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The effect of IGL-1 preservation solution on outcome after kidney transplantation: A retrospective single-center analysis

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Accepted Article

Abbreviations

CTS	Collaborative Transplant Study
DGF	delayed graft function
eGFR	estimated glomerular filtration rate
fDGF	function delayed graft function
HLA	human leukocyte antigen
HTK	histidine tryptophan ketoglutarate solution
IGL-1	Institut Georges Lopez solution-1
IPTW	inverse probability of treatment weighting
ROS	reactive oxygen species
PEG	polyethylene glycol
UNOS	United Network of Organ Sharing
UW	University of Wisconsin solution

Abstract

Institut Georges Lopez-1 solution (IGL-1) is increasingly used for kidney preservation, though little information on outcomes is available. Outcomes of all deceased donor kidneys preserved by IGL-1, University of Wisconsin solution (UW), or histidine-tryptophan-ketoglutarate (HTK) and transplanted in our center (2000-2018) were analyzed. Multivariable analysis for delayed graft function (DGF), functional DGF, estimated glomerular filtration rate (eGFR, CKD-EPI equation), proteinuria, acute rejection, death-censored graft loss and patient survival were performed. A double robust approach, consisting of propensity score weighting and correction for confounders, minimized the risk of bias.

1943 transplants were included: 234 with IGL-1, 1046 with UW, and 663 with HTK. As IGL-1 was only introduced in 2014, a pre-specified sensitivity analysis of 917 kidneys (2010-2018) was performed using the same statistical approach. After weighting, IGL-1 retained a higher proportion of kidneys donated after circulatory death (DCD).

IGL-1 was not independently associated with any of the outcomes when compared to UW or HTK. Sensitivity analysis between 2010 and 2018 (n=917) showed similar results.

In this retrospective analysis, using robust methodology to reduce the risk of bias, IGL-1 preservation results in equal outcomes compared to UW or HTK, despite more DCD-transplants in the IGL-1 group.

Introduction

Cold storage, the most frequently used form of kidney preservation slows down cellular metabolism, protecting the organ from anoxia. Organ preservation solutions have been developed to counteract the detrimental consequences of hypothermia and anoxia, namely interstitial and cellular edema, acidosis, and reactive oxygen species (ROS) production at reperfusion. The most defining characteristics of these solutions are their impermeants (usually colloids, saccharides, or anions) and electrolyte composition (either an intracellular (low Na⁺, high K⁺) or an extracellular electrolyte composition (high Na⁺, low K⁺)).(1)

Abdominal organs are most often preserved by either University of Wisconsin (UW) or histidine-tryptophan-ketoglutarate (HTK).(2) In 2003, Institut Georges Lopez-1 (IGL-1) solution was introduced in clinical practice. IGL-1 combines an extracellular electrolyte composition with a phosphate buffer and the colloids polyethylene glycol (PEG 35kDa, 1g/L), saccharides and anions.(3) IGL-1 has a viscosity lower than UW and higher than HTK.(4) In IGL-1, ROS-scavengers (glutathione and allopurinol) are present in the same concentrations as in UW.(5) Additionally, PEG might also reduce ROS-induced damage as reduced lipid peroxidation was observed in isolated hepatocytes and in a kidney perfusion model.(6-8) Isolated perfusion models of rat and porcine kidneys as well as pig kidney autotransplant models show improved creatinine clearance, glomerular filtration rates and fractional sodium excretions with IGL-1 or PEG-containing extracellular solutions (with different PEG lengths and concentrations) compared to UW.(6, 9, 10) Additionally, in pig kidney autotransplant models where PEG was added to an extracellular solution, a significant reduction in MHC class II expression on epithelial tubule cells has been observed with a reduced influx of CD4⁺ and CD8⁺ cells compared to UW.(9, 11, 12) Furthermore, addition of PEG is associated with reduced interstitial fibrosis after pig kidney autotransplantation.(11, 12). As such, IGL-1 might improve both short and longer-term after kidney transplantation. IGL-1 was introduced in clinics in 2003 and has gained a significant place on the market in Europe (Belgium, France, Switzerland, Norway, Sweden, Spain) and Brazil. In all these countries, except Spain, IGL-1 is now the first choice for abdominal organ preservation. (G. Olive of the IGL-1-group, personal communication) Nevertheless, very few clinical outcome data have been published precluding any firm conclusions to be drawn on the superiority of IGL-1 as a preservation solution for kidneys.(13) We set out to compare outcomes of kidneys transplanted in our center after storage in either IGL-1, UW, or HTK.

