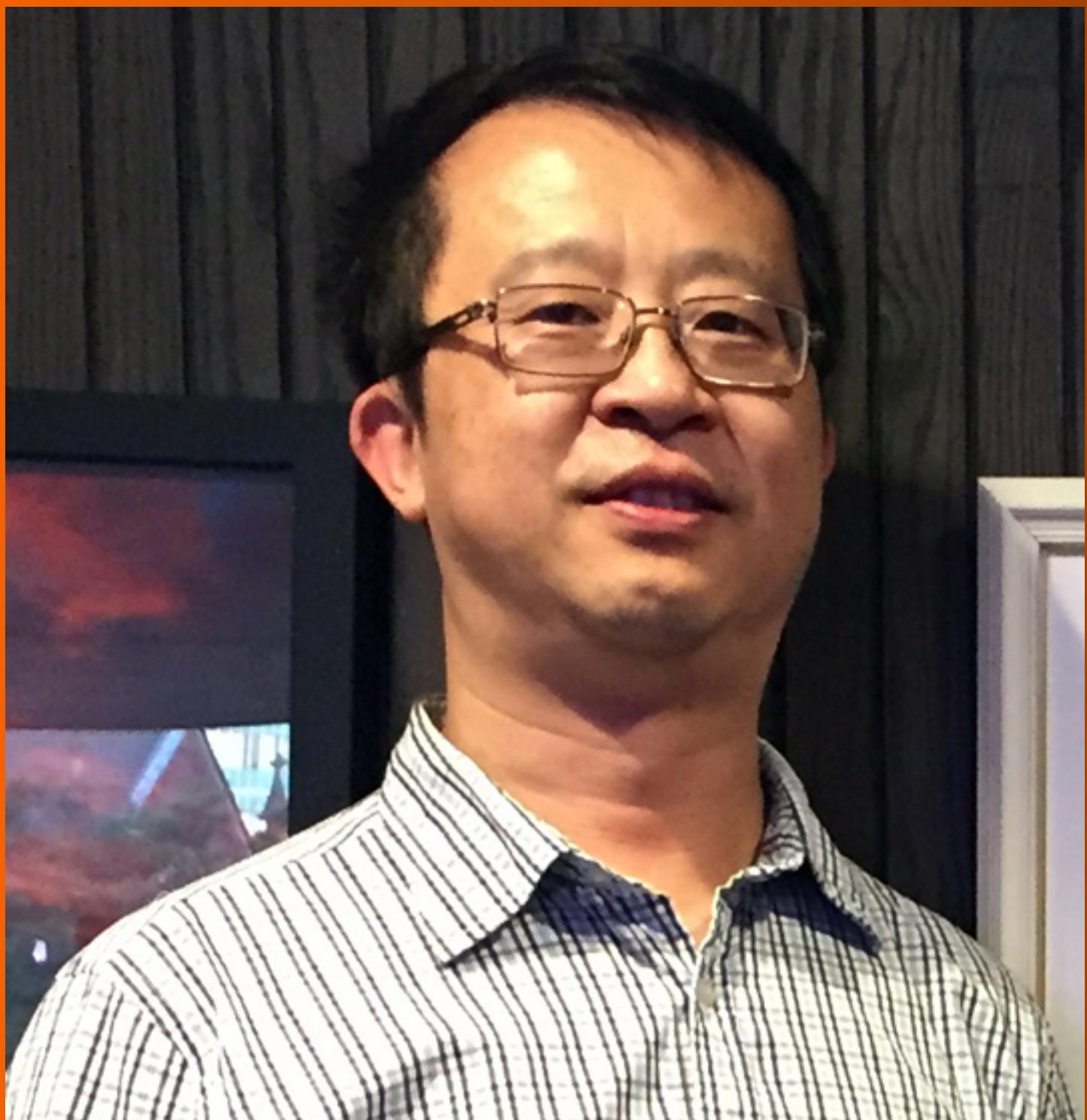


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EDITORIAL

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ORIGINAL ARTICLE

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Retrospective Study

Impact of Medicaid expansion on kidney transplantation in the State Oklahoma

Hyoshin Kwon, Zoya Sandhu, Zonna Sarwar, Oya M Andacoglu

Specialty type: Transplantation**Provenance and peer review:**

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Abstract

BACKGROUND

There is no data evaluating the impact of Medicaid expansion on kidney transplants (KT) in Oklahoma.

