

Assessment of Current Practices for Perioperative Antibiotic Prophylaxis in Kidney Transplantation in China: Results from a Nationwide Survey

Wenjing Hou^{1,2,*}, Jiayu Yang^{3,*}, Kuifen Ma^{1,2,4}, Xiangduan Liu^{2,5}, Hui Yang^{2,6}, Qing Qian^{2,7}, Pan Chen^{2,8}, Fang Zeng^{2,9}, Rongrong Wang^{2,4}, Guangzhao Wang^{2,10}, Aiping Wen¹

¹Department of Pharmacy, Beijing Friendship Hospital, Capital Medical University, Beijing, 100050, People's Republic of China; ²National Alliance of Transplant Pharmacists, Zhejiang, People's Republic of China; ³Department of Pharmacy, Beijing Tiantan Hospital, Capital Medical University, Beijing, 100070, People's Republic of China; ⁴Department of Clinical Pharmacy, The First Affiliated Hospital, Zhejiang University School of Medicine, Hangzhou, 311500, People's Republic of China; ⁵Department of Pharmacy, Fifth Clinical College of Henan University of Traditional Chinese Medicine (Zhengzhou People's Hospital), Zhengzhou, 450000, People's Republic of China; ⁶Department of Pharmacy, Beijing Chao-Yang Hospital, Capital Medical University, Beijing, 100020, People's Republic of China; ⁷Department of Pharmacy, The First People's Hospital of Changzhou, Changzhou, Jiangsu, 213003, People's Republic of China; ⁸Department of Pharmacy, The First Affiliated Hospital, Sun Yat-Sen University, Guangzhou, 510080, People's Republic of China; ⁹Department of Pharmacy, Union Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, 430022, People's Republic of China; ¹⁰Department of Pharmacy, The First People's Hospital of Yulin, Yulin, Guangxi, 537000, People's Republic of China

*These authors contributed equally to this work

Correspondence: Aiping Wen, Department of Pharmacy, Beijing Friendship Hospital, Capital Medical University, 95# Yongan Street, Beijing, 100050, People's Republic of China, Email wenaiping@ccmu.edu.cn

Background: Current guidelines support routine perioperative antibiotic prophylaxis (PAP) to minimize surgical site infection in kidney transplantation (KT), though data regarding the current practices of PAP is lacking in China.

Objective: To survey the routine PAP strategies in KT, and analyze main clinical considerations associated with adjusted antibiotic dosing regimens in different Chinese hospitals.

Methods: A nationwide survey was conducted on behalf of the National Alliance of Transplant Pharmacists. An online questionnaire was created via Wen Juan Xing (<http://www.wjx.cn>) and sent to all pharmacists in the Alliance.

Results: Twenty-three pharmacists from different teaching hospitals with Grade IIIA participated in the survey, with a response rate of 46.0%. There were wide differences in routine dosing regimens and clinical considerations. Six strategies were involved in living-donor KT and monotherapy was most often used (80.9%), while combination therapy was most common (69.6%) among the ten strategies in deceased-donor KT. Of fifteen antibiotics submitted in the survey, eight agents were prescribed with different doses and/or frequencies among different hospitals. Only 37.5% and 23.1% of the hospitals would stop PAP within 72 hours in living-donor KT and deceased-donor KT, respectively. Among 28 preset factors, four factors were considered significantly important to decide PAP regimens, and eight factors were considered significantly unimportant ($P < 0.05$).

Conclusion: There was wide variability in routine dosing regimens and clinical considerations in PAP decisions in KT. Further investigations are warranted to obtain high-quality evidence and to make PAP in KT more rational.

Keywords: perioperative antibiotic prophylaxis, clinical consideration, kidney transplant, nationwide survey

Introduction

Solid-organ transplantation is the best therapeutic option for patients with end-stage organ disease. The rate of surgical site infection (SSI) was the lowest (3.0%~11.0%) in kidney transplant recipients (KTRs) among all the organ transplant

types.^{1,2} However, it is also crucial to carry out perioperative infection prevention to minimize the risk of SSIs because SSIs are associated with prolonged hospitalization and reduced graft survival.³

There are some guidelines on perioperative antibiotic prophylaxis (PAP) in kidney transplantation (KT), though specific recommendations are inconsistent.^{1,2,4–7} (1) first-generation cephalosporin for 24 hours or less,^{2,4,7} (2) first- or second-generation cephalosporins or penicillins with beta-lactams (BLs) for single dose or within 72 hours,⁶ (3) first- or second-generation cephalosporins in living donor KTRs and beta-lactam/beta-lactamase inhibitor combinations (BL/BLIs) in deceased donor KTRs for single dose or within 72 hours,¹ (4) using single-dose, rather than multi-dose.⁵ Owing to the complexity of host, recipient and surgery associated factors, especially the challenge caused by multi-drug-resistant organisms, it was recommended to appropriately upgrade and strengthen PAP protocols in KT in current guidelines,^{1,2} while the timing and the specific recommendation is unknown because robust evidence is lacking. Therefore, it was difficult to determine dosing regimens in clinical practice especially in complicated situations. Some studies showed there were inconsistent PAP strategies in different hospitals, such as a single dose of first-generation cephalosporin, a third-generation cephalosporin for 7 days, duration, ampicillin-sulbactam for 24–48 hours postoperatively, or multi-drug regimens of a carbapenem combined with teicoplanin and echinocandins for up to 7–14 days, etc.^{8–11}

Nationwide data regarding the current practices of PAP in KT is lacking in China. Therefore, our main aim was to assess the routine protocols and analyze main clinical considerations in Chinese kidney transplant centers.

