Retrospective analysis of surgical complications following cadaveric kidney transplantation in the modern transplant era

Domingo Hernández1,3, Margarita Rufino1,3, Silvia Armas1, Ana González1, Pedro Gutiérrez2,3, Pablo Barbero1, Sofía Vivancos2, Concepción Rodríguez1, José Rodríguez de Vera2 and Armando Torres1,3

1Department of Nephrology, 2Department of Urology, Research Unit, Hospital Universitario de Canarias, Instituto Reina Sofía de Investigación and 3University of La Laguna, La Laguna, Tenerife, Spain

Abstract

Background. Risk factors for surgical complications (SCs) following kidney transplantation in the modern transplant era need to be identified to perform appropriate prophylactic interventions.

Methods. Records from 870 consecutive adult cadaveric kidney transplants done at a single centre were reviewed. SCs were classified into four groups: (i) vascular (12%, thrombosis or stenosis); (ii) haemorrhagic (12%); (iii) ureteral (7.5%, leaks and stenosis) and (iv) wound (16%, lymphoceles or dehiscences).

Results. One or more SCs occurred in 299 (34%) patients, with multiple SCs in 65 (7.4%). By logistic regression analysis, recipient vessel atherosclerosis and delayed graft function (DGF) were significantly associated with both thrombotic complications [odds ratio (OR) 4, 95% confidence interval (CI), 1.4–11, \( P = 0.010 \) and OR 3.8, 1.3–12, \( P < 0.00001 \), respectively] and graft artery stenosis (OR 2.9, 1.2–6.8, \( P = 0.015 \) and OR 5.6, 2.3–13.4, \( P < 0.0001 \), respectively). Acute rejection increased the risk of graft artery or ureteral stenosis by 2.5 (CI 1.02–6.4, \( P = 0.045 \)) and 3.3 (CI 1.1–10, \( P = 0.034 \)), respectively. Older recipients were related to urinary leak (OR 1.04, CI 1.01–1.07, \( P = 0.011 \)). Difficult bench surgery, DGF and the use of antiplatelet drugs increased the risk of bleeding by 3.6 (CI 1.9–6.4, \( P < 0.0001 \)), 2.7 (CI 1.5–4.7, \( P < 0.0001 \)) and 1.8 (CI 1.03–3.29, \( P = 0.038 \)), respectively. Each month on dialysis increased the risk by 1.02 (CI 1.01–1.03, \( P = 0.002 \)). Sirolimus increased the risk for wound SCs by 4.1 (CI 2.1–8.3, \( P < 0.0001 \)) and obesity, retransplant and acute rejection were additional risk factors.

Conclusions. Adult renal transplant recipients at risk for SCs can be identified by age, DGF, graft vessel and recipient atheromatosis, difficult bench surgery, obesity, rejection and the use of antiplatelet drugs and rapamycin.

Keywords: immunosuppression; kidney transplantation; surgical complications

Introduction

Despite improvements in surgical and diagnostic techniques, surgical complications (SCs) following kidney transplantation remain an important clinical problem that may increase morbidity, hospitalization and costs [1]. Depending on the stage of the transplant process these complications may have an origin in back-table work to prepare the allograft, the dissection of the renal bed and vascular anastomosis or in the restoration of the continuity of the urinary tract. However, SCs do not necessarily imply a surgical procedure-related technical problem. Several risk factors such as older donor and recipients with atheromatosis and obesity are increasingly observed among kidney transplant candidates [2]. This may lead to both vascular thrombotic events and ureteral complications after surgery. Moreover, potential kidney recipients have unfavourable cardiovascular profiles and, frequently, they have to be treated with antiplatelet agents which may predispose to perioperative bleeding complications.

