Analysis of Complications in Patients With a History of Cannabis Use and Tobacco Use Undergoing Implant-Based Breast Reconstruction

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Abstract

Background: There is limited information regarding the perioperative effects of marijuana in breast reconstructive surgeries.

Objectives: The objective of this study was to explore the association between a history of cannabis use and postoperative complications in the setting of implant-based breast reconstruction.

Methods: Two databases, TriNetX and PearlDiver, were queried for patients undergoing implant-based breast reconstruction. Patients were divided into 4 groups based on active ICD-10 diagnostic codes: (1) cannabis use only, (2) tobacco use only, (3) cannabis and tobacco use, and (4) neither cannabis nor tobacco use. Associations with postoperative complications were analyzed with a logistic regression test.

Results: TriNetX search revealed that 327 patients had an active diagnosis of cannabis use only and 1118 had an active diagnosis of tobacco use only. Patients in the cannabis only cohort had a significantly increased risk of developing surgical site infection. Patients in the tobacco only cohort had significantly increased risk of developing wound dehiscence, need for debridement, and surgical site infection. The PearlDiver search included 472 patients who had an active diagnosis of both cannabis and tobacco use and 17,361 patients with a diagnosis of tobacco use only. Patients with a diagnosis of cannabis and tobacco use had a significantly increased risk of developing postoperative complications including surgical site infection, wound dehiscence, need for incision and drainage, and debridement.

Conclusions: Patients undergoing implant-based breast reconstruction with an active diagnosis of cannabis with or without tobacco use were at increased risk of developing postoperative complications, and the risk was even higher in patients using both tobacco and cannabis.

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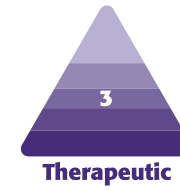

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Cannabis is the most utilized recreational drug in the United States; 48.2 million people, or about 18% of Americans, reported use at least once in 2019. As of 2022, 19 states and the District of Columbia had enacted measures to regulate recreational cannabis use, with an additional 19 states with medical and/or decriminalized use.[1]

With ever-changing legislative developments regarding cannabis use and the ever-growing cannabis-using population, it is pertinent to understand the adverse effects of cannabis use. Although the association between tobacco exposure and postoperative complications is clear, the association between cannabis use and postoperative complications remains unclear.[2,3] The current literature suggests that cannabis use increases the risk of cardiovascular disease, including myocardial infarction and arrhythmias.[4,5] Additionally, cannabis exposure has been shown to induce endothelial dysfunction, atherosclerosis, cardiomyopathy, and metabolic dysfunction in animal models.[6,7] Other authors have identified similar trends related to perioperative complications following inpatient spinal surgeries, with increased perioperative morbidity that included thromboembolism and septicemia.[8]

Each year, nearly 300,000 people are diagnosed with breast cancer, many of whom undergo mastectomies followed by breast reconstruction.[9] With the prevalence of breast cancer and its associated procedures, it is imperative to understand the potential effects of cannabis use in a surgical setting. The purpose of this study was to utilize 2 retrospective healthcare databases, TriNetX (TriNetX, LLC; Cambridge, MA) and PearlDiver (Colorado Springs, CO), to explore the association between a history of cannabis use and postoperative complications in the setting of implant-based breast reconstruction.

METHODS

TriNetX

TriNetX database is a healthcare database representing over 250 million patients across the globe from 2002 to 2023. The database is compliant with the Health Insurance Portability and Accountability Act (HIPAA) and maintains an Information Security Management System (ISMS) to protect and deidentify patients' personal information. In TriNetX, the 2 groups were further stratified based on active ICD-9 and ICD-10 diagnostic codes at the time of surgery: (1) patients with a diagnosis of cannabis use only, and (2) patients with a diagnosis of tobacco use only. Patients with a diagnosis of both cannabis and tobacco use were excluded to characterize the association of cannabis use with postoperative outcomes, and to prevent confounding with tobacco's effects. Propensity score matching of cohorts was performed by sex, age, and race/ethnicity.

