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The Effect of Hepatic Vascular Inflow Occlusion on Liver Tissue pH, Carbon Dioxide, and Oxygen Partial Pressures: Defining the Optimal Clamp/Release Regime for Intermittent Portal Clamping[1]

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Background. **The optimal duration of hepatic vascular inflow occlusion (Pringle maneuver) and reperfusion during liver resection are not defined. The aim of this study was to describe the changes that occur in liver tissue pH, partial pressure of carbon dioxide (P_LCO_2), and partial pressure of oxygen (P_LO_2) and by using the P_LCO_2 as a predictor of hepatocellular damage define the optimal clamp/release regime for intermittent portal clamping during liver resection.**

Methods. **Continuous pH, P_LCO_2, and P_LO_2 measurements were obtained using a Paratrend multiparameter sensor (Diametrics Medical Inc., Roseville, MN) in 13 patients undergoing elective partial liver resection. Patients were randomly allocated to undergo a 10-min clamp/5-min release regime (group 1) or a 20-min clamp/10-min release regime (group 2).**

Results. **In group 1 (n = 6) P_LCO_2 increased and pH decreased significantly after 10 min of clamping and returned to baseline within 5 min of reperfusion. In group 2 (n = 7) the P_LCO_2 increased and pH decreased significantly after 10 min of clamping, with a further significant change after 20 min. Following 10 min of reperfusion, pH and P_LCO_2 had not returned to baseline. P_LO_2 did not change significantly with either intermittent portal clamping regime.**

Conclusions. **A reperfusion of 5 min is sufficient to restore the P_LCO_2 and liver tissue pH to normal after 10 min of clamping, but more than 10 min of reperfusion is required after 20 min of clamping. To minimize hepatic ischemia during liver resection, a 10-min clamp/5-min release regime should be used.**

Key Words: **intermittent portal clamping; Pringle maneuver; monitoring; tissue carbon dioxide.**

INTRODUCTION

A number of vascular occlusive techniques have been described to minimize bleeding during liver resection. These include inflow occlusion using hepatic pedicle clamping (Pringle maneuver) and simultaneous inflow/outflow occlusion (total vascular exclusion) [1–5]. Of these, the Pringle maneuver is the method of choice, being better tolerated in the majority of patients [1, 5].

The major complication of hepatic vascular occlusion is hepatic ischemia, which increases with longer and continuous periods of clamping and may manifest in a spectrum ranging from mild dysfunction to lethal organ failure [6–9]. This is particularly true in patients with abnormal liver parenchyma, as this group is acutely sensitive to ischemia [9]. In order to limit hepatic ischemia intermittent portal clamping (IPC) regimes were developed. In a study comparing IPC (15-min clamp/5-min release) with continuous portal clamping (CPC), patients who underwent CPC had significantly higher rates of liver dysfunction than the IPC group [6]. However the optimal clamp release regime has not yet been defined.

Using a Paratrend multi-parameter sensor (Diametrics Medical Inc., Roseville, MN), we have previously reported the changes that occur in pH, P_LCO_2, and P_LO_2 in response to variations in F_iO_2 and end-tidal carbon dioxide and that, upon application of the Prin-

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gle maneuver, P_LCO_2 increases with time [10]. In animal models, such prolonged increases in P_LCO_2 are associated with hepatocellular damage [11]. The aim of this study was to describe the changes that occur in liver tissue pH, P_LCO_2, and P_LO_2 during IPC and to define the optimal IPC regime, using P_LCO_2 as a predictor of hepatocellular damage.

METHODS

The study was undertaken at Queens Medical Centre, University Hospital, Nottingham, United Kingdom. Patients with American Society of Anesthesiologists grade >2, preexisting parenchymal liver disease, and nonmetastatic disease were excluded from the study. Following ethical committee approval, 13 patients scheduled for elective liver resection for colorectal metastases gave written, informed consent. Baseline characteristics were collected, and the patients were then randomly allocated to undergo either a 10-min clamp period followed by 5-min reperfusion (group 1) ($n = 6$) or a 20-min clamp period followed by 10-min reperfusion (group 2) ($n = 7$).

All patients underwent a standardized anesthetic, including induction of anesthesia with propofol and maintenance with isoflurane and nitrous oxide in oxygen. An infusion of atracurium was used for muscle relaxation and analgesia was with a continuous thoracic epidural infusion of 0.25% bupivacaine. Central venous pressure was maintained between 0 and 5 mmHg, and blood pressure was maintained within 20% of the preoperative value using an ephedrine infusion at 0-30 mg h^{-1}.

