Clinical Kidney Journal, 2019, vol. 12, no. 3, 437–442

doi: 10.1093/ckj/sfy107
Advance Access Publication Date: 15 November 2018
Original Article

ORIGINAL ARTICLE

Should donors who have used marijuana be considered candidates for living kidney donation?

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ABSTRACT

Background. The use of marijuana in the USA has been steadily increasing over the last 10 years. This study is the first to investigate the effect of marijuana use by live kidney donors upon outcomes in both donors and recipients.

Methods. Living kidney donor transplants performed between January 2000 and May 2016 in a single academic institution were retrospectively reviewed. Donor and recipient groups were each divided into two groups by donor marijuana usage. Outcomes in donor and recipient groups were compared using *t*-test, Chi-square and mixed linear analysis ($P < 0.05$ considered significant).

Results. This was 294 living renal donor medical records were reviewed including 31 marijuana-using donors (MUD) and 263 non-MUDs (NMUD). It was 230 living kidney recipient records were reviewed including 27 marijuana kidney recipients (MKRs) and 203 non-MKRs (NMKR). There was no difference in donor or recipient perioperative characteristics or postoperative outcomes based upon donor marijuana use ($P > 0.05$ for all comparisons). There was no difference in renal function between NMUD and MUD groups and no long-term difference in kidney allograft function between NMKR and MKR groups.

Conclusions. Considering individuals with a history of marijuana use for living kidney donation could increase the donor pool and yield acceptable outcomes.

Keywords: cannabis, living donors, nephrectomy, outcomes, renal transplantation

INTRODUCTION

There is a current shortage of kidneys available for transplantation. End-stage renal disease (ESRD) patients can wait ≥5 years to get a deceased donor kidney. Additionally, the prevalence of ESRD has increased 600% from 1980 to 2009 [1]. Living kidney donation has helped to increase the donor pool; however, there is still a great disparity between supply and demand.

The prevalence of marijuana use has more than doubled between 2001–02 and 2012–13 [2]. In addition, 54.1% of adolescents initiate marijuana use by the age of 21 years, with the mean age of onset being 16.5 years [3]. Based on National Kidney Registry

Received: 25.7.2018; Editorial decision: 17.9.2018

recommendations that exclude substance abusers from donation [4], many transplant institutions refuse live kidney donors who have a history of marijuana use; however, there is no evidence pertaining specifically to the donor or recipient outcomes.

A growing body of evidence demonstrates the harmful effects of donor and recipient tobacco use [5–10]. When donors continue to use tobacco post-donation, they are more likely to develop complications or experience increased mortality rates [5, 6]. For the recipients, donor tobacco use is significantly correlated with delayed graft function, allograft rejection and early mortality [7–9, 11]. Although live kidney donor tobacco use has been linked to worse outcomes for both the donor and the recipient [10], there has not been any investigation into the effect of marijuana use by living kidney donors. Considering the wider general use and increasing legality of marijuana, clarifying the effect of donor marijuana use on the donor and recipient is important.

Marijuana and tobacco are both primarily consumed by inhalation. As such, our hypothesis was that if the donor used marijuana, then they and their recipient would experience different outcomes than their abstaining counterparts. One may assume that tobacco users would smoke more and therefore accumulate more exposure, but that may not always be the case. It has been previously shown that recreational marijuana use in recipients had no effect upon outcomes in the recipients of kidney transplants [12]. However, no prior study has examined the effect of marijuana use by living kidney donors upon the outcomes of kidney donors and their recipients. The purpose of this study is to investigate renal transplant outcomes of donors and recipients, when the donor has a history of marijuana use.

MATERIALS AND METHODS

Following institutional review board approval, a retrospective medical record review was performed on patients who underwent renal transplant and their living donors between January 2000 and May 2016 at a single institution. Donors were divided into two groups, marijuana-using donors (MUD) and non-MUDs (NMUD). A MUD was defined as a patient who self-reported a history of marijuana use beyond sampling the drug or had a positive drug screen for cannabinoids. Recipients were also divided into two groups, those who got a kidney from a marijuana kidney recipient (MKR) and those who got a kidney from a non-MKR (NMKR). Demographic data such as age, body mass index (BMI), ethnicity and gender were collected and included in the analysis for all patients. Intra-operative values such as estimated blood loss, operative time and warm and cold ischemia time were also reviewed. The number and severity of rejections (Banff criteria) were recorded. Donor serum creatinine values were measured at multiple intervals including preoperatively and 1, 6 and 12 months postoperatively. Recipient serum creatinine values were measured at multiple intervals including preoperatively, at discharge, and 1, 6, 12 and ≥60 months postoperatively. Insufficient follow-up was defined as not having one of the aforementioned follow-up intervals for both donors and recipients.