PearlDiver

PearlDiver database is a commercially available healthcare database that represents 122 million patients across the United States and all payer types. The database uses unique patient identifier codes allowing for longitudinal tracking from 2010 to 2020, while maintaining HIPAA compliancy. In PearlDiver patients undergoing implant-based breast reconstruction were stratified as (1) patients with a diagnosis of cannabis and tobacco use, and (2) patients with a diagnosis of tobacco use only. Patients with a diagnosis of both cannabis and tobacco use were included. Patients with an active diagnosis of cannabis use only were excluded from this study given the very small sample size, because PearlDiver is unable to provide data in sample sizes of less than 10 patients to comply with HIPAA regulations. Cohorts were matched by age, gender, region, insurance plan, and Elixhauser Comorbidity Index.

Institutional review board approval was not required for this study because both databases are publicly available and completely deidentified. A retrospective analysis was completed with the TriNetX and PearlDiver databases to identify patients undergoing implant-based breast reconstruction (CPT codes 11970, 19340, 19342, and 19357).[10] For both databases, only patients with an active diagnosis of cannabis and/or tobacco use within the 3 months before surgery were included in the study. Patients with a history of cannabis or tobacco use greater than 3 months before surgery were excluded. This helped ensure that only recent use of cannabis or tobacco was taken into account.

A logistic regression analysis was performed to determine the association between the preoperative diagnosis of tobacco and/or cannabis use and postoperative complications. Common postoperative complications reviewed

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Table 1. TriNetX Demographics by Cohort

Cannabis cohort	Characteristics	Patients with Cannabis diagnosis $n = 327$	Control population before propensity score matching $n = 48,963$	Control population after propensity score matching $n = 327$
	Female, *n* (%)	313 (96)	45,736 (95)	313 (96)
	Age (years), mean	51.2	56.7	51.2
	Race/ethnicity, *n* (%)			
	White	241 (74)	36,794 (77)	242 (74)
	Black or African American	53 (16)	4239 (9)	52 (16)
	Hispanic or Latino	22 (7)	4565 (10)	21 (6)
	Unknown/Other	29 (9)	5593 (12)	29 (9)

Tobacco cohort	Characteristics	Patients with tobacco diagnosis $n = 1,118$	Control population before propensity score matching $n = 48,963$	Control population after propensity score matching $n = 1,118$
	Female, *n* (%)	1116 (99)	40,822 (93)	1116 (99)
	Age (years), mean	54.4	56.8	54.4
	Race/ethnicity, *n* (%)			
	White	849 (76)	36,226 (76)	849 (75)
	Black or African American	126 (11)	4226 (9)	126 (11)
	Hispanic or Latino	76 (7)	4512 (10)	75 (7)
	Unknown/Other	125 (11)	5562 (12)	124 (11)

% = frequency.

included surgical site infection, wound dehiscence, need for incision and drainage, and need for debridement. All patient cohorts (ie, Cannabis Only, Tobacco Only, and Cannabis/Tobacco) were compared to patients who had no diagnosis of either cannabis or tobacco use. Statistical significance was defined as a *P* value of less than .05 in all analyses.

RESULTS

TriNetX

A total of 50,416 patients underwent implant-based breast reconstruction. Of those, 327 patients had an active diagnosis of cannabis use only and 1118 had an active diagnosis of tobacco use only. The average ages for the Cannabis Only Cohort and the Tobacco Only Cohort were 51.2 and 54.4, respectively. There were 313 females and 14 males in the Cannabis Only Cohort, whereas the Tobacco Only Cohort had 1116 females and 2 males. The predominant race/ethnicity in both cohorts was White (Table 1). A statistical comparison of the complication rates in each cohort was conducted via logistic regression (Supplemental Table 1, available at www.aestheticsurgeryjournal.com).

Patients in the Cannabis Only Cohort had significantly increased risk of surgical site infection (odds ratio [OR] 2.18, [95% CI 1.01-4.70]). Patients in the Tobacco Only Cohort had significantly increased risk of developing surgical site infection (OR 2.840, [95% CI 1.91-4.23]), wound dehiscence (OR 3.596, [95% CI 2.29-5.66]), and need for debridement (OR 1.611, [95% CI 1.01-2.58]) (Table 2).

