PART X

TRANSPLANTATION: Complications

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           J Ahonen
SURGICAL COMPLICATIONS IN 500 KIDNEY TRANSPLANTATIONS

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Summary

The surgical complications in a series of 500 transplantations done by a single transplantation unit with over ten years' experience in the field are reported. The complications are divided into vascular, urological and gastrointestinal. In addition, renal rupture, primary wound infections and operative deaths are reported. Most of the losses of transplants caused by surgical complications are due to renal rupture and vascular complications, accounting for 3.6 and 2 percent of losses respectively out of the 500 kidney transplants. The urological complications caused a loss of the remaining 1.2% of a total of 6.8%. The overall mortality was highest in gastrointestinal complications with 6% of the total of 10% deaths following surgical complications. The mortality rate in the group of patients with gastrointestinal bleeding and perforations and with acute pancreatitis was extremely high. More accurate screening for potential candidates for gastroduodenal ulceration and better prophylactic treatment is needed. More active treatment of acute pancreatitis is suggested.

Introduction

The surgical complications in a series of 500 kidney transplantations are reported. The first kidney transplantation in our unit was performed in December 1964 and the 500th in October 1976. Since only four transplantations were done during the years 1964 to 1966, the series effectively consists of ten year material with at least six months follow up. Only surgical complications needing operative treatment or close surgical attention for a longer period of time are reported.

Material and Methods

Material

Five hundred renal transplantations were performed on 434 patients aged 9-72 years,
using living donor kidneys in 107 (21%) and cadaveric donor kidneys in 393 (79%). The number of retransplantations (from one to three) was 66 (13%). The patient survival was 61% and graft survival 53%. The oldest functioning living donor graft was 10 years and the oldest cadaveric donor graft has been functioning for 9 years.

Surgery

The surgical technique for transplantation was conventional, with end-to-side vein anastomosis and end-to-end arterial anastomosis to the recipient’s iliac vessels. Ureterocystostomy was done using an anterolateral cystotomy and introducing the ureter through an oblique punchhole with a short submucosal tunnel into the bladder. The spatulated end of the ureter was firmly fixed with two chromic catgut sutures to the locally de-epithelialised bladder wall and thereafter adapted with three sutures to the edges of the bladder mucosa. An indwelling ureteral catheter was brought through the bladder wall. This catheter was kept for the first 3 post-operative days. Urethral drainage was continued for two additional days.

Grafts with multiple arteries were encountered in 70 of the 500 transplants. Sixty-one had two main arteries, eight had three and one, four arteries. Usually the multiple arteries could be reconstructed to one artery for the final anastomosis to the recipient’s internal iliac artery. The use of a vein graft for reconstruction was exceptional.

Immunosuppressive treatment

Immunosuppression with methylprednisolone sodium succinate (for a patient of 70 kg bodyweight) was as follows: on the day of transplantation the recipient received 200 mg (40 mg pre-operatively, 120 mg at re-establishment of the blood supply to the transplant and 40 mg post-operatively) and on the first and second post-operative day, 120 mgs divided into three doses intravenously. Oral treatment was started on the third post-operative day with a single dose of 68 mg a day, up to the beginning of the third post-operative week, when the dose was lowered weekly, being 24 mg by the eighth week. Depending on donor sources, match grade, rejection periods and drug side-effects, variations were made. From the fifth week the doses may be alternating, with a lower dose every second day (for example 20 and 4 mg at the eighth week). Starting from the third month a dose of 20 mg was given only every second day and diminished each month and later, each year, to a very small dose, if the patient did well and the follow up was uneventful.

In cases of rejection the recipient received 1000 mg every second day to a total of 3000 mg. At the same time systemic heparinisation is started and additionally furosemide given in doses of 250 mg (up to 500 mg) four times a day.

This regimen was started from March 1975; before this date the doses of corticosteroids had been larger.
The azathioprine dose was 50 mg three times a day. If there was a rise in serum liver enzymes, the dose was lowered, but had to be totally abandoned and changed to cyclophosphamide in 5 patients only.

**Surgical complications (Table I)**

*Operation Deaths*

Two patients died on the operating table, one in cardiac failure and one from a subarachnoid bleed during the operation. Three deaths from heart failure and one from a ruptured arterial ligature occurred in the early post-operative days.

