Fluorescence-based bowel anastomosis perfusion evaluation: results from the IHU-IRCAD-EAES EURO-FIGS registry

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Abstract

Background Anastomotic leakage (AL) is one of the dreaded complications following surgery in the digestive tract. Near-infrared fluorescence (NIRF) imaging is a means to intraoperatively visualize anastomotic perfusion, facilitating fluorescence image-guided surgery (FIGS) with the purpose to reduce the incidence of AL. The aim of this study was to analyze the current practices and results of NIRF imaging of the anastomosis in digestive tract surgery through the EURO-FIGS registry.

Methods Analysis of data prospectively collected by the registry members provided patient and procedural data along with the ICG dose, timing, and consequences of NIRF imaging. Among the included upper-GI, colorectal, and bariatric surgeries, subgroup analysis was performed to identify risk factors associated with complications.

Results A total of 1240 patients were included in the study. The included patients, 74.8% of whom were operated on for cancer, originated from 8 European countries and 30 hospitals. A total of 54 surgeons performed the procedures. In 83.8% of cases, a pre-anastomotic ICG dose was administered, and in 60.1% of cases, a post-anastomotic ICG dose was administered. A significant difference ($p < 0.001$) was found in the ICG dose given in the four pathology groups registered (range: 0.013–0.89 mg/kg) and a significant ($p < 0.001$) negative correlation was found between the ICG dose and BMI. In 27.3% of the procedures, the choice of the anastomotic level was guided by means of NIRF imaging which means that in these cases NIRF imaging changed the level of anastomosis which was first decided based on visual findings in conventional white light imaging. In 98.7% of the procedures, the use of ICG partly or strongly provided a sense of confidence about the anastomosis. A total of 133 complications occurred, without any statistical significance in the incidence of complications in the anastomoses, whether they were ICG-guided or not.

Conclusion The EURO-FIGS registry provides an insight into the current clinical practice across Europe with respect to NIRF imaging of anastomotic perfusion during digestive tract surgery.

Keywords Fluorescence-guided surgery · Near-infrared fluorescence imaging · Image-guided surgery · Registry

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Introduction

One of the most dreaded complications following surgery in the digestive tract is anastomotic leakage (AL), which has an incidence of up to 20% for esophageal surgery [1–3], 15% for gastric surgery [4–6], and up to 20% for colorectal surgery [7–10]. AL is a severe complication, associated with increased post-operative morbidity and mortality, resulting in prolonged hospital stay and extra costs. In the long term, there is an increased risk of worsened oncological and functional outcomes. Known risk factors for anastomotic leakage include smoking, adjuvant chemotherapy, male sex, chronic steroid use, preoperative weight loss, ASA (American Society of Anesthesiologists) score above 1, anastomosis location, and a prolonged operating time [11–14]. In spite of extensive research, the pathogenesis of AL is still not fully understood. It is hypothesized that an improved vascularization of the anastomosis will contribute to fewer anastomotic leaks [15, 16]. Near-infrared fluorescence (NIRF) imaging is a promising modality that is being explored as a mean to intraoperatively enhance the visualization of the esophageal, gastric or colorectal perfusion with the objective of possibly reducing the incidence of anastomotic leaks. In systematic reviews [17, 18], it was concluded that NIRF imaging for the assessment of bowel perfusion in colorectal resection surgery was feasible and easy-to-use, and based on the reports thus far, it holds great potential in the prevention of anastomotic leaks. However, at the moment, there is no definitive conclusion to support its routine use in gastrointestinal surgery [19].

In order to collect high-volume data, share experiences about the current practices of NIRF imaging across Europe and facilitate collaborations among surgical centers, a European registry on Fluorescence Image-Guided Surgery (EURO-FIGS: www.euro-figs.eu) has been launched. This registry is a collaboration between the Research Institute against Digestive Cancer (IRCAD, Strasbourg), the Institute of Image-Guided Surgery (IHU-Strasbourg), and the Technology Committee of the European Association of Endoscopic Surgery (EAES) and is funded by the Association for Cancer Research (ARC, France). At the moment, the registry is collecting data on the following: (I) near-infrared cholangiography of which the preliminary results were published in 2019 [20]; (II) anastomotic perfusion evaluation (III) fluorescence-based lymphography; data collection on additional clinical applications will be added soon.

In this manuscript, we present the current results of the data collection on NIRF anastomotic perfusion (NIRF-P) evaluation.

Methods

The registry

The EURO-FIGS registry (www.euro-figs.eu) is a secured online platform with the primary aim to allow an easy and centralized collection of safety and efficacy data of fluorescence guidance in various surgical applications. In this database, which is accessible to members only, cases performed using FIGS are collected anonymously and all registered data are provided with informed consent from patients, retrieved by the submitting institution. The use of this registry was approved by the University of Strasbourg and by the French authority protecting privacy, which reports to the French Data Protection Authority (CNIL: Commission Nationale de l'Informatique et des Libertés), under the reference number 2007309v0. Additionally, the registry is endorsed by the European Association for Endoscopic Surgery (EAES), which is one of the major leading surgical societies in Europe. Participants in the network of the principal investigator (MD) were invited to register their cases. Along with the invitation letter, participants received a consent form to be signed by patients whose data would be added to the registry. The consent form was originally prepared in English, Italian, and French. When required, the contributors translated it into the language of their country of practice.

Technology application

Given the descriptive, non-interventional, nature of the registry, surgeons were left free to use FIGS without technical restrictions. NIRF was performed after the i.v. bolus injection of ICG. The choice about timing, dosing, distance of the camera to the target organ and all other procedural steps as well as the fluorescence imaging equipment used depended on the preferences of the surgeon.

Data collection and analysis

Through a collection of multiple choice and open-ended questions (Appendix A), the participants were asked to register anonymized patient demographic data and procedure-related information as presented in Table 1. Descriptive statistics were used to analyze the data derived from the registry concerning overall cohort demographics, operative and technical details, and overall outcomes.