AIM

To investigate the impact of Medicaid expansion on KT patients in Oklahoma.

METHODS

The UNOS database was utilized to evaluate data pertaining to adult KT recipients in Oklahoma in the pre-and post-Medicaid eras. Bivariate analysis, Kaplan Meier analysis was used to estimate, and cox proportional models were utilized.

RESULTS

There were 2758 pre- and 141 recipients in the post-Medicaid expansion era. Post-expansion patients were more often non-United States citizens (2.3% vs 5.7%), American Indian, Alaskan, or Pacific Islander (7.8% vs 9.2%), Hispanic (7.4% vs 12.8%), or Asian (2.5% vs 8.5%) ($P < 0.0001$). Waitlist time was shorter in the post-expansion era (410 vs 253 d) ($P = 0.0011$). Living donor rates, pre-emptive transplants, re-do transplants, delayed graft function rates, kidney donor profile

index values, panel reactive antibodies levels, and insurance types were similar. Patients with public insurance were more frail. Despite increased early (< 6 months) rejection rates, 1-year patient and graft survival were similar. In Cox proportional hazards model, male sex, American Indian, Alaskan or Pacific Islander race, public insurance, and frailty category were independent risk factors for death at 1 year. Medicaid expansion was not associated with graft failure or patient survival (adjusted hazard ratio: 1.07; 95%CI: 0.26-4.41).

CONCLUSION

Medicaid expansion in Oklahoma is associated with increased KT access for non-White/non-Black and non-United States citizen patients with shorter wait times. 1-year graft and patient survival rates were similar before and after expansion. Medicaid expansion itself was not independently associated with graft or patient survival outcomes. Ongoing research is necessary to determine the long-term effects of Medicaid expansion.

Key Words: Medicaid expansion; Oklahoma; Kidney transplant

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Core Tip: The Medicaid Expansion had a significant impact on several kidney transplant (KT) recipients in Oklahoma. There was greater access to KTs for non-white population (Hispanics, Asians, American Indian, Alaskan, or Pacific Islanders), and Non-United States citizens. Male sex, race, frailty category and insurance type were associated with increased mortality at 1 year after transplant. Medicaid expansion was not associated with 1 year outcomes, however, further research is needed to investigate the long-term impact of Medicaid expansion on Oklahoma.

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INTRODUCTION

Health insurance in the United States is a competitive market that includes private and public insurance options. In 2010, the affordable care act (ACA) was introduced by the United States government to achieve the goal of providing more coverage to its citizens, especially those in a lower income bracket. Medicaid is a government program (albeit often administered by private insurance companies that offer Medicaid managed care services). One of the goals of ACA was to expand Medicaid, however expansion of Medicaid has been highly variable among the states. The expansion of Medicaid provided more eligibility to various health care specialties for more individuals and the impact of this expansion has been studied widely[1-5]. The ACA expanded eligibility to include individuals with an income up to 138% of the federal poverty level[1,4]. Based on reported data, the percentage of uninsured adults aged 18-64 decreased from 20.4% to 12.1% from 2013 to 2017[1]. The overall decrease in uninsured adults occurred among all races. Hispanics had the most significant percentage drop of 40.6% to 24.1%, followed by non-Hispanic black and non-Hispanic Asians. Furthermore, there was an increase in Medicaid enrollment among end-stage renal disease (ESRD) patients with Medicare in the first year after the 21st Century Cures Act, which particularly showed increased enrollment in black, Hispanic, and dual-eligible individuals[3]. In states with Medicaid expansion, there was a significantly higher portion of patients listed with Medicaid than private insurance in transplant surgery[6,7]. This phenomenon is explained as more patients who are previously uninsured and needed transplant surgery became eligible for Medicaid under ACA expansion[8]. Earlier reports suggested an increased number of patients covered by Medicaid with low socioeconomic status may be associated with lower survival rates after solid-organ transplants[9]. Furthermore, there is evolving evidence about the impact of Medicaid expansion on transplant outcomes and increased interest in social-economic determinants that influence not just post-transplant outcomes but also transplant referrals[8,9]. According to studies, similar relationships between patient demographics, such as race/ethnicity, socioeconomic status, functionality, kidney function or ESRD, and the health outcome of the KT are shown[9-11]. With more eligibility for Medicaid after the expansion, changing in patient demographic is suspected, which results in a different outcome for Medicaid patients for KT. Furthermore, studies suggest Medicaid expansion affects non-patient changes, such as preemptive waiting list, waitlist time, and others which eventually impact the health outcome of KTs in Medicaid patients[11,12].

