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# Quantitative Intraoperative Microperfusion Analysis in Open Aortic Repair to Prevent Colonic Ischemia

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## Abstract

**Objective:** With an incidence of 1.6 to 7.6%, postoperative colonic ischemia is a rare but dangerous complication after infrarenal open aortic repair (OAR) with a mortality rate of up to 50%. A potential risk factor is intraoperative ligation of the inferior mesenteric artery (IMA). The aim of this study is to determine the feasibility of the standardized intraoperative assessment of colonic microperfusion by laser Doppler flowmetry with "oxygen to see (O2C)" to facilitate the decision regarding IMA reimplantation.

**Methods:** In this prospective pilot study, twenty-five patients underwent elective OAR. Measurements with the O2C were performed on the serosa of the sigmoid colon before and after OAR. If reimplantation of the IMA was necessary, a third measurement was performed accordingly. The decision regarding reimplantation was made by the surgeon using the O2C parameters flow, velocity, SO2, and rHb in combination with the macroscopic findings (backflow from the IMA and sigmoid color).

**Results:** Significant relative changes in the O2C microperfusion parameters SO2, rHb, flow, and velocity were detected ($P < .0001$) intraoperatively after OAR. No reimplantation of the IMA was deemed necessary on the basis of macroscopic findings alone. However, low or decreasing O2C values in combination with the respective macroscopic findings led to three IMA reimplantations. In patients with IMA reimplantation, rHb and flow were significantly lower after OAR ($P = .0335$; $P = .0265$). No sigmoid ischemia occurred in any of the patients. The 30-day mortality rate was 0%. Overall, one or more minor complications (Clavien-Dindo grades I and II) occurred in 5 patients (20%). Major complications (grades III, IV, and V) did not occur postoperatively in any of the patients (0%).

**Conclusions:** Objective measurement parameters obtained by O2C can be used to guide decisions regarding the need for IMA reimplantation. Further studies are needed to investigate the validity of the parameters.

**Keywords:** Tissue spectrophotometry; Microcirculation, Microvascular blood flow; Postoperative complication; Prevention

## Introduction

Open abdominal aortic repair (OAR) is mainly performed in patients with a ruptured abdominal aortic aneurysm (AAA) or with an intact one at risk of rupture, as well as in severe arterial occlusive disease of the aortic bifurcation [1]. Less common indications are aortic ulcers, dissections, infections, and aortoenteric fistulas. The rate of minor and major postoperative complications

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after OAR varies between 9 and 34% [2-4]. The most frequent complications after OAR include pneumonia (9%), respiratory insufficiency (6.5%), and renal deterioration (8 to 13%) [4,5]. Colonic ischemia (CI) remains another serious complication after OAR, which occurs mainly in the sigmoid colon [6]. Its incidence is reported to be in the range between 1.6 and 7.6% [5,7], but the mortality rate from CI is 21 to 51% [5,7,8]. Apart from the potentially fatal consequences for the patient, the health economic impact is immense. According to a prior publication, the average treatment costs were doubled when CI occurred postoperatively [9]. The development of CI is most likely multifactorial and finally based on an imbalance of oxygen supply and demand. Intraoperative factors that increase the risk of postoperative CI include operating time, perioperative hypotension, and high blood loss. Patient-specific risk factors include female sex, higher age, current smoking, arterial hypertension, renal insufficiency, and heart failure [5, 10]. Intraoperative ligation of the inferior mesenteric artery (IMA) during OAR is an obvious intervention, which is widely discussed as being a risk factor for CI [11-14]. Various studies indicate a protective effect of reimplantation and high long-term patency of the IMA, without increasing transfusion requirements or critically prolonging operating time [11,15,16]. The European Association for Cardio-Thoracic Surgery states that IMA reimplantation has shown benefits in certain patient subgroups (i.e., reduced backflow, visual signs of intraoperative CI), but does not give a clear recommendation regarding decision making. The Society for Vascular Surgery's (SVS) practice guidelines recommend that reimplantation of a patent IMA should be considered when there is an increased risk of CI [17]. However, there is no clear consensus as to which specific factors contribute to such a suspicion. Thus, the identification of patients who might benefit from IMA reimplantation is still unclear in open aortic surgery. For this purpose, various techniques have been studied, aiming to quantify colonic microperfusion intraoperatively [18,-22].[18-22] Despite the availability of multiple measurement methods, there is currently no uniformly applied technique for measuring colonic perfusion during OAR. This pilot study examines the intraoperative application of the tissue spectrometry device "Oxygen to see" (O2C), which combines both a laser doppler flowmeter and a spectrophotometer. The aim of this study was to investigate to what extent the values for the intraoperative O2C microperfusion parameters of the sigmoid colon change before and after replacement of the infrarenal aorta and whether these parameters are suitable for quantifying colonic microperfusion in comparison to macroscopic assessment. The ultimate question is whether this quantitative assessment tool can guide the decision making on IMA reimplantation.

