Quantitative Fluorescence Angiography with Indocyanine Green for the Analysis of Ureterovesical Anastomosis Complications in Kidney Transplantation

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Abstract

Relevant issues following kidney transplantation include urine leakage and ureteral stenosis. There is currently no accepted definition of ureterovesical anastomosis issues following kidney transplantation. This study was created to show the quantitative Indocyanine Green (ICG) fluorescence angiography's prediction ability. 196 kidney transplantations were included in this bicentric historical cohort analysis, which was carried out between November 2015 and December 2019. In the context of donor, recipient, periprocedural, and postoperative features, the relationships between quantitative perfusion parameters of near-infrared fluorescence angiography with ICG and the occurrence of various grades of ureterovesical anastomosis problems were assessed. In 18% of cases, ureterovesical anastomosis problems followed the transplant. Three categories of complications have been established and graded. They had a connection to the length of time spent on dialysis (p = 0.0025), the kind of donor (p = 0.0404), and the quantity of postoperative dialysis sessions (p = 0.0173). In patients with complications, the median ICG ingress at the proximal ureteral third was 14.00 (5.00-33.00 AU) whereas in patients without issues, it was 23.50 (4.00-117.00 AU) (p = 0.0001, cutoff: 16 AU, sensitivity: 70%, specificity: 70%, AUC: 0.725, p = 0.0011). In order to allow for accurate comparisons between research, the recommended definition and grading of post-transplant ureterovesical anastomosis problems has been developed. ICG Fluorescence Angiography enables quantitative intraoperative evaluation of ureteral microperfusion after kidney transplantation and has the ability to foretell the likelihood of difficulties with ureterovesical anastomosis.

Keywords Near-infrared • Renal transplantation • Perfusion assessment

Introduction

The best option for treating end-stage renal illness is kidney transplantation. The majority of surgical transplant procedures are largely standardized, making them comparable across transplant centers and resulting in generally low complication rates. One approach that is continuously being improved upon is the anastomosis between the ureter and the bladder. Major urological problems such ureteral stenosis or urinary fistulas typically occur between 1% and 13% of the time. The routine use of ureteric stents is first: According to a recent Cochrane study, ureteric stent use can lower ureteric anastomosis complication rates from 7%-9% to roughly 1.5%. This improvement carries the risk of stent migration, bladder discomfort, and malpositioning, as well as growing infection rates. The second point is the surgical procedure used to implant the transplant ureter into the bladder: Different approaches, such as the "Taguchi" ureteroneocystostomy and the two most popular antireflux procedures, Politano-Leadbetter (PL) and Lich-Gregoir (LG), have been reported. Compared to antireflux procedures, Taguchi ureteroneocystostomy involves a smaller bladder incision and is simpler to carry out.

There is now insufficient data to support either the Taguchi or the LG methods, according to a systematic review comparing the two approaches. The majority of studies comparing the most widely used PL and LG techniques show that the LG approach is superior because shorter ureters can be employed, which reduces the risk of ischemia injury. This approach was found to have a decreased risk of urine leakage and hematuria in a meta-analysis. The European Association of Urology therefore recommends the LG method for kidney transplantation.

Malperfusion of the ureter during organ procurement is another problem that may result in ureteroneocystostomy problems. However, no standardized technique has yet been used to visualize ureter perfusion during the transplant surgery. Indocyanine Green (ICG)-based near-infrared fluorescence angiography is a new method for monitoring intraoperative perfusion following kidney transplantation. This method has been shown to allow intraoperative prediction of delayed graft function following kidney transplantation. Detection of early ureteral ischemia showed promising outcomes in a recently published study.

The purpose of this study was to evaluate the concept of ureteral malperfusion as a risk factor using the intraoperative results of ICG fluorescence angiography for the assessment of the graft ureteral microperfusion and to identify risk factors for post-transplant ureterovesical anastomosis complications retrospectively on the basis of a new clinical definition of this complication.

