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Ileal pouch-anal anastomosis with fluorescence angiography: a case-matched study

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ABSTRACT:

Aim

An anastomotic leak in ileoanal pouch surgery may lead to pouch failure. Constructing a tension-free ileal pouch-anal anastomosis (IPAA) reduces this risk but can be technically challenging, balancing pouch vascularization with ileal mesenteric length and site of vessel ligation. Fluorescence angiography (FA) may help the clinician make a more balanced judgement.

Methods

Thirty-two patients undergoing minimally invasive completion proctectomy with FA guided-IPAA at two academic centres were matched and compared on a 1:1 basis to an historical group undergoing the same procedure without the use of this technique.

Results

Ligation of the ileocolic vessels (ICV) was safely performed in 15/32 (47%) with FA patients compared with 5/32 patients (16%) in historical controls. One patient underwent intraoperative IPAA reconstruction after FA detected ischaemia. No anastomotic leak occurred with FA but there was only one in the historical controls (P=0.31). Postoperative complication rate was similar between the two groups (P= 0.60).

Conclusion

FA is applicable to IPAA surgery and may help to reduce perfusion-related anastomotic leaks. A prospective randomized trial should be warranted.

KEY-WORDS: restorative proctocolectomy, fluorescence angiography, pouch surgery, Indocyanine green; ulcerative colitis; Familial Adenomatous Polyposis.

Originality statement:

To our knowledge, this is the first study to report the feasibility and potential value of fluorescence angiography in ileal pouch construction and the ileal pouch-anal anastomosis.

1. INTRODUCTION:

Restorative proctocolectomy with ileal pouch-anal anastomosis (IPAA) is standard surgery for patients with ulcerative colitis (UC) and familial adenomatous polyposis (FAP)(1,2.) Initially open, IPAA can be safely carried out using laparoscopic techniques, commonly multiport but in some centres as a double single-port trans-stomal and transanal procedure (3). Irrespective of the approach, restorative proctocolectomy is challenging and has a significant complication rate (4). A retrospective study of 3707 IPAA procedures reported pelvic sepsis in 6.4%, anastomotic leak in 4.8% and pouchitis in 33.9%. Early complications occurred in 33.5%, delayed complications in 29.1% and the mortality rate was 0.1% (5).

When it occurs, an anastomotic leak may necessitate radiological drainage or re-operation for sepsis and can compromise long-term pouch function (6). In some patients, pouch failure leads to excision and a permanent stoma.

Ileo-anal anastomotic dehiscence can occur if there is tension in the mesentery after the pouch has been delivered into the the pelvis. This can result in pouch hypoperfusion with acute or chronic ischaemia (7). Mesenteric lengthening manouevres to enable the pouch to reach the pelvic floor can

also impair vascularization (8). Even if the pouch remains viable and the anastomosis intact, chronic ischaemia is undesirable as it has been associated with the development of pouchitis (9).

There have been a number of reports in the colorectal literature in which fluorescein angiography (FA) and near infra-red angiography NIR have been used to study colonic vascular perfusion (10–13). A recent multicentre phase II trial used indocyanine green (ICG) and near-infrared angiography to assess vascular perfusion in the proximal limb reported a change in the level of the transection line in 5.8% of the cases (14). Studies suggest that this technology could be applied more generally to reduce ischaemia-related anastomotic leaks.

We have recently described the use of FA in IPAA (15). The aim of this study was to investigate the feasibility and the value of using FA while performing an IPAA, discussing in detail the technical steps of the procedure and possible pitfalls. Post-operative outcomes were compared to a case-matched historical cohort of patients undergoing IPAA without the use of FA.

2. METHODS:

This was a retrospective analysis of a prospectively maintained database of patients undergoing IPAA with the use of FA from December 2015 to September 2017 . The group was matched, on a 1:1 basis, with an historical cohort of patients undergoing an IPAA procedure without fluorescence between 2011 and 2015. Groups were matched on age and body mass index (BMI). Ethical approval was obtained from the local Research Ethics Committee. Participants gave written informed consent prior to surgery.

The following variables were analysed: underlying pathology (UC or FAP), presence of associated adenocarcinoma and surgical procedure (restorative proctocolectomy vs completion proctectomy). Restorative proctocolectomy with IPAA and loop ileostomy was defined as a 2-stage procedure. Completion proctectomy (following a prior total colectomy) with IPAA and loop ileostomy was

defined as a 3-stage procedure. Perioperative data, including operative time, conversion to open procedure and ileocolic vessels (ICV) ligation were collected. Postoperative data included length of stay (LoS), 90-day complications according to the Dindo-Clavien classification, readmission and reoperation (16).

