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ORIGINAL ARTICLE

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# Postoperative recovery of microcirculation after gastric tube formation

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**Abstract** *Background and aims:* The formation of a gastric tube is associated with partial devascularisation of the stomach and impaired tissue perfusion in the anastomotic region. The aim of the study was to gain data on the time interval of microcirculatory recovery of the normal gastric conduit. *Patients and methods:* Twenty-nine out of 49 consecutive patients who had undergone oesophagectomy and reconstruction with a gastric tube and intrathoracic oesophagogastrostomy were selected. Inclusion criterion was an uncomplicated postoperative course. After the patients' admission to ICU, continuous measurement of mucosal $pCO_2$ ($pCO_2I$) was commenced, with the use of recirculating gas analysis with a TONOCAP device. $pCO_2I$ values (in mmHg and kPa) were recorded hourly and related to the arterial $pCO_2$ ($\Delta pCO_2 = pCO_2I - pCO_2a$). In addition, mean arterial pressure (MAP), cardiac output (CO) and systemic vascular resistance (SVR) were measured by pulse contour analysis. *Results:* $pCO_2I$ was monitored over an average period of 79 h (total 2,288 measurements). The mean $\Delta pCO_2$ before extubation was 12.4 mmHg (1.7 kPa) ± 8.7 SD (1.2 kPa). After extubation, there was an increase in $\Delta pCO_2$ values in all 29 patients. The peak $\Delta pCO_2$ of 27.4 mmHg (3.7 kPa) ± 12.6 SD (1.7 kPa) was observed 18 h after extubation. This was followed by a steady decline in $\Delta pCO_2$ values that almost reached baseline $\Delta pCO_2$ values after 4 days of monitoring. Changes in $\Delta pCO_2$ did not correlate with changes in MAP, CO and SVR. *Conclusions:* High levels of $pCO_2I$ indicate an impaired postoperative microcirculation in normal gastric tubes. After initial deterioration, gastric microcirculation takes approximately 4 days to recovery. These data are important for the implementation of ischaemic conditioning prior to gastric tube formation and gastric pull-up.

**Keywords** Oesophagectomy · Gastric interposition · Microcirculation · Tonometry · Mucosal $pCO_2$ measurement

## Introduction

The formation of a gastric tube as standard reconstruction after subtotal oesophagectomy induces microcirculatory changes in the gastric fundus. This is due to partial devascularisation of the stomach, in particular the ligation of the left gastric artery [1]. The intraoperative reduction of tissue perfusion and tissue oxygenation has been demonstrated in several clinical and animal studies [2–6] and is well accepted as the main cause of anastomotic leakage. However, although almost all patients demonstrate this intraoperative impairment, only a minority develop, postoperatively, a leakage of the oesophagogastrostomy. This suggests that even a reduced tissue perfusion is sufficient

for adequate anastomotic healing in the majority of gastric conduits if microcirculation recovers during the early postoperative course. Experimental data have shown that, after devascularisation of the stomach and delayed formation of the gastric conduit, microcirculation has improved at the time of reconstruction [7–9]. This therapeutic principle, known as ischaemic conditioning of the gastric interposition, might help to reduce the rate of anastomotic break down.

However, no data exist about the time interval of microcirculatory recovery of the gastric conduit. This is mainly due to a lack of appropriate and well-established methods that sufficiently monitor microcirculation of the gastric interposition during the postoperative course. In contrast to intraoperative measurement of tissue perfusion, which can be done on the serosal surface, postoperative monitoring has to be done from the endoluminal mucosal site. Intestinal tonometry measuring the mucosal $pCO_2$ ($pCO_2I$) has proven to reflect the balance between intestinal metabolism, intestinal perfusion and alveolar ventilation [10, 11]. With regard to the gastric conduit, the validity of continuous tonometry was demonstrated in an intraoperative study in which changes in $pCO_2I$ were observed after ligation of the left gastric artery [12]. A second observational study on 49 patients with oesophageal carcinoma was done to evaluate the predictive value of $pCO_2I$ measurement in the diagnosis of anastomotic leakage during the postoperative course [13]. Out of this group of consecutive patients a cohort was selected that was characterised by a postoperative course without any complications. The aim of the present study was to analyse the course of mucosal $pCO_2$ in that patient group and to gain data on the microcirculatory recovery of the normal gastric conduit during an uncomplicated postoperative period.