The complications collected were ileus, fever, signs of local or generalized peritonitis, fecal or purulent drainage from wound and/or drain, need of any post-operative radiological investigation (with: absence of radiological complications, perianastomotic abscess or fluid collection, perforation, post-operative ileus (air-fluid levels)). For these complications the management options for treatment that could be selected, were no need for treatment, non-surgical treatment or surgical treatment.

The definition used for ileus in this registry was specified as ''flatus/stool and oral diet tolerance not experienced until 3rd post-operative day'' [21].

Table 1 Descriptive data of the whole population and distribution according to pathology

Part AVariable	Overall ($n=1240$)	Esophageal cancer ($n=21$)	Gastric cancer ($n=45$)	Colorectal cancer ($n=861$)	Colic inflammatory disease ($n=169$)	Bariatric surgery ($n=129$)
Part A						
Age years—mean (SD)	64.5 (13.9)	64.7 (9.5)	64.5 (14.2)	68.3 (12.1)	59.7 (13.9)	46.4 (8.6)
BMI kg/m^2—mean (SD)	27.8 (6.8)	27.2 (6.4)	25.0 (4.2)	25.9 (4.0)	25.7 (4.1)	43.5 (4.3)
Gender						
Female	578 (46.6%)	4 (19.0%)	23 (51.1%)	372 (43.2%)	89 (52.7%)	83 (64.3%)
Male	662 (53.4%)	17 (81%)	22 (48.9%)	489 (56.8%)	80 (47.3%)	46 (35.7%)
Comorbidities						
No	412 (33.2%)	3 (14.3%)	27 (60.0%)	583 (67.7%)	88 (52.1%)	101 (78.3%)
Yes	828 (66.8%)	18 (85.7%)	18 (40.0%)	278 (32.3%)	81 (47.9%)	28 (21.7%)
Smoking						
No	1072 (86.5%)	12 (57.1%)	41 (91.1%)	759 (88.2%)	151 (89.3%)	97 (75.2%)
Yes	168 (13.5%)	9 (42.9%)	4 (8.9%)	102 (11.8%)	18 (10.7%)	32 (24.8%)
Atherosclerosis						
No	1157 (93.3%)	20 (95.2%)	44 (97.8%)	790 (91.8%)	161 (95.3%)	129 (100%)
Yes	83 (6.7%)	1 (4.8%)	1 (2.2%)	71 (8.2%)	8 (4.7%)	0 (0.0%)
Diabetes						
No	1022 (82.4%)	19 (90.5%)	39 (86.7%)	709 (82.3%)	161 (95.3%)	82 (63.6%)
Yes	218 (17.6%)	2 (9.5%)	6 (13.3%)	152 (17.7%)	8 (4.7%)	47 (36.4%)
Hypertension						
No	710 (57.3%)	6 (28.6%)	26 (57.8%)	471 (54.7%)	119 (70.4%)	77 (59.7%)
Yes	530 (42.7%)	15 (71.4%)	19 (42.2%)	390 (45.3%)	50 (29.6%)	52 (40.3%)
Other comorbidities						
No	963 (77.7%)	13 (61.9%)	35 (77.8%)	681 (79.1%)	141 (83.4%)	82 (63.6%)
Yes	277 (22.3%)	8 (38.1%)	10 (22.2%)	180 (20.9%)	28 (16.6%)	47 (36.4%)
Part B						
Anastomosis technique						
Manual	199 (16%)	4 (19.0%)	5 (11.1%)	107 (12.4%)	2 (1.2%)	78 (60.5%)
Stapled	1041 (84%)	17 (81.0%)	40 (88.9%)	754 (87.6%)	167 (98.8%)	51 (39.5%)
Anastomosis location						
Extracorporeal	219 (17.7%)	6 (28.6%)	10 (22.2%)	183 (21.3%)	13 (7.7%)	0 (0.0%)
Intracorporeal	1021 (82.3%)	15 (71.4%)	35 (77.8%)	678 (78.7%)	156 (92.3%)	129 (100%)
Anastomosis type						
Side to side	363 (29.3%)	7 (33.3%)	22 (48.9%)	301 (35.0%)	14 (8.3%)	18 (14.0%)
Side to end	131 (10.6%)	6 (28.6%)	2 (4.4%)	107 (12.4%)	14 (8.3%)	0 (0.0%)
End to side	100 (8.1%)	2 (9.5%)	20 (44.4%)	13 (1.5%)	5 (3.0%)	58 (45.0%)
End to end	635 (51.2%)	6 (28.6%)	1 (2.2%)	434 (50.4%)	136 (80.5%)	49 (38.0%)
Anastomosis evaluation						
Serosal in laparoscopic view	773 (62.3%)	14 (66.7%)	35 (77.8%)	501 (58.2%)	88 (52.1%)	129 (100%)
Serosal in open view	450 (36.3%)	6 (28.6%)	9 (20.0%)	346 (40.2%)	81 (47.9%)	0 (0.0%)
Mucosal intraluminally	17 (1.4%)	1 (4.8%)	1 (2.2%)	14 (1.6%)	0 (0.0%)	0 (0.0%)
Pre-anastomotic injection						
No	201 (16.2%)	2 (9.5%)	11 (24.4%)	63 (7.3%)	20 (11.8%)	104 (80.6%)
Yes	1039 (83.8%)	19 (90.5%)	34 (75.6%)	798 (92.7%)	149 (88.2%)	25 (19.4%)
Need for reinjection						
No	1212 (97.7%)	19 (90.5%)	42 (93.3%)	839 (97.4%)	168 (99.4%)	129 (100%)
Yes	28 (2.3%)	2 (9.5%)	3 (6.7%)	22 (2.6%)	1 (0.6%)	0 (0.0%)
Post-anastomotic injection						
No	495 (39.9%)	15 (71.4%)	27 (60.0%)	353 (41.0%)	63 (37.3%)	25 (19.4%)

Table 1 (continued)

