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Cannabis Use and Risk of Acute Kidney Injury in Patients with Advanced Chronic Kidney Disease Transitioning to Dialysis

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Abstract

Background: The current social and legal landscape is likely to foster the medicinal and recreational use of cannabis. Synthetic cannabinoid use is associated with acute kidney injury (AKI) in case reports; however, the association between natural cannabis use and AKI risk in patients with advanced chronic kidney disease (CKD) is unknown.

Materials and Methods: From a nationally representative cohort of 102,477 U.S. veterans transitioning to dialysis between 2007 and 2015, we identified 2215 patients with advanced CKD who had undergone urine toxicology (UTOX) tests within a year before dialysis initiation and had inpatient serial serum creatinine levels measured within 7 days after their UTOX test. The exposure of interest was cannabis use compared with no use as ascertained by the UTOX test. We examined the association of this exposure with AKI using logistic regression and inverse probability of treatment weighting with extensive adjustment for potential confounders.

Results: The mean age of the overall cohort was 61 years; 97% were males, 51% were African Americans, 97% had hypertension, 76% had hyperlipidemia, and 75% were diabetic. AKI occurred in 56% of the cohort, and in multivariable-adjusted analysis, cannabis use (when compared with no substance use) was not associated with significantly higher odds of AKI (odds ratio 0.85, 95% confidence interval 0.38–1.87; $p = 0.7$). These results were robust to various sensitivity analyses.

Conclusions: In this observational study examining patients with advanced CKD, cannabis use was not associated with AKI risk. Additional studies are needed to characterize the impact of cannabis use on risk of kidney disease and injury.

Keywords: chronic kidney disease; acute kidney injury; end-stage kidney disease; cannabinoids; urine toxicology; multinomial propensity score weights

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Introduction

Chronic kidney disease (CKD) is a global public health problem.[1–3] Acute kidney injury (AKI) is a risk factor for development of CKD, and experiencing AKI may worsen CKD progression and hasten the development of end-stage kidney disease.[4–7] The rise in cannabis use is also a rapidly evolving public health concern that may impact various health problems, including CKD.[8] The increasing number of people using cannabis over the past two decades is most likely related to a persistent trend toward legalization of cannabis (both medicinal and recreational) in the United States and worldwide.[8,9]

In light of the current legal trends, it is expected that cannabis use will continue to increase in the coming years. This is especially the case in older adults with multiple comorbidities[10,11] given the growing medicinal applications of this substance and its related components. This patient population will include greater numbers of individuals with chronic diseases.[11] In this regard, patients with advanced CKD are often prescribed opioids and non-steroidal anti-inflammatory drugs (NSAIDs) for pain management.[12] However, these medications can induce many adverse effects including opioid dependence which may lead to addiction and potential nephrotoxic properties which limits their safe use in CKD.[13] Given the potentially less severe adverse effect profile associated with cannabis when compared with the traditional pain control medications, patients with advanced CKD may opt for cannabis-based regimens for their symptoms.[8,14] The increased likelihood for exposure of patients with CKD to cannabis highlights the need for a deeper understanding of the real-world effects of cannabis use on kidney outcomes.

