A Pilot Study into the Use of Intraoperative Indocyanine Green Fluorescence Angiography in Young Infants & Neonates

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This study aims to investigate whether the intraoperative use of indocyanine green fluorescence angiography (ICG-FA) is feasible and safe in neonates. Feasibility is therein defined as practically possible use of ICG-FA, resulting in clear and…

Ethical review	Approved WMO
Status	Pending
Health condition type	Gastrointestinal vascular conditions
Study type	Interventional

Summary

ID

NL-OMON56951

Source
ToetsingOnline

Brief title
IMAGINE Study

Condition

- Gastrointestinal vascular conditions
- Gastrointestinal therapeutic procedures

Synonym
Surgical gastrointestinal disorders; Disorders of the gastrointestinal system requiring surgery

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Groningen
Source(s) of monetary or material Support: Stryker,Stryker European Operations Limited

Intervention

Keyword: Fluorescence Angiography, Gastrointestinal Surgery, Indocyanine Green, Pediatric Surgery

Outcome measures

Primary outcome

The primary endpoints of this study will be measured by the following

parameters:

1. Regarding feasibility:

a. Comparison of the number of procedures in which it was a priori possible

to perform ICG-FA imaging and the number of procedures in which the device was

eventually used intraoperatively (applicability);

b. Possibility for the researchers to assess intestinal perfusion based on the

intraoperative ICG-FA images (clarity);

c. Possibility for the researchers to point out a specific location for

resection of the bowel based on visualization of perfusion in the ICG-FA images

(interpretability);

d. Interference with intraoperative Near Infrared Spectroscopy (NIRS) brain

monitoring (compatibility).

2. Regarding safety:

a. Number of complications directly related to use of the device or extension

of operative time for ICG-FA imaging, occurring within 24 hours after surgery

in the patients involved in this study;

b. Measurement of the prolonged OR time associated with intraoperative ICG-FA.

Secondary outcome

Regarding postoperative evaluation: Comparing the visual assessment

(conventional image) with the perfusion assessment of ICG-FA in order to

identify whether ICG-FA, if applied for decision-making, would have confirmed

or altered intraoperative decision making.

Study description

Background summary

A fluorescence imaging device, in combination with intravenous injection of indocyanine green (ICG), can visualize perfusion in real-time during surgery. [1] Perfusion assessment is of major importance for prevention of complications in gastrointestinal surgery. Specifically, a fluorescence imaging device can determine the tissue perfusion rate of anastomoses. [2,3]. Therefore, such a device can reduce the risk of complications such as anastomotic leakage, stricture and bowel ischemia. [4-6] Furthermore, it has the potential of improving intraoperative decision-making regarding anastomotic location. A review on the use of ICG-fluorescence angiography (FA) for assessment of colorectal anastomosis perfusion rate has shown that ICG-FA use causes on intraoperative change in surgical plan in 10.8% of cases as well as a 4% leakage reduction. [7] Furthermore, a 2020 RCT showed an intraoperative change in transection line in 19.3% of patients undergoing colorectal resection surgery, as well as a leakage reduction for low colorectal anastomoses. [8]

Although these results in the adult population are promising, the use of ICG-FA for assessment of intestinal perfusion in neonates has barely been researched in this particularly vulnerable patient group. However, in neonates, severe gastrointestinal diseases associated with a decreased perfusion can occur. One might think of necrotizing enterocolitis (NEC), a fulminant and often life-threatening disease mostly occurring in preterm infants, during which intestinal ischaemia and subsequent perforation can occur. Resection of the avital tissue followed by either a primary anastomosis (when bowel vitality allows) or ostomy creation is required. Resection of too much bowel is

undesirable as it can cause severe complications such as Short Bowel Syndrome (SBS). [9] The decision whether bowel is still viable is a subjective one, based on the surgeons macroscopic assessment of perfusion. Other intestinal diseases in the newborn requiring surgery and are e.g. intestinal atresia, malrotation/volvulus and spontaneous intestinal perforation (SIP). In all of these disorders, assessment of the viability of the resection margins which are subsequently anastomosed is paramount yet subjective. An objective measurement to assess bowel perfusion, outlining which intestine is still viable and which is not adequately perfused, can therefore significantly increase our surgical abilities. In the future such a tool might significantly decrease complications such as anastomotic leakage or stricture, as well as prevent unnecessary resection of viable tissue thereby decreasing the risk for short bowel syndrome. ICG-FA might be such a tool, as has been demonstrated in adults.

A review of current literature has confirmed the lack of available studies on indocyanine green fluorescence angiography (ICG-FA) use in pediatric gastrointestinal surgery. However, the available literature does show that its use might be safely used for intraoperative decision-making as well as for intraoperative perfusion assessment. It may even be more useful than conventional clinical assessment of intestinal perfusion. The safety profile of ICG in neonates furthermore looks promising, as no serious complications or adverse events have been reported to date. [10] Prospective studies are necessary to further investigate the feasibility of ICG-FA in neonatal gastrointestinal surgery [10]. The goal of this study is to follow up on the review by further investigating the feasibility and safety of ICG-FA in neonatal gastrointestinal surgery in two academic pediatric surgical centers with a wide experience in such surgery.

Study objective

This study aims to investigate whether the intraoperative use of indocyanine green fluorescence angiography (ICG-FA) is feasible and safe in neonates. Feasibility is therein defined as practically possible use of ICG-FA, resulting in clear and interpretable results, with the future potential to improve clinical outcome and benefits for the patient.