Methodology

Study population

All patients who received a deceased-donor kidney-only transplant at the University Hospitals Leuven between January 1, 2000 and December 31, 2018 were included in this retrospective cohort study of prospectively collected data. Transplants with kidneys preserved by a preservation solution other than IGL-1, UW, or HTK, were excluded. Patients provided written consent to use their clinical data for study purposes. This study was approved by our institution's Ethical Committee (s62400). Kidneys were procured in standard fashion as part of multi-organ procurements after an aortic cold flush with cold preservation solution. The standard immunosuppression regimen is described in the Appendix.

Clinical data

Data were prospectively collected in electronic clinical patient charts, which were used for clinical patient management and directly linked to the database used in this study. All post-transplantation data were collected during routine clinical follow-up. The kidney donor risk index (KDRI) was calculated.⁽¹⁴⁾ Primary non-function was defined as failure to regain function by 3 months post-transplantation. Delayed graft function (DGF) was defined as need for dialysis within the first seven days after transplantation. We also looked at a stricter definition of DGF, defined as the need of at least two dialysis sessions in the first seven days post-transplantation. Functional DGF (fDGF) was defined as the absence of 3 consecutive eGFR decreases of >10% during the first week.⁽¹⁵⁾ To prevent misclassification in patients with good early graft function, a known limitation of this definition (16, 17), creatinine evolutions reaching an eGFR of <2 mg/dL/1.73m² on day 3 were considered to not have fDGF. Graft function was determined at 3 and 12 months post-transplant to reflect the estimated glomerular filtration rate (eGFR; CKD-EPI) (18), with a nominal value of 10 mL/min/1.73m² imputed in case the graft had failed. End-stage renal disease (ESRD) was defined as an eGFR<30 mL/min/ 1.73m² at one-year post-transplantation. Acute rejection occurring within 3 months of transplantation was analyzed. These were clinically treated rejections of which all but 3% were biopsy-proven. Time to graft loss was taken as time from transplantation to graft nephrectomy or return to dialysis, whichever was earlier and was censored for patient death with a functioning graft. Survival of the patient was defined as time from transplantation until death or last follow-up. Follow-up analysis of the study population ended January 4th, 2019.

Statistical analysis

Logistic regression models were used for comparison of DGF and fDGF; a multivariate model for longitudinal data for comparison of eGFR and proteinuria. Proteinuria models were fit on transformed

values (inverse hyperbolic sign) and results back-transformed to original scales and therefore differences are presented as ratios. Cox regressions were used for duration of post-transplant dialysis, graft loss and patient survival. For time-to-event analyses in which there are competing risks, cumulative incidence curves were used and results from Fine and Gray regression models are given in addition to Cox regression. Kaplan-Meier curves were created for patient survival. Survival analyses were limited to 5 years post-transplant as IGL-1 was introduced in 2014. Tukey adjustments for confidence intervals and p-values were used for pairwise comparisons.

In each of the models, the risk of bias in this retrospective study was reduced by using inverse probability of treatment weighting. Weights were based on propensity scores and obtained with an approach proposed by McCaffrey et al and variables used in the models were prespecified (19, 20) (Supplementary Appendix). Additionally, these variables were added as covariates in each of the models (double robust approach). Further, donor center was added as random effect. In the Fine and Gray models, adding donor center as a random effect was computationally unfeasible.

As IGL-1 was only introduced in 2014, a pre-specified sensitivity analysis of recipients receiving their kidney graft between January 1, 2010 and December 31, 2018 was performed using the same statistical approach.

All analyses were performed using SAS software, version 9.4 of the SAS System for Windows (SAS Institute Inc., Cary, USA). All reported p-values are two-sided.