The main psychotropic active ingredient in cannabis (tetrahydrocannabinol [THC]) exerts its effects by acting on cannabinoid receptors type 1 (CB_1) and type 2 (CB_2), which are expressed in multiple organs throughout the body, including the kidneys.[11,15–17] These receptors can also be activated by other compounds commonly found in cannabis collectively referred to as cannabinoids (e.g., cannabinol [CBN]),[11,17] and endogenous ligands that are commonly referred to as endocannabinoids (ECs). The cannabinoid receptors together with the endogenous ligands that act on these receptors and the machinery involved in their synthesis and breakdown comprise the EC system.[11,17,18] There is accumulating evidence that the EC system plays a significant role in maintaining normal homeostasis, and alterations of this system can lead to various pathological conditions including CKD and AKI.[11,17,18] Previous research using *in vitro* and *in vivo* preclinical models of kidney disease has found that alterations of CB_1 and CB_2 receptors (e.g., in the localization or expression of CB receptors or downstream signaling subunits of CB receptors) can play a role in the pathogenesis of various renal conditions including AKI. Also, previous preclinical research has shown that inhibition of CB_1 receptor and/or activation of CB_2 receptor have shown to be renoprotective.[11,19–22] Despite the abundance of preclinical data, clinical studies evaluating the impact of cannabis and cannabinoids on kidney disease and injury are limited. More recently, there have been series of case reports linking exposure to synthetic cannabinoids (SCBs) to increased risk of AKI and the need for renal replacement therapy.[11,23–26] These reports have raised concern over the impact of cannabis use on kidney function and on the pathogenesis of kidney disease including AKI, especially in patients with preexisting kidney disease.

There is a paucity of epidemiological studies exploring the association between natural/non-SCBs use and AKI. The aim of this study was to examine the association between cannabis use and the incidence of AKI in a large cohort of patients with advanced CKD. We hypothesized that cannabis use would be associated with higher incidence of AKI.

Materials and Methods

Study population

We examined a nationally representative cohort of U.S. veterans with incident end stage renal disease (ESRD) who transitioned to renal replacement therapy from October 1, 2007, through March 31, 2015 (Transition of Care in Chronic Kidney Disease [TC-CKD]).[27,28] The TC-CKD cohort consisted of 102,477 U.S. veterans identified from the United States Renal Data System (USRDS).[29] Applying various inclusion and exclusion criteria (Supplementary Methods) resulted in a study population of 2251 patients. Figure 1 describes the sample selection criteria.

Exposure

Our primary analysis compared patients with a cannabis-only positive toxicology screen with patients whose toxicology screens were negative for all tested substances. In patients who had undergone a urine toxicology (UTOX) test in the 1-year prelude, cannabis status (positive vs. negative, based on 50 ng/mL cutoff