On the other hand, newer and more potent immunosuppressive drugs, such as mycophenolate mofetil (MMF) and sirolimus (SRL) have contributed to decrease the acute rejection rate and improve kidney graft function. However, recent reports show a strong association between these agents and increased incidence of wound complications and lymphocele formation [3–5]. Thus, it is plausible that an additive effect between these newer agents and risk factors
related either to donor or recipient characteristics may magnify the development of SCs in this population. Retrospective studies have reported the incidence and risk factors for a particular SC in adult renal-transplant recipients, but most of them do not provide complete information for global perioperative troublesome complications [3–10]. In addition, not all studies have included the newer immunosuppressants in their analysis [6–10], which may underestimate the incidence of SCs in this population. Therefore, an analysis of all SCs in the modern transplant era, including newer immunosuppressive agents, would be desirable to ascertain multiple risk factors with the ultimate goal of applying preventive measures which reduce the incidence of SCs.

The purpose of this study was to document a retrospective analysis of early SCs following adult cadaveric kidney transplants in order to assess the overall incidence of these complications and to identify multiple risk factors related to donor and recipient characteristics in the modern transplant era.

Subjects and methods

Study population

We conducted a retrospective cohort study with 870 consecutive Caucasian patients (18–76 years old) who received a cadaveric kidney between January 1996 and December 2004 in a regional transplant centre (Hospital Universitario de Canarias, Spain). This period was relatively homogeneous in terms of general clinical management following kidney transplantation.

Grafts were flushed with cold University of Wisconsin solution and preserved in cold solution until the transplants. All transplants were performed by one of four senior surgeons sufficiently trained for kidney transplantation. Assistant surgical support was provided by a second attendant. The four senior surgeons involved have a wide range of experience and have worked in this transplant programme since 1981. All of them used standard surgical techniques for transplantation. Briefly, kidneys were placed in either the right or the left iliac fossa using an extraperitoneal approach. The renal graft vessels were anastomosed end-to-side to the recipient external or common iliac vessels. Multiple arteries in the graft were anastomosed individually or to each other before being sewn to the recipient vessels. Fine sutures of prolene (5/0 or 6/0) were used for vascular anastomoses. Vascular bench surgery was performed before transplantation was performed when vascular abnormalities, multiple arteries or harvesting injury were present using finer sutures of prolene (7/0 or 8/0). A standard Lich-Gregoir ureteroneocystostomy was performed in all cases. Thereafter, a double-J stent (Medical Engineering Corp., New York, NY) was systematically inserted and removed 2 weeks later. All recipients were given prophylactic broad-spectrum parenteral antibiotics in the operating room at the time of transplant. Proper hydration was provided to all patients during the periooperative period. There was no routine use of post-operative anti-coagulation therapy unless clearly, medically or surgically indicated.

After surgery, the patients were monitored clinically and biochemically. In addition, all patients underwent a color Doppler flow study within the first 24 h. Immediate haemorrhagic complications were clinically detected in the first hours after surgery and, consequently, treated as an emergency. After this period, when cases of vascular or haemorrhagic complications were suspected computerized tomography, magnetic resonance imaging or angiography study were performed to confirm the diagnosis. Thereafter, additional SCs (including ureteral and wound SCs) during follow-up were diagnosed by means of echography, isotope scanning, angiography and antegrade pyelography as appropriate.

Data collection

Demographic and clinical data were collected at the time of transplantation and during hospitalization until discharge, by chart review. The parameters evaluated in this study were:

(i) Donor variables: age, gender, cause of death (cerebral vascular or not), serum creatinine before harvesting and atherosclerosis of graft vessels.

(ii) Recipient characteristics: age, gender, cause of kidney failure, dialysis modality, time on dialysis, previous transplants, the human leukocyte antigens (HLA) mismatches, maximal pre-transplant anti-lymphocytic antibodies, cytomegalovirus (CMV) status, dyslipidaemia, pre-transplant cardiovascular disease (ischaemic heart disease, heart failure, stroke and peripheral artery disease) defined by standard criteria [11], obesity [body mass index (BMI) > 30 kg/m²], use of pre-transplant antiplatelet drugs and hypertension (blood pressure > 140/90 mmHg or need for anti-hypertensive therapy) and atherosclerosis of the vessels. The recipient was considered atherosclerotic when either vascular calcifications or atherosclerotic lesions of the iliac–femoral axis during surgery were present.

