Prescribing patterns and impact of glucagon-like peptide-1 receptor agonists in a kidney transplant evaluation cohort in British Columbia, Canada: A single-center experience

Hyunwoong Harry Chae[1], Cindy Luo[2], David Harriman[3], Christopher Nguan[3]
[1]Faculty of Medicine, University of British Columbia, Vancouver, BC, Canada; [2]Faculty of Pharmaceutical Sciences, University of British Columbia, Vancouver, BC, Canada; [3]Department of Urologic Sciences, University of British Columbia, Vancouver, BC, Canada

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Corresponding author: Dr. Christopher Nguan, Department of Urologic Sciences, University of British Columbia, Vancouver, BC, Canada; chris.nguan@ubcurology.com

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ABSTRACT

Introduction: Glucagon-like peptide-1 receptor agonists (GLP-1RA) have demonstrated weight loss and cardiometabolic benefits in specific subpopulations. Studies of GLP-1RAs in Canadian end-stage renal disease (ESRD) and kidney transplantation (KT) patients are limited.

Methods: This is a retrospective cohort study of patients evaluated for potential KT at the Vancouver General Hospital (VGH) between January 2014 and August 2024. We analyzed prescription patterns, weight changes, and post-transplant outcomes.

Results: At evaluation, 63/2789 (2.3%) patients were on a GLP-1RA. The proportion of GLP-1RA users increased from 0% in 2014–2018, 0.3% (1/366) in 2019, and 8.7% (20/231) in 2024. There was a mean weight change of -1.82 kg (1.93%, 95% confidence interval [CI] -3.46 to -0.19, p=0.031; n=26) at six months and -2.50 kg (2.62%, 95% CI -4.47 to -0.52, p=0.016; n=25) at 12 months post-initiation. Twenty-six patients received a KT and had a median followup of 1.14 (interquartile range [IQR] 0.19−1.79) years. Only 11 patients were on a GLP-1RA at one year post-transplant and had available post-transplant outcome data. No significant differences were detected in estimated glomerular filtration rate (eGFR) (67, IQR 65.5−78 vs. 59, IQR

KEY MESSAGES

- GLP-1RA prescribing amongst a kidney transplant evaluation cohort in BC increased markedly after 2019.
- GLP-1RA use was associated with modest weight loss at six and 12 months in these potential kidney transplant candidates.
- No significant differences in one-year post-transplant outcomes were detected between GLP-1RA users and non-users.

45−75 mL/min/1.73 m², p=0.18), graft failure (0% vs. 4.6%, p=1) and mortality (0% vs. 3.0%, p=1) between GLP-1RA users vs. non-users at one year post-KT.
Conclusions: GLP-1RA use in BC's KT evaluation cohort increased since 2019 and was associated with modest weight loss at six and 12 months post-initiation. No significant differences in post-transplant outcomes were detected. This provides preliminary support for GLP-1RAs as a potentially safe weight management strategy for Canadian KT candidates.

INTRODUCTION

Glucagon-like peptide 1 receptor agonists (GLP-1RA) are a relatively new class of medications primarily used as a glucose-lowering agent for type 2 diabetes mellitus (T2DM). It has been shown to effectively provide improved glycemic control, weight loss, and cardiovascular benefits in these patient groups.[1–3] In recent years, multiple trials have found similar metabolic and cardiovascular benefits amongst non-diabetic patients.[4,5] As such, studies have begun exploring the use of this medication in diverse patient populations, and have found improved clinical outcomes in heart failure patients, obstructive sleep apnea, non-alcoholic liver steatohepatitis, polycystic ovarian syndrome (PCOS), and antipsychotic use-associated obesity.[6–9]

Kidney transplant (KT)-related populations, including both potential candidates with end-stage renal disease (ESRD) or advanced chronic kidney disease (CKD G4–G5) and KT recipients, are another patient group that may benefit from the previously identified positive impacts of this medication in other clinical contexts. First, KT is pursued for patients with ESRD who are dialysis-dependent or those with advanced CKD undergoing pre-emptive transplantation. Even after KT, recipients remain at risk for allograft injury due to persistent comorbidity and transplant-specific factors such as immunosuppression, rejection, and recurrent disease. The two most common causes of CKD are hypertension and diabetes mellitus, and as such, the previously demonstrated protective effects of GLP-1RAs on metabolic and cardiovascular health suggest that these medications may be useful for KT- related populations. Second, obesity is a significant barrier to KT accessibility, as is considered a relative contraindication to KT in many transplant programs, contributing to delays or denial of waitlisting and transplantation.[10] As such, GLP-1RA use in obese, marginal KT candidates may not only improve their metabolic and cardiovascular health, but if safe and sustainable weight loss can be achieved on this medication, it could potentially increase KT accessibility.