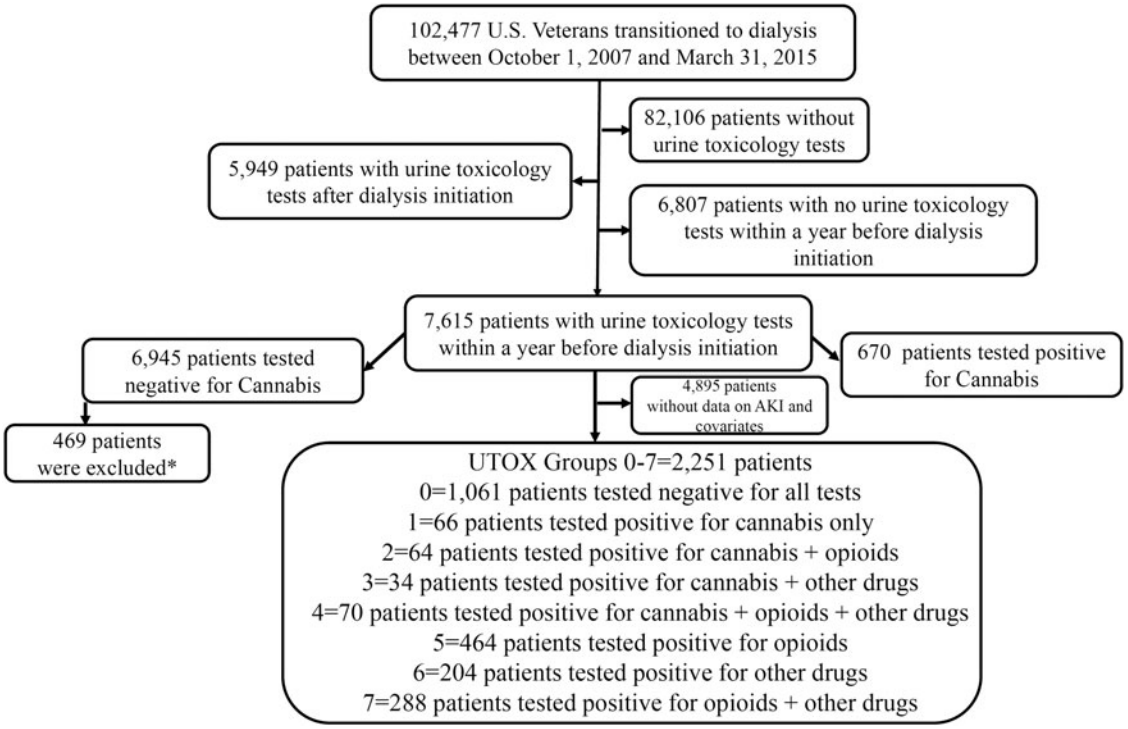

FIG. 1. Study population for AKI outcome. *Four hundred sixty-nine patients tested positive for cannabis any time before 365 days of dialysis initiation or after dialysis initiation. AKI, acute kidney injury.

for cannabinoids, CBN, cannabis, and THC) was ascertained by the validated algorithm by Morasco et al.[30] Of the 2251 patients, 1061 patients had negative test results for all the toxicology tests and 234 patients tested positive for cannabis. Of the 234 cannabis-positive patients, 66 patients tested positive for cannabis use only. Previous research has shown that cannabis users are more prone to polysubstance use.[31] Hence, we further classified the rest of 168 cannabis users as combined users of opioids and/or other drugs. The remaining 956 patients were opioids/other polysubstance users without cannabis exposure and served as positive controls in our analyses (Fig. 2 and Supplementary Methods).

Covariates

Multivariable models were adjusted for *a priori* specified variables including sociodemographics, comorbidities, medications, and vital signs, as listed below.[8,24,32–35] Data from the USRDS Patient and Medical Evidence file were used to determine patients' baseline information on age, sex, and race at a year before dialysis initiation (1-year prelude). Pre-existing comorbidities (Supplementary Methods) were identified from the VA Inpatient and Outpatient Medical SAS Datasets, and the VA/CMS databases, using *International Classification of Disease, Ninth Revision, Clinical Modification* (ICD-9-CM) diagnostic and *Current Procedural Terminology* codes. The Charlson comorbidity index scores were estimated using the Deyo modification for administrative data sets without including kidney disease.[36] Smoking information was extracted from VA health factors data.[37,38] Vascular access data were obtained from the USRDS Patient and Medical Evidence Form 2728.[39] Information about potentially nephrotoxic medication[40,41] use (at least one prescription, Supplementary Methods) during the year before dialysis initiation was collected from both VA pharmacy dispensation records and CMS Medicare Part D files.[40,42–44] The VA Vital Status file was used to obtain data on systolic blood pressure, diastolic blood pressure, body mass index, and pain score. We used the mean value of all measurements performed within a year before dialysis initiation for each of these variables. Estimated glomerular filtration rate (eGFR) was calculated by the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI),