Materials and Methods

Study Design

An online survey was conducted to collect data about clinical practice for PAP in KT on behalf of the National Alliance of Transplant Pharmacists.

Questionnaire Design

The questionnaire was designed by the research team, who are all members of the standing committee in the alliance, which contained three primary sections and 40 questions. The first section gathered the basic information of the respondents and their hospitals. Section 2 was designed to gather information on routine PAP strategies in living-donor and deceased-donor KT, including the names, doses, frequencies, and duration of prophylactic antimicrobial agents. Section 3 requested the respondents to identify the factors associated with adjusted PAP strategies in their hospitals. This section involved 28 independent variables, which were divided into 3 sets (the host factors, recipient factors and surgical factors) based on guidelines.^{1,2} Moreover, first-line medication for pneumocystis carinii pneumonia (PCP) and adjusted protocols for people who had a history of sulfonamide allergy were collected. Most questions were in multiple-choice format, which allowed the respondents to choose and a free-text response was provided. Skip logic was utilized to minimize survey fatigue and reduce completion time.

Survey Participants

The participants were the members of the alliance, which was spontaneously established by Chinese transplant pharmacists in December 2022. Until May 2023, a total of 76 transplant pharmacists from 57 hospitals in 23 provinces or province-level municipalities in China were involved. All members were required to provide pharmaceutical care for transplant recipients for more than one year. In the alliance, most members were kidney transplant pharmacists (58/76) who were from 50 hospitals.

Survey Implementation

The online questionnaire (ID: 211761213) was created via Wen Juan Xing (<http://www.wjx.cn>), a widely used online survey platform in China. The picture with the link and two-dimensional code for the survey was sent to the WeChat group, which had been built since the alliance was established. In addition, the main purpose of this survey was clearly introduced, and related questions were answered. The survey was carried out over 38 days, and three reminder messages

were sent throughout the study period. The anonymity of the respondents and the confidentiality of their responses were guaranteed.

Statistical Analyses

Data was exported from Wen Juan Xing (<http://www.wjx.cn>) into a Microsoft Excel file. All categorical variables were presented as numbers and/or percentages. Free-text responses were grouped based on the contents. If two or more pharmacists in the same hospital participated in the survey, the data submitted by transplant pharmacists with more experience was adopted. Data was analyzed with descriptive statistics and chi-square tests. Statistical analysis was performed using SAS software version 9.4 (SAS Institute, Cary, North Carolina). A P value <0.05 was considered statistically significant.

Results

In total, data from 23 hospitals were obtained, with the overall response rate 46.0% (23 of the 50 hospitals in the alliance). Questions in Section 1 and 3 were completed by all the respondents. Two respondents did not describe the empirical PAP protocols in living-donor KTRs as only deceased-donor KT was performed in their hospitals. All other analyses were unaffected; therefore, they were excluded only from this question in Section 2.

Descriptive Characteristics

The characteristics of the respondents and responding hospitals are shown in Table 1. Twenty-one of the respondents (91.3%) had more than 5 years of KT pharmaceutical care practice. The hospitals were located in both northern (10 of 23 [43.5%]) and southern regions (13 of 23 [56.5%]), and they were all teaching hospitals with Grade IIIA. In fourteen hospitals (60.9%), 100 or more KTs were performed every year.

Routine PAP Protocols in Responding Hospitals

The names, doses, frequencies, and duration of prophylactic antimicrobial agents in living-donor and deceased-donor KT were collected. Detailed information is shown in Table 2.

There were six kinds of protocols in living-donor KT. A single antibacterial agent as monotherapy was used by 80.9% (17/21) of responding hospitals and BL/BLIs were most often selected (10/21 [47.6%]). Ten kinds of protocols were involved in deceased-donor KT. Combination therapy was used in 69.6% (16/23) of responding hospitals, among which

Table 1 Characteristics of the Respondents and Responding Hospitals (N = 23)

Characteristic		N (%)
Respondents	Professional title	
	Pharmacist	1 (4.35)
	Pharmacist-in-charge	11 (47.8)
	Associate professor of pharmacy	10 (43.5)
	Professor of pharmacy	1 (4.35)
	Years of working	
	≥ 10	13 (56.5)
	5~9	8 (34.8)
	1~4	2 (8.7)
	Full-time clinical pharmacist	
	Yes	21 (91.3)
	No	2 (8.7)
	Experience as a transplant pharmacist (years)	
	≥ 10	2 (8.7)
	5~9	13 (56.5)
	1~4	8 (34.8)

(Continued)

Table 1 (Continued).