Results

In the study period, 2015 single deceased-donor kidney transplants were performed. After exclusion of 72 cases with a different solution than IGL-1, UW, or HTK, 1943 transplants in 1868 patients were available for analysis (Table S1). Of these, 468 were re-transplantations. Table 1 presents donor and recipient characteristics. Imbalances in baseline characteristics were corrected after weighting, except a higher proportion of donations after controlled donated after circulatory death (DCD) remained in IGL-1 (Table S2). Median donor aortic flush volumes used were 5L (4-6) with IGL-1 (9 missing), 4L (2-4) with UW (37 missing), and 10L (8-10) with HTK (19 missing). The sensitivity analysis looked at 917 single deceased donor kidney transplants performed between 01/01/2010 and 31/12/2018 (Table S3). After weighting, the IGL-1 group of this cohort had recipients who were transplanted with a slightly shorter cold ischemia time and more HLA-mismatches (Table S4).

Primary non function

Unweighted incidence of primary non function was 0.9% (2/234) with IGL, 0.3% (3/1046) with UW, and 0.9% (6/663) with HTK ($p=0.21$). After weighting, these were 0.5%, 0.3%, and 0.7% ($p=0.41$), respectively. No multivariable analyses were performed because of low numbers. Sensitivity analysis showed similar results (data not shown).

Delayed graft function

Unweighted incidence of DGF was 17.1% with IGL-1, 16.3% with UW, and 24.6% with HTK ($p<0.001$). After weighting, these were 17.7%, 16.9%, and 23.2% ($p=0.02$), respectively. In multivariable analyses, these differences were not significant, neither without nor with additional correction for the considered confounders (Table 2). These results did not change when 7 patients transplanted pre-emptively (IGL-1: 2; UW: 2; HTK: 3) were excluded (data not shown). Unweighted incidence of this DGF, requiring at least 2 dialysis sessions, was 7.3% with IGL-1, 9.9% with UW, and 14.2% with HTK ($p=0.003$). After weighting, these were 7.8%, 10.4%, 13.3% ($p=0.11$), respectively. In multivariable analyses, these differences were not significant (Table 2). The sensitivity analysis showed similar results (Tables S5-S6). There is no evidence that preservation solution is an independent risk factor for DGF.

The median unweighted duration of post-transplant dialysis in patients with DGF was 2 (1-12) days with IGL-1, 9 (1-24) with UW, and 6 (1-18) with HTK. Multivariable analyses suggest IGL-1 is associated with shorter dialysis in main and sensitivity analysis, though the Cox estimates are not significant, the Fine&Gray estimates are (Table 2, S6-S8).

Unweighted incidence of fDGF was 42.9% with IGL-1, 29.6% with UW, and 35.0% with HTK ($p<0.001$). After weighting, these were 35.1%, 30.4%, and 33.3% ($p=0.44$), respectively. In multivariable analyses, these differences were not significant (Table 2). The sensitivity analysis showed similar results (Tables S5-S6). There is no evidence that preservation solution is an independent risk factor for fDGF.

Kidney graft function

Unweighted eGFR at 3 months was 41.7 mL/min/1.73m² (95% CI: 38.7-44.7) with IGL-1, 45.9 (95% CI: 44.0-47.7) with UW, and 43.9 (95% CI: 42.1-46.7) with HTK ($p=0.005$). After weighting, these were 45.8 (95% CI: 42.6-49.0), 45.4 (95% CI: 43.3-47.4), and 42.9 (95% CI: 40.9-44.9) ($p=0.04$), respectively.

At 1 year post-transplantation, unweighted eGFR with IGL-1, UW, and HTK was 46.7 mL/min/1.73m² (95% CI: 43.4 to 50.0), 50.6 (95% CI: 48.7 to 52.5), and 49.5 (95% CI: 47.6 to 51.4) ($p=0.05$), respectively. After weighting, these were 50.9 mL/min/1.73m² (95% CI: 47.4 to 54.4), 49.9 (95% CI: 47.8 to 52.0), and 48.5 (95% CI: 46.3 to 50.6) mL/min/1.73m² ($p=0.30$), respectively. There was no evidence that the differences

between the three solutions depended on the timepoint ($p=0.26$). Averaged over the two timepoints, differences were not significant (Table 2). The sensitivity analysis showed similar results (Tables S5-S6).