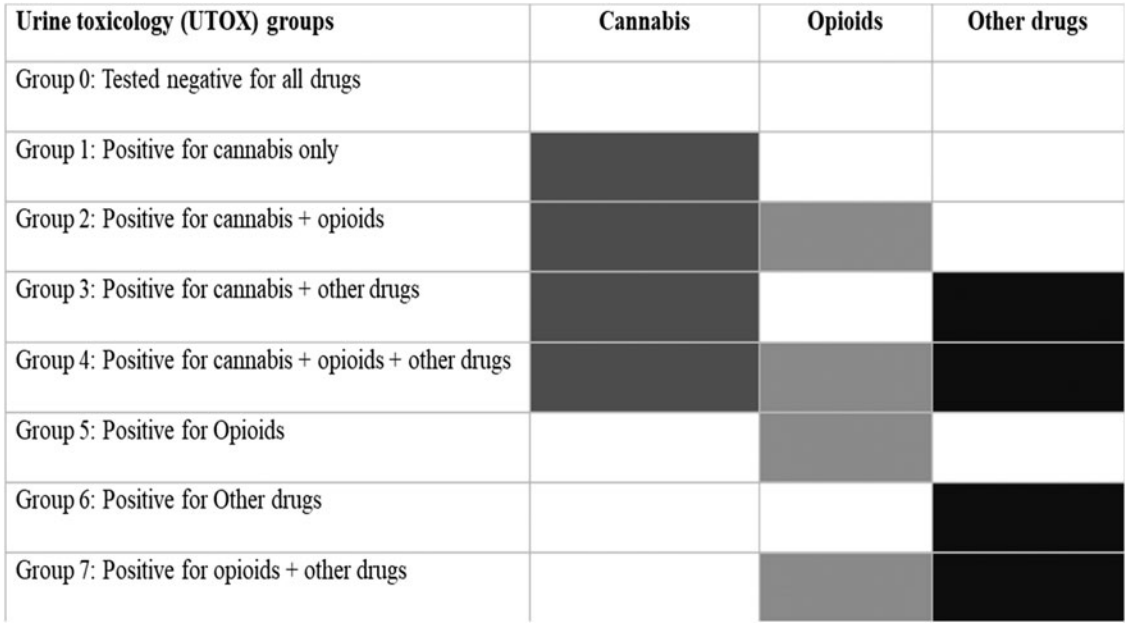

FIG. 2. Color matrix for the UTOX groups. Description of UTOX groups 0–7. UTOX, urine toxicology.

using outpatient serum creatinine values.[45] Baseline eGFR was defined as the intercept estimated from a mixed-effects model of all outpatient eGFR values measured during the last prelude year.

Outcome

The outcome of interest was incidence of AKI within 7 days of the UTOX test. Natural cannabinoids can be detected in the urine as long as 3 days after a single use, 7 days after multiple uses, 14 days in frequent users, and 30 days in heavy daily users.[46,47] A 7-day window was used as the estimated time window in which cannabis could be expected to remain in the body following a positive urine test and hence exert biological effects on kidney function. As a sensitivity analysis, we also repeated analyses using a 3-day window for the detection of AKI. AKI was defined per the Kidney Disease Improving Global Outcomes (KDIGO) guidelines.[4,48] In the current study, due to the low number of patients in various exposure groups, we only used the binary definition (presence or absence) of AKI as an outcome. For descriptive purposes, we also staged AKI events according to the KDIGO guidelines.

Statistical analyses

Baseline data are presented for the entire cohort and by UTOX group as a number (percent) for categorical variables and mean (standard deviation [SD]) or median (Q1–Q3), as appropriate. Inverse probability of treatment weighting (IPTW) was used to adjust for differences between baseline covariates (listed above). We used generalized boosted modeling, a nonparametric method to calculate the weights with more than two treatment groups (using the "twang" package in R), which is referred to as multinomial propensity score weights.[49,50] To correctly interpret IPTW weights as probability weights, we used survey packages/methods.[50] We assessed the odds ratios of AKI associated with UTOX groups using logistic regression models (crude and adjusted). Specifically, we used the survey logistic procedure in the SAS software with UTOX group 0 (negative for all tested substances) as reference. We performed various levels of adjustments categorized as main and sensitivity analyses to examine the association between cannabis use and AKI. The main analysis examined the association of cannabis exposure (alone and in combination with opioids or other illicit substances) versus no exposure to any illicit substances with AKI in unadjusted and IPTW weights-adjusted analyses. Details of the various sensitivity analyses are provided in the Supplementary Methods. p-Values of <0.05 were used as a threshold of statistical significance for most statistical analyses. We also performed additional analyses to control for multiple comparisons

between the eight UTOX groups (described in detail in the Supplementary Methods). All analyses were conducted in SAS Enterprise Guide v7.1 (SAS Institute, Cary, NC, USA), STATA/MP Version 15 (STATA Corporation, College Station, TX, USA), and R-Studio 1.0.153. The study was approved by the institutional review boards of the Memphis and Long Beach VA Medical Centers, with exemption from informed consent.