(iii) Perioperative factors: left or right kidney, graft anatomy (number of arteries and veins), difficult bench surgery (presence of vascular abnormalities or major vascular injury requiring repair), graft biopsy, cold ischaemia time and graft revascularization time.

(iv) Post-transplant factors: Presence of delayed graft function (DGF), defined as the need for dialysis in the first week after surgery and/or failure of creatinine clearance to rise above 10 ml/min within the first 5 post-operative days irrespective of dialysis need, acute rejection, and serum creatinine and immunosuppressants at discharge. The diagnosis of DGF was confirmed in all cases by ultrasound, isotope scanning and/or graft biopsy.

Finally, we identified all recipients with a documented SC during the first 3 months after surgery. This included analysis of patients with prolonged stays after kidney transplantation and re-admissions.

Immunosuppression

The provided immunosuppressive treatment was similar in all patients and consisted of prednisone plus anti-lymphocytic antibodies followed by calcineurin inhibitor drugs (microemulsion Neoral or tacrolimus) and MMF
(before 1997, azathioprine) or SRL. Anti-T-cell induction therapy was administered in most patients. This therapy was usually given for the first 7 days and included either anti-thymocyte globulin at 1 mg/kg/day (Thymoglobulin, Genzyme Corporation, Boston, MA), basiliximab at 20 mg on days 0 and 4 (Simulect, Novartis, Inc., Basel, Switzerland) or daclizumab at 1 mg/kg on day 0 and all 14 days at four doses (Zenapax, Hoffman-La-Roche, Nutley, NJ, USA). The Neoral microemulsion (Novartis, Inc., Basel, Switzerland) was orally administered at 4 mg/kg per day in divided doses, to keep C0 levels between 125 and 175 ng/ml. According to our local immunosuppression policy, re-transplants, patients with high immunological risk or known intolerance to Neoral received tacrolimus instead of Neoral microemulsion. Tacrolimus (Prograf, Fujisawa Healthcare, Deerfield, IL, USA) was started at 0.1 mg/kg per day to maintain levels between 6 and 8 ng/ml. MMF (Cellcept, Hoffman La-Roche, Nutley, NJ, USA) was begun on the first post-operative day, 1 g twice a day, and remained at that dose the first year unless side effects warranted dose reduction. SRL (Rapamune, Wyeth, Radnor, PA, USA) was administered after May 2000 to avoid calcineurin inhibitor agents in the case of a marginal donor. SRL was started with 12 mg oral loading dose followed by 3 mg daily to achieve plasma levels between 8 and 10 ng/ml, and dosage reductions and levels below 8 ng/ml were targeted if cytopenia or other toxicities unrelated to wound healing were observed. Finally, intravenous methylprednisolone at a dose of 250 mg was given on day 0. Thereafter, 20 mg/day doses were systematically tapered to a maintenance dose of 0.1 mg/kg/day at 1 year. Acute rejection episodes were initially treated with three boluses of 500 mg of intravenous methylprednisolone. Resistant episodes were treated with a 7-day course of OKT3 (5 mg/day) (Muromonab CD3; Ortho Pharmaceutical, Raritan, NJ, USA).

Between 1996 and 1997, recipients received high-dose oral acyclovir (800–3200 mg/day, adjusted according to renal function) after i.v. ganciclovir as anti-CMV prophylaxis. After 1997, oral ganciclovir after i.v. ganciclovir was used in patients whose donor was seropositive, with the dose adjusted for renal function.

Classification and definitions

**Group I: vascular complications.** These included vascular thrombosis and renal artery stenosis, including significant kinking of the artery during graft placement. Primary renal allograft thrombosis whether arterial, venous or both, was identified as the cause of transplant failure only if the result of the graft’s histopathology had excluded any sign of rejection. Likewise, pre-operative hypercoagulable states were ruled out. Anastomotic or post-anastomotic renal artery stenosis was defined as a narrowing of the graft artery. Early scintigraphy or angiography were systematically performed when vascular complications were suspected. When the diagnosis was doubtful, surgical exploration was performed. The renal allograft was removed as soon as non-correctable vascular occlusion was identified.