## Materials and methods

### Patients

Twenty-nine patients with oesophageal carcinoma were included in this prospective, observational study. They were selected from a series of 49 consecutive patients undergoing postoperative $pCO_2I$ measurement postoperatively. Data from those 49 patients have been described elsewhere [13]. Selection criterion for the 29 out of the consecutive series of 49 patients was an uncomplicated postoperative course, which was defined as follows [14]: mechanical ventilation <24 h, stay on intensive care and/or intermediate care unit (ICU) <7 days, no anastomotic leakage, no re-operation, no re-admission to ICU. Twenty-five patients were male, four patients female. The mean age was 53.2 years (range: 38–75 years). Twenty-one patients (72.4%) had an adenocarcinoma, and eight patients (17.6%) a squamous cell carcinoma. Because of a locally advanced tumour 12 patients (41.4%) received neoadjuvant radiochemotherapy according to a standardised protocol. The study protocol was approved by the local institutional human research committee.

### Surgery

In all 29 patients a standardised transthoracic oesophagectomy with two-field lymphadenectomy of the abdominal and mediastinal compartment was performed. The operating technique is described in detail elsewhere [15].

In brief, after laparotomy the hiatus was opened to confirm resectability of the primary tumour. Then, the stomach was completely mobilised. This included the preservation of the right gastric artery as well as the gastroepiploic arcade along the greater curvature. The short gastric arteries and the left gastric artery were dissected. A partial lymphadenectomy of the abdominal compartments I and II was performed. After closure of the abdomen the patient was moved into a left lateral position and an anterolateral thoracotomy through the fifth intercostal space was performed. After en-bloc mobilisation of the intrathoracic oesophagus and mediastinal lymph nodes, the oesophagus was transsected in the upper mediastinum above the level of the azygos vein, and the mobilised stomach was pulled into the chest. A circular stapler (CEEA 28, Tyco, Germany) was inserted through the lesser curvature, and a stapler oesophagogastrostomy was performed between the gastric fundus and oesophageal stump. The procedure was completed by resection of the lesser curvature with the adherent oesophagus, by use of a linear stapler (TA 90, Tyco). After the intrathoracic anastomosis had been completed, a 16F tonometry nasogastric tube (Datex Ohmeda, Duisburg, Germany) with a silicone balloon at its distal end was placed in the gastric conduit. Under bi-manual palpation, the upper edge of the silicone balloon was positioned 2 cm below the anastomosis. A postoperative chest X-ray confirmed the correct position of the nasogastric tube. In all patients a complete resection of the primary tumour could be achieved (R0 resection).

### Recirculating gas tonometry

Immediately after each patient's admission to ICU, $pCO_2I$ measurement was initiated. Continuous tonometry was based on recirculating gas analysis with a TONOCAP device (Datex Ohmeda). The TONOCAP measures the gradient between balloon and luminal $CO_2$ concentration of hollow visceral organs, which is closely related to the mucosal $CO_2$, somewhat reflecting a regional metabolic state. The measured $CO_2$ concentration was expressed as partial pressure in millimetres of mercury (kPa). The cycle of measurement was repeated at 15-min intervals. According to the manufacture's instruction, calibration of the TONOCAP required three to four cycles of recirculating gas analysis, so the $pCO_2I$ values of the first hour were not included for further statistical analysis. Thereafter, the first measured $pCO_2I$ value for each hour was documented. According to international standards [10, 11] $pCO_2I$ was related to the arterial $pCO_2$ ($\Delta pCO_2 = pCO_2I - pCO_2a$). Arterial $pCO_2$ (in millimetres of mercury) was obtained by blood gas analysis taken routinely six hourly. All patients received a daily dose of 40 mg omeprazole, intravenously, until oral intake was begun on postoperative days 7–9. Postoperative tonometry was performed for as long the patient required the nasogastric tube or was treated on ICU. The decision to remove the nasogastric tube was entirely based on clinical judgement and was not influenced by the study protocol.

### Haemodynamic monitoring

For the first eight patients of this series, cardiac output, systemic vascular resistance (SVR) and mean arterial pressure (MAP) were measured so that the influence of the haemodynamic parameters on $pCO_2I$ measurement could be excluded. This was done with the PICCO device (Pulsion Medical System, Munich, Germany). For

calibration, the device measured transcardiopulmonary cardiac output (TCPCO) based on thermodilution. Recalibration was done 24 hourly. For continuous measurement of CO the pulse contour method (PCCO) was used. Based on continuous PCCO measurement, SVR was calculated by the PICCO device. Haemodynamic parameters were documented hourly, time matched with $pCO_2I$ measurement.

### Statistical analysis

Data are presented as mean and standard deviation if not otherwise noted. The time course of the $\Delta pCO_2$ was analysed after the measurements had been grouped in 6 h intervals. Since postoperative mechanical ventilation ranged from 9 h to 29 h (average of 15.4±4.5 h) the first group included all measurements obtained 6 h prior to extubation. This group was defined as baseline value. Variance analysis was performed so that significant differences between the groups could be evaluated. If variance analysis showed significant differences, post-hoc subgroup evaluation was done with the Bonferroni method. A $P<0.05$ was considered to be significant. Regression analysis (Pearson's) was performed in order that correlation between haemodynamic parameters and $pCO_2I$ could be analysed. All calculations were done with SPSS for Windows, version 10.0.7 (SPSS, Chicago, Ill., USA, 1999).

