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The effect of cannabis use on postoperative complications in patients undergoing spine surgery: A national database study

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ABSTRACT

Background: With the increased use of cannabis in the US, there is a significant need to understand the medical complications associated with its use in relationship to a surgical population. Cannabis has mainly been studied with respect to its qualities of pain treatment, yet few studies have investigated post-surgical complications associated with its use. Therefore, the purpose of this study was to explore the effect of cannabis use on complications in spine surgery, and compare these complications rates to opioid-related complications.

Methods: This was a retrospective study conducted using the PearlDiver Database. Using ICD codes 40,989 patients that underwent lumbar spine fusion between January 2010 and October 2020 were identified and divided into 3 study groups (i.e., control, patients with known opioid use disorder, and patients identified as cannabis users). Differences in the incidence of complications within 30 days of the index procedure and pseudarthrosis rates at 18 months postindex procedure were assessed among study groups using a multivariate logistic regression.

Results: Of 12.4% study population used cannabis and 38.8% had a known opioid use disorder. Results indicated increased odds of experiencing a VTE, hypoxia, myocardial infarction, and arrhythmia for both opioid and cannabis users compared to controls; however, when controlling for tobacco use there were no increased odds of complications within the cannabis group. The pseudarthrosis rate was greater in cannabis users (2.4%) than in controls (1.1%).

Conclusions: The pseudarthrosis rate was significantly greater in patients using cannabis and opioids compared to the control group. However, when controlling for tobacco use, results suggested a possible negative synergistic between cannabis use and concomitant tobacco use that may influence bone fusion.

Background

Postoperative complications in spine surgery can have significant repercussions on a patient's postoperative recovery and can create significant economic burden for both the patient and society [1–3]. Preoperative patient optimization to identify potential modifiable risk factors associated with poor surgical outcomes has become more common in an effort to reduce postoperative complications [4]. In regards to patients undergoing spine fusions, it is not uncommon for patients to be on some type of pain control for lower back pain, and in many cases this pain management is opioid-based. Continued opioid use in this patient population has been shown to increase both postoperative complications and the potential for prolonged opioid use and/or addiction [5–7]. As a

result of the need for improved opioid stewardship many surgeons are seeking alternatives to opioid-based pain management.

Within the United States, the legal landscape concerning the use of cannabis and cannabinoid products, has drastically shifted over the last decade with a significant increase in both legalization and access to these products in both a medical and recreational setting [8]. Recent studies have focused on the potential benefits of cannabis use with studies suggesting a possible positive synergistic effect between cannabis and a reduction in opioid use [9]. However, there is only a small number of studies that have investigated the potential risks associated with preoperative cannabis use [10,11]. Studies have demonstrated an increased risk of medical complications of myocardial infarction, thromboembolism, respiratory complications, and stroke among patients who

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underwent orthopedic and spine-related procedures [12,13]. Suggesting that preoperative cannabis use may be as harmful as it is helpful in this patient population. However, none of these studies have looked into the influence of concomitant tobacco and cannabis use which has been shown to be common [3,10,11,14]. Furthermore, studies have indicated that concomitant opioid and tobacco increases the risk of postoperative complications [15,16], and therefore understanding tobacco’s influence on cannabis related complications is essential to optimizing patients for surgery.

Given that previous studies have suggested that cannabis use may reduce postoperative opioid use; thereby reducing the risk of postoperative opioid addiction [9], studies exploring cannabis’ effect on postsurgical complication are necessary before recommending cannabis use as a potential alternative to opioid based pain control. Therefore, the purpose of this study was to better understand how preoperative cannabis use influenced perioperative and postoperative complications in patients undergoing single level lumbar spine fusion, in comparison to the complication rates associated noted in patients with opioid use disorder. It was hypothesized that the complication rates would be lower in patients using cannabis compared to those with an opioid use disorder. It was also hypothesized that patients using cannabis would have similar complication rates to patients that had no history of cannabis use, opioid use disorders, or drug abuse. A secondary aim of this study was to determine if there was a mediating influence of tobacco use and cannabis use that would further influence postoperative complication rates.