## Material and Methods

### Study design and procedure

This single-center prospective cohort study investigates the feasibility of using O2C to assess the intraoperative microperfusion of the sigmoid colon before and after OAR. Due to the exploratory design of this observational clinical pilot trial and the lack of reference values concerning the O2C method, no sample size calculation has been carried out and the trial has not been registered. Preoperative diagnostics, patient preparation, and intra- and postoperative management followed the internal clinical standards of our center and its current guidelines. In each patient, a preoperative computed tomography angiography (CTA) scan was available for surgical planning and the assessment of the visceral and iliac arteries by a radiologist. Microperfusion was evaluated twice during each surgery. The first O2C measurement took place after laparotomy and before implantation of the aortic graft. The second measurement was performed after implantation of the graft. Simultaneously, the cardiocirculatory parameters were documented. If the IMA was reimplantated, a third measurement was performed after reimplantation. Patients were admitted to the intermediate care (IMC) or intensive care unit (ICU) for postoperative surveillance. Postoperative morbidity (e.g., wound complications, cardiopulmonary complications) and mortality were graded according to Clavien-Dindo and documented for all the patients during the clinical follow up period of 30 days. Ischemic colitis was diagnosed via endoscopy. CI was defined as colonic malperfusion that was diagnosed clinically or by endoscopy and that subsequently required colon resection. A postoperative sigmoidoscopy and/or CT scan was only performed upon clinical suspicion.

### Patient selection

The study population consisted of patients scheduled for infrarenal OAR at the Division of Vascular Surgery of the Surgical Department at the University Medical Center Mannheim (Germany). The surgeries took place between January 2020 and May 2021. Only elective repair cases (i.e., no ruptured AAA) were assessed for eligibility. Further inclusion criteria were the intraoperative availability of the O2C and a surgeon who was familiar with the device. Patients were excluded in cases of bilateral internal iliac artery occlusions, previous endovascular aneurysm repair (EVAR), colon resection, or inflammatory bowel disease. The flow diagram is presented in Figure 1. The study was performed in accordance with the Declaration of Helsinki and conducted after approval by the Ethics Committee of the Medical Faculty Mannheim, University of Heidelberg (2019-639N).

### Surgical technique

Open aortic repair (OAR) was carried out under general anesthesia and sterile conditions. Intraoperative blood salvage was performed in each operation. The abdominal aorta and common iliac arteries were exposed by a midline incision. Before aortic clamping, heparin was administered

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systemically (100 IU/kg). The proximal aortal clamp was placed just below the renal arteries. The distal clamps were placed on the common iliac arteries, followed by IMA division and cross-clamping. Then the aneurysmal sac was opened longitudinally. A collagen-, silver-, and triclosan-coated vascular graft (Intergard Synergy knitted, Getinge AB, Göteborg, Sweden) was used to replace a portion of the infrarenal aorta. Straight tube grafts were used in patients with AAA limited to the infrarenal aorta. If the iliac arteries were involved, patients received bifurcation grafts. IMA reimplantation into the graft was only performed in selected cases (see below). Otherwise, the IMA was ligated. Finally, retroperitoneal and abdominal wall closure was performed.

