Intraoperative Assessment of Gastric Sleeve Oxygenation Using Hyperspectral Imaging in Esophageal Resection: A Feasibility Study

Frank Schwandner Sebastian Hinz Maria Witte Mark Philipp
Clemens Schafmayer Eberhard Grambow

Department of General, Visceral, Vascular and Transplantation Surgery, University Medical Center Rostock, Rostock, Germany

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tissue oxygenation before gastroesophageal anastomosis and might reduce the incidence of anastomotic failure in the gastrointestinal tract.

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Abstract

Introduction: Sufficient tissue oxygenation is essential for anastomotic healing in visceral surgery. Hyperspectral imaging (HSI) is a noncontact, noninvasive technique for clinical assessment of tissue oxygenation in real time. **Methods:** In this case series, HSI was used in 4 patients who were admitted for either esophageal cancer or cardiac carcinoma (AEG type I or II). Thoraco-abdominal surgical esophageal resection was performed after staging and neoadjuvant therapy. Intraoperative oxygenation of superficial (StO₂) and underlying tissue (NIR perfusion index) of the gastric sleeve were studied intrathoracic by means of the TIVITA® Tissue HSI camera. This was performed prior to esophagogastric anastomosis. The postoperative course, especially in view of surgical complications, was recorded. **Results:** Assessment of StO₂ and NIR perfusion index was performed in 4 regions of interest per gastric sleeve, aboral and oral of the clinically determined resection line. It allowed the fast quantification of gastric oxygenation prior gastroesophageal anastomosis. Median StO₂ aboral of the determined resection line was 69%, while median StO₂ in the oral part of the gastric sleeve was found at 53%. In contrast, the median NIR perfusion index was similar aboral (80) and oral (82) of the resection line. In none of the 4 studied patients, an anastomotic failure appeared. **Discussion/Conclusion:** This report suggests that HSI is a feasible technique for intraoperative assessment of

Introduction

Curative surgical therapy of esophageal cancer and cardiac carcinoma (AEG type I or II) involves thoracoabdominal operation with resection of tumor and lymph nodes and preparation of the gastric sleeve for esophago-gastric anastomosis. Thereby, anastomosis failure is a major complication. Especially in upper gastrointestinal surgery, anastomotic failure is associated with markedly increased morbidity and mortality for the patient, resulting in significant burden to the health system [1, 2]. It requires a fast detection and respective surgical or endoscopic therapy. Reasons for anastomotic failure are multifactorial and include technical aspects like tension of the anastomosis, the used type of suture material, the technique of anastomosis, as well as patient-derived characteristics such as liver cirrhosis, smoking behavior, alcohol abuse, cachexia, systemic infections, immunosuppression, chronic kidney disease, arterial hypertension, or diabetes mellitus. Other external circumstances affecting anastomotic healing are neoadjuvant radiation or chemotherapy, perioperative volume therapy, and blood transfusion [3]. However, impaired perfusion of gastroesophageal anastomoses or the gastric sleeve is one of the most important factors for anastomotic complications [4–6]. A

Table 1. Characteristics of the 4 studied patients

	Patient 1	Patient 2	Patient 3	Patient 4
Age, years	63	69	48	72
Gender	Male	Male	Male	Female
Diagnosis	Esophageal carcinoma (squamous cell carcinoma)	Cardiac carcinoma AEG II (adenocarcinoma)	Cardiac carcinoma AEG I (adenocarcinoma)	Cardiac carcinoma AEG I (adenocarcinoma)
Neoadjuvant therapy	Radiochemotherapy	Chemotherapy (4x cycle FLOT)	Chemotherapy (6x cycle FLOT)	Chemotherapy (4x cycle FLOT)
Comorbidity	Arterial hypertension	Arterial hypertension Aortic valve insufficiency grade II Mitral valve insufficiency grade II	–	Arterial hypertension Diabetes mellitus
Operation	Thoracoabdominal esophageal resection, gastric sleeve, cholecystectomy, jejunal catheter	Thoracoabdominal esophageal resection, gastric sleeve, cholecystectomy, jejunal catheter	Thoracoabdominal esophageal resection, gastric sleeve, cholecystectomy, jejunal catheter, atypical lung resection	Thoracoabdominal esophageal resection, gastric sleeve, jejunal catheter
Histology	ypT0 pN0(0/18) L0 V0 Pn0 R0	G2 ypT3 ypN1(2mi/27) L0 V0 Pn0 R0	G3 pT3 pN1(2mi/44) L1 V0 Pn0 R1	ypT0 ypN0(0/22) L0 V0 Pn0 R0

sufficient intraoperative evaluation of esophageal and gastric perfusion is essential to reduce the risk for anastomotic failure. Recently, hyperspectral imaging (HSI), a noninvasive, noncontact technique for quantification of tissue perfusion, was successfully tested for intraoperative assessment of bowel perfusion during colorectal resections [7, 8] and during esophagectomy [6]. Here, we report the results of the first 4 cases of intraoperative HSI measurement to analyze gastric sleeve perfusion intraoperatively during esophageal resection in our department.