Oklahoma only recently passed a Medicaid expansion bill as of 2020[4]. More than 300000 individuals became eligible to enroll for Medicaid beginning on July 1st of 2021 according to Oklahoma Healthcare Agency[4]. There is no published data on the impact of Medicaid expansion in KTs in Oklahoma.

Our aim was to investigate the impact of Medicaid expansion on KT patients in Oklahoma. We specifically investigated: (1) Transplant patients' demographics before and after expansion; (2) 1-year graft and patient survival rates before and after Medicaid expansion; and (3) investigate the association of Medicaid expansion and other variables with 1-year graft and patient survival.

MATERIALS AND METHODS

The Scientific Registry of Transplant Recipients (SRTR) and United Network of Organ Sharing (UNOS) data were used. We compared the recipients with KT before and after the Medicaid expansion in Oklahoma. We included adults only (> 18 years old), kidney only transplant recipients. We excluded pediatric recipients (< 18 years old), simultaneous transplants with other organs. The evaluated data includes patient demographics, information specific to diseases, graft and patient survival in 1 year follow-up. We included the following variables into our analysis: Citizenship at transplant, recipient age, recipient body mass index (BMI), race, recipient primary payment source at transplant, ESRD diagnosis, history of previous KT (re-do transplant), distance donor hospital to transplant center, deceased donor kidney biopsy, donor kidney glomerulosclerosis %, human leukocyte antigens mismatch level, recipient creatinine at discharge, most recent calculated panel reactive antibodies (PRA), delayed graft function determined by dialysis in first week after transplant, pre-emptive transplant, kidney donor profile index, work for income, calculated estimated post-transplant survival (EPTS), functional status of recipients at registration at transplant, and at follow up, insurance types, organ share types, cold ischemic time (in hours), and waitlist times, rejection within 6 months post-transplant, donor type [live donor, deceased donor, donation after cardiac death (DCD)]. Functional status and frailty were grouped into 3 categories using the Karnofsky performance scale. Group 1 included recipients who could carry on normal activity and work with no special care needed. Group 2 included recipients who were unable to work but able to live at home and care for most personal needs with varying amounts of assistance needed. Group 3 included recipients who were unable to care for themselves and required the equivalent of institutional, or hospital care with rapidly progressing diseases. Insurance was categorized as: Public (Department of Veterans Affairs and Medicaid), Private and Other (self, donation, Freecare and pending). All data were compared between pre-expansion (before July 2021) and post-expansion (after July 2021) eras. The supplemental data were obtained from the Center for Disease Control and Prevention to further compare demographics. University of Oklahoma Health Sciences Center Research Institutional review board was obtained (No. 15049).