Surgical procedure and ICG fluorescence angiography

For preoperative diagnostics, organ sourcing, and the transplantation surgery, standard techniques were applied. Only surgeons with extensive kidney transplantation experience carried out the surgical procedures. Under sterile settings, a transurethral catheter was inserted into the bladder. The periureteral fat and blood arteries were preserved with great care throughout bench dissection.

Five minutes following reperfusion, the allograft underwent intraoperative ICG fluorescence angiography using the SPY Elite system (STRYKER, Kalamazoo, MI, USA). ICG was given intravenously in a single bolus at a normal dose of 0.02 mg/kg body weight (ICG-Pulsion, Pulsion Medical Systems AG, Munich, Germany, or Verdye, Diagnostic Green, Aschheim, Germany). As previously mentioned in detail, the assessments were carried out in accordance with a defined protocol under equivalent circulatory conditions in a shaded operating room to prevent interference from ambient light. In order to track the influx and outflow of ICG, 138 seconds of intraoperative films were taken. The kidney allograft and the ureter were both placed in a region of the camera field where they were at the proper distance from the camera head (25cm–35cm), with the help of the integrated laser targeting device, to enable later assessment of the perfusion. The graft ureter was shortened as much anatomically as possible after fluorescence angiography. Because the quantification was done postoperatively, the results of the perfusion analysis had no impact on the decision of the degree of ureteral shortening made during surgery.

The transplanted ureter was fitted with a double-J ureteric stent. The ureterovesical anastomosis was performed using the "Lich-Gregoir" method. The ureterovesical anastomosis was situated close to a surgical drain. At least five days were spent with transurethral catheters in place. Following the removal of the transurethral catheter, the surgical drain was taken out. Three weeks to four weeks following the transplant, the double-J ureteric stent was removed. In order to rule out allograft hydronephrosis, kidney allograft ultrasonography was performed on every

patient multiple times in the initial days following transplantation during postoperative surveillance on the IMC unit and at least once before discharge. Additionally, it was done in any patient who had issues urinating following surgery and after the ureteric stent was removed.

Analysis of fluorescence angiography video sequences and the ureteral perfusion

With the help of the integrated SPY-Q analysis tool-kit, the postoperative analysis of the fluorescence angiography recordings was done utilizing a grey scale of 256 different shades (SPY-Q, Stryker). The SPY-Q software's quantitative analysis defines "Ingress," "Ingress Rate," "Egress," and "Egress Rate" as the four microperfusion parameters. Prior investigations have detailed the analysis of cortical microperfusion of the kidney transplant and quantification. In a manner similar, quantitative evaluation of graft ureter microperfusion was carried out. In terms of the rise in fluorescence intensity per second, the ingress rate quantifies the intake (increase in grey stats per second). The rate at which blood leaves the body is known as the egress rate, and it is quantified by how much fluorescence intensity decreases each second. Egress is the difference between the maximum intensity and the end intensity, and ingress is the difference between the original baseline fluorescence intensity and the maximum intensity assessed. By choosing regions of interest, microperfusion was assessed independently for the kidney's top pole, middle section, and lower pole as well as for each third of the ureter (proximal/medial/distal) (ROI).

Grading of post-transplant ureterovesical anastomosis complications

Both the perioperative transplant and the patient's characteristics were evaluated. Up to a year following a kidney transplant, the ureter function was observed. As a result, all ureter revision operations following allograft transplantation were documented. The type of ureteral problem was divided into three categories (Grade A-C) based on clinical factors, as indicated in Table 1. If the intraoperatively implanted double-J stent was withdrawn within 4 weeks of transplantation without sonographic evidence of allograft hydronephrosis, a normal postoperative course (no ureteral complication) was attested.

