



Cohort Study

Anastomotic leak test using indocyanine green during laparoscopic Roux-en-Y gastric bypass: A cohort study

Giovanna Pavone^a, Alberto Fersini^a, Mario Pacilli^a, Pasquale Cianci^b, Antonio Ambrosi^a, Nicola Tartaglia^{a,*}

^a Department of Medical and Surgical Sciences, University of Foggia, Viale Pinto, 71122, Foggia, Italy

^b General Surgery Unit, Bonomo Hospital, Viale Istria, 76123, Andria, BT, Italy



ARTICLE INFO

Keywords:

Laparoscopic Roux-en-Y Gastric Bypass
 Indocyanine green test
 Anastomotic fistula
 Gastro-jejunal leak

ABSTRACT

Background: Indocyanine green (ICG) can be injected into the human bloodstream and it allows us to show stomach vascularity in real time. The aim of our study is to observe the preliminary results of the application of indocyanine green fluorescence (IGF) during laparoscopic Roux-en-Y Gastric Bypass (RYGB in our center and how the perfusion of the gastro-jejunal anastomosis affects the onset of fistula.

Materials and methods: 30 consecutive patients underwent RYGB with ICG fluorescence angiography at our center from January 2020 to December 2021. 5 ml of ICG were then injected intravenously to identify the blood supply of the stomach and the gastro-jejunal anastomosis. The UIN for [ClinicalTrials.gov](https://clinicaltrials.gov) Protocol Registration and Results System is: NCT05476159 for the Organization UFoggia.

Results: In the RYGB tested with ICG, we all have adequate perfusion but despite this a methylene blue test was positive and allowed us to reinforce the suture of the gastro-jejunal anastomosis.

Conclusion: Intraoperative ICG testing during laparoscopic RYGB may be helpful in determining which patients are at an increased risk for leakage but multiple factors concur to the pathophysiology and the incidence of gastric fistula not only the perfusion.

1. Introduction

Morbid obesity has become a major global health threat that leads to severe morbidity including diabetes, hypertension, obstructive sleep apnea, degenerative joint dis-ease and cardiovascular diseases [1].

Bariatric surgery is recognized as the most effective treatment for morbid obesity, maintaining a stable weight reduction in the long term and reducing comorbidities, with a favorable impact on mortality [2–4].

Gastric Bypass is a common operation for weight loss in patients with severe obesity. The procedure was developed in the 1960s by Drs. Mason and Ito who observed significant weight loss in a patient undergoing partial gastrectomy for peptic ulcer disease.

As expected, any increase in the frequency of a procedure usually unveils a significant number of related complications. Most of the complications of bariatric surgery are usually observed in the post-operative period.

Ninety-day mortality is very low (less than 0.5%). The morbidity of

the procedure is classified into early complications and late complications [5].

Early complications (0–30 days):

- Venous thromboembolism (VTE)
- Anastomotic leak
- Infection
- Intestinal blockage
- Stenosis Gastro-Jejunal

Late complications.

- Intestinal blockage
- Dumping syndrome
- Marginal ulcer
- Gastrointestinal fistula
- Gallstones

* Corresponding author. Viale Pinto 1, 71122, Foggia, Italy.

E-mail addresses: giovanna.pavone@unifg.it (G. Pavone), alberto.fersini@unifg.it (A. Fersini), mario.pacilli@unifg.it (M. Pacilli), ciancidoc1@virgilio.it (P. Cianci), antonio.ambrosi@unifg.it (A. Ambrosi), nicola.tartaglia@unifg.it (N. Tartaglia).

<https://doi.org/10.1016/j.amsu.2022.104939>

Received 31 August 2022; Received in revised form 24 October 2022; Accepted 12 November 2022

Available online 17 November 2022

2049-0801/© 2022 The Authors. Published by Elsevier Ltd on behalf of IJS Publishing Group Ltd. This is an open access article under the CC BY license (<http://creativecommons.org/licenses/by/4.0/>).

- Incisional hernia
- Nutritional deficiencies

More information on complications after gastrectomy is beyond the scope of this review article. These are very complex pathological processes with specific etiologies, pathophysiology and treatments.

