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APPLICATION OF INDOCYANINE GREEN FLUORESCENCE FOR URETER IMAGING: REVIEW

A.D. Smagulov[1], M.S. Rysmakhanov[1, 2], Zh.M. Koishybayev[1], Y.B. Sultangereyev[2], N.M. Mussin[1]

[1] West Kazakhstan Medical University, Aktobe, Kazakhstan

[2] Department of Surgery and Transplantation, Aktobe Medical Center, Aktobe, Kazakhstan

Introduction. Indocyanine green has been used in medicine for more than 70 years in cardio-thoracic surgery, hepatobiliary and colorectal surgery, urology, gynecology, transplantology, etc. This review based on literature dates describing the use of ICG for intraoperative imaging and evaluation of the ureteral perfusion. **Method.** The research searched in the electronic database PubMed, Scopus, Elsevier, Springer, and Web of Science between January 2000 and December 2020, using the following search terms: ICG imaging, ureteral vessels. Additional literature data identified from separately published sources. **Results.** There are 21 articles were obtained in the specified database: 9 – with intravenous ICG, 12 – with intraureteral administration. The use of intravenous ICG followed by next clinical situation: ureteral imaging is described for ureteral strictures, for isolation and preservation of the ureteral branch of the uterine artery during radical hysterectomy, for robotic radical cystectomy with ureteroenterostomy, for laparoscopic removal of ureteral endometriosis, for evaluation of ureteral perfusion during kidney transplantation, and for identification and prevention of ureteral damage during pelvic surgery in patients with colorectal tumors and gynecological pathologies. **Conclusions.** Both intravenous and intraureteral ICG imaging are safe, easy to perform, and easily reproducible. It allows objectively identifying the degree of perfusion of the ureteral wall, clearly determining the boundaries of the stricture. It is effectively helps in the prevention of ureteral wall damage in extraurinal surgical interventions.

Keywords: ICG, ICG fluorescence, ureter detection.

INTRODUCTION

Indocyanine green (ICG) has been used in clinical medicine for more than 70 years, when it was first used to assess cardiac and hepatic function [1–3]. ICG is a tricarbocyanine molecule with a half-life of 150–180 seconds, completely excreted into the bile by the liver [4]. The literature also describes the metabolism of ICG in the renal parenchyma, which occurs with the participation of the protein bilitranslocase [5]. Intravenous administration of ICG is non-toxic and effective at low doses [6]. It was also shown that ICG has an effective intraoperative contrast identifier in real time with the possibility of penetration into tissues up to 5 mm [7].

The first report on the use of ICG for perfusion evaluation of a kidney transplant was reported in 2004 [8]. In the future, this method was used to assess the blood flow of the renal parenchyma during partial nephrectomy, donor nephrectomy, and vascular anastomoses of the renal graft [9–12]. Although there are many reports on the use of ICG in urology, there are few studies on the visualization and assessment of the ureteral condition.

This review focuses on the current literature that describes the use of ICG to intraoperative visualize and evaluate the condition of the ureter.

To do this, a search was conducted for studies in the electronic database PubMed, Scopus, Elsevier, Springer and Web of Science in the period from January 2000 to December 2020, using the following search terms: «ICG imaging, ureteral». Additional literature data were identified from separately published sources. As a result, 21 articles were received in the specified database. Of these, 9 articles describe the use of ICG imaging of the ureter with intravenous administration, 12 – with intraureteral administration.

VISUALIZATION OF THE URETER DURING INTRAVENOUS ADMINISTRATION OF ICG

Sekijima M. et al. reported in 2004 on the use of intravenous ICG (IV-ICG) to visualize the urinary system in a kidney transplant recipient. This method made it possible to record and reproduce images of organ vessels in real time during the operation [8].

