JOURNAL OF LAPAROENDOSCOPIC & ADVANCED SURGICAL TECHNIQUES
Volume 00, Number 00, 2019

DOI: 10.1089/lap.2018.0624

Indocyanine Green Fluorescence Lymphography: A New Technique to Perform Lymphatic Sparing Laparoscopic Palomo Varicocelectomy in Children

Ciro Esposito, MD, PhD, Francesco Turrà, MD, Fulvia Del Conte, MD, Serena Izzo, MD, Francesca Gargiulo, MD, Alessandra Farina, MD, Giovanni Severino, MD, Mariapina Cerulo, MD, and Maria Escolino, MD

Abstract

Background: Laparoscopic Palomo varicocelectomy is one the most common approaches adopted to treat pediatric varicocele, but postoperative hydrocele still remains a potential problem with this procedure. This study aimed to evaluate the outcome of a new technique of lymphography using indocyanine green (ICG)-enhanced fluorescence to perform lymphatic sparing laparoscopic Palomo varicocelectomy.
Patients and Methods: The records of 25 patients who underwent laparoscopic left varicocelectomy in our unit from March 2017 to March 2018 were retrospectively evaluated. The average patients' age was 13.7 years (range 12–16). All patients had a high degree varicocele associated with left testicular hypotrophy and symptoms. All procedures were performed in laparoscopy using three trocars. After trocars' positioning, 2 mL of ICG solution was directly injected into the left testicle. Using ICG fluorescence, the lymphatic vessels were clearly identified and spared, and then the entire spermatic bundle was clipped and divided according to Palomo's principle.
Results: The average operative time was 18 minutes (range 10–25). No conversions to open surgery and no allergy or other adverse reactions induced by ICG were reported. At a maximum follow-up of 18 months, no recurrence of varicocele or postoperative hydrocele was recorded.
Conclusions: Our preliminary experience showed that ICG fluorescence lymphography is a safe and effective option to perform lymphatic sparing laparoscopic Palomo varicocelectomy in children and adolescents with high degree varicocele. The intratesticular injection of ICG and use of fluorescence vision allowed identification of lymphatic vessels in 100% of cases. No allergy to ICG or postoperative hydrocele was reported in our experience.

Keywords: varicocele, children, hydrocele, lymphography, indocyanine green, fluorescence

Introduction

Laparoscopic treatment of varicocele according to Palomo technique is probably one of the most common approaches adopted in children to treat high degree varicocele.[1,2] Palomo technique, according to the reports of the literature, gives excellent results in children, with success rates >95% but with a 20%–30% incidence of postoperative hydrocele, requiring redo surgery in most cases.[3–5] For this reason, in recent years, lymphatic sparing procedures have been applied for varicocele repair, to decrease the incidence of secondary hydrocele and ensure a better andrological outcome for children.[6–8]

In a recent article, we reported the standardization of lymphatic sparing Palomo technique using preoperative intradartoic/intratesticular injection of isosulfan blue.[9] This procedure gives excellent results with the only disadvantage that the patients' urines are blue/green for 2–3 days after surgery and the patients have a blue slick on the scrotum for about 1–2 weeks postoperatively.

Indocyanine green (ICG) has traditionally been used to assess liver function. In recent years, ICG fluorescence has been adopted in adults to perform angiography in case of tumors and to check the anomalies of biliary tract during laparoscopic cholecystectomy.[10,11] More recently, a novel method to measure human lymphatic pumping using a solution of ICG with fluorescence video control has been described.[12,13]

Use of ICG angiography has been reported in microsurgical subinguinal varicocelectomy in adult population, resulting in a

Pediatric Surgery Unit, ''Federico II'' University of Naples, Naples, Italy.

safer and quicker surgery.[14,15] To date, there are no reports in the international literature regarding application of this technique during laparoscopic varicocele repair in the pediatric population.

This study aimed to evaluate the outcome of ICG-enhanced fluorescence lymphography to perform lymphatic sparing laparoscopic Palomo varicocelectomy in pediatric patients.

Patients and Methods

We retrospectively reviewed the records of 25 patients, who underwent laparoscopic left Palomo varicocelectomy in our unit from March 2017 to March 2018. Patients' age ranged between 12 and 16 years (average 13.7 years). All patients had a high degree varicocele at clinical examination (Grade II or Grade III according to the Dubin clinical classification), all were symptomatic with left testicular pain or discomfort, and all had a left testicular hypotrophy defined as 20% volume or greater differential between testicles. All patients received preoperatively a testicular ultrasound (US) to assess the testicular volume and a testicular venous Doppler to assess the venous reflux.