**Table I. Surgical complications in 500 kidney transplants**

<table>
<thead>
<tr>
<th>Complication</th>
<th>Per cent of 500 transplants</th>
<th>Per cent of 434 transplant patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Operative deaths</td>
<td>0.4</td>
<td>0.46</td>
</tr>
<tr>
<td>Vascular complications</td>
<td>4.6</td>
<td>5.3</td>
</tr>
<tr>
<td>Urological complications</td>
<td>8.2</td>
<td>9.4</td>
</tr>
<tr>
<td>Gastrointestinal complications</td>
<td>8.8</td>
<td>10.1</td>
</tr>
<tr>
<td>Transplant rupture</td>
<td>4.2</td>
<td>4.8</td>
</tr>
<tr>
<td>Miscellaneous complications</td>
<td>0.8</td>
<td>0.9</td>
</tr>
</tbody>
</table>

*Wound infection*

Excluding cases with other causes for wound infections, eg. urinary fistulas, the incidence of primary wound infection was 2.8 per cent, which is equal to the rate of wound infection in elective surgery at our general surgery clinic.

*Transplant ruptures*

Rupture of the kidney transplant appeared within the first ten post-operative days, with the exception of two late ruptures. Because of severe shock and intense pain and swelling of the wound, 21 transplants were explored. Fifteen ruptured kidneys were removed and of the rest, three additional kidneys were lost. Only three of the ruptured transplants survived.

*Vascular complications (Table II)*

*Arterial complications* appeared in 20 kidneys, 12 early and 8 late after the transplantation. Of the early arterial complications, there were 5 cases of arterial thrombosis followed by death of one patient and loss of the graft in four other patients. In three the renal artery was thrombosed. In one case,
TABLE II. Vascular complications

<table>
<thead>
<tr>
<th>Complication</th>
<th>Number of patients</th>
<th>Lost Grafts</th>
<th>Deaths</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Arterial</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Early</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Renal Artery thrombosis</td>
<td>3</td>
<td>3</td>
<td>-</td>
</tr>
<tr>
<td>Anastomotic bleeding</td>
<td>4</td>
<td>-</td>
<td>1</td>
</tr>
<tr>
<td>Aortoiliac thrombosis</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Undetected main branch</td>
<td>1</td>
<td>1</td>
<td>-</td>
</tr>
<tr>
<td>Arterial stenosis &amp; rejection</td>
<td>3</td>
<td>2</td>
<td>-</td>
</tr>
<tr>
<td>Late</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Renal artery stenosis</td>
<td>8</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td><strong>Venous</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Venous thrombosis</td>
<td>3</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td><strong>Lymphatic</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lymphocele</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>23</td>
<td>10</td>
<td>4</td>
</tr>
</tbody>
</table>

after opening the blood supply it was found that one main arterial branch had been undetected. The reconstruction failed, leading to necrosis of the lower pole, urinary fistulation and later to loss of the graft. In one case an aorto-iliac thrombendarterectomy had been performed in connection with the transplantation. This patient died one and a half months later of aorto-iliac thrombosis. In the cases with anastomotic bleeding, three kidneys were saved by resuturing of the rupture. In one, a ruptured arterial branch ligature diagnosed at autopsy caused the patient's death. In three early cases stenosis of the arterial anastomosis was found by arteriography. Exploration revealed a 180 degree twist of the renal artery in two of the cases, and an insignificant stenosis in one. All three kidneys showed signs of rejection. Resection and re-anastomosis saved only one of the kidneys.

In the eight late arterial complications, arteriography for hypertension showed a significant stenosis of the transplant renal artery. High renin values were found in seven. After reconstructive surgery one kidney was lost from a technical failure and the patient died. Successful reconstruction of the renal artery was performed in the other seven cases.
Venous thrombosis occurred in three cases affecting the renal outflow. Only one was diagnosed pre-operatively. The patient had sudden swelling of the leg on the side of the kidney transplant followed by haematuria and subsequent anuria. After venous thrombectomy the kidney function restarted but the patient died a month later following wound infection and sepsis. In the other two cases of venous thrombosis the kidneys were lost.

Lymphatic complications did not occur in our series.

Urological complications (Table III)

Massive bleeding into the bladder was observed in two cases and needed operation. In one case recurrent bleeding from the ureteric artery needed operative ligation five weeks after transplantation.

