# Amikacin Prophylaxis and Risk Factors for Surgical Site Infection After Kidney Transplantation

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**Background.** Antibiotic prophylaxis plays a major role in preventing surgical site infections (SSIs). This study aimed to evaluate antibiotic prophylaxis in kidney transplantation and identify risk factors for SSIs. **Methods.** We evaluated all kidney transplantation recipients from January 2009 and December 2012. We excluded patients who died within the first 72 hr after transplantation, were undergoing simultaneous transplantation of another organ, or were below 12 years of age. The main outcome measure was SSI during the first 60 days after transplantation. **Results.** A total of 819 kidney transplants recipients were evaluated, 65% of whom received a deceased-donor kidney. The antibiotics used as prophylaxis included cephalosporin, in 576 (70%) cases, and amikacin, in 233 (28%). We identified SSIs in 106 cases (13%), the causative agent being identified in 72 (68%). Among the isolated bacteria, infections caused by extended-spectrum β-lactamase–producing Enterobacteriaceae predominated. Multivariate analysis revealed that the risk factors for post-kidney transplantation SSIs were deceased donor, thin ureters at kidney transplantation, antithymocyte globulin induction therapy, blood transfusion at the transplantation procedure, high body mass index, and diabetes mellitus. The only factor associated with a reduction in the incidence of SSIs was amikacin use as antibiotic prophylaxis. Factors associated with reduced graft survival were: intraoperative blood transfusions, reoperation, human leukocyte antigen mismatch, use of nonstandard immunosuppression therapy, deceased donor, post-kidney transplantation SSIs, and delayed graft function. **Conclusion.** Amikacin prophylaxis is a useful strategy for preventing SSIs.

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In recent times, advances in surgical technique and improved immunosuppression resulted in increased survival rates for kidney transplantation (KTx) recipients. However, the incidence of health care–associated infection (HAI), especially surgical site infection (SSI) after KTx, has remained stable, implying a negative impact on the survival of the graft and the recipient.[1-3]

Although the reported incidence of SSI after KTx ranges from 2.6% to 20%, it is typically below 10%.[3-7] The main agents isolated from SSIs are *Staphylococcus aureus*, coagulase-negative *staphylococci*, *Enterococcus* species, *Enterobacteriaceae* (*Klebsiella pneumoniae, Escherichia coli*) and *Pseudomonas aeruginosa*.[2,4,5,8] Risk factors associated with posttransplantation SSI in KTx recipients include high body mass index (BMI), diabetes mellitus (DM), acute cellular rejection, reoperation, delayed graft function (DGF), sirolimus use, deceased donor, female recipient, recipient age, prolonged cold ischemia time, and urinary fistula.[1,2,4,7-10]

General principles of asepsis and antisepsis are used in KTx, but there are only a few references in the literature about more specific approaches to reduce SSI after KTx. Such measures include the use of chlorhexidine for skin antisepsis, modifying the surgical technique, using antibiotic-impregnated surgical material, implementing protocols for SSI prevention, adopting a checklist for safe surgery, improving preoperative patient health status; and optimizing the antibiotic prophylaxis.[11-16] Prophylaxis of SSI is aimed at reducing the size

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of the bacterial inoculum at the surgical site, thereby decreasing the risk of infection. Therefore, it is important that the antimicrobial agent is active against the major pathogens colonizing the skin and the operative site. Cephalosporins are the antibiotics that have been most widely indicated for surgical prophylaxis because of their broad spectrum, good bioavailability, and low toxicity.[17]

In recent years, the incidence of community-acquired infection caused by extended-spectrum β-lactamase (ESBL)–producing *Enterobacteriaceae* has increased. In this context, cephalosporins might have become less effective as surgical prophylaxis, especially for populations in which *Enterobacteriaceae* infections and antibiotic use are common, as they are in patients with end-stage renal disease.[18,19] The aim of this study is to evaluate the impact of the antibiotic prophylaxis modification in KTx and identify risk factors for SSI.

## RESULTS

A total of 903 KTx were performed between January 2009 and December 2012. We excluded 84 cases: 10 cases of recipient death within the first 72 hr after transplantation, 49 cases of simultaneous organ transplantation, and 25 pediatric transplantations. The casuistic consisted of the remaining 819 cases. Of those, six patients lost follow-up in a period lower than 60 days; they were retained in analysis because the median time follow-up of these cases was 29.5 days. Of 819 KTx, 430 (52.5%) were men. The median age was 47 years (12 to 79). The most common pretransplant diagnosis is glomerulonephritis. (see **Table S1, SDC,** http://links.lww.com/TP/B42).