Characteristic	N (%)
Responding Hospitals	
Geographic regions	
North	10 (43.5)
South	13 (56.5)
Classification of Chinese hospitals	
Grade IIIA hospital	23 (100)
Other	0 (0)
Teaching hospital	
Yes	23 (100)
No	0 (0)
Number of beds in total	
≥2000	15 (65.2)
1000–1999	5 (21.7)
<1000	3 (13.1)
Number of beds in kidney transplantation ward	
≥100	2 (8.7)
50–99	3 (13.0)
<50	18 (78.3)
40–49	2 (8.7)
30–39	6 (26.1)
20–29	5 (21.7)
10–19	2 (8.7)
<10	3 (13.1)
Annual count of kidney transplant procedures	
≥500	2 (8.7)
400–499	0 (0)
300–399	2 (8.7)
200–299	4 (17.4)
100–199	6 (26.1)
<100	9 (39.1)
50–99	5 (21.7)
0–49	4 (17.4)
AMS in hospital	
Yes	21 (91.3)
No	2 (8.7)
AMS in the transplant ward	
Yes	10 (43.5)
No	13 (56.5)

Abbreviation: AMS, antimicrobial stewardship.

dual-combination therapy (11/23 [47.8%]) was comprised of one antibacterial agent and one antifungal agent (echinocandins), while triple combination therapy (5/23 [21.7%]) was comprised of two antibacterial agents with different antibacterial spectra and one antifungal agent (echinocandins).

Fifteen agents were collected (10 in living-donor KT and 13 in deceased-donor KT, with 8 duplicate agents). Seven agents were prescribed with same doses and frequencies among different hospitals: cefuroxime 0.75 g q8h; cefoxitin 2 g q8h; ceftizoxime 2 g q12h; mezlocillin/sulbactam 3.75 g q8h; imipenem/cilastatin 0.5 g q6h; linezolid 0.6 g q12h; teicoplanin 400 mg q12h for the first 3 doses, then 400 mg once daily. The usage for the other eight agents differed among hospitals whether in living-donor or deceased-donor KT: cefazolin 2 g q12h or 2g q8h; cefotaxime 1 g q8h or 2 g q12h; piperacillin/tazobactam 2.25 g q8h, 4.5 g q12h or 4.5 g q8h; cefoperazone/sulbactam 1 g q12h, 1.5g q12h, 2 g q12h, 3 g q12h or 3g q8h; meropenem 0.5 g q12h, 0.5 g q8h or 1 g q8h; daptomycin 0.5g once every other day or 0.35 g once daily; caspofungin 50 mg once daily, or first dose 70 mg, then 50 mg once daily), micafungin 50 mg once daily or 100 mg once daily.

Table 2 The Routine PAP Protocols in Responding Hospitals

Prophylactic Antibacterial Agents N (%)			
Living-donor kidney transplant (N=21)		Deceased-donor kidney transplant (N=23)	
Monotherapy	17 (80.9)	Monotherapy	7 (30.4)
First/second-generation cephalosporins ^a	4 (19.1)	Cephamycins ^b	1 (4.3)
Cephamycins ^b	1 (4.8)	BL/BLIs ^d	6 (26.1)
Third-generation cephalosporins ^c	2 (9.5)		
BL/BLIs ^d	10 (47.6)		
Combination therapy	4 (19.1)	Combination therapy	16 (69.6)
Dual combinations	4 (19.1)	Dual combinations	11 (47.8)
Third-generation cephalosporins ^c + echinocandins ^e	1 (4.8)	First-generation cephalosporins ^a + echinocandins ^e	1 (4.3)
BL/BLIs ^d + echinocandins ^e	3 (14.3)	Third-generation cephalosporins ^c + echinocandins ^e	2 (8.7)
		BL/BLIs ^d + echinocandins ^e	6 (26.1)
		Carbapenems ^f + echinocandins ^e	2 (8.7)
Triple combinations	0	Triple combinations	5 (21.7)
		[BL/BLIs ^d or Carbapenems] ± daptomycin + echinocandins ^e	1 (4.3)
		Carbapenems ^f + daptomycin + echinocandins ^e	1 (4.3)
		Carbapenems ^f + teicoplanin + echinocandins ^e	1 (4.3)
		Carbapenems ^f + linezolid + echinocandins ^e	2 (8.7)
Duration (days) N (%)			
Living-donor kidney transplant (N=16)		Deceased-donor kidney transplant (N=13)	
≤3	6 (37.5)	3	3 (23.1)
5–7	8 (50.0)	7	4 (30.7)
10	2 (12.5)	10	3 (23.1)
		14–15	3 (23.1)

Notes: ^aFirst/second-generation cephalosporins: cefazolin, cefuroxime. ^bCephamycins: cefoxitin. ^cThird-generation cephalosporins: ceftizoxime; cefotaxime. ^dBeta-lactam/beta-lactamase inhibitor combinations (BL/BLIs): mezlocillin/sulbactam, piperacillin/tazobactam, cefoperazone/sulbactam. ^eEchinocandins: caspofungin, micafungin. ^fCarbapenems: meropenem; imipenem/cilastatin.