Potential recipients who were active users of tobacco, marijuana or other illicit substances at the time of evaluation for transplant were eliminated from consideration for kidney transplant. Use was determined by both historical questioning and toxicology screening. Prior to donation, each donor underwent a full psychological work-up and evaluation with a social worker to make sure that they were mentally, emotionally and socially fit to undergo kidney donation. If the patients failed any of these evaluations or were found to have addictive personality traits, then they were not allowed to donate. All donor nephrectomies were performed using the hand-assisted laparoscopic approach in the 45° lateral decubitus position. Most recipients received the same tacrolimus-based postoperative immunosuppression regimen. Acute rejection was confirmed by kidney allograft biopsy and classified according to Banff criteria.

Patients were grouped and stratified based on the donor's reported yearly marijuana use. Estimated glomerular filtration rate (eGFR) in mL/min/1.73 m^2 was calculated using the Chronic Kidney Disease Epidemiology Collaboration creatinine equation (2009). Recipients <18 years of age were excluded; however, they were not recipients of MUD kidneys. The primary endpoint evaluated was the change in renal function using absolute change in eGFR. Baseline values for the donor population were their preoperative values, and baseline values for the recipient population were their 1-week postoperative values.

Univariate analysis between the two groups was performed using Student's *t*-test for continuous variables and the Chi-square test for categorical variables. Multivariate analysis was performed using a mixed effects linear regression model. Both univariate and multivariate analysis were done using SPSS software (Version 22, IBM Corporation, Armonk, NY, USA) with $P < 0.05$ considered significant.

RESULTS

The medical records of 658 patients were reviewed. After review, 35 donors and 99 recipients with insufficient follow-up data were excluded from the analysis. After exclusion, there were 294 living donors and 230 of their paired recipients. Among the living donors, there were 31 MUDs and 263 NMUDs. In the recipients, there were 27 MKRs and 203 NMKRs. Ten MUDs were identified over the first 11 years, compared with 21 over the last 5.3 years. All MUDs reported inhalation as their method of consumption. No MUDs were lost to follow-up.

No significant difference was found between the donor groups with respect to age, BMI, gender, baseline eGFR or baseline creatinine (Table 1). Marijuana usage in the MUD cohort ranged from 1 to 400 exposures per year with an average of 92. Recipient groups were similar in all regards except age; the MKR group was significantly older than the NMKR group (49.9 versus 42.9 years old; $P = 0.027$) (Table 1). Ethnicity in both donor and recipient groups was evaluated, the majority of patients being either Hispanic (49 and 51%) or Caucasian (39 and 34%) and the minority being African-American (6 and 8%) or Asian (5 and 6%). The percentage of patients experiencing acute rejection between MKR and NMKR groups was similar (7.4% versus 8.4%; $P = 0.864$) at latest follow-up. Graft and patient survival was 100% at latest follow-up. Mean follow-up times were 2.1 years for donors and 5.2 years for recipients. No recipients in either group had any respiratory complications postoperatively. No recipients in any group had any respiratory complications that were directly related to donor marijuana use.

Univariate analysis showed a trend toward significance between the MUD and NMUD cohorts in serum creatinine change at 1 month (0.38 versus 0.46; $P = 0.051$). However, there was no significant difference at 6 months (0.31 versus 0.38; $P = 0.493$) or 12 months (0.37 versus 0.34; $P = 0.694$), respectively. Between the MUD and NMUD cohorts, there was no significant difference regarding change in eGFR at follow-up times of 1 month (−36.5 versus −41.8 mL/min/1.73 m^2; $P = 0.112$), 6 months (−31.9 versus −36.2 mL/min/1.73 m^2; $P = 0.640$) or 12 months (−36.3 versus −32.4 mL/min/1.73 m^2; $P = 0.559$), respectively (Table 2). Additionally, at 12-month follow-up, no donors had experienced pulmonary,

Table 1. Demographics and preoperative characteristics of 524 patients at a single institution, including 294 kidney donors and 230 of their recipients (after exclusion of recipients < 18 years of age)