At 1-year post-transplantation, unweighted incidence of grafts with an $\text{eGFR} < 30 \text{ ml/min/1.73m}^2$ at 1-year post-transplantation with IGL-1, UW, and HTK was 18.7%, 12.6%, and 16.7%, ($p=0.02$), respectively. After weighting, these were 12.4%, 12.3%, 18.9% ($p=0.009$), respectively. There was no evidence that IGL-1 reduced the risk of a 1-year $\text{eGFR} < 30 \text{ ml/min/1.73m}^2$, however, UW was an independent protective factor compared to HTK (Table 2). The sensitivity analysis showed similar odd ratios though UW was no longer an independent protective factor compared to HTK (Tables S5-S6).

For patients with a functioning graft at 1-year post-transplantation, unweighted proteinuria was 0.21 g/24h (95% CI: 0.16 to 0.27) with IGL-1, 0.22 (95% CI: 0.19 to 0.23) with UW, and 0.25 (95% CI: 0.22 to 0.28) with HTK ($p=0.12$). Weighted concentrations were 0.21 g/24h (95% CI: 0.16 to 0.25) 0.22 (95% CI: 0.19 to 0.24), and 0.25 (95% CI: 0.22 to 0.27) ($p=0.18$), respectively. There is no evidence that preservation solution is an independent predictor of proteinuria at 1 year for grafts that are still functioning (Table 2). Sensitivity analysis showed similar results (Table S5-S6).

Acute rejection within three months of transplantation

Unweighted incidence of acute rejection was 22.2% with IGL-1, 24.9% with UW, and 24.4% with HTK ($p=0.70$). After weighting, these were 22.7%, 24.7%, and 24.6% ($p=0.87$), respectively. In multivariable analyses, these differences were not significant (Table 2). The sensitivity analysis showed similar results (Tables S5-S6).

Graft loss and patient survival

Overall graft loss rates at 1, 3, and 5 years were 4.9% (95% CI: 4.0 to 5.9), 8.0% (95%CI: 6.7 to 9.2), and 10.8% (95%CI: 9.3 to 12.2), respectively. Graft loss within 3 years was 6.5% (95% CI: 3.2 to 9.8), 7.2% (95% CI: 5.6 to 8.8), 9.2% (95% CI: 6.9 to 11.4), for IGL-1, UW and HTK respectively (Fig 1). When correcting for confounding variables, HTK was an independent risk factor for graft loss when compared to UW, with similar hazard ratios in the sensitivity analysis (Table 2, S9-S10). There is no evidence that IGL-1 is independently associated with graft loss.

Overall patient death rates at 1, 3, and 5 years were 3.5% (95% CI: 2.7 to 4.4), 8.2% (95% CI: 6.9 to 9.4), 13.9% (95% CI, 12.2 to 15.5), respectively. Patient survival was similar for patients who received a kidney preserved by IGL-1, UW, or HTK (**Error! Reference source not found.**). There is no evidence that

preservation solution was an independent risk factor patient death (Table 2). The sensitivity analysis showed similar results (Tables S6).

Discussion

In this single-center analysis, evaluating the post-transplant outcome of 1943 kidneys, preservation with IGL-1 results in equal outcomes compared to UW or HTK despite a higher proportion of DCD donors after weighting with IGL-1. In multivariable analysis, correcting for all considered potential confounders with the double robust approach, IGL-1 could not be identified as an independent factor determining the risk of DGF, fDGF, lower eGFR, lower proteinuria, acute rejection, graft loss or patient death. As far as we are aware, this is the first study to look at the effect of IGL-1 on all these outcome parameters. It contradicts the main finding of a very recently published French registry study. Legeai et al. report that IGL-1 was associated with the lowest risk of DGF compared to other preservation solutions, with no differences in 1-year eGFR and 1-year overall graft survival; functional DGF, acute rejection and proteinuria were not investigated.(21) Although our study included outcomes of 234 IGL-1 kidneys, it might be that any effect of IGL-1 remained hidden as DGF rates were relatively low. Unweighted incidences of DGF remained below 25% in all groups, with incidences <20% in IGL-1 and UW. This is considerably lower compared to the DGF-rates reported by Legeai et al (23.0% with IGL-1, 28.9% with UW, and 35.5% with HTK).(21) Although we do not have a clear explanation for these comparatively low DGF rates, it could be that the relatively low median cold ischemia times in our cohort compared to the cohort reported by Legeai et al. contributed. Also, compared to the wide range of DGF rates (13%-73%) reported in a systematic review and meta-analysis in which the effect of different preservation solutions on outcome after kidney transplantation was compared, the DGF rate in our study are on the lower end.(22). Additionally, as far as we are aware, this is the first study to compare IGL-1 with other preservation solutions outside of France and therefore in a different organ allocation region (i.e. Eurotransplant). Although we did correct for a random donor center effect, there might be differences in practice between the two allocation organisations that we could not correct for. The discrepancy might also be a consequence of the rigorous statistical methods used to maximally reduce the risk of bias in our retrospective study, as bias is also a relevant issue in registry analyses. Indeed, the strength of this retrospective cohort study lies with all efforts taken to reduce the risk of bias by using a double robust approach, consisting of inverse probability of treatment weighting and additional correction for confounders. A sensitivity analysis, analyzing transplants between 2010 and 2018, was performed to reduce any potential era-effect as IGL-1 was only introduced in 2014. This sensitivity analysis confirmed the results of the overall analysis and no important

