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Intraoperative Laser Doppler Flowmetry: A Predictor of Ischemic Injury in Acute Mesenteric Infarction

Key Words
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Abstract
Mesenteric ischemia following intestinal infarction caused by occlusion of the superior mesenteric artery is a rare and devastating disease. The overall mortality is a high as 80%. The purpose of this prospective study was to investigate erythrocyte flux to defined areas of the intestine immediately after laparotomy by using laser Doppler flowmetry (LDF) assessment. We tried to predict the intestinal viability and recovery of the small bowel, and further tried to define the level of critical perfusion below which intestinal resection is indicated. 13 patients undergoing surgery for acute mesenteric ischemia were prospectively studied. Multiple LDF assessment of bowel blood flow (4 records/segment) were performed on 48 ischemically injured bowel segments intraoperatively. All patients underwent a second-look procedure within 48 h to define the viability of the previously suspicious segments. All 18 resected bowel segments were histologically evaluated for the extent of ischemia. In addition clinical judgement as well as histological findings were compared with the laser Doppler records. There was a 19% (9 of 48) incidence of histologically proven nonviable bowel segments with a significant decrease in intestinal erythrocyte flux below 50 perfusion units intraoperatively in all those patients. But there was a 50% (9 of 18) incidence of nonviable segments among the clinically proven viable and subsequently resected segments, only. Therefore, clinical judgement alone had a overall accuracy of 87% and a predictive value of only 69%, compared to the 100% overall accuracy, sensitivity and predictive values of LDF assessment. The results of this study demonstrate that LDF is a sensitive guide and feasible method to evaluate and define the viability of ischemically injured intestine.

Introduction

Mesenteric ischemia and infarction following either thrombotic or embolic occlusion of the superior mesenteric artery (SMA) is a rare and devastating disease that is a challenge to early diagnosis.

The overall mortality is reported to be as high as 80% [1–4], and one factor limiting the successful management of such patients is the difficulty in accurately predicting intestinal recovery from ischemic injury following surgical treatment of the underlying disease. Only immediate recognition and aggressive management can prevent the

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often fatal outcome. The difficulties in establishing the clinical diagnosis of visceral ischemia and in assessing intestinal viability intraoperatively have lead to several technically cumbersome methods to identify small intestinal viability [5–8]. Despite these efforts none of the methods has found clinical application. Laser Doppler flowmetry (LDF), which was introduced by Shepard and Riedel [9] in 1982, is a safe, quantitative and reproducible method to measure blood flow in various abdominal organs under sterile conditions. It has been shown to correlate with other flow measurements like fluorescein ultraviolet fluorescence, Doppler ultrasound flowmetry or the isotope washout technique, all of which have been tried in formal clinical trials in patients with intestinal ischemia [5, 6, 10, 11].

Therefore we investigated the microvascular perfusion of 48 suspicious small bowel segments using LDF in a consecutive series of 13 patients undergoing surgery for acute mesenteric ischemic disease. We tried to predict the intestinal viability and recovery of the small bowel, and further tried to define the level of critical perfusion below which the resection of intestine is indicated.

Material and Methods

Thirteen consecutive patients undergoing surgery for acute mesenteric ischemia were prospectively analyzed in this study. Only patients with surgically correctable underlying disease were included in the study. The decision to resect intestinal segments and the extent of resection was based on clinical grounds and after sufficient reperfusion of the revascularized bowel, and was always independent of LDF measurements. Proximal and distal resection margins within 1 cm as well as clinically suspicious intestinal segments were evaluated by LDF before and 15 and 30 min after revascularization and reconstruction. Following these criteria 48 intestinal segments were investigated in 13 patients.

Measurements of the intestinal blood flow were performed intraoperatively on the antimesenteric side of the bowels using a Periflux 4001 Master (Fa. Perimed, Stockholm, Sweden) with a PF 415:1 probe. For detailed description of the LDF technique see Shepard and Riedel [9], Johannson et al. [10], Nilsson et al. [12] and Ahn et al. [13]. Briefly, light generated by a laser diode (780 nm wavelength with a maximum emission of 0.8 mW) penetrates the tissue where it is reflected by circulating blood cells. The reflected light is returned to a photodetector in the instrument and transformed to an electrical signal. The electrical signal is proportional to the number of blood cells moving in the measured volume X the mean velocity of the cells. Analog laser Doppler flow signals were digitalized with an UIM 100 (Biopac. Inc., Galeto, Calif.) and processed with a MP 100 WSW software on a personal computer. Recording of blood flow was performed by a separate surgeon and did not increase operation time. Each segment was recorded by LDF for 30 s and the mean value of flux signals with standard deviations were used. Arterial blood pressure and oxygen saturation were monitored in all patients at the time of recording the LDF signals, and electrolyte solutions were infused to keep the mean arterial pressure between 70 and 90 mm Hg.