Results

Baseline characteristics

The mean (SD) age of the overall cohort was 61 years (9); 97% were males, 51% were African Americans, 97% had hypertension, 76% had hyperlipidemia, 75% were diabetic, 54% were current smokers, 92% were analgesics users (68% aspirin users; 46% acetaminophen users; 67% opioid users; no NSAID users), 90% used diuretics, and 56% were prescribed psychiatric medications. Cannabis-only positive patients (UTOX group 1) were more likely to be younger, less likely to be White, and more likely to be smokers (Table 1). The baseline characteristics of the remaining UTOX groups (polysubstance use including/excluding cannabis use) are provided in Supplementary Table S1.

Table 1. Cohort Baseline Characteristics

Characteristic	All ($N=2251$)	Tested negative for all tests (ref) ($N=1061$)	Tested positive for cannabis alone ($N=66$)
Demographics			
Mean age (SD), years	61 (9)	63 (10)	57 (7)
Males, *n* (%)	2184 (97)	1034 (98)	63 (96)
Race, *n* (%)			
Whites	1045 (46)	575 (54)	33 (50)
African Americans	1143 (51)	441 (42)	32 (49)
Other	63 (3)	45 (4)	1 (2)
Comorbidities, *n* (%)			
Chronic pulmonary disease	1206 (54)	540 (51)	25 (38)
Liver disease	634 (28)	219 (21)	24 (36)
Diabetes	1686 (75)	820 (77)	39 (59)
Hyperlipidemia	1700 (76)	850 (80)	39 (59)
Hypertension	2186 (97)	1030 (97)	62 (94)
PTSD	467 (21)	160 (15)	15 (23)
CCI score, median (25th–75th percentile)	5 (3–7)	5 (3–7)	4 (2–5)
Access type, *n* (%)			
AVF	304 (14)	153 (14)	10 (15)
AVG	51 (2)	17 (2)	4 (6)
Catheter	1741 (77)	821 (77)	47 (71)
Other	14 (1)	9 (1)	0 (0)
Missing	141 (6)	61 (6)	5 (8)
Baseline eGFR mL/min/1.73 m^2, mean (SD)	29 (21)	28 (21)	30 (23)
Smoking, *n* (%)			
Never	570 (25)	342 (32)	6 (9)
Current	1212 (54)	432 (41)	50 (76)
Past	462 (21)	282 (27)	9 (14)
Missing	7 (0)	5 (0)	1 (2)
Medication use, *n* (%)			
Analgesics	2079 (92)	958 (90)	57 (86)
Psychiatric medications	1255 (56)	499 (47)	36 (55)
Antimicrobials	885 (39)	407 (38)	18 (27)
Antiretrovirals	5 (0)	1 (0)	1 (2)
Cardiovascular medications	1934 (86)	934 (88)	50 (76)
Chemotherapeutics	16 (1)	6 (1)	1 (2)
Diuretics	2029 (90)	949 (89)	60 (91)
Proton pump inhibitors	1566 (70)	692 (65)	48 (73)
H2 receptor blockers	560 (25)	263 (25)	12 (18)
Warfarin	240 (11)	122 (12)	5 (8)
Anticoagulants	1793 (80)	838 (79)	46 (70)
Antihistamines	543 (24)	222 (21)	15 (23)
Benzodiazepines	580 (26)	236 (22)	15 (23)
Vital signs, mean (SD)			
SBP, mmHg	146 (17)	146 (17)	150 (19)
DBP, mmHg	79 (11)	77 (11)	83 (11)
BMI, kg/m^2	28 (7)	29 (7)	26 (5)
Pain score	2 (2)	1 (1)	2 (2)

AVF, arteriovenous fistula; AVG, arteriovenous graft; BMI, body mass index; CCI, Charlson comorbidity index; DBP, diastolic blood pressure; eGFR, estimated glomerular filtration rate; H2 receptors, histamine 2 receptors; IQR, interquartile range; PTSD, post-traumatic stress disorder; SBP, systolic blood pressure; SD, standard deviation.