Despite GLP-1RAs being an actively discussed and studied medication in recent years, with increasing utilization in different clinical settings, there are a limited number of studies characterizing prescribing patterns of this medication in potential KT candidates (advanced CKD and ESRD) and KT recipients.[11,12] To our knowledge, no such study exists in the Canadian context thus far.

Furthermore, while there have been large trials demonstrating improved metabolic and cardiovascular outcomes with GLP-1RA use in CKD patients,[13,14] the evidence base for ESRD and KT patients remains limited, with most existing studies being small scale trials or observational cohorts reporting heterogenous findings. Some studies of ESRD and dialysis patients have identified weight loss and improved cardiometabolic parameters with GLP-1RA use, although reported effects have varied widely.[15–19] Existing data remains similarly limited for KT recipients; while one large retrospective registry study on KT recipients suggested improved graft outcomes and survival rates in GLP-1RA users, they did not evaluate metabolic outcomes.[20] Some retrospective cohort studies have identified mild improvements in renal function, cardiovascular health, weight, graft outcomes and survival; however, many studies had limited sample sizes and reported inconsistent findings.[11,12,21–23]

To address these gaps, the objectives of this single-centre study were to characterize prescribing patterns of GLP-1RA in patients being evaluated for KT and KT recipients in BC, evaluate the association of GLP-1RA use and changes in weight, and compare post-transplant outcomes between KT recipients who were GLP-1RA users vs. non-users.

METHODS

Study design

This is a single-center, retrospective cohort study of patients evaluated for potential KT at the Vancouver General Hospital (VGH) between 2014/01-2024/08. All patients who have ESRD, are on dialysis, or have advanced CKD approaching ESRD are referred to the VGH KT clinic, where they are evaluated for eligibility for KT. Institutional records and the provincial transplant database were reviewed for data collection.

Demographic variables were collected at time of evaluation for potential KT, and included age, sex, race/ethnicity, blood group, weight and BMI at time of evaluation, primary etiology for CKD, and co-morbid diabetes.

Patient records were screened for patient weights and presence of GLP-1RA medication prescriptions. Trends in annual prescription prevalence of GLP-1RA medications in our cohort were analyzed by calculating the number of first-time evaluations for potential KT in which the patient was receiving a GLP-1RA at the time of evaluation, divided by the total number of evaluations performed in the same calendar year.

Weight changes at 6 months and 12 months from prescription imitation were recorded. For each time point (i.e. time of GLP-1RA initiation, 6 months post-initiation, 12 months post-initiation), the weight measurement closest to the target date within a ±3-month window was used. Patients with incomplete weight data or those who discontinued their medication prior to each time point were excluded.

Post-transplant outcomes at 1-year post-transplant, including estimated glomerular filtration rate (eGFR), graft failure, mortality, were compared between (1) KT recipients who were receiving a GLP-1RA at time of initial evaluation and remained on a GLP-1RA at the 1-

year post-transplant timepoint, and (2) KT recipients who never received a GLP-1RA during the study period. Patients with incomplete 1-year post-transplant data or those who discontinued their GLP-1RA medication prior to the 1-year post-transplant timepoint were excluded.

Statistical analysis

Descriptive statistics were utilized to summarize demographics data. Prescription prevalence trends were presented descriptively, and annual trends were assessed via logistic regression modelling. Paired t-tests were utilized for weight change analyses. Post-transplant outcomes were compared via two-sample t-test or Wilcoxon rank-sum test for continuous outcomes and Chi-square or Fisher's exact tests for categorical outcomes, with each test selected appropriately based on the data characteristics and underlying assumptions. Analyses were conducted using R 4.0.4 (R Foundation for Statistical Computing, Vienna, Austria). $P<0.05$ was considered statistically significant.