### Visual evaluation of sigmoid perfusion and IMA reimplantation

The individual collateral colonic blood supply was assessed by grading the intensity of backflow from the IMA after its division. The backflow was categorized by the surgeon as either “pulsatile,” “moderate,” “drop by drop,” or “none.” Simultaneously to each O2C measurement, the color of the sigmoid colon’s serosal surface was evaluated visually by the surgeon (“viable”, “marbled”). Based on the clinical judgement and visual assessment, the surgeon made an intraoperative decision regarding IMA reimplantation in each patient.

### Intraoperative assessment of microperfusion with Oxygen to See (O2C)

The tissue spectrometry device O2C (LEA Medizintechnik GmbH, Giessen, Germany) consists of a computer system, two light sources, and a fiber optic probe transmitting white (wavelength range: 500-630 nm; optical resolution: 1.5 nm) and laser (wavelength: 830 nm) light. It has been approved as a class IIa medical device (EU Regulation 2017/745). The O2C is designed for non-invasive assessment of microperfusion by quantifying microcirculatory blood flow and oxygenation saturation. During the measurement, the tissue is irradiated via the fiber optic probe and the remitted light signals are detected by a sensor integrated in the system [23]. Based on this data, the following four parameters are calculated: SO2 (postcapillary oxygen saturation, in %), rHb (relative amount of capillary hemoglobin in AU [arbitrary units]), flow (microcirculatory blood flow, in AU), and velocity (microcirculatory blood flow velocity, in AU). Measurements were taken according to a standardized protocol under ambient light with the surgical lights directed away from the measuring site. A sterile LFX-54 probe was placed manually on the serosal surface of the antimesenteric border of the sigmoid colon without pressure (Figure IIA). The probe’s optical fibers for light emission and detection are separated by 1.2 mm, delivering a catchment volume depth of about 0.8-1.0 mm depending on the optical properties of the irradiated tissue. The measurements were taken over a period of 10 s. The average values of the aforementioned perfusion parameters were calculated by the device and displayed immediately on the live monitor (Figure IIB).

### Statistical analysis

Statistical analysis was conducted using SAS statistical software, release 9.4 (SAS Institute Inc., Cary, NC, USA). Mean values and standard deviations were calculated for continuous variables. In case of skewed distributions, median values are presented together with interquartile range (Q1 - Q3) or minimum and maximum. Nominal and ordinal categorical data are presented as absolute frequencies and percentage values. The Chi2 test was used to compare binary factors in two independent groups. If the requirements for a Chi2 test were not met, Fisher´s exact test was performed instead. An exact Wilcoxon 2-sample test was conducted for quantitative variables. A Cochran-Armitage trend test was performed for ordinally scaled characteristics with few states of expression. In order to compare differences (i.e., before and after OAR or before and after IMA reimplantation), a paired t test or Wilcoxon test for 2 paired samples was used, as appropriate. Pearson’s correlation coefficient was used to quantify the strength of a correlation between continuous variables of perfusion and cardiocirculatory assessment. The significance level for all tests was set at alpha = .05.