Of the 819 KTx, 61 (7.4%) and 6 (0.7%) had been previously submitted to one and two kidney transplants, respectively; 530 (64.7%) were from a deceased donor, and 289 (35.3%) were from a living donor. Of the 289 living-donor kidneys, 84 (29.1%) were from an unrelated donor and 205 (70.9%) were from a related donor. Induction immunosuppression therapy was performed in 798 recipients (97.4%), of whom 307 (38.5%) used antithymocyte globulin (ATG) and 491 (61.5%) were treated with basiliximab.

The antibiotic prophylaxis used was as follows: broad-spectrum antibiotic because of active infection at transplantation in 8 (0.9%); tetracycline, because of an adverse drug reaction to standard prophylaxis in 1 (0.1%); cefazolin, in 519 (63.4%), for a mean duration of 3.2 days (1–17); ceftriaxone, in 57 (7.0%) for a mean duration of 2.8 days (1–12); and amikacin, in 233 (28.4%) for a mean duration of 2.1 days (1–5).

Eighty five (36.5%) patients that used amikacin for surgical prophylaxis developed DGF. The frequency of DGF was lower in patients that used cephalosporin for surgical prophylaxis, 169 (29.2%) (*P* 0.05) (see **Table S2, SDC,** http://links.lww.com/TP/B42). No other side effect of amikacin was detected in the period of study.

We identified 106 (12.9%) SSIs, which we classified as organ or space SSIs in 81 cases (76.4%), as deep incisional primary SSIs in 11 (10.4%), and as superficial incisional primary SSIs in 14 (13.2%). The incidence of SSI in 2009, 2010, 2011, and 2012 was 13.4%, 16.4%, 12.7%, and 10.0%, respectively (*P*=0.19). Incidence density rate of SSI in the period was 2.39 per 1000 patient-days; patients that used amikacin for surgical prophylaxis had 0.52 SSI by multidrug-resistant (MDR) incidence rate compared with 1.07 of those that used other antibiotic prophylaxis (*P* 0.06) (see **Table S2, SDC,** http://links.lww.com/TP/B42).

The median time between KTx and SSI was 20 days (range, 7–60 days). A total of 17 infections were diagnosed after 30 days; 14 (82.3%) were classified as space-organ and three (17.7%) as incision infection, all those subcutaneous abscesses. The causative agent was identified in 72 SSIs (67.9%), of which 68 (83.9%) were organ or space SSIs and 4(16%) were incisional infections. Among the 68 organ or space SSIs, the causative agent was isolated in the bloodstream as well in 32 (39.5%). *Enterobacteriaceae* was the most common family of bacteria isolated from SSIs, ESBL-producing *Enterobacteriaceae* being predominant (Table 1). Of the 19 *K. pneumoniae* isolated, 8 (42.1%) were ESBL producers and 7 (36.8%) were carbapenem-resistant. Of the 57 *Enterobacteriaceae* identified, 55 (96.5%) were sensitive to amikacin. We identified a trend toward a lower proportion of SSIs caused by MDR bacteria in 2012 than in the previous years (Figure 1).

In the multivariate analysis, the risk factors associated with SSI after KTx were deceased donor, thin ureters at transplantation, ATG use in the induction therapy, blood transfusion during transplantation, a high BMI, and DM (Table 2). The only factor associated with a reduction in the incidence of SSI was amikacin use as the surgical prophylaxis. The risk factors associated with reduced graft survival were a significant amount of blood transfused during transplantation, previous KTx, human leukocyte antigen (HLA) mismatch, use of nonstandard immunosuppression therapy, deceased donor, SSI after KTx, and DGF (Table 3). The graft survival curve is shown in Figure 2. The risk factors associated with mortality in the first year after KTx were advanced recipient age, deceased donor, HAI within the first 60 days after transplantation, graft function loss, and a significant amount of

**TABLE 1.**

**Microorganisms isolated from 106 surgical site infections occurring after kidney transplantation**

| Microorganism | Total | MDR |
|---|---|---|
| *Klebsiella pneumoniae*, n (%) | 19 (18) | 15 (79) |
| *Enterococcus faecium*, n (%) | 16 (15) | 11 (69) |
| *Escherichia coli*, n (%) | 14 (13) | 6 (43) |
| *Enterobacter cloacae*, n (%) | 9 (8) | 1 (11) |
| *Pseudomonas aeruginosa*, n (%) | 6 (6) | 2 (33) |
| *Enterococcus faecalis*, n (%) | 5 (5) | 1 (20) |
| *Morganella morganii*, n (%) | 4 (4) | 0 |
| *Acinetobacter baumannii*, n (%) | 4 (4) | 3 (75) |
| Non-albicans *Candida* species, n (%) | 4 (4) | — |
| *Staphylococcus epidermidis*, n (%) | 3 (3) | 0 |
| *Proteus mirabilis*, n (%) | 3 (3) | 1 (33) |
| *Candida albicans*, n (%) | 3 (3) | — |
| *Klebsiella oxytoca*, n (%) | 2 (2) | 2 (100) |
| *Enterobacter aerogenes*, n (%) | 2 (2) | 1 (50) |
| *Serratia marcescens*, n (%) | 2 (2) | 0 |
| *Staphylococcus aureus*, n (%) | 2 (2) | 1 (50) |
| Anaerobic bacteria, n (%) | 2 (2) | 0 |
| Other GPC, n (%) | 4 (4) | 0 |
| Other GNB, n (%) | 3 (3) | 0 |