Gastric fistulas are the most common complication observed after gastric sleeve surgery. A meta-analysis of almost 10,000 sleeve gastrectomies conducted by Parikh et al. revealed that 2.2% of these procedures were posteriorly complicated by fistula development. In regards to Roux-en-Y gastric bypass (RYGB), anastomotic leaks are their most common complications with an incidence of 0–8% [6,7].

Indocyanine green fluorescence angiography (ICG) is an emerging technology that has been used in an attempt to reduce the incidence of anastomotic leaks. ICG is a water-soluble tricarbocyanine dye that remains in the intravascular compartment until excretion and has a plasma half-life of between 3 and 5 min [8]. Importantly, the ICG absorbs light at a wavelength of excitation between 750 and 800 nm while emitting light at emission wavelengths greater than 830 nm or more [9]. Using near-infrared imaging systems, vascular perfusion to the gastro-jejunal anastomosis can be assessed intraoperatively, allowing surgeons to anastomose a well perfused bowel or to reshape a poorly perfused anastomosis. 5 ml of ICG were then injected intravenously to identify the blood supply of the stomach and the gastro-jejunal anastomosis.

The aim of our study is to observe the preliminary results of the application of indocyanine green fluorescence (IGF) during laparoscopic Roux-en-Y Gastric Bypass (RYGB) in our center and how the perfusion of the gastro-jejunal anastomosis affects the onset of fistula.

2. Materials and Methods

We conducted a cohort study with 30 consecutive patients underwent RYGB with ICG fluorescence angiography at our center from January 2020 to December 2021.

During the period of interest, 10 male and 20 female patients underwent RYGB by the same surgical team with the same standardized technique.

The mean age was 43.6 in the male group and 37.6 in the female group (mean 39.18).

The mean preoperative BMI was roughly the same in the two groups (45.16 in the male group vs 45.06) (in the female group).

At least one major comorbidity was found in all patients: the most represented was hypertension (19 patients, 63.33%), followed by diabetes (6 patients, 20%), COPD and/or OSAS (4 patients, 12, 3%) and osteoarthritis (1 patient, 3.33%).

2.1. Five patients had previous sleeve gastrectomy surgeries

Adequate perfusion was defined as “the direct and clear visualization of the fluorescence along the gastric tube and the anastomosis, relative to the excised specimen, after an estimated time of 150–180 s after i.v. Administration injection” (Fig. 1a–b).

In case of inadequate perfusion, our expected options were binding reinforcement with fibrin glue or with sutures.

A methylene blue test is routinely performed after fluorescence.

The procedure ended with the placement of an intra-abdominal drain along the suture line.

On the second postoperative day, a routine swallow test with Gastrografin is performed.

After the Gastrografin swallow test, if negative, patients were given a liquid diet for 1 day, then a semi-liquid diet and were discharged on the third postoperative day.

Our follow-up was performed routinely with blood tests and clinical examination at 3-6-12 months. The UIN for [ClinicalTrials.gov](https://clinicaltrials.gov) Protocol Registration and Results System is: NCT05476159 for the Organization

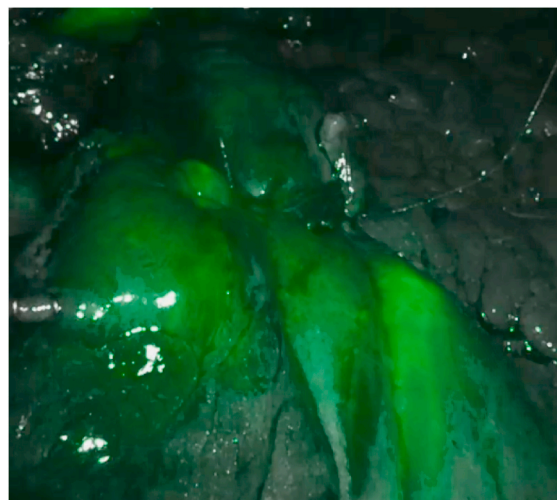


Fig. 1a. Evaluation of perfusion of gastro-jejunal by using Indocyanine green test. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

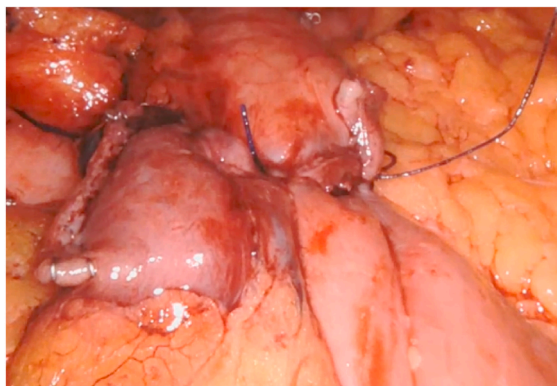


Fig. 1b. Intraoperative picture of the gastro-jejunal anastomosis.