Association of cannabis use with AKI

Inpatient AKI (definition: 7-day window) occurred in 56% of the overall cohort ($N=1270$). AKI occurred in 50% of cannabis-alone users ($N=33$) and in 54% of no substance users ($N=569$). When applying a 3-day evaluation window to define AKI, the outcome was detected in 1230 patients (55%) of the overall cohort ($N=33$ [50%] of cannabis-alone users and $N=547$ [52%] of no substance users). Of 56% (overall cohort) who had AKI, 88% ($N=1115$) had stage 1, 8% ($N=107$) had stage 2, and 4% ($N=48$) had stage 3 AKI.

Table 2 shows the association between cannabis use and AKI risk. In the unadjusted model, cannabis-alone use (vs. no substance use) was not associated with higher odds of AKI (odds ratio [OR] 0.87, 95% confidence interval [CI] 0.53–1.42; $p=0.6$). In the IPTW weights-adjusted analysis, a similar statistically nonsignificant association was observed (OR 0.85, 95% CI 0.38–1.87; $p=0.7$). Similar trends of associations were observed in all the sensitivity analyses (incrementally adjusted multivariable analysis, adjusted for winsorized IPTW weights, and doubly robust model).

Cannabis use combined with opioids (Supplementary Table S2) or with other drugs (Supplementary Table S3) or with both opioids and other drugs (Supplementary Table S4) showed no significant association with the odds of AKI in both the main and sensitivity analyses.

Opioid use excluding cannabis use (Supplementary Table S5) showed no significant association with AKI.

Table 2. Association of Cannabis Use with Acute Kidney Injury

Cannabis use versus negative for all substance use	Unadjusted/Model 1, OR (95% CI)	*p*	Adjusted (IPTW weights), OR (95% CI)	*p*
Main analysis	0.87 (0.53–1.42)	0.6	0.85 (0.38–1.87)	0.7
Sensitivity analyses				
Double robust estimation			0.79 (0.34–1.83)	0.6
Adjusted (winsorized IPTW weights)			0.81 (0.46–1.43)	0.5
DRE (winsorized IPTW weights)			0.79 (0.34–1.83)	0.6
Incremental analysis (weights not included)				
Model 2			0.84 (0.51–1.39)	0.5
Model 3			0.91 (0.55–1.51)	0.7
Model 4			0.93 (0.55–1.57)	0.8
Model 5			0.83 (0.48–1.41)	0.5

IPTW weights are calculated from the variables shown in Table 1. Doubly robust estimation: "doubly robust" means the model includes all the variables used to calculate IPTW weights and weights too. Winsorized weights: Weights adjusted at 90 percentiles, respectively, for each group. Model 1: Unadjusted analysis. Models 2–5 presented here are incrementally adjusted, as follows: Model 2: Model 1 + demographics (sex, race, and age). Model 3: Model 2 + comorbidities (chronic pulmonary disease, liver disease, diabetes, hyperlipidemia, hypertension, and post-traumatic stress disorder) + access type + smoking. Model 4: Model 3 + use of medications (analgesics, psychiatric drugs, antimicrobials, antiretrovirals, cardiovascular medications, chemotherapeutic inhibitors, diuretics, proton pump inhibitors, H2 receptor blockers, warfarin, anticoagulants, and benzodiazepines). Model 5: Model 4 + vital signs (mean systolic blood pressure, mean DBP, mean BMI, and mean pain score) + baseline eGFR (eGFR intercept). DRE, doubly robust estimation; IPTW, inverse probability of treatment weighting.