RESULTS

There were 2758 pre- and 141 post-Medicaid expansion adult KT recipients. Compared to pre-expansion patients, there were more non-United States citizen patients (2.3% vs 5.7%, $P = 0.0188$) with a significant increase in Hispanic (7.4% vs 12.8%), Asian (2.5% vs 8.5%) and American Indian, Alaskan, or Pacific Islanders population (7.8% vs 9.2%, $P < 0.0001$). There were no significant differences in median age, gender distribution, or median BMI between pre- and post-Medicaid expansion recipients (Table 1). There were more patients with EPTS $> 20\%$ in the post-expansion era (24.4% vs 56.7%, $P < 0.0001$). Functional status at transplant and at the most recent follow-up was similar between pre-and post-expansion recipients. More regional (3.7% vs 17.0%) and national (8% vs 34.8%) organ sharing was observed with resultant longer cold ischemic time (12 vs 16 h) (all $P < 0.0001$). Wait time was shorter in the post-expansion era (410 vs 253 d, $P = 0.0011$). Living donor rates, DCD grafts, history of previous KTs, pre-emptive transplant, delayed graft function rates, kidney donor profile index values, and PRA levels were all similar between the pre- and post-expansion era (Table 1). Although there was less public insurance in the post-expansion era, (69.7% vs 66.7%) this was statistically not significant ($P > 0.05$) (Table 1). Despite increased early (< 6 months) rejection rates, 1-year graft (94.6% vs 97.2%) and patient survival rates (95% vs 98.6%) were similar before and after Medicaid expansion, respectively (Figures 1 and 2).

We also evaluated frailty, and insurance among race groups. Non-white groups had public insurance more commonly ($P = 0.0003$). Although frailty scores were similar among racial categories, patients with public insurance had significantly worse frailty scores ($P = 0.0003$) (Tables 2-4). Cox proportional hazards model was performed and after controlling for other variables male sex [adjusted hazard ratio (aHR): 1.186, 95%CI: 1.01-1.40], American Indian/Alaska Native/Pacific Islanders race (aHR: 1.521, 95%CI: 1.18-1.97), public insurance (aHR: 1.536, 95%CI: 1.25-1.88), and frailty category (aHR: 2.134, 95%CI: 1.09-4.20) were independent risk factors for mortality at 1 year after transplant. Medicaid expansion itself was not associated with higher risk of graft failure or patient survival (aHR: 1.07; 95%CI: 0.26-4.41) (Table 5).

DISCUSSION

This is the first report analyzing the impact of the Medicaid expansion on KT in Oklahoma after it was implemented in 2021. This is also the first report analyzing the impact of Medicaid expansion on the American Indian population after KT. We report several important findings: We report that an increased number of patients from underrepresented minorities received KTs after the Medicaid expansion. Non-United States citizens, American Indian, Alaskan and Pacific Islander, Hispanic, and Asian recipients received more KTs in the post-expansion era. Similar findings are reported in other studies. Harhay *et al*[12] reported that more low-income United States patients with chronic kidney disease received KT before requiring dialysis after Medicaid expansion. Harhay *et al*[12] also reported that pre-emptive KT recipients from expansion states were more likely to be from minority groups. The OPTN/SRTR 2021 Annual report found that the proportion of Asian and Hispanic candidates on the kidney waiting list has gradually increased, accompanied by a decline in the proportion of White candidates[13].

We also report that waitlist times decreased after Medicaid expansion in Oklahoma. Several other studies also reported similar results. OPTN/SRTR 2020 Annual Kidney Report shows that patients waiting less than 1 year comprise most of the waitlist KT candidates. On the other hand, 10% of the patients have been waiting for more than 5 years[14]. The 2021

Table 1 Statistical analysis of pre-and post-Medicaid expansion in adult kidney transplant recipients for the state of Oklahoma

