Use of indocyanine green angiography in microsurgical subinguinal varicocelectomy - lessons learned from our initial experience

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Abstract
Microsurgical subinguinal varicocelectomy (MSV) is generally considered the gold standard nowadays in view of the lower risk of complications and recurrence. To achieve complete ligation of veins while preserving testicular artery (TA) during the procedure remains challenging despite the application of high power optical magnification and micro-Doppler ultrasonography. The use of intraoperative indocyanine green angiography (ICGA) with infrared fluorescence operative microscope in MSV potentially lowers the incidence of TA injury and shortens the learning curve of novice surgeons. We present our initial experience in the application of the technique in nine patients and explore the potential of the new adjunct.

Keywords:
Varicocele; Microsurgery; Indocyanine Green

INTRODUCTION
Subinguinal microsurgical varicocelectomy (MSV) became the gold standard technique for varicocelectomy nowadays in view of the lower rate of recurrence and complications compared with open or laparoscopic techniques (1, 2). On one hand, subinguinal approach allows exposure of external spermatic and gubernacular veins and the lack of fascial incision results in less pain postoperatively. On the other hand, the more difficult dissection with a greater number of internal spermatic arteries and veins subinguinally (3) poses challenges to the operating surgeons. Injury to the testicular artery (TA) is a major complication of the procedure and a potential cause of testicular atrophy, but the incidence is unclear (4). It is believed that accidental arterial injury may go unnoticed and underreported particularly in non-microscopic varicocelectomy with inadequate optical magnification (5). Inspection of the cord for presence of arterial pulsations under high power magnification with irrigation of papaverine solution and the use of micro-Doppler (6, 7) are the most commonly adopted and effective means to locate the testicular artery (TA). However, the techniques require a certain level of experience and the result can be operator dependent. The application of indocyanine green angiography (ICGA) in MSV has been recently reported in the literature.
The objective images provided by ICGA potentially simplify TA localization and decrease the incidence of inadvertent TA injury.

**Surgical Technique**

Between September 2016 and January 2017, nine patients had unilateral MSV and ICG performed on left grade 2 to 3 varicoceles in our unit. Four of the nine patients suffered from infertility with abnormal semen parameters. Two patients who presented with incidental finding of grade 3 left varicocele and oligozoospermia preferred surgical intervention after counseling. One patient was operated on due to bothersome discomfort associated with left grade 3 varicocele. Two varicocelectomies in adolescents were performed in view of testicular size discrepancy.

The procedures were performed under general anesthesia. The infrared fluorescence operative microscope (Zeiss OPMI Pentero 900, Oberkochen, Germany) was brought into the field after incision of skin and spermatic fasciae. The vas deferens and its vessels were protected. ICGA was performed when the possible TA was identified. A pack of 25mg of indocyanine green (ICG) (Diagnogreen, Tokyo, Japan) was dissolved in 10mL of water. Each angiography required 5mL (12.5mg) of ICG solution which was prepared and administered by an anesthetist in a bolus via a peripheral line. The Infrared 800 mode of the microscope was activated and the fluorescence angiography was recorded and analyzed. ICGA was repeated if necessary and at the end of the procedure to confirm a successful TA preservation.

Testicular artery was clearly identified by ICGA in all patients (Figure-1). Two testicular arteries were visualized in one patient while a single TA was identified in the remaining eight cases. The maximal diameter of the TA identified was no more than 1mm. All TA were shown up within one minute upon injection of ICG with a mean time of 36.3 seconds. Cremasteric and deferential arteries were visualized during intraoperative ICGA in most of the patients (Figure-1). The real-time angiographic images could be recorded and analyzed with the assistance of the built-in computer program of the operating microscope (Figure-2). The data could...
Figure 2 - Built-in fluorescence modules of the operating microscope provided analysis of the vascular dynamics. 
A) Infrared 800 module demonstrates the relative intensity of indocyanine green signal. 
B) Flow 800 module illustrates the sequences the flow dynamics into a visual map. 
C) Interpretation of specific area on the angiographic image can be marked and 
D) Flow dynamic of each region can be illustrated in the form of curves.
be presented in different formats by comparing
the relative intensity and time to visualization of
each vessel.