Donors	MUD	NMUD	P-value
N	31	263	
Age, mean (years)	35.1	37.4	0.276
BMI, mean (kg/m^2)	25.8	26.6	0.256
Sex (% male)	45	34	0.195
Hypertension (% have)	0	0	NA
Diabetes (% have)	0	0	NA
Baseline eGFR (mL/min/1.73 m^2)	107.4	108.3	0.740
Baseline creatinine (mg/dL)	0.80	0.76	0.192
Recipients	**MKR**	**NMKR**	**P-value**
N	27	203	
Age, mean (years)	49.9	42.9	0.027
BMI, mean (kg/m^2)	27.3	27.4	0.987
Sex (% male)	59	58	0.911
Hypertension (% have)	89	93	0.504
Diabetes (% have)	41	27	0.145
Warm ischemia time (min)	34.9	41.5	0.227
Cold ischemia time (min)	237.0	224.5	0.461
Total ischemia time (min)	271.6	265.5	0.757
Rejections (%)	7.4	8.4	0.864
Baseline eGFR (mL/min/1.73 m^2)	69.1	68.8	0.947
Baseline creatinine (mg/dL)	1.29	1.46	0.452
Percentage on dialysis	100	94	0.369

NA, not applicable.

Table 2. Creatinine and eGFR change between MUD and NMUD at 1, 6 and 12 months

Donors	Time (months)	MUD	NMUD	P-value
Mean creatinine change (mg/dL)	1	0.381	0.456	0.051
	6	0.313	0.378	0.493
	12	0.367	0.339	0.694
Mean eGFR change (mL/min/1.73 m^2)	1	−36.5	−41.8	0.112
	6	−31.9	−36.2	0.640
	12	−36.3	−32.4	0.559

Table 3. Creatinine and eGFR change between MKR and NMKR at 1, 6, 12 and ≥60 months

Recipients	Time (months)	MKR	NMKR	P-value
Mean creatinine change (mg/dL)	1	−0.022	−0.195	0.089
	6	0.084	−0.087	0.284
	12	0.041	−0.105	0.427
	≥60	−0.020	−0.115	0.801
Mean eGFR change (mL/min/1.73 m^2)	1	−4.91	3.43	**0.010**
	6	−8.76	−3.88	0.357
	12	−5.01	−4.12	0.879
	≥60	4.74	−2.92	0.387

Note: Bold values are P-values < 0.05.

infectious or other complications following donation that could be attributed to donor marijuana use.

In univariate analysis, there was a trend toward significance between the MKR and NMKR cohorts regarding the difference in serum creatinine at 1 month (−0.02 versus −0.19 mg/dL; P = 0.089). However, there was no significant difference at follow-up of 6 months (0.08 versus −0.09 mg/dL; P = 0.284), 12 months (0.04 versus −0.11 mg/dL; P = 0.694) or ≥60 months (−0.02 versus −0.12 mg/dL; P = 0.801), respectively (Table 3). Upon multivariate analysis, the near significance was due to variances in BMI and diabetic status of the recipients, whereas donor marijuana status was not a factor (Table 4).

Table 4. A multivariate analysis of MKRs and NMKRs and the effects of age, BMI, hypertension, diabetes, donor smoking status, donor marijuana status and warm ischemia time on creatinine and eGFR showing P-values

Effect	Creatinine	eGFR
Age	0.837	**0.001**
BMI	**0.047**	**0.001**
HTN	0.395	0.887
Diabetes	**0.002**	**0.035**
Donor smoking status	0.280	0.204
Donor marijuana status	0.695	0.245
Warm ischemia	0.054	0.123

Note: Bold values are P-values < 0.05.

Compared with hospital discharge, at 1 month, there was a significant decrease in eGFR for the MKR cohort (−4.9 mL/min/1.73 m^2) compared with an increase in the NMKR cohort (3.4 mL/min/1.73 m^2) (P = 0.010). However, at 6 and 12 months, there was no difference in eGFR change between MKR (−8.7, −5.0 mL/min/1.73 m^2) and NMKR (−3.9, −4.1 mL/min/1.73 m^2) cohorts (P = 0.357, P = 0.879), respectively. At follow-up of ≥60 months, the difference in eGFR between the two groups was not significant (P = 0.387) (Table 3). Upon multivariate analysis, the early difference was due to variances in age, BMI and diabetic status of the recipients, with donor marijuana status not playing a role (Table 4).

