Immunohumoral Response During Laparoscopic and Open Living Donor Nephrectomy: An Experimental Model

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ABSTRACT
Measurement of interleukins (IL) and C-reactive protein (CRP) have demonstrated that a laparoscopic approach may induce less surgical stress than an open approach. The potential influence of this observation in living donor nephrectomy has scarcely been analyzed. The aim of the study was to analyze the immunohumoral response induced by laparoscopic versus open donor nephrectomy in an experimental model. Twenty pigs underwent left nephrectomy, 10 by laparoscopy and 10 by an open approach. In both groups the following parameters were measured: CRP, IL-2, IL-10, tumour necrosis factor α (TNF α), and endothelin-1 (ET-1). The determinations were done at different times: basal, immediately as well as on the first, third, fifth, and seventh days after the procedure. A comparative analysis between groups demonstrated a significant increases among the open group in the following markers: CRP (1.44 ± 0.88 vs 1.32 ± 0.14 mg/dL, P = .046); TNF α (131.14 ± 41.37 vs 57.19 ± 23.71 pg/mL; P > .001); and ET-1 (0.91 ± 0.49 vs 0.56 ± 0.5 fmol/mL; P = .001). The laparoscopic group showed higher levels of IL-2 than the open group. In conclusion, open donor nephrectomy produced a greater immunohumoral response than a laparoscopic approach. The influence of these observations on ischemia-reperfusion injury or on immediate graft function after kidney transplantation has not been clearly established.

Graft survival seems to be better after living donor nephrectomy. Laparoscopic and open donor nephrectomies are performed with good results. However, the laparoscopic approach may induce less surgical stress than an open approach. Different interleukins (IL) and C-reactive protein (CRP) have been reported to be surgical stress markers.1,2 The potential influence of this immunohumoral response during living donor graft harvest has been rarely analyzed. Endothelin 1 (ET-1), a powerful vasoconstrictor produced by renal endothelium, has been reported to be increased during laparoscopy secondary to parenchymal compression from the pneumoperitoneum.3,4 Its utility as a marker of surgical stress has not been previously evaluated. The aim of the study was to analyze the immunohumoral responses induced by laparoscopic versus open donor nephrectomy in an experimental model.

METHODS
A left nephrectomy was performed in 20 Landrace pigs, including 10 cases by an open approach (control group) and 10 cases by laparoscopy (study group). Open nephrectomy was performed through a midline laparotomy with the animal in the decubitus position. Laparoscopic nephrectomy was performed with the animal in a left lumbotomy position. The intra-abdominal pressure was fixed at 12 mm Hg. Peripheral blood samples were obtained previous to surgery, immediately after the procedure, and at the first, third, fifth and seventh days postsurgery for IL2, IL10, tumor necrosis factor (TNF) α and ET-1 levels measured by enzyme-linked immunosorbent assay, polymerase chain reactions (PCR) on agglutination.

RESULTS
PCR values increased progressively after open nephrectomy, reaching significant differences at the fifth day.

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IMMUNOHUMORAL RESPONSE

Some molecules such as IL or CRP, have been considered to be mediators of acute phase response induced by major surgery. CRP is synthesized mainly in the liver. It functions to neutralize inflammatory agents, helping to minimize local damage in regenerating tissues. IL-2 is a proinflammatory pleiotropic cytokine produced by T cells that induces T- and B-cell growth and differentiation. IL-10 is an anti-inflammatory pleiotropic cytokine produced by T cells that functions to neutralize inflammatory agents, helping to minimize local damage in regenerating tissues. IL-10 values did not show significant differences between groups. Fornara et al reported no differences in human laparoscopic and open nephrectomy in a comparative study. There are no previous reports measuring IL-10 in porcine models comparing both accesses.

DISCUSSION

In conclusion, open donor nephrectomy produces a greater immune response than a laparoscopic approach. Levels of CRP, TNF, and IL-1 were higher after open compared with laparoscopic nephrectomy, probably as an expression of major surgical stress. The influence of these factors on donor morbidity or graft function after kidney transplantation has not been clearly established of present. Further studies are necessary to obtain a deeper knowledge of the mechanisms involved in this process.

REFERENCES


Table 1. Average Stress Markers of Laparoscopic and Open Nephrectomy

<table>
<thead>
<tr>
<th></th>
<th>Laparoscopic Nephrectomy</th>
<th>Open Nephrectomy</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>PCR (mg/dL)</td>
<td>1.32 ± 0.14</td>
<td>1.44 ± 0.88</td>
<td>.046</td>
</tr>
<tr>
<td>IL-2 (pg/mL)</td>
<td>2.51 ± 0.12</td>
<td>2.35 ± 0.04</td>
<td>.001</td>
</tr>
<tr>
<td>IL-10 (pg/mL)</td>
<td>4.99 ± 0.19</td>
<td>4.85 ± 0.12</td>
<td>NS</td>
</tr>
<tr>
<td>TNF (pg/mL)</td>
<td>57.19 ± 23.71</td>
<td>131.14 ± 41.37</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>ET-1 (fmol/mL)</td>
<td>0.56 ± 0.5</td>
<td>0.91 ± 0.49</td>
<td>.001</td>
</tr>
</tbody>
</table>

(1.46 ± 0.53 vs 1.3 ± 0.15 mg/dL, P = .013). The average PCR, of both groups showed a significant differences being higher for open approach (1.44 ± 0.88 vs 1.32 ± 0.14 mg/dL, P = .046; Table 1).

Laparoscopic nephrectomy showed higher average values of IL-2 (2.35 ± 0.04 vs 2.51 ± 0.12 pg/mL, P = .001), a difference that was maximal at the third day (2.32 ± 0.06 vs. 2.5 ± 0.28 pg/mL, P = .001).

There were no significant differences in the levels of IL-10 between the open and laparoscopic nephrectomies.

TNF α average values were significantly higher among the open nephrectomy group (151.14 ± 41.37 vs 57.19 ± 23.71 pg/mL, P < .001). The major difference was observed at the fifth day (163.47 ± 38.46 vs 28.1 ± 2.74 pg/mL, P = .01), although differences were evident from the immediate postsurgery value to the fifth day. ET-1 average levels were higher during open nephrectomy (0.91 ± 0.49 vs 0.56 ± 0.5 fmol/mL, P = .04) and remained significant during the entire postoperative period (Table 1).