Regarding the follow-up, all patients were seen 1 week postoperatively for surgical wound check. Clinical controls were performed thereafter at 1, 6, and 12 months after surgery, assessing for varicocele persistence or recurrence or development of new onset hydrocele. Testicular US was repeated when possible. The study received the appropriate Institute Review Board (IRB) approval at Federico II University of Naples.

Surgical technique

All the procedures were performed under general anesthesia with orotracheal intubation. Patients were placed in supine position with slight Trendelenburg and three trocars were always adopted. The first 5- or 10-mm trocar for the 0° optic was placed at umbilical level using open technique and thereafter other two 5-mm working trocars were placed under vision in triangulation with the optic port. After pneumoperitoneum induction, the posterior peritoneum covering the inner spermatic vessels (ISV) was opened performing a 2-cm T-shaped incision with the monopolar hook, at a distance of about 3–4 cm from the internal inguinal ring. After this step, a vial of ICG (5 mg/dL) was diluted with 10 mL of distilled water and only 2 mL of this solution was directly injected into the body of the left testicle using a 23G needle. Using the near-infrared mode, the lymphatic vessels appeared fluorescent and were clearly identified and spared; then the entire spermatic bundle was clipped and divided according to Palomo's principle (Fig. 1). Also using the standard white light mode, the lymphatics were clearly visible because they appeared green (Fig. 2). The ICG is commonly metabolized by the liver; for this reason, the patients' urine was normally colored after surgery and also the injection site on the scrotum presented no sign of the dye. The trocars orifices were closed using resorbable sutures, steri-strips or glue. All steps of the surgical procedure are reproduced in the Supplementary Video S1; Supplementary Data available online at www.liebertpub.com/lap.

Results

All the procedures were completed in laparoscopy with no conversion to open surgery or intraoperative complications. In 2/25 patients (8%), lysis of adhesions of colon covering the ISV was performed as additional procedure during the same surgery. The average operative time was 18 minutes (range 10–25 minutes). All procedures were performed by 1 senior surgeon. About 20–30 seconds after the intratesticular injection of ICG, the fluorescence of the lymphatics was clearly detected in 100% of the patients. The lymphatic vessels appeared fluorescent using the near-infrared mode (Fig. 1) and green using the standard white light mode (Fig. 2). In some patients, after a time interval of about 60 seconds from lymphatic visualization, also gonadal veins were observed using ICG fluorescence, although somewhat dully. In all patients, about two to three lymphatic vessels were identified and spared during the procedure. All patients restarted full oral feeding mean 2 hours postoperatively and the average analgesic requirement was 12 hours (range 8–28 hours). The average length of hospital stay was 36 hours (range 22–48 hours). No allergy or other adverse events induced by ICG were observed in our series. No patients in our series experienced any testicular pain secondary to the intratesticular injection, either early or late after surgery. At a maximum follow-up of 18 months, no recurrence or persistence of varicocele was recorded and no postoperative hydrocele was observed. One patient (4%) presented postoperatively umbilical port-site infection, treated with oral antibiotics and local therapy (II Clavien). All patients were highly satisfied with the postoperative cosmetic appearance of the umbilicus.

Discussion

Varicocele is a frequent pathology in pediatric population, with an incidence of $\sim$15%–20%[16] and is associated with testicular damage and subsequent testicular hypotrophy. Several reports stated that varicocele is related to sperm DNA disorders and male infertility, which are improved by surgical repair.[17–19] Three different surgical techniques have been described for the treatment of pediatric varicocele: high ligation (suprainguinal), microsurgical low ligation (subinguinal), and laparoscopy.[15] In recent years, several authors have reported the safety and efficacy of laparoscopy for the surgical correction of pediatric varicocele.[1,2]

Laparoscopic Palomo technique is the most common approach adopted in children.[1,16] According to the reports of the international literature, the laparoscopic Palomo procedure resulted in a significant decrease of the operative failure rate compared with the artery-sparing procedures, with no increase in the incidence of testicular hypotrophy/atrophy.[1,16] The main disadvantage reported with Palomo procedure was the high rate of postoperative hydrocele (10%–30%) since during this technique no attempt is made to preserve the lymphatic vessels that are difficult to identify, because they are similar to small veins.[3–5] Therefore, lymphatic sparing procedures have been applied for varicocele repair to decrease the incidence of postoperative hydrocele.[6–9] Different vital dyes have been applied to perform lymphography during lymphatic-sparing varicocelectomy, including methylene blue, patent V, or its isomer isosulfan blue.[19–23]