## Results

For 29 patients, a total of 2,288 $pCO_2I$ measurements was recorded. Based on hourly documentation, the gastric conduit of each patient was monitored over an average period of 79 h (range 17–156 h). The mean $pCO_2I$ was 61.9 mmHg (8.3 kPa) ± 13.5 SD (1.8 kPa); the mean $\Delta pCO_2$ was 20.2 mmHg (2.7 kPa) ± 12.2 SD (1.6 kPa).

The mean $\Delta pCO_2$ during mechanical ventilation and before extubation ($n$=425 measurements) was 12.4 mmHg (1.7 kPa) ± 8.7 SD (1.2 kPa) (Fig. 1). After extubation an increase in $\Delta pCO_2$ values occurred in all 29 patients. The peak $\Delta pCO_2$, at 27.4 mmHg (3.7 kPa) ± 12.6 SD (1.7 kPa) was observed 18 h after extubation, corresponding to 24 h after initiation of measurement on ICU (Fig. 1). The values at 18, 24 and 36 h were significantly different from the baseline values before extubation. After that, a continuous decline in $\Delta pCO_2$ values could be demonstrated. Eighty-four hours after extubation $\Delta pCO_2$ measurement reached its minimum, at 18.2 mmHg (2.4 kPa) ± 7.1 SD (1.0 kPa). This was significantly different from the peak $\Delta pCO_2$ at 18, 24 and 36 h ($P<0.001$) but was not statistically different from the baseline $\Delta pCO_2$ 6 h before extubation (Fig. 1).

For the first eight patients the number of measurements, the mean values of MAP, CO and SVR and the correlation coefficients are displayed in Table 1. In general, changes in $\Delta pCO_2$ did not correlate with changes in haemodynamic parameters.

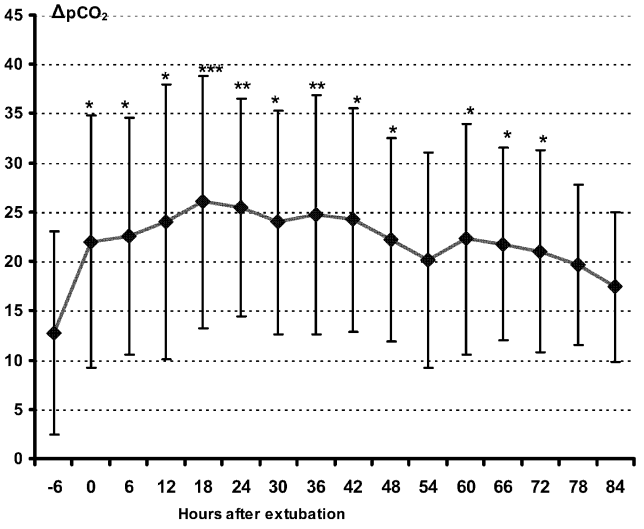


**Fig. 1** Postoperative $\Delta pCO_2$ measurement (mean ± SD), at 6 h intervals, of 29 patients with uncomplicated ICU course after oesophagectomy and reconstruction with a gastric conduit (* significantly different from values at −6 h, ** significantly different from values at −6 and 84 h, *** significantly different from values at −6, 54, 78 and 84 h

**Table 1** Correlation coefficients of haemodynamic parameters with $\Delta pCO_2$ measurements

| Parameter | $n$ | Mean ± SD | $r^2$ |
|---|---|---|---|
| Cardiac output (l/min) | 572 | 6.3±1.8 | 0.001 |
| SVR (dyne × s/cm$^2$) | 572 | 1,065±451 | 0.03 |
| MAP (mmHg) | 572 | 86±13 | 0.07 |

## Discussion

Anastomotic leakage of an oesophagogastrostomy is still the major surgical complication after subtotal oesophagectomy and reconstruction with a gastric tube. The leakage rate depends on the localisation of the anastomosis and ranges from 5% to 25% [15, 16]. The main cause of this complication is the partial devascularisation of the lesser curvature with ligation of the left gastric artery [16]. However, this step of reconstruction is unavoidable, in order for the gastric pull-up to be performed. Therefore, scientific interest focuses on the question of how tissue perfusion and tissue oxygen tension in the gastric fundus can be improved so that the leakage rates of oesophagogastrostomy can be reduced.