Part AVariable	Overall ($n = 1240$)	Esophageal cancer ($n = 21$)	Gastric cancer ($n = 45$)	Colorectal cancer ($n = 861$)	Colic inflammatory disease ($n = 169$)	Bariatric surgery ($n = 129$)
Yes	745 (60.1%)	6 (28.6%)	18 (40.0%)	508 (59.0%)	106 (62.7%)	104 (80.6%)
Choice of the anastomotic level						
ICG unrelated	902 (72.7%)	19 (90.5%)	39 (86.7%)	580 (67.4%)	124 (73.4%)	127 (98.4%)
ICG-guided	338 (27.3%)	2 (9.5%)	6 (13.3%)	281 (32.6%)	45 (26.6%)	2 (1.6%)
Surgeons' sense of confidence						
No	10 (0.8%)	0 (0.0%)	10 (22.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Partial	122 (9.8%)	1 (4.8%)	2 (4.4%)	32 (3.7%)	10 (5.9%)	77 (59.7%)
High	626 (50.5%)	9 (42.9%)	20 (44.4%)	467 (54.2%)	93 (55.0%)	37 (28.7%)

A p value of < 0.05 was considered as being statistically significant. The correlation between complications and gender, comorbidities, type of pathology, anastomotic characteristics, neoadjuvant treatment, ICG injection characteristics, and surgeons' opinions were analyzed. A multivariate regression model was then created and only variables with a $p < 0.1$ at univariate analysis were included.

The GraphPad Prism software (GraphPad Software, Inc.) and SPSS software (IBM SPSS Statistics for Windows) were used to analyze and present the data.

Results

From March 2017 to January 2020, a total of 54 surgeons from 30 different hospitals across 8 European countries recorded NIRF-P data in the registry. A combined total of 1240 patients (578 women/662 men) with a mean age of 64.52 ± 13.95 years and a mean BMI of 27.77 ± 6.81 kg/m^2 (mean BMI 25.90 ± 4.1 kg/m^2 when excluding bariatric patients and BMI of 43.50 ± 4.3 kg/m^2 for bariatric patients) were registered (Table 1). The distribution of registered cases per country was as follows: Italy ($n = 832$), Spain ($n = 331$), Romania ($n = 27$), Switzerland ($n = 17$), Germany ($n = 13$), Slovenia ($n = 13$), Portugal ($n = 6$), and Greece ($n = 1$). The mean number of inclusions per center was 41 patients with a range of 1–197 (Fig. 1).

Indications for surgery

Out of 1240 patients, there were 927 cases of cancer (21 esophageal, 45 gastric, 861 colorectal), 169 cases of inflammatory disease (160 cases of diverticulitis, 9 cases of inflammatory bowel disease (IBD)), and 129 cases of patients who underwent bariatric surgery.

In the case of cancer, 127 patients received neoadjuvant chemoradiotherapy, 14 patients received only neoadjuvant radiotherapy, and 24 patients received only neoadjuvant chemotherapy. This makes a total of 141 patients receiving a form of neoadjuvant chemotherapy (with or without radiotherapy) and 151 patients receiving a form of neoadjuvant radiotherapy (with or without chemotherapy).

Colorectal resections were the most common procedures performed ($n = 1030$). In Table 2, a subdivision of the indications for colorectal surgery is provided.

Type of anastomosis

Considering the technical characteristics of the anastomosis, 1041 were mechanical and 199 were made manually. A total of 1021 anastomoses were created intracorporeally and 219 were created extracorporeally.

NIR cameras

Several models of NIR cameras were used: D-Light-P (KARL STORZ, Germany, $n = 741$), SPY (Stryker, USA, $n = 217$), Firefly (Intuitive Surgical, USA, $n = 179$), PINPOINT (Novadaq, Canada, $n = 65$), VISERA ELITE (Olympus, Japan, $n = 31$), Artemis Spectrum® (Quest Medical Imaging BV, The Netherlands, $n = 3$), and EleVision™ (Medtronic, USA, $n = 1$).

FIGS

The evaluation of perfusion was mainly performed from the serosal side of the bowel, 773 (62.3%) cases in laparoscopic view and 450 (36.3%) cases in open field view; 17 (1.4%) low colorectal anastomoses were evaluated intraluminally with NIRF assessment of the mucosa using the NIR laparoscope.

Surgeons reported that the level and creation of the anastomosis was guided by means of NIRF-P in 27.3% ($n = 338$) of cases.

Out of the 758 available answers, the use of ICG contributed to a full sense of confidence concerning the anastomotic perfusion in 626 cases (82.6%), only partial

Hospital ID	mean	SD	sample size	95% CI
1	0.280	0.044	5	[0.241; 0.319]
2	0.165	0.091	19	[0.124; 0.206]
3	0.300	0.000	95	
4	0.500	0.000	19	
5	0.095	0.012	17	[0.089; 0.101]
6	0.146	0.068	6	[0.092; 0.200]
7	0.228	0.107	35	[0.193; 0.263]
8	0.054	0.078	27	[0.025; 0.083]
9	0.300	0.000	6	
10	0.269	0.046	92	[0.260; 0.278]
11	0.167	0.143	93	[0.138; 0.196]
12	0.269	0.069	13	[0.231; 0.307]
13	0.197	0.083	88	[0.180; 0.214]
14	0.300	0.000	2	
15	0.274	0.069	20	[0.244; 0.304]
16	0.200	0.000	175	
17	0.200	0.000	5	
18	0.400	0.000	50	
19	0.148	0.049	13	[0.121; 0.175]
20	0.415	0.296	109	[0.359; 0.471]
21	0.250	0.122	6	[0.152; 0.348]
22	0.170	0.033	12	[0.151; 0.189]
23	0.172	0.025	18	[0.160; 0.184]
24	0.100	0.000	3	
25	0.060	0.000	1	
26	0.300	0.000	15	
27	0.262	0.074	8	[0.211; 0.313]
28	0.130	0.082	197	[0.119; 0.141]
29	0.200	0.000	13	
30	0.124	0.163	78	[0.066; 0.160]
Random effects model				**[0.162; 0.235]**
Prediction interval				**[0.029; 0.369]**