Methods

This study was performed as a database study using the PearlDiver Mariner Patient Claims Database (PearlDiver Technologies, Colorado Springs, CO). PearlDiver is a proprietary web-based research platform that accesses adjudicated medical claims data from a national repository of commercial, Medicare, Medicaid, government, and cash payer types. At the time this study was performed, there were over 151 million HIPAA compliant records available between 2010 and 2020. Patients were identified using both Current Procedural Technology (CPT) and International Classification of Diseases-Ninth and Tenth Revisions codes (ICD-9 and ICD-10). This study was submitted to the Institutional Review Board and was deemed “Not human subject research” and therefore exempt due to the nature of the data used in this investigation.

Patient records that indicated that a patient had underwent either a posterior or anterior, single level lumbar fusion were queried from the orthopedic subgroup of PearlDiver from January 1, 2010 through October 30, 2020 using CPT codes 22,633 (Arthrodesis, combined posterior or posterolateral technique with posterior interbody technique including laminectomy and/or discectomy sufficient to prepare interspace (other than for decompression), single interspace and level; lumbar), 22,612 (Posterior, Posterolateral or Lateral Transverse Process Technique Arthrodesis Procedures on the Spine [Vertebral Column]), 22,630 (Arthrodesis, posterior interbody technique, including laminectomy

and/or discectomy to prepare interspace (other than for decompression), single interspace; lumbar), and 22,558 (Anterior or Anterolateral Approach Technique Arthrodesis Procedures on the Spine [Vertebral Column]).

Patients were excluded if they: were under the age of 18 at the time of surgery, required a fusion due to a pathological fracture or had a history of cancer. Additionally, data were filtered to ensure that none of the patients in this sample had a multilevel fusion. To ensure that none of the patients had a multilevel fusion all patients that had CPT codes for additional segments fused within the same record were excluded. Furthermore, all records were indexed to only include the first record of a spine fusion to address the potential for duplicated patient records. Finally, patients were also excluded if they had an additional fusion within 14 days of their index procedure, to ensure that none of the patients included in the final study cohort had a staged procedure. Demographic data pertaining to the patient’s sex, age, and insurance status were obtained for the final study sample.

Patients that had previously used cannabis products were identified using both ICD-9 and ICD-10 diagnosis codes (ICD9-D-30520, ICD9-D-30430, ICD10-D-F1210, ICD10-F1220, and ICD10-F1290). The codes used were selected as they indicated use, abuse, or dependence without associated complications. Patients that had a previous diagnosed addiction to opioids were also identified using both ICD-9 and ICD-10 codes (ICD9-D-30550, ICD9-D-30400, ICD10-D-F1110, ICD10-D-F1120). Using Boolean language 3 study groups were created based on cannabis use and opioid use. The first group of patients consisted of patients coded as isolated cannabis users (CU) prior to their lumbar fusion. The CU group excluded any patients with a history of opioid addiction, drug abuse, and patients that had used opioid at any time during the 3 months preceding their indexed spine fusion. The second group of patients consisted of patients that had a diagnosis of opioid use disorder (OU), prior to their lumbar fusion. The OU group excluded any patients that also had previous diagnoses for cannabis use, or drug abuse. The final study group, was a representative sample of the remaining lumbar fusion patients that did not have a formal diagnosis of cannabis use, opioid use disorder, drug abuse, or had used any opioid-based medication within the preceding 3 months. Given that this sample was considerably larger than either the CU or OU study groups, PearlDiver was coded to randomly choose 20,000 patients from the remaining patients to construct the control group. Once the 3 study groups were established an additional query was performed to determine the number of patients in each group with concomitant tobacco use.

The primary outcomes of interest for this study were postoperative medical complications that occurred within 30 days following the index procedure and included: acute venous thromboembolism (VTE), bronchospasm, laryngospasm, stroke, anoxic brain injury, myocardial infarction (MI), cardiac arrhythmia, and delirium. All complications were identified using ICD-9 and ICD-10 codes (Table 1). Additionally, early pseudarthrosis occurring 18 months postindex procedure, was also queried using ICD-9 and ICD-10 codes (Table 1).

Table 1
ICD-9 and ICD-10 diagnosis codes used to define complications within this paper.