Materials and Methods

Patient Characteristics

All 4 patients were admitted to the Department for General, Visceral, Vascular and Transplantation Surgery at the University Medical Center Rostock, Rostock, Germany, for operation with the diagnosis of esophageal cancer or cardiac carcinoma (AEG type I or II). The detailed patient characteristics are given in Table 1. In short, all cases were discussed in our multidisciplinary tumor board, and surgical resection after neoadjuvant therapy was recommended.

HSI Camera System

Oxygenation of the gastric sleeve was assessed by means of the TIVITA® Tissue HSI camera (Diaspective Vision, Am Salzhaff, Germany). The TIVITA® Tissue provides precise reproducible parameters with high spatial resolution allowing for highly reliable determinations of the perfusion state of the measured tissue and for the analysis of spatial perfusion distribution. The camera system includes an internal push broom imaging spectrograph used for spectral data acquisition along the x-axis that acquires a full spectrum for every point of the row in parallel, a high-quality infrared enhanced CMOS megapixel camera sensor, integrated in an intelligent camera with USB3-data transfer for high recording speed and an internal stepper motor moving the slit of the spectrograph

at the first image plane of the optical setup along the y-axis to realize the image acquisition. With this system, a hyperspectral image can be acquired without the need of moving the camera or the patient. The distance between the camera and the investigated tissue is standardized at 50 cm. This distance is defined by 2 LED lights (red and green) that fuse to 1 light point on the investigated tissue when the respective distance of 50 cm is reached. The measurement creates the so-called 3-dimensional hyperspectral data cube with the spatial x- and y-axis as well as the spectral λ -axis. The hyperspectral data cube has an image resolution of 640×480 and comprises a spectral range from 500 to 1,000 nm with a resolution of 5 nm (100 spectral bands). The parameter calculation was developed by an empirical approach considering the known optical properties of tissues and blood and was calibrated by occlusion tests with healthy volunteers against a commercial tissue oximeter [9].

It is a noninvasive, noncontact imaging technique that enables spectroscopical measurement of tissue oxygenation over a larger area without the need for contrast agents or radiation. The TIVITA® Tissue is designed to detect and measure the chromophores hemoglobin with its derivatives oxyhemoglobin O₂Hb and deoxyhemoglobin HHb and water to provide a 2-dimensional map of oxygenation pattern (StO₂ and NIR perfusion index). StO₂ and NIR perfusion index describe the relative oxygen saturation of hemoglobin in the microcirculatory system of the examined area in superficial tissues about 1 mm (StO₂) and deeper tissues about a 3-mm depth (NIR perfusion index) [10].

Intraoperative Procedure of HSI

In principle, resection was performed as standard Ivor-Lewis operation. The abdominal preparation of the gastric sleeve was performed by means of the Echelon Flex Powered stapler (Johnson & Johnson, New Brunswick, NJ, USA). After positioning of the gastric sleeve in the thorax, tissue perfusion was assessed by means of HSI before shortening it to the optimal length for the esophago-gastric anastomosis. The resection line for the anastomosis was determined by clinical examination of the gastric sleeve and was not affected by the assessed oxygenation parameters. The oxygenation was assessed in 4 regions of interest (ROI) with a standardized diameter of 30 pixel. They were positioned oral and aboral of the clinically defined resection line of the gastric sleeve. The dis-

tance between the ROIs was chosen individually with respect to the length of the gastric sleeve. After the HSI measurement, the transection of the sleeve was also performed using an Echelon Flex Powered stapler, and the anastomosis was created using a 25-mm Echelon Circular Powered stapler (Johnson & Johnson, New Brunswick, NJ, USA).

Results

Patient 1

A 63-year-old male patient with a low-grade squamous cell carcinoma of the esophagus was discussed in our multidisciplinary tumor team and a neoadjuvant chemoradiotherapy prior surgical tumor resection was conducted. As a comorbidity, an arterial hypertension existed. After a cumulative radiotherapy with 41.4 Gy and carboplatin/paclitaxel treatment, the restaging after neoadjuvant therapy revealed no metastases. The preoperative esophagoscopy showed a persistent stenosis 29 cm from the incisors. Therefore, a thoracoabdominal esophageal resection was indicated and performed according to standard. After positioning the gastric sleeve in the thorax, HSI was performed (Fig. 1A). Postoperatively, the patient was admitted to the intensive care unit (ICU) for 3 days. The postoperative course was uneventful. Histologic analysis defined the tumor stage ypT0 pN0 (0/18) L0 V0 Pn0 R0. In the postoperative tumor board conference, an oncologic surveillance was recommended. The patient was discharged 19 days after the surgery.