However, polysubstance use excluding cannabis use (Supplementary Tables S6 and S7) was associated with higher odds of AKI. However, none of the associations between AKI and pairwise comparisons of UTOX groups were statistically significant in Tukey's adjustment for pairwise comparisons (Supplementary Fig. S1). Similar trends of association were observed between cannabis/combined cannabis use and AKI when AKI was determined using a 3-day window (Supplementary Tables S8–S14 and Supplementary Fig. S2).

Discussion

In this nationally representative cohort of U.S. veterans with advanced CKD who transitioned to dialysis, we did not observe a statistically significant association between cannabis use and AKI risk, whether modeling cannabis exposure alone or in combination with other drugs. Similar nonsignificant associations were observed for exposure to other types of illicit drugs besides cannabis.

Based on prior studies, the likely targets for the ingredients found in cannabis would be their cognate receptors, CB_1 and CB_2, which are known to be differentially expressed throughout the tubular epithelial cells of the nephron, interstitial cells, and vasculature in the kidney.[11] Similar binding patterns to CB_1 and CB_2 can be observed with the EC system.[11,26] Functionally, increased expression of CB_1 or CB_2 receptors and their associated activity were detected in various forms of kidney disease and injury.[26,51–53] At this time, there is increasing evidence that the activation of CB_1 receptors plays a causal role in both acute[51] kidney disease[54–56] so blockade of the receptor has been shown to ameliorate disease progression. Conversely, CB_2 receptor activation has an opposing function to CB_1 and elicits protective properties in animal models of AKI, including cisplatin-induced nephrotoxicity[57,58] and renal ischemia–reperfusion injury.[59–61]

Based on the findings of these above-mentioned preclinical studies, we postulated that the exposure to cannabis and its active ingredients would be associated with an increased risk of kidney injury and progression of CKD. However, our findings did not support this hypothesis. The reasons for a lack of association with AKI may be attributed to the distribution pattern and complex activation states of both the CB_1 and CB_2 in the kidney, where many of the major chemical constituents of cannabis have the capability to activate either of the receptors to varying degrees. Moreover, the effect of cannabis and its active ingredients may have been complicated by the presence of other drugs and underlying disease pathologies. Therefore, relying on the activity pattern or lack thereof for each receptor to predict the overall renal impact can be misleading,[62] especially since we could not determine the expression profile of these receptors in the patients being studied. With that said, there is a strong possibility that both CB_1 and CB_2 are involved in the pathogenic effects seen with SCBs in several published case reports.[11,23–26] First, SCBs are known to have much higher potency than naturally occurring THC in cannabis and therefore elicit a much more intense CB activity resulting in renal toxicity. Second, binding of SCBs to CB receptors may lead to a differential intracellular signaling event compared with THC and other ingredients that would normally be found in different amounts. Finally, SCBs are unregulated drugs that may contain other chemical diluents and excipients that may mediate the toxic renal effects leading to AKI. These observations highlight the critical need for clinical and translational studies, which can bridge the gap between preclinical results and relevant patient findings.

A novel aspect of our study is the examination of the association between the combined use of cannabis with opioids or with other illicit drugs, which was not previously studied, although a higher risk of AKI associated with both opioid overdose[63] and with exposure to other illicit drugs[64] has been reported. The combined use of cannabis with opioids leads to potential synergistic interactions, and studies have shown that while administering lower doses of THC or morphine alone may not be effective in treating pain,[8] when the same small doses of both THC and morphine were administered together, they produced a significant reduction in pain.[65,66] In our study, we observed a nonsignificant association between the risk of AKI with combined cannabis use and either opioids or other illicit drugs. Possible explanations for the lack of significant associations include differences in the cohorts studied. Also, the combined use of cannabis with opioids/other drugs may result in the consumption of lower doses of each substance compared with individual use of each substance, thus mitigating the adverse effects of opioids and/or other illicit substances.