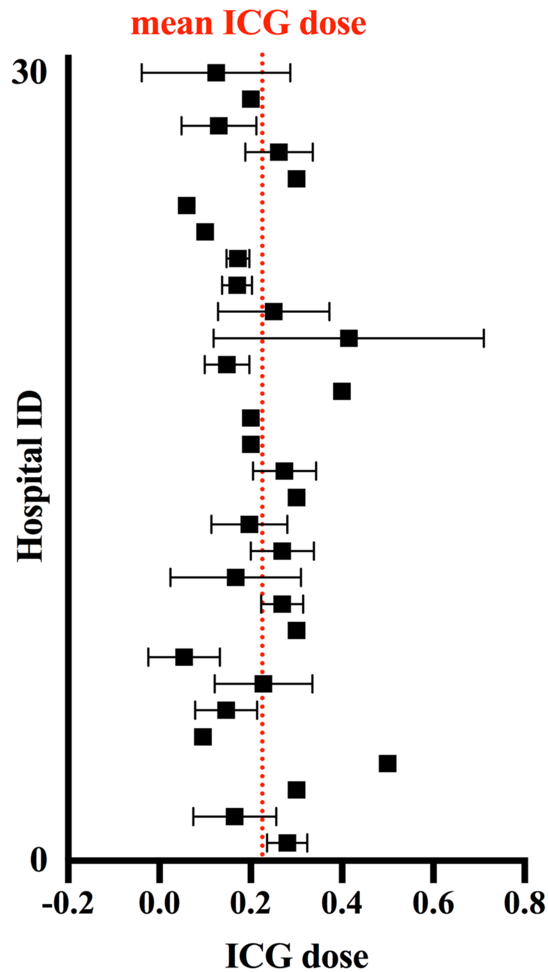

Fig. 1 Distribution of included cases and ICG dose per including center

Table 2 Colorectal resections subdivided into type and indication for surgery

Type of resection	Cancer	Inflammatory disease
Ileocecal resection	3	5
Right hemicolectomy	209	5
Extended right hemicolectomy	48	0
Transverse colon resection	38	0
Left hemicolectomy	159	50
Extended left hemicolectomy	15	0
Sigmoidectomy	63	96
High RAR (> 10 cm)[a]	108	7
Low RAR (5 > = 10 cm)[a]	135	1
Ultralow RAR (< = 5 cm)[a]	73	1
Total colectomy	5	1
Other	2	3

RAR radical anterior resection; missing data $n = 3$

[a]Distance given is measured from the anal verge

confidence in 122 cases (16.1%), and no confidence in 10 cases (1.3%). These data are included in Table 1.

A total of 1039 (99.9%) patients received ICG injection before anastomosis creation with 28 (2.2%) cases requiring a second ICG injection before anastomosis creation. A total of 745 (60.1%) ICG injections were performed after anastomosis creation.

ICG dose

The dose of ICG in the registered cases ranged from 0.013 to 0.89 mg/kg (Fig. 2).

A significant difference ($p < 0.001$) in the median dose of ICG was found for the different pathologies: a median dose of 0.2 mg/kg (IQR (interquartile range) 0.17) for cancer, 0.085 mg/kg (IQR 0.11) for morbid obesity, and 0.2 mg/kg (IQR 0.10) for inflammatory disease, respectively.

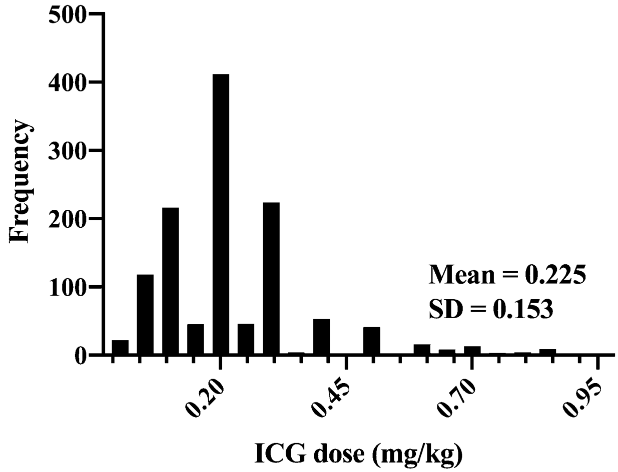

Fig. 2 Frequency of ICG doses used

Complications

No adverse events related to the administration of ICG were reported.

At univariate analysis, the cases with and cases without complications had a statistically significant difference ($p < 0.001$) in median age (71 (IQR 18) vs. 60 years (IQR 20)). The variables showing a p value < 0.1 are presented in Table 3.

For all registered cases, 133 patients (10.7%) had one or more complications including ileus ($n = 48$), fever ($n = 51$), peritonitis ($n = 32$), hemorrhagic anemia ($n = 12$), and fecal purulent drainage ($n = 3$ 7). To assess the need for treatment, we divided these complications according to the Clavien-Dindo classification [22]: Clavien-Dindo grade 1 (no need for treatment) ($n = 57$), Clavien-Dindo grade 2 (requiring medical intervention) and grade 3a (requiring surgical, endoscopic or radiological intervention not under general anesthesia) ($n = 58$), Clavien-Dindo grade 3b (requiring intervention under general anesthesia) ($n = 17$). For one complication, the Clavien-Dindo classification could not be scored due to missing information on the treatment. Although the majority of complications were found in the anastomosis group which was not ICG-guided, there was no statistically significant difference ($p = 0.958$) in the incidence of complications between the two groups (Table 4).

Esophageal cancer

Out of 21 surgical procedures in this subgroup, surgeons reported 15 (71.4%) procedures following the Ivor-Lewis technique and 6 (28.6%) procedures following the McKeown esophagectomy. No inferential statistics were performed due to the low number of cases and adverse events.