IV-ICG imaging has proven to be particularly useful in robotic surgery in cases of ureteral scar strictures. At

Corresponding author: Myltykbay Rysmakhanov. Address: 68, Maresyev str., 030019, Aktobe, Kazakhstan.
Phone: +77770365690. E-mail: transplantaktobe@gmail.com

the same time, it allows you to completely resect the scar-altered ureteral tissue and perform ureteral reimplantation with preserved perfusion. Marc A. Bjurlin et al. 42 robotic operations for the reconstruction of the upper urinary tract were performed using this technique. At the same time, perioperative complications occurred in 14.3% of cases. The authors of this study hypothesized that the use of NIRF imaging can prevent postoperative ureteral stricture, especially during repeated operations, and also helps to ensure adequate blood flow in the area of the urinary anastomosis [13]. Although the authors indicate a lack of clinical data for long-term follow-up.

In two cases report by Ying Long et al. successful isolation and preservation of the ureteral branch of the uterine artery during radical hysterectomy with IV-ICG angiography for cervical cancer was demonstrated [14]. This procedure prevents damage to the ureteral branch with subsequent ischemia of the distal ureter leading to its necrosis and stricture. During 4 months of follow-up of these patients, there were no complications associated with the ureter.

After a robotic radical cystectomy with urinary diversion (RCUD), a severe complication is the development of ureteral anastomosis stricture. Jim K. Shen et al. conducted a comparative study of patients who underwent ureteroenterostomy in two groups of n = 93 in each: with IV-ICG imaging of the ureter, and without IV-ICG [15]. In the group of patients with IV-ICG imaging with a median follow-up of 12.0 months, there was no complication from ureteroenterostomy. While in the group without IV-ICG imaging (median follow-up 24.3 months), the number of complications was 7.5% ($p = 0.01$). Thus, the use of the IV-ICG method of visualization of ureteral perfusion allowed to significantly reduce the frequency of ureteroenterostomy strictures.

Another study analyzed 345 cases of ureteroenterostomy during robot-assisted radical cystectomy, of which 89 cases used IV-ICG imaging to assess vascularization of the distal ureter [16]. According to the results of this study, there was a significant decrease in the frequency of ureteral anastomosis strictures from 10.6% to 0% after IV-ICG evaluation of vascularization of the distal ureter. This highlights the clinical significance of this strategy for minimizing the complications of robot-assisted radical cystectomy.

The use of IV-ICG imaging of ureteral blood flow in open radical cystectomy with urinary diversion Chirag P. Doshi et al. studied in a group of 31 patients with 62 ureteroenteroanastomoses [17]. In the group with IV-ICG, ureteroenteroanastomosis stricture was observed in 3.2% of cases, in the group without IV-ICG – 16.7%. This study also confirms a decrease in the frequency of formation of ureteroenteroanastomosis structures when using the IV-ICG imaging technique to assess vascularization of the distal ureter.

Diego Raimondo et al. in preliminary study was conducted in 23 women who underwent laparoscopic removal of ureteral endometriosis using ICG for intraoperative assessment of ureteral perfusion [18]. Intraoperative assessment of the degree of ureteral blood flow made it possible to optimally choose the tactics of further surgical approach after removal of the endometrioid noudle: Double J ureteral stenting – 3 patients, ureteral stenting – 2 patients. In the remaining 28 cases (90.3%), the blood flow was assessed as satisfactory (regular fluorescence) and did not require any intervention. NIR-ICG has proven to be a safe and feasible tool for assessing residual ureteral vascularization after conservative surgery for ureteral endometriosis.

Currently, there are two preliminary studies on the use of ICG to assess ureteral perfusion in kidney transplantation. In the study (preliminary experience) Vignolini G. et al. 6 recipients with robotic kidney transplantation from a living donor were included [19]. The second study, conducted by H. Boullenois et al., included 11 recipients, 10 of which were conducted from a cadaveric donor (Fig. 1) [20]. In both studies, the use of ICG visualization of ureteral perfusion did not take time, and allowed objective and reliable visualization of ureteral vascularization. However, the correlation between ICG fluorescence and postoperative complications could not be studied due to the small number of patients, which requires further larger studies studies.

