

Indocyanine green angiography for preserving the ureteral branch of the uterine artery during radical hysterectomy

Two case report

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Abstract

Rationale: Conventional radical hysterectomy is frequently associated with postoperative ureteral ischemic necrosis, urinary fistula, stenosis, and kidney seeper. Some have suggested that preserving the ureteral branch during radical hysterectomy may reduce the incidence of ureteral complications. However, the feasibility of such preservation has not been explored using intraoperative imaging techniques.

Patient concerns: Two cervical cancer patients aged 45 and 53 years were selected to undergo surgery in our hospital in October 2017. Both patients showed normal function of major organs and no special treatment was deemed necessary based on their subjective symptoms and preoperative examination.

Diagnoses: Both patients were diagnosed with cervical cancer in stage Ib1 according to the staging scheme of the International Federation of Gynecology and Obstetrics (FIGO 2009).

Interventions: Two patients underwent ureteral branch-sparing radical hysterectomy. During surgery, indocyanine green (ICG) fluorescence angiography was used to identify the ureteral branch and evaluate perfusion of the uterine artery, its ureteral branch and the ureter.

Outcomes: The uterine artery and ureteral branch were clearly labeled by green fluorescence, as were the distal serous layer of the ureter and tissue supplied by the ureteral branch. During 4-month follow-up, neither patient suffered hydronephrosis, ureteral fistula or stricture.

Lessons: ICG angiography is a useful intraoperative imaging technique for identifying the ureteral branch and evaluating the branch-sparing surgery. Based on real-time angiography, sparing the ureteral branch can maintain blood supply to the ureter distal serous layer and neighboring tissues.

Abbreviations: CTA = computed tomography angiography, FIGO = International Federation of Gynecology and Obstetrics, ICG = indocyanine green, MRI = magnetic resonance imaging.

Keywords: ICG, imaging, sparing, the ureteral branch

1. Introduction

Conventional radical hysterectomy is the standard surgical procedure for treating early stage cervical cancer. The procedure involves removal of the uterus, upper part of the vagina, as well as

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nearly all uterosacral, cardinal, and uterovesical ligaments. The surgery involves cutting the uterine artery, separating the ureter tunnel, and performing radical parametrial resections. The procedure is frequently associated with postoperative insufficiency of ureteral blood supply and repair problems. This can lead to significant ureteral complications, such as postoperative ischemic necrosis, urinary fistula, stenosis and kidney seeper.^[1-3]

Some have suggested that the incidence of these complications can be reduced by preserving the ureteral branch of the uterine artery during radical hysterectomy.^[2,4] We are unaware of studies in which this approach is guided by intraoperative imaging techniques. Taking advantage of the recent use of indocyanine green (ICG) intraoperative imaging to assess uterine blood flow and perfusion,^[5] we decided to apply the same technique to ureteral branch-sparing radical hysterectomy. Here we describe 2 cases in which we observed, in real time, perfusion of the uterine artery, its ureteral branch and the ureter using ICG fluorescence angiography.

2. Case presentation

This report of 2 cases was approved by the Institutional Review Board of the Affiliated Tumor Hospital of Guangxi Medical

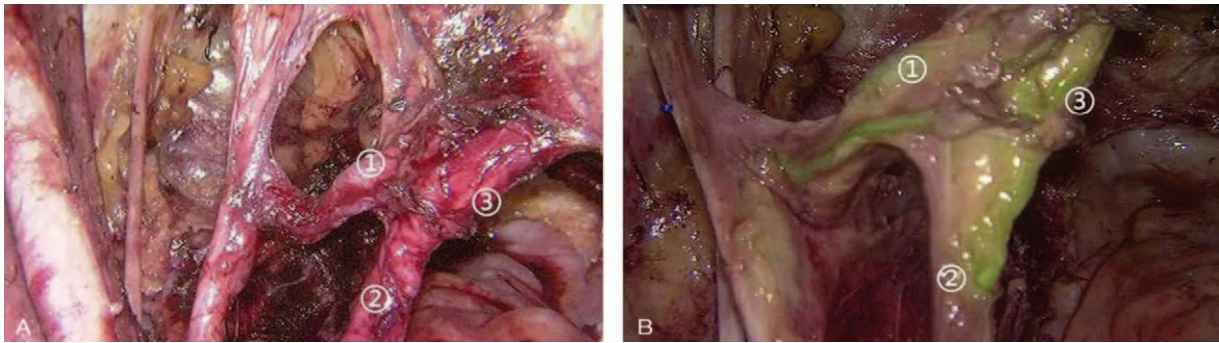


Figure 1. Representative images of one patient (A) before and (B) after ICG injection. ①, uterine artery; ②, ureter; ③, ureteral branch. ICG=indocyanine green.