Complication	Codes
Venousthromboembolism	ICD-9-D-4532,ICD-9-D-4533,ICD-9-D-4534,ICD-9-D-45382,ICD-9-D-45384,ICD-9-D-45385,ICD-9-D-45386,ICD-10-D-126:ICD-10-D-12699,ICD-9-D-4151:ICD-9-D-4159,ICD-10-D-126:ICD-10-D-1269
Hypoxia	ICD-10-D-J9601, ICD-10-D-J9691
Bronchospasm	ICD-9-D-51911, ICD-10-D-J9801
Laryngospasm	ICD-10-D-J385, ICD-9-D-47875
Stroke	ICD-9-D-43491, ICD-10-D-I6781
Anoxic brain injury	ICD-9-D-3481, ICD-10-D-G931
Myocardial infarction	ICD-9-D-41001, ICD-9-D-41011, ICD-9-D-41021, ICD-9-D-41031, ICD-9-D-41041, ICD-9-D-41051, ICD-9-D-41081, ICD-9-D-41091, ICD-10-D-I219, ICD-10-D-I214
Arrhythmia	ICD-9-D-4279, ICD-10-D-I499, ICD-10-D-I498
Delirium	ICD-9-D-2930, ICD-9-D-2931, ICD-9-D-29281, ICD-10-D-F11121, ICD-10-D-F12121, ICD-10-D-F13121, ICD-10-D-F13221
Pseudarthrosis	ICD-10-D-M960

All statistical analyses were performed using the PearlDiver application. PearlDiver's native application used R studio software version 3.6.1. Descriptive statistics were used to describe each study group and univariate analyses were used to determine baseline differences in demographics among groups. To determine if study groups were at a greater risk of developing a complication within 30 days of the index procedure a multivariate logistic regression was used. The outcome variables within the model were the incidence of complications and the dependent variables were the 3 study groups. The control group was chosen as the reference group for which the cannabis users group and opioid use disorder group were compared against. To account for possible confounding factors related to complications due to both age and sex, the logistic regression model was expanded to control for both age and sex differences among the study groups. The logistic regression model provided both a p-value as well as an odds ratio with an associated 95% confidence interval. A p-value of .05 or less was considered to be statistically significant.

A secondary analysis was also performed to better understand the influence of tobacco use on the risk of developing a postoperative complication. In this analysis the logistic regression model previously used was expanded to also account for patients that were tobacco users in each of the 3 study groups, again a p-value of .05 or less was considered statistically significant.

Results

A total of 40,989 patients who underwent elective lumbar fusion were included in this study (Table 2). There were significant differences in age distribution among groups with both the CU and OU groups having a larger proportion of younger patients, patients between the ages of 20 and 50 years old, compared to the control group ($p < .001$). It was noted that only 19.4% of the control group was in this age range compared to 43.6% of the CU group and 30.6% of the OU group. The CU group was also found to have a different sex distribution than both the OU and control groups ($p < .001$). The CU group had significantly more males (53.3%) compared to the 42% noted in both the OU and control groups. It was also noted that the CU group had the largest number of tobacco users (89%) followed by the OU group and then the control group ($p < .001$).

The results concerning postsurgical medical complications occurring within 30 days of the index surgical procedure indicated that both the OU and CU group had a greater incidence of medical complications than the control group (Table 3). Results indicated that patients with an opioid use disorder were 50% more likely to have a VTE, 50% more

likely to develop and arrhythmia, 230% more likely to experience hypoxia, and 250% more likely to have an MI compared to the control group. However, there was no increased odds of experiencing a bronchospasm, laryngospasm, stroke, anoxic brain injury, or postoperative delirium (Table 3). Similarly, patients in the CU group had a 35% increased chance of having a postoperative MI, 50% increased chance of experiencing a VTE, 90% increased chance of hypoxia, and a 240% increased chance of developing a postoperative arrhythmia (Table 3).

When controlling for concomitant tobacco use, the overall incidence rates of complications remained consistent between the control group and opioid use disorder group while the incidence rates decreased in the cannabis use group (Table 4). The results of the logistic regression indicated that patients using cannabis were at no greater odds of developing a postoperative medical complication compared to the control group (Table 4). However, results did indicate that those patients in the OU group still had a 40% increased chance of developing hypoxia, and a 35% increased chance of developing a postoperative acute VTE (Table 4).