GPC, gram-positive cocci; GNB, gram-negative bacilli; MDR, multidrug-resistant.

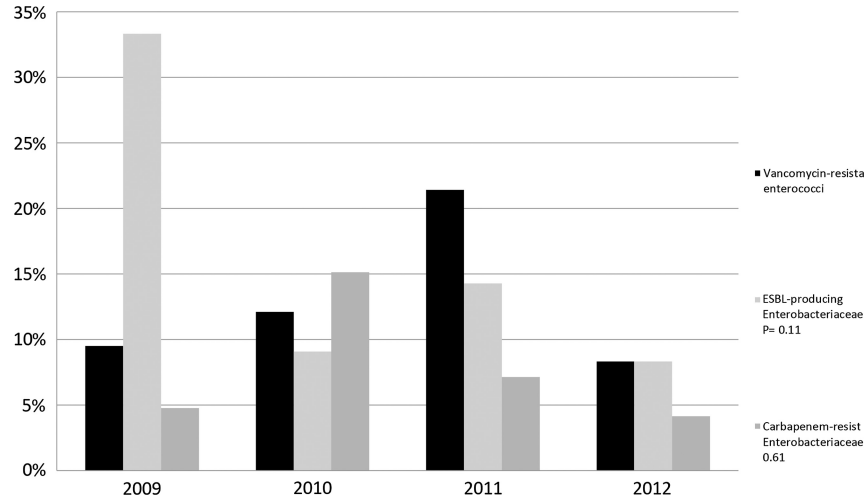


**FIGURE 1.** Proportion of multidrug-resistant bacteria as the causative agents of 819 cases of surgical site infection after kidney transplantation over the 2009 to 2012 study period.

blood transfused during transplantation (see **Table S3, SDC,** http://links.lww.com/TP/B42). The recipient survival curve is shown in **Figure S1,** (**SDC,** http://links.lww.com/TP/B42).

## DISCUSSION

In the present study, the incidence of SSI after KTx was 12.9%, which is consistent with the 2% to 20% reported in the literature.[3-7] There is no consensus regarding the criteria used in defining SSI after KTx or even the ideal duration of the follow-up. This rate was increased due in part to the 60-day period of follow up, if we used only the traditional 30-day period of follow-up, the incidence of SSI dropped to 10.7%. Our decision to maintain surveillance of SSI over the first 60 postoperative days was based on the observation that infections tend to occur later at our facility, the median time from transplantation to infection being 20 days.

The causative agents identified in our study are the same as those described by other authors, except for the unusual predominance of *K. pneumoniae* in relation to others *Enterobacteriacae*, especially *E. coli*. Among the *K. pneumoniae* isolated from SSI, we noted a high frequency of ESBL-producing isolates and carbapenem-resistant strains.[2,4,5,8]

Solid-organ transplant recipients are described as being at a higher risk for ESBL-producing *Enterobacteriaceae* infections. Also, the risk of acquiring ESBL-producing *K. pneumoniae* has been shown to be higher among patients on dialysis.[20,21] Considering solid-organ transplant recipients, ESBL-producing *K. pneumoniae* infections are most common in KTx, the typical site of such infections being the urinary tract.[22,23] It is estimated that the ESBL-producing *Enterobacteriaceae* are responsible for up to one third of all post-KTx urinary tract infections.[22] A high incidence of infection with *Enterobacteriacae*, especially ESBL-producing *K. pneumoniae*, has been reported in numerous studies of KTx recipients.[22,24,25] A recent Brazilian study reported that 80% of all *K. pneumoniae* isolates from SSIs are ESBL producers.[9] Another study of urinary tract infection after KTx showed that the incidence of infection with ESBL-producing *Enterobacteriaceae* has increased over time.

More recently, the increase in the incidence of infections with carbapenem-resistant *K. pneumoniae* has been observed among solid-organ transplant recipients, especially KTx recipients, and the most common site of such infections is also the urinary tract. The mechanisms of carbapenem resistance vary from metallo-β-lactamase-producing bacteria to carbapenemase producing *K. pneumoniae*.[26-28] In the present study, seven cases of infection with carbapenemase producing *K. pneumoniae* were identified, representing one third of all the *K. pneumoniae* infections.