Discussion

Urological issues frequently arise following kidney transplantation. The incidences in the most current literature range from 3.6% to 15.5%, but rates as high as 30% have been documented. When they occur in immunosuppressed patients, they are linked to meaningful morbidity, including consequences for short- and long-term graft survival and even a higher mortality risk. The findings of this investigation support the primary risk factors for post-transplant ureterovesical anastomosis difficulties following kidney transplantation as being ureteral malperfusion and the length of cold ischemia. Future implementation of intraoperative fluorescence angiography with ICG as a technique for identifying individual risk factors is possible. It is challenging to compare our findings with those from earlier research since there is no accepted definition of ureterovesical anastomosis issues following renal transplantation. The wide range of incidence rates reported in various trials also reflects this. The two most frequent subtypes of ureterovesical anastomosis problems are urine leakage/fistula and stenosis/stricture/obstruction. About 3% of cases of fistula or leakage are caused by stenosis. Similar management techniques for all subtypes include surgical revision in addition to ureteric stenting. Unspecific laboratory results, such as elevated serum creatinine, any event necessitating surgical revision or percutaneous nephrostomy, or the concomitant occurrence of symptomatic events and the need for intervention are signs of pertinent ureteral complications or they can be used to categorize the anatomic site of the lesion.

However, the vast majority of publications fail to include a definition at all. To the best of our knowledge, this is the first study to propose a uniform clinical definition of problems related to ureterovesical anastomosis following kidney transplantation. We categorize post-transplant ureterovesical anastomosis complications into three classes, according to the existing classifications of lymphatic issues following kidney transplantation. The severity grading is based on the invasiveness of the management strategies, specifically the requirement for prolonged ureteric stent placement (grade A), the requirement for antegrade (endo)urologic interventions, including percutaneous nephrostomy (grade B), and the requirement for additional operations (grade C).

According to our proposed definition, which includes all patients, even those with a little aberrant postoperative course, the total rate of ureterovesical anastomosis problems is 18%, which is relatively high in comparison to the earlier research stated above (grade A). In our analysis, there were 6% of serious problems (grade C), which is comparable to the findings of other studies that discuss the frequency of surgical revisions. In addition to technical errors, ureteral malperfusion is thought to be one of the primary pathogenic processes for all subtypes of problems. This condition might result in segmental ureteral stenosis or urine leakage because of necrosis or poor anastomotic repair. It has been technically challenging to evaluate ureteric perfusion objectively in order to directly support this notion, though. A developing technology for this purpose is fluorescence angiography, which satisfies the criteria for enabling in situ, real-time, noninvasive, quantitative tissue perfusion measurements without subjecting the patients to the pertinent adverse effects. According to a recently published study, ICG fluorescence angiography had a sensitivity of 100% and a specificity of 93% for the detection of ureteral ischemia. The study compared the results of intraoperative ureteral ICG perfusion assessment with the histopathological findings of 31 sections of dissected ureters. According to the scientists, only the proximal 14 cm of the ureters were able to sustain optimum perfusion. Our findings from intraoperative ureteral and allograft perfusion imaging demonstrate a considerable reduction in ICG fluorescence signal with ureteral length.

Additionally, we demonstrated that the ICG ingress in the proximal ureter demonstrates prognostic power for problems associated with ureterovesical anastomosis. Only the inflow parameters (ingress, ingress rate) seem to be representative for the ureteral perfusion analysis with ICG. This observation might be explained by the fact that venous drainage is still developing at this early stage (five minutes after reperfusion), especially at the distal portions of the ureter. The lower kidney pole's intensity of perfusion and the ureter were found to be correlated. Complications from ureterovesical anastomosis were independently predicted by the perfusion of the lower kidney pole. The ureteral vascularization hypothesis can be used to explain these data.

Therefore, it is best to refrain from performing extensive periureteric dissection in order to protect the arterial blood flow during harvesting and bench dissection. Our findings imply that graft ureters should be as short as possible while still allowing tension-free anastomosis to the bladder, despite the fact that ureteral length alone was unable to explain ureteral problems in earlier investigations.