The results indicated that the pseudarthrosis rate 18-month postindex procedures was the highest in the OU group, followed closely by the CU group, and both the CU and OU groups had significantly higher rates of pseudarthrosis compared to the control group (Table 5). More specifically, cannabis users were 230% more likely to have a pseudarthrosis and opioid users were 290% more likely compared to the control group. However, when controlling for concomitant tobacco use, the pseudarthrosis rate decreased for all groups, with the largest decrease noted in the CU group (Table 5). The regression analysis indicated that patients in the OU group were still 290% more likely to have a pseudarthrosis compared to the control group while there was no longer a significant odds of pseudarthrosis in the CU group compared to the control.

Discussion

Postoperative complications in spine surgery are a significant burden for patients as well as an economic burden for society; as a result there is constant investigation to not only identify risk factors associated with complication but also to mitigate these risks [16,17]. This study sought to explore how cannabis use in patients undergoing elective lumbar fusion may effect complications rates. Additionally, this study also sought to understand if tobacco use had a mediating effect on medical complications among patients with a diagnosis of opioid use disorder as well as cannabis use. Among the cohort of spine patients in the PearlDiver Medical Claim database it was noted that patients using cannabis had similar

Table 2
Demographic comparison of the study groups.

	Control group	Cannabis use group	Opioid use disorder group	p-value
N	20,000	5,080	15,909	
Age Range				
18–19	41 (0.2%)	23 (0.5%)	7 (0.1%)	<0.001
20–29	284 (1.4%)	290 (5.7%)	317 (2.0%)	
30–39	1,106 (5.5%)	736 (14.5%)	1,516 (9.5%)	
40–49	2,499 (12.5%)	1,189 (23.4%)	3,046 (19.1%)	
50–59	4,541 (22.7%)	1,700 (33.5%)	5,109 (32.2%)	
60–69	5,909 (29.5%)	958 (18.9%)	4,032 (25.3%)	
70–79	5,318 (26.7%)	170 (3.3%)	1,740 (10.9%)	
≥80	302 (1.5%)	14 (0.2%)	142 (0.9%)	
Sex				
Male	8,517 (42.6%)	2,706 (53.3%)	6,760 (42.5%)	<0.001
Female	11,483 (57.4%)	2,374 (46.7%)	9,149 (57.5%)	
Insurance type				
Commercial	13,202 (66.0%)	3,354 (66.0%)	10,754 (67.6%)	<0.001
Medicare	5,422 (27.1%)	725 (14.3%)	3,005 (18.9%)	
Medicaid	754 (3.8%)	844 (16.7%)	1,650 (10.4%)	
Government	417 (2.1%)	63 (1.2%)	259 (1.6%)	
Unknown	191 (1.0%)	86 (1.8%)	224 (1.5%)	
Tobacco Users	8,974 (45%)	4,550 (89%)	11,405 (71%)	<0.001

Table 3
Comparison of 30 day complications following the index procedures.

Outcome	Study group	Incidence	P-value	Odds ratio	95% confidence interval
VTE	Control	153 (0.8%)		Ref.	Ref.
	Cannabis	52 (1.0%)	<0.001	1.5	1.1–2.1
	Opioid	161 (1.0%)	<0.001	1.5	1.1–1.9
Hypoxia	Control	37 (0.2%)		Ref.	Ref.
	Cannabis	63 (1.2%)	<0.001	1.9	1.4–2.4
	Opioid	188 (1.2%)	<0.001	2.3	1.9–2.6
Bronchospasm	Control	<11			
	Cannabis	<11			
	Opioid	<11			
Laryngospasm	Control	0			
	Cannabis	0			
	Opioid	0			
Stroke	Control	15 (0.1%)			
	Cannabis	<11	0.289		
	Opioid	12 (0.1%)	0.056		
Anoxic Brain Injury	Control	<11			
	Cannabis	<11			
	Opioid	<11			
MI	Control	14 (0.1%)		Ref.	Ref.
	Cannabis	14 (0.3%)	<0.001	1.35	1.1–2.3
	Opioid	44 (0.3%)	<0.001	2.5	1.6–4.1
Arrhythmia	Control	49 (0.2%)		Ref.	Ref.
	Cannabis	42 (0.9%)	<0.001	2.4	1.6–3.5
	Opioid	100 (0.6%)	0.004	1.5	1.1–2.0
Delirium	Control	13 (0.1%)			
	Cannabis	<11	0.154		
	Opioid	23 (0.1%)	0.687		

Ref.= Reference group by which the other groups were compared.