DISCUSSION

As of 2018, there are nearly 100 000 patients on the waiting list for deceased donor kidney transplants, with an average wait time of 3–10 years depending on region and blood type [13]. Some patients do not survive long enough on dialysis to receive a transplant [14]. Occasionally, patients are fortunate enough to have a family member or friend who is both a match and willing to donate a kidney. Living donor transplants decrease the time the recipient spends on dialysis and increase the small donor pool. In addition, outcomes of the recipient and their graft are better when receiving a living donor kidney over a deceased donor kidney [15].

As per National Kidney Registry guidelines, donors should not donate a kidney if they have a substance abuse problem [4]. However, because the guidelines and minimum exclusion criteria are not written in specifics, variability in practice has arisen due to the lack of information pertaining to outcomes. Some transplant programs adhere to the mainstream idea that any marijuana use constitutes drug abuse and will refuse live kidney donation by an individual with a history of marijuana use, stating that the decision is in the best interest of the donor and their recipient [16]. In addition, most institutions do not publish specific donor marijuana use criteria, making it difficult to clarify how many programs accept donors who are using marijuana.

Multiple studies have shown that tobacco use causes endothelial injury and can lead to hypertension, tubular damage, atherosclerosis and increase the progression to chronic renal disease [17, 18]. Furthermore, studies comparing marijuana and tobacco exposure have demonstrated that the changes seen to

endothelial cells are similar when exposure time and amount are held constant [19, 20]. However, therein lies one of the major differences between tobacco and marijuana use: consumption patterns.

Although it is somewhat commonplace to smoke a pack or more of cigarettes per day, even an avid user of marijuana will be less likely, or even be able to consume marijuana at these levels. This was recently confirmed in a study that showed chronic, persistent users of marijuana smoked less than one-third as much when compared to their cigarette-consuming counterparts [21]. Given that the exposure time to marijuana is less, there are likely fewer negative vascular consequences from smoking marijuana, due to this factor alone. This idea was shown by the similar clinical outcomes of the MUDs compared with their NMUD counterparts in this study. In addition, the average yearly exposure of MUDs to marijuana amounted to once every 4 days, which is significantly less exposure than a patient with a history of even one cigarette per day. Furthermore, on multivariate analysis, donor marijuana smoking did not demonstrate any deleterious effects on donor or recipient outcomes. Multiple studies have illustrated the differences in consumability by demonstrating that smoking tobacco significantly decreases renal function [22–24], but smoking marijuana does not significantly decrease eGFR even in the most avid users [25].

There is no denying the increasing prevalence of marijuana use and acceptance among the US population. Our numbers support this idea of increasing prevalence, with two-thirds of our MUD cohort coming from the last 5 years of the 15-year study. People in the USA spent an estimated 40.6 billion dollars on black-market marijuana in 2010 alone [26]. Business analysts project that legal recreational and medicinal marijuana will be a 44 billion dollar business in the USA by 2020 [27]. The greatest increase in use has been seen in those aged 18–29 years, with a use rate of 21.2% in 2013 [2]. According to a representative survey done on more than 2000 randomly selected adults in 2014, more than half believed that marijuana should be legalized for recreational use [28]. Almost 60% of the 50 states have already made medical marijuana legal [29, 30]. Additionally, 8 states have also made recreational use legal, with 11 more believed to be following suit in the near future [31]. Furthermore, 17 more states have provisions in place which allow medical use of strains that are low in tetrahydrocannabinol and high in cannabidiol, thus bringing the total states that allow marijuana in some form to 46 [29]. In 2016, the state of California passed a bill that prohibited exclusion of recipients from transplant lists due to use of medical marijuana [32]. With the changing views on the drug, it is essential for medical professionals to be aware of the consequences of marijuana use and be able to treat the growing population of users. Our study has the most relevance in the realm of living kidney donors and the criteria for accepting or rejecting them.

The average age of living kidney donors in the USA is currently in the early to mid-30s [33, 34]. Keeping this in mind, within the next 10 years, the current population of 18- to 29-year-olds will be the largest group of living kidney donors. This is the same group of people that are currently using marijuana at a prevalence of >21%, before allowing for further projected increases in use. In addition, a survey showed that only 22% of the general American population would refuse a cannabis user's kidney, whereas 44% would refuse a cocaine user's kidney [35].

