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Oral/oesophageal candidiasis is a risk factor for severe infection after kidney transplantation

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Abstract

Aim: Bacterial and fungal infections are serious, life-threatening conditions after kidney transplantation. The development of oral/oesophageal candidiasis after kidney transplantation is not a reported risk factor for subsequent severe infection. This study was performed to investigate the relationship between oral/oesophageal candidiasis after kidney transplantation and the development of subsequent infection requiring hospitalization.

Methods: This retrospective study included 522 consecutive patients who underwent kidney transplantation at Japanese Red Cross Aichi Medical Center Nagoya Daini Hospital from 1 January 2010 to 1 February 2019. Ninety-five percentage of patients were living donor transplant recipients. Visual examination was performed to detect oral candidiasis, beginning immediately after kidney transplantation; upper gastrointestinal endoscopy was performed 8–10 months after kidney transplantation. Twenty-five patients developed candidiasis (Candida-onset group) and 497 did not (non-Candida-onset group). The follow-up periods were 67 (37–86) months in the Candida-onset group and 55 (34–89) months in the non-Candida-onset group. Severe infection was defined as bacterial or fungal infection requiring hospitalization; viral infections were excluded.

Results: Severe infection developed in 9/25 (36%) patients in the Candida-onset group and in 77/497 (15%) patients in the non-Candida-onset group ($p = .006$). Binomial logistic analysis revealed that Candida infection (odds ratio [OR] 2.53, 95% confidence interval [CI] 1.06–6.06; $p = .037$) and use of rituximab (OR 1.81, 95% CI 1.12–2.93; $p = .016$) were significant predictors of subsequent severe infection.

Conclusion: Oral/oesophageal candidiasis is a risk factor for severe infection after kidney transplantation and suggests an over-immunosuppressive state, which should prompt evaluation of immunosuppression.

KEYWORDS
immunosuppression, kidney transplantation, oesophageal diseases, oral candidiasis, rituximab

SUMMARY AT A GLANCE

This paper concludes that oral/oesophageal candidiasis is a risk factor for severe infection following kidney transplantation. The authors suggest that the presence of oral/oesophageal candidiasis indicates an over-immunosuppressed state, which should prompt a review of immunosuppression.

1 | INTRODUCTION

Kidney transplantation is the only radical treatment for patients with end-stage kidney disease and has a better prognosis, compared with dialysis therapy. The number of kidney transplant patients in Japan is increasing yearly, and management of complications after kidney transplantation is extremely important. Bacterial and fungal infections are serious complications of kidney transplantation that can affect the function of the transplanted kidney and may be life-threatening. Various risk factors for post-kidney transplantation infection have been reported, including immunosuppressive drug use, older recipient age, rituximab use, and prolonged haemodialysis before transplantation.[1–3] However, there are no reports regarding whether oral/oesophageal candidiasis is a risk factor for severe bacterial or fungal infection after kidney transplantation. Oral/oesophageal candidiasis may indicate over-immunosuppression. Understanding the association between the onset of oral/oesophageal candidiasis after kidney transplantation and subsequent severe bacterial or fungal infection may allow prevention of bacterial and fungal infections and correction of over-immunosuppression. The purpose of this study was to evaluate the association between the onset of oral/oesophageal candidiasis after kidney transplantation and subsequent development of severe bacterial and fungal infections.

2 | PATIENTS AND METHODS

2.1 | Study design

In total, 959 patients underwent kidney transplantation at the Japanese Red Cross Aichi Medical Center Nagoya Daini Hospital from 1 January 2010 to 1 February 2019. Exclusion criteria included age under 20 years ($n = 42$), presence of oral/oesophageal Candida before transplantation ($n = 2$), second transplantation cases ($n = 28$), use of immunosuppressive drugs before transplantation ($n = 72$), and transfer to another hospital during the observation period ($n = 293$). The remaining 522 consecutive patients were observed retrospectively. Censoring was at the end of the observation period, death, or reintroduction of haemodialysis.