PearlDiver does not provide a specific count for groups of less than 11 and this is noted in the table below as <11.

Table 4
Comparison of 30 day complications following the index procedures adjusting for tobacco use.

Outcome	Study group	Incidence	p-value	Odds ratio	95% confidence interval
VTE	Control	90 (0.8%)		Ref.	Ref.
	Cannabis	<11	0.111	–	–
	Opioid	53 (1.0%)	0.016	1.35	1.1–2.1
Hypoxia	Control	30 (0.2%)		Ref.	Ref.
	Cannabis	<11	0.078	–	–
	Opioid	45 (1.0%)	<0.001	1.4	1.1–2.0
Bronchospasm	Control	<11			
	Cannabis	0			
	Opioid	<11			
Laryngospasm	Control	0			
	Cannabis	0			
	Opioid	0			
Stroke	Control	<11			
	Cannabis	<11			
	Opioid	<11			
Anoxic brain injury	Control	<11			
	Cannabis	<11			
	Opioid	<11			
MI	Control	12 (0.1%)			
	Cannabis	<11	0.922	–	–
	Opioid	15 (0.3%)	0.237	–	–
Arrhythmia	Control	27 (0.2%)			
	Cannabis	<11	0.418	–	–
	Opioid	18 (0.4%)	0.341	–	–
Delirium	Control	<11			
	Cannabis	<11			
	Opioid	<11			

Ref.= Reference group by which the other groups were compared.

PearlDiver does not provide a specific count for groups of less than 11 and this is noted in the table below as <11.

medical complication rates as those with an opioid use disorder within 30 days of their index procedure. Results also suggested that cannabis did not influence the incidence of bronchospasm, laryngospasm, anoxic brain injury, or delirium.

Patients using opioids had the highest pseudoarthrosis rate followed closely by cannabis users; both groups had significantly higher rates of pseudoarthrosis compared to the control group. However, the results

demonstrated a potential synergistic affect between cannabis and tobacco. Data indicated that when tobacco use was taken into account, the pseudoarthrosis rate decreased by 1.2%, whereas the control group only decreased by 0.2% and those with an opioid use disorder decreased by 0.3%. Additionally, results of the multivariate regression suggested that cannabis users were 230% (95% CI: 190%–280%) more likely to have a pseudoarthrosis compared to the control group; however, when

Table 5
Comparison of pseudarthrosis rate with and without tobacco use control at 18-month postindex procedure among study groups.

	Study group	Incidence	p-value	Odds ratio	95% confidence interval
Pseudarthrosis	Control	270 (1.4%)		Ref.	Ref.
	Cannabis	163 (3.6%)	<0.001	2.3	1.9–2.8
	Opioid	626 (3.9%)	<0.001	2.9	2.5–3.4
Pseudarthrosis controlling for tobacco use	Control	137 (1.1%)		Ref.	Ref.
	Cannabis	13 (2.4%)	0.224	–	–
	Opioid	164 (3.6%)	<0.001	2.9	2.4–3.8

Ref.= Reference group for comparison against other study groups.

controlling for tobacco use the cannabis use was no longer at a significantly increased risk of pseudarthrosis compared to the control. The regression analysis did indicate that regardless of tobacco use patients with an opioid use disorder were at a 290% (95% CI: 250%–340%) increased risk of pseudarthrosis compared to the control group.

This national database study paints a different picture than data that has been previously presented. With regard to medical complications, there was a significant increased risk of acute VTEs in both cannabis users and those with an opioid use disorder in within 30 days post-op. However, similar to the pseudarthrosis finding, these findings must be tempered against the fact that 89% of the CU group also used tobacco products. When adjusting for tobacco use cannabis users no longer were at a greater risk of an acute VTE event compared to the control group; whereas the opioid use disorder group remained at nearly a 50% greater risk compared to the control group regardless of tobacco use. Therefore, the results suggest that isolated cannabis use does not affect VTE risk in patients undergoing lumbar spine fusion.