Technical aspects of FA

Fluorescence assessment was carried out using the following equipment: PINPOINT endoscopic fluorescence imaging system (Stryker, Kalamazoo, MI, USA); Laparoscopic SPIES system (Karl Storz GmbH & Co. KG, Tuttlingen, Germany) and full high definition camera system (IMAGE 1 SPIESTM, Karl Storz), with xenon light source (D-LIGHT P SCB, Karl Storz).

The perfusion of the small bowel selected for pouch construction was assessed after vascular clamping as follows (figure 1). Twenty-five mg of indocyanine green (ICG) lyophilized powder (VERDYE, Diagnostic Green) was dissolved in 10 ml of water. A bolus of ICG equivalent to 0.2-0.1 mg/Kg was injected intravenously in accordance with manufacturer recommendations and ileal perfusion at the transection line confirmed by fluorescence uptake (visualized about 30 seconds after the injection and subjectively assess by the surgeon). (A second study was performed to verify the vascularization of the J- pouch. To construct the J-pouch, the ileum was folded into two portions of about 15 cm. A side-to-side anastomosis of the two portions of distal ileum was created, usually with 2 fires of a 100-mm linear stapler (ILA™ 100 Stapler, Medtronic Inc., MN, USA) or 3 fires of an Echelon 60mm blue (Ethicon, Sommerville NJ, USA) (figure 2). A 31mm (or 29mm) anvil was placed at the apex of the pouch. A double purse string end-to-end single stapling anastomosis, according to the transanal approach technique, was created with a circular stapler that was advanced through the anus. In the rest of the cases, when proctectomy was performed with transabdominal approach, the anastomosis was created by conventional double stapling technique or handsewn. The anastomosis was performed when the surgeon subjectively judged there was sufficient

fluorescein recorded in the pouch. A third ICG bolus was given enable pouchoscopy to assess the mucosal perfusion after the IPAA had been performed (with the same time-window described above)(figure 3).

Statistics Continuous non-parametric data were presented as mean and standard deviation, whereas nominal data were presented as percent frequency of occurrence. Categorical data were analysed with Fisher's exact test or $\chi 2$ test, continuous variables analysed using the Mann–Whitney–Wilcoxon test with $P< 0.05$ stastically significant. Analysis was performed using the Statistical Package for Social Science 17.0 (SPSS Inc., Chicago, Illinois, USA).

RESULTS

Between December 2015 and November 2017, 32 patients (21 male,11 female; mean age 39.4± 14.09 years) underwent FA-guided IPAA surgery. Twenty four patients had UC: most were uncomplicated but two had dysplasia and two had developed adenocarcinoma. The remaining eight patients had FAP. Twelve patients underwent a 2-stage approach. The remaining 20 patients had a completion proctectomy, IPAA and loop ileostomy after initial subtotal colectomy (3-stage procedure).

The historical group comprised 32 consecutive patients (17 male, 15 female; mean age 45.75 ± 15.9 years) undergoing IPAA between 2011 and 2015. 16 patients underwent minimally invasive surgery. Demographic and operative characteristics are summarized in table 1. Conversion to open surgery occurred in 4/32 cases in the FA-guided group (12.5%) and in 2/16 (12.5%) patients of the historical group (NS). Mean operative time (mins) was similar between the two groups (315±16 vs 351±18, P=0.14).

After visualizing the mesenteric blood flow using FA, ligation of the ICV was performed in 15/32 (47%) patients. In the historical group, fewer patients (5/32 (16%) underwent ICV ligation in order to achieve sufficient length for the pouch to reach the pelvis (P<0.05).

After IPAA had been performed,, FA was undertaken in all patients to assess the pouch mucosa transanally.. In one patient, a new ileal pouch was immediately constructed after FA detected partial pouch ischaemia (figure 4). This patient did not experience any postoperative complication.

Postoperative complications were similar in both arms of the study and are depicted in table 2. In the FA group, 6 patients had grade I complications (3 urinary retention, 3 superficial wound infection) 6 patients had grade 2 II complications (2 postoperative ileus managed conservatively, 2 altered stoma output, 1 extravasation of intravenous drugs, 1 pelvic collection treated conservatively with antibiotics) and one IIIb complication (52 yr male with FAP and an associated rectal pT2N0M1 carcinoma who went back to theatre for postoperative, intrabdominal bleeding but who incidentally had positive nodes in the ICV pedicle).