The duration for PAP also varied widely among different hospitals. In living-donor KT, 37.5% (6/16) of responding hospitals limited the prophylactic duration to 3 days or less, and 50% stopped antimicrobial prophylaxis within 5 to 7 days. In deceased-donor KT, nearly half of the responding hospitals (6/13 [46.2%]) used prophylactic antimicrobial agents for 10 days or more.

Compound sulfamethoxazole was widely used in the prevention of PCP, with the most common single dose “1 tablet” (17/23) and frequencies “once daily” (19/23). The most common duration of PCP prophylaxis was “three to six months” (15/18), and “nine months” or “one year” was also selected (3/18). For people who have a history of sulfonamide allergy, adjusted protocols were “starting with small dose” (10/23), “no prophylactic agents” (7/23), “using second-line agents” (3/23) or “desensitization” (3/23). And second-line agents included “clindamycin”, “clindamycin combined with caspofungin”, “micafungin” or “azithromycin”.

Clinical Considerations Associated with Adjusted Antibiotic Dosing Regimen

Nine host factors, thirteen recipient factors, and six surgical factors were preset as option to investigate which factors were considered when changing empirical PAP protocol. The results are shown in [Figure 1](#).

Among donor-associated factors, “history of infection” and “active infections at the time of procurement” were associated with adjustment in prophylaxis protocol ($P<0.05$), while “abnormal donor kidney conditions”, “local epidemiology” and “intestinal perforation/rupture” were not considered. As for recipient-associated factors, “preoperative infection history” was the only consideration ($P<0.05$) and three other factors were not considered ($P<0.05$), including “malnutrition”, “obesity” and “re-operation at the transplant site”. Among surgical factors, “Contamination at the

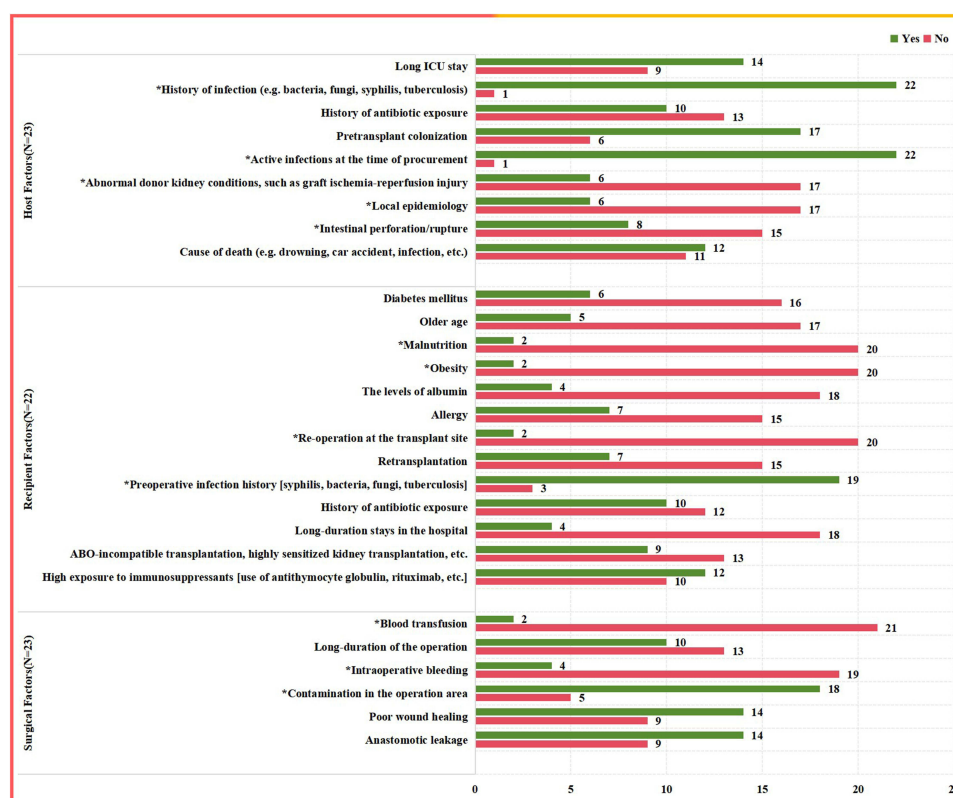


Figure 1 Clinical considerations associated with adjusted antibiotic dosing regimen in responding hospitals, there was statistically significant difference with respect to twelve factors with an asterisk.

operation area” was the only factor associated with PAP change, while “blood transfusion” and “intraoperative bleeding” were not associated with adjustment ($P < 0.05$).

Discussion

In this study, the detailed PAP protocols in KT among 23 Chinese hospitals were revealed. To our knowledge, this is the first nationwide survey on perioperative infection prevention in KT in China.

Routine PAP Strategies in KT

In the present study, we found wide variability in the names, doses, frequencies, and duration of prophylactic antimicrobial agents, which was similar with the results from Europe¹² and South Korea.¹³ As mentioned above, one important explanation was the absence of international consensus on the use of prophylactic antimicrobial agents in KT because of relatively weak evidence.^{12,14} Besides, individualized medication for KTRs was needed because of complex risk factors in clinical practice. Until now, guidance is lacking about when and how to appropriately upgrade and strengthen PAP. Different from the two existing surveys,^{12,14} routine PAP strategies in this study were separately analyzed in living-donor KT and deceased-donor KT based on Chinese experts’ consensus,¹ which was in line with the clinical practice.