**Group II: haemorrhagic complications.** Post-operative bleeding complication was defined as any haematoma related to the surgical transplant procedure that needed re-intervention, aspiration or blood transfusions.

**Group III: ureteral complications.** These included urinary leaks and ureteral obstruction (due to either kinking of the ureteral anastomosis or stenosis). The urinary leak was defined as the exteriorization of urine through the drainage system or by the appearance of a liquid collection on ultrasound documented by aspiration and biochemical analysis. Antegrade pyelography was systematically performed to confirm the diagnosis and to allow the placement of a decompression nephrostomy tube. Additionally, retrograde cystography was systematically performed to check the bladder and to rule out a possible vesical fistula.

**Group IV: surgical wound complications.** It included impaired wound healing, lymphocele, dehiscence or incisional hernia, that needed repeated aspiration and drainage, ethanol sclerosis or surgical repair. A collection was designated as lymphocele if the cell counts from direct aspirates proved lymphatic content.

This study was approved by the Ethics Committee of the University Hospital of the Canary Islands, and was conducted in accordance with the provisions of the Declaration of Helsinki. Medical record review was performed according to Spanish law with reference to clinical data confidentiality protection.

**Statistical analysis**

Both univariate and multivariate analyses were used to assess the significance of multiple risk factors for SCs following kidney transplantation. In particular, univariate assessment of categorical variables was analysed using the chi-square test, and when applicable, the Fisher’s exact test. Continuous variables were analysed parametrically using the Student’s t-test. Candidate variables, including the surgeon effect (identified when two-tailed \( P < 0.15 \)), were then included in a stepwise logistic regression model. In the final analysis, risk factors for SCs with a two-tailed \( P < 0.05 \) were considered statistically significant. Results are reported as means ±SD. Statistical analysis was performed using SPSS 12.0 (Chicago, IL, USA).

**Results**

Table 1 displays descriptive statistical data of the donors and recipients. One or more SCs occurred in 299 of the 870 transplants (34%) with multiple SCs in 65 (7.4%). Re-intervention was required in 126 (14.5%) and 37 grafts (4.3%) were lost by major SCs (vascular or haemorrhagic complications). A longer hospitalization was observed in patients who had a SC, because most of them occurred during the admission (29 ± 22 vs 18 ± 13 days, \( P < 0.0001 \)).

**Group I**

Overall there were 87 vascular complications in 83 patients, an incidence of 10%. Renal artery thrombosis and vein thrombosis developed in 26 (3%) and 16 (1.8%) patients, respectively. In addition, renal artery stenosis (including significant kinking or torsion of the graft artery) occurred in...
Univariate and multivariate analysis of risk factors for vascular complications are summarized in Table 2. Recipient vessel atherosclerosis and DGF were related to both thrombotic complications (artery or vein thrombosis) and renal transplant artery stenosis. Additionally, acute rejection and atherosclerosis of graft vessels were significantly associated with renal artery stenosis (Table 2).

**Group II**

Haemorrhagic complications occurred within the first 48 h after surgery in 128 patients (14.7%) and many of them underwent re-intervention (44%). The risk of bleeding increased almost 4-fold when difficult bench surgery was performed. Patients with DGF were more than twice as likely to have a bleeding complication. Each additional month on dialysis increased the risk by 2%, and the use of antiplatelet drug, pre-transplant, almost doubled the risk for haemorrhagic complications after surgery (Table 3).