One anastomotic leak was observed in the historical group. There was none in the FA-guided group (p=0.31). The anastomotic leak occurred in a patient with a defunctioning ileostomy and was treated conservatively with antibiotics. In our study, there was no 30-day readmission.

LoS was similar between FA and historic controls (p =0.80).

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4. DISCUSSION:

There has been increasing interest in the use of ICG near-infrared fluorescence in colorectal surgery since it may have a role in evaluating bowel perfusion and directing the level of transection prior to performing a colorectal anastomosis (11). Along with our previous case report, this is the

first description of ICG near-infrared fluorescence to map the vascularization of the mesentery during IPAA surgery, especially after lengthening manoeuvres such as ICV ligation (15).

ICG fluorescence in pouch construction was feasible in all of the cases regardless of the surgical strategy (2- vs 3-stage procedures, minimally invasive vs. open procedure), Although more minimally invasive procedures (including single port) were performed in the FA IPAA group and took an average 36 minutes longer to perform than historic controls this did not reach statistical significance.

Absence of tension and sufficient perfusion play a crucial role in anastomotic healing, challenging and sometimes impossible to perform in patients with a short mesentery (17). Although it is our practice to carry out ligation of the ileocolic vessels to achieve a tension-free anastomosis, there are several other pouch lengthening surgical steps including the stepladder technique and ligation of the superior mesenteric pedicle (18,19). All of these procedures can perversely also put at risk the blood supply to the pouch. The main role of FA is to visualize mesenteric blood flow before and after ICV ligation and would be applicable if additional mesenteric lengthening manoeuvres were employed.

In our series, the use of ICG fluorescence led to a safe ligation of the ICV in 15/32 (47%) patients. Pouch perfusion was assessed after application of the vascular pedicle to rather than after be vessel transection. More patients in the FA group underwent ligation of ICV during pouch construction in comparison to the historical group. This difference may be because the surgeon was reassured that it was safe to do so, by virtu of FA assessment. Carrying out this manoeuvre did not significantly affect postoperative outcome.

FA can be used to assess the viability of a colorectal anastomosis at the time of surgery. Indeed, in a multicentre study assessing the FA in laparoscopic colorectal resection, the technique changed the operative strategy in 5.8% of patients (14). In our series, one patient in the FA group had a successful redo pouch after ischaemia was detected during the transanal (figure 4). Despite

this, there was still no difference in postoperative anastomotic complications between the two cohorts.

There are limitations to this study. It is a retrospective and case matched rather than randomized. The cohorts are relatively small. Despite the increasing use in colorectal surgery, the use of ICG for IPAA is still in its infancy. Our follow up is short and it remains to be seen if the technique might prevent long term complications such as pouchitis and stricture.

5. CONCLUSIONS:

Fluorescence ICG imaging is feasible in IPAA surgery and may guide the surgeon in selecting particular mesenteric lengthening procedures. Furthermore, the technique could reduce anastomotic leak rates by recognising pouch and anastomotic ischaemia at the time of surgery. Prospective randomized control studies are needed to provide more solid evidence.

Disclosure

Antonino Spinelli has acted as consultant or speaker for Ethicon, Olympus, Frankenman, Transenterix (not active), Tigenyx, Pfizer, Takeda, Sandoz.

Paulo Gustavo Kotze has been lecturer for Abbvie, Janssen, Pfizer and Takeda and is a member of the advisory board for Abbvie, Pfizer and Takeda.

Isacco Montroni, has served as instructor for Olympus Europe SE &co courses.

Michele Carvello, Marco Montorsi, Frederic Ris and Nicolas Buchs have nothing to disclose.

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Table 1: Demographics and operative characteristics. (UC: ulcerative colitis, FAP: familial adenomatous polyposis, IPAA: ileal pouch-anal anastomosis, BMI: body mass index, Dys: Dysplasia, CRC: colorectal cancer, ASA: American Society of Anesthesiologists, ICV: ileocolic vessels)