RESULTS

Demographics

Demographic characteristics of the study cohort are summarized in Table 1. Between 2014/01 to 2024/08, 63/2789 (2.3%) patients evaluated for potential KT were on a GLP-1RA at time of evaluation. Twenty-six (26/63, 41.3%) subsequently received a KT within the study period and were followed up for a median of 1.14 (IQR 0.19-1.79) years post-transplant. The median age at time of initial evaluation for this cohort was median 61.0 (IQR 48.5, 68.6) years, and 36/63 (57.1%) patients were male. The most common race/ethnicities reported were White (17/63, 27.0%), Southeast Asian (12/63, 19.0%), and East Asian (6/63, 9.5%), although many patients' race/ethnicity were unknown or unreported (20/63, 31.7%). ABO blood group was most commonly O (28/63, 44.4%), A1 (16/63, 25.4%), B (13/63, 20.6%), and AB (6/63, 9.5%). The median weight and BMI at the time of evaluation was 100 (IQR 80.4,115) kg and 34.9 (IQR 29.1,38.7) kg/m^2. The most common primary etiology of chronic kidney disease included diabetes (46/63, 73.0%), glomerulonephritis (5/63, 7.9%), hypertension (3/63, 4.8%), and cystic kidney disease (3/63, 4.8%). Most patients had comorbid type 2 diabetes mellitus (55/62, 88.7%), with 3/62 (4.8%) having type 1 diabetes mellitus.

Prescription prevalence

Annual proportions of patients evaluated for potential KT who were on a GLP-1RA during the study period are presented in Figure 1. Between 2014-2018, no patient evaluated for potential KT were on any GLP-1RAs. The proportion of GLP-1RA users at time of initial evaluation rose to 0.3% in 2019 (1/366) and 0.9% in 2020 (2/223), then increasing to 4.4% in 2021 (9/203), 4.3% in 2022 (8/184), 6.2% in 2023 (23/372), and 8.7% in 2024 (20/231). In a logistic regression restricted to 2019–2024 (excluding years with no GLP-1RA users from 2014-2018), each additional calendar year was associated with increased GLP-1RA use (OR 1.65, 95% CI 1.39–2.00; $p<0.001$).

Weight change

Changes in weight of GLP-1RA users at 6 months and 12 months post-initiation are presented in Figures 2 and 3. Mean weight change among GLP-1RA users with paired measurements was −1.82 kg (−1.93%; 95% CI −3.46 to −0.19; p=0.031; n=26) at 6 months post-initiation, and -2.50 kg (-2.62%; 95% CI -4.47 to -0.52; p=0.016; n=25) at 12 months post-initiation.

Post-transplant outcomes

Estimated glomerular filtration rate at 1-year post-transplant was numerically higher in patients who remained on GLP-1RAs at the 1-year post-transplant timepoint compared to non-users; however, the difference was not statistically significant (median 67 (IQR 65.5–78) mL/min/1.73 m² in GLP-1RA users (n=11) vs 59 (45–75) for non-users (n=1225); p=0.18; Figure 4). No graft failures (0/11, 0% vs 60/1316, 4.6%; p=1.00; Figure 5) or deaths (0/11, 0% vs 39/1316, 3.0%; p=1.00; Figure 6) occurred among GLP-1RA users at 1-year post-transplant; however, the difference in graft failure and mortality rates between users vs. non-users was not statistically significant.

DISCUSSION

In this single-centre retrospective cohort study of all patients evaluated for potential KT at VGH (2014/01-2024/08), we identified that while the cumulative GLP-1RA prescription prevalence during the study period was low with 2.3%, utilization has been rapidly increasing from 2019-2024, with 8.7% prevalence in 2024. GLP-1RA use was associated with modest weight loss at both 6 and 12-months after initiation, however, we did not detect a significant difference for 1-year post-transplant outcomes such as eGFR, graft failure, and mortality.

Although the literature is limited for ESRD patients and KT recipients, our finding of increasing utilization of GLP-1RAs in our KT evaluation cohort (consisting of advanced CKD and ESRD patients and KT recipients) aligns with existing studies in diabetics, CKD patients, and KT recipients in other geographical contexts. One nationwide U.S. study of KT recipients with T2DM identified that GLP-1RA utilization increased from 2.8% in 2014 to 12.5% in 2023.[24] Another multinational cohort study (Japan, Europe, and the U.S.) of CKD patients with T2DM demonstrated steadily increasing utilization of GLP-1RAs from 2012-2021.[25] In the Canadian context, a previous national study identified increasing prescription prevalence of GLP-1RAs across general populations in all provinces from 2018-2021,[26] and another national utilization analysis conducted by the Canadian Agency of Drugs and Technologies in Health (CADTH) identified a 5-fold increase in GLP-1RA claimants from 2019-2021.[27] In British Columbia, one previous study of treatment patterns for T2DM patients between 2001-2020 identified similar trends as our findings, as GLP-1RA use as first line treatment of T2DM was less than 1% until 2015, then rising to 10% cumulative use between 2016-2020.[28] Our study adds novel insights into the utilization patterns of this medication in KT-related populations, as to the best of our knowledge, no such study specifically assessing ESRD patients or KT recipients have been conducted in British Columbia nor Canada thus far. Furthermore, given that existing