University. Both patients gave informed consent for their cases to be published.

2.1. Patients

Two patients aged 45 and 53 years were diagnosed with cervical cancer in stage Ib1 according to the staging scheme of the International Federation of Gynecology and Obstetrics (FIGO 2009) and were selected to undergo ureteral branch-sparing radical hysterectomy in our hospital in October 2017. Both patients showed normal function of major organs and no special treatment was deemed necessary based on their subjective symptoms and preoperative examination.

2.2. Surgical methods

After pelvic lymphadenectomy, we identified the uterine artery at its origin by pulling the atresia of the umbilical artery, then we freed the uterine artery to the inside of the ureter. We divided the anterior leaf of the vesico-uterine ligament and pulled the uterine artery to reveal the ureteral branch. We cut the concomitant superficial uterine vein, and excised connective and adipose tissue around the artery. We isolated the ureteral branch of the uterine artery running cranially from the uterine artery to the ureter.

Since the ureteral branch runs from the uterine artery at the intersection of the uterine artery and ureter, we clamped and cut the uterine artery on the inside of the ureter. This procedure spared the ureteral branch. Pushing the ureter laterally from the cervix, we separated the uterus deep vein and cut it off. Subsequent surgical steps were those commonly practiced in conventional radical hysterectomy. A bipolar coagulation device and Harmonic 1 system (ERBE Elektromedizin, Germany) were used with both patients.

2.3. Intra-operative ICG fluorescence imaging

ICG (25 mg; Dandong Yichuang, Dandong, China) was mixed with 10 mL sterile water, and 3 mL of the dilution was injected intravenously into each patient. The dye was tracked intraoperatively in real time using an infrared fluorescence laparoscopic system (Endoscope Camera Fluorescent System; OptoMedic, Guangdong, China) in order to reveal blood flow in the uterine artery, the ureteral branch and the ureter. The fluorescent signals were processed by a digital video system and displayed on a TV monitor in real time.

ICG fluorescence peaked at 2 to 3 minutes after injection. The uterine artery and ureteral branch were clearly labeled by green

fluorescence, as were the distal serous layer of the ureter and tissue supplied by the ureteral branch. Representative images before and after ICG injection are shown in Figure 1A and B.

2.4. Follow-up

Patients were followed up for 4 months. Neither patient suffered hydronephrosis, ureteral fistula or stricture.

3. Discussion

Conventional radical hysterectomy involves ligating the uterine artery and veins and cutting them at their origin from the internal iliac artery. This stops blood perfusion from the ureteral branch of the uterine artery. In addition, dividing the ureter tunnel requires blindly inserting a clamp into the tissue around the ureter and clamping this tissue, which injures the serous layer of the distal ureter. This surgical procedure can lead to insufficient ureteral blood supply postoperatively. It can also lead to serious postoperative hydronephrosis and it can compromise ureter repair, leading to ureter fibrosis or even necrosis and fistula.^[1,2] To avoid these problems, a procedure to spare the ureteral branch of the uterine artery during radical hysterectomy was developed.^[2,4] However, this procedure requires further validation to demonstrate that clinicians can safely recognize the ureteral branch, which can be quite thin and easily damaged, and to confirm that sparing the ureteral branch can maintain blood supply to the ureter distal serous layer and neighboring tissues. We reasoned that we could achieve both objectives using real-time intraoperative imaging.

Computed tomography angiography (CTA)^[6] and magnetic resonance imaging (MRI)^[7] have been used to image uterine vessels and assess uterine perfusion after radical trachelectomy. CTA requires radiation, which raises safety and shielding issues, while MRI requires lengthy analysis. These disadvantages make both techniques less suitable for real-time intraoperative imaging. In addition, whether CTA or MRI can clearly resolve the quite thin ureteral branch is unclear.