PearlDiver

A total of 95,662 patients underwent implant-based breast reconstruction. Of those, 472 patients had an active diagnosis of both cannabis and tobacco use and 17,361 patients had a diagnosis of tobacco use only. The average ages for the Cannabis and Tobacco Cohort and the Tobacco Only Cohort were 46 and 52.8, respectively. There were 472 females and 0 males in the Cannabis and Tobacco Cohort, whereas there were 17,359 females and 2 males in the

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Table 2. Regression Analysis Evaluating Associations Between an Active Diagnosis of Cannabis Use and Tobacco Use Following Implant-based Breast Reconstruction in TriNetX

Complications	Odds ratio	95% CI	*P* value
Surgical site infection			
Cannabis	2.18[a]	(1.01-4.70)	.043
Tobacco	2.84[a]	(1.91-4.23)	<.0001
Wound dehiscence			
Cannabis	1.52	(0.67-3.44)	.308
Tobacco	3.60[a]	(2.29-5.66)	<.0001
Incision and drainage			
Cannabis	1.31	(0.57-3.03)	.524
Tobacco	1.22	(0.66-2.24)	.533
Debridement			
Cannabis	1.63	(0.73-3.65)	.230
Tobacco	1.61[a]	(1.01-2.58)	.046

[a]$P < .05$. CI, confidence interval.

Tobacco Only Cohort. The majority of patients were from the southern region of United States and the predominant health insurance coverage for both cohorts was commercial (Table 3). A statistical comparison of the complication rates in each cohort was conducted via logistic regression (Supplemental Table 2, available at www.aestheticsurgeryjournal.com).

Patients with a diagnosis of cannabis and tobacco use had a significantly increased risk of developing postoperative complications including surgical site infection (OR 1.72, [95% CI 1.08-2.74]), wound dehiscence (OR 5.53, [95% CI 3.27-9.37]), need for incision and drainage (OR 2.39, [95% CI 1.51-3.79]), and need for debridement (OR 2.22, [95% CI 1.41-3.51]) (Table 4). Relative to the control cohort, patients with a diagnosis of cannabis and tobacco use were at higher risk for developing the studied postoperative complications than patients using tobacco alone.

DISCUSSION

This study, to the best of our knowledge, was the first in the literature to utilize 2 different large databases and investigate the associations between a history of cannabis use and postoperative complications in patients undergoing breast reconstruction procedures. The use of 2 databases allowed for the cross-referencing of results and strengthened conclusions. This analysis elucidated the increased risk of postoperative complications associated with cannabis use alone and when employed in combination with tobacco. Most patients with an active diagnosis of cannabis use also presented with a concurrent diagnosis of tobacco use, which is consistent with previous studies showing a positive relationship between cannabis and tobacco use.[11,12] In fact, our findings suggest that cannabis use potentiates the effects of tobacco when both are taken.

Our results showed that patients who underwent implant-based breast reconstruction and used cannabis were 2.18 times more likely to have surgical site infection than patients who did not use cannabis. Patients who used tobacco were at high risk of surgical site infection, wound dehiscence, and need for debridement. There was not a significant increase in the need for incision and drainage in either cohort. Even though cannabis use did not increase the risk of wound dehiscence or the need for incision and drainage or debridement, our study illustrated that cannabis use increases the risk of postoperative infections and procedures related to that or the eventual development of a wound. It is prudent for patients to be aware of these complications because they can have devastating effects on recovery, more so for implant-based reconstruction because the reconstruction might fail, requiring removal of the device.

A similar relationship between cannabis use and postoperative complications has been identified in other surgical specialties, some of which are also reconstructive. For instance, in patients undergoing treatment for ruptured intracranial aneurysms, those who were in the cannabis group were more likely to experience adverse surgical outcomes.[13] In the orthopedic literature, patients who used cannabis and underwent primary total knee arthroplasties were found to have a higher frequency and statistically significant odds ratio of prosthetic joint infection, among other medical complications.[14] Unfortunately, in a review assessing whether cannabis use is contradicted in bariatric surgery, no conclusions could be drawn based upon the available data at the time.[15] In several studies, the effects of cannabis use on cardiovascular function and inflammatory pathways have been investigated, which may provide insight into the increased risk of several postoperative complications.

A number of reports have demonstrated that cannabinoids and their endogenous counterparts can modulate plaque development in experimental models of atherosclerosis.[16] Additionally, studies have described peripheral atherosclerotic disease, known as cannabis arteritis, which is indistinguishable from thromboangiitis obliterans, after cannabis use. Cannabis arteritis presents with claudication, Raynaud's phenomenon, and ischemic ulcers or digital necrosis.[7] The underlying mechanisms of these cannabis-induced cardiovascular effects is still relatively unknown but may be related to the disruption of endothelial function and cannabinoid receptor 1–activated inflammatory cytokines.[6,17] Surprisingly, whereas cannabinoid receptor 1 activation results in increased inflammatory cytokines,