Canadian GLP-1RA utilization studies largely include data only through 2021, real-world prescribing patterns may have changed substantially since then in this rapidly evolving field. With early evidence suggesting not only improved glycemic control and weight loss, but also cardiovascular and renal benefits in CKD, ESRD, and KT recipients, clinical practice may be changing accordingly.[14,20,29] As such, our study provides a timely update on GLP-1RA prescribing patterns in KT-related populations in a Canadian context.

We identified modest weights loss (-1.82 kg at 6 months and -2.50 kg at 12 months post-initiation) in patients evaluated for KT on GLP-1RAs. Weight loss has been a proven benefit of GLP-1RAs in both T2DM patients and non-diabetic populations according to recently published trials.[5,30] In KT-related populations, however, existing studies are limited by small sample sizes. Reported weight loss at 12 months post-initiation in post-KT patients have been heterogenous, ranging from no statistically significant loss to -8.8 kg.[31–35] Reported weight loss in ESRD patients also had mixed findings, including no statistically significant weight loss at 12 weeks, −4.6 kg at 12 weeks, and -4.9 kg at a median of 17.4 months.[15,16,19] Compared to existing studies, the weight loss observed in our study was within the lower end of reported ranges. This variability may reflect differences across published studies in GLP-1RA agent and titration, treatment duration and adherence, baseline BMI, study design (randomized trials vs retrospective cohorts), and follow-up intervals, which may limit our ability for direct comparisons with existing literature.

Our study did not identify statistically significant differences in post-transplant outcomes at 1-year between GLP-1RA users vs non-users. Nonetheless, the GLP-1RA user group had numerically higher post-transplant eGFR compared to non-users and had zero mortality or graft failure events at 1-year post-transplant. These findings may be due to our study's limited sample size, as there were only 11 patients who were on GLP-1RAs at 1-year post-transplant and had available post-transplant outcome data, and our analyses were likely underpowered to detect any significant differences. Some observational studies have recently reported lower incidences in mortality and graft failure rates, composite renal outcomes (including rejection, dialysis, re-transplantation, mortality), and major adverse kidney events (including eGFR <15, and mortality) in GLP-1RA using KT recipients in the U.S., Taiwan, and Israel.[20,36,37] Despite limited power, our study provides novel preliminary Canadian data on GLP-1RA use and potential associations with post-transplant outcomes in KT-related populations, as to the best of our knowledge, no such study has been conducted thus far in the Canadian setting. These findings provide context-specific insights into the early impact of GLP-1RA medications on KT-related populations in British Columbia and Canada more broadly, where population demographics, medication access pathways and availabilities, prescribing practices, and transplant care processes may differ from other healthcare systems and geographical contexts.

The established metabolic and cardiovascular benefits associated with GLP-1RA use in T2DM, non-diabetic, and CKD patients have driven the recent interest in exploration of GLP-1RA use amongst ESRD patients and KT recipients.[3–5,14,38] If similar benefits extend to KT-related populations, GLP-1RAs could help mitigate risk of allograft injury in KT recipients, but

it may also provide improved transplant eligibility for obese, marginal KT candidates. As most Canadian transplant programs have been reported to use BMI thresholds of 35-40 kg/m^2 for wait-list eligibility,[39,40] and with approximately 33% of the general Canadian population being classified as obese (BMI ≥ 30 kg/m^2),[41] obesity is a significant barrier to transplant accessibility. Furthermore, even amongst KT recipients, obesity has been associated with worse post-transplant outcomes, including higher rates of delayed graft function, graft loss, and post-operative complications.[42,43] There are recent studies suggesting early evidence that the metabolic and cardiovascular benefits of GLP-1RA's may indeed be conferred in KT recipients and ESRD patients.[20,31,34,36,37] Our analyses were unable to identify clear post-transplant safety signals for KT recipients on GLP-1RAs in this small sample size cohort, as we found modest weight loss at 6 and 12 months post-initiation and increased GLP-1RA utilization in our cohort in recent years, these findings may support the feasibility of GLP-1RA use as a potentially safe avenue for weight loss for obese, marginal KT candidates. Future studies with larger sample sizes, standardized exposures, and longer follow-ups on KT recipients and advanced CKD and ESRD patients should be conducted to clarify our understanding of the impact of these medications on KT-related populations.