Variables	Before medicaid expansion (n = 2758)	After medicaid expansion (n = 141)	P value
Recipient age, median (IQR)	53.0 (21.0)	51.0 (22.0)	0.3999 ^c
Gender			
Female	1089 (39.5)	56 (39.7)	0.9563
Male	1669 (60.5)	85 (60.3)	
Recipient BMI, Median (IQR)	27.8 (7.6)	28.4 (8.0)	0.1549 ^c
Race			
White	1708 (61.9)	75 (53.2)	< 0.0001
Black	531 (19.3)	22 (15.6)	
Amer Ind/ Alaska Native/Pacific Islander	215 (7.8)	13 (9.2)	
Hispanic	204 (7.4)	18 (12.8)	
Asian	68 (2.5)	12 (8.5)	
Multiracial	32 (1.2)	1 (0.7)	
Citizenship at transplant			
United States citizen	2696 (97.8)	133 (94.3)	0.0188 ^a
Non-United States citizen	62 (2.3)	8 (5.7)	
ESRD diagnosis			
Other	1423 (51.8)	85 (60.3)	0.0646
Diabetes	778 (28.3)	26 (18.4)	
Hypertension	546 (19.9)	30 (21.3)	
History of a previous kidney transplant	306 (11.1)	14 (9.9)	0.6665
Recipient pretransplant dialysis	2303 (83.9)	110 (78.0)	0.0673
Initial calculated EPTS			
< 20%	2086 (75.6)	61 (43.3)	< 0.0001
≥ 20%	672 (24.4)	80 (56.7)	
PRA, median (IQR)	0.0 (27.0)	0.0 (37.0)	0.3133 ^c
Recipient functional status at transplant			
Able to carry on normal activity and to work. No special care needed	2158 (80.6)	11 (80.9)	0.5848
Unable to work; able to live at home and care for most personal needs; varying amount of assistance needed	499 (18.6)	27 (19.2)	
Unable to care for self; requires equivalent of institutional or hospital care; diseases may be progressing rapidly	20 (0.8)	0 (0.0)	
Recipient functional status-most recent at follow-up			
Able to carry on normal activity and to work. No special care needed	1025 (80.8)	116 (82.3)	0.1781
Unable to work; able to live at home and care for most personal needs; varying amount of assistance needed	197 (15.5)	24 (17.0)	
Unable to care for self; requires equivalent of institutional or hospital care; diseases may be progressing rapidly	46 (3.6)	1 (0.7)	
Total days on waiting list/including inactive time, median (IQR)	410.0 (683.0)	253.0 (621.0)	0.0011 ^c
Donor type			
Deceased donor	2098 (76.1)	111 (78.7)	0.4705
Living donor	660 (23.9)	30 (21.3)	

DCD donor	469 (22.4)	33 (29.7)	0.0708
Deceased donor kidney biopsy	681 (32.5)	46 (41.4)	0.0497
Donor kidney glomerulosclerosis, %			
≤ 20	709 (98.6)	52 (100.0)	1.0000 ^a
> 20	10 (1.4)	0 (0.0)	
HLA mismatch level			
0	199 (7.2)	9 (6.4)	0.0161
1	70 (2.5)	1 (0.7)	
2	203 (7.4)	7 (5.0)	
3	439 (16.0)	21 (15.0)	
4	678 (24.7)	54 (38.6)	
5	800 (29.1)	31 (22.1)	
6	362 (13.2)	17 (12.1)	
Delayed graft function	408 (14.8)	27 (19.2)	0.1578
KDPI			
Low < 20%	648 (31.0)	40 (36.0)	0.4063
Moderate 20%-85%	1375 (65.7)	69 (62.2)	
High > 85%	69 (3.3)	2 (1.8)	
KDPI, median (IQR)	34.0 (40.0)	34.0 (50.0)	0.9930 ^c
Share type			
Local	2437 (88.4)	68 (48.2)	< 0.0001
Regional	101 (3.7)	24 (17.0)	
National	220 (8.0)	49 (34.8)	
Kidney cold ischemic time (hours), median (IQR)	12.0 (12.5)	16.0 (12.9)	< 0.0001 ^c
Rejection within 6 months	176 (7.5)	9 (16.4)	0.0344 ^a
Post TX			
Recipient primary insurance at transplant			
Private insurance	835 (30.3)	47 (33.3)	0.5142 ^b
Public insurance	1921 (69.7)	94 (66.7)	
Other	2 (0.1)	0 (0.0)	
Working for income	876 (34.7)	57 (42.2)	0.0752

^aP for Fisher exact test.^bP for Monte Carlos exact test.^cP for Wilcoxon Rank sum test.

IQR: Inter quartile range; BMI: Body mass index; ESRD: End Stage Renal Disease; EPTS: Estimated Post Transplant Survival; PRA: Panel Reactive Antibodies; DCD: Donation after Cardiac Death; HLA: Human Leukocyte Antigens; KDPI: Kidney Donor Profile Index; TX: Transplant.