Table 3 Variables and their association with complications in all registered cases

Variables	Complications		No complications		*p*
	%	*n*	%	*n*	
Comorbidities					
No	75.9	101/133	65.7	727/1107	**0.018**
Yes	24.1	32/133	34.3	380/1107	
Type of pathology					
Cancer	86.8	112/129	74.4	815/1096	**< 0.001**
Morbid obesity	0	0/129	11.8	129/1096	
Inflammatory disease	13.2	17/129	13.9	152/1096	
Neoadjuvant radiotherapy					
No radiotherapy	79.7	106/133	89.7	993/1107	**0.001**
Use of radiotherapy	20.3	27/133	10.3	114/1107	
Neoadjuvant chemotherapy					
No chemotherapy	78.9	105/133	88.9	984/1107	**0.001**
Use of chemotherapy	21.1	28/133	11.1	123/1107	
Pre-anastomotic injection					
No	6	8/133	17.4	193/1107	**0.001**
Yes	94	125/133	82.6	914/1107	
Anastomosis					
Extracorporeal	23.3	31/133	17	188/1107	**0.071**
Intracorporeal	76.7	102/133	83	919/1107	

Bariatric surgery

Out of 129 surgical procedures in this subgroup, surgeons reported 124 Roux-en-Y gastric bypass procedures (96.1%) and 5 sleeve gastrectomies (3.9%). No inferential statistics were performed due to the low number of cases and adverse events.

Colorectal cancer

Surgeons reported 861 colorectal resections for cancer, which was the largest subgroup registered. At univariate

Table 4 Subdivision of registered cases guided by ICG vs. cases not guided by ICG, with respective complications according to the Clavien-Dindo classification

Complications	ICG guidance	No ICG guidance	*p*
No complications	302	806	0.958
Clavien-Dindo grade 1	19	38	
Clavien-Dindo grades 2-3a	14	44	
Clavien-Dindo grade 3b	3	14	
Total	338	902	

analysis, the difference among cases with and without complications had statistically significant associations with several variables listed in Table 5.

After selecting the associations with $p < 0.1$ listed in Table 5, a multivariate analysis was performed. The risk of complications was 57% lower in the absence of comorbidities ($p = 0.018$). The risk of complications was found to be 72% lower when the surgeon stated that they had a high sense of confidence concerning NIRF-P and the anastomosis in comparison to cases where the surgeon was only partially confident ($p = 0.002$). The predictive ability of this model is 87.2%.

We analyzed the variables associated with the need for ICG reinjection prior to the creation of the anastomosis in colorectal cancer cases. The variables independently associated with the need for reinjection included smoking, in which smokers had a fourfold higher probability of requiring a reinjection ($p = 0.013$). In cases where the choice of the anastomotic level was ICG-guided, the probability of a reinjection was found to be three times higher ($p = 0.048$). Finally, in cases where surgeons reported a high sense of confidence in the anastomosis, the probability of a reinjection was found to be 79% lower as compared to cases where the surgeon was only partially confident ($p = 0.019$). The predictive ability of this model is 96.8%.

Table 5 Variables and their association with complications in colorectal procedures for cancer

Variables	Complications		No complications		*p*
	%	*n*	%	*n*	
Gender					
Female	34	36/106	44.5	336/755	**0.040**
Male	66	70/106	55.5	419/755	
Comorbidities					
No	22.6	24/106	33.6	254/755	**0.023**
Yes	77.4	82/106	66.4	501/755	
Smoking					
No	81.1	86/106	89.1	673/755	**0.017**
Yes	18.9	20/106	10.9	82/755	
Neoadjuvant radiotherapy					
No radiotherapy	74.5	79/106	86.6	654/755	**0.001**
Use of radiotherapy	25.5	27/106	13.4	101/755	
Neoadjuvant chemotherapy					
No chemotherapy	74.5	79/106	87	657/755	**0.001**
Use of chemotherapy	25.5	27/106	13	98/755	
Surgeons' sense of confidence based on ICG					
Partial	15.6	10/64	5.1	22/435	**0.001**
High	84.4	54/64	94.9	413/435	
Anastomosis					
Manual	17.9	19/106	11.7	88/755	**0.067**
Stapled	82.1	87/106	88.3	667/755	

Colonic inflammatory diseases

In the subgroup of colonic inflammatory diseases, a total number of 160/169 cases of diverticulitis (94.7%) and 9/169 cases of inflammatory bowel disease (5.3%) were reported. At univariate analysis, the difference among cases with and without complications had statistically significant associations with the variables presented in Table 6.

After selecting the variables with $p < 0.1$, a multivariate analysis was performed. No variables independently associated with complications were found.

Gastric cancer

Out of 45 surgical procedures in this subgroup, surgeons reported 27 (60.0%) subtotal gastrectomies and 16 (35.6%) total gastrectomies. There were 2 cases (4.4%) of missing data.

At univariate analysis, the cases with and without complications had a statistically significant difference ($p = 0.014$) in median BMI (31.0 kg/m^2 (IR 7.9) vs. 24.5 kg/m^2 (IR 5.2)). In addition, the presence of comorbidities was significantly associated with a complicated outcome ($p = 0.032$).

Discussion

In the present study, the results of the EURO-FIGS registry on the use of FIGS during digestive tract surgery for the visualization of anastomotic perfusion are presented.

Table 6 Variables significantly associated with complications in colorectal resections for inflammatory disease

Variables	Complications		No complications		*p*
	%	*n*	%	*n*	
Anastomosis					
Manual	11.8	2/17	0	0/152	**< 0.001**
Stapled	88.2	15/17	100	152/152	
Extracorporeal	23.5	4/17	5.9	9/152	**0.01**
Intracorporeal	76.5	13/17	94.1	143/152	
Side to side	0	0/17	9.2	14/152	**0.003**
Side to end	5.9	1/17	8.6	13/152	
End to side	17.6	3/17	1.3	2/152	
End to end	76.5	13/17	81.2	123/152	
Surgeons' sense of confidence					
Partial	30	3/10	7.5	7/93	**0.023**
High	70	7/10	92.5	86/93	

The importance of the existence of a registry such as the EURO-FIGS is mostly in the possibility to exchange experiences in the international network that could help to rapidly collect large volumes of data. These can be used to draw conclusions beneficial to the clinical practice and reach consensus. Analysis of this registry has provided several insights into the current use of NIRF for anastomosis evaluation.