<table>
<thead>
<tr>
<th>Complication</th>
<th>Number of patients</th>
<th>Number of reoperations</th>
<th>Lost grafts</th>
<th>Deaths</th>
</tr>
</thead>
<tbody>
<tr>
<td>Massive urinary bladder bleeding</td>
<td>3</td>
<td>3</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Urinary bladder fistula</td>
<td>18</td>
<td>6</td>
<td>-</td>
<td>4</td>
</tr>
<tr>
<td>Ureteric fistula</td>
<td>14</td>
<td>38</td>
<td>5</td>
<td>3</td>
</tr>
<tr>
<td>Renal pelvic fistula</td>
<td>2</td>
<td>2</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Ureteric obstruction or stricture</td>
<td>4</td>
<td>4</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>41</strong></td>
<td><strong>53</strong></td>
<td><strong>6</strong></td>
<td><strong>8</strong></td>
</tr>
</tbody>
</table>

Urinary fistulation from the bladder was either caused by rupture of the anterior cystotomy or leakage from the ureterovesical junction. Out of 12 cases treated with urethral catheter drainage of the bladder, 11 healed. Only one patient died following infection and sepsis. Six patients were operated upon, three recovered completely and the other three died with wound infection, though myocardial infarction was the ultimate cause in two patients.

Ureteral fistulation occurred in 14 cases. In these multiple arteries were present in seven. Eight had ureteric necrosis with total sloughing of the distal part of the ureter. In the rest there was fistulation from necrosis of the ureteric wall. From a total of 38 operations for correction, only seven of the kidneys could be saved. In the other seven cases 5 grafts were lost and three patients died,
two of them with functioning grafts.

*Pelvic fistulation* occurred in two cases, one due to leakage from a primary uretero-pelvic anastomosis and one due to segmental necrosis of the transplanted kidney. The first patient died following infection and sepsis. In the other, corrective surgery was unsuccessful and the graft was lost.

*Urinary obstruction* needing surgery occurred in 4 patients. In one patient obstruction was caused by a kink from an unduly long ureter. A new cystostomy with shortening of the ureter was done on the first post-operative day. In one case a pyonephrosis developed due to debris obstructing the ureterovesical junction. The patient was cured by surgical removal of the debris and temporary urinary diversion through a pyelostomy. In the remaining two cases there were late complications with hydronephrosis following ureteric stricture. Both transplants were saved by corrective surgery.

*Gastrointestinal complications*

The most life-threatening surgical complications in our series were gastrointestinal, especially those connected with peptic ulceration, reported elsewhere in this volume. The overall morbidity was 14% and mortality 6% in all types of gastrointestinal complications. Complications other than those connected with peptic ulceration were as follows: acute pancreatitis in five (4 died), ileus in three (2 died), iatrogenic caecal fistula in three (no deaths) and spontaneous colonic perforation with survival in one. A case of pneumatosis cystoides of the caecum is of interest, a rare condition characterised by multiple gas-filled cysts in the intestinal wall. Surgical exploration performed for pain in the right abdomen and the unexplained finding of ‘intra-abdominal air’, was followed by a protracted caecal fistula. In the cases of peptic ulceration, 48 in all, 14 of the patients had no complications of the disease. The mortality from gastrointestinal bleeding and perforation was very high. Half of the patients with ulcer bleeding and all the patients with perforation died. Acute rejection was connected with 11 episodes of bleeding out of 25 and 6 ulcer perforations out of 7 were connected with acute rejection. Additional complications occurred in 40%. This explains why the diagnosis of perforation in five of the cases was established first at autopsy.

**Discussion**

In our series of 500 kidney transplants on 434 recipients, every fourth patient had complications needing surgery or prolonged surgical attention. The graft loss due to surgical complications was 7% and the overall mortality from these complications was 10%.

The graft loss was highest in cases of kidney rupture needing surgery. 18 grafts out of 21 were lost (86%). The total percentage of kidney loss from this
complication was 3.6% compared with a loss from vascular complications of 2% and urological complications of 1.2%. There was no correlation of the ruptures with the ischaemic period in these kidney transplants. Capsulotomy was not performed routinely in our series.

The operative deaths were only two, with four additional deaths in the early post-operative days. In our series the time available for conditioning the patient for cadaveric kidney transplantation was only 12 to 36 hours, depending on the often long patient journeys from all over Finland to our centre in Helsinki.

Some of the vascular complications appearing in the early post-operative period could, technically, have been avoided. Difficulties arose from incorrect donor nephrectomy, especially where the cut-off of the renal vessels had been performed before reaching the main renal artery. One kidney had four very short branches. Reconstructive measures were difficult and arterial thrombosis appeared shortly after transplantation. In the late vascular complications, seven out of eight cases of hypertension due to renal artery stenosis were successfully reconstructed. Exploration of the transplant artery should be avoided for insignificant stenoses, where the hypertension is attributable to the patients' own kidneys. Selective renin studies of blood samples from the transplant and the patient's own kidneys are conclusive in questionable cases of transplant artery stenosis2.