The marijuana dilemma is not limited to kidney transplantation alone. A prior study on heart transplantation showed no difference in survival rates between recipients who received a MUD or NMUD heart [36]. Furthermore, a similar study demonstrated similar findings for MUD versus NMUD lungs [37]. Currently, eight states have passed laws that prohibit denial of medical marijuana users from being put on any organ transplant list [38]. However, nearly one-third of heart transplant surgeons believe this should not be the case [39].

Despite the many controversies surrounding the interplay between marijuana use and organ donation, it is hoped that the results of this study may encourage open dialog, and ultimately increase the kidney donor pool. Including these patients as potential, living kidney donors could help alleviate the strain on the current deceased donor waiting list and also increase the scarce pool of living donors. This study was the first to address the effect donor marijuana use has on recipient or donor renal function postoperatively; consequently, it will open the door for future prospective multicenter studies.

The results of this study should not be extrapolated to promote or support marijuana use. The purpose of this study was to determine the consequences of using living kidney donors with a history of marijuana use, and if doing so would compromise either donor or recipient outcomes. Marijuana remains a mind-altering substance that can lead to psychosis, neurodegeneration, poor cognitive development and long-term cognitive deterioration even after a long period of abstinence [40–43]. The cognitive impairment is great enough that driving under the influence of marijuana has been associated with increased traffic accidents and fatalities [42]. In addition, smoking marijuana leads to an increased risk of lung cancer, emphysema and chronic obstructive pulmonary disease [44]. Marijuana has been shown to cause vascular changes that increase the risk of myocardial infarction, stroke and transient ischemic attack [45]. Use during pregnancy causes delayed mental development in the fetus and is associated with problem behavior in toddlers [46–48]. Legal ramifications from possessing and using the drug still exist despite the increasing legality at a statewide level; marijuana is a Drug Enforcement Agency schedule 1 controlled substance and remains illegal under federal law [49].

Although kidney donation is a lifesaving treatment for the recipient, donation does not come free of risk. Donors are vetted appropriately to make sure that they are ready for the ordeal of kidney transplantation. In preparation, each donor meets with a financial analyst, a dietician, a social worker, a nephrologist, their surgeon as well as an independent living donor advocate. This team identifies and eliminates from consideration donors who demonstrate addictive behaviors, recent loss of employment, degeneration of relationships, financial problems stemming from substance use or accidents related to substance use. Having a multifaceted team perform evaluations prior to donation minimizes donor regret and ensures that the donor will have adequate physical, financial, emotional and spiritual support following donation. While one could potentially draw the conclusion that marijuana could be a risk factor for poor follow-up, none of the donors who were lost to follow-up was from the MUD cohort.

This study has potential limitations. First, the study was a retrospective medical record review and therefore brings some unavoidable bias due to design. In addition, all transplants and donor nephrectomies were performed at a single institution with an experienced transplant team. Outcomes in larger, prospective randomized trials will be required to confirm these results. In addition, once kidney donation has taken place, the donors could start smoking marijuana again, posing a theoretical risk to themselves. In addition, the cumulative effects of marijuana use over many years could not be evaluated as the average donor follow-up was 24 months (consistent with Organ Procurement and Transplantation Network guidelines). Also,

there was no way to assess the amount of marijuana smoke consumed per use. Another limitation of this study is that it was performed specifically on inhalational marijuana use and not synthetic cannabinoids, which have been reported to cause acute renal failure. Synthetic cannabinoids would need to be further evaluated to determine their effects upon kidney donors and recipients [50]. One final caveat to the data was that the MKR group was significantly older (7 years older) than the NMKR group; however, this may make an even stronger case for allowing users who have used marijuana to donate. This is because age is the key factor affecting long- and short-term allograft function, with younger patients having much greater function posttransplant [51].

CONCLUSION

There is no difference in renal function between MUD and NMUD groups following kidney donation. In addition, there is no difference between MKR and NMKR groups following transplant. If current trends persist into the future, then there will be a further increase in both recreational and medicinal marijuana use. For this reason, the growing population of marijuana users will become an even more significant segment of the potential living kidney donor pool. Subsequently, consideration of marijuana using kidney donors could increase the donor pool.

ACKNOWLEDGEMENTS

The authors would like to thank Ji Liang for his assistance and expertise with the statistical analysis.

FUNDING

This study was funded in part through a grant from the Walter McPherson Society at Loma Linda University Health.

CONFLICT OF INTEREST STATEMENT

The authors have no conflicts of interest to disclose. Funding was departmental. This research and these results have not been published previously in whole or part, except in abstract format.

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