In a recent article, we reported the standardization of lymphatic sparing Palomo technique using preoperative intradartoic/intratesticular injection of isosulfan blue.[9] This procedure reported excellent results with a 0% rate of postoperative hydrocele.[9,16] No adverse event related to isosulfan blue injection such as orchitis, allergy, or anaphylactic shock was reported in our series.[9,16]

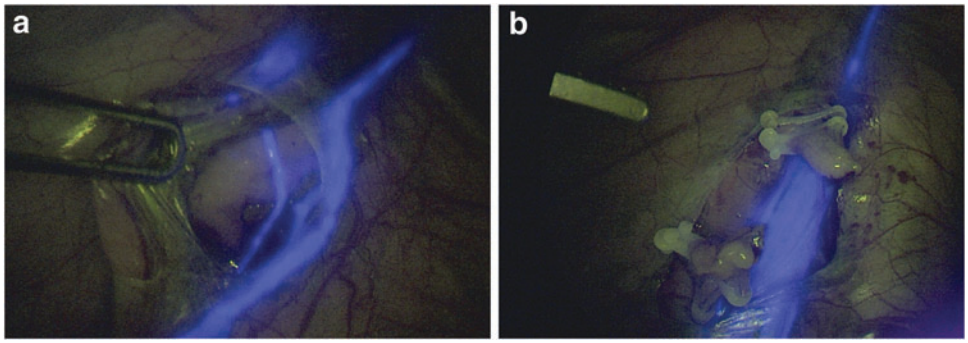

FIG. 1. After intratesticular ICG injection, lymphatic vessels appear fluorescent using the near-infrared mode, before **(a)** and after **(b)** spermatic vessels' division. ICG, indocyanine green.

In recent years, ICG-enhanced fluorescence has been introduced in laparoscopic surgery to improve visualization and provide detailed anatomical information during surgery.[24,25] The ICG dye can be injected into the human blood stream with practically no adverse effects.[12] ICG becomes fluorescent once excited with light of a specific wavelength in the near-infrared spectrum delivered by a Xenon light source.[26] After intravenous injection, ICG is rapidly bound to plasma proteins, especially lipoproteins. ICG is rapidly extracted unaltered through the liver and almost completely excreted without conjugation in bile about 8 minutes after injection.[12] Fluorescence can be detected using specific scopes and cameras and then transmitted to a video screen, thus enabling the observer to visualize areas of anatomical interest where the dye has accumulated (biliary ducts, vessels, and lymph nodes). For visualization of efferent lymphatic vessels, ICG is injected in the peritumoral area, commonly reaching the nearest draining lymph node within 15 minutes.[11] ICG-enhanced fluorescence imaging has been used in the past few years for improved visualization of the biliary duct system during laparoscopic cholecystectomy, intraoperative evaluation of lymphatic drainage, sentinel lymph node mapping in case of tumors, identification of vascular anatomy and for perfusion control of solid organs, colon, and rectum.[10–12,24–26] To date, no data about use of ICG to perform lymphography in pediatric patients affected by varicocele have been reported. We decided to adopt intratesticular injection of ICG to visualize lymphatic vessels during lymphatic-sparing laparoscopic Palomo varicocelectomy. We also standardized the technique of injection of ICG, as we already reported for isosulfan blue,[9] and we outlined the differences between the two vital dyes. The main difference is that isosulfan blue is metabolized by the kidney and consequently the urines appear blue for 1–2 days after surgery, whereas ICG is metabolized by the liver and the urines remain normal after surgery. Isosulfan blue injection leaves a blue slick on the scrotum for about 1–2 weeks postoperatively, whereas the scrotum appears normally colored after ICG injection.

After ICG injection, there are two modalities of visualization of lymphatics: they appear fluorescent using the near-infrared mode (Fig. 1), whereas they appear green at the standard white light mode (Fig. 2). Switching from standard white light mode to near-infrared mode is simply done through foot-pedal control. The onset of fluorescence of lymphatics is about 20–40 seconds after ICG injection, and the duration of fluorescence is about 15 minutes. In this way, it is sufficient a single injection to allow completion of the entire procedure with no loss of the fluorescence. In addition, the modality of administration of ICG, which is directly injected into the testicular parenchyma, is technically easier compared with the intradartoic/intratesticular injection previously described for isosulfan blue.

We also standardized the amount of product to be injected to optimize the visualization of lymphatics, as we already reported in the methods. As for disadvantages related to the use of ICG, special equipment, including a camera system that can be operated in dual mode for both white light and fluorescence imaging and an ICG laparoscope equipped with a special filter for optimal reproduction during INC-enhanced fluorescence and standard white light imaging, are needed in the operative theatre.