This study has limitations. First, the sample size of this cohort is limited, with 63 total patients evaluated for KT on GLP-1RA, 26 ultimately receiving KT, and only 11 having available 1-year post-transplant data. Second, heterogeneity in patients along the transplant evaluation pathway (evaluated, waitlisted, received KT), and our retrospective study design necessitated non-standardized timing of weight measurement intervals (using the closest available weight measurement to each timepoint). Additionally, there was variability in GLP-1RA agents, dosing, and treatment durations across patients. Together, these factors may have introduced measurement variability and limited comparability of weight change estimates amongst patients and timepoints. Third, while the study period ended in August 2024, given the rapidly evolving literature on this topic, practice patterns and local guidelines and policies around the use of these medications may have continued to shift after our study period window. As such, the estimates of prescription prevalence reported in this study may not fully reflect current extent of utilization amongst KT-related populations. Fourth, due to the single-centre, retrospective design of this study, there is potential for selection bias, as all patients were from a single transplant program, and potential confounders such as baseline differences between GLP-1RA users and non-users (e.g., baseline metabolic health, transplant candidacy, patient motivation, engagement with care). In the context of these limitations, these findings should be interpreted as preliminary, hypothesis-generating observational data that may inform future, more robust studies, rather than definitive evidence regarding the safety or efficacy of these medications in the KT population.

CONCLUSIONS

Among the KT evaluation cohort at the VGH KT Program in British Columbia, Canada, utilization of GLP-1RAs has increased significantly between 2019-2024, and use was associated

with modest weight loss at 6 and 12 months post-initiation. Among KT recipients, we did not detect significant differences between GLP-1RA users and non-users in 1-year post-transplant eGFR, graft failure, or mortality. Studies with larger patient populations must be conducted to clarify the safety profile and clinical impact of GLP-1RAs in KT-related populations.

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Declaration of generative AI and AI-assisted technologies in the writing process:
During the preparation of this work, the author(s) used ChatGPT for checking of grammatical and spelling errors. After using this tool/service, the author(s) reviewed and edited the content as needed and take(s) full responsibility for the content of the published article.

FIGURES AND TABLES

Figure 1. Proportion of patients evaluated for potential kidney transplantation who were on a GLP-1RA at time of evaluation. CI: confidence interval; OR: odds ratio.

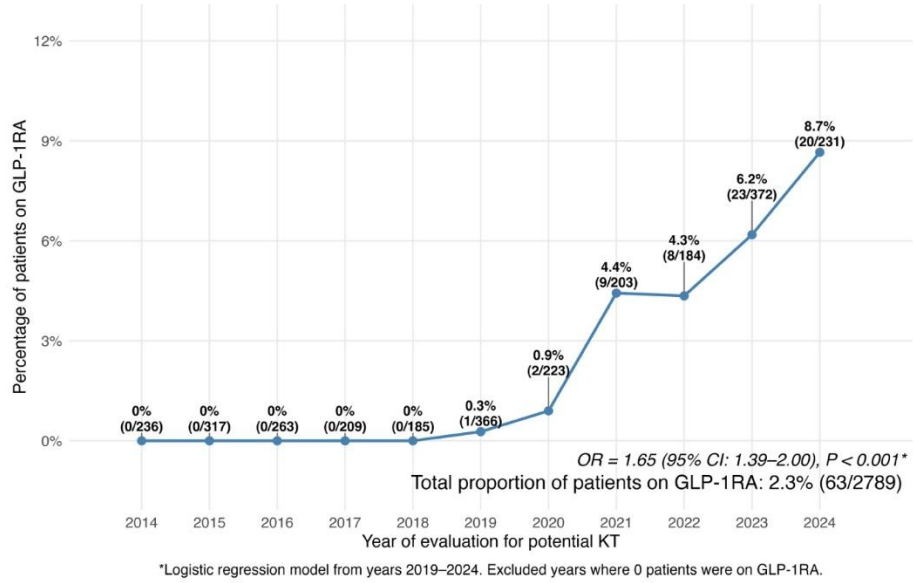

Figure 2. Weight change among GLP-1RA users 6 months after initiation. OR: odds ratio.

