^{28,29} Of note, patients with an Elixhauser score of 2 or 3 had significantly decreased odds of experiencing complications. Developed in 1998, the Elixhauser Comorbidity Index utilizes a set of 38 predetermined comorbidities from which patients are assigned a score based on the total number of comorbidities relevant to the patient based on hospital administrative data. These comorbidities were originally included in this index because they were identified as having impacts on resource allocation and clinical outcomes. This index has previously been used to meaningfully predict in-hospital mortality, length of stay, and other adverse events.³⁰ Our analysis found elevated Elixhauser comorbidity scores in HIV-positive patients, relative to HIV-negative patients, in line with previous studies that posit greater comorbidity burden in individuals, and women in particular, who live with HIV.^{31–33}

In our assessment, Elixhauser comorbidity scores of three or fewer were protective against complications, whereas Elixhauser scores of four or more were associated

with increased odds of complications. Likewise, Elixhauser scores above one were correlated with elevated odds of revision. Typically, patients with increased Elixhauser scores are associated with worse outcomes, but it is possible that this level of score allows patients to be identified by the healthcare team as vulnerable patients at risk for complications. This would allow for closer care management that lowers their risk for complications. Above a certain threshold of Elixhauser score, however, this protective factor likely becomes negligible and increases the patient's risk for complications.

Limitations

The Merative MarketScan Research Databases enable an unprecedented analysis of breast reconstruction outcomes in a considerable sample of HIV-positive and -negative individuals. Nevertheless, the authors note several important limitations. First, the MarketScan Research Databases are not nationally representative and notably exclude many insurance modalities, such as Medicare and Medicaid, entities under which many individuals undergo breast reconstruction in the United States. Second, we utilized ICD and CPT codes to identify HIV diagnoses, breast reconstruction procedures, and other associated characteristics and outcomes. As such, inconsistencies and inaccuracies in coding practices could yield potential misclassification. Third, our cohort only includes patients who underwent surgery, and so those deemed to be at excessive risk for operation were excluded. Therefore, our study's findings may not apply to all individuals with HIV considering breast reconstruction. Fourth, we assumed that all patients with HIV diagnoses undergoing reconstructive breast surgery would be undergoing HAART therapy because surgeons are unlikely to operate on individuals with uncontrolled HIV. However, this assumption is not guaranteed. Fifth, MarketScan Research Databases do not include qualitative data, and thus, we were unable to assess multifactorial patient and provider decision-making that is central to this topic.

CONCLUSIONS

As demonstrated by the results in this study, when other confounding factors are taken into account, HIV status and HAART utilization do not increase the odds of a patient experiencing complications after breast reconstruction. This furthers the notion that breast reconstruction is both a safe and efficacious step in management for patients experiencing breast cancer while living with HIV and utilizing HAART. HIV and non-HIV-related malignancies continue to be a problem in the HIV-infected population utilizing HAART and require further research. By means of reducing HIV viral load, delaying the disease progression to AIDS, and restoring immunity, HAART increases survivability and decreases mortality among HIV-infected individuals.^{34–36} The increased lifespan of those living with HIV on HAART also increases the burden of non-AIDS-defining malignancies in the population, including breast cancer. As breast reconstruction grows to be an increasingly popular component of postmastectomy care, future studies should continue to investigate trends

and outcomes of breast reconstruction in this emerging subpopulation that will seek out plastic surgery as a part of their care.³⁷

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REFERENCES

- Pantanowitz L, Schlecht HP, Dezube BJ. The growing problem of non-AIDS-defining malignancies in HIV. *Curr Opin Oncol*. 2006;18:469–478.
- Murphy EL, Collier AC, Kalish LA, et al. Highly active antiretroviral therapy decreases mortality and morbidity in patients with advanced HIV disease. *Ann Intern Med*. 2001;135:17–26.
- Park LS, Tate JP, Sigel K, et al. Time trends in cancer incidence in persons living with HIV/AIDS in the antiretroviral therapy era: 1997–2012. *AIDS*. 2016;30:1795–1806.
- Shiels MS, Engels EA. Evolving epidemiology of HIV-associated malignancies. *Curr Opin HIV AIDS*. 2017;12:6–11.
- Polesel J, Clifford GM, Rickenbach M, et al. Non-Hodgkin lymphoma incidence in the Swiss HIV cohort study before and after highly active antiretroviral therapy. *AIDS*. 2008;22:301–306.
- Cobucci RNO, Lima PH, de Souza PC, et al. Assessing the impact of HAART on the incidence of defining and non-defining AIDS cancers among patients with HIV/AIDS: a systematic review. *J Infect Public Health*. 2015;8:1–10.
- Shiels MS, Islam JY, Rosenberg PS, et al. Projected cancer incidence rates and burden of incident cancer cases in HIV-infected adults in the United States through 2030. *Ann Intern Med*. 2018;168:866–873.
- Robbins HA, Pfeiffer RM, Shiels MS, et al. Excess cancers among HIV-infected people in the United States. *J Natl Cancer Inst*. 2015;107:dju503.
- Engels EA, Biggar RJ, Hall HI, et al. Cancer risk in people infected with human immunodeficiency virus in the United States. *Int J Cancer*. 2008;123:187–194.
- Dauby N, De Wit S, Delforge M, et al. Characteristics of non-AIDS-defining malignancies in the HAART era: a clinic-epidemiological study. *J Int AIDS Soc*. 2011;14:16.
- Winters S, Martin C, Murphy D, et al. Breast cancer epidemiology, prevention, and screening. *Prog Mol Biol Transl Sci*. 2017;151:1–32.
- Pantanowitz L, Sen S, Crisi GM, et al. Spectrum of breast disease encountered in HIV-positive patients at a community teaching hospital. *Breast*. 2011;20:303–308.
- Zhang L, Liu BC, Zhang XY, et al. Prevention and treatment of surgical site infection in HIV-infected patients. *BMC Infect Dis*. 2012;12:115.
- Sayyed AA, Shin S, Abu El Hawa AA, et al. Postoperative outcomes following a multidisciplinary approach to HIV-positive breast cancer patients. *Plast Reconstr Surg Glob Open*. 2022;10:e4552.