Annual Kidney Report found that the proportion of candidates prevalent on the waiting list with waiting time less than 1 year rose to 34.2% in 2021 from 31.4% in 2020 and 33.9% in 2019, while 13.6% on the waiting list at some point in 2021 have been waiting 5 years or longer, a proportion that has been decreasing in recent years[13]. The decrease in waitlists nationally is a result of allocation policy changes, but also could be affected by Medicaid expansion as well, for instance higher priority patients may be getting more access to transplant because of expansion. Although, in our study, PRA levels and re-do transplant rates were similar before and after expansion. Findings may change in the longer-term follow-up.

We analyzed frailty scores among different racial and insurance groups. In our report, frailty scores were similar in pre- and post- Medicaid expansion eras and among different racial groups; however, frailty and public insurance were associated with worse outcomes in Oklahoma. Dubay *et al*[9] also found that in renal transplant patients, public insurance was associated with a 1.4% lower survival rate, and Medicaid itself was associated with a higher mortality hazard ratio

Table 2 Post-expansion recipient functional status at transplant by different insurance types

Functional status at transplant	Private insurance (%)	Public insurance (%)	Other (%)	P value
Able to carry on normal activity and to work. No special care needed	1083 (86.4)	1184 (75.9)	5 (100.0)	0.0003 ^b
Unable to work; able to live at home and care for most personal needs; varying amount of assistance needed	168 (13.4)	358 (23.0)	0 (0.0)	
Unable to care for self; requires equivalent of institutional or hospital care; diseases may be progressing rapidly	2 (0.2)	18 (1.2)	0 (0.0)	

^bP for Monte Carlo exact test.

Table 3 Post-Medicaid expansion recipients' insurance types, n (%)

Insurance	White 1783 (61.6)	Black 553 (19.1)	AI/NH/PI (0.08)	Hispanic (0.08)	Asian (0.03)	Multiracial (0.01)	P value
Private insurance	905 (50.8)	181 (32.7)	91 (39.9)	80 (36.0)	35 (43.8)	7 (21.2)	0.0003
Public insurance	874 (49.0)	371 (67.1)	137 (60.1)	142 (64.0)	45 (56.3)	26 (78.8)	
Other	4 (0.22)	1 (0.18)	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)	

AI/NH/PI: American Indian/Alaska Native/Pacific Islander.

Table 4 Post-expansion recipient functional status at Transplant by different race, n (%)

Recipient functional status transplant	White 1783 (61.6)	Black 553 (19.1)	AI/NH/PI (0.08)	Hispanic (0.08)	Asian (0.03)	Multiracial (0.01)	P value
Able to carry on normal activity and to work. No special care needed	1391 (80.5)	435 (79.7)	178 (81.3)	178 (81.7)	65 (85.5)	25 (78.1)	0.8401 ^b
Unable to work; able to live at home and care for most personal needs; varying amount of assistance needed	322 (18.7)	108 (19.8)	40 (18.3)	39 (17.9)	11 (14.5)	6 (18.8)	
Unable to care for self; requires equivalent of institutional or hospital care; diseases may be progressing rapidly	14 (0.81)	3 (0.55)	1 (0.46)	1 (0.46)	0 (0.00)	1 (3.1)	

^bP for Monte Carlo exact test.

AI/NH/PI: American Indian/Alaska Native/Pacific Islander.