In the registered cases, 84% of patients with an anastomosis underwent a stapled anastomosis and the remaining patients had a hand-sewn anastomosis. These findings are in line with the findings of the European Society of Coloproctology (ESCP) international snapshot audit of left colon, sigmoid, and rectal resections, which was performed recently [8]. The surgical procedures were performed by 54 surgeons from 30 centers in eight different countries.

A total of 1039 patients received a pre-anastomotic ICG injection with subsequent NIRF-P, and only 28 required a reinjection. In 745 cases, an ICG injection was performed after the creation of the anastomosis, to check its vascularization even if the resection lines were decided independently. As a result, in the majority of cases, both a pre- and post-anastomotic injection was considered necessary to evaluate anastomotic perfusion. Additionally, surgeons reported that the anastomosis level and creation was guided by means of NIRF-P in 27.3% of cases ($n=338$). Out of the 758 answers available, surgeons stated that FIGS provided a full sense of confidence concerning anastomotic perfusion in 626 cases, only partial confidence in 122 cases, and no confidence in only ten cases. These findings highlight the perceived role of NIRF-P in the current clinical practice in which NIRF-P is considered beneficial in a considerable number of cases.

Overall, in > 60% of cases and in 84% of complicated colorectal cases, surgeons stated they had a partial to high sense of confidence in their anastomosis after NIRF-P. Paradoxically, although the risk of complications was lower in cases where surgeons reported to have a high sense of confidence in the anastomosis, a considerable number of complications were still found in this subgroup. This underlines the subjectivity of the appraisal of fluorescence imaging, which can be deceptive as the surgeon's clinical evaluation has a low predictive accuracy for anastomotic leakage [23]. Although NIRF-P has shown promising results in various studies [17, 18, 24–27], the absence of a validated and widely used quantification method for the fluorescence signal is one of the main issues to be solved before understanding the real impact of this technique on anastomotic complications. In this registry, perfusion was evaluated in a static fashion, which is based on fluorescence intensity, without considering the diffusion of ICG in the tissue over time. This may result in an overestimation of perfusion, which may potentially lead to the creation of an anastomosis in a less perfused area than assumed, based on visual findings. For instance, NIRF-P in the assessment of gastric conduit perfusion in esophageal surgery has been used for both qualitative analysis and for quantitative measures, based on the time of perfusion. Kumagai et al. [28] demonstrated that blood flow in the reconstructed gastric tube is sufficient if the anastomosis is made in the area where NIRF-P demonstrates perfusion within 60 s after ICG dye administration. A quantitative approach to assess bowel perfusion was demonstrated by several studies such as the fluorescence-based enhanced reality (FLER) approach [29–36]. FLER is a fluorescence videography technique, which integrates NIRF imaging and a specific software which generates a virtual perfusion cartogram based on time-to-peak (TTP) fluorescence. The TTP is a measure for the time required to reach a peak in the FI of a certain region of interest. The perfusion cartography can be superimposed onto real-time images and help the surgeon define the exact location of a well-perfused anastomosis. The feasibility and accuracy in the clinical setting has been recently demonstrated [37].

We found a large variability in the ICG dose administered (range: 0.013–0.89 mg/kg) and a statistically significant difference in the median dose of ICG for the different pathology groups was defined in this registry. A mean dose of 0.2 mg/kg was used in cancer and inflammatory disease surgery, while a mean dose of 0.085 mg/kg is used in bariatric surgery. In studies on NIRF-P so far the average dose of ICG administered was 0.2–0.5 mg/kg of bodyweight [38, 39]. A logical explanation for the lower concentration of ICG used in obese patients in this registry is that a fixed total dose of ICG was used in the majority of included cases, which results in a lower concentration per kg of body weight in the obese patient. We therefore recommend the use of a dose calculated per kilogram rather than a fixed total dose, in order to overcome this variability between patients and to increase the uniformity of NIRF-P.

The application of NIRF imaging is easy to learn, and in all registered cases, no complications related to the use of ICG occurred, which is consistent with the findings of a review showing adverse events in less than 1 in 40,000 patients [40].

The present study has some limitations. Although all digestive tract procedures requiring an anastomosis can be registered in this registry, the majority of cases involved colorectal procedures. Consequently, only 5.3% of cases were esophageal or gastric procedures, which prevented a subgroup analysis for these pathologies due to the low number of included cases. The vast majority of the registered cases were performed in two countries (Italy and Spain), which is not representative of NIRF-P use in Europe. In addition, several surgeons who registered their cases are internationally known to be advocates of NIRF imaging. Consequently, in order to have a better insight into the performance and use of NIRF-P across Europe, future inclusions from a greater number of European centers should be added along with an increased heterogeneity of cases and surgeons.

In this registry, complications occurred in 10.7% of cases including fever, bleeding, peritonitis, as signs of anastomotic dehiscence. However, although these signs may be suggestive of AL, it was not specifically defined as such in the registry, and as a result it is uncertain to conclude on the exact percentage of ALs which have occurred, which is a limitation of this registry. However, to have a better understanding of the severity of complications, we scored the complications according to the Clavien-Dindo classification. The analysis of these complications showed no statistical difference in the incidence of complications in the cases which were guided by ICG and the cases which were not guided by ICG.

In 2.2% of the cases a second ICG injection was performed prior to the creation of the anastomosis. The reason for this was not provided in this registry.

Inherently to the design of this registry, only cases of NIRF-P were reported without the inclusion of cases in which no NIRF-P was used. This limits the understanding of the findings of this registry in relation to the standard surgical care protocols.