This study was performed in accordance with the Declaration of Helsinki. All patients accepted into this study provided written informed consent for their laboratory results to be reviewed. This clinical study was approved by the Ethics Committee of the Japanese Red Cross Aichi Medical Center Nagoya Daini Hospital (approval number: 1467).

2.2 | Definitions

In this study, severe infection was defined as new-onset bacterial or fungal infection requiring hospitalization; viral infections were excluded. Oral candidiasis was defined as a case diagnosed by visual inspection and treated with amphotericin B syrup. Oesophageal candidiasis was diagnosed by macroscopic findings during upper gastrointestinal endoscopy. Visual examination was performed to detect oral candidiasis beginning immediately after kidney transplantation; upper gastrointestinal endoscopy was performed 8–10 months after kidney transplantation, then every 1–2 years thereafter.

2.3 | Immunosuppression

Standard maintenance immunosuppressants used in blood group-matched transplants included steroids, calcineurin inhibitors (cyclosporine [CsA] or tacrolimus [TAC]), and metabolic antagonists (mycophenolate mofetil [MMF] or everolimus [EVR]). For blood group-incompatible transplantation, in addition to the standard immunosuppressive therapy for blood group-matched transplantation, steroids and MMF were administered orally beginning 2 weeks before surgery. In patients with anti-blood group antibody titres of 1:32 or higher, rituximab 100 mg was administered 2 weeks before surgery and on the day before surgery. Rituximab 100 mg was administered on the day before surgery in patients with blood group antibody titres of 1:16 or lower. For donor-specific antibody-positive cases, in addition to immunosuppressive therapy similar to the therapy used in blood group-incompatible transplantation, rituximab 200 mg was administered 2 weeks before surgery and on the day before surgery. In all cases, steroids (methylprednisolone, 1000 mg intravenously) were administered intraoperatively. Basiliximab was also used in all cases.

2.4 | Target levels of calcineurin inhibitors, MMF, and EVR, and steroid dose

The target levels of immunosuppressive drugs used in our hospital during the study period were as follows. For TAC, the target area under the concentration–time curve during the first 4 h after administration (AUC_{0-4}) was 80 ng · h/ml for the first 3 months, then the maintenance dose was reduced to achieve 50 ng · h/ml. For TAC Extended Release (ER), the target AUC_{0-4} was 250 ng · h/ml, then the maintenance dose was reduced to achieve 200 ng · h/ml. For CsA, the target AUC_{0-4} was 3500 ng · h/ml for the first 3 months, then the maintenance dose was reduced to achieve 2000 ng · h/ml. The MMF

was adjusted to achieve a target AUC_{0-4} of 40–80 μg · h/ml. EVR was adjusted to achieve a trough level of 3–5 ng/ml. When used in combination with EVR, for TACER, the target AUC_{0-4} was 200 ng · h/ml for the first 3 months, then the maintenance dose was reduced to achieve 150 ng · h/ml; for CsA, the target AUC_{0-4} was 3000 ng · h/ml for the first 3 months, then the maintenance dose was reduced to achieve 1500 ng · h/ml.

Prednisolone (PSL) was started at 60 mg/day; it was then reduced to 10 mg/day at 3 weeks after surgery, 7.5 mg/day at 1 month after surgery, 6 mg/day at 2 months after surgery, and to a maintenance dose of 5 mg/day at 3 months after surgery.

2.5 | Measurements

The clinical features and laboratory results of recipients during hospitalization for kidney transplant surgery were considered baseline values. Clinical features examined in this study included age at transplant, age at onset of candidiasis, sex, primary disease leading to kidney failure, type of immunosuppressive drug administered, rituximab use, living/deceased kidney transplant, preemptive kidney transplantation, dialysis period, blood group-compatible/incompatible transplant, number of human leukocyte antigen mismatches, and rejection within 1 year. The following blood test results were evaluated: serum albumin, serum creatinine, estimated glomerular filtration rate (eGFR), haemoglobin A1c (HbA1c), C-reactive protein (CRP), and serum immunoglobulin G (IgG). To evaluate serum creatinine and eGFR, the results on Day 21 after surgery were used. For HbA1c, CRP, and serum IgG, the results during hospitalization for kidney transplantation were used. We also examined IgG and lymphocyte counts at 6 months after kidney transplantation.