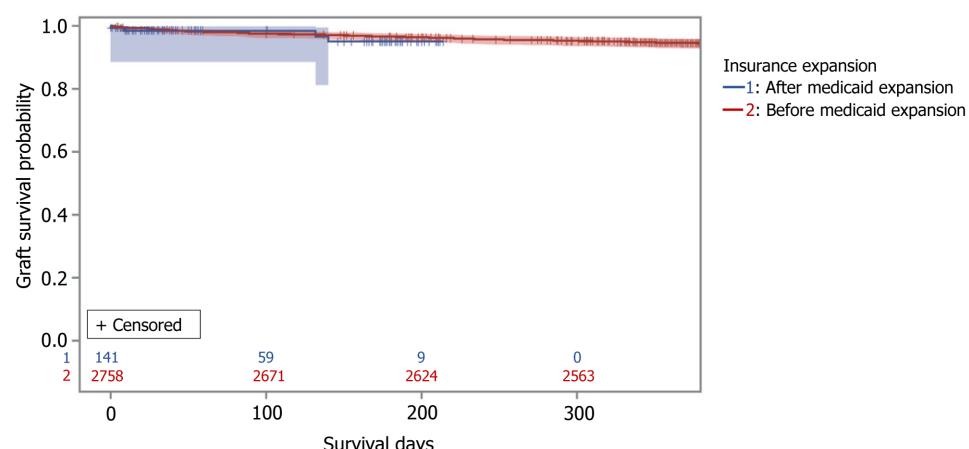
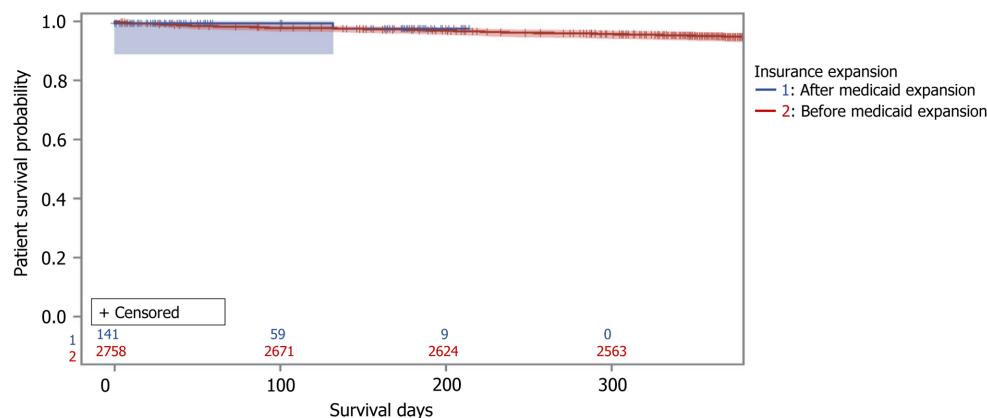
**Figure 1 1-year graft survival of kidney transplant recipients between pre- and post-Medicaid expansion in Oklahoma.**

Table 5 Cox proportional hazards model for a hazard ratio of variables for 1-year patient survival

Variables	aHR (95%CI)	P value
Age	1.04 (1.03, 1.05)	< 0.0001
Sex		
Female	Reference	
Male	1.19 (1.01, 1.40)	0.0426
Race		
White	Reference	
Black	0.98 (0.87, 1.20)	0.8699
Amer Ind/Alaska Native/Pacific Islander	1.52 (1.18, 1.97)	0.0014
Hispanic	0.82 (0.58, 1.17)	0.2748
Asian	0.73 (0.40, 1.33)	0.3056
Multiracial	1.05 (0.34, 3.32)	0.9289
Insurance		
Private insurance	Reference	
Public insurance	1.54 (1.25, 1.88)	< 0.0001
Recipient functional status at transplant		
Able to carry on normal activity and to work. No special care needed	Reference	
Unable to work; able to live at home and care for most personal needs; varying amount of assistance needed	1.53 (1.27, 1.84)	< 0.0001
Unable to care for self; requires equivalent of institutional or hospital care; diseases may be progressing rapidly	2.13 (1.09, 4.20)	0.0281
Medicaid expansion		
Before medicaid expansion	Reference	
After medicaid expansion	1.07 (0.26, 4.41)	0.9290

aHR: Adjusted hazard ratio.

**Figure 2** 1-year patient survival in kidney transplant patients in between pre- and post-Medicaid expansion in Oklahoma.

when compared to private insurance. Frailty is an important status when evaluating patients for transplant. Frailty is associated with reduced access to the waiting list and higher waiting list mortality[15]. In a study of 7078 individuals who were evaluated at three transplant centers between 2009 and 2018, frail individuals were almost half as likely as non-frail individuals to be placed on a KT waiting list[16]. Pérez-Sáez *et al*[17] also found that in KT candidates, pre-frailty and frailty according to both the PFP and the FRAIL scale were associated with poorer results while listed. While it is critical to improve access to transplant for all patient groups including frail patients, ongoing strategies are necessary to improve outcomes in this patient population.