Specifically, the feasibility and safety for use of ICG-FA in neonates undergoing laparotomy as treatment for necrotizing enterocolitis (NEC), intestinal atresia, spontaneous intestinal perforation (SIP) and malrotation will be investigated.

If ICG-FA turns out to be feasible and safe for the population investigated in this study, a follow-up study will be conducted with the aim to explore the potential benefits of this technique on the postoperative outcome and intraoperative decision-making.

Study design

This is a prospective single-arm multicenter feasibility study, including all neonates undergoing laparotomy for intestinal diseases within the first three months of life. The study will be performed in two academic pediatric surgical centers: University Medical Center Groningen (UMCG) and University Medical Center Utrecht (UMCU). Due to the exploratory nature of the study, there is no control group.

This clinical investigation is a drug-device combination study. The objective is to visualize perfusion in the bowel using a hand-held imaging device (SPY-PHI, Stryker® Endoscopy) with the aid of the fluorescent dye indocyanine green (Verdye®, Diagnostic Green)
As the visualization of perfusion in the bowel is the main objective, the SPY-PHI® medical device has the primary functionality in the study and the study is therefore considered a medical device study. This decision is further supported by the medical device being used off-label in this study (not indicated for use in neonates), while the fluorescent dye (Verdye®) is being used on label.

Intervention

After the standard-of-care visual bowel inspection, study participants will undergo an additional 5-10 minutes of bowel fluorescence angiography (FA) with the aid of intravenous indocyanine green (ICG) injection (on-label, non-investigational) and a specific imaging camera, the SPY-PHI (Stryker® Endoscopy) - the investigated medical device. There will be no physical contact between the study participant and the SPY-PHI camera, and heat release and radiation exposure are not applicable. In principle, the obtained ICG-FA images will not have any therapeutic implications as this is a safety and feasibility study. An unexpected signifcant discrepancy between visual inspection and ICG-FA may prompt a change in surgical plan as ICG-FA has already been proven superior to visual assessment only in adults.

Study burden and risks

The investigational device does not touch the patient at all and therefore does not constitute many potential risks for participants in this trial. For the use of the SPY-PHI camera, the potential risks are:
- Minimal prolonged OR time
- Device malfunction
- Non-sterile drapes

If the device malfunctions (ADE), no results of the participant involved will be available afterwards. However, the patient will still receive the same care all other participants and non-participants receive. The only change in

treatment that occurs when a child participates in this study is the injection of ICG and limited prolongation of operative time. The assessment of vitality of the bowel and further surgical and therapeutic management of the patient does not change.

The device is always covered in sterile drapes before use during the surgery. To mitigate any risk of contamination of the surgical field, in case the drapes are touched by the device they will be immediately replaced by new sterile drapes.
Last, the use of the device prolongs the operative time with approximately 5-10 minutes. Prolonged operative time may cause additional risks, such as development of a surgical site infection (SSI). However, the mean operating time for the diseases studied is 120 minutes. A 10-minute extension is thus less than 10% additional operating time. This will have a negligible effect on the complication risks. A 2020 systematic review on the incidence of abdominal surgical site infections after abdominal birth defects surgery in infants showed the total proportion of wound infection in these surgeries is 6%, which is a low risk already. [14]

More importantly, the length of procedure does not seem to determine this risk in this systematic review. For example, the Kasai procedure for biliary atresia takes approximately 4 hours, whereas pull-through surgery for Hirschsprung*s disease takes approximately 2.5 hours. Still, the individual SSI rate for biliary atresia surgery is lower than the individual SSI rate for Hirschsprung*s disease. A <10% extension of operating time for this study is thus not expected to cause an additional risk in SSI. However, to mitigate any risk, ICG-FA will not be performed if the patient is assessed unstable by the operating team intraoperatively. If so, the patient will be excluded.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Babies and toddlers (28 days-23 months)
Newborns
Premature newborns (<37 weeks pregnancy)

Inclusion criteria

1. Written informed consent is obtained by both patient*s parents or legal guardians (as applicable);
2. Patient is a neonate (< 1 month of age) or young infant (<3 months of age);
3. Patient is suffering from necrotizing enterocolitis, intestinal atresia, malrotation or spontaneous intestinal perforation;
4. Patient requires laparotomy for management of the disease.

Exclusion criteria

General exclusion criteria
1. Patient is suffering from clinically significant (treatment necessary) hyperbilirubinemia;
2. Patient is suffering from thyroid or liver disease;
3. Patient is allergic to the active substance indocyanine green or sodium iodide or iodine;
4. Patient has abdominal wall defects;
5. Patient can be treated non-surgically;
6. During the preoperative multidisciplinary meeting with the team, including the pediatric anesthetist, patient is deemed not stable enough hemodynamically to perform the ICG-FA measurements
Intra-operative exclusion criterium
7. Patient is assessed unstable by operating team intraoperatively.

Study design

Design

Study type: Interventional

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-09-2024
Enrollment:	20
Type:	Anticipated

Medical products/devices used

Generic name:	SPY-PHI
Registration:	Yes - CE outside intended use

Ethics review

Approved WMO

Date:	15-08-2024
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
ClinicalTrials.gov	NCT05734118
CCMO	NL83678.000.24