2.6 | Outcomes

The primary endpoint was defined as new-onset bacterial or fungal infection requiring hospitalization before 1 September 2020. The rates of kidney graft survival, haemodialysis reintroduction, and mortality in both groups were also examined.

2.7 | Statistical analysis

Data are expressed as numbers with percentages or medians with interquartile ranges (25%–75%). The χ^2 test and Mann–Whitney *U* test were used for comparisons between the two groups. Binomial logistic analysis was performed to evaluate predictors of severe bacterial or fungal infection, and odds ratios (ORs) with 95% confidence intervals (CIs) were calculated. The Kaplan–Meier method was used to calculate the cumulative probability of developing severe bacterial/fungal infection, and the log-rank test was used to compare differences between the two groups. All statistical analyses were performed with IBM SPSS Statistics, version 24. *p* Values <.05 were considered statistically significant.

3 | RESULTS

3.1 | Patient characteristics

Five hundred and twenty-two patients were followed-up and examined through 1 September 2020. In the 522 patients, immunosuppressive therapy was combined PSL, TAC, and MMF in 50%; PSL, TAC, and EVR in 5%; PSL, CsA, and MMF in 34%; and PSL, CsA, and EVR in 11%.

Twenty-five patients developed oral/oesophageal candidiasis after kidney transplantation (Candida-onset group; 2 cases of oral candidiasis and 23 cases of oesophageal candidiasis); the remaining 497 patients did not develop candidiasis (non-Candida-onset group).

In candida-onset group, oral/oesophageal candidiasis occurred 16 (8–37) months after kidney transplantation. One of the 23 patients with oesophageal candidiasis had heartburn, while the remaining 22 were asymptomatic. The remaining 497 cases were in the non-Candida-onset group. The median observation periods from time of kidney transplantation were 67 (37–86) months in the Candida-onset group and 55 (34–89) months in the non-Candida-onset group; this difference was not statistically significant ($p = .82$). There were no differences between the groups in the primary disease that led to end-stage kidney disease. The age at kidney transplantation was significantly older in the Candida-onset group than in the non-Candida-onset group ($p = .01$).

CsA was used significantly more frequently in the Candida-onset group ($n = 18$, 72%) than in the non-Candida-onset group ($n = 213$, 42.9%; $p = .004$). Rituximab was used by a higher proportion of patients in the Candida-onset group than in the non-Candida-onset group ($p = .01$). There were no differences in trough levels at 6 months after transplantation between the Candida-onset group and non-Candida-onset groups: TAC (ng/ml), 6.0 (4.3–6.2) versus 5.2 (4.3–6.0; $p = .47$); CsA (ng/ml), 79 (68–110) versus 86 (61–106; $p = .34$); and MMF (μg/ml), 3.0 (2.0–4.9) versus 3.2 (2.4–4.4; $p = .69$). EVR was used in only one patient in the Candida-onset group; thus, it was not possible to compare trough levels between the groups. The trough level of EVR in the non-Candida-onset group was 4.6 ng/ml (3.5–5.5). There was no difference in MMF dose at 6 months after transplantation between the Candida-onset group and non-Candida-onset groups: MMF (mg/day), 1500 (1000–1500) versus 1500 (1000–1500; $p = .36$). There were no differences in IgG level or lymphocyte count at 6 months after transplantation between the Candida-onset group and non-Candida-onset groups (Table 1).