Routine PAP Strategies in Living-Donor KT

In the available guidelines, prophylactic use of first- or second-generation cephalosporins for single dose or within 72 hours was the most common recommendation to prevent perioperative infection. In this survey, the guideline adherence rate on selection of antimicrobial agents was 42.9% in living-donor KT, and only 37.5% of the responding hospitals would stop PAP within 72 hours after transplantation.

In living-donor KT, the time frame of evaluation of living donors is relatively non-urgent, and the operation time is controllable, which allows thorough screening and corresponding treatment for both donors and recipients.¹⁵ Liu et al⁸ reported the incidence of perioperative infection was significantly lower in living-donor KTRs than in deceased-donor KTRs (5.69% vs 12.78%). In general, an increased risk of postoperative infections may occur in living-donor KTRs prescribed with rituximab. A study showed even for these high-risk living-donor KTRs, the efficacy of single-dose perioperative antimicrobial therapy (ampicillin/sulbactam 750 mg or cefazolin 500 mg once daily) is acceptable for prophylaxis of infections compared with multiple doses up to 7 days.¹⁶ These results infer that prolonged duration may not be necessary in living-donor KT.

Routine PAP Strategies in Deceased-Donor KT

In contrast to living-donor KT, BL/BLIs were also recommended except for first- or second-generation cephalosporins in current guidelines, with the same duration of prophylactic use. In this survey, 26.1% of the responding hospitals selected recommended antimicrobial agents in the guidelines, only 23.1% of the hospitals would stop PAP within 72 hours and 53.8% stopped PAP within 7 days in deceased-donor KT. Situations for donors are sometimes more complex in deceased-donor KT. Some researchers thought that recommendations in existing guidelines were only suitable for uncomplicated situations,^{8,14} whereas the optimal antibiotic regimen is yet unknown for complex circumstances.

In some studies, deceased donors were the only source of donor type.^{8,17,18} Results from these earlier studies were consistent with recommendation. A randomized, controlled clinical trial showed that the incidences of SSI and urinary tract infection were similar in the single-dose regimen group (n=103) and multi-dose antibiotic regimen group (n=102) selecting cefazolin 2 g or cefotaxime 1 g for prophylaxis, thus single-dose regimen was preferred at least in study population (non-diabetic, non-morbidly obese, adult renal transplant recipients).¹⁷ The conclusion was the same as another retrospective case-control study in 254 deceased donor KTRs between October 2015 and August 2018, and researchers found that single-dose first-generation cephalosporin (cefazolin 2.0 g) can be safe and was associated with a relatively low prevalence of SSIs when compared with the third-generation cephalosporin (ceftriaxone) by same dosage.¹⁸ Similarly, another retrospective research from January 2015 to March 2019 showed that there was no statistically significant difference in the incidence of infection when using different antibiotics [name unknown] during the perioperative period of deceased-donor kidney transplantation (10.47% vs 14.89%, $P=0.374$),⁸ these two agents are located in different grades based on Antibiotics Classification Management Lists in China.

However, donor-derived infections (DDI) gained great concern in recent years, with the increasing challenge of more complications and high mortality by MDROs. Some centers adjusted cephalosporins-based antibiotic prophylaxis to face the increased incidence of infection caused by extended-spectrum beta-lactamase (ESBL)-producing Enterobacteriaceae. Freire et al¹⁹ evaluated the antibiotic prophylaxis in 819 living-donor or deceased-donor KTRs (1:3) from January 2009 and December 2012 and confirmed amikacin prophylaxis was a useful strategy for preventing SSIs. However, eighty-five (36.5%) KTRs using amikacin developed DGF in this study from Brazil, which was the main shortcoming for KTRs. In the same situation, Sanclemente et al²⁰ described that they changed surgical prophylaxis from cefazolin 2 g to ertapenem 1 g in 2014. In this observational study, 223 KTRs were recruited with approximately equal quantities of living-donor and deceased-donor KTRs, and found that a single dose of ertapenem was effective at preventing SSI and the incidence of early infections due to ESBL-producing Enterobacteriaceae was reduced.

In China, deceased donation was the main source and DDI, it was trickier to select prophylactic antibiotics, especially the main pathogen carbapenem-resistant Enterobacteriaceae (CRE) can cause serious adverse events such as graft removal, and recipient death.^{8,14} Although BL/BLIs were recommended for deceased donor KTRs in China,¹ a “one-size-fits-all” approach cannot be implemented in these special populations.²¹ It was advised for transplant centers to optimize their protocol based on the infection and colonization status of recipients and donors, the presence of nosocomial pathogens, and local resistance patterns.¹⁸ However, there are few studies with high-quality evidence, the reporting strategies are yet to be verified; on the other hand, clinician generally fears of the worst-case scenario such as graft loss, which may strongly influence decision-making.^{21,22} Thus, some customized protocols with high-grade antibiotics were established based on their experience in many transplant centers. It is noteworthy that not all deceased-donor KTRs need “full coverage” prophylaxis with long-term, multi-dose regimens to cover Gram-positive,

and Gram-negative organisms and fungus. Due to frequent antibiotic and healthcare system exposures, KTRs are at high risk for antimicrobial resistance and toxicity associated with antibiotics, and limiting antimicrobial duration may mitigate the detrimental effects of antibiotics.²³