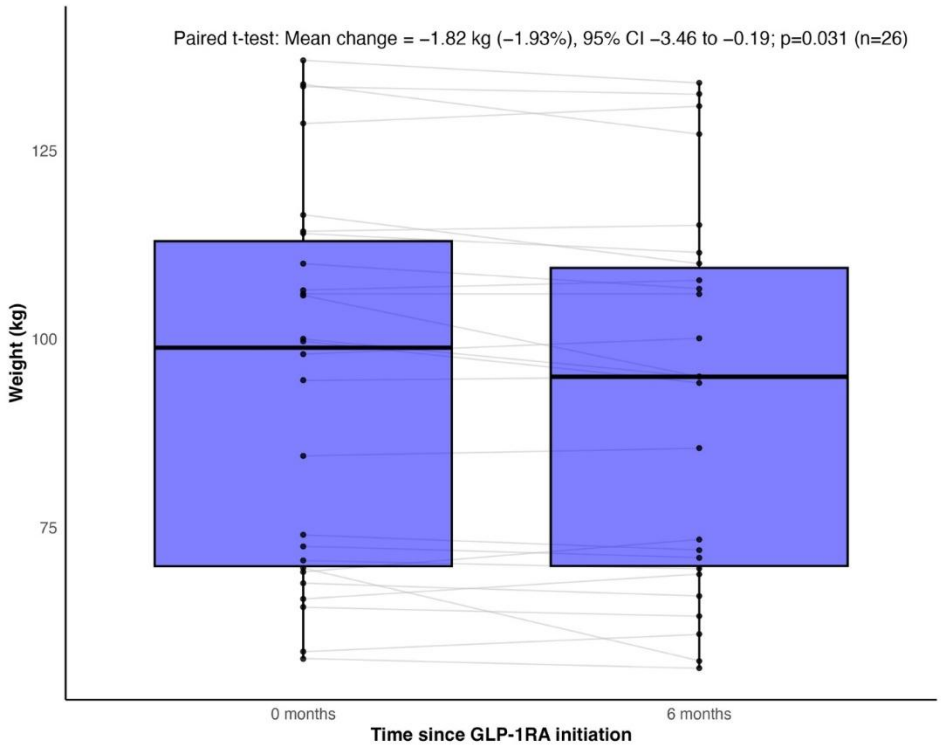

Figure 3. Weight change amongst GLP-1RA users 12 months after initiation. CI: confidence interval; OR: odds ratio.

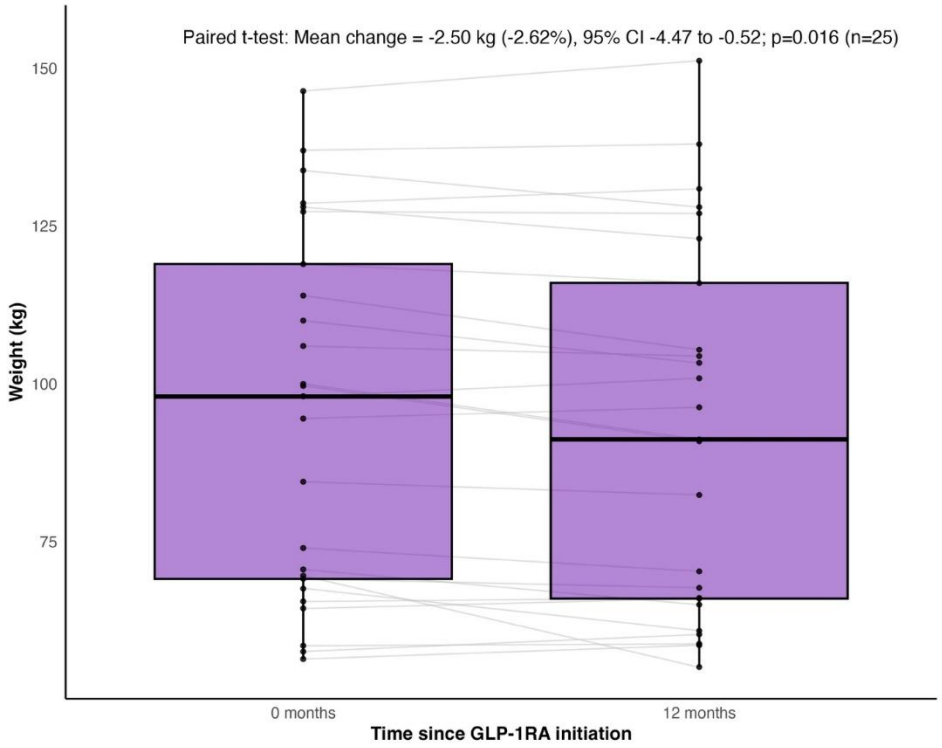

Figure 4. Estimate glomerular filtration rate at 1-year post-transplant.