Finally, various commercially available systems were used for NIRF imaging. These systems are equipped with different light sources to excite the fluorophores. These different technologies may influence the sensitivity of the devices and the consequent appraisal of the imaging. In this registry, there was an inhomogeneous spread of the systems with the majority of cases being performed with D-Light-P, SPY or Firefly technology, preventing statistical comparative analyses of these devices in relation to their impact on the procedures.

Conclusions

The EURO-FIGS registry provides an insight into the current clinical practice across several European centers with respect to NIRF-P imaging. The main findings of this analysis show that this technique is safe and that it has guided the surgical procedure in a considerable number of cases. The majority of respondents stated that they had a high sense of confidence in their anastomosis after NIRF-P. This registry may be a valuable tool to promote consensus guidelines and monitor NIRF-P across Europe, in the light of the increasing technological developments and widespread diffusion of this imaging modality.

Appendix A: List of items registered

- Patient age.
- Patient gender.
- Patient BMI.
- Patient comorbidities.
- Diagnosis requiring surgery.
- Neoadjuvant radiotherapy?
- Neoadjuvant chemotherapy?
- Surgical procedure performed.
- Type of anastomosis.
- Near-infrared camera model.
- Evaluation of anastomotic perfusion?
- ICG dose (mg/kg).
- Pre-anastomotic ICG injection?
- Reinjection?
- Post-anastomotic ICG injection?
- Adverse events of ICG administration?
- Did ICG influence the transection line?
- Did ICG provide you with a sense of confidence concerning the perfusion of your anastomosis?
- Did your patient present any clinical sign of post-operative complications?
- Did your patient need any post-operative radiological investigation?
- Do you have any other comment?

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Compliance with ethical standards

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References

1. Kassis ES, Kosinski AS, Ross P Jr, Koppes KE, Donahue JM, Daniel VC (2013) Predictors of anastomotic leak after esophagectomy: an analysis of the society of thoracic surgeons general thoracic database. Ann Thorac Surg 96(6):1919–1926
2. Biere SS, Maas KW, Cuesta MA, van der Peet DL (2011) Cervical or thoracic anastomosis after esophagectomy for cancer: a systematic review and meta-analysis. Dig Surg 28(1):29–35
3. Orringer MB, Marshall B, Chang AC, Lee J, Pickens A, Lau CL. Two thousand transhiatal esophagectomies: changing trends, lessons learned. Ann Surg. 2007;246(3):363–72; discussion 72–4.
4. Lang H, Piso P, Stukenborg C, Raab R, Jahne J (2000) Management and results of proximal anastomotic leaks in a series of 1114 total gastrectomies for gastric carcinoma. Eur J Surg Oncol 26(2):168–171
5. Haga Y, Wada Y, Takeuchi H, Ikejiri K, Ikenaga M (2011) Prediction of anastomotic leak and its prognosis in digestive surgery. World J Surg 35(4):716–722
6. Inokuchi M, Otsuki S, Fujimori Y, Sato Y, Nakagawa M, Kojima K (2015) Systematic review of anastomotic complications of esophagojejunostomy after laparoscopic total gastrectomy. World J Gastroenterol 21(32):9656–9665
7. McDermott FD, Heeney A, Kelly ME, Steele RJ, Carlson GL, Winter DC (2015) Systematic review of preoperative, intraoperative and postoperative risk factors for colorectal anastomotic leaks. Br J Surg 102(5):462–479
8. European Society of Coloproctology Collaborating G (2018) The 2017 European Society of Coloproctology (ESCP) international snapshot audit of left colon, sigmoid and rectal resections—executive summary. Colorectal Dis 20(6):13–41
9. Kang CY, Halabi WJ, Chaudhry OO, Nguyen V, Pigazzi A, Carmichael JC et al (2013) Risk factors for anastomotic leakage after anterior resection for rectal cancer. JAMA Surg 148(1):65–71
10. Park JS, Choi GS, Kim SH, Kim HR, Kim NK, Lee KY et al (2013) Multicenter analysis of risk factors for anastomotic leakage after laparoscopic rectal cancer excision: the Korean laparoscopic colorectal surgery study group. Ann Surg 257(4):665–671
11. Buchs NC, Gervaz P, Secic M, Bucher P, Mugnier-Konrad B, Morel P (2008) Incidence, consequences, and risk factors for anastomotic dehiscence after colorectal surgery: a prospective monocentric study. Int J Colorectal Dis 23(3):265–270
12. Midura EF, Hanseman D, Davis BR, Atkinson SJ, Abbott DE, Shah SA et al (2015) Risk factors and consequences of anastomotic leak after colectomy: a national analysis. Dis Colon Rectum 58(3):333–338
13. Turrentine FE, Denlinger CE, Simpson VB, Garwood RA, Guerlain S, Agrawal A et al (2015) Morbidity, mortality, cost, and survival estimates of gastrointestinal anastomotic leaks. J Am Coll Surg 220(2):195–206
14. Pommergaard HC, Achiam MP, Burcharth J, Rosenberg J (2015) Impaired blood supply in the colonic anastomosis in mice compromises healing. Int Surg 100(1):70–76
15. Karliczek A, Benaron DA, Zeebregts CJ, Wiggers T, van Dam GM (2009) Intraoperative ischemia of the distal end of colon anastomoses as detected with visible light spectroscopy causes reduction of anastomotic strength. J Surg Res 152(2):288–295
16. Trencheva K, Morrissey KP, Wells M, Mancuso CA, Lee SW, Sonoda T et al (2013) Identifying important predictors for anastomotic leak after colon and rectal resection: prospective study on 616 patients. Ann Surg 257(1):108–113
17. van den Bos J, Al-Taher M, Schols RM, van Kuijk S, Bouvy ND, Stassen LPS (2018) Near-infrared fluorescence imaging for real-time intraoperative guidance in anastomotic colorectal surgery: a systematic review of literature. J Laparoendosc Adv Surg Tech A 28(2):157–167
18. Blanco-Colino R, Espin-Basany E (2018) Intraoperative use of ICG fluorescence imaging to reduce the risk of anastomotic leakage in colorectal surgery: a systematic review and meta-analysis. Tech Coloproctol 22(1):15–23
19. Shen R, Zhang Y, Wang T (2018) Indocyanine green fluorescence angiography and the incidence of anastomotic leak after colorectal resection for colorectal cancer: a meta-analysis. Dis Colon Rectum 61(10):1228–1234
20. Agnus V, Pesce A, Boni L, Van Den Bos J, Morales-Conde S, Paganini AM et al (2019) Fluorescence-based cholangiography: preliminary results from the IHU-IRCAD-EAES EURO-FIGS registry. Surg Endosc. 34:3888–3896
21. Gero D, Gie O, Hubner M, Demartines N, Hahnloser D (2017) Postoperative ileus: in search of an international consensus on definition, diagnosis, and treatment. Langenbecks Arch Surg 402(1):149–158
22. Clavien PA, Barkun J, de Oliveira ML, Vauthey JN, Dindo D, Schulick RD et al (2009) The Clavien-Dindo classification of surgical complications: five-year experience. Ann Surg 250(2):187–196
23. Karliczek A, Harlaar NJ, Zeebregts CJ, Wiggers T, Baas PC, van Dam GM (2009) Surgeons lack predictive accuracy for anastomotic leakage in gastrointestinal surgery. Int J Colorectal Dis 24(5):569–576
24. Jafari MD, Wexner SD, Martz JE, McLemore EC, Margolin DA, Sherwinter DA et al (2015) Perfusion assessment in laparoscopic left-sided/anterior resection (PILLAR II): a multi-institutional study. J Am Coll Surg. 220(1):82-92 el
25. Zehetner J, DeMeester SR, Alicuben ET, Oh DS, Lipham JC, Hagen JA et al (2015) Intraoperative assessment of perfusion of the gastric graft and correlation with anastomotic leaks after esophagectomy. Ann Surg 262(1):74–78
26. Noma K, Shirakawa Y, Kanaya N, Okada T, Maeda N, Ninomiya T et al (2018) Visualized evaluation of blood flow to the gastric conduit and complications in esophageal reconstruction. J Am Coll Surg 226(3):241–251
27. Van Daele E, Van Nieuwenhove Y, Ceelen W, Vanhove C, Braeckman BP, Hoorens A et al (2019) Near-infrared fluorescence guided esophageal reconstructive surgery: a systematic review. World J Gastrointest Oncol 11(3):250–263
28. Kumagai Y, Hatano S, Sobajima J, Ishiguro T, Fukuchi M, Ishibashi KI et al (2018) Indocyanine green fluorescence angiography of the reconstructed gastric tube during esophagectomy: efficacy of the 90-second rule. Dis Esophagus. https://doi.org/10.1093/dote/doy052
29. Diana M, Agnus V, Halvax P, Liu YY, Dallemagne B, Schlagowski AI et al (2015) Intraoperative fluorescence-based enhanced reality laparoscopic real-time imaging to assess bowel perfusion at the anastomotic site in an experimental model. Br J Surg 102(2):e169–e176
30. Diana M, Dallemagne B, Chung H, Nagao Y, Halvax P, Agnus V et al (2014) Probe-based confocal laser endomicroscopy and fluorescence-based enhanced reality for real-time assessment