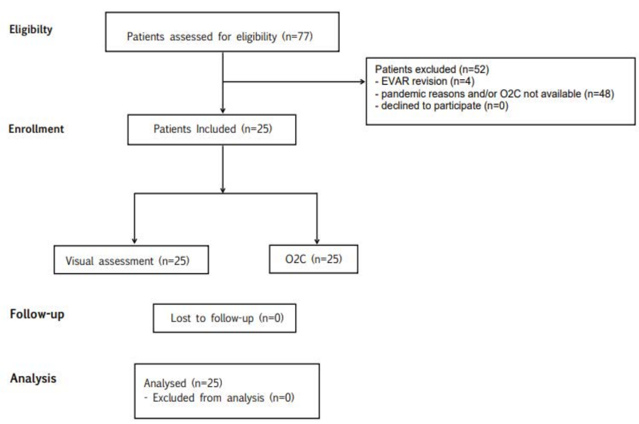


**Figure 1:** Flow diagram.

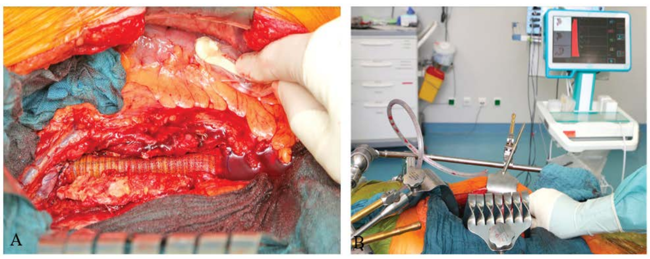


**Figure 2:** Intraoperative setting of O2C measurements during open aortic repair. The sterile fiber optic microprobe was placed directly on the serosal surface of the sigmoid colon during measurements (A). Perfusion parameters were calculated by the device and displayed immediately on the monitor (B).

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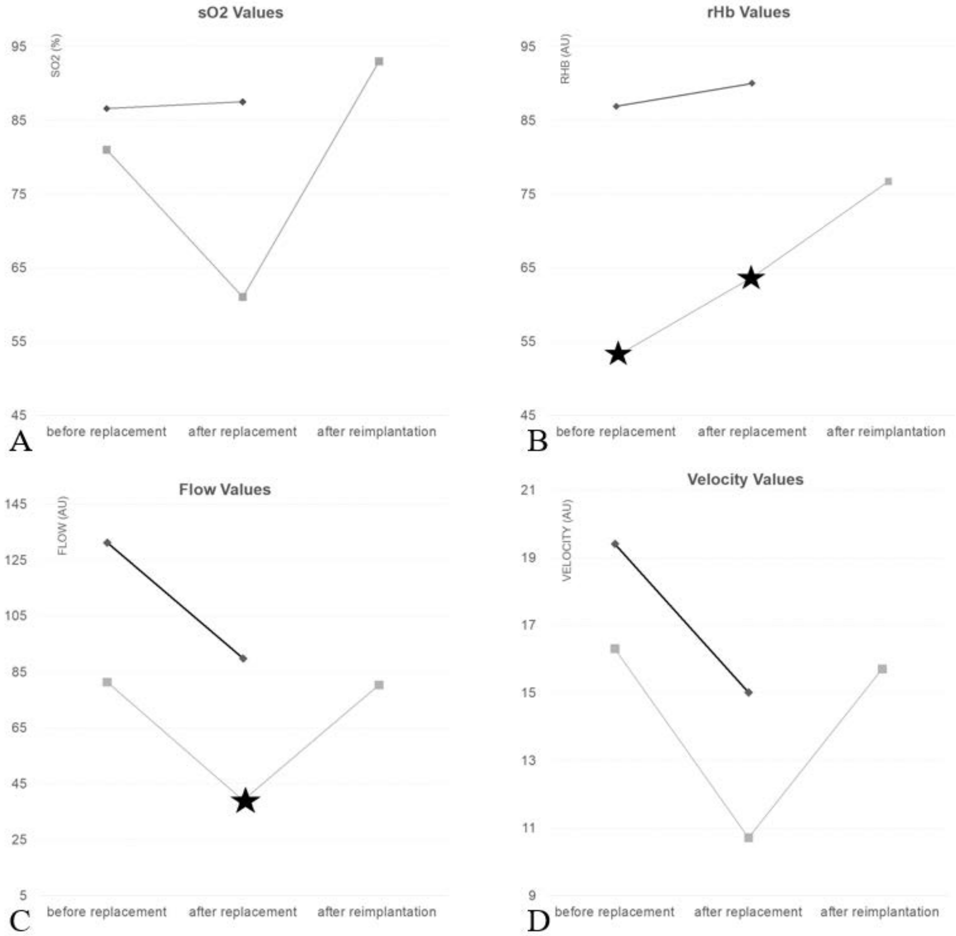


**Figure 3:** Comparison of the mean intraoperative O2C perfusion parameters SO2 (A), rHb (B), Flow (C), and Velocity (D) before and after aortic replacement (OAR) between patients without IMA reimplantation (black graph, n = 22) and with IMA reimplantation (grey graph, n = 3). Black Stars: significant difference.