The absence of lymphoceles and lymphatic fistulas in contrast with other reports3,4 seems to justify our policy of never dividing the lymphatics along the external iliac artery. If the lymphatics are well-developed and have to be cut to reach the iliac vein, they are clamped and carefully ligated.

The principal urological complication was urinary fistulation in accordance with other reports5,6. Fistulas arising from the anterior cystotomy and from the ureterovesical junction may often heal with urethral catheter drainage of the bladder for a longer period. The ureteric fistulas heal with more difficulty and need surgical correction. The use of the ipsilateral recipient ureter for reconstruction was the most successful procedure. In one case the contralateral ureter was used for successful ureteropyelostomy. No reconstructive measures should be done during a period of infection and tissue destruction in the wound. In these cases the operative wound has to be widely opened and drained. In three cases the surface of the transplanted kidney was seen in the open wound. By later covering the skin defect with a sliding barrel type of skin graft, a clean fistula was left. Finally the fistula was excised, followed by ureteric reconstruction. These procedures saved the kidneys. Of 14 ureteric fistulas, 7 kidneys were saved by ureteric reconstruction. There were multiple arteries in seven of the 14 grafts that developed ureteric necrosis. Improved harvesting techniques for cadaveric kidneys should diminish this kind of complication7.

The highest overall mortality was in the group of gastrointestinal complications, being 6%, when the corresponding percentage from vascular complications was 0.9% and urological 1.8%. The mortality rate was extremely high for the gastrointestinal group, being 56%, compared with 17.3: in the vascular and 19.5% in the urological group of complications.

The mortality rate is especially high in those with bleeding gastroduodenal
ulcers or ulcer perforations. Effective therapeutic measures are not possible with surgical procedures. The new H₂-blocking agents may possibly be the therapeutic tool needed for prophylaxis. It seems desirable to evaluate the prospective transplant patients by gastric secretion studies, serum gastrin analysis and endoscopy to identify potential candidates for gastroduodenal ulceration.

In our series, acute pancreatitis was a rare but serious complication. Four out of five cases with this complication died. Our experience of pancreatitis in clinical surgery suggests that a more active approach, i.e., surgical cannulation and dialysis of the abdominal cavity or subtotal pancreatic resection, is necessary, although the mortality remains high.

References

7 Hrisko, GM, Birtch, AG, Bennett, AH and Wilson, RE (1973) Ann. Surg. 178, 609

Open Discussion

CUCCIARI (Rome) I want to ask something about spontaneous rupture of the kidney. What are the later results after suture?

LINDFORS We considered rupture to be connected with rejection, so that is why they are not presented in this paper. We had 21 of them and lost 15 grafts.

JIRKA (Prague) Congratulations on your low figures concerning wound infection. Did you use antibiotics prophylactically?

LINDFORS Yes, we used them for the first five days, as long as we had urinary catheters.

MASSRY (Los Angeles) Do you have any information on aseptic necrosis of the head of the femur?

LINDFORS They are quite rare in our material, but they are due to the immunosuppressive treatment, and not the topic of this paper.

MASSRY You showed us eleven patients with hypertension. I understand they had renal artery stenosis.

LINDFORS They had radiologically definite arterial stenosis.
MASSRY  What about the overall incidence of hypertension in transplant recipients?

LINDFORS  It depends on many factors, the steroid medication, whether the patient has his own kidneys removed, and many other factors. About 30% overall.

BURCK (Kiel) What consequences do you draw from the large number of gastrointestinal problems? Is it your policy now to gastrectomise all patients who have a gastrointestinal history before transplantation?

LINDFORS  This topic is going to be presented by another member of our team.

WALASLEWSKI (Warsaw) I want to come back to the renal artery stenosis. You have shown us relatively small numbers of renal artery stenoses in your material; 4.5% or something like that. How did you investigate them? Was the only indication for angiography hypertension, or did you routinely investigate all the transplants?

LINDFORS  No, we don’t investigate all the transplants. If the patient is normotensive we do not investigate them by angiography. But if we have any reason to suspect arterial troubles then we do angiography.

BAKER (London) How long do you leave the ureteric splint and bladder catheter in after transplantation?

LINDFORS  Now it is 3 to 4 days.