The rate of rejection within 1 year was 2/25 (8.0%) in the Candida-onset group and 29/497 (5.8%) in the non-Candida-onset group ($p = .65$). In the two cases of rejection within 1 year after kidney transplantation in the Candida-onset group, the trough values at 6 months after kidney transplantation were CsA 162 (ng/ml) + MMF 1.9 (μg/ml) and Tac 4.7 (ng/ml) + MMF 3.9 (μg/ml), respectively. In the non-Candida-onset group of rejection within 1 year after kidney transplantation, the trough values at 6 months after kidney transplantation were Tac (ng/ml), 5.1 (4.5–6.3); CsA (ng/ml), 63 (46–124.3); MMF (μg/ml), 3.2 (2.2–3.7); and EVR (ng/ml), 3.5

TABLE 1 Patient characteristics in the whole study population ($n = 522$)

	Candida-onset group ($n = 25$)	Non-Candida-onset group ($n = 497$)	p value
Age at transplantation (years)	62 (50–66)	52 (42–62)	.01
Age at onset of Candida (years)	62 (54–70)	-	-
Male sex (%)	11 (44)	310 (62.3)	.06
Living donor (%)/deceased donor (%)	24 (96)/1 (4)	470 (94.5)/27 (5.5)	.75
PEKT (%)/HD or PD (%)	9 (36)/16 (64)	199 (40)/298 (60)	.68
Dialysis period (months)	19 (7.2–103)	26 (7–70.5)	.98
Blood group-compatible transplant (%)	12 (48)	324 (65.1)	.08
HLA mismatch	4 (3–5)	4 (3–5)	.82
Rejection within 1 year, total (TCMR/ABMR)	2 (0/2)	29 (18/11)	.65
Serum albumin (mg/dl)	3.81 (3.63–4.07)	3.81 (3.53–4.11)	.90
Serum creatinine (mg/dl)	1.05 (0.92–1.28)	1.26 (1.02–1.55)	.05
eGFR (ml/min/1.73 m^2)	45 (40.8–54)	45.1 (37.3–53.7)	.61
HbA1c (%)	5.5 (5.2–6.1)	5.5 (5.2–5.9)	.66
CRP (mg/dl)	0.2 (0.2–0.42)	0.2 (0.2–0.32)	.46
IgG (mg/dl)	733 (612–851)	720 (586–832)	.77
IgG (mg/dl) at 6 months after transplantation	959 (846–1156)	961 (795-–1108)	.52
Lymphocyte count, /μl at 6 months after transplantation	1160 (830–1530)	1290 (960–1635)	.19
Diagnosis			
DM (%)	8 (32)	143 (29)	.73
CGN (%)	6 (24)	161 (32)	.38
ADPKD (%)	2 (8)	40 (8)	.99
Renal sclerosis (%)	1 (4)	40 (8)	.46
Other (%)	8 (32)	113 (22.7)	.28
Immunosuppression			
TAC/CsA (%)	7 (28)/18 (72)	284 (57.1)/213 (42.9)	.004
MMF/EVR (%)	24 (96)/1 (4)	415 (83.5)/82 (16.5)	.09
Rituximab (%)	14 (56)	158 (31.8)	.01
MMF dose at 6 months	1500 (1000–1500)	1500 (1000–1500)	.36
Trough level			
TAC trough (ng/ml)	6.0 (4.3–6.2)	5.2 (4.3–6.0)	.47
CsA trough (ng/ml)	79 (68–110)	86 (61–106)	.34
MMF trough (μg/ml)	3.0 (2.0–4.9)	3.2 (2.4–4.4)	.69
EVR trough (ng/ml)	-	4.6 (3.5–5.5)	-

Note: Values shown are median (interquartile range) or number (proportion). For continuous variables, the Mann–Whitney U test was performed to assess the significance of inter-group differences. Categorical variables are expressed as percentages and were compared using the χ^2 test.
Abbreviations: ABMR, antibody-mediated rejection; ADPKD, autosomal dominant polycystic kidney disease; CGN, chronic glomerular nephritis; CRP, c-reactive protein; CsA, cyclosporine; DM, diabetes mellitus; eGFR, estimated glomerular filtration rate; EVR, everolimus; HD, haemodialysis; HLA, human leukocyte antigen; MMF, mycophenolate mofetil; PD, peritoneal dialysis; PEKT, preemptive kidney transplantation; TAC, tacrolimus; TCMR, T-cell mediated rejection.

