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CHAPTER 4

Effect of gentamicin-containing collagen sponges on surgical site infection after hand-assisted laparoscopic donor nephrectomy

V.P. Alberts, R.C. Minnee, F.J. Bemelman, K.A.M.I. van der Pant and M.M. Idu

ABSTRACT
Postoperative surgical site infection (SSI) can be considered a frequent complication of hand-assisted laparoscopic donor nephrectomy (HALDN). Since 2007, our center routinely used a gentamicin-containing collagen sponge (GCCS) when closing the wound. The effect of GCCS on SSI is not elucidated clearly. In this retrospective cohort study we assessed the effects of GCCS on SSI after HALDN.

Between December 2004 and November 2007 we treated 100 patients without GCCS, and from November 2007 to July 2010 there were 100 patients with GCCS placed after HALDN. SSI was defined as an incisional infection that required an intervention such as opening of the wound or antibiotic treatment within 90 days after surgery.

Implantation of a GCCS resulted in a statistically significant reduction of the SSI rate, from 6% to 0% (P = 0.01). All infections occurred in the Pfannenstiel incision site. There was no significant difference in creatinine concentration after three months between both groups.

The use of a GCCS reduces the risk of SSI significantly after HALDN without compromising kidney function.

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INTRODUCTION

Living donor renal transplantation has increased over the last years, as it provides better patient and graft survival than organs from deceased donors. The introduction of the hand-assisted laparoscopic donor nephrectomy (HALDN) technique has decreased donor morbidity substantially compared with the open technique.\(^1,2\) Additionally, HALDN results in a shorter operating time, less blood loss, fewer conversions to open nephrectomy, and a shorter warm ischemia time than total laparoscopic donor nephrectomy while maintaining low morbidity and a short hospital stay.\(^1,2\)

Postoperative surgical site infections (SSI) are a common complication after donor nephrectomy. Such an infection increases the duration of hospital stay, the postoperative recovery period, the risk of wound dehiscence, and costs.\(^3\) Furthermore, as the donors undergo an operation without personal benefit, it is even more important to minimize the risks of complications after kidney donation. With the serious medical and psychological implications of post-operative infection in healthy kidney donors, it is imperative that measures, including the use of prophylactic antibiotics, be taken to prevent infection.

To reduce the likelihood of SSI after HALDN, our center now applies gentamicin-containing collagen sponges (GCCS) routinely when closing the incision. However, the effect of GCCS on SSI has not been elucidated clearly, and the reported results from various studies are inconsistent.\(^4-8\) In this study we retrospectively assessed the effect of GCCS on the incidence of SSI after HALDN.

METHODS

In November 2007 we started routine insertion of a GCCS during HALDN. We compared 100 consecutive donors with a GCCS placed routinely (November 2007 to July 2010) with the 100 consecutive donors before this period (December 2004 to November 2007) when no GCCS was used. All procedures were done at the Academic Medical Center, Amsterdam.

Preoperatively, the surgical field was treated with iodine directly after the pubic hair was removed on the table by electric hair clippers. No systemic antibiotic prophylaxis was given. The surgical team members washed their hands with chlorhexidine soap and an alcohol hand solution was applied. The HALDN was carried out transperitoneally. One surgeon (MMI) performed all procedures. Before the start of the study period, the surgeon had a personal experience of at least 70 HALDNs. The handport (Omniport\(^\text{®}\), Advanced Surgical Concepts, Wicklow, Ireland) was placed in a 7 to 8 cm long Pfannenstiel incision, the length of which was standardized to the width of the surgeon’s left hand (glove size 7). The non-dominant hand of the surgeon was introduced through the handport
in all operations. Two trocars were placed, one of 10 mm for the videoscope, and one of 12 mm for the ultrasonic dissection device (UltraCision® Harmonic Scalpel, Ethicon Endosurgery, Inc) in the surgeon’s dominant hand. A maximum insufflation pressure of 12 mmHg was used. The kidney was extracted through the handport. During closure of the incision in the more recent 100 cases, one GCCS (Garacol®, EUSA Pharma Ltd, Oxford, UK) was placed. This sponge is made of pepsin-treated collagen, measures 10 · 10 · 0.5 cm, and contains 130 mg of gentamicin. The sponges were divided in three pieces. The first piece was placed pre-peritoneally behind the rectus abdominis muscles, the second between the rectus abdominis muscles and the anterior rectus sheath, and the third was placed subcutaneously. No drains were placed. The subcutis was closed such as to obliterate dead space. The skin was closed intracutaneously and a dry dressing was applied. The operation technique and environment were identical throughout the study, as was the anesthesiology protocol (volume administration and body temperature regulation methods). No patients in either group needed a peri-operative red blood cell transfusion and no conversions to an open procedure were required.