## Results

### Patients and procedure characteristics

The characteristics of the 25 patients included in this trial are presented in Table I, and the intra- and postoperative parameters in Table II.

### Preoperative vascular status

The coeliac artery (CA) and SMA were patent in all cases. Concerning the IMA, eight patients (32%) had an osteal occlusion in preoperative CTA. Intraoperatively, another patient was documented to have an osteal IMA occlusion, which was not conclusive from the CTA scan.

### Intraoperative visual assessment of sigmoid perfusion

Sigmoid perfusion was described as sufficient in all patients at both measurements. Retrograde IMA backflow by collateral supply was pulsatile in 18 patients (72%), moderate in two patients (8%), and in drops in one patient (4%). There was no backflow in four patients (16%).

### Intraoperative assessment of sigmoid microperfusion by O2C

With regard to all patients, the O2C perfusion parameters were slightly lower after OAR, except for rHb, which increased. Mean values are provided as supplementary material (Supplemental Table I).

In two patients, there were marked decreases of more than 30% for at least two O2C parameters while the macroscopic perfusion assessment was uncritical. In one patient, there was a 20% decrease in two O2C parameters in combination with a reduced IMA backflow "in drops" (Supplemental Table II). Both situations led to the intraoperative decision in favor of IMA reimplantation in these three patients. Comparing patients with and without IMA reimplantation, rHb was significantly lower before and after OAR ($P = .0257$; $P = .0335$), and flow was significantly lower after OAR ($P = .0265$). The values normalized after IMA reimplantation (Figure 3). When comparing absolute changes before and after OAR for all patients (n = 25), significant results were

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obtained for change in flow (P = .0002) and for velocity (P < .0001). For patients without IMA reimplantation (n = 22), the corresponding P values are P = .0008 (flow) and P = .0003 (velocity). In contrast, relative changes proved to be statistically significant for each parameter, both for the entire group and for patients without IMA reimplantation (each P < .0001).

## Intraoperative hemodynamic parameters

Mean intraoperative hemodynamic parameters before and after OAR, which are possible confounders, are presented in Table III. Blood pressure was not significantly different at the various O2C assessments. There were significant differences in norepinephrine rates; no significant correlations, however, were found between each of the four O2C parameters and the corresponding norepinephrine rates. Relative change in Hb correlated significantly with flow (r= -0.43038; p= .0317) after OAR. Since the relative change was calculated as postoperative Hb/preoperative Hb, a stronger perioperative decrease in hemoglobin was associated with a higher flow value. In addition, velocity after OAR showed a significant correlation with intraoperative blood loss (r= 0.52082; p= .0076).

## Postoperative results and complications

No patients developed postoperative CI or ischemic colitis. The 30-day mortality was 0%. No postoperative complications were found in 20 (80%) patients. Minor complications (Clavien-Dindo grade I-II) occurred in five (20%) cases, as presented in Table II. There were no major complications.

**Table 1:** Patient characteristics (n = 25). Continuous variables are expressed as a mean and standard deviation. For categorical variables, absolute (numbers) and relative (percentage) frequencies are given.

| Patient characteristics | |
|---|---|
| Age (Years) | 68.3 (± 7.9) |
| Gender (m;f) | 20 (80%); 5 (20%) |
| Body Mass Index (kg/m$^2$) | 26.2 (± 4.2) |
| Aneurysm size (mm) | 57.2 (± 7.6) |
| ASA-Score | |
| ASA 2 | 14 (56%) |
| ASA 3 | 8 (32%) |
| ASA 4 | 3 (12%) |
| **Clinical Presentation** | |
| Symptomatic | 7 (28%) |
| Asymptomatic | 18 (72%) |
| **Comorbidities** | |
| Hypertension | 20 (80%) |
| Diabetes | 5 (20%) |
| Chronic kidney disease | 4 (16%) |
| Coronary Heart Disease | 9 (36%) |
| COPD | 6 (24%) |
| Peripheral arterial occlusive disease | 7 (28%) |
| Hyperlipidemia | 2 (8%) |
| Hernia | 5 (20%) |
| Adipositas | 7 (28%) |
| Smoking | 16 (64%) |
| Packyears (n=20); median **(**Q1 – Q3) | 44 (40 – 57.5) |
| Legend: ASA, American Society of Anesthesiologists Physical Status Classification System; Adipositas diagnosed if BMI > 30 kg/m2 | |