The cannabis group was also noted to have a similar distribution of MI and arrhythmias when compared to the opioid use disorder group. Regression results indicated that cannabis users were 35% more likely to experience a postoperative MI compared to the control group while patients in the opioid use disorder group were at a 250% increased risk compared to the control. These findings do support current literature that suggests that opioid consumption increases the risk of heart disease [17,18]. However, current literature indicates that the relationship between cannabis use and cardiac issues is inconclusive [19]. Taken at face value, the data presented in the current study would suggest that cannabis use may have a significant effects on cardiac complications postlumbar spine surgery. However, when controlling for tobacco use cardiac events (i.e., MI, arrhythmia, and stroke) were extremely uncommon, less than 11 patients that were isolated cannabis users experienced MI, arrhythmia, or stroke. Additionally, the regression analysis demonstrated that isolated cannabis users were at no greater risk of cardiac events compared to the control group. Given the significant influence that tobacco has on cardiac events, the results of this study suggest that isolated cannabis use does not influence postoperative cardiac events within 30 days of an elective lumbar spine fusion.

The effect of cannabis products on bone health and healing has been extensively studied [20]. In an animal model for fracture healing, Kogan et al. found that CBD enhanced fracture healing with regards to maximal load and work to failure; whereas other studies have provided contradictory results demonstrating that cannabis products decreased bone health and time to healing [21,22]. The results of this study suggest that cannabis products may have some influence on pseudarthrosis. Despite the prevalence of tobacco use in the cannabis users group, even when controlling for cannabis use the pseudarthrosis incidence was still double that of the control group; however, the results of the regression analysis suggested that isolated cannabis users were not at an increased risk of developing a pseudarthrosis within 18 months of their index spine fusion. Therefore, additional research is necessary to further explore the relationship between pseudarthrosis rates and cannabis to determine if there is a causal relationship, which cannot be fully evaluated using the large database design employed in this study. Additionally, the potential that cannabis use along with concomitant tobacco use may have a

negative synergistic effect on bone healing and fusion rates should also be further explored as this could have significant implications on pre-operative optimization for patients undergoing lumbar spine fusions.

This study is not without limitations, this was a large database study and thus limited by design. The data analyzed in this study was provided in aggregate form and deidentified; limiting the ability to perform patient-level analysis. Additionally, the PearlDiver database is based on billed ICD-9/10 and CPT codes and as a result coding errors could affect data quality. There may also be some selection bias to patients that are included in the 2 study groups (i.e., cannabis and opioid use disorder groups) as those patients have formal billed diagnoses for their conditions; therefore, there is the potential especially in regards to the cannabis use group that some patients in the control group were not coded for cannabis use, or those patients with a cannabis code may represent a group that uses cannabis products to a much greater extent than those that do not have a formal diagnosis. Although both study groups were based on formal diagnoses there was no ability to quantify the amount of frequency of use by these patients which could drastically influence the study results.

It is also important to note that within Pearldiver controlling for additional intervening procedures becomes increasingly difficult the further out from the index procedure; therefore, the definition of pseudarthrosis occurring within 18 months may not be reflective of the true pseudarthrosis rate should this variable have been followed out for 3 or more years postindex procedure. Finally, this study was designed with very stringent definitions for patient inclusion, and as a result while this produces the most accurate results, the conservative approach employed in this study design may limit generalizability to a larger patient population.

A final limitation to consider was that controlling for various known confounders, such as demographic data (e.g., race or socio-economic status) or medical parameters (e.g., amount of cannabis used per day, type of cannabis product used, or amount of tobacco consumed per day) is impossible given that this data is not available in the PearlDiver database. Therefore, future work should be directed toward better understanding how quantities of cannabis product used by patients influences their postsurgical complications.

Conclusions

In summary, patients that only used cannabis products prior to their lumbar spine fusions were at no greater risk of developing medical complications during the immediate postoperative period compared to a control group. However, those patients that used both cannabis and tobacco products had significantly greater complication rates when compared to the control group and were similar to the complication rates of patients with opioid use disorders. Therefore, suggesting that cannabis and tobacco use may have a synergistic affect that could amplify the ill effect of both products, and further research should be directed towards better understanding this relationships.

The pseudoarthrosis rate was significantly greater in cannabis and tobacco users and patient with opioid use disorders compared to a control group. However, patients that were isolated cannabis users also showed a significantly greater pseudarthrosis rate than the control group, but

the rate was lower than that of the cannabis and tobacco users; suggesting the possibility of a negative synergistic effect on bone fusion for concomitant cannabis and tobacco use.

Declaration of Competing Interest

The authors declare no conflicts of interest.

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