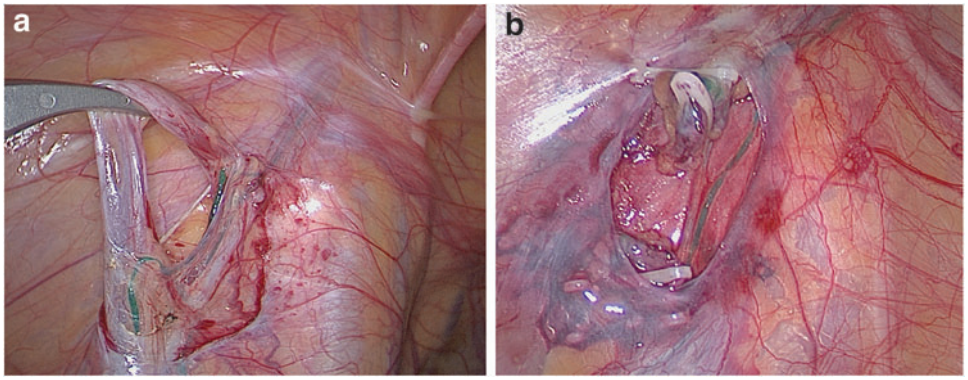

FIG. 2. After intratesticular ICG injection, lymphatic vessels appear green using the standard white light mode, before **(a)** and after **(b)** spermatic vessels' division. ICG, indocyanine green.

In conclusion, our preliminary experience showed that lymphatic sparing laparoscopic Palomo varicocelectomy using ICG fluorescence lymphography is a feasible and versatile technique to adopt for treatment of children and adolescents with varicocele. The intratesticular injection of ICG and use of fluorescence vision resulted in a safe and effective method, allowing identification of lymphatic vessels in 100% of cases in our series. In addition, no allergy to ICG or postoperative hydrocele was reported after a mid-term follow-up.

Disclosure Statement

No competing financial interests exist.