UFoggia (<https://clinicaltrials.gov/ct2/show/NCT05476159>).

This work is fully compliant with the STROCSS criteria [10].

2.2. Eligibility criteria

Adult patients of both genders with morbid obesity defined as BMI > 40 kg/m² or BMI > 35 kg/m² with at least one associated major comorbidity were included. We excluded patients with secondary obesity due to endocrine and psychological disorders and patients unwilling to comply with postoperative diet and exercise program.

3. Results

The procedure was performed in all patients without ICG-related adverse events.

The mean operative time was 123 min. No conversion to laparotomy was performed.

The blood supply was rated “satisfactory and adequate” in 29 patients, only 1 patient showed ischemic areas at the anastomosis, confirmed by intraoperative methylene blue test positive, a suture reinforcement of the gastro-jejunal anastomosis was performed with Vycril stitches.

Routine swallowing of Gastrografin on the second postoperative day was negative for leaks in all patients.

No patient showed signs or symptoms of leaks at the gastro-jejunal

anastomosis.

Analyzing our database, we performed 26 RYGBs without ICG tests from 2017 to 2019; the total number of leakage was 0 and our leakage rate was 0%.

In the RYGB tested with ICG, we have only 1 case of inadequate anastomotic perfusion with a positive methylene blue test and allowed us to reinforce the suture of the gastro-jejunal anastomosis (Fig. 1a - b).

4. Discussion

Anastomotic leaks following RYGB can be caused by a number of factors including those compromising healing such as mechanical tension and ischemia [11–14] but are also associated with other factors such as BMI, age and the postoperative course [15].

The reported incidence of gastro-jejunal leakages after LRYGB has been reported to range between 1 and 3% [16–19].

The diagnosis of gastrointestinal leak after bariatric surgery can be challenging. The patient's presentation varies according to the type and timing of the leak and the patient's systemic inflammatory response. Patients with morbid obesity may show uncertain presentations, leading to late diagnosis and potentially catastrophic consequences.

There is still uncertainty about the pathophysiology of anastomotic leak after RYGB: the cause may vary from person to person. It may be caused by a problem with the tool or materials used to close the anastomosis during surgery. It may be because of problems with the blood flow in the area after surgery. Or it may be linked to other reasons for poor wound healing, such as diabetes or smoking [20–23].

The use of routine intraoperative methylene blue leak testing is still discussed as it may be useful for identifying suture line rupture but not for identifying areas at increased risk of subsequent leakage [24].

Recently, much interest has been focused on the possibility of assessing blood supply during surgery with the use of ICG fluorescence angiography, which is a real-time, inexpensive and feasible method of establishing vascularity in an area [25]. It has been fully and positively approved in most laparoscopic procedures [26] but there is still little literature on its usefulness in the bariatric procedure.

Therefore, our aim was to evaluate whether intraoperative ICG fluorescence angiography could lead to estimating the ischemic area [27,28].

In our study we tested 30 patients undergoing RYGB with ICG tests and only 1 patient showed an ischemic area at the anastomosis confirmed by the methylene blue test, therefore we considered it necessary to reinforce with Vycril points. This solution in this case proved to be sufficient to avoid the anastomotic leak.

Despite this, the cause of the anastomotic leak during RYGB is multifactorial, therefore not only the use of the ICG test can be a valid tool to avoid the leak caused by ischemia. A limitation of this study is the low number of patients.

5. Conclusions

We can conclude that ICG test in our study proved to be a valid tool to identify a possible ischemic area of the anastomosis confirmed by a positive methylene blue test, this forced us to reinforce the anastomosis. But multiple factors contribute to the pathophysiology and incidence of anastomotic fistula in the context of the RYGB operation. Therefore, intraoperative testing of the ICG can be helpful in determining which patients are at greater risk for anastomotic leak and whether additional measurement is needed during surgery, but further studies are needed to determine if the ICG test predicts leak due to the ischemia.