Patient 2

A 69-year-old male patient with a cardiac carcinoma AEG II was discussed in our multidisciplinary tumor team, and a neoadjuvant chemotherapy (4x cycle FLOT) was conducted prior to the surgical tumor resection. As a comorbidity, arterial hypertension, aortic valve insufficiency grade II, and a mitral valve insufficiency grade II existed. A thoracoabdominal esophageal resection was indicated and performed according to standard as described for patient 1. Tissue perfusion was assessed like in patient 1 by means of HSI (Fig. 1B). Postoperatively, the patient was admitted to the ICU for 2 days. The postoperative course was uneventful except for a wound healing disorder, which was treated conservatively. Histologic analysis defined the tumor stage G2 ypT3 ypN1(2mi/27) L0 V0 Pn0 R0. In the postoperative tumor board conference, an adjuvant chemotherapy was recommended. The patient was discharged 11 days after the surgery.

Patient 3

A 48-year-old male patient with a cardiac carcinoma AEG I was discussed in our multidisciplinary tumor team, and a neoadjuvant chemotherapy (6x cycle

FLOT) was conducted prior to surgical tumor resection. No comorbidity existed. Thoracoabdominal esophageal resection was indicated and performed according to standard and then tissue perfusion was assessed by means of HSI (Fig. 1C). Postoperatively, the patient was admitted to the ICU for 22 days. The postoperative course was characterized by an acute respiratory distress syndrome (ARDS) with pneumonia followed by dilatative tracheotomy. A gastroscopy due to increased infection signs on the 7th postoperative day showed an inconspicuous anastomosis. Histologic analysis defined the tumor stage G3 pT3 pN1(2mi/44) L1 V0 Pn0 R1. Due to the R1 situation, the postoperative tumor board conference recommended a local radiation therapy. The patient was discharged 32 days after the surgery.

Patient 4

A 72-year-old female patient with a cardiac carcinoma AEG I was discussed in our multidisciplinary tumor team, and a neoadjuvant chemotherapy (4x cycle FLOT) was conducted prior to surgical tumor resection. As comorbidities, diabetes mellitus (dietary) and arterial hypertension existed. Thoracoabdominal esophagus resection was indicated and performed according to standard and also tissue perfusion was assessed by means of HSI (Fig. 1D). Postoperatively, the patient was admitted to ICU for 9 days. The postoperative course was characterized by a pneumonia and chyle fistula, both treated conservatively. A gastroscopy due to increased infection signs on the 6th postoperative day showed an inconspicuous anastomosis. Histologic analysis defined the tumor stage ypT0 ypN0(0/22) L0 V0 Pn0 R0. In the postoperative tumor board conference, a completion of adjuvant chemotherapy was recommended. The patient was discharged 25 days after the surgery.

Intraoperative Oxygenation Assessment

The intraoperative oxygenation parameters StO₂ and NIR perfusion index are shown in Figure 1. Referring to the defined resection line, quantification of both parameters in the aboral part of the gastric sleeve revealed a StO₂ range from 51 to 84% and a NIR perfusion index range from 70 to 89 in all 4 patients. The median StO₂ in the aboral part was 69% (25% percentile: 65.5%; 75% percentile: 75.5%), the median NIR perfusion index was 80 (25% percentile: 74.5; 75% percentile: 84.5). In contrast, the oxygenation parameters oral of the resection line were found lower, with StO₂ ranging from 40 to 71% and NIR perfusion index ranging from 70 to 83 (Table 2). Here median StO₂ was 53% (25% percentile: 51%; 75% percentile: 67%), median NIR perfusion index was found at 82 (25% percentile: 80; 75% percentile: 83).

Fig. 1. Hyperspectral analysis of gastric sleeve perfusion. In all 4 patients (**A–D**, respectively), intraoperative red-green images show the gastric sleeve before resection and subsequent esophagogastric anastomosis. The clinically defined resection line is shown dashed. Hyperspectral assessment included analysis of superficial (StO_2) and deeper (NIR perfusion index) tissue oxygenation in 4 ROIs.