We also report that several independent risk factors that were associated with worse graft and patient outcomes at 1 year in the post-Medicaid expansion era such as male sex and race, specifically American Indian, Alaskan, or Pacific Islander group. These results differ from other studies. Seipp *et al*[18] analyzed the KT outcomes for indigenous patients in the United States and found that cardiovascular, graft and infectious outcomes were similar between white and American Indian groups. While the impact of sex in KT outcomes is not consistent, in some studies it is suggested that the male sex is considered an independent factor for poor survival outcomes after KT[19]. Increased long term mortality after KT is observed in Native Americans when no confounders are adjusted[20]. We were not able to analyze specific variables per racial groups in our study due to sample size.

We report that 1-year patient and graft survival rates were similar in the pre- and post-Medicaid expansion eras, despite increased early rejection rates. Other studies show worse outcomes for Medicaid patients. Medicaid organ transplant beneficiaries had significantly lower survival compared with privately insured beneficiaries[21]. The more severe organ failure among Medicaid beneficiaries at the time of listing suggested a pattern of late referral, which might account for worse outcomes[9]. A higher portion of patients with low socioeconomic factors received transplants through Medicaid. Social factors such as social, race, and education levels can play a role in determining transplantation outcomes and individuals with low socioeconomic factors were found to be associated with worse health care outcomes overall[22-24].

Lastly, we found that 1-year patient and graft survival were similar in the pre- and post-Medicaid expansion eras. This contrasts with other studies that reported better or worse survival for the Medicaid population[9,25,26]. Trivedi *et al*[6] found that states that expanded Medicaid under the ACA had a significant increase in the proportion of patients listed with Medicaid and better 1-year waiting list survival. That highlights the need for further long-term studies.

Our limitations include: (1) Study only reflects short-term follow-up since Medicaid expansion as it was only recently implemented in Oklahoma; and (2) we had a relatively small sample size in the post expansion era due to the aforementioned limitation. Therefore, to address the true impact of this expansion, further research is needed to fully understand the long-term impact of Medicaid expansion on KT outcomes, as well as the potential challenges that may arise as more patients become eligible for transplantation services. Although this research didn't analyze global data, the preliminary results in this study imply that access to healthcare for underrepresented minorities leads to more KTs. Further research would be needed to analyze the global impact of Medicaid or affordable healthcare.

CONCLUSION

The Medicaid Expansion had a significant impact on KT recipients in Oklahoma: (1) More access to KT for non-United States citizens, and non-white population (Hispanics, Asians, American Indian, Alaskan, or Pacific Islander); (2) there were shorter waitlist times for patients regardless of distance and local sharing; (3) similar 1-year graft and patient survival in pre and post-expansion eras; (4) Medicaid expansion itself is not associated with one-year outcomes; and (5) male sex, American Indian/Alaska Native/Pacific Islanders race, public insurance and frailty category are risk factors for mortality at 1 year after transplant in Oklahoma. Further research is necessary to investigate the long-term impact of the Medicaid expansion on adult KT patients in Oklahoma.

FOOTNOTES

Author contributions: Kwon H, Sandhu Z, Andacoglu OM, and Sarwar Z designed the project together; Sarwar Z collected the data and provided Tables and Figures; Kwon H, Sandhu Z and Andacoglu OM interpreted results together, contributing to the results/discussion and conclusion sections of the manuscript. All authors drafted and reviewed the manuscript. Kwon H and Sandhu Z are co-first authors because they contributed to most manuscript drafting, data analysis and submission together. Equal effort and time were spent by both Kwon H and Sandhu Z to create this manuscript. Kwon H and Sandhu Z were essential to the submission and communication between all team members. Designating Kwon H and Sandhu Z as co-first authors recognize the amount of time, energy and resources that these authors dedicated to this manuscript.

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