Provenance and peer review

Not commissioned, externally peer-reviewed.

Ethical approval

The ethics committee of our institution approved the study.

Sources of funding

GIOVANNA PAVONE, ALBERTO FERSINI, MARIO PACILLI, PASQUALE CIANCI, ANTONIO AMBROSI, NICOLA TARTAGLIA. declare haven't been funded.

Author contribution

- (I) Conception and design: GIOVANNA PAVONE.
- (II) Administrative support: ANTONIO AMBROSI.
- (III) Provision of study materials or patients: ALBERTO FERSINI.
- (IV) Collection and assembly of data: PASQUALE CIANCI.
- (V) Data analysis and interpretation: MARIO PACILLI.
- (VI) Manuscript writing: All authors.
- (VII) Final approval of manuscript: NICOLA TARTAGLIA.

Registration of research studies

Name of the registry: [ClinicalTrials.gov](https://clinicaltrials.gov)
 Unique Identifying number or registration ID: NCT05476159
 Hyperlink to your specific registration (must be publicly accessible and will be checked): <https://clinicaltrials.gov/ct2/show/NCT05476159>

Consent

Informed consent was obtained from all individual participants included in the study.

Guarantor

The Guarantors are Professor Nicola Tartaglia and Professor Antonio Ambrosi.

Declaration of competing interest

GIOVANNA PAVONE, ALBERTO FERSINI, MARIO PACILLI, PASQUALE CIANCI, ANTONIO AMBROSI, NICOLA TARTAGLIA. declare no conflict of interests.

Acknowledgments

None.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.amsu.2022.104939>.

References

- [1] F. Younis, M. Shnell, N. Gluck, S. Abu-Abeid, S. Eldar, S. Fishman, Endoscopic treatment of early leaks and strictures after laparoscopic one anastomosis gastric bypass, *BMC Surg.* 20 (1) (2020 Feb 21) 33, <https://doi.org/10.1186/s12893-020-0686-2>. PMID: 32085769; PMCID: PMC7035723.
- [2] H. Buchwald, Y. Avidor, E. Braunwald, M.D. Jensen, W. Pories, K. Fahrenbach, et al., Bariatric surgery: a systematic review and meta-analysis, *JAMA* 292 (14) (2004) 1724–1737.
- [3] N.V. Christou, J.S. Sampalis, M. Liberman, D. Look, S. Auger, A.P. McLean, et al., Surgery decreases long-term mortality, morbidity, and health care use in morbidly obese patients, *Ann. Surg.* 240 (3) (2004) 416–423, discussion 423–4.
- [4] L. Sjostrom, K. Narbro, C.D. Sjostrom, K. Karason, B. Larsson, H. Wedel, et al., Effects of bariatric surgery on mortality in Swedish obese subjects, *N. Engl. J. Med.* 357 (8) (2007) 741–752.