Prophylactic Use of Antifungal Agents in KT

In the present study, echinocandins were used for living-donor KTRs in 19.1% of respondent centers, and for deceased-donor KTRs, the proportion was up to 69.6%. The results were similar to one research in Korea, in their study, triazoles ± amphotericin B was used to prevent fungal infections for KTRs in 42% of centers (13/31).¹³ According to the American Society of Transplantation Infectious Disease Community of Practice, the incidence of *Candida* infection was 25.7% in KTRs, but routine *Candida* prophylaxis is not recommended because the incidence of invasive candidiasis is too low for this population.²⁴ In China, targeted use of agents to prevent fungal infection is not necessary for all KTRs, but routinely treated with antifungal agents was recommended for deceased-donor KTRs.²⁵ There was no recommendation about the specific agent. Given that the targeted approach is preferred to universal prophylaxis, it is essential to identify high-risk patients who need antifungal prophylaxis. Therefore, we advised selecting the antimicrobial agents according to the current guideline in all living-donor KTRs and part of deceased-donor KTRs without known risk factors for SSI, the upgraded selection of prophylactic antibiotics was only used for deceased-donor KTRs with known risk factors.

Compound sulfamethoxazole is the first-line agent to prevent PCP in clinical practice, which is consistent with the guideline.²⁶ Second-line agents are dapsone, atovaquone, pentamidine, and clindamycin plus pyrimethamine. However, there is often no choice for people with a history of sulfonamide allergy, because of cross-reactivity between the compound sulfamethoxazole and dapsone, and the poor availability of other drugs in China. Leoung GS reported two methods (dose escalation and direct rechallenge) for compound sulfamethoxazole reintroduction, and it may be feasible for some patients other than severe drug reactions resulting from compound sulfamethoxazole.²⁷ Some patients may have to choose no prophylaxis, but it is associated with a higher incidence of PCP in the first 180 days after kidney transplantation.²⁸ Other prophylactic protocols such as clindamycin plus caspofungin or not, micafungin, or azithromycin are reported in few studies. These protocols are not recommended in the guidelines and are only used in three responding hospitals.

Factors That May Influence Decisions on Prophylaxis Protocol

It was advised that the risk factors associated with SSIs should be fully screened before prophylactic antibiotics are selected in kidney transplantation, especially for deceased-donor KTRs. Freire et al identified six risk factors for post-kidney transplantation SSIs: deceased donor, high body mass index, diabetes mellitus, thin ureters at kidney transplantation, blood transfusion at the transplantation procedure, and anti-thymocyte globulin induction therapy by multivariate analysis.¹⁹ However, Ostaszewska et al also determined risk factors for SSIs by multivariable logistic regression and showed that statistically significant differences were present between reoperated and non-reoperated patients, thus reoperation was identified as an individual risk factor for SSI after kidney transplantation.¹⁸ Many kinds of other risk factors were mentioned in different studies, but it is unknown how these factors are considered in prophylaxis protocol adjustment in current practices.

In the present study, we evaluated 9 host factors, 13 recipient factors, and 6 surgical factors according to existing guidelines and research. In responding hospitals, we found that twelve factors existed statistically significant differences between selecting the “yes” group and selecting the “no” group. Four factors played a role in protocol adjustment, including “history of infection” and “active infections at the time of procurement” for donors, “preoperative infection history” for recipients, and “Contamination in the operation area”. Conversely, other eight factors were excluded when making medication decisions, including “abnormal donor kidney conditions”, “local epidemiology” and “intestinal perforation/rupture” for donors, “malnutrition”, “obesity” and “reoperation at the transplant site” for recipients, and “blood transfusion” and “intraoperative bleeding” for surgical factors. Similar studies on medication decision analysis have not been found. The same as that of non-transplanted surgical patients, appropriate antimicrobial prophylaxis was one of the infection control measures, and SSIs cannot be prevented only by the administration of a broader spectrum or

longer duration of peri-operative prophylactic antibiotics. Although consistent with the basic principles of surgical antibiotic prophylaxis, there is no doubt that these results need to be confirmed.

Limitations

There were several limitations in our study. First, the sample size is relatively small. By November 15, 2023, there were 149 medical institutions qualified for kidney transplantation in China, and they were mainly distributed in Guangdong (18), Beijing (13), Shandong (10), Hunan (10), Zhejiang (9) and Shanghai (8).²⁹ As far as we know, not all these hospitals routinely implement kidney transplantation, and the exact number was difficult to obtain and we were unable to contact all institutions. Given that responding hospitals could represent most of the geographic areas in China, the bias may have been minimized. Second, our survey was distributed to clinical pharmacists in the alliance, so the results were inevitably influenced by subjective factors. Based on the responsibility for pharmacists in antimicrobial stewardship in China, we believed these pharmacists were familiar enough with current practices for perioperative antibiotic prophylaxis in their hospitals, meanwhile, they were advised to discuss with doctors, when necessary, to verify the actual situation. Taking this into consideration, survey results would be close to the actual situation. Lastly, further research is needed to determine whether reporting risk factors in the present study should be considered to adjust the routine perioperative antibiotic selection. To the best of our knowledge, this is the only study to describe the current practices in perioperative antibiotic prophylaxis for KTRs in China, and the results can be hopeful for kidney centers when establishing or adjusting their protocols.