**Table 2**: Peri- and postoperative characteristics and course after open aortic repair (n = 25). Continuous variables are expressed as a mean and standard deviation, or as the median with minimum and maximum, or Q1 and Q3, as appropriate. Categorical variables are expressed as absolute (numbers) and relative (percentage) frequencies.

| **Periprocedural characteristics** | |
|---|---|
| Operative time (minutes) | 167 (134-183) |
| Intraoperative blood loss (ml) | 1000 (700-1400) |
| Tube graft | 13 (52%) |
| Bifurcated graft | 12 (48%) |
| Number of red cell concentrates transfused median (min-max) | 0 (0 – 10) |
| Number of fresh frozen plasma transfused median (min-max) | 0 (0 – 8) |
| Cellsaver autotransfusion (ml) median (Q1-Q3) | 300 (200-550) |
| Preoperative Hb (mg/dl)* | 13.47 (± 2.33) |
| Postoperative Hb (mg/dl)* | 11.79 (± 1.99) |
| **Postoperative diagnostics, results, and complications** | |
| Length of hospital stay (days) | 11 (8-43) |
| Sigmoidoscopy | 5 (20%) |
| CT-Imaging | 6 (24%) |
| Ketoacidosis | 1 (4%) |
| Postoperative ileus** | 1 (4%) |
| Cardial (echocardiographic right ventricular stress)** | 1 (4%) |
| Pulmonary (pleural effusion, pulmonary embolism)** | 2 (8%) |
| Wound healing disorder** | 2 (8%) |
| * Pre- and postoperative Hb (hemoglobin) were measured outside the operating room (before and after procedure). **all minor (Clavien-Dindo grade I-II). | |

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**Table 3:** Intraoperative hemodynamic parameters before and after open aortic repair (n = 25). Continuous variables are expressed as a mean and standard deviation. P values were derived by paired t tests.

| Intraoperative parameters | Before OAR | After OAR | P value |
|---|---|---|---|
| Hb (mg/dl) | 12.14 (± 2.16) | 11.24 (± 2.08) | 0.0037 |
| Systolic blood pressure (mmHg) | 120.0 (± 18.4) | 123.4 (± 16.8) | 0.5578 |
| Diastolic blood pressure (mmHg) | 63.2 (± 10.9) | 64.4 (± 13.8) | 0.7562 |
| Mean arterial pressure (mmHg) | 81.5 (± 12.0) | 83.3 (± 12.9) | 0.6474 |
| Heart rate (/min) | 59.5 (± 11.0) | 65.3 ± (13.2) | 0.0004 |
| SaO2 (%) | 97.5 (± 1.9) | 98.2 (± 1.9) | 0.0676 |
| Body temperature | 36.3 (± 0.5) | 36.0 (± 0.5) | 0.0365 |
| Norepinephrine rate (mg/h) | 0.28 (± 0.20) | 0.58 (± 0.34) | 0.0001 |

Hb (hemoglobin) before OAR and after OAR were both measured intraoperatively using blood gas analysis; OAR, open aortic repair; SaO2, blood-oxygen concentration