VISUALIZATION OF THE URETER DURING INTRAURETHRAL ADMINISTRATION OF ICG

Recently, intraurethral administration of ICG (IU-ICG) has been used for diagnostic purposes. The first mention in the available literature of ICG imaging with intraurethral administration describes a series of 7 patients with ureteral stricture who underwent robot-assisted reconstructive surgery [21]. Subsequently, intraoperative IU-ICG imaging was used to identify various ureteral pathologies in a larger cohort (8 and 25) of patients (Fig. 2) [22–25]. IU-ICG imaging made it possible to quickly and accurately identify the ureter, localize the level of structure with less tissue damage and protect its blood supply, and the technique itself is safe and easy to perform. This technique has been successfully used in operations on pathological kidneys [25, 26, 27].

The IU-ICG technique has been successfully used to identify and prevent ureteral damage during pelvic surgery in patients with colorectal tumors and gynecological pathologies [28–32]. Intraureteral ICG imaging was effective for intraoperative identification of the ureter in complex gynecological and colorectal operations.

CONCLUSION

Thus, based on the described literature review, it can be concluded that ICG imaging (both intravenous and intraureteral) is safe, simple to perform and easily reproducible. It allows you to objectively identify both the degree of perfusion of the ureteral wall, and clearly determine the boundaries of the stricture. In case of extraurinary surgical interventions, such visualization effectively helps in the prevention of damage to the ureteral wall. Based on this, the use of ICG imaging in kidney transplant recipients will be the subject of our further study.

The authors declare no conflict of interest.

Fig. 1. Projection on a transplant diagram of an intraoperative image of indocyanin green fluorescence of a ureter in semiquantitative analysis: a – complete and intense fluorescence of the ureter except the last centimeters in favor of good vascularization; b – partial and weak fluorescence of the ureter in favor of weak and partial vascularization; c – zero fluorescence of the ureterand the lower pole of the transplant in favor of no vascularization of the ureter and the lower pole of the transplant. Illustration: H. Boullenois et al. 2020

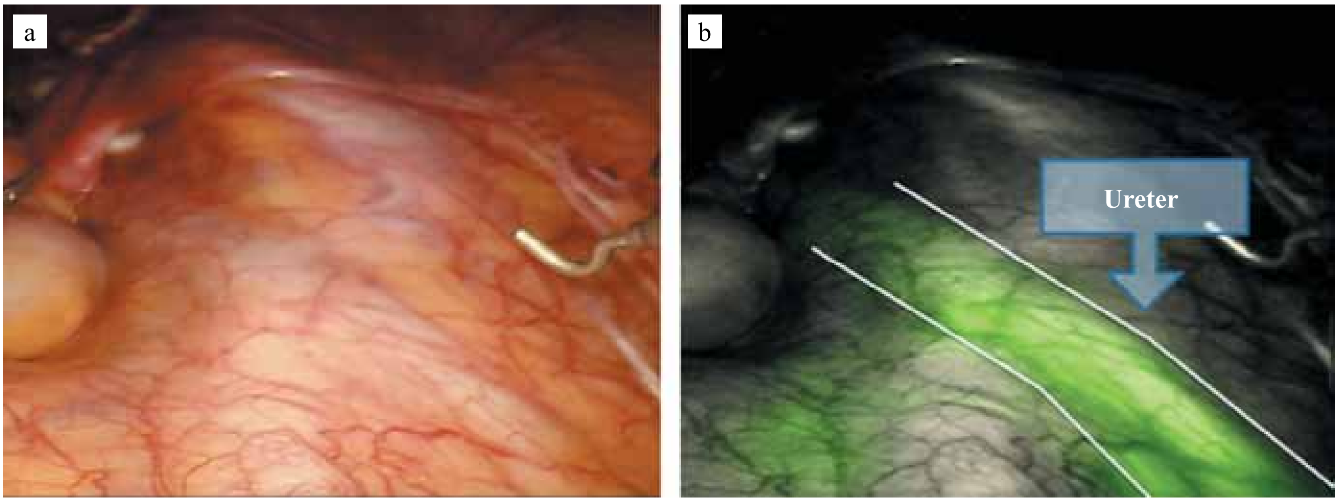

Fig. 2. Ureteral identification (a) in the absence of near-infrared fluorescence (NIRF) and (b) under NIRF. Reproduced with permission from Ziho Lee et al. 2015

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