**Group III**

A total of 75 ureteral complications were reported in 67 patients, (8.7%) (Table 4). In particular, distal urinary leak occurred in 38 (4.4%) and distal ureteral obstruction in 37 (4.3%) patients, requiring prolongation of stay or re-admission in the majority of the cases. For each additional year of recipient age at transplantation, the risk increased by 4%. Likewise, a longer time on dialysis was also associated with urinary leak. Interestingly, patients with acute rejection were more than three times as likely to have ureteral stenosis. Conversely, a shorter revascularization time

### Table 2. Risk factors for vascular complications following kidney transplantation

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>Univariate analysis</th>
<th>Multivariate analysisa</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Patients with</td>
<td>Patients without</td>
</tr>
<tr>
<td></td>
<td>complication (%)</td>
<td>complication (%)</td>
</tr>
<tr>
<td>Arterial or venous thrombosis (n=42)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Recipient vessel atherosclerosis</td>
<td>9 (21)</td>
<td>87 (10)</td>
</tr>
<tr>
<td>DGF</td>
<td>31 (73)</td>
<td>256 (31)</td>
</tr>
<tr>
<td>Difficult bench surgery</td>
<td>13 (30)</td>
<td>134 (16)</td>
</tr>
<tr>
<td>Revascularization time (min)</td>
<td>43 ± 13</td>
<td>39 ± 11</td>
</tr>
<tr>
<td>Graft artery stenosis (n=45)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Recipient vessel atherosclerosis</td>
<td>18 (40)</td>
<td>80 (10)</td>
</tr>
<tr>
<td>DGF</td>
<td>10 (23)</td>
<td>83 (10)</td>
</tr>
<tr>
<td>Acute rejection</td>
<td>10 (25)</td>
<td>77 (10)</td>
</tr>
<tr>
<td>Right kidney</td>
<td>29 (64)</td>
<td>371 (45)</td>
</tr>
<tr>
<td>Revascularization time (min)</td>
<td>44 ± 13</td>
<td>39.5 ± 11</td>
</tr>
</tbody>
</table>

aStepwise logistic regression model.
bAdjusted for all risk factors listed in the table. A relative risk >1.00 or <1.00 indicates a higher or lower risk for vascular complications, respectively. Other variables included in the analysis, but not in the table, were donor and recipient age, primary renal disease, HLA-mismatches, multiple renal arteries, pre-transplant cardiovascular disease, dialysis modality, re-transplant, CMV status, obesity, graft biopsy, cold ischaemia time, immunosuppressants and individual surgeons (each with P > 0.15). DGF, delayed graft function.
was related to lower risk for these complications due likely to an easier surgical procedure.

**Group IV**

Surgical wound complications were observed in 92 patients (10.5%), including isolated lymphoceles in 51 (6%). Major wound-healing problems requiring additional surgical repair occurred in 23 (28%) patients. The most significant risk factor for these complications was the use of rapamycin, which increased the risk 4-fold for this complication. Other immunosuppressants were not related to these complications. Other important risk factors were re-transplant, obesity and the presence of acute rejection (Table 5).

Finally, no SC-related deaths occurred and there was graft loss in 35 and 20% of groups I and II, respectively. As a consequence, the 1-year and 5-year graft survival rate for those with SCs was 75 and 62% compared with 93 and 78% for the remainder of our transplant populations, respectively (log rank test: 29.2, \( P < 0.0001 \)).

**Discussion**

This retrospective analysis shows that overall the incidence of SCs in adult kidney transplants is higher than that reported previously [1], which may reflect significant changes in donor organ harvesting and recipient characteristics in the modern transplant era. Otherwise, this difference may also be explained by ascertainment biases. Indeed, many studies do not provide complete information about potential risk factors for global SCs during different stages of the transplant process [3–10]. Moreover, not all reports have included the newer immunosuppressant agents in their analysis [6–10]. Thus, the true incidence for overall SCs following kidney transplantation might have been underestimated.
We collected detailed information from medical records throughout the whole transplant process. Consequently, we identified multiple intertwined risk factors for SCs from donor and recipient characteristics as well as the perioperative period and from newer immunosuppressants such as rapamycin. For example, one-third of our cases had either graft or recipient vessel atheromatosis or multiple arteries. Difficult bench surgery was needed in 20%; the use of antiplatelet drugs pre-transplantation was documented in 37% of the patients, and more than half received anti-proliferative immunosuppressants. Thus, an additive effect between multiple risk factors and immunosuppression for developing SCs, appears likely. The surgeons themselves are one of the most important risk factors for any SC, but we did not find an association between this factor and SC in the univariate and multivariate analysis (data not shown).