In all patients a second-look procedure was performed within 48 h after the initial operation. Viability at the resection margins and previously suspicious areas were again evaluated clinically including visible arterial pulsation, bowel peristalsis and normal color as well as by LDF. In the first procedure the intestinal wall of each suspicious segment was marked (Prolen 5-0) so that exactly the same intestinal segment was found for remeasurement during the second-look laparotomy in cases with full recovery.

During the second-look operation clinically nonviable bowel was also resected. All resected segments were immediately fixed in 3% formaldehyde. Sections were stained with hematoxylin and eosin and histologically evaluated for the extent of ischemia and necrosis according to Bulkley et al. [14] and Krohg-Sorensen et al. [15].

Statistics

The sensitivity (percentage of nonviable segments correctly detected), specificity (percentage of viable segments correctly detected), the predictive value (percentage of ischemic segments scored as nonviable) and the overall accuracy (percentage of correct evaluation) are expressed in confidence limits (± 95%) determined by a binomial distribution. LDF results are given as mean ± SD in perfusion units for each point measured. Student's t test and ANOVA were used to calculate differences for different time points and locations as well as patient subgroups. p values of <0.05 were considered to be statistically significant.

Results

This series contains 9 male and 4 female patients with a mean age of 73 years (range 46–84 years). Ten patients had acute mesenteric ischemia due to thrombotic or embolic SMA occlusion. 1 patient had a combined embolism into the celiac axis and the SMA. One patient had type-b aortic dissection with suprarenal reentry. Another patient had nonocclusive mesenteric ischemia of unknown underlying cause. The mean delay between onset of symptoms and operation was 30 h (± 1.5 h). Embolectomy of the SMA was done in 9 cases, SMA reconstruction in 2 and aortic reconstruction including replacing of the SMA stump in another case.

This series therefore included 13 patients with 48 analyzed intestinal segments. 18 small bowel segments were resected and investigated histologically. Seven small bowel resection were performed in 4 patients at the first laparotomy, 11 small bowel segments were resected in 9 patients during the second-look operation.

The overall mortality was 69%. Six of 13 patients died within 3 days after operation, 3 survived between 15 and 22 days, and 4 patients are still alive.

During first laparotomy, LDF evaluations were made in all 48 bowel segments and gave reproducible signals in all specimens but recorded a decreased erythrocyte flux

below 50 perfusion units (PU) in all clinically doubtful but unresected segments. In these segments erythrocyte flux did not increase significantly after revascularization of the SMA.

At relaparotomy, all these segments still showed laser Doppler flux below 50 PU and were clinically found to be necrotic. All of the resected bowel segments thought clinically to be nonviable at the operation site, but which were histologically viable, had a statistically significantly higher LDF signal (121.23 ± 13.76 PU, mean ± SD) than the critical level of 50 PU.

All patients with clinically viable segments had an increase in bowel perfusion after revascularization and an even higher flow at the second look. There was a 19% (9 of 48) incidence of histologically proven nonviable bowel segments with a significant decrease in intestinal erythrocyte flux below 50 PU intraoperatively in all those patients (fig. 1). The histological assessment of the resected segments revealed that only 9 of 18 segments (50%) had a severe form of intestinal infarction. The other segments were not ischemically damaged and did not pass the histological criteria for nonviable or necrotic bowel. Four of the seven (57%) resected segments at the initial operation and 5 of the 11 (45%) segments at the relaparotomy were histologically viable, although they were clinically proven to be ischemically injured bowel segments. Therefore 50% of the clinically proven nonviable segments were viable and resected. In our series planned reexploration resulted in a negative second laparotomy in 4 of 13 patients (30.8%) in whom the full recovery and viability of the dubious segments was predicted by LDF assessment.

Clinical judgement alone had an overall accuracy of 87% (42 of 48) and a predictive value of 69% (9 of 13) only. The predictive value of clinical judgment at the first laparotomy was even lower (58%). The LDF method could predict persisting ischemia at the first operation in 100%. The clinical assessment during the first laparotomy missed 9 of 18 (50%) subsequently resected segments at the initial operation, while LDF correctly identified all 9 ischemic segments in the first session as having a perfusion level of <50 PU.

In this study the LDF method was superior to clinical judgement in determining the ischemic extend in small bowel segments. Differences in specificity ($p < 0.002$), sensitivity ($p < 0.001$), and predictive value ($p < 0.001$) were statistically significant compared to clinical assessment.

Fig. 1. The histological specimen of a patient developing severe mesenteric infarction of a small bowel segment with submucosal edema, hemorrhages and severe inflammation of the muscle layer. Clinically predicted as viable and defined as nonviable by LDF measurement at the initial operation.

Discussion

The difficulty in establishing an early diagnosis in acute mesenteric ischemia is probably the most important cause of the high mortality, which varies from 60 to 80% [1–4], and an additional delay in the decision for explorative laparotomy further increases the impairment of splanchnic perfusion. Unfortunately, most cases of acute intestinal ischemia are only diagnosed intraoperative, at a time when full mesenteric infarction has already been established. Also the severity and extent of ischemically injured intestine may be difficult to determine intraoperatively.