A superficial incisional SSI was defined as an infection that required an intervention such as opening of the incision or antibiotic treatment within 90 after surgery. A deep incisional infection was defined as an infection of abdominal wall muscle or fascia. Furthermore, we assessed the length of the postoperative hospital stay and the serum creatinine concentration three months after surgery. No donors were lost to follow-up and the mean follow-up was 2.7 years.

The χ² test was used to compare data between groups. Comparison of continuous variables was performed with the Mann-Whitney U test. A P value of less than 0.05 was considered statistically significant. Statistical analyses were performed using SPSS 16 for Windows (SPSS, Chicago, IL, USA).

<table>
<thead>
<tr>
<th>Table 1 Baseline characteristics of donors</th>
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<tr>
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<tr>
<td></td>
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<tr>
<td>Female sex</td>
</tr>
<tr>
<td>Mean age in years (± SD)</td>
</tr>
<tr>
<td>Mean BMI in kg/m² (± SD)</td>
</tr>
<tr>
<td>Smoking</td>
</tr>
<tr>
<td>Hypertension</td>
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<tr>
<td>Mean duration of surgery in minutes (± SD)</td>
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</tbody>
</table>

GCCS = gentamicin-containing collagen sponge, SD = standard deviation, BMI = body mass index
RESULTS

The study groups were similar with regard to baseline characteristics (Table 1). Implantation of a GCCS resulted in a statistically significant reduction of the SSI rate, from 6% to 0% (P = 0.01; Table 2). All infections occurred in the Pfannenstiel incision, and all were opened (partially). In the cultures we found Staphylococcus aureus in two patients, Pseudomonas aeruginosa in one patient, Streptococcus milleri in one patient, and no micro-organisms in the remaining two patients.

No deep incisional SSI occurred. Two persons with SSI developed an incisional hernia. In addition, we found nine other complications of which five were in the non-GCCS group (5%) and four in the GCCS group (4%; odds ratio (OR) 0.80; 95% confidence interval (CI) 0.21 to 3.07). These complications were four cases of pneumonia, one ileus, one iatrogenic gallbladder perforation with leakage, one leakage of chyle, one ventral hematoma, and one case of atrial fibrillation. There was no significant difference in the duration of surgery between the two groups (P = 0.68), and the postoperative hospital stay was similar (P = 0.36). The mean postoperative serum creatinine concentrations after three months were 1.18 mg/dL (standard deviation (SD) ± 0.22) in the group without GCCS and 1.19 mg/dL (SD ± 0.24) in the group with GCCS (P = 0.68).

<table>
<thead>
<tr>
<th>Table 2 Postoperative outcomes</th>
<th>No GCCS (n = 100)</th>
<th>GCCS (n = 100)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Surgical site infections</td>
<td>6</td>
<td>0</td>
<td>0.01</td>
</tr>
<tr>
<td>Other complications</td>
<td>5</td>
<td>4</td>
<td>0.75</td>
</tr>
<tr>
<td>Overall complications</td>
<td>11</td>
<td>4</td>
<td>0.07</td>
</tr>
<tr>
<td>Median hospital stay in days (IQR)</td>
<td>4 (4 - 5)</td>
<td>4 (3 - 5)</td>
<td>0.36</td>
</tr>
<tr>
<td>Mean creatinine levels after three months in mg/dL (± SD)</td>
<td>1.18 ± 0.22</td>
<td>1.19 ± 0.24</td>
<td>0.68</td>
</tr>
</tbody>
</table>