Finally, we classified SCs in different categories and analysed SC risk in each group individually, which may help to clarify the pathogenesis in each one. Taken together, these factors could well explain an ongoing increase in the incidence of SCs following cadaveric kidney transplantation as observed in our study.

Renal allograft vascular thrombosis is a serious complication following kidney transplantation that ultimately leads to graft loss. The incidence of thrombotic complications (arterial or venous) in our study was 4.8%, which is within the range previously reported (0.5–6%). In cadaveric transplantation, many risk factors have been associated with thrombotic sequelae [7,9,12]. We did not find a relationship with other known causes of this complication such as, severe rejection, difficult vascular bench surgery, pro-coagulant immunosuppressants, multiple arteries or cold ischaemia, among others. In addition, we did not include paediatric recipients nor patients with pre-transplant hypercoagulability state. Atherosclerosis has been also suggested as one of the risk factors for vascular complications [13]. In the current study, graft and recipient vessel atheromatosis were important contributing factors for developing both vascular thrombosis and renal transplant artery stenosis. This latter complication occurred in 5% of our series, similar to the previous studies [1,14]. Besides atherosclerosis, several risk factors for renal artery stenosis have been suggested in both cadaveric and live donor transplantation, including acute rejection [14,15]. Accordingly, a relationship between immunological dysfunction and this complication was also observed in this study. Although merely speculative, inflammation of the endothelium may lead to intimal hyperplasia and narrowing of the vascular lumen as has been previously suggested [15]. In favour of this view, the majority of the stenoses in our study were found distal to the surgical anastomosis.

An interesting finding in this study was the significant association of vascular complications—thrombosis and graft artery stenosis—with DGF. A similar relationship has been previously established in both paediatric and adult kidney recipients [9,16]. The reasons for this finding are not clear. Our definition of DGF was sufficiently precise and Doppler ultrasound performed within the first post-operative 24 h could verify graft vascular flow in all cases. Whether vascular complications, in particular thrombotic events, may be the result of haemodynamic instability, inflammatory response or interstitial oedema attributed to severe acute tubular necrosis remain undefined. Alternatively, DGF may be a consequence rather than the cause of these SCs. Meanwhile, when allografts are suffering from early DGF an effort should always be made to rule out vascular causes especially in the presence of other risk factors.

Although we did not use routine prophylactic heparinization after surgery, the incidence of haemorrhagic complications, including collections that only needed aspiration or transfusion, was 14.7%. The pathogenesis of bleeding after kidney transplantation has been poorly studied in the

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>Univariate analysis</th>
<th>Multivariate analysis*</th>
<th>P value</th>
<th>ORb (95% CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Patients with complication (%)</td>
<td>Patients without complication (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>n = 92</td>
<td>n = 778</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Recipient age (years)</td>
<td>51 ± 13</td>
<td>46.6 ± 14</td>
<td>0.010</td>
<td>1.02 (0.9–1.04)</td>
<td>0.112</td>
</tr>
<tr>
<td>Recipient obesity</td>
<td>16 (20)</td>
<td>74 (9)</td>
<td>0.012</td>
<td>2.1 (1.2–4)</td>
<td>0.017</td>
</tr>
<tr>
<td>Acute rejection</td>
<td>13 (16)</td>
<td>66 (8)</td>
<td>0.053</td>
<td>1.9 (1.01–3.8)</td>
<td>0.049</td>
</tr>
<tr>
<td>Re-transplant</td>
<td>16 (20)</td>
<td>66 (8)</td>
<td>0.003</td>
<td>2.9 (1.5–5.6)</td>
<td>0.001</td>
</tr>
<tr>
<td>Rapamycin used initially</td>
<td>15 (18.5)</td>
<td>47 (6)</td>
<td>0.000</td>
<td>4.1 (2.1–8.3)</td>
<td>0.000</td>
</tr>
<tr>
<td>MMF used initially</td>
<td>52 (64)</td>
<td>328 (48)</td>
<td>0.006</td>
<td>1.4 (0.8–2.3)</td>
<td>0.211</td>
</tr>
</tbody>
</table>