We noticed that the substitution by amikacin as prophylaxis led to a reduction in the proportion of MDR bacteria as the causative agents of SSI, particularly by MDR *Enterobacteriaceae* and vancomycin-resistant *Enterococci*.

Surgical prophylaxis can modify the etiology of SSI in two ways: the first is the effect of the antimicrobials on the flora of patients undergoing KTx that facilitates colonization by antimicrobial-resistant organisms. Cephalosporin use has been associated with an increased incidence of MDR bacterial infection like vancomycin-resistant *Enterococci*, ESBL-producing or carbapenem-resistant *Enterobacteriaceae*.[29-32] The other mechanism is the direct intraoperative effect of surgical prophylaxis on microorganisms possibly present at the surgical site. The aminoglycosides are active against ESBL-producing *Enterobacteriaceae* and are marginally effective against *Enterococci*. Antibiotic prophylaxis that is more effective against the flora of the patient can reduce not only the incidence of infection caused by these bacteria but also the overall incidence of SSI. Recent studies comparing amikacin and cephalosporin as surgical prophylaxis in other surgical procedures have demonstrated that amikacin is the most effective, especially in urologic procedures.[33,34] In the present study, the efficacy of amikacin in reducing the incidence of SSI was confirmed on the multivariate analysis for SSI risk factors.

Although amikacin was efficient in decreased SSI, particularly SSI caused by MDR bacteria, aminoglycosides were more toxic than cephalosporin, especially in relation of nephrotoxicity. This is an important issue, once KTx patients are susceptible to renal injury. In this study, patients that used amikacin in surgical prophylaxis evolved more frequently

