Liver tissue partial pressure of oxygen and carbon dioxide during partial hepatectomy

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Background. Data on tissue oxygen partial pressure (\(P_{tO2}\)) and carbon dioxide partial pressure (\(P_{tCO2}\)) in human liver tissue are limited. We set out to measure changes in liver \(P_{tO2}\) and \(P_{tCO2}\) during changes in ventilation and a 10 min period of ischaemia in patients undergoing liver resection using a multiple sensor (Paratrend® Diametrics Medical Ltd, High Wycombe, UK).

Methods. Liver tissue oxygenation was measured in anaesthetized patients undergoing liver resection using a sensor inserted under the liver capsule. \(P_{tO2}\) and \(P_{tCO2}\) were recorded with \(F_{IO2}\) values of 0.3 and 1.0, at end-tidal carbon dioxide partial pressures of 3.5 and 4.5 kPa and 10 min after the onset of liver ischaemia (Pringle manoeuvre).

Results. Data are expressed as median (interquartile range). Increasing the \(F_{IO2}\) from 0.3 to 1.0 resulted in the \(P_{tO2}\) changing from 4.1 (2.6±5.4) to 4.6 (3.8±5.2) kPa, but this was not significant. During the 10 min period of ischaemia \(P_{tCO2}\) increased significantly (\(P<0.05\)) from 6.7 (5.8±7.0) to 11.5 (9.7±15.3) kPa and \(P_{tO2}\) decreased, but not significantly, from 4.3 (3.5±12.0) to 3.3 (0.9±4.1) kPa.

Conclusion. \(P_{tO2}\) and \(P_{tCO2}\) were measured directly using a Paratrend® sensor in human liver tissue. During anaesthesia, changes in ventilation and liver blood flow caused predictable changes in \(P_{tCO2}\).

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Tissue hypoxia may be an important cause of the systemic inflammatory response and multiple organ dysfunction1 and it also reflects poor blood flow and hypovolaemia.2 Tissue oxygen partial pressure (\(P_{tO2}\)) and carbon dioxide partial pressure (\(P_{tCO2}\)) and pH have been measured through a fibreoptic sensor in brain,3 skin4 and muscle5 but there are only limited reports of these measurements being made in intra-abdominal tissues in man.6

We measured changes in liver \(P_{tCO2}\), \(P_{tO2}\), and pH measured using a Paratrend® multi-sensor (Diametrics Medical, High Wycombe, UK) placed beneath the liver capsule during liver resection surgery. We changed the inspired gas mixture and measured the effect of clamping the hepatic vascular inflow for 10 min.

Methods

Following ethical committee approval, 11 patients scheduled for elective liver resection for colorectal metastases gave written, informed consent.

We used a standardized anaesthetic method, including induction of anaesthesia 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 bupivacaine 0.25%. Central venous pressure was maintained between 0 and 5 mm Hg and blood pressure within 20% of the preoperative value using an ephedrine infusion 0–30 mg h⁻¹.

The liver was mobilized using standard surgical techniques. The hepatic inflow was controlled with a sling.
Insertion and removal of the probe from the liver was associated with minimal, self-limiting bleeding only and no other significant morbidity.

Discussion

We found that in healthy patients during anaesthesia, when the $F_{\text{IO}_2}$ is 0.3, $P_{\text{aO}_2}$ is approximately 16 kPa and the median liver $P_{\text{tO}_2}$ is 4.1 kPa. In six of the nine patients studied, the $P_{\text{tO}_2}$ was not altered by increasing $F_{\text{IO}_2}$ to 1.0. The median liver $P_{\text{tCO}_2}$ is 1.7–2.1 kPa greater than the $P_{\text{aCO}_2}$ when the median values are 3.9 and 4.7 kPa, respectively. Application of a clamp to the hepatic vascular inflow for 10 min increased the liver $P_{\text{tCO}_2}$ to greater than 10 kPa in five of eight subjects in whom the measurement was made. The tissue pH broadly followed the changes in $P_{\text{tCO}_2}$. The wide spread of initial pH values may be a result of tissue metabolism and blood flow, but more patients would need to be studied to be sure about this.