* Stepwise logistic regression model (n = 870 transplants and 92 surgical wound complications).

b Adjusted for all risk factors listed in the table. A relative risk >1.00 or <1.00 indicates a higher or lower risk for surgical wound complications, respectively. Other variables included in the analysis, but not in the table, were donor age, cause of donor death, atherosclerosis of graft vessels, primary renal disease, HLA-mismatches, pre-transplant cardiovascular disease, dialysis modality, time on dialysis, delayed graft function, use of anti-platelet drugs, CMV status, graft anatomy, achievement of graft biopsy, bench surgery, cold ischaemia time, revascularization time, renal function, other immunosuppressants and individual surgeons (each with a relative risk >1.00 or <1.00).
Wound complications are now probably the most common type of post-transplant complications. Important risk factors for these SCs include older recipients, obesity, re-operation and the use of anti-platelet drugs [3–5,8]. Although all immunosuppressive agents inhibit wound healing, SRL has a unique anti-proliferative and anti-mitotic action by inhibiting growth factor-induced proliferation of several cell types, including fibroblasts [20]. Thus, SRL may lead to either impaired wound healing or failure to seal perivascular lymphatic channels after kidney transplantation. Accordingly, the incidence of these complications in our study was 10.5% and the risk factors we identified were not surprising. The use of SRL was the most significant risk factor by multivariate analysis and no other immunosuppressants were associated with these SCs. Overdosing of SRL did not seem to be a factor for a higher surgical complication rate in our series, because early SRL levels were well within the therapeutic range (data not shown). In our current clinical practice, we used SRL when marginal donors were transplanted in an older recipient. Although our results cannot be necessarily extrapolated to other renal recipients, it may be clinically relevant, as recipients with a high risk for wound complications (e.g. those who are older, obese, re-transplants or with a high immunological risk) could be treated with an immunosuppressive regimen that avoids this agent. Whether delayed introduction of SRL minimizes these SCs is undetermined. Therefore, future lower-risk induction strategies should be tested in this population.

Although no direct mortality was attributable to global SCs, a significant decrease in graft survival was observed for both vascular and haemorrhagic complications, as previously reported [7]. In any case, other SCs may cause significant morbidity and may lead to prolonged hospitalization, re-interventions and high cost as seen in our study. Obviously, all these factors must stimulate targeting prophylactic interventions in kidney recipients.

This is a retrospective study which constitutes an important limitation. However, we obtained complete information from our database, which is updated yearly and used a proper model regression to minimize biases inherent to this type of analysis. Second, this approach may differ in the setting of live donor transplantation or paediatric kidney transplant which could be another limitation of this study.

Under this retrospective analysis, several promising approaches could prevent SC after adult kidney transplants. They may include the following: (i) to perform a more meticulous surgical procedure and vascular bench surgery in atherosclerotic patients who receive anti-platelet drugs or when atherosclerotic graft vessels are present, so that vascular and haemorrhagic complications could be minimized; (ii) adequate perioperative management in order to reduce DGF, haemodynamic instability and acute rejection and (iii) to individualize immunosuppression with SRL, avoiding or delaying its use in obese and older recipients. In any case, whether these merging manoeuvres reduce SCs following kidney transplantation deserves future clinical trials.

Acknowledgements. The authors thank Antonio Rodríguez and Carmen Abad for their work in data collection. The authors also thank the Renal Transplant team from the Canary Islands for their collaboration. This study was supported by grant (FIS 02/1350 and C03/03) from Spanish Ministry of Health and grant (PI2003/008) from Consejería de Educación, Cultura y Deportes del Gobierno de Canarias.

Conflict of interest statement. None declared.

References


Received for publication: 9.12.03
Accepted in revised form: 15.5.06