**TABLE 2.**

**Univariate and multivariate analyses of risk factors for surgical site infection after kidney transplantation**

| | Surgical site infection | | | | | | |
|---|---|---|---|---|---|---|---|
| | Yes | No | | | Multivariate analysis | | |
| Variable | (n=106) | (n=713) | RR | *P* | OR | 95% CI | *P* |
| Age at transplantation, yr, median (range) | 50.5 (19–77) | 44.4 (12–79) | — | <0.001 | | | |
| White race, n (%) | 71 (67) | 504 (70.7) | 0.98 (0.92–1.04) | 0.42 | | | |
| Male sex, n (%) | 46 (43.4) | 384 (53.9) | 0.95 (0.90–1.00) | 0.05 | | | |
| Diabetes mellitus, n (%) | 35 (33) | 115 (16.1) | 1.17 (1.07–1.28) | <0.001 | 1.94 | 1.01–3.73 | 0.05 |
| Hepatitis C virus infection, n (%) | 12 (11.3) | 37 (5.2) | 1.16 (0.99–1.31) | 0.01 | | | |
| Smoking, n (%) | 11 (10.4) | 82 (11.5) | 0.99 (0.91–1.07) | 0.73 | | | |
| A+ blood type, n (%) | 43 (40.6) | 245 (34.4) | 1.04 (0.98–1.10) | 0.21 | | | |
| Dialysis before transplantation, n (%) | 101 (95.3) | 647 (90.7) | 1.08 (1.00–1.15) | 0.14 | | | |
| Previous kidney transplantation, n (%) | 11 (10.4) | 50 (7.0) | 1.07 (0.95–1.20) | 0.22 | | | |
| BMI, kg/m$^2$ at transplantation, median (range) | 26.8 (16.6–54.3) | 24.3 (13.3–52.1) | — | <0.001 | 1.10 | 1.04–1.16 | 0.001 |
| Donor age, yr, median (range) | 46.2 (8–740) | 42.8 (4–71) | — | 0.03 | | | |
| Deceased donor, n (%) | 93 (87.7) | 437 (61.3) | 1.16 (1.11–1.21) | <0.001 | 7.35 | 2.55–21.15 | < 0.001 |
| HLA-DR mismatch, n (%) | 50 (47.2) | 314 (44.0) | 1.01 (0.96–1.07) | 0.61 | | | |
| HLA-A mismatch, n (%) | 78 (73.6) | 498 (69.8) | 1.02 (0.96–1.08) | 0.62 | | | |
| HLA-B mismatch, n (%) | 73 (68.9) | 489 (68.6) | 1.00 (0.94–1.06) | 0.92 | | | |
| Total HLA mismatch, median (range) | 2.8 (0–6) | 2.6 (0–7) | — | 0.35 | | | |
| ASA physical status, median (range) | 3 (2–5) | 3 (2–4) | — | 0.05 | | | |
| Cold ischemia time, hr, median (range) | 21.1 (0.2–41) | 15.3 (0.3–48) | — | <0.001 | | | |
| Surgical time, min, median (range) | 227.4 (75–510) | 219.6 (60–840) | — | 0.08 | | | |
| Anatomic anomalies of the urinary tract, n (%) | 25 (23.6) | 185 (25.9) | 0.98 (0.93–1.04) | 0.60 | | | |
| Use of Belzer perfusion solution, n (%) | 82 (77.3) | 504 (70.0) | 1.04 (0.99–1.10) | 0.17 | | | |
| Ureteral dysfunction at transplantation, n (%) | 15 (14.2) | 58 (8.1) | 1.11 (0.98–1.25) | 0.04 | 2.27 | 1.05–4.87 | 0.04 |
| Ureteroneocystostomy (Lich-Gregoir technique), n (%) | 97 (91.5) | 669 (94.0) | 0.89 (0.73–1.09) | 0.15 | | | |
| Graft location (left iliac fossa), n (%) | 50 (47.2) | 364 (51.1) | 0.98 (0.93–1.03) | 0.45 | | | |
| Vena cava patch, n (%) | 59 (55.7) | 287 (40.3) | 1.09 (1.03–1.15) | 0.002 | | | |
| Arterial anastomosis (external iliac artery), n (%) | 89 (84) | 593 (83.2) | 1.01 (0.93–1.10) | 0.80 | | | |
| Aortic patch, n (%) | 64 (60.4) | 361 (50.6) | 1.06 (1.00–1.12) | 0.04 | 0.55 | 0.27–1.12 | 0.1 |
| Intraoperative blood transfusion, n (%) | 10 (9.4) | 20 (2.8) | 1.31( 1.00–1.74) | 0.003 | 3.73 | 1.20–11.59 | 0.02 |
| Experienced (senior) surgeon, n (%) | 27 (25.5) | 238 (33.4) | 0.95 (0.91–1.00) | 0.10 | 0.46 | 0.22–1.02 | 0.07 |
| Amikacin prophylaxis, n (%) | 17 (16) | 216 (30.3) | 0.92 (0.87–0.96) | 0.002 | 0.37 | 0.15–0.92 | 0.03 |
| ATG induction therapy, n (%) | 62 (58.5) | 245 (34.4) | 2.35 (1.82–3.03) | <0.001 | 2.23 | 1.23–4.06 | 0.008 |
| Standard immunosuppression therapy, n (%) | 93 (87.7) | 661 (92.7) | 0.91 (0.80–1.03) | 0.07 | | | |
| Surgical drain, n (%) | 41 (38.7) | 247 (34.6) | 1.02 (0.97–1.08) | 0.44 | | | |
| Ureteral stent use, n (%) | 28 (26.4) | 165 (23.1) | 1.03 (0.96–1.09) | 0.45 | | | |
| Surgical intervention after transplantation, n (%) | 28 (26.4) | 102 (14.3) | 1.13 (1.03–1.24) | 0.001 | 1.98 | 0.95–4.13 | 0.07 |
| Acute cellular rejection, n (%) | 11 (10.4) | 146 (20.5) | 0.99 (0.91–1.07) | 0.83 | | | |
| CMV infection, n (%) | 2 (1.9) | 121 (17.0) | 0.91 (0.85–0.98) | 0.15 | | | |
| Delayed graft function, n (%) | 57 (53.8) | 197 (27.6) | 1.18 (1.10–1.26) | <0.001 | | | |

ASA, American Society of Anesthesiologists; BMI, body mass index; OR, odds ratio; 95% CI, 95% confidence interval; HLA, human leukocyte antigen; CMV, cytomgalovirus; ATG, antithymocyte globulin.

with DGF. However, amikacin surgical prophylaxis had no impact in graft survival during whole study period (Table 3) or first 30 days after KTx (data not shown).

Some of the risk factors identified in our study, including BMI, reoperation rates and DM, have been previously associated with an increased incidence of SSI after KTx.[1,4,7,9] Technical surgical challenges and intraoperative complications also increase the risk of SSI. This study evaluated a large number of variables related to the surgical technique to identify which ones might be associated with SSI. Among them, only thin ureters at KTx and the need of blood transfusion during transplantation were identified as risk factors for SSI. Thin ureters demanded correction (reduction of ureteral length) to reduce the risk of ischemia after transplantation. This factor can increase the risk of SSI. Transfusion itself plays an immunosuppressive role and, in the case of SSI, is an indirect marker of intraoperative complication. Other studies of solid organ transplantation have identified an association between multiple transfusions during transplantation and a higher risk of SSI.[35,36] In addition, the risk of SSI is higher among patients receiving induction therapy with ATG compared to those receiving basiliximab or those that received no induction therapy. Although the use of ATG has rarely been associated with post-KTx SSI, various studies have demonstrated that the overall incidence of bacterial infection is lower in patients receiving basiliximab compared to those receiving ATG.[37] Basiliximab is a chimeric highly specific anti-CD25 monoclonal antibody that blocks the