Therefore we turned to ICG angiography, which detects fluorescence from the tri-carbocyanine dye ICG, which shows an absorption peak at 805 nm and a fluorescence emission peak at 835 nm. ICG binds to proteins in the plasma, and it glows green in the near-infrared spectrum when illuminated with light at 806 nm. ICG angiography is simple to perform without the need for radiation shielding, and the fluorescence images can be processed and displayed in real time during surgical procedures. It has already been used in gynecological oncology intraoperatively to

map sentinel lymph nodes^[8] and to detect tumor nodules or tumor scar tissues.^[9] It has also been used to analyze uterine perfusion during uterine artery-sparing radical trachelectomy.^[5]

The primary contraindication and side effect of ICG is allergic reaction. The dye is contraindicated for patients with history of iodine allergy, because the dye preparation contains a small amount of iodine. The dye should be used with care in patients with a history of severe allergy to penicillin and sulfa drugs, even though ICG does not show obvious cross-reaction with these drugs. We suggest the following selection criteria for ureteral branch-sparing radical hysterectomy guided by ICG angiography: stage Ib1-IIa2 disease, normal function of major organs, and no history of severe allergy to iodine or any drugs. The technique appears to be safe: neither of our cases showed any of the intra- or postoperative side effects that have been reported for surgical treatment of gynecological tumors.^[5,8–10]

The safety and efficacy of the intervention described here should be considered preliminary until the results from these 2 cases can be verified and extended in larger, prospective studies. We acknowledge that ICG angiography faces challenges when evaluating blood flow. The gold standard for measuring intraoperative blood flow in vascular anastomosis is Doppler ultrasonography, which can allow calculation of flow velocity and indices, but this technique is usually performed in large, straight arteries and veins. In contrast, most vessels of the female reproductive system are curved and slender. Future work should examine possibilities for real-time evaluation of blood flow during ureteral branch-sparing radical hysterectomy.

Our 2 cases demonstrate that ICG angiography can provide real-time images of the uterine artery, its ureteral branch, the ureter distal serous layer and tissue supplied by the ureteral branch. This imaging confirms that the ureteral branch is spared and that this preserves blood supply to the distal ureter. No ureter-related complications occurred in either patient during 4-month follow-up. We plan to verify and extend these findings in a larger clinical study.

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Author contributions

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Supervision: De-sheng Yao.

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References

- [1] Likic IS, Kadija S, Ladjevic NG, et al. Analysis of urologic complications after radical hysterectomy. *Am J Obstet Gynecol* 2008;199:644.e1–3.
- [2] Yoo S, Terai Y, Tanaka T, et al. Role of the two-point pull-up technique for treating the uterine arteries during radical hysterectomy and trachelectomy. *Eur J Obstet Gynecol Reprod Biol* 2013;170:544–9.
- [3] Fujii S, Takakura K, Matsumura N, et al. Precise anatomy of the vesico-uterine ligament for radical hysterectomy. *Gynecol Oncol* 2007;104:186–91.
- [4] Cai HB, Chen HZ, Zhang F, et al. [Clinical report of the modified Piver class III hysterectomy on invasive cervical cancer]. *Zhonghua Fu Chan Ke Za Zhi* 2010;45:511–4.
- [5] Escobar PF, Ramirez PT, Garcia ORE, et al. Utility of indocyanine green (ICG) intra-operative angiography to determine uterine vascular perfusion at the time of radical trachelectomy. *Gynecol Oncol* 2016;143:357–61.
- [6] Tang J, Li J, Wang S, et al. On what scale does it benefit the patients if uterine arteries were preserved during ART. *Gynecol Oncol* 2014;134:154–9.
- [7] Makino H, Kato H, Furui T, et al. Assessment of uterine enhancement rate after abdominal radical trachelectomy using dynamic contrast-enhanced magnetic resonance imaging. *Arch Gynecol Obstet* 2016;293:625–32.
- [8] Buda A, Bussi B, Di MG, et al. Sentinel lymph node mapping with near-infrared fluorescent imaging using indocyanine green: a new tool for laparoscopic platform in patients with endometrial and cervical cancer. *J Minim Invasive Gynecol* 2016;23:265–9.
- [9] Mery E, Jouve E, Guillermet S, et al. Intraoperative fluorescence imaging of peritoneal dissemination of ovarian carcinomas. A preclinical study. *Gynecol Oncol* 2011;122:155–62.
- [10] Veys I, Pop FC, Vankerckhove S, et al. ICG-fluorescence imaging for detection of peritoneal metastases and residual tumoral scars in locally advanced ovarian cancer: a pilot study. *J Surg Oncol* 2018;117:228–35.