## Discussion

The results of this feasibility trial show that intraoperative O2C tissue spectrometry on the serosal surface of the sigmoid colon is a sensitive and practical method to quantify colonic perfusion during OAR. We were able to detect minimal, yet significant changes in the intraoperative perfusion parameters after OAR, making them a real-time surrogate parameter reflecting different factors influencing colonic microperfusion, such as intraoperative blood loss, hemoglobin, hemodynamic parameters, and macroperfusion. In three cases, however, a marked decrease in O2C perfusion parameters influenced the operating surgeon to perform IMA reimplantation although a macroscopic assessment alone would not have led to the same decision. The parameters rHb and flow might guide the decision regarding IMA reimplantation since these parameters were significantly lower after OAR in patients with IMA reimplantation. Possibly as a result of intraoperative O2C spectrometry, no case of postoperative CI was observed in this cohort of 25 patients. The current guidelines (EACTS and SVS) do not recommend routine reimplantation of the IMA during OAR [17,242]. Common practice is visual assessment of the serosal surface and of the quality of arterial backflow from the IMA. As known from gastrointestinal surgery, visual evaluation by the surgeon has a low predictive ability for anastomotic healing and bowel viability [25]. This observation is in line with the present study concerning the discriminatory power of the macroscopic rating of IMA backflow and sigmoidal color. Consequently, there is a need for objective tools to guide the intraoperative decision on IMA reimplantation.

Since the end of the 20th century, different methods have been investigated for this purpose. In a study from 1978, measurement of intra-arterial pressure of the IMA was used during OAR to predict colonic ischemia [21]. The measurement was successful in 39 of 52 patients. One patient developed postoperative CI. This was also the only subject whose intra-arterial IMA stump pressure after graft implantation was less than 40 mmHg. The use of indocyanine green (ICG) has been validated for measuring intraoperative perfusion. In recent years, ICG has been used to analyze the perfusion of various organs including the bowel and the extremities. Most recently, a study of ten patients undergoing elective AAA repair observed a delayed ICG perfusion time (> 3 min) in one patient, who developed colonic ischemia postoperatively [22]. In an early study from 1979, an ultrasound Doppler flowmeter was used to determine the intraoperative perfusion of the serosa and mesentery in 130 patients [18]. Transient occlusion of the IMA during OAR was associated with a marked decrease in left-sided colonic perfusion in eight patients. In these patients, patency of the IMA was subsequently restored. No complications occurred during the postoperative course. Another trial from 1989 employed a laser-Doppler flowmeter (LDF) in 16 patients undergoing OAR. The LDF visualized a significant reduction in sigmoid perfusion in patients with IMA ligation compared to cases in which the artery could be preserved. Three of all of the patients showed symptoms of CI and lower relative flux units (RFU < 3.3) than the asymptomatic ones (RFU > 5) [19,18,21,22]. Spectrometry with O2C, which also includes the LDF technique, has been tested with regard to various indications. In 1988 it was validated in open cardiac surgery for judging the supply of myocardial oxygen [26]. Threshold values have also been published concerning the prediction of wound healing after amputations of the lower limb [27]. The device has been further validated for the assessment of bowel perfusion in low anterior rectum resection in a prospective study of 40 patients. The authors identified an O2C flow below 164.43 AU at the serosa of the descending colon as a predictor for postoperative anastomotic insufficiency. However, the authors used a different probe (LFX-55), and values cannot necessarily be compared to our results, which are generally lower [20]. This study has several limitations. Firstly, the small sample size only allows us to make a limited

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statement regarding the average microperfusion in the total patient population. Moreover, it was impossible to calculate O2C threshold values for predicting CI because, fortunately, none of the patients in this cohort suffered from a postoperative CI. It is possible that all patients happened to have resilient microperfusion and would not have developed ischemic complications even without reimplantation. Therefore, there is no way to prove whether the patients who received IMA reimplantation would have otherwise developed CI.

## Conclusion

In summary, O2C spectrometry of the sigmoid colon has been shown to be a feasible procedure for quantifying colonic microperfusion during OAR. The additional use of O2C parameters may increase the discriminatory power for identifying patients at risk of CI. Macroscopically inconspicuous deficits in perfusion can be detected and addressed immediately by revascularization. Future studies are warranted to define threshold values to identify patients at risk for CI. This study may serve as a basis for sample size calculations to design larger studies to confirm the benefit of O2C to guide decisions regarding the need for inferior mesenteric artery reimplantation to prevent colonic ischemia.

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## Conflicts of interest: None

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