Another human study reported tissue measurements following orthotopic liver transplantation. The mean values for $P_{\text{tO}_2}$ and $P_{\text{tCO}_2}$ recorded were consistent with the findings of our study but without a period of liver ischaemia. These authors also commented on the lack of correlation between changes in arterial oxygen tension and liver oxygen tension. Similar studies have been performed in human brain, muscle and skin. The findings from liver tissue are within the ranges that would be expected from data published examining brain tissue.

Studies in pigs have shown that the liver tissue oxygen varied between 4.8 and 10 kPa when $F_{\text{IO}_2}$ was 1.0, and $P_{\text{tCO}_2}$ values were more consistent at approximately 7.5 kPa when normocapnia was maintained. Soller and colleagues calculated critical values associated with the onset of tissue dyoxia during experimental shock. They reported the critical value for oxygen as being 1.5–1.7 kPa and for carbon dioxide the critical value was 8.5–10 kPa. They noted that the time for which $P_{\text{tCO}_2}$ was greater than this critical value predicted a poor outcome.

Our study has some limitations. First, the probes were fragile so that some data were lost. However, with the insertion method described, we obtained more than 95% of the possible data points in the last six patients studied. Second, the sensor uses optodes that have a limited area of

### Results

Eleven patients were recruited. Data were obtained from nine patients. Complete sets of data were collected in six patients. Six data points out of 108 measurements were missing because of probe malfunction or damage.

The median values for arterial and liver pH and oxygen and carbon dioxide partial pressures are shown in Table 1. The changes in liver $P_{\text{tCO}_2}$ with increasing $E'_{\text{CO}_2}$ and during clamping of hepatic blood flow were statistically significant ($P<0.005$). There was a clear change in arterial partial pressure of oxygen ($P_{\text{aO}_2}$) as $F_{\text{IO}_2}$ was increased from 0.3 to 1.0. However, neither this change nor clamping the vascular inflow resulted in a statistically significant change in $P_{\text{tO}_2}$.

### Table 1

<table>
<thead>
<tr>
<th>Inspired oxygen fraction/end-tidal carbon dioxide partial pressure (kPa)</th>
<th>0.3/3.5</th>
<th>1.0/3.5</th>
<th>1.0/4.5</th>
<th>10 min clamp</th>
</tr>
</thead>
<tbody>
<tr>
<td>Liver pH</td>
<td>7.28 (7.16–7.35)</td>
<td>7.26 (7.21–7.31)</td>
<td>7.25 (7.22–7.32)</td>
<td>7.02 (6.93–7.11)</td>
</tr>
<tr>
<td>Arterial pH</td>
<td>7.48 (7.47–7.50)</td>
<td>7.5 (7.45–7.52)</td>
<td>7.4 (7.38–7.45)</td>
<td>7.4 (7.38–7.45)</td>
</tr>
<tr>
<td>$P_{\text{CO}_2}$ (kPa)</td>
<td>5.7 (5.4–6.0)</td>
<td>5.6 (5.4–5.8)</td>
<td>6.7 (5.8–7.0) ($P&lt;0.05$)</td>
<td>11.5 (9.7–15.3) ($P&lt;0.05$)</td>
</tr>
<tr>
<td>$P_{\text{aCO}_2}$ (kPa)</td>
<td>4.0 (3.9–4.2)</td>
<td>3.9 (3.6–4.2)</td>
<td>4.7 (4.6–5.2)</td>
<td>4.7 (4.6–5.2)</td>
</tr>
<tr>
<td>$P_{\text{aO}_2}$ (kPa)</td>
<td>4.1 (2.6–5.4)</td>
<td>4.6 (3.8–5.2) ($P&gt;0.05$)</td>
<td>4.3 (3.5–12.0)</td>
<td>3.3 (0.9–4.1) ($P&gt;0.05$)</td>
</tr>
<tr>
<td>$P_{\text{tO}_2}$ (kPa)</td>
<td>16.7 (15.5–19.6)</td>
<td>44.8 (39.3–51.8)</td>
<td>51.7 (39.3–52.7)</td>
<td>51.7 (39.3–52.7)</td>
</tr>
</tbody>
</table>