- [5] R. Peterli, B.K. Wölnerhanssen, T. Peters, D. Vetter, D. Kröll, Y. Borbély, B. Schultes, C. Beglinger, J. Drewe, M. Schiesser, P. Nett, M. Bueter, Effect of laparoscopic sleeve gastrectomy vs laparoscopic roux-en-Y gastric bypass on weight loss in patients with morbid obesity: the SM-BOSS randomized clinical trial, *JAMA* 319 (3) (2018 Jan 16) 255–265, <https://doi.org/10.1001/jama.2017.20897>. PMID: 29340679; PMCID: PMC5833546.
- [6] M. Parikh, R. Issa, A. McCrillis, J.K. Saunders, A. Ude-Welcome, M. Gagner, Surgical strategies that may decrease leak after laparoscopic sleeve gastrectomy: a systematic review and meta-analysis of 9991 cases, *Ann. Surg.* 257 (2013) 231–237 [PubMed] [Google Scholar].
- [7] P. Montravers, P. Augustin, N. Zappella, et al., Diagnosis and management of the postoperative surgical and medical complications of bariatric surgery, *Anaesth. Crit. Care Pain Med.* 34 (2015) 45–52 [PubMed] [Google Scholar].
- [8] D.S. Keller, T. Ishizawa, R. Cohen, M. Chand, Indocyanine green fluorescence imaging in colorectal surgery: overview, applications, and future directions, *Lancet Gastroenterol. Hepatol.* 2 (2017) 757e766.
- [9] J.T. Alander, I. Kaartinen, A. Laakso, et al., A review of indocyanine green fluorescent imaging in surgery, *Int. J. Biomed. Imag.* (2012), 940585.
- [10] G. Mathew, R. Agha, for the STROCSS Group, Strocsc 2021: strengthening the Reporting of cohort, cross-sectional and case-control studies in Surgery, *Int. J. Surg.* 96 (2021), 106165.
- [11] R. Gonzalez, L.G. Nelson, S.F. Gallagher, et al., Anastomotic leaks after laparoscopic gastric bypass, *Obes. Surg.* 14 (2004) 1299–1307.
- [12] C. Ballesta, R. Berindoague, M. Cabrera, et al., Management of anastomotic leaks after laparoscopic Roux-en-Y gastric bypass, *Obes. Surg.* 18 (2008) 623–630.
- [13] N. Tartaglia, G. Pavone, A. Di Lascia, F. Vovola, F. Maddalena, A. Fersini, M. Pacilli, A. Ambrosi, Robotic voluminous paraesophageal hernia repair: a case report and review of the literature, *J. Med. Case Rep.* 14 (1) (2020 Feb 4) 25, <https://doi.org/10.1186/s13256-020-2347-6>. PMID: 32019608; PMCID: PMC6998085.
- [14] R. Singhal, I. Omar, B. Madhok, C. Ludwig, A.A. Tahrani, K. Mahawar, GENEVA Collaborators, Effect of BMI on safety of bariatric surgery during the COVID-19 pandemic, procedure choice, and safety protocols - an analysis from the GENEVA Study, *Obes. Res. Clin. Pract.* 16 (3) (2022 May-Jun) 249–253, <https://doi.org/10.1016/j.orcp.2022.06.003>. Epub 2022 Jun 8. PMID: 35718696; PMCID: PMC9174153.
- [15] D.R. Flum, S.H. Belle, W.C. King, et al., Perioperative safety in the longitudinal assessment of bariatric surgery, *N. Engl. J. Med.* 361 (2009) 445–454.
- [16] R.F. Alizadeh, S. Li, C. Inaba, P. Penalosa, M.W. Hinojosa, B.R. Smith, M.J. Stamos, N.T. Nguyen, Risk factors for gastrointestinal leak after bariatric surgery: MBASQIP analysis, *J. Am. Coll. Surg.* 227 (1) (2018 Jul) 135–141, <https://doi.org/10.1016/j.jamcollsurg.2018.03.030>. Epub 2018 Mar 30. PMID: 29605723.
- [17] R. Singhal, I. Omar, B. Madhok, Y. Rajeev, Y. Graham, A.A. Tahrani, C. Ludwig, T. Wiggins, K. Mahawar, GENEVA Collaborators, Safety of bariatric surgery in ≥ 65-year-old patients during the COVID-19 pandemic, *Obes. Surg.* 32 (7) (2022 Jul) 1–13, <https://doi.org/10.1007/s11695-022-06067-z>. Epub 2022 May 5. PMID: 35513762; PMCID: PMC9071248.