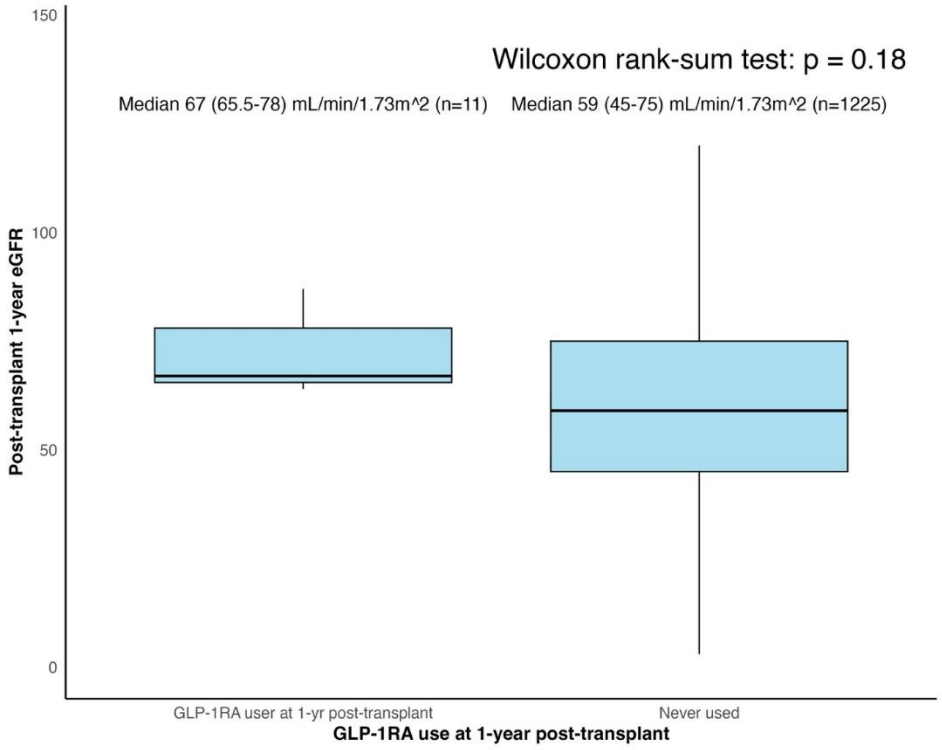

Figure 5. Graft failure at 1-year post-transplant

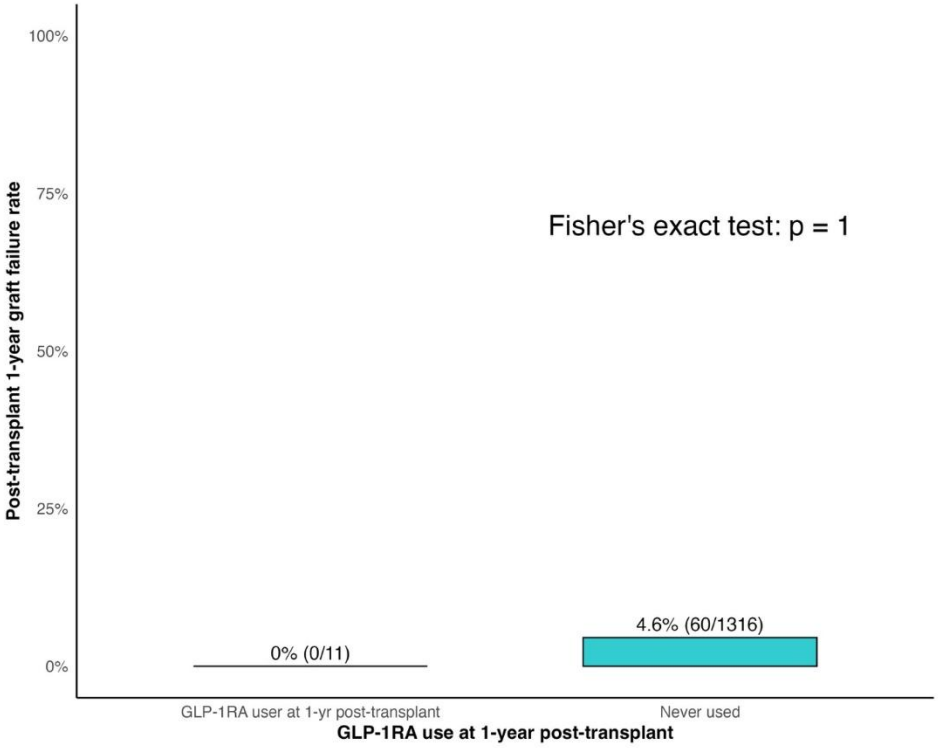

Figure 6. Mortality at 1-year post-transplant.

