International Journal of Surgery 48 (2017) 210–214

Contents lists available at ScienceDirect

International Journal of Surgery

journal homepage: www.elsevier.com/locate/ijsu

Original Research

Indocyanine green tissue angiography affects anastomotic leakage after esophagectomy. A retrospective, case-control study

Ioannis Karampinis[a], Ulrich Ronellenfitsch[b], Christina Mertens[a], Andreas Gerken[a], Svetlana Hetjens[c], Stefan Post[a], Peter Kienle[a], Kai Nowak[a,*]

[a] Department of Surgery, Mannheim University Medical Centre, University of Heidelberg, Theodor Kutzer Ufer 1-3, 68167, Mannheim, Germany
[b] Department of Vascular and Endovascular Surgery, University of Heidelberg, Im Neuenheimer Feld 110, 69120, Heidelberg, Germany
[c] Institute of Medical Statistic and Biomathematics, Mannheim University Medical Centre, University of Heidelberg, Ludolf-Krehl Strasse 13-17, 68167, Mannheim, Germany

ARTICLE INFO

Keywords:
Gastric conduit
Esophagectomy
Anastomotic leakage
Indocyanine green
Fluorescence angiography

ABSTRACT

Purpose: Optimal perfusion of the gastric conduit during esophagectomy is elementary for the anastomotic healing since poor perfusion has been associated with increased morbidity due to anastomotic leaks. Until recently surgical experience was the main tool to assess the perfusion of the anastomosis. We hypothesized that anastomoses located in the zone of optimal ICG perfusion of the gastric conduit ("optizone") have a reduced anastomotic leakage rate after esophagectomy.

Methods: Indocyanine green (ICG) fluorescence tissue angiography was used to evaluate the anastomotic perfusion in 35 patients undergoing esophagectomy with gastric conduit reconstruction. The transition point of the "optizone" to the malperfused area of the conduit was defined macroscopically and with the use of ICG angiography during the operation. The anastomosis was performed in the optizone whenever possible. The results of the ICG patients were retrospectively reviewed and compared with 55 patients previously operated without ICG angiography.

Results: The visual assessment of the conduit perfusion concurred with the ICG angiography in 27 cases. In 8 cases (22.8%) the ICG angiography deviated from the visual aspect. One case of anastomotic leakage was observed in the group of patients in which the anastomosis could be performed in the optizone (1/33; 3%) compared with 10 cases in the control group (18%; $p = 0.04$). In two cases we had to perform the anastomosis in an area of compromised ICG perfusion. Both patients developed an anastomotic leakage.

Conclusions: ICG tissue angiography represents a feasible and reliable technical support in the evaluation of the anastomotic perfusion after esophagectomy. In this retrospective analysis we observed a significant decrease in anastomotic leakage rate when the anastomosis could be placed in the zone of good perfusion defined by ICG fluorescence. A prospective trial is needed in order to provide higher level evidence for the use of ICG fluorescence in reducing leakage rates after esophagectomy.

1. Introduction

Esophageal carcinoma incidence has been rising during the past decade in the western world [1]. Despite various innovative therapeutic modalities, surgical resection remains the only curative solution. Progress in perioperative treatment and complication management has reduced the operative risk in patients undergoing esophagectomy. However, anastomotic leaks still remain a major cause of morbidity in esophageal surgery [2].

Cervical anastomosis has been historically associated with higher rates of anastomotic leaks and remains probably the most challenging anastomosis in gastrointestinal surgery [3]. However, it is sometimes preferred because the clinical consequences for the patient are usually less severe. Leaks from intrathoracic anastomosis, on the other hand, are less common than cervical leaks, but more often lead to severe complications [3].

It is widely accepted that the main factors influencing the healing of the anastomotic region are the arterial perfusion and the tension of the

* Corresponding author.
E-mail addresses: Ioannis.karampinis@umm.de (I. Karampinis), Ulrich.ronellenfitsch@med.uni-heidelberg.de (U. Ronellenfitsch), Christina.mertens@umm.de (C. Mertens), Andreas.gerken@umm.de (A. Gerken), Svetlana.hetjens@medma.uni-heidelberg.de (S. Hetjens), Stefan.post@umm.de (S. Post), Peter.kienle@umm.de (P. Kienle), kai.nowak@umm.de (K. Nowak).

https://doi.org/10.1016/j.ijsu.2017.11.001
Received 2 August 2017; Received in revised form 15 October 2017; Accepted 2 November 2017
Available online 13 November 2017
1743-9191/

anastomosis. The right gastric and gastroepiploic arteries are the only vessels supporting the anastomosis after formation of a gastric conduit. However, the vascular arcade rarely reaches the proximal stomach, which is mainly supplied by a submucosal plexus [4–6]. Several procedures ranging from intraoperative oxygen saturation measurements, intraoperative Doppler sonography, conventional and CT angiography up to ischemic preconditioning of the stomach have been tested in order to objectify and measure the perfusion of the anastomotic region, but none of these methods has been implemented in the everyday surgical practice [7].

Lately, intraoperative indocyanine green (ICG) fluorescence angiography has been introduced for the assessment of the blood supply in open and minimally invasive procedures [8,9]. After intravenous injection, ICG can be visualized using a near-infrared camera, offering the surgeon real-time information regarding the blood supply of the anastomotic region.