differences in outcome between kidneys preserved in IGL-1, UW, or HTK could be found. However, this does not prove any equivalence between the three solutions. Ideally, a sensitivity analysis should have been done between 2014 and 2018, though this was not feasible as the number of subjects decreased too much. Therefore, bias by the era-effect is potentially not resolved by our statistical approach. Furthermore, although our statistical approach was optimized, potential bias inherent of a retrospective single center analysis remains.

The difficulty to show superiority of one kidney preservation solution over the other, especially regarding graft survival, is nicely illustrated by the ongoing debate whether UW is superior to HTK. While reported meta-analysis was not able to show superiority of one preservation solution over the other when considering the development of DGF (22), there is less clarity when considering graft loss. While randomized controlled trials (23, 24) showed no differences in graft survival rates – probably because they were underpowered – registry analyses do suggest superiority of UW over HTK.(2, 25) A United Network of Organ Sharing (UNOS)-registry analysis showed that the use of HTK is an independent risk factor for death-censored graft loss at 1 year as compared with UW solution (25), while analyses of Collaborative Transplant Study (CTS) data showed UW to result in improved graft survival up to 3 years after transplantation compared to HTK only if cold ischemia times were longer than 24 hours.(2) Similar findings were already reported by our center, suggesting that a short CIT makes it more difficult to unmask superiority of one preservation over the other.(26) The analyses comparing UW with HTK in our cohort are in line with registry data, showing a decreased risk of graft loss with UW compared to HTK, confirming the validity of this dataset.(2) Our analysis loses some power given that numbers at risk for graft loss in the IGL-1 group decreases rapidly over time compared to the UW and HTK groups.

As IGL-1 is used in multi-organ procurements, its effect on liver, pancreas, and intestinal grafts is important. The scarce literature shows IGL-1 is safe to store liver, pancreas, and intestinal grafts.(4, 13, 27-30) There is some suggestion that IGL-1 reduces ischemia-reperfusion injury in liver and pancreas transplantation.(28, 29)

In conclusion, this single-center study shows that IGL-1 can be safely used to preserve kidney grafts. More data are needed to elucidate whether IGL-1 is superior to UW or HTK. In the absence of sufficiently powered randomised trials, large cohort studies with appropriate design to reduce risk of bias and case-control studies would be helpful.

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Disclosure

The authors of this manuscript have conflicts of interest to disclose as described by the *American Journal of Transplantation*. Professor J. Pirenne, co-author of this paper holds a KU Leuven chair of the IGL company. The other authors have no conflicts of interest to disclose.

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Figure Legends

Fig 1 Cumulative incidence curve for graft loss of 1943 single deceased donor kidneys transplanted between 2000 and 2018 (unweighted), restricted to 3 years post-transplantation.

Fig 2 Kaplan-Meier curve for patient survival of 1943 recipients of single deceased donor kidneys transplanted between 2000 and 2018 (unweighted), restricted to 3 years post-transplantation.

Data Availability Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Supporting Information

Additional supporting information may be found online in the Supporting Information section at the end of the article.

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Tables

Table 1 Donor and recipient characteristics of 1943 single kidney transplants performed between 2000 and 2018.