(3.4–4.1). It was difficult to compare the groups because there were only two patients in the Candida-onset group.

3.2 | Outcomes

During the observation period, severe bacterial or fungal infection occurred in 9 of 25 patients (36%) in the Candida-onset group and in 77 of 497 patients (15%) in the non-Candida-onset group. Two patients in the Candida-onset group had severe infections before developing oral/oesophageal candidiasis. The above two patients developed oesophageal candidiasis. No severe infections were found after the onset. The incidence of severe bacterial or fungal infection was significantly higher in the Candida-onset group than in the non-Candida-onset group ($p = .006$; Table 2). The interval from the onset of candidiasis to the diagnosis of a severe infection was 17 (4–50)

TABLE 2 Outcomes

	Candida-onset group	Non-Candida-onset group	*p* value
Severe infection requiring admission (%)	9 (36)	77 (15)	.006
Age at onset of severe infection (years)	64 (46–69)	59 (46–67)	.66
Haemodialysis reintroduction (%)	1 (4)	14 (3)	.72
Kidney graft survival (%)	22 (88)	470 (94.5)	.17
Death (%)	2 (8)	13 (3)	.11
Observation period (months)	67 (37–86)	55 (34–89)	.82
Time to onset of Candida infection (months)	16 (8–37)	-	-
Interval from kidney transplantation to onset of severe infection (months)	52 (20–67)	22 (10–51)	.33

Note: Values shown are median (interquartile range) or number (proportion). For continuous variables, the Mann–Whitney U test was performed to assess the significance of inter-group differences.

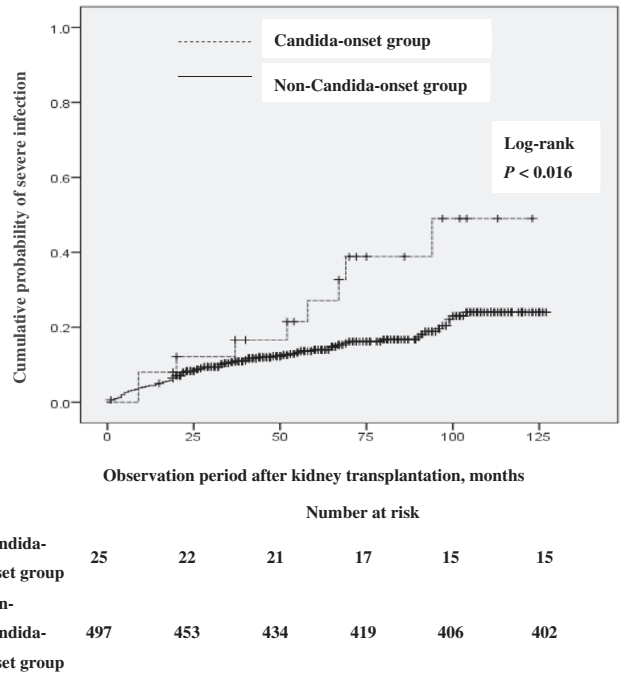

FIGURE 1 The proportion of patients who developed severe infection was significantly higher in the Candida-onset group than in the non-Candida-onset group (9 patients [36%] vs. 77 patients [15%], respectively; $p = .006$). The cumulative prevalence of severe bacterial or fungal infection was significantly higher in the Candida-onset group than in the non-Candida-onset group ($p < .016$)

TABLE 3 Risk factors for severe infection

	Odds ratio	95% CI	*p* value
Age at transplantation	1.01	0.99–1.03	.215
Previous Candida infection	2.53	1.06–6.06	.037
Use of rituximab	1.81	1.12–2.93	.016

Note: Data shown are the odds ratio, 95% CI, and *P* value from binomial logistic regression analysis.
Abbreviation: CI, confidence interval.

months (Supporting Information 2). The log-rank test showed that the cumulative prevalence of severe bacterial or fungal infection was significantly higher in the Candida-onset group than in the non-Candida-onset group ($p < .016$; Figure 1).