**TABLE 3.**

**Univariate and multivariate analyses of death-censored graft survival after kidney transplantation**

| | Graft loss | | | | Multivariate analysis | | |
|---|---|---|---|---|---|---|---|
| | Yes | No | | | | | |
| Variable | (n=78) | (n=741) | HR (95% CI) | *P* | HR | 95% CI | *P* |
| Hepatitis C virus infection, n (%) | 41 (52.6) | 41 (5.5) | 1.92 (0.92–3.98) | 0.08 | | | |
| Diabetes mellitus, n (%) | 12 (8) | 66 (9.9) | 0.89 (0.48–1.65) | 0.71 | | | |
| BMI, kg/m$^2$ at transplantation, median (range) | 23.2 (15.8–54.3) | 23.8 (13.3–51.1) | 1.00 (0.96–1.05) | 0.88 | | | |
| Male sex, n (%) | 46 (59.0) | 384 (51.8) | 0.77 (0.49–1.21) | 0.26 | | | |
| Age at transplantation, yr, median (range) | 47 (15–74) | 48 (12–79) | 1.01 (0.99–1.03) | 0.42 | | | |
| ASA physical status, median (range) | 3 (2–5) | 3 (2–4) | 1.18 (0.66–2.11) | 0.57 | | | |
| Previous kidney transplantation, n (%) | 13 (16.7) | 48 (6.5) | 2.75 (1.51–4.99) | 0.001 | 2.27 | 1.13–4.59 | 0.022 |
| Smoking, n (%) | 10 (12.8) | 83 (11.2) | 1.12 (0.58–2.18) | 0.73 | | | |
| Deceased donor, n (%) | 66 (84.6) | 464 (62.6) | 3.46 (1.87–6.41) | <0.001 | 2.47 | 1.09–5.59 | 0.03 |
| Donor age, yr, median (range) | 49 (16–72) | 43 (4–74) | 1.04 (1.02–1.05) | <0.001 | | | |
| Total HLA mismatch, median (range) | 3 (0–6) | 3 (0–6) | 1.14 (1.02–1.29) | 0.02 | 1.20 | 1.03–1.39 | 0.017 |
| Dialysis before transplantation, n (%) | 75 (96.2) | 673 (90.8) | 2.53 (0.80–8.03) | 0.12 | | | |
| Cold ischemia time, hr, median (range) | 22 (0–33) | 20 (0–48) | 1.03 (1.01–1.06) | 0.001 | | | |
| Surgical time, min, median (range) | 215 (75–420) | 210 (60–840) | 1.01 (0.99–1.04) | 0.64 | | | |
| Aortic patch, n (%) | 50 (64.1) | 375 (50.6) | 1.81 (1.13–2.91) | 0.01 | | | |
| Anatomical anomalies of the urinary tract, n (%) | 23 (29.5) | 187 (25.2) | 1.28 (0.78–2.08) | 0.33 | | | |
| Vena cava patch, n (%) | 46 (59.0) | 300 (40.5) | 2.01 (1.27–3.18) | 0.003 | | | |
| Ureteral dysfunction at transplantation, n (%) | 10 (12,8) | 63 (8.5) | 1.63 (0.84–3.17) | 0.15 | | | |
| Ureteroneocystostomy (Lich-Gregoir technique), n (%) | 71 (91) | 696 (93.9) | 0.60 (0.22–1.65) | 0.33 | | | |
| Ureteral stent use, n (%) | 21 (26.9) | 172 (23.2) | 1.36 (0.83–2.26) | 0.23 | | | |
| Experienced (senior) operating surgeon, n (%) | 10 (12.8) | 103 (13.9) | 0.74 (0.45–1.22) | 0.24 | | | |
| Intraoperative blood transfusion (units), median (range) | 0 (0–2) | 0 (0–4) | 1.91 (1.38–2.64) | <0.001 | 1.92 | 1.33–2.76 | <0.001 |
| Amikacin prophylaxis, n (%) | 18 (23.1) | 215 (29.0) | 0.69 (0.41–1.17) | 0.17 | | | |
| ATG induction therapy, n (%) | 40 (51.3) | 268 (36.2) | 1.88 (1.21–2.94) | 0.005 | | | |
| Standard immunosuppression therapy, n (%) | 65 (83.3) | 689 (93.0) | 2.51 (1.38–4.56) | 0.002 | 2.37 | 1.17–4.81 | 0.016 |
| Surgical intervention after transplantation, n (%) | 48 (61.5) | 111 (15.0) | 7.51 (4.76–11.87) | <0.001 | | | |
| Acute cellular rejection, n (%) | 18 (23.1) | 150 (20.2) | 1.03 (0.61–1.74) | 0.92 | | | |
| CMV infection, n (%) | 9 (11.5) | 128 (17.3) | 0.62 (0.31–1.24) | 0.17 | | | |
| Health care–associated infection, n (%) | 40 (51.3) | 178 (24.0) | 3.20 (2.05–5.00) | <0.001 | | | |
| Surgical site infection, n (%) | 30 (38.5) | 76 (10.3) | 4.86 (3.08–7.68) | <0.001 | 1.85 | 0.99–3.46 | 0.05 |
| Delayed graft function, n (%) | 43 (55.1) | 211 (28.5) | 2.92 (1.87–4.57) | <0.001 | 1.93 | 1.08–3.43 | 0.027 |