Variable	IGL-1	UW	HTK	p-value
Number	234	1046	663	
Donor Characteristics				
Age (y)	56 (44-64)	48 (36-58)	51 (37-58)	<0.001
Gender, n (%)				0.71
Male	136 (58)	592 (57)	366 (55)	
Female	98 (42)	454 (43)	297 (45)	
Donor type; n (%)				<0.001
DBD	162 (69)	1010 (97)	484 (73)	
DCD	72 (31)	36 (3)	179 (27)	
Donor warm ischemia time (in DCD) (min)	14.5 (9.5-21.5)	15.0 (10.5-21.0)	14.0 (10.0-22.0)	0.94
History of arterial hypertension; n (%)	54 (24)	199 (20)	138 (29)	<0.001
Cause of death; n (%)				<0.001
Anoxia	61 (26)	90 (9)	102 (15)	
Cerebrovascular accident	107 (46)	527 (50)	358 (54)	
Trauma	36 (15)	234 (22)	95 (14)	
Other	30 (13)	195 (19)	108 (16)	
Last creatinine (mg/dL)	0.70 (0.58-0.87)	0.79 (0.62-1.00)	0.73 (0.59-0.94)	<0.001
Donor risk category; n (%)				<0.001
ECD	105 (45%)	297 (16%)	192 (29%)	
SCD	128 (55%)	733 (70%)	422 (64%)	
unknown	1 (0.4%)	16 (2%)	49 (7%)	
KDRI	1.32 (0.99-1.62)	1.09 (0.88-1.40)	1.16 (0.93-1.42)	<0.001
Recipient Characteristics				
Age (y)	61 (54-67)	56 (45-65)	56 (46-63)	<0.001
Gender, n (%)				0.35
Male	153 (65)	632 (60)	401 (60)	

Female	81 (35)	414 (40)	262 (40)	
Dialysis vintage (y)	2.8 (1.5-5.4)	3.1 (1.8-4.8)	3.4 (2.0-5.8)	0.004
Transplant Characteristics				
Re-transplantation, n (%)	30 (13)	305 (29)	133 (20)	<0.001
Number HLA-mismatches	3 (3-4)	3 (2-3)	3 (2-3)	<0.001
Cold ischemia time (h)	11.4 (7.6-15.2)	14.6 (11.8-17.9)	15.7 (12.9-18.5)	<0.001
Implantation time (min)	32 (28-36)	33 (30-38)	34 (30-39)	<0.001

Median (interquartile range) is given for continuous variables.

DBD, donation after brain death; DCD, donation after circulatory death; ECD, expanded criteria donor; HLA; human leukocyte antigen; KDRI, kidney donor risk index; SCD, standard criteria donor.

Table 2 Regression models for outcomes after transplantation of 1943 single kidneys between 2000 and 2018.

	IPTW		Double robust	
	Odds Ratio (95% CI)	p-value	Odds Ratio (95% CI)	p-value
Delayed graft function		0.07		0.09
IGL-1vs UW	1.10 (0.70 to 1.743)	0.86	1.15 (0.72 to 1.84)	0.77
IGL-1vs HTK	0.80 (0.49 to 1.32)	0.55	0.84 (0.50 to 1.40)	0.69
UW vs HTK	0.73 (0.52 to 1.01)	0.06	0.73 (0.52 to 1.02)	0.07
DGF, ≥2 dialysis sessions needed		0.19		0.30
IGL-1vs UW	0.77 (0.41 to 1.43)	0.58	0.81 (0.43;1.54)	0.73
IGL-1vs HTK	0.62 (0.32 to 1.20)	0.21	0.67 (0.34;1.32)	0.34
UW vs HTK	0.80 (0.54 to 1.19)	0.39	0.82 (0.55;1.23)	0.48
Functional DGF		0.25		0.34
IGL-1vs UW	1.24 (0.87 to 1.77)	0.34	1.25 (0.85 to 1.82)	0.36
IGL-1vs HTK	1.08 (0.74 to 1.58)	0.87	1.13 (0.76 to 1.68)	0.75
UW vs HTK	0.88 (0.68 to 1.13)	0.43	0.91 (0.70 to 1.18)	0.65
Acute rejection within 3 months		0.83		0.75
IGL-1vs UW	0.90 (0.60 to 1.35)	0.83	0.89 (0.58 to 1.35)	0.78
IGL-1vs HTK	0.93 (0.60 to 1.45)	0.92	0.94 (0.60 to 1.49)	0.95
UW vs HTK	1.03 (0.77 to 1.38)	0.96	1.06 (0.79 to 1.44)	0.88
	Difference (95% CI)	p-value	Difference (95% CI)	p-value
eGFR 3 months (CKD-EPI) (mL/min/1.73m²)		0.04		0.15
IGL-1vs UW	0.48 (-2.29 to 3.24)	1.00	0.27 (-2.27 to 2.82)	1.00
IGL-1vs HTK	3.00 (-0.12 to 6.13)	0.41	2.11 (-0.76 to 4.98)	0.70
UW vs HTK	2.53 (0.46 to 4.60)	0.16	1.83 (-0.11 to 3.78)	0.43
eGFR 1 year (CKD-EPI) (mL/min/1.73m²)		0.30		0.59
IGL-1vs UW	0.96 (-2.17 to 4.09)	0.99	0.82 (-2.01;3.64)	0.99
IGL-1vs HTK	2.43 (-1.05 to 5.90)	0.75	1.58 (-1.56;4.72)	0.92
UW vs HTK	1.47 (-0.76 to 3.70)	0.79	0.76 (-1.29;2.81)	0.98
Proteinuria at 1 year(g/24h)\$		0.11		0.08
IGL-1vs UW	0.99 (0.94 to 1.04)	0.94	1.00 (0.95 to 1.05)	1.00
IGL-1vs HTK	0.96 (0.91 to 1.01)	0.28	0.96 (0.91 to 1.02)	0.53
UW vs HTK	0.97 (0.94 to 1.00)	0.13	0.96 (0.93 to 1.00)	0.08