of intestinal microcirculation in a porcine model of sigmoid ischemia. Surg Endosc 28(11):3224–3233
31. Diana M, Halvax P, Dallemagne B, Nagao Y, Diemunsch P, Charles AL et al (2014) Real-time navigation by fluorescence-based enhanced reality for precise estimation of future anastomotic site in digestive surgery. Surg Endosc 28(11):3108–3118
32. Diana M, Noll E, Agnus V, Liu YY, Kong SH, Legner A et al (2017) Reply to letter: "Enhanced Reality Fluorescence Videography to Assess Bowel Perfusion: The Cybernetic Eye." Ann Surg 265(4):e49–e52
33. Diana M, Noll E, Diemunsch P, Dallemagne B, Benahmed MA, Agnus V et al (2014) Enhanced-reality video fluorescence: a real-time assessment of intestinal viability. Ann Surg 259(4):700–707
34. Hayami S, Matsuda K, Iwamoto H, Ueno M, Kawai M, Hirono S et al (2019) Visualization and quantification of anastomotic perfusion in colorectal surgery using near-infrared fluorescence. Tech Coloproctol 23(10):973–980
35. Seeliger B, Agnus V, Mascagni P, Barberio M, Longo F, Lapergola A et al (2020) Simultaneous computer-assisted assessment of mucosal and serosal perfusion in a model of segmental colonic ischemia. Surg Endosc 34(11):4818–4827
36. Iwamoto H, Matsuda K, Hayami S, Tamura K, Mitani Y, Mizumoto Y et al (2020) Quantitative indocyanine green fluorescence imaging used to predict anastomotic leakage focused on rectal stump during laparoscopic anterior resection. J Laparoendosc Adv Surg Tech A 30(5):542–546
37. D'Urso A, Agnus V, Barberio M, Seeliger B, Marchegiani F, Charles AL et al (2020) Computer-assisted quantification and visualization of bowel perfusion using fluorescence-based enhanced reality in left-sided colonic resections. Surg Endosc. https://doi.org/10.1007/s00464-020-07922-9
38. Foppa C, Denoya PI, Tarta C, Bergamaschi R (2014) Indocyanine green fluorescent dye during bowel surgery: are the blood supply "guessing days" over? Tech Coloproctol 18(8):753–758
39. Boni L, David G, Mangano A, Dionigi G, Rausei S, Spampatti S et al (2015) Clinical applications of indocyanine green (ICG) enhanced fluorescence in laparoscopic surgery. Surg Endosc 29(7):2046–2055
40. Benya R, Quintana J, Brundage B (1989) Adverse reactions to indocyanine green: a case report and a review of the literature. Cathet Cardiovasc Diagn 17(4):231–233

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