GCCS = gentamicin-containing collagen sponge, IQR = interquartile range, SD = standard deviation

DISCUSSION

Application of a GCCS during HALDN results in significantly fewer postoperative SSI. Since the introduction of GCCS during HALDN in our center, not one SSI occurred in 100 consecutive HALDN procedures. The 6% SSI rate in the group without a GCCS is similar to that in other studies, where incidence rates between 2.6% and 7.5% have been described. In a study by Zomorrodi et al. an SSI rate of 2% to 4% was reported after donor nephrectomy with systemic antibiotic prophylaxis.
The use of systemic antibiotic prophylaxis in (donor) nephrectomy is a subject of discussion. Nephrectomies are clean-contaminated procedures, because they cross a presumably uninfected genito-urinary tract. However, some authors advocate routine systemic antibiotic prophylaxis.\textsuperscript{12} We did not use preoperative systemic prophylactic antibiotics because earlier studies demonstrated that there was no beneficial effect on SSI, especially in clean laparoscopic surgery in low-risk (American Society of Anesthesiologists class I) patients.

Previous studies in patients undergoing abdominal surgery for rectal cancer found a reduction of SSI with application of a GCCS.\textsuperscript{4,5} In addition, one study found a significant reduction of overall postoperative complications when a GCCS was used.\textsuperscript{5} A study by Schimmer et al. found that GCCS significantly reduced the incidence of SSI in cardiac surgery patients.\textsuperscript{6} However, two studies from Bennett-Guerrero et al. found no effect of GCCS in patients undergoing cardiac surgery and a significant increase in SSI with the use of GCCS in colorectal surgery.\textsuperscript{7,8} Those authors hypothesized that this effect may be the result of selection of more resistant bacteria, a loss of effectiveness secondary to rapid elution of the gentamicin, or a mechanical barrier effect of collagen, delaying effective closure of the incision.

In this study, no evidence of nephrotoxicity was found as there was no significant difference in creatinine concentrations between the GCCS group and the non-GCCS group. Swieringa et al. demonstrated that application of one GCCS with 130 mg gentamicin does not result in a toxic serum gentamicin concentration.\textsuperscript{15} The advantage of GCCS is a locally high concentration of antibiotics in the surgical area, avoiding a high systemic concentration that can be associated with nephrotoxicity. In the pharmacokinetic study of Jørgensen et al. the local gentamicin concentration of one GCCS containing 130 mg of gentamicin exceeded the minimum inhibitory concentration (MIC) for most bacteria normally considered resistant to gentamicin.\textsuperscript{16} These high MIC values were sustained for two to three days. These findings diminish the predictive value of the regular in-vitro testing and contradict the hypothesis of rapid elution of gentamicin.

The use of a handport in the abdominal wall causes tension on the skin around the surgical site and might result in poor microperfusion of the skin around the incision during the procedure. Consequently, this area is possibly more susceptible to infection by ordinary microorganisms such as S. aureus. Cavanaugh et al. demonstrated in an experimental study that GCCS was more effective than systemic antibiotic treatment in decreasing the local number of colony-forming units of Staphylococcus Aureus.\textsuperscript{17} These findings, combined with the hypothetical negative effect of the handport on the local incision conditions in an otherwise-sterile operation, were the basis of starting the use of GCCS in our hospital. However, previous studies failed to demonstrate a higher risk of SSI after HALDN compared with standard laparoscopic donor nephrectomy without the use of a handport.
A limitation of our study is that no randomization was performed, since the analyses were done in two consecutive groups. This could have induced bias secondary to a cohort effect. There is a possibility that the sequential design of the study has been a confounder. However, we assumed that this was unlikely, because the operating surgeon had a personal experience of 70 procedures before starting the study and therefore had completed the learning curve.

In conclusion, we found a clear benefit of the use of one 130 mg GCCS in HALDN. It reduced the risk of postoperative SSI and therefore lowered postoperative morbidity. Routine application of a GCCS in HALDN is a safe procedure that does not compromise kidney function.

REFERENCES