Discussion/Conclusion

HSI bears the benefits of a noninvasive, mobile, easy to use technique that can visualize tissue oxygenation saturation in real time without the need for any contrast

agents. This could be a benefit compared to other methods for intraoperative assessment of perfusion during esophagectomy like the indocyanine green (ICG) fluorescence technique [11]. ICG angiography indirectly measures tissue perfusion by emission of excitation of the ex-

Table 2. Intraoperative oxygenation parameter of the gastric sleeve

	StO ₂ , %	NIR perfusion index
<i>Patient 1</i>		
Aboral	74	72
	69	74
	67	70
Oral	51	70
<i>Patient 2</i>		
Aboral	75	78
	69	85
	76	89
Oral	71	83
<i>Patient 3</i>		
Aboral	84	80
	79	75
Oral	67	82
	40	83
<i>Patient 4</i>		
Aboral	54	82
	51	84
	64	85
Oral	53	80

StO₂ and NIR perfusion index were assessed in the gastric sleeve aboral and oral from the clinically defined resection line.

ogenously supplied fluorescent dye. In contrast, HSI allows direct quantification of tissue oxygenation. The hyperspectral dataset as well as the quantitative analysis are stored in the camera system which is an important aspect for postoperative recapitulation of intraoperative tissue perfusion and might have legal relevance in future when it comes to the question of intraoperative tissue perfusion. Due to these aspects, the camera system is actually tested in different clinical settings. It comprises analysis of wounds to predict wound perfusion and healing [12, 13], detection of brain cancers [14, 15], depth assessment of thermal wounds [16], and microcirculatory effects of postoperative therapy in Dupuytren's disease [17]. Our own group previously showed the feasibility of HSI for detection of peripheral artery disease [10].

In visceral surgery, the TIVITA® Tissue was already used for evaluation of colon perfusion and during esophagectomy [6, 7]. Jansen-Winkel et al. [7] have recently showed that HSI allows precise quantification of bowel perfusion in colorectal surgery. Therefore, it could be used to determine of the optimal resection margin with respect to tissue oxygenation. The technical details of this camera system were previously described in detail [10, 18]. Intraoperative assessment of this parameters took about 1 min, including positioning of the camera, record of the hyperspectral data, and quantification of StO₂ and

NIR perfusion index by means of the software TIVITA® suit that is included in the camera system. The intraoperative gained data allowed a direct visualization and quantification of the gastric sleeve. As indicated by the figure, HSI analysis was performed after positioning of the sleeve in the thorax (Fig. 1). The circular ROI for quantification of StO₂ and NIR perfusion index of the gastric sleeve were defined after clinical determination of the resection line for subsequent esophagogastric anastomosis. Over all 4 patients, StO₂ was found lower in the resected oral part of the gastric sleeve. In the aboral part of the gastric sleeve, the median StO₂ in this case series was comparable to the median StO₂ described by Koehler et al. [6] in the group without ischemic preconditioning. Although the studied patient group is small, this accounts for the comparability of oxygenation values in the gastric tube assessed by HSI. In 1 of the 4 patients (patient 3), the NIR perfusion index was slightly higher in the oral part than in the aboral part, respectively to the resection line. The other 3 patients showed a lower or similar NIR perfusion index in the oral part than in the aboral part of the resection line. The intraoperative orientation of the camera differed between the different images (Fig. 1). However, this did not affect the oxygenation analysis of the gastric sleeve. This case series shows that the oxygenation is different in the gastric sleeve tissue. Therefore, the HSI technique could enable the surgeon to correct the location of the anastomosis due to quantitative assessment of tissue perfusion if oxygenation is insufficient. Although the intraoperative use of HSI was successful and surgical treatment of the patients was uneventful, prospective studies with large, convincing numbers of studied cases are needed to establish standard and cutoff values for the oxygenation parameters StO₂ and the NIR perfusion index. As catecholamine treatment affects organ perfusion due to vasoconstriction, further studies should also account for the intraoperative catecholamine therapy and circulatory parameters, including arterial blood pressure, central venous pressure, and heart frequency, which were not addressed in this study. Another important aspect that should be considered for future studies is the standardized positioning of the ROI with identical distances between each ROI. This will improve the standardized oxygenation assessment as well as the comparability and the documentation of the gained data between different patients, respectively.

In summary, this is a proof-of-principle study that successfully illustrates and supports the promising use of intraoperative HSI technique for oxygenation assessment during esophageal resection in visceral surgery. In future, this technique could be a valuable tool to reduce the still relevant high incidence of anastomotic leakage that is associated to a significant increase in morbidity and mortality.

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Statement of Ethics

The study was conducted ethically in accordance with the World Medical Association Declaration of Helsinki. The patient gave written informed consent to publish this case (including publication of the images).

Disclosure Statement

The authors have no conflicts of interest to declare.

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Author Contributions

All authors planned the hyperspectral analysis in the presented case. F.S. and E.G. contributed to writing and drafting of the manuscript and performed the hyperspectral analysis.

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