Conclusions

Specific antibiotic regimens and factors influencing antibiotic-prescribing decisions vary widely across transplant centers in China. Stratified recommendation is essential.

Abbreviations

PAP, perioperative antibiotic prophylaxis; KT, kidney transplantation; SSI, surgical site infection; KTRs, kidney transplant recipients; BLs, beta-lactams; BL/BLIs, beta-lactam/beta-lactamase inhibitor combinations; PCP, pneumocystis carinii pneumonia; DDI, donor-derived infections; ESBL, extended-spectrum beta-lactamase; CRE, carbapenem-resistant Enterobacteriaceae.

Ethics Approval

This study was approved by the institutional ethical committee of Beijing Friendship Hospital. The questionnaires were completed by clinical pharmacists based on their work experience, which did not affect the diagnosis and treatment for KTRs. Before participating in the survey, respondents were requested to read the full information and carefully decide. If a respondent entered the online survey site, it was assumed that they agreed to participate in the survey. Ethics approval was obtained for the waiver of a signature on the consent form.

Acknowledgments

We thank all the pharmacists who took part in the survey.

Funding

This study did not receive any specific grant from funding agencies.

Disclosure

The authors report no conflicts of interest in this work.

References

1. Branch of Organ Transplant Physicians of Chinese Medical Doctor Association, Branch of Organ Transplantation of Chinese Medical Association. Chinese experts consensus on the management of surgical site infection in solid organ transplantation (2022 edition). *Organ Transplant*. 2023;1:11–23,48. doi:10.3969/j.issn.1674-7445.2023.01.002
2. Abbo LM, Grossi PA. AST ID community of practice. Surgical site infections: guidelines from the American Society of Transplantation Infectious Diseases Community of Practice. *Clin Transplant*. 2019;9:e13589. doi:10.1111/ctr.13589
3. Carugati M, Arif S, Sudan DL, et al. Epidemiology of surgical site infections after solid organ transplants in the period 2015–2019: a single-center retrospective cohort study. *Am J Transplant*. 2022;12:3021–3030. doi:10.1111/ajt.17189
4. Del Toro López MD, Arias Díaz J, Balibrea JM, et al. Executive summary of the consensus document of the Spanish Society of Infectious Diseases and Clinical Microbiology (SEIMC) and of the Spanish Association of Surgeons (AEC) in antibiotic prophylaxis in surgery. *Enfermedades Infecciosas y Microbiología Clínica*. 2021;1:29–40. doi:10.1016/j.eimc.2020.02.017
5. EAU Guidelines. EAU guidelines on renal transplantation. [EB/OL]. Available from: <https://uroweb.org/guidelines/renal-transplantation/chapter/citation-information>. Accessed December 4, 2024.
6. Yamamoto S, Shigemura K, Kiyota H, et al. Essential Japanese guidelines for the prevention of perioperative infections in the urological field: 2015 edition. *Int J Urol*. 2016;10:814–824. doi:10.1111/iju.13161
7. Bratzler DW, Dellinger EP, Olsen KM, et al. Clinical practice guidelines for antimicrobial prophylaxis in surgery. *Am J Health Syst Pharm*. 2013;3:195–283. doi:10.2146/ajhp120568
8. Liu -Y-Y, Yue H-J, Chen C, et al. Analysis of perioperative infection risk factors and rationality of prophylactic antibiotics in renal transplant recipients. *J Med Postgrad*. 2020;11:1181–1186. doi:10.16571/j.cnki.1008-8199.2020.11.012
9. Tan L, Xie X, Peng L, et al. Distribution and therapy strategy of culture microorganisms of kidney perfusion fluid. *Chin J Organ Transplant*. 2018;3:135–139. doi:10.3760/cma.j.issn.0254-1785.2018.03.002
10. Guo C, Liu J, Ji J, et al. Analysis and clinical significance of culture results of donor renal perfusate. *Chin J Organ Transplant*. 2018;10:602–605. doi:10.3760/cma.j.issn.0254-1785.2018.10.006
11. Graziano E, Peghin M, Grossi PA. Perioperative antibiotic stewardship in the organ transplant setting. *Transplant Infect Dis*. 2022;5:e13895. doi:10.1111/tid.13895
12. Bachmann F, Adam T, Friedersdorff F, et al. Perioperative antibiotic prophylaxis in renal transplantation: a single-center comparison between two regimens and a brief survey among the Eurotransplant renal transplantation centers. *World J Urol*. 2018;5:957–967. doi:10.1007/s00345-018-2440-2
13. Huh K, Jeong SJ, Kim YJ, et al. Nationwide survey of infection prevention protocols in solid organ transplantation in South Korea. *Korean J Transplant*. 2022;3:212–220. doi:10.4285/kjt.22.0036
14. Anesi JA, Blumberg EA, Abbo LM. Perioperative antibiotic prophylaxis to prevent surgical site infections in solid organ transplantation. *Transplantation*. 2018;1:21–34. doi:10.1097/tp.0000000000001848