All patients underwent a laparotomy to exclude extrahepatic metastases and intraoperative ultrasound (Aloka, CT) to confirm the number and location of metastases. The Paratrend multiparameter sensor (Diametrics Medical Inc.) was calibrated automatically and inserted as described previously in ref. 9. The probe was sited well away from the tumor mass in the lobe that was to be resected. The measurements were taken before starting the liver resection and during the measurement period no surgical interventions were performed.

The probe required a 20-min period to achieve stable readings. The Pringle maneuver was applied using a Rummel tourniquet secured around the hepatic pedicle. In group 1 the Pringle maneuver was applied for 10 min followed by 5 min of reperfusion; in group 2 the Pringle maneuver was applied for 20 min followed by 10 min of reperfusion. During monitoring of the P_LCO_2, the inspired oxygen concentration ($F_iO_2 = 1.0$), end-tidal CO_2 partial pressure (33.8 mmHg), inspired volatile concentration, and blood pressure were maintained at constant values. Following completion of data collection, the probe was removed and the liver resection commenced. No further readings were taken during the liver resection.

Data were analyzed using the Student's *t*-test and Mann–Whitney test with the Statistical Package for Social Sciences, SPSS (Version 11.0 for Windows; GmbH, Munich, Germany) and are presented as median (IQR) unless otherwise stated.

TABLE 1

Summary of Patient Demographics

	Group 1 Mean (range)	Group 2 Mean (range)
Age	67.3 (55–77)	68.3 (63–75)
Sex		
M	5	5
F	1	2

TABLE 2

Pre-operative and Day 2 Post-operative Bilirubin and ALT Levels for Group 1 and Group 2 Patients

	Group 1		Group 2	
	Mean (SD)	*N*	Mean (SD)	*N*
Preoperative bilirubin (μmol/L)	8.5 (6.0)	4	7.0 (3.34)	5
Preoperative ALT (IU/L)	33.5 (19.1)	4	26.3 (9.6)	5
Day 2 postoperative bilirubin (μmol/L)	37.3 (26.3)	4	71.6 (45.0)	5
Day 2 postoperative ALT (IU/L)	416.5 (298.6)	4	903.4 (933.4)	5

ALT = alanine aminotransferase.

RESULTS

Thirteen patients took part in the study. Their demographics are summarized in Table 1. All patients were scheduled to undergo formal partial hepatectomy for colorectal metastases: group 1 (1 left + 5 right hepatectomies) and group 2 (2 left + 5 right hepatectomies). Insertion and removal of the probe from the liver was associated with only minimal, self-limiting bleeding and no significant morbidity. Pre- and day 2 postoperative liver function tests are summarized in Table 2.

In group 1 the median preclamp pH was 7.03 (IQR 0.18). This decreased significantly to 6.77 after 10 min of clamping ($P = 0.01$). After 5 min of reperfusion the pH had returned to baseline (Fig. 1A). In group 2 the median preclamp pH was 7.29 (IQR 0.08). This decreased significantly to 6.71 (IQR 0.36) after 20 min of clamping ($P < 0.001$) and remained significantly reduced after 10 min of reperfusion ($P = 0.014$) (Fig. 2A).

In group 1 the preclamp median P_LCO_2 was 63.06 (IQR 41.65) mmHg. This increased significantly to 131.75 (IQR 56.48) mmHg ($P = 0.008$) after 10 min of clamping. After 5 min of reperfusion the P_LCO_2 had returned to baseline (Fig. 1B). In group 2 the preclamp median P_LCO_2 was 52.04 (IQR 11.6) mmHg. This increased significantly to 177.17 (IQR 45.4) mmHg ($P < 0.001$) after 20 min of clamping. This was significantly greater than the P_LCO_2 after 10 min of clamping ($P = 0.035$). After 10 min of reperfusion the P_LCO_2 only returned to baseline in two of the seven patients (Fig. 2B).

In group 1 the median preclamp P_LO_2 was 42.04 (IQR 49.35) mmHg. There was no significant change in P_LO_2 after 10 min of clamping or 5 min of reperfusion. In group 2 the median P_LO_2 was 34.53 (IQR 29.47)