HR, hazard ratio; CI, confidence interval ASA, American Society of Anesthesiologists; BMI, body mass index; 95% CI, 95% confidence interval; HLA, human leukocyte antigen; CMV, cytomgalovirus; ATG, antithymocyte globulin.

interleukin 2 receptor, thereby reducing the effect on CD8 lymphocytes compared to the less specific effect of ATG, which interacts with all types of T lymphocytes.[38]

This study found the incidence of SSI to be higher among patients who received kidneys from deceased donors than among those receiving kidneys from living donors. Ho et al.[7,39] also identified a lower incidence of SSI in KTx recipients from living donors, and Silva et al.[7,39] reported a higher incidence of bloodstream infection in recipients from deceased-donor kidneys. That association could be explained by the long cold ischemia time in deceased donors, the better control of previous infectious of the living-donor recipient, and the need for more potent immunosuppression in recipients of kidneys from deceased donors.

In the present study, we have demonstrated that SSI after KTx has a significant impact on the survival of grafts and recipients. Other authors have described this correlation.[1] However, to our knowledge, there have been no studies using a multivariate model for survival analysis that found this correlation. This is important because graft survival can be influenced by a number of variables, such as recipient sex, acute cellular rejection rates, donor age, HLA mismatches, cytomegalovirus (CMV) infection, time on dialysis, recipient age, DGF, and panel-reactive antibodies.[40,41]

Humar et al.[1] reported that SSI reduces graft survival within the first 30 days, as well as within the first 5 years, after KTx. In the present study, recipients were followed up for 4 years after KTx, during which time, SSI was correlated with graft function loss even when included in a multivariate model. The reduced graft survival was related to SSI even after excluding the cases of graft function loss within the first 30 days ($P<0.001$) (data not shown).

We analyzed risk factors for death in the first year after KTx and identified risks related to the graft, recipient, and surgical approach to KTx. Of the risk factors identified, the only one not typically described in the literature is blood transfusion during transplantation. However, it is reasonable to assume that difficulties in the surgical approach and intraoperative complications are implicated in alterations in graft function and worse recipient outcomes.

In this cohort, HAI within first 60 days after KTx had a significant impact on recipient survival. The SSI cases

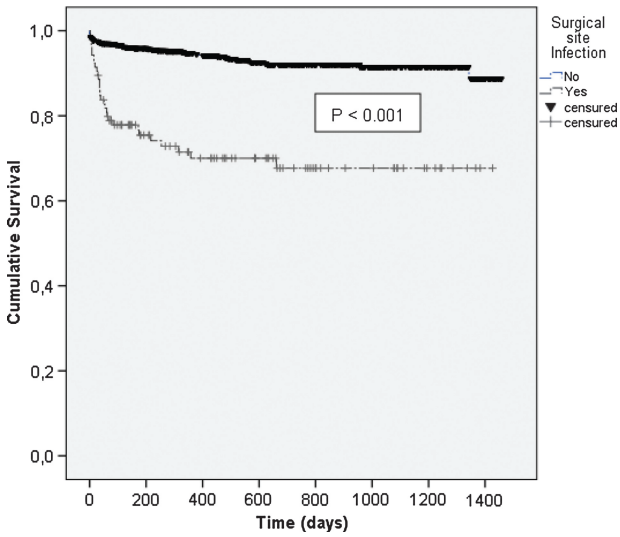


**FIGURE 2.** Kaplan-Meier estimate of cumulative probability of death-censored graft survival after kidney transplantation, stratified by surgical site infection within the first 60 days after transplantation.

accounted for 49.1% of the HAI in the evaluated patients. Other early posttransplantation infections, such as bloodstream infection and pneumonia, have also been found to correlate with a negative impact in recipient survival.[39,42] It is therefore possible that, although SSI was the most common type of post-KTx infection, other infections can contribute to a negative outcome in the early postoperative period after KTx.