15. Zeng X, Xia Q, Li H, et al. Prognosis and risk analysis of living-donor kidney transplantation recipients. *Pract J Organ Transplant*. 2021;6:491–495. doi:10.3969/j.issn.2095-5332.2021.06.016
16. Nishimura S, Wada K, Araki M, et al. Use of single-dose perioperative antimicrobial therapy is acceptable in recipients of living-donor renal transplants in the rituximab era. *J Infect Chemother*. 2019;4:247–252. doi:10.1016/j.jiac.2018.11.013
17. Orlando G, Manzia TM, Sorge R, et al. One-shot versus multidose perioperative antibiotic prophylaxis after kidney transplantation: a randomized, controlled clinical trial. *Surgery*. 2015;1:104–110. doi:10.1016/j.surg.2014.06.007
18. Ostaszewska A, Domagała P, Zawistowski M, Karpeta E, Wszola M. Single-center experience with perioperative antibiotic prophylaxis and surgical site infections in kidney transplant recipients. *BMC Infect Dis*. 2022;1:199. doi:10.1186/s12879-022-07182-z
19. Freire MP, Antonopoulos IM, Piovesan AC, et al. Amikacin prophylaxis and risk factors for surgical site infection after kidney transplantation. *Transplantation*. 2015;3:521–527. doi:10.1097/tp.0000000000000381
20. Sanclemente G, Bodro M, Cervera C, et al. Perioperative prophylaxis with ertapenem reduced infections caused by extended-spectrum betalactamase-producing Enterobacteriaceae after kidney transplantation. *BMC Nephrol*. 2019;1:274. doi:10.1186/s12882-019-1461-4
21. So M, Hand J, Forrest G, et al. White paper on antimicrobial stewardship in solid organ transplant recipients. *Am J Transplant*. 2022;1:96–112. doi:10.1111/ajt.16743
22. Porto APM, Tavares BDM, de Assis DB, et al. Brazilian perspective: antimicrobial stewardship in solid organ transplant. *Transplant Infect Dis*. 2022;5:e13874. doi:10.1111/tid.13874
23. Imly H, Spellberg B. Shorter is better: the case for short antibiotic courses for common infections in solid organ transplant recipients. *Transplant Infect Dis*. 2022;5:e13896. doi:10.1111/tid.13896
24. Aslam S, Rotstein C. Candida infections in solid organ transplantation: guidelines from the American Society of Transplantation Infectious Diseases Community of Practice. *Clin Transplant*. 2019;9:e13623. doi:10.1111/ctr.13623
25. Chinese Society of Organ Transplantation, China Medical Association. Technical specifications for clinical diagnosis and treatment of invasive fungal infection for solid organ transplantation recipients (2019 edition). *Organ Transplant*. 2019;3:227–236. doi:10.3969/j.issn.1674-7445.2019.03.002
26. Fishman JA, Gans H. Pneumocystis jirovecii in solid organ transplantation: guidelines from the American Society of Transplantation Infectious Diseases Community of Practice. *Clin Transplant*. 2019;9:e13587. doi:10.1111/ctr.13587
27. Leoung GS, Stanford JF, Giordano MF, et al. Trimethoprim-sulfamethoxazole (TMP-SMZ) dose escalation versus direct rechallenge for Pneumocystis Carinii pneumonia prophylaxis in human immunodeficiency virus-infected patients with previous adverse reaction to TMP-SMZ. *J Infect Dis*. 2001;8:992–997. doi:10.1086/323353
28. Chen RY, Li DW, Wang JY, et al. Prophylactic effect of low-dose trimethoprim-sulfamethoxazole for Pneumocystis jirovecii pneumonia in adult recipients of kidney transplantation: a real-world data study. *Int J Infect Dis*. 2022;125:209–215. doi:10.1016/j.ijid.2022.10.004
29. National Health Commission of the People's Republic of China. List of medical institutions qualified to carry out organ transplants. Available from: <http://www.nhc.gov.cn/wjw/qgyzjg/202010/452dcb0bb3604f86b10de4d0d5a5a8ed.shtml>. Accessed December 4, 2024.

Infection and Drug Resistance

Dovepress

Publish your work in this journal

Infection and Drug Resistance is an international, peer-reviewed open-access journal that focuses on the optimal treatment of infection (bacterial, fungal and viral) and the development and institution of preventive strategies to minimize the development and spread of resistance. The journal is specifically concerned with the epidemiology of antibiotic resistance and the mechanisms of resistance development and diffusion in both hospitals and the community. The manuscript management system is completely online and includes a very quick and fair peer-review system, which is all easy to use. Visit <http://www.dovepress.com/testimonials.php> to read real quotes from published authors.

Submit your manuscript here: <https://www.dovepress.com/infection-and-drug-resistance-journal>