The types of severe infections in both groups are summarized in Supporting information 1. Binomial logistic analysis was performed to evaluate age at transplantation, rituximab use, and previous Candida infection (all of which were significantly different between groups in univariate analysis) as predictors of severe bacterial or fungal infection. The results showed that previous Candida infection (OR 2.53, 95% CI 1.06–6.06; $p = .037$) and rituximab use (OR 1.81, 95% CI 1.12–2.93; $p = .016$) were significant risk factors for severe bacterial or fungal infection (Table 3).

Kidney graft survival occurred in 22 (88%) patients in the Candida-onset group and in 470 (94.5%; $p = .17$) patients in the non-Candida-onset group. Reintroduction of haemodialysis was performed in 1 (4%) patient in the Candida-onset group and in 14 (3%; $p = .72$) patients in the non-Candida-onset group. Mortality occurred in 2 (8%) patients in the Candida-onset group and in 13 (3%; $p = .11$) patients in the non-Candida-onset group (Table 2).

4 | DISCUSSION

This retrospective study showed that oral/oesophageal candidiasis after kidney transplantation was significantly associated with subsequent severe bacterial or fungal infection. Oral/oesophageal candidiasis may be a risk factor for subsequent severe bacterial or fungal infection. Rituximab use was also found to increase the risk of severe bacterial or fungal infection.

In this study, viral infections were not considered severe infections because death and kidney graft loss after kidney transplantation are often caused by bacterial infections.[4,5] In contrast, herpesvirus, herpes zoster virus, and cytomegalovirus are common viral infections after kidney transplantation, but they are rarely life-threatening. In addition, cytomegalovirus infection after kidney transplantation is difficult to evaluate appropriately because

the risk of onset and treatment modifications, such as prophylactic administration of antiviral drugs, depend on the patient's background (e.g., antibody presence or absence in donor and recipient).

In this study, we excluded second kidney transplantation patients because immunosuppressive therapy before kidney transplantation causes reductions in cell-mediated immunity and humoral immunity, which may affect the baseline patient background. Previous reports have suggested that infection is a major factor in graft loss in multiple transplants.[6]

Patients with kidney transplantation are two to three times more likely to develop cancer, compared with the general population,[7] and regular gastrointestinal tract examination after kidney transplantation is important. Oral/oesophageal candidiasis is often found on regular examination after kidney transplantation, although it may be asymptomatic. Previous studies found that kidney transplant recipients had a high prevalence of oral/oesophageal candidiasis.[8] Kidney transplant recipients taking immunosuppressive drugs, individuals with diabetes, HIV patients, stem cell therapy patients, patients taking corticosteroids, and patients with solid tumours have an increased risk of developing candidiasis.[9]

In this study, the Candida-onset group was significantly older at the time of kidney transplantation; however, binomial logistic analysis revealed no significant difference in terms of age at transplantation as a risk factor for severe infections. We presume that this is because the risk of bacterial and fungal infections is more affected by the decline in cell-mediated immunity related to the use of immunosuppressive drugs, rather than by the effects of aging.

Candida infections include superficial candidiasis (e.g., oral/oesophageal candidiasis, vulvovaginitis, and balanitis) and invasive candidiasis (e.g., candidemia and invasive candidiasis). Superficial candidiasis is controlled by cell-mediated immunity, whereas invasive candidiasis is controlled by neutrophils.[10,11] Invasive candidiasis is less likely to occur after kidney transplantation because neutrophil function remains almost unchanged; however, oral/oesophageal candidiasis, which is a superficial candidiasis, is more likely to occur.[10,11]

The prevalence of oral candidiasis was not high in this study. At our hospital, we do not perform candidiasis prophylaxis early after transplantation. Previous reports have indicated that prophylactic administration of antifungal drugs is non-inferior with respect to the development of oral candidiasis.[12] However, it is possible that over-immunosuppressive conditions may be overlooked in facilities where antifungal drugs are administered prophylactically after kidney transplantation.