All patients were discharged the same
day after the operation. No adverse reaction was
observed after injection of ICG. No clinical re-
currence and complication was recorded upon
follow-up at 4 weeks after the operation.

COMMENTS

The use of ICGA as an adjunct to MSV
seems a promising technique in our initial
experience. Localization of TA was achieved in all
patients. The technique repeatedly demonstrated
its ability in clearly identifying small TA of
less than 1mm diameter. It was applicable to
both adults and adolescents. ICGA is unique in
providing an objective real-time assessment and
images of arterial flow in the cord compared
to direct visualization of pulsation under high
power magnification and micro-Doppler. The
intraoperative pictures can be recorded and are
particularly useful for training and documentation

purposes. It may facilitate transfer of technique
to training surgeons and potentially shorten the
learning curve. The technique of ICGA is not
operator dependent and easy to administer with
minimal prior preparation. Each ICGA spent no
more than a few minutes and did not significantly
prolong the operating time. The high-contrast
images provided by the angiography allow
simple interpretation to most surgeons. ICG has
low toxicity with LD$_{50}$ of 50-80mg/kg in animals
(9). Confinement to the vascular compartment
through binding with plasma proteins and rapid
excretion via bile explained the safe nature of
ICG. The safety (10) and short plasma half-life of
ICG allows repeated ICG administration without
compromising the quality of images. Its use
was particularly valuable in patients with dense
adhesion among intermingled arteries and veins
(Figure-3). The adhesion rendered the identification
of TA difficult by damping the arterial pulsation.
The pulsation may appear weak and the exact
localization of a particular pulsating artery may be
difficult before the vessels were freely separated.
ICGA may be superior in this scenario since the

Figure 3 - Intraoperative indocyanine green angiography may facilitate early identification of testicular artery. A) Microscopic
view showing dense adhesions among intermingled artery and dilated veins which render the identification of arterial pulsation
extremely difficulty. B) Indocyanine green angiography showed a single testicular artery among the densely adhered vessels.
arterial flow is not obscured by adhesion among vessels. Small TA could be visualized before the adhesion was completely lysed. The whole course of TA across the operating field was shown up clearly most of the time. An earlier and more precise identification of TA during the procedure will reduce the risk of inadvertent arterial injury. Further comparative studies among the different strategies in TA preservation is required in delineating the potential advantages of ICGA in facilitating earlier TA identification and/or decreasing the risk of TA injury.

The recent advancement in fluorescence angiography lays in the analysis of ICG fluorescence dynamics. The built-in computer modules of the operating microscope provide data of flow dynamics of each vessel in the operating field. Although the significance of relative flow among testicular/deferential/cremasteric arteries in testicular blood supply is unknown, the demonstration of an intact collateral flow may be of importance in case of TA injury. An intact deferential and cremasteric supply may predict less probability of testicular atrophy and impairment of spermatogenesis after TA injury. In addition, ICGA may have a role in TA repair in case of accidental injury by localizing the abdominal end of the transected artery. The confirmation of intact deferential artery is preferred in the presence of prior groin or scrotal surgery when the status of the collateral supply is doubtful. The assessment of collateral arterial supply to the testes is not feasible with the technique of optical magnification and micro-Doppler.

The vascular anatomy and ICG dynamics illustrated by ICGA could be a research tool in better understanding the intraoperative microanatomy and physiology of varicocele. The information of microanatomy may further refine and decrease the complication of varicoceleectomy.

ICGA may prove to be a more cost effective than the use of other adjunct such as micro-Doppler. Although the set-up of an infrared fluorescence operative microscope is more costly compared to a micro-Doppler machine (USD $283,000 versus $11,600), the microscope can be shared among different specialties in the setting of a multi-disciplinary hospital. The running cost of ICGA is much lower than micro-Doppler for each procedure. A pack of 25mg Diagnogreen costs around USD $43 in our locality and usually one to two packs were consumed for each procedure while a disposable micro-Doppler probe costs USD $386.

In conclusion, the use of intraoperative ICGA is safe and consistently provides objective assessment of testicular artery. The technique facilitates early identification and preservation of TA, and may decrease the incidence of TA injury during MSV. ICGA is potentially superior to and provides additional information compared to the current technique of TA identification with direct visualization of pulsation under high power magnification and micro-Doppler.

CONFLICT OF INTEREST

None declared.

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