15. King JT, Perkal MF, Rosenthal RA, et al. Thirty-day postoperative mortality among individuals with HIV infection receiving anti-retroviral therapy and procedure-matched, uninfected comparators. *JAMA Surg.* 2015;150:343–351.
16. Kigera JWM, Straetemans M, Vuhaka SK, et al. Is there an increased risk of post-operative surgical site infection after orthopaedic surgery in HIV patients? A systematic review and meta-analysis. *PLoS One.* 2012;7:e42254.
17. Awale MA, Makumbi T, Rukundo G, et al. Postoperative sepsis among HIV-positive patients with acute abdomen at tertiary hospital in sub-saharan Africa: a prospective study. *SN Compr Clin Med.* 2019;1:465–472.
18. Regan JP, Casaubon JT. Breast reconstruction. In: *StatPearls*. Treasure Island, FL: StatPearls Publishing; July 23, 2023. Available at <https://www.ncbi.nlm.nih.gov/books/NBK470317>
19. Chen W, Lv X, Xu X, et al. Meta-analysis for psychological impact of breast reconstruction in patients with breast cancer. *Breast Cancer.* 2018;25:464–469.
20. Cooper DC, Qureshi AA, Sharma K, et al. Impact of breast reconstruction patients on cosmetic practice. *Plast Reconstr Surg Glob Open.* 2021;9:e3614.
21. Shmakova A, Germini D, Vassetzky Y. HIV-1, HAART and cancer: a complex relationship. *Int J Cancer.* 2020;146:2666–2679.
22. Wilson EMP, Sereti I. Immune restoration after antiretroviral therapy: the pitfalls of hasty or incomplete repairs. *Immunol Rev.* 2013;254:343–354.
23. Thapa S, Shrestha U. Immune reconstitution inflammatory syndrome. In: *StatPearls*. Treasure Island, FL: StatPearls Publishing; January 2, 2023. Available at <https://www.ncbi.nlm.nih.gov/books/NBK567803/>
24. Stanford Center for Population Health Sciences. MarketScan databases. Published online February 2023.
25. Elixhauser A, Steiner C, Harris DR, et al. Comorbidity measures for use with administrative data. *Med Care.* 1998;36:8–27.
26. Jacob R, Chandler K, Medawar N, et al. Incidence of complications and revision surgery in HAART compliant HIV patients undergoing primary total hip and knee arthroplasty: an institutional review. *Arch Orthop Trauma Surg.* 2022;143:3803–3809.
27. Ifarraguerra AM, Malyavko A, Stoll WT, et al. Impact of human immunodeficiency virus on 2-year revision rates following lumbar fusion for degenerative spine conditions: a retrospective cohort study. *J Spine Surg.* 2021;7:475–484.
28. Congiusta DV, Amer KM, Otero K, et al. Differences in the predictive value of Elixhauser comorbidity index and the Charlson comorbidity indices in patients with hand infections. *J Clin Orthop Trauma.* 2021;16:27–34.
29. Mrad MA, Al Qurashi AA, Shah Mardan QNM, et al. Predictors of complications after breast reconstruction surgery: a systematic review and meta-analysis. *Plast Reconstr Surg Glob Open.* 2022;10:e4693.
30. Sharma N, Schwendimann R, Endrich O, et al. Comparing Charlson and Elixhauser comorbidity indices with different weightings to predict in-hospital mortality: an analysis of national inpatient data. *BMC Health Serv Res.* 2021;21:13.
31. Collins LF, Palella FJ, Mehta CC, et al. Aging-related comorbidity burden among women and men with or at-risk for HIV in the US, 2008-2019. *JAMA Netw Open.* 2023;6:e2327584.
32. Roomaney RA, van Wyk V, Pillay-van Wyk V. Aging with HIV: increased risk of HIV comorbidities in older adults. *Int J Environ Res Public Health.* 2022;19:2359.
33. Webel A, Schexnayder J, Cioe PA, et al. A review of chronic comorbidities in adults living with HIV: state of the science. *J Assoc Nurses AIDS Care.* 2021;32:322–346.
34. Abaasa AM, Todd J, Ekoru K, et al. Good adherence to HAART and improved survival in a community HIV/AIDS treatment and care programme: the experience of the AIDS Support Organization (TASO), Kampala, Uganda. *BMC Health Serv Res.* 2008;8:241.
35. Panos G, Samonis G, Alexiou VG, et al. Mortality and morbidity of HIV infected patients receiving HAART: a cohort study. *Curr HIV Res.* 2008;6:257–260.
36. Malta M, da Silva CMFP, Magnanini MM, et al. Improvement of HAART in Brazil, 1998-2008: a nationwide assessment of survival times after AIDS diagnosis among men who have sex with men. *BMC Public Health.* 2015;15:226.
37. Qin Q, Tan Q, Lian B, et al. Postoperative outcomes of breast reconstruction after mastectomy: a retrospective study. *Medicine (Baltim).* 2018;97:e9766.