Diabetes is also a risk factor for the development of oral/oesophageal candidiasis and other infectious diseases in general.[13] However, in this clinical study, there were no significant differences in the rates of diabetic nephropathy or HbA1c levels between the two groups.

The incidence of candidiasis was high in patients using CsA. Previous reports have indicated that patients using CsA have a higher level of Candida in saliva, compared with patients using than TAC,[8] which may enhance the onset of candidiasis associated with dry mouth.[14,15] We presume that this led to more frequent candidiasis onset in patients using CsA.

Previous studies have reported that the onset of oral candidiasis is a risk factor for subsequent severe infection in patients on immunosuppressive therapy for anti-neutrophil cytoplasmic antibody-associated vasculitis.[16] To our knowledge, this is the first report of oral/oesophageal candidiasis as a predictor of severe bacterial or fungal infection in kidney transplant recipients taking immunosuppressive drugs. Severe bacterial and fungal infections are serious conditions that affect transplanted kidney function and may be life-threatening in kidney transplant recipients, and the results of this study may help to prevent the onset of severe bacterial or fungal infection. If new-onset oral/oesophageal candidiasis is confirmed after kidney transplantation, the possibility of over-immunosuppression with the current immunosuppressive therapy must be considered. It is necessary to consider optimization by measuring the concentration of immunosuppressive drugs; however, no available test can fully evaluate the degree of immunosuppression achieved with multiple immunosuppressive drugs. Furthermore, it is difficult to completely determine the degree of immunosuppression according to the concentration of immunosuppressive drug alone. Therefore, evaluation of oral/oesophageal candidiasis is another useful tool in understanding the immunosuppressive state. Oral/oesophageal candidiasis could be a good surrogate marker for the overall immunosuppressive status. The median time to onset of candidiasis was 16 months in this study; thus, candidiasis onset may be a sign of over-immunosuppression and risk of bacterial/fungal infection, rather than an early immunosuppressive marker.

The presence of candidiasis may be diagnosed with regular upper gastrointestinal endoscopy, which also enables screening for gastrointestinal cancer after kidney transplantation. Oral candidiasis is often asymptomatic,[17] and endoscopy examination often shows that transplant patients with asymptomatic oral candidiasis have oesophageal candidiasis.[18] Because of the high incidence and mortality of gastric cancer in Japan,[19] regular upper gastrointestinal endoscopy is common. It is important to detect malignant tumours of the gastrointestinal tract; it is also important to perform regular upper gastrointestinal endoscopy that can detect oral/oesophageal candidiasis. However, oral/oesophageal candidiasis as a risk factor for subsequent severe infections may not be suitable for clinical practice in areas where regular gastroscopy is not performed on a regular basis.

There were several limitations in this study. This was a single-centre study, and additional studies are needed to confirm our findings. In addition, it was not possible to show specific measures for the type of immunosuppressive drug used and the extent of dose reduction in recipients who developed oral/oesophageal candidiasis after kidney transplantation. Because this was a retrospective case–control study, rather than an intervention study, it was not possible to investigate the reduction in the incidence of severe bacterial or fungal infection after immunosuppressive drug optimization. Additionally, there might be uncaptured confounders.

In conclusion, oral/oesophageal candidiasis after kidney transplantation is a risk factor for the subsequent development of severe bacterial or fungal infection. The onset of oral/oesophageal candidiasis is a sign of over-immunosuppression, and optimization of immunosuppressive medications is recommended.

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CONFLICT OF INTEREST

The authors declare no conflicts of interest.

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SUPPORTING INFORMATION

Additional supporting information may be found in the online version of the article at the publisher's website.

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