Conventional clinical assessment, like the color of the intestine, motility, pulsation and bleeding of the mucosa, proved to be reasonably reliable, but in most cases prediction of subsequent ischemia of the remaining intestine is not possible. Several sophisticated methods, including fluorescein angiography, transserosal tissue oxygen tension measurements (TpO_2) and isotope-labeled protein have been evaluated to predict the nonviability of bowel segments, but most require an experienced investigator

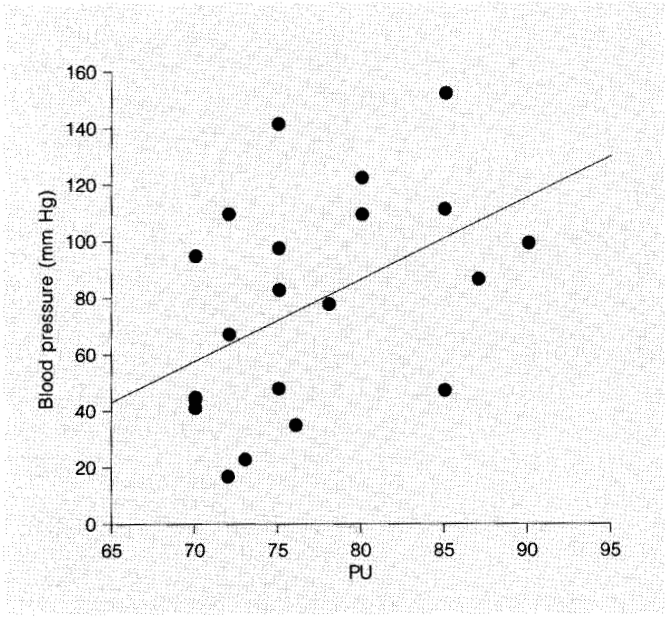

Fig. 2. The relationship between actual mean arterial pressure and laser Doppler flowmetry signals given in a linear fashion of mean arterial blood pressure (MAP) and LDF recorded perfusion units (PU) at different times and different MAP ($p < 0.0005$; correlation coefficient 0.69).

for correct evaluation. One of the most promising methods that has recently been introduced into microvascular research is LDF. Blood flow measurements by laser Doppler was first described by Shepard and Riedel [9] and has since been developed into a valuable noninvasive tool to investigate microvascular perfusion in various abdominal organs [15–18]. Blood flux ranged between 100 and 150 PU is small bowel segments measured in experimental models in pigs [15]. With an identical set-up and the same calibration method as in the study of Krohg-Sorensen et al. [15], baseline blood flux in non-diseased bowel segments of hemodynamically stable patients ranged between 142 ± 19 PU in the ileum and 187 ± 42 in the jejunum segments.

In the intestinal tract microvascular flux assessed by LDF was demonstrated to correlate in a linear fashion with the total blood flow in the respective organ [10] (fig. 2) and ischemic tissue necrosis of intestinal segments could be predicted when the LDF-assessed blood flux was below 50 PU.

At initial laparotomy it may be difficult to judge whether ischemic bowel will recover or progress to full-thickness necrosis, leaving the surgeon with the decision to unnecessarily resect viable intestine or to excise all dubious bowel segments. This often ends in intestinal insufficiency, whereas failure to resect necrotic bowel segments might lead to fatal bowel perforation. Therefore, many institutions routinely perform a second-look operation to evaluate whether further resection is required.

The high rate of negative relaparotomies (31%) in our series may allow a selective policy of relaparotomy to reduce the number of negative second-look operations, but in several studies also shows the low overall accuracy [19, 20].

Recently, MacSweeney and Postlethwaite [21] suggested that a second-look procedure was diagnostic in the assessment of intestinal viability after the initial operation for acute mesenteric ischemia. We have not done this in this series, but have found laparoscopy to be difficult after previous surgery due to adhesions and inaccessibility of all bowel sections. Also assessment of bowel viability can be difficult for optical reasons.

However, the accuracy, sensitivity and specificity calculations show that LDF is more accurate and more reliable than intraoperative clinical judgement as demonstrated in this study. We have shown that clinical judgement of intestinal viability at the initial operation detects the viable segments with a specifity of 86%, but has a poor predictive value (58%) resulting in unnecessary bowel resections or negative second-look operations. In fact, clinical judgement alone led to 50% unnecessary small bowel segment resections and 31% negative relaparotomies. Unlike this experience, LDF evaluated and predicted the intestinal viability of suspicious bowel segments in all 13 patients with a 100% overall accuracy, sensitivity and predictive value.

The failure to identify ischemically injured bowel segments by clinical judgement and to decide the extent of bowel resection at the initial operation continues to be a problem after surgery of acute mesenteric ischemia.

In this study, we demonstrated for the first time that intraoperative LDF is a new and easily applicable method to evaluate critical intestinal blood flow in suspicious bowel segments during the initial or second-look operation of acute mesenteric ischemia. LDF has the advantage of predicting ischemic bowel injury during the initial operation and thus obligates the need for a second-look operation in elderly or multimorbid patients.

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