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Table 3. PearlDiver Demographics by Cohort

Cannabis and tobacco cohort	Characteristic	Patients with diagnosis $n = 472$	Control population before matching $n = 77,827$	Control population after matching $n = 472$
	Female, *n* (%)	472 (100)	77,827 (100)	472
	Mean age (years)	46 (10)	50.05	46.06
	Region in US, *n* (%)			
	Midwest	144 (31)	19,167 (25)	144 (31)
	Northeast	98 (21)	13,676 (18)	98 (21)
	Southern	150 (32)	34,148 (44)	150 (32)
	Western	79 (17)	10,832 (14)	79 (17)
	Insurance, *n* (%)			
	Commercial	344 (73)	75,057 (96)	419 (89)
	Medicaid	94 (20)	1760 (2)	25 (5)
	Medicare	24 (5)	863 (1)	17 (4)
	Unknown/Other	10 (2)	147 (0.1)	11 (2)

Tobacco only cohort	Characteristic	Patients with diagnosis $n = 17,361$	Control population before propensity score matching $n = 77,827$	Control population after matching $n = 17,361$
	Female, *n* (%)	17,359 (99)	77,827 (100)	17,359 (99)
	Mean age (years)	52.84	50.05	52.84
	Region in US, *n* (%)			
	Midwest	5146 (30)	19,167 (25)	5146 (30)
	Northeast	3496 (20)	13,676 (18)	3496 (20)
	Southern	6496 (37)	34,148 (44)	6496 (37)
	Western	2166 (12)	10,832 (14)	2166 (12)
	Insurance, *n* (%)			
	Commercial	14,248 (82)	75,057 (96)	15,052 (87)
	Medicaid	1343 (8)	1760 (2)	612 (4)
	Medicare	1383 (8)	863 (1)	1248 (7)
	Unknown/Other	387 (2)	147 (0.1)	404 (2)

% = frequency.

agonism of cannabinoid receptor 2 results in decreased infiltration by neutrophils and macrophages, as well as decreased expression of monocyte chemotactic protein MCP-1, stromal cell-derived factor SDF-1, interleukin IL-6, IL-1β, tumor necrosis factor TNF-α, transforming growth factor TGF-β,1 and vascular endothelial growth factor VEGF-A.[16] Lastly, similar to inhaled tobacco smoke, inhaled cannabis smoke decreases myocardial oxygen delivery and increases myocardial oxygen demand.[5] Based on the above literature, one can postulate that the increased risk of postoperative complications in patients who undergo breast reconstruction and use cannabis may be attributed to cannabis-driven cardiovascular dysfunction and dysregulation of inflammatory pathways.

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Table 4. Regression Analysis Evaluating Associations Between an Active Diagnosis of Cannabis and Tobacco Use and Tobacco Use Only Following Implant-based Breast Reconstruction in PearlDiver

Complications	Odds ratio	95% CI	*P* value
Surgical site infection			
Cannabis & tobacco	1.72[a]	(1.08-2.74)	.028
Tobacco	1.49[a]	(1.34-1.66)	<.0001
Wound dehiscence			
Cannabis & tobacco	5.53[a]	(3.27-9.37)	<.0001
Tobacco	2.02[a]	(1.83-2.23)	<.0001
Incision and drainage			
Cannabis & tobacco	2.39[a]	(1.51-3.79)	.0002
Tobacco	1.54[a]	(1.41-1.67)	<.0001
Debridement			
Cannabis & tobacco	2.22[a]	(1.41-3.51)	.0006
Tobacco	1.72[a]	(1.58-1.87)	<.0001

[a]$P < .05$. CI, confidence interval.

Although less is known about the effects of cannabis on wound healing in postoperative patients, the perioperative and postoperative risks associated with tobacco are well documented. Previous studies in cosmetic surgery population illustrated that smokers had a higher risk of major complications after body procedures and that smoking was found to be an independent predictor of surgical site infections.[18] In a prospective study that followed patients who underwent abdominoplasties, the risk of postoperative infection was 12 times higher for patients who smoked cigarettes.[19] Comparably, in a randomized controlled trial investigating the relationship between tobacco abstinence and incisional wound infections, the tobacco cohort had significantly increased rates of infection.[20] This trend is further supported in other plastic surgery procedures and across surgical specialties.[21]