The Paratrend® probe was calibrated automatically and inserted through an 18G cannula (Arrow™ Pennsylvania, USA) aseptically, until the distal 25 mm was exposed. A 14G cannula (Abbocath™ Sligo, Republic of Ireland) was inserted into the liver, away from the tumour mass, to a depth of approximately 50 mm. The probe, in the protective 18G cannula, was inserted through the 14G Abbocath cannula into the liver tissue.

The probe required a period of up to 20 min, without surgery, to achieve stable readings. The ventilator settings were adjusted to control the inspired oxygen concentration ($F_{\text{IO}_2}$) and the end-tidal carbon dioxide partial pressure ($E'_{\text{CO}_2}$). For each ventilation setting, steady-state tissue measurements were obtained, shown by a steady output. Arterial blood gases were sampled at steady state for each ventilatory change. Three steady-state measurements were made with the following ventilation settings: (i) $F_{\text{IO}_2}$ 0.3, $E'_{\text{CO}_2}$ 3.5 kPa; (ii) $F_{\text{IO}_2}$ 1.0, $E'_{\text{CO}_2}$ 3.5 kPa; (iii) $F_{\text{IO}_2}$ 1.0, $E'_{\text{CO}_2}$ 4.5 kPa. Once these measurements were complete, a Pringle manoeuvre was performed for 10 min, after which tissue partial pressures were recorded. Following completion of the data collection the probe was removed.

The oxygen and carbon dioxide partial pressures during the respiratory and clamping manoeuvres were analysed using Dunn’s multiple comparisons. Statistical analysis was performed using GB stat v. 7.0 (Dynamic Microsystems Inc.).

Studies in pigs have shown that the liver tissue oxygen varied between 4.8 and 10 kPa when $F_{\text{IO}_2}$ was 1.0, and $P_{\text{tCO}_2}$ values were more consistent at approximately 7.5 kPa when normocapnia was maintained. Soller and colleagues calculated critical values associated with the onset of tissue dyoxia during experimental shock. They reported the critical value for oxygen as being 1.5–1.7 kPa and for carbon dioxide the critical value was 8.5–10 kPa. They noted that the time for which $P_{\text{tCO}_2}$ was greater than this critical value predicted a poor outcome.
examination. Thus, the sensor position in relation to local arterial supply may affect tissue readings, as described in other tissues.7

It was surprising that tissue oxygenation did not decrease significantly during application of the clamp across the vascular inflow. This may be the result of back flow from the hepatic veins maintaining partial liver perfusion,10 or alternatively, incomplete vascular pedicle occlusion. However, the recorded $P_{tO2}$ values are also at the lower limit of the sensitivity of the probe. At a $PO_2$ less than 3 kPa the linearity of the probe output cannot be assumed.

The increase in $P_{tCO2}$ to 10 kPa following 10 min vascular occlusion may be significant when Soller and colleagues’ work9 is considered. However, this study was not designed to examine the effect of tissue carbon dioxide on liver cell function in humans. Hepatic vascular inflow may be stopped for periods of 20 min or more, depending on the surgical technique. This may affect patients subjected to large resections or those with underlying liver disease and would warrant further study.

We found that human liver $P_{tO2}$ and $P_{tCO2}$ can be measured directly using a Paratrend® probe, and $P_{tCO2}$ changes predictably with changes in arterial and expired gas tensions and with decreased liver blood flow. These observations support the use of this method to assess tissue metabolism.

Acknowledgements

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