- [18] N. Tartaglia, A. Di Lascia, P. Cianci, A. Fersini, M. Pacilli, G. Pavone, A. Ambrosi, Hemoperitoneum caused by spontaneous rupture of hepatocellular carcinoma in noncirrhotic liver. A case report and systematic review, *Open Med.* 15 (1) (2020 Aug 3) 739–744, <https://doi.org/10.1515/med-2020-0202>. PMID: 33336031; PMCID: PMC7712383.
- [19] M. Pacilli, N. Tartaglia, A. Gerundo, G. Pavone, A. Fersini, A. Ambrosi, Energy based vessel sealing devices in thyroid surgery: a systematic review to clarify the relationship with recurrent laryngeal nerve injuries, *Medicina* 56 (12) (2020 Nov 27) 651, <https://doi.org/10.3390/medicina56120651>. PMID: 33260912; PMCID: PMC7760641.
- [20] R. Singhal, A.A. Tahrani, C. Ludwig, K. Mahawar, GENEVA collaborators, Global 30-day outcomes after bariatric surgery during the COVID-19 pandemic (GENEVA): an international cohort study, *Lancet Diabetes Endocrinol.* 9 (1) (2021 Jan) 7–9, [https://doi.org/10.1016/S2213-8587\(20\)30375-2](https://doi.org/10.1016/S2213-8587(20)30375-2). Epub 2020 Nov 27. PMID: 33253631; PMCID: PMC7832244.
- [21] R. Singhal, C. Ludwig, G. Rudge, G.V. Gkoutos, A. Tahrani, K. Mahawar, GENEVA Collaborators, et al. 30-Day Morbidity and Mortality of Bariatric Surgery During the COVID-19 Pandemic: a Multinational Cohort Study of 7704 Patients from 42 Countries, *Obes. Surg.* 31 (10) (2021 Oct) 4272–4288, <https://doi.org/10.1007/s11695-021-05493-9>. Epub 2021 Jul 30. PMID: 34328624; PMCID: PMC8323543.
- [22] N. Tartaglia, G. Pavone, V. Lizzi, F. Vovola, F. Tricarico, M. Pacilli, A. Ambrosi, How emergency surgery has changed during the COVID-19 pandemic: a cohort study, *Ann. Med. Surg. (Lond)* 60 (2020 Dec 5) 686–689, <https://doi.org/10.1016/j.jamsu.2020.12.001>. PMID: 33312562; PMCID: PMC7719013.
- [23] F. Benedix, D.D. Benedix, C. Knoll, et al., Are there risk factors that increase the rate of staple line leakage in patients undergoing primary sleeve gastrectomy for morbid obesity? *Obes. Surg.* 24 (2014) 1610–1616.
- [24] N. Sakran, D. Goitein, A. Raziq, et al., Gastric leaks after sleeve gastrectomy: a multicenter experience with 2,834 patients, *Surg. Endosc.* 27 (1) (2013) 240–245, <https://doi.org/10.1007/s00464-012-2426-x>.
- [25] S. Delle Monache, A. Calgani, P. Sanità, et al., Adipose-derived stem cells sustain prolonged angiogenesis through leptin secretion, *Growth Factors* 33 (3–4) (2016) 87–96, <https://doi.org/10.1080/08977194.2016.1191481>.
- [26] R. Singhal, T. Wiggins, J. Super, A. Alqahtani, E.P. Nadler, C. Ludwig, A. Tahrani, K. Mahawar, GENEVA Collaborative. 30-Day morbidity and mortality of bariatric metabolic surgery in adolescence during the COVID-19 pandemic - the GENEVA study, *Pediatr. Obes.* 16 (12) (2021 Dec), e12832, <https://doi.org/10.1111/ijpo.12832>. Epub 2021 Jul 8. PMID: 34240553.
- [27] R. Singhal, V.R. Cardoso, T. Wiggins, J. Super, C. Ludwig, G.V. Gkoutos, K. Mahawar, GENEVA Collaborators, 30-day morbidity and mortality of sleeve gastrectomy, Roux-en-Y gastric bypass and one anastomosis gastric bypass: a propensity score-matched analysis of the GENEVA data, *Int. J. Obes.* 46 (4) (2022 Apr) 750–757, <https://doi.org/10.1038/s41366-021-01048-1>. Epub 2021 Dec 15. PMID: 34912046; PMCID: PMC8671878.
- [28] L. Cobianchi, F. Dal Mas, M. Massaro, P. Fugazzola, F. Coccolini, Y. Kluger, A. Leppäniemi, E.E. Moore, M. Sartelli, P. Angelos, F. Catena, L. Ansaloni, Team Dynamics Study Group, Team dynamics in emergency surgery teams: results from a first international survey, *World J. Emerg. Surg.* 16 (1) (2021 Sep 16) 47, <https://doi.org/10.1186/s13017-021-00389-6>. Erratum in: *World J Emerg Surg.* 2021 Nov 1;16(1):55. PMID: 34530891; PMCID: PMC8443910.