In conclusion, we found SSI to be a major adverse event in early postoperative period after KTx, with a significant impact on recipient and graft survivals. We also found that risk factors for SSI after KTx were related to characteristics of the recipient, the conditions under which KTx is performed, the type of donor and the type of immunosuppression. Amikacin prophylaxis was found to be an efficient choice in preventing SSI in scenario of MDR bacteria.

## MATERIALS AND METHODS

We evaluated all patients who underwent KTx between January 2009 and December 2012 at the University of São Paulo School of Medicine Hospital das Clínicas. We excluded patients who died within the first 72 hr after transplantation, were undergoing simultaneous transplantation of another organ, or were below 12 years of age. Follow-up started at hospital admission and continued until the end of posttransplant month 2. Infections were identified through active surveillance on the KTx ward and review of outpatient records. For the analysis of graft and patient survival, we reviewed all patient records from the time of KTX up through January 2013. The criteria used to identify and classify HAIs were those outlined by the (United States) National Healthcare Safety Network.[43] The criteria used for CMV infection and disease were those defined by Ljungman et al.[44] We defined the category of MDR bacteria according to the criteria established by the Centers for Disease Control and Prevention and European Centre for Disease Prevention and Control.[45]

From January 2009 to July 2012, the standard surgical prophylaxis in use was a 3-day course of cefazolin. Thereafter, amikacin became the standard. Amikacin was administered 30 min before surgery, and the dosing used was 1000 mg or 15 mg/kg for patients weighting less than 70 kg; patients that had creatinine clearance over 30 mL per min and urinary output in first day after KTx received an amikacin second dose adjusted for creatinine clearance rate. The prophylaxis protocol was modified for cases in which patients underwent KTx during treatment for an infection as well as for those in which the donor had a confirmed infection. In such cases, the antibiotic used for prophylaxis was the same as that used for the treatment of the infection in question. Between January 2009 and December 2010, the prophylaxis was also changed from cefazolin to ceftriaxone or amikacin when considered appropriate by the surgeon. Prophylaxis for CMV was administered to all patients classified as being at a high risk for CMV infection, to recipients in whom the serology was negative for CMV (negative immunoglobulin G), and to those receiving induction immunosuppression or rejection therapies with ATG. The standard immunosuppression regimen consisted of tacrolimus, mycophenolate mofetil, and a corticosteroid.

We calculated infection rates on the basis of the number of SSIs in relation to the total number of KTxs performed during the study period. We evaluated the following variables related to the surgical procedure: cold ischemia time, number of units of blood transfused during transplantation, reoperation, previous KTx, level of experience of the lead surgeon, American Society of Anesthesiologists physical status classification, surgical time, use of an aortic patch, use of a vena cava patch, thin ureters at transplantation that required reduction of ureteral length and or stenting, anatomic variation in the genitourinary tract of the recipient, ureteroneocystostomy technique, type of arterial anastomosis, donor type (living or deceased), donor age, and the type of surgical prophylaxis. We also evaluated variables related to the recipient: age, sex, DM, dialysis before KTx, smoking and other underlying diseases, proportion of HLA mismatch, and BMI at transplantation. In addition, we evaluated the following variables related to transplantation procedure: use of induction immunosuppression therapy, the need for dialysis, the duration of abdominal drain, acute cellular rejection, CMV disease, and type of initial immunosuppression therapy (standard vs. nonstandard).

The main outcome measure was SSI during the first 60 days after transplantation. For dichotomous variables, we performed univariate analysis with chi-square or Fisher exact test as appropriate. For continuous variables, we used the Mann-Whitney *U* test. Multivariate analysis was performed by stepwise binary logistic regression. The criterion for inclusion in the multivariate analysis was *P* less than 0.2 in the univariate analysis. Variables that reduced the −2*log-likelihood error or had a value of *P* less than 0.05 were retained in the model. Survival was evaluated by Cox proportional-hazard regression, criteria used for inclusion variables in multivariate model was the same as described for binary logistic regression. For patient survival analysis, endpoint used was death in 1 year, and for graft survival, endpoint was return to dialysis in any time during the 4-year study period. Receptor age and graft lost was treated as a time-dependent variable in patient survival analysis.

We constructed survival curves by Kaplan-Meier test, calculating *P* values with the log-rank test. All statistical analyses were performed with the Statistical Package for the Social Sciences, version 17.0 (SPSS Inc., Chicago, IL).

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