	Odds Ratio (95% CI)	p-value	Odds Ratio (95% CI)	p-value
eGFR < 30ml/min/1.73m² at 1 year		0.002		0.001
IGL-1vs UW	1.01 (0.56;1.84)	1.00	1.13 (0.59;2.15)	0.90
IGL-1vs HTK	0.62 (0.34;1.14)	0.15	0.66 (0.35;1.26)	0.29
UW vs HTK	0.61 (0.44;0.86)	0.002	0.58 (0.41;0.83)	0.001
	Hazard Ratio (95% CI)	p-value	Hazard Ratio (95% CI)	p-value
Duration of post-transplant dialysis in DGF*		0.03		0.08
IGL-1vs UW	1.63 (1.06 to 2.52)	0.02	1.54 (0.97 to 2.44)	0.07
IGL-1vs HTK	1.55 (0.99 to 2.41)	0.05	1.51 (0.94 to 2.42)	0.10
UW vs HTK	0.95 (0.70 to 1.28)	0.90	0.98 (0.72 to 1.33)	1.00
All cause graft loss		0.02		0.02
IGL-1vs UW	0.70 (0.30 to 1.62)	0.58	0.67 (0.27 to 1.66)	0.56
IGL-1vs HTK	0.48 (0.20 to 1.13)	0.11	0.45 (0.18 to 1.13)	0.10
UW vs HTK	0.68 (0.47 to 0.99)	0.04	0.66 (0.45 to 0.98)	0.040
Patient survival		0.09		0.07
IGL-1vs UW	0.33 (0.10 to 1.09)	0.08	0.37 (0.11 to 1.23)	0.13
IGL-1vs HTK	0.34 (0.10 to 1.13)	0.09	0.43 (0.13 to 1.44)	0.23
UW vs HTK	1.03 (0.82 to 1.29)	0.95	1.16 (0.89 to 1.51)	0.38

Results from regression models with inverse probability of treatment weighting (IPTW). Odds ratios, differences between mean values and hazard ratios were reported for the appropriate outcome measures. The double robust approach refers to the weighted analysis with all variables involved in the construction of the propensity-based weights added as confounders in the model. Tukey adjustments were used for the p-values of the pairwise comparisons.

* note that a hazard ratio > 1 denoted a shorter time on dialysis.

§ Subgroup analysis in patients with a functioning graft at 1 year; the difference is presented as a ratio because the data were transformed in the models

DGF, delayed graft function; eGFR; estimated glomerular filtration rate; HTK, histidine-tryptophan-ketoglutarate solution; IGL-1, Institut Georges Lopez-1 solution; UW, University of Wisconsin solution

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