Patients characteristics	FA (n = 32)	Non FA (n = 32)	P value
Age, year, mean ± SD (Range)	39.41 ± 14.09 (29-49)	45.75 ± 15.9 (32-58.5)	NS
Female, n (%)	34.3% (11)	46.8% (15)	NS
BMI, kg/m^2, mean ± SD	22.16 ± 0.7	22.84 ± 0.52	NS
ASA grade, n (%)			NS
1- No disturbance	25% (8)	31.25% (10)	
2- Mild disturbance	71.87% (23)	65.62% (21)	
3- Severe disturbance	3.12% (1)	3.12% (1)	
4- Life threatening	-	-	
Diagnosis, n (%)			
Ulcerative colitis	62.5% (20)	71.87% (23)	
Ulcerative colitis and dysplasia/cancer	12.5% (4)	25% (8)	
Polyposis and cancer	25% (8)	3.12% (1)	
Institution	ICH (19) HUG (13)	ICH (32)	
Surgery Characteristics			
Surgical technique, n (%)			NS
2 stage	37.5% (12)	40.62% (13)	
3 stage	62.5% (20)	59.37% (19)	
Type of surgery, n (%)			
Open	-	50% (16)	
Multiport	65.62% (21)	40.62% (13)	
Singleport	34.37% (11)	9.37% (3)	
Conversion, n (%)	12.5% (4)	12.5% (2)	NS*

Ileocolic vessel ligation, n (%)	47% (15)	16% (5)	0.0442
Operative time, min, mean ± SD	315.2 ±16.52	351.3 ± 18.36	NS

* Statistical analysis performed only on patients treated by minimally invasive approach (multiport + singleport) (FA= 32; non FA= 16)

Table 2: postoperative outcomes

Post-operative outcome			
Length of stay, days, median (range)	6.5 (4-20)	8 (6-19)	NS
Post-operative complication, n (%)			
-None	59.37% (19)	68.75% (22)	NS
- Dindo Clavien I	18.75% (6)	15.62% (5)	
- Dindo Clavien II	18.75% (6)	9.37% (3)	
- Dindo Clavien III	-	6.25% (2)	
- Dindo Clavien IIIa	-	-	
- Dindo Clavien IIIb	3.12% (1)	-	
- Dindo Clavien IV	-	-	
- Dindo Clavien IVa	-	-	
- Dindo Clavien IVb	-	-	
- Dindo Clavien V	-	-	
Re-admission, n (%)	-	3.12% (1)	
Re-operation, n (%)	3.12% (1)	-	
Anastomotic leak	0	3.12% (1)	
Follow up time, months, median (range)	9.5 (1-43)	39.5 (5-80)	

Figure 1. ICG assessment of the small bowel loop designated for pouch construction after vascular ligations and elongation procedures.

Figure 2 Preserved vascularization assessed by ICG fluorescence during clamping (a) and division (b) of the ileocolic vessels

Figure 3. ICG assessment after pouch construction

Figure 4. Transanal ICG assessment of the anastomosis

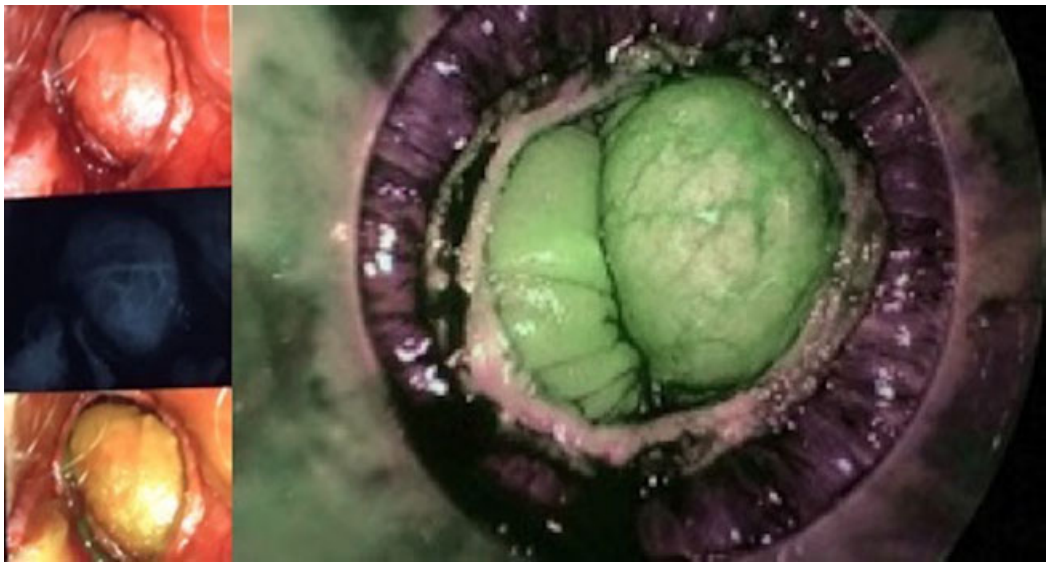

Figure 5. Sectorial ischemia of the IPAA detected intraoperatively