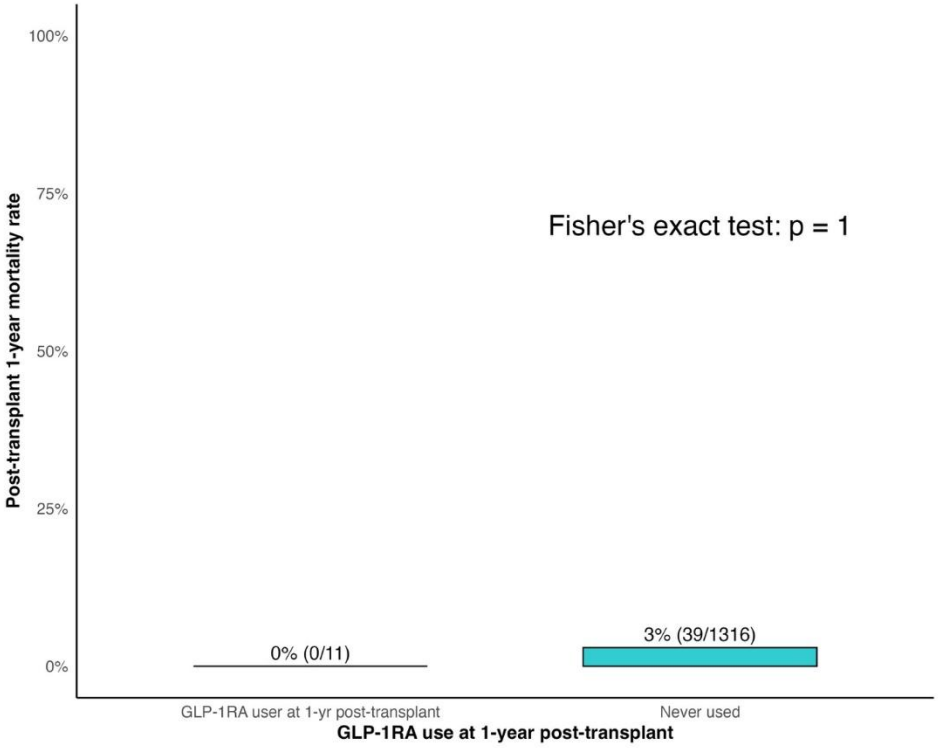

Table 1. Demographics of GLP-1RA users at time of evaluation for potential kidney transplant	
	On GLP-1RA at time of evaluation for potential KT (n=63)
Age (years)	
Median [Q1,Q3]	61.0 [48.5,68.6]
Sex	
Male	36/63 (57.1%)
Female	27/63 (42.9%)
Missing	0 (0%)
Race/ethnicity	
White	17/63 (27.0%)
Black	1/63 (1.6%)
East Asian	6/63 (9.5%)
South Asian	4/63 (6.3%)
Southeast Asian	12/63 (19.0%)
Middle Eastern/North African	0/63 (0.0%)
Hispanic/Latino ethnicity	0/63 (0.0%)
Indigenous	3/63 (4.8%)
Unknown	20/63 (31.7%)
ABO blood group	
A1	16/63 (25.4%)
A2	0/63 (0.0%)
AB	6/63 (9.5%)
B	13/63 (20.6%)
O	28/63 (44.4%)
Missing	0 (0%)
Weight	
Median [Q1,Q3]	100 [80.4,115]
Missing	2 (3.2%)
BMI	
Median [Q1,Q3]	34.9 [29.1,38.7]
Missing	2 (3.2%)
Primary etiology of chronic kidney disease	
Diabetes	46/63 (73.0%)
Glomerulonephritis	5/63 (7.9%)
Hypertension	3/63 (4.8%)
Cystic kidney disease	3/63 (4.8%)
Congenital	1/63 (1.6%)
Obstruction	2/63 (3.2%)

Drug/toxin induced	0/63 (0.0%)
Reflux	0/63 (0.0%)
Other	3/63 (4.8%)
Unknown	0/63 (0.0%)
Comorbid diabetes	
No diabetes	4/62 (6.5%)
Type 1 diabetes	3/62 (4.8%)
Type 2 diabetes	55/62 (88.7%)
Missing	1 (1.6%)