Different surgical techniques have emerged to overcome this problem. Fundus rotation gastroplasty does not require dissection of the left gastric artery and results in an increased tissue perfusion of the gastric fundus, compared to the standard gastric tube [4, 17]. The disadvantage of this procedure is an incomplete lymphadenectomy along the lesser curvature and the left gastric artery, which are known to be the major sites of abdominal

metastases in squamous cell cancer and adenocarcinoma of the oesophagus [18, 19]. Another surgical technique is the formation of additional microvascular anastomoses to the upper part of the gastric conduit, which increases the arterial and venous flow along the arcade of the greater curvature [20]. This option requires special microsurgical skills and extends the operation time considerably. Application of pharmacological agents such as prostaglandin E1 has been suggested to induce vasodilation of the splanchnic region, improving tissue perfusion at the anastomotic site [21].

Ischaemic conditioning (delay phenomenon) of the gastric interposition is a concept that might help to reduce the leakage rate of the oesophagogastric anastomosis. This concept is based on performing a gastric pull-up with oesophagogastric anastomosis, after a definite time interval, to the gastric preparation and partial devascularisation of the conduit. In a rodent model, Urschel et al. could demonstrate that gastric tissue perfusion gradually increases after acute gastric devascularisation [22] and that ischaemic conditioning improves the wound healing of oesophagogastrostomy [8]. Akiyama et al. realised the concept of ischaemic conditioning in a series of patients in whom the left gastric and splenic artery were preoperatively embolised [7, 8]. However, the optimal time interval between partial gastric devascularisation and completion of reconstruction is still not known.

The investigation of gastric recovery is limited by methodological difficulties in the continuous monitoring of the microcirculation of the gastric tube during the postoperative course [23, 24]. In recent studies, measurement of mucosal $pCO_2$ by continuous tonometry has been proved to be a valuable tool for the monitoring of the gastric conduit during the intra-operative and postoperative course [12, 13]. It is generally accepted that $pCO_2I$ should be measured by automated air tonometry, which is based on recirculating gas analysis [10, 11, 25]. This method allows a semi-continuous monitoring of $pCO_2I$ and is more reliable than the balloon saline technique that has been widely used in published works of the past [12, 13]. Most of the past clinical work that assessed tonometry as a prognostic factor is also based on mucosal pH (pHi). Since pHi calculation is affected by systemic acid–base status, several authors recommended that the pHi concept be abandoned and that simply the mucosal $pCO_2$ be monitored [10, 11]. Furthermore, it is well accepted that $pCO_2I$ has to be referenced to the arterial $pCO_2$, thereby giving $CO_2$ gap values. This gap reflects, most accurately, an imbalance between gastric mucosal perfusion and metabolism [10, 11]. So that the influence of haemodynamic parameters on $pCO_2I$ measurement could be excluded, MAP, CO and SVR were recorded time matched with tonometric data. It could be demonstrated that the observed changes in mucosal $pCO_2$ are "true" changes and not secondary to changes in cardiac output, MAP and SVR.

The present study included a homogeneous group of 29 patients with oesophageal carcinoma who were selected from a larger cohort of consecutive patients and characterised by an uncomplicated postoperative course. Based on hourly documentation, each patient was continuously monitored over an average period of more than 3 days. One of the main results is that even markedly elevated $pCO_2I$ levels of the gastric conduit are not indicative of a complicated postoperative course. The average $\Delta pCO_2$ of 20 mmHg (2.7 kPa) and the average peak of $\Delta pCO_2$ at 27 mmHg (3.7 kPa) in this series clearly exceed a $pCO_2$ gradient of 1.2 kPa, which has been defined as an upper normal limit [26]. The rise in $pCO_2I$ levels is initiated by the intraoperative devascularisation of the stomach and the gastric pull-up to the upper mediastinum [12]. However, it is not known whether prolonged high $pCO_2I$ levels are due to low tissue perfusion, with a low "wash out" of intracellular $pCO_2$, or indicate a switch from aerobic to anaerobic metabolism with an increase in intracellular $pCO_2$ concentration.

Comparing the results of continuous tonometry with the published data on laser Doppler flowmetry it is obvious that even small changes in $pCO_2I$ levels are equivalent to a severe impairment of microcirculation in terms of tissue perfusion [2, 4, 5, 7]. This fact is important for the interpretation and understanding of $pCO_2I$ changes, as demonstrated for patients with an uncomplicated postoperative course after gastric tube formation. After the patients had been admitted to ICU, their $pCO_2I$ levels of the gastric conduit still increased, which was associated with a change from controlled mechanical ventilation to spontaneous ventilation [13].

In conclusion, the most critical impairment of the microcirculation of normal gastric conduits in patients with an uncomplicated postoperative course was observed 24 h after their admission to ICU. This was followed by a slow but constant recovery that almost reached the baseline values of the microcirculation in terms of $pCO_2I$ levels. Four days after partial devascularisation, microcirculation of the gastric conduit and, therefore, requirements for anastomotic healing, are improved. These data are important in the implementation of ischaemic conditioning into the surgical therapy of oesophageal reconstruction.

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