References

1. Parrilli A, Roberti A, Escolino M, Esposito C. Surgical approaches for varicocele in pediatric patient. Transl Pediatr 2016;5:227–232.
2. Borruto FA, Impellizzeri P, Antonuccio P, Finocchiaro A, Scalfari G, Arena F, Esposito C, Romeo C. Laparoscopic vs open varicocelectomy in children and adolescents: Review of the recent literature and meta-analysis. J Pediatr Surg 2010;45:2464–2469.
3. Esposito C, Valla JS, Najmaldin A, Shier F, Mattioli G, Savanelli A, Castagnetti M, McKinley G, Stayaert H, Settimi A, Jasonni V, Guys JM. Incidence and management of hydrocele following varicocele surgery in children. J Urol 2004;171:1271–1273.
4. Esposito C, Monguzzi G, Gonzalez-Sabin MA, Rubino R, Montinaro L, Papparella A, Esposito G, Settimi A, Mastroianni L, Zamparelli M, Sacco R, Amici G, Damiano R, Innaro N. Results and complications of laparoscopic surgery for pediatric varicocele. J Pediatr Surg 2001;36:767–769.
5. Nees SN, Glassberg KI. Observations on hydroceles following adolescent varicocelectomy. J Urol 2011;186:2402–2407.
6. Liang Z, Guo J, Zhang H, Yang C, Pu J, Mei H, Zheng L, Tong Q. Lymphatic sparing versus lymphatic non-sparing laparoscopic varicocelectomy in children and adolescents: A systematic review and meta-analysis. Eur J Pediatr Surg 2011;21:147–153.
7. Lisle R, Mahomed A. Lymphatic sparing laparoscopic Palomo varicocelectomy. J Pediatr Surg 2010;45:285.
8. Tong Q, Zheng L, Tang S, Du Z, Wu Z, Mei H, Ruan Q. Lymphatic sparing laparoscopic Palomo varicocelectomy for varicoceles in children: Intermediate results. J Pediatr Surg 2009;44:1509–1513.
9. Esposito C, Iaquinto M, Escolino M, Cortese G, De Pascale T, Chiarenza F, Cerulo M, Settimi A. Technical standardization of laparoscopic lymphatic sparing varicocelectomy in children using isosulfan blue. J Pediatr Surg 2014;49: 660–663.
10. Ishizawa T, Bandai Y, Ijichi M, Kaneko J, Hasegawa K, Kokudo N. Fluorescent cholangiography illuminating the biliary tree during laparoscopic cholecystectomy. Br J Surg 2010;97:1369–1377.
11. Tanaka E, Choi HS, Fujii H, Bawendi MG, Frangioni JV. Image-guided oncologic surgery using invisible light: Completed pre-clinical development for sentinel lymph node mapping. Ann Surg Oncol 2006;13:1671–1681.
12. Groenlund JH, Telinius N, Skov SN, Hjortdal V. A validation study of near-infrared fluorescence imaging of lymphatic vessels in humans. Lymphat Res Biol 2017;15:227–234.
13. Unno N, Nishiyama M, Suzuki M, Tanaka H, Yamamoto N, Sagara D, Mano Y, Konno H. A novel method of measuring human lymphatic pumping using indocyanine green fluorescence lymphography. J Vasc Surg 2010;52:946–952.
14. Cho CL, Ho KL, Chan WK, Chu RW, Law IC. Use of indocyanine green angiography in microsurgical subinguinal varicocelectomy—Lessons learned from our initial experience. Int Braz J Urol 2017;43:974–979.
15. Shibata Y, Kurihara S, Arai S, Kato H, Suzuki T, Miyazawa Y, Koike H, Ito K, Nakamura T, Suzuki K. Efficacy of indocyanine green angiography on microsurgical subinguinal varicocelectomy. J Invest Surg 2017;30:247–251.
16. Esposito C, Escolino M, Castagnetti M, Cerulo M, Settimi A, Cortese G, Turrà F, Iannazzone M, Izzo S, Servillo G. Two decades of experience with laparoscopic varicocele repair in children: Standardizing the technique. J Pediatr Urol 2018;14:10.e1–e10.e7.
17. Smit M, Romijn JC, Wildhagen MF, Veldhoven JL, Weber RF, Dohle GR. Decreased sperm DNA fragmentation after surgical varicocelectomy is associated with increased pregnancy rate. J Urol 2010;183:270–274.
18. La Vignera S, Condorelli R, Vicari E, D'Agata R, Calogero AE. Effects of varicocelectomy on sperm DNA fragmentation, mitochondrial function, chromatin condensation, and apoptosis. J Androl 2012;33:389–396.
19. Capolicchio JP, El-Sherbiny M, Brzezinski A, Eassa W, Jednak R. Dye-assisted lymphatic-sparing laparoscopic varicocelectomy in children. J Pediatr Urol 2013;9:33–37.
20. D'Alessio A, Piro E, Beretta F, Brugnoni M, Marinoni F, Abati L. Lymphatic preservation using methylene blue dye during varicocele surgery: A single-center retrospective study. J Pediatr Urol 2008;4:138–140.
21. Golebiewski A, Krolak M, Komasara L, Czauderna P. Dye-assisted lymph vessels sparing laparoscopic varicocelectomy. J Laparoendosc Adv Surg Tech A 2007;17:360–363.
22. Chiarenza SF, Giurin I, Costa L, Alicchio F, Carabaich A, De Pascale T, Settimi A, Esposito C. Blue patent lymphography prevents hydrocele after laparoscopic varicocelectomy: 10 years of experience. J Laparoendosc Adv Surg Tech A 2012;22:930–933.
23. Oswald J, Korner I, Riccabona M. The use of isosulphan blue to identify lymphatic vessels in high retroperitoneal ligation of adolescent varicocele-avoiding postoperative hydrocele. BJU Int 2001;87:502–504.
24. Schaafsma BE, Mieog JS, Hutteman M, van der Vorst JR, Kuppen PJ, Lowik CW, Frangioni JV, van de Velde CJ, Vahrmeijer AL. The clinical use of indocyanine green as a near-infrared fluorescent contrast agent for image-guided oncologic surgery. J Surg Oncol 2011;104:323–332.
25. Verbeek FP, Schaafsma BE, Tummers QR, van der Vorst JR, van der Made WJ, Baeten CI, Bonsing BA, Frangioni JV, van de Velde CJ, Vahrmeijer AL, Swijnenburg RJ. Optimization of near-infrared fluorescence cholangiography for open and laparoscopic surgery. Surg Endosc 2014;28:1076–1082.
26. Luo S, Zhang E, Su Y, Cheng T, Shi C. A review of NIR dyes in cancer targeting and imaging. Biomaterials 2011; 32:7127–7138.

Address correspondence to:
Ciro Esposito, MD, PhD
Pediatric Surgery Unit
''Federico II'' University of Naples
Via Pansini 5
Naples 80131
Italy

E-mail: ciroespo@unina.it