Molecularly, tobacco affects nearly every aspect of wound healing, from hemostasis, inflammation, wound contraction, proliferation, to remodeling.[2] It has been shown that tobacco decreases tissue oxygenation and aerobic metabolism temporarily.[2] It also affects the inflammatory healing response, which is attenuated by a reduced inflammatory cell chemotactic responsiveness, migratory function, and oxidative bactericidal mechanisms.[2] Additionally, the proliferative response is impaired by a reduced fibroblast migration and proliferation in addition to a downregulated collagen synthesis and deposition.[2] Therefore, the increased risk of all postoperative complications of interest does not come with any surprise, nor does the synergistic effect of cannabis and tobacco use. Our findings are concurrent with the established mechanisms of increased wound-healing complications in patients who use tobacco products. Interestingly, we found that patients who underwent implant-based reconstruction with active diagnoses of cannabis and tobacco use had an increased risk of all outcomes of interest relative to patients who only used tobacco (Table 4). Inquiring about the use of such products in the preoperative period and educating the patients about their implications for postoperative recovery is crucial.

Limitations

This study was not without limitations. Due to the nature of deidentified, aggregate patient data, we were unable to obtain certain longitudinal information, such as the frequency or amount of cannabis use. This study explored only the association of cannabis and/or tobacco use in relation to postoperative complications. Much of the literature examining the effects of cannabis is limited by frequency of use, inconsistent formulation, route, and timing. Further research is needed to investigate the effects of route of administration, dose, duration, and timing of cannabis use among surgical patients. We must also consider that cannabis use is underreported because of its federally illegal status. Diagnoses of cannabis and/or tobacco use rely heavily upon self-reporting, likely in a preoperative setting within this patient population. Self-reporting use of cannabis and/or tobacco increases the likelihood of selection bias within TriNetX and PearlDiver, bringing into question the reliability of some of the information available within these databases.

Additionally, given that the PearlDiver software is based on insurance claim data, the data is only as accurate as is allowed by proper CPT coding for included procedures. Moreover, the large database does not account for surgeon-specific factors such as surgical techniques that could confound the results. Another important limitation is that the database does not differentiate between small complications that can be treated with outpatient management vs clinically significant complications requiring a return to the operating room. Additionally, due to sample sizes, the PearlDiver database was not capable of differentiating the effects of cannabis from those of tobacco. Nevertheless, the authors perceive this data as valuable and potentially more reflective of the patients commonly encountered in clinical settings, because it reveals a positive correlation between the simultaneous use of tobacco and cannabis.[11,12] Furthermore, the analysis completed via the TriNetX database allowed us to differentiate the effects of cannabis through the cannabis only group.

Of note, due to differences in database design, cohorts in TriNetX and PearlDiver could not be matched in the same

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manner (ie, PearlDiver cannot match patients by race/ethnicity, whereas TriNetX can). However, although patients could not be matched by race/ethnicity within PearlDiver, a predominant number of the experimental and control cohorts had commercial insurance. Recently, the US Census Bureau illustrated that the rates of commercial insurance coverage are greatest among Caucasian/White people.[22] Given the distribution of commercial insurance in PearlDiver and coverage rates among the Caucasian/White population in the United States, one could presume the cohort demographics within PearlDiver are comparable to those in TriNetX. Last, experimental and control cohorts were not matched according to common comorbid conditions (hypertension, diabetes, obesity, etc) because this function was not available in PearlDiver. Further investigation is required to determine how the rates of common comorbidities may affect surgical outcomes in patients who have a history of cannabis and/or tobacco use.

CONCLUSIONS

In conclusion, understanding the impact of cannabis and tobacco use in patients undergoing breast reconstruction is imperative for providers to adequately identify associated risk factors, stratify patients, and provide adequate counseling. In their impactful role in patient's lives, surgeons have a duty to look beyond their actions in the operating room and be cognizant of the predisposing factors to postoperative complications. By providing an investigation of the postoperative risks of cannabis use, our results suggest that not only does cannabis increase the risk of surgical site infections and wound healing complications, but it also potentiates the negative effects of tobacco. Surgeons should discuss the implications of use of cannabis and tobacco with this patient population and encourage them to avoid use of such products in the perioperative period to minimize the risk of complications. Further studies are necessary to not only understand the mechanisms related to complications from cannabis use, but also to determine the cessation timing for reducing the potential for postoperative complications.

Supplemental Material

This article contains supplemental material located online at www.aestheticsurgeryjournal.com.

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