In the current investigation, the variables postoperative dialysis requirement, type of donation, and time since dialysis initiation were linked to post-transplant ureteral problems. As previously demonstrated, prolonged dialysis can cause bladder atrophy, which raises the possibility of ureterovesical anastomosis difficulties. The male recipient gender, technical parameters, cold ischemia time, extended criteria donors, donor age, and delayed graft function have all been linked to an increased incidence of general postoperative urological problems following kidney transplantation. In contrast to other research, our patient group's vascular multiplicity did not affect the development of ureterovesical anastomosis issues, although this is likely because so few of the patients in this cohort had this trait. In the current investigation, significant ureterovesical anastomosis problems were linked to cold ischemia period (grade C).

Clinical practice may be impacted by the routine use of quantitative intraoperative fluorescence angiography during kidney transplantation. Before and after the completion of the ureterovesical anastomosis, the approach can be used as an objective intraoperative quality check of the kidney transplant and ureteral microperfusion. Before conducting the anastomosis, this approach would enable fluorescence-guided interventive decision-making on the ideal length of the ureter. If there is only minimal perfusion, ICG angiography can be repeated, allowing for additional shortening or lowering of tension once the anastomosis is complete. Although the feasibility of intraoperative decision-making was not assessed in this investigation, our results support the success of future prospective studies that make use of the standardized endpoint definition presented here. In the current investigation, we concentrated on the proximal ureteral microperfusion's ability to predict difficulties related to postoperative anastomosis. Our findings can be applied to situations where the transplant ureter cannot be further constrained anatomically during surgery. With the purpose of facilitating postoperative treatment, an individual risk prediction can be made in following circumstances based on the intraoperative perfusi-

-usion assessment: Prolonged ureteric stenting may be advantageous in preventing the manifestation of urinary leaks or stenosis in patients with a decreased intraoperative ICG ingress at the proximal ureter and/or the manifestation of additional risk factors, especially given that outpatient ureteric stent removal is a procedure that can be done safely. The validity of this study was limited by its retrospective nature. However, its architecture is suitable for risk analysis as well as for the adoption of a definition. Additionally, some potentially important risk factors for ureterovesical anastomosis complications, such as the impact of the surgeon's experience, the surgical technique for ureteral implant, and the influence of the preoperative bladder volume capacity, could not be assessed here due to the retrospective setup and the focus on perfusion assessment. It is advised that more research be done in order to prospectively validate the definition and evaluate the impact of all identified risk variables. The results of the ROC analysis conducted here demonstrate the predictive efficacy of ICG ingress for postoperative problems with a good AUC and a substantial p-value. These findings are clinically applicable since they can be used to assess individual risk early during surgery and provide postoperative care. However, only 70% of the threshold values were sensitive and particular. In order to alter the postoperative care of ureteral problems, they need be verified in additional prospective trials. The depth of near-infrared light's penetration limits the use of ICG fluorescence angiography. The best way to obtain ureteral transplants is with a layer of surrounding fatty tissue. Sometimes, this tissue can make fluorescence imaging challenging. This occurrence might have had an impact on the quantification results. Furthermore, the ureteral microcirculation would likely suffer from even a slight amount of anastomotic stress.

For quality assurance and to enable intraoperative decision-making, the SPY-Q quantification analysis may also be conducted. However, in the current investigation, there was no second perfusion assessment performed prior to anastomosis completion because it was outside the purview of this trial to evaluate ICG fluorescence as a tool for intraoperative decision making, but it might be used in future trials.

Conclusion

The uniform definition of post-transplant ureterovesical anastomosis complications that is being proposed should standardise the reporting of this complication while allowing comparison with the findings from various studies. This study further shows that ICG fluorescence angiography can be used in a safe manner to objectively document ureteral microperfusion quality during kidney transplant surgery during the course of the operation. In order to anticipate issues from ureterovesical anastomosis, this study is the first to provide threshold values for ICG ingress at the lower pole of the kidney and the proximal third of the ureter. The postoperative care of patients who have undergone kidney transplantation may be improved by using these findings for intraoperative quality control, decision-making, and individual postoperative risk stratification.

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