There are several unique features in the current study that contributed to the strength of this investigation. First, we used UTOX tests to ascertain the use of cannabis, opioids, other/illicit drugs, and the combination of these, using a validated algorithm. Prior literature on the effects of cannabis is primarily based on the self-reported exposure by the participants,[24,32–35] which is known to be an inaccurate method from research using patients with chronic pain.[67] Besides self-reporting, drug use can be ascertained through biological specimens, including urine, blood, breath, oral fluid, nail, and hair, with the most commonly used drug-testing specimen being urine. Advantages of urine specimens include the noninvasive nature of specimen collection, a higher concentration of the parent drug and its metabolites, and longer drug detection times.[46,47] The second strength of our study is the definition of AKI using serial serum creatinine measurements during an inpatient hospitalization following the UTOX screen. To the best of our knowledge, this is the first study to ascertain cannabis/combined cannabis use with opioid/other drugs via UTOX tests and to examine the association between various combinations of exposures and the risk of AKI using IPTW. Furthermore, the current study is also the first study to explore these associations in patients with advanced CKD.

Even with these strengths, we recognize that our study has several limitations. First, even though UTOX tests are more sensitive than self-reported use, there is still a possibility of misclassification due to false positive or negative test results. Second, the low number of AKI events also resulted in limited statistical power, and we were not able to assess the risk of AKI stages. Third, we had no information about frequency of cannabis use, and thus, the degree of exposure to cannabis or dose/level of cannabis cannot be ascertained for the full evaluation period for AKI (7 days). To mitigate this limitation, we repeated analyses after defining AKI using a 3-day post-toxicology test period, which showed similar results. Fourth, as the study cohort was restricted to predominantly male U.S. veterans and all of our patients transitioned to dialysis, our study findings may have limited generalizability. Fifth, as we used observational data for this study, we cannot infer causality. Finally, while we used extensive adjustment for confounders, there remains a possibility of residual confounding by unmeasured covariates.

In summary, this study shows that cannabis use alone or combined with opioids/other drugs was not significantly associated with a risk of AKI. These findings remained robust after extensive adjustment for covariates. Additional clinical studies are needed to better characterize the association of cannabis and cannabinoids with kidney injury and markers of chronic disease in different patient cohorts.

Authors' Contributions

Research idea and study design: P.K.P., C.P.K., H.M., F.P., C.K., and F.T. Data acquisition: P.K.P., E.S., K.K.-Z., and C.P.K. Data analysis/interpretation: P.K.P., C.P.K., H.M., F.P., C.K., F.T., and K.S. Statistical analysis: P.K.P. Supervision or mentorship: K.K.-Z. and C.P.K. Each author contributed important intellectual content during article drafting or revision, accepts personal accountability for the author's own contributions, and agrees to ensure that questions pertaining to the accuracy or integrity of any portion of the work are appropriately investigated and resolved. All authors reviewed and approved the final version of this article.

Disclaimer

The interpretation and reporting of these data are the responsibility of the authors and in no way should be seen as official policy or interpretation of the Department of Veterans Affairs (VA) or the U.S. government. The results of this article have not been published previously in whole or part.

Author Disclosure Statement

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Supplementary Material

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Abbreviations Used

AKI = acute kidney injury
AVF = arteriovenous fistula
BMI = body mass index
CB_1 = cannabinoid receptors type 1
CB_2 = cannabinoid receptors type 2
CBN = cannabinol
CKD = chronic kidney disease
CI = confidence interval
DBP = diastolic blood pressure
EC = endocannabinoid
eGFR = estimated glomerular filtration rate
H2 receptors = histamine 2 receptors
IPTW = inverse probability of treatment weighting
IQR = interquartile range
NSAID = non-steroidal anti-inflammatory drug
OR = odds ratio
SBP = systolic blood pressure
SCB = synthetic cannabinoid
SD = standard deviation
TC-CKD = Transition of Care in Chronic Kidney Disease
THC = tetrahydrocannabinol
USRDS = United States Renal Data System
UTOX = urine toxicology