In this trial we assessed the feasibility and reliability of ICG fluorescence angiography for the evaluation of the perfusion of the gastric conduit during open and minimal-invasive esophagectomy. We defined a zone in the peripheral part of the gastric conduit macroscopically (visually) and with the use of ICG fluorescence angiography (optizone). We hypothesized that anastomoses located in the zone of optimal ICG perfusion of the gastric conduit (optizone) show a reduced anastomotic leakage rate after esophagectomy.

2. Material and methods

2.1. Patient characteristics

90 patients with primary esophageal carcinoma undergoing esophagectomy in our department were enrolled in this study. 35 patients were operated between August 2014 and December 2016 with intraoperative ICG fluorescence angiography. The results were compared to a consecutive cohort of 55 patients who had been operated between 2010 and 2014 without intraoperative ICG tissue angiography. The inclusion criterion for the trial was scheduled esophagectomy for resectable esophageal cancer. The study was approved by the local ethics committee. Patients gave their informed consent for the use of their data. The research is being reported in line with the STROBE criteria.

2.2. Surgical procedure

A 3- to 5-cm wide gastric conduit was created under preservation of the right gastric (when possible) and gastroepiploic artery. Linear staplers were used to prepare the gastric conduit and the staple lines were oversewn with PDS 4-0 sutures (Ethicon, Norderstedt, Germany). Patients with distal esophageal cancer were operated with a transthoracic approach with an anterolateral thoracotomy in supine position [10]. The tubularized gastric conduit was brought up to the posterior mediastinum and a stapler was used for the anastomosis (25mm intraluminal circular stapler, Ethicon, Norderstedt, Germany). Patients with tumor of the proximal or upper thoracic esophagus were operated thoracoscopically in prone position [11]. After pull-up of the gastric conduit to the neck, a cervical end to end hand-sewn single layer anastomosis was performed.

2.3. Intraoperative assessment of the conduit perfusion in the ICG group

After preparation of the gastric conduit, the PinPoint system (Novadaq, Ontario, Canada) was used to assess the blood perfusion. The PinPoint imaging system is designed to acquire fluorescent images in minimally invasive or open surgery using indocyanine green (ICG) as fluorescent agent. Upon intravascular administration, ICG is rapidly bound to plasma proteins (> 98%). Peak spectral absorption of ICG in blood is at 800–810nm. ICG is taken up by the liver and excreted unchanged into the bile. The plasma half-time is 3–5 minutes. Images are acquired using a charge coupled device video camera sensitive to near infrared light and are displayed real time on a monitor. The system provides simultaneously the natural white light image, a black/white contrast fluorescence mode, a fluorescence green enhanced white light mode and an additional semi-quantitative colorized fluorescence mode. The sequences are automatically saved to allow further analysis, review and archiving.

The time between gastric tube creation and ICG angiography was approximately 20 minutes. Image caption began at central-line injection of 7.5mg ICG which was immediately followed by a 10ml flushing with normal saline. Hemodynamic parameters and catecholamine support were recorded during the operation.

The zone of optimal perfusion of the proximal gastric conduit (optizone) was defined with the use of ICG angiography and the lower margin of the optizone was marked. This spot identified the transition from the optizone to the malperfused area (Fig. 2). An effort was made to place the anastomosis proximal to this transition point, within the optizone area. ICG Angiography was always performed in the abdomen, before the pull up of the gastric conduit. If our macroscopic assessment of the perfusion changed after the pull up, we repeated the ICG angiography in order to rule out damage of the conduit and ensure that the zone of optimal perfusion still concurs with the initial assessment. The conduit was always shortened after the pull up, respecting the findings of the ICG angiography whenever possible.

2.4. Assessment of anastomotic healing

Nasogastric tubes were routinely removed within 24 hours after the operation. 5-7 days postoperatively all patients received methylene-blue dye dissolved in tea (200ml). Drainage fluid was intensively observed for coloring. If the drainage fluid remained clean and there was no clinical evidence for leakage, transition to oral diet was performed. If a leak was assumed due to clinical signs an upper endoscopy was performed.

Comorbidities and risk factors for poor anastomotic healing were evaluated, including ASA score, cardiopulmonary disorders, smoking status, alcohol abuse, neoadjuvant treatment (radiotherapy, chemotherapy).

2.5. Statistics

Data were collected from our prospective upper-GI database. Quantitative variables are presented by mean values ± standard deviation. For approximately normally distributed data two-sample t-tests were used in order to compare the mean values of two groups. For skewed variables Mann–Whitney U-tests were performed instead. For the comparison of qualitative parameters Fisher's exact tests were applied. Logistic regression was performed as a multivariable model in order to analyze two factors for a binary outcome simultaneously. All statistical calculations were done with the SAS software, release 9.3 (SAS Institute Inc. Cary, NC, USA). Statistical significance was assumed for p values less than 0.05.

3. Results

3.1. ICG group

35 consecutive patients with primary esophageal carcinoma were operated in our department between August 2014 and December 2016 with intraoperative ICG fluorescence angiography. The anastomotic leakage rate of the complete cohort was 8.57% (3 cases). In 33 cases the anastomosis could be performed within the optizone area with one leakage observed (3%). In 2 patients undergoing esophagectomy with cervical anastomosis the gastric conduit could not be shortened and the anastomosis was placed beyond the optizone area within an area of reduced ICG perfusion. Those patients were analyzed separately.