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Infectious disease events in people with HIV receiving kidney transplantation: Analysis of the Swiss HIV Cohort Study and the Swiss Transplant Cohort Study

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Abstract

Background Since the implementation of universal antiretroviral therapy, kidney transplantation (K-Tx) has become a valuable option for treatment of end-stage kidney disease for people with HIV (PWH) with similar patient and graft survival as compared to HIV-uninfected patients. Little is known about the hazards and manifestations of infectious disease (ID) events occurring in kidney transplant recipients with HIV.

Methods Using linked information collected in the Swiss HIV Cohort Study (SHCS) and the Swiss Transplant Cohort Study (STCS), we described in-depth demographical and clinical characteristics of PWH who received a K-Tx since 2008. Further, we performed recurrent time to event analyses to understand whether HIV was an independent risk factor for ID events.

Results Overall, 24 PWH with 57 ID events were included in this study (100% match of SHCS to STCS). Of these, 17 (70.8%) patients had at least one ID event: 22 (38.6%) viral (HIV not counted), 18 (31.6%) bacterial, one (1.8%) fungal and 16 (28.1%) probable infections. Most ID events affected the respiratory tract (25, 37.3%) or the urinary tract (13, 19.4%). Pathogen types and infection sites were similar in PWH and a matched control group of HIV-uninfected patients. HIV was not an independent risk factor for ID events (adjusted hazard ratio 0.94, $p = 0.9$).

Conclusion By linking data from two large national Swiss cohorts, we provided in-depth information on ID events in PWH receiving a K-Tx in Switzerland. HIV infection was not associated with an increased hazard for ID events after K-Tx.

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Summary
In a matched analysis based on longitudinal data from the Swiss HIV and Transplant Cohort Studies including all people with HIV who received a kidney transplantation, HIV was not an independent risk factor for infectious disease events post-transplant.

Keywords Kidney transplantation, HIV, Infectious disease events

Introduction

Solid organ transplant (SOT) recipients are at increased risk to experience life-threatening infectious disease (ID) events post-transplant [1], due to the long-term immunosuppressive treatment. Van Delden et al. [2] investigated the manifestations and occurrence of ID events in all SOT recipients in Switzerland between 2008 and 2014. In the first year post-transplant, more than half of the 3541 SOT recipients had at least one clinically relevant ID event, highlighting the burden of ID events in post-transplant clinical care. While most of the ID events were attributed to common bacterial infections, opportunistic infections occurred only rarely in the first year post-transplant.

For a long time, an HIV infection was considered a contraindication for receiving a SOT. However, since implementation of universal antiretroviral therapy (ART) and continuous improvement of care for people with HIV (PWH) leading to a recovery of the immune system, transplantation in PWH became a valuable option for treatment of end-stage organ disease. The patient and graft survival was shown to be comparable to people without HIV [3, 4]. For example, in a review and meta-analysis by Zheng et al. [5], 27 studies on kidney transplantation (K-Tx) in PWH were included. Based on these publications, the authors estimated that after 1 year, patient survival was 97% and graft survival 91%. However, infectious complications were observed in 41% of patients in the first year post-transplant, again highlighting the high burden of ID events post-transplant. Studies comparing ID events of kidney transplant recipients with HIV and kidney transplant recipients without HIV are scarce. Ailioaie et al. reported ID events of kidney transplant recipients with HIV and compared these with a matched control group of HIV-negative kidney transplant recipients [6]. Limitations of their study were the monocentric and retrospective design. Details on manifestations of ID events in kidney transplant recipients with HIV are currently lacking, such as risk factors for ID events and detailed description of causative pathogens and patient characteristics.

In this study, we linked data collected in two representative nation-wide cohort studies in Switzerland, the Swiss Transplant Cohort Study (STCS) and the Swiss HIV Cohort Study (SHCS). Our main study hypothesis was that kidney transplant recipients with HIV are more prone to ID events after transplantation as compared to kidney transplant recipients without HIV. Hence, our main aim was to compare the occurrence of ID events with a matched control group of HIV-uninfected kidney transplant recipients. Further, we aimed to provide a comprehensive characterisation of ID events in kidney transplant recipients with HIV including detailed information on HIV-specific parameters, such as ART regimen and viral loads.

Methods

Swiss transplant cohort study (STCS)

The Swiss Transplant Cohort Study (STCS), a multicentric cohort study established in 2008, covers information on more than 93% of all solid organ transplant recipients in Switzerland [7, 8], from all Swiss transplant centres (Basel, Bern, Geneva, St. Gallen, Lausanne, and Zurich). The STCS collects longitudinal information in pre-defined follow-up visits post-transplant, including in-depth information on infectious complications and immunosuppressive treatment. STCS data is collected at local participating transplant clinics by trained physicians and study nurses based on medical records. The data is then transferred to the national STCS database, where data is harmonised, encoded and exported for research purposes (see www.stcs.ch for details). Uniform definitions of ID events are applied in all involved centres [2]. For this study, we included the following ID events: (a) proven bacterial infections (clinically apparent infections combined with detection of the causative bacterium and initiation of targeted antimicrobial treatment); (b) symptomatic viral infections (probable viral infections, proven viral infections and viral syndromes); (c) proven and probable invasive fungal diseases; and (d) probable infections (clinical presentations with suspected infectious aetiology resulting in the initiation of antimicrobial treatment, but no causative pathogen being identified in routine diagnostics). We also performed a subset analysis focusing on potentially opportunistic infections: these encompassed infections due to herpesviruses, polyomaviruses, *Toxoplasma gondii*, *Pneumocystis jirovecii*, yeasts or moulds, and mycobacteria.

Swiss HIV cohort study (SHCS)

The Swiss HIV Cohort Study (SHCS) is a nationwide longitudinal cohort study enrolling adult people with HIV (PWH) living in Switzerland. The cohort study was

established in 1988 and covers approximately 70% of all people ever diagnosed with HIV in Switzerland, with cumulatively more than 21'000 participants [9]. In biannual follow-up visits at participating clinics, in-depth clinical, demographic, lifestyle, and laboratory endpoints are collected by trained personnel. The data is then stored centrally at the datacentre of the SHCS, and monthly data exports of harmonised and encoded data are provided to researchers for pre-defined projects (see www.shcs.ch the details).

Patient selection

All PWH with a K-Tx between 2008 and 2022 registered in the SHCS were identified and linked with the respective study identifier in the STCS, in order to obtain detailed information on both, HIV-related parameters and transplant-related parameters. Linkage was performed using the birthdate, transplantation date and further demographic and clinical variables available in both cohort studies. For unclear cases, the treating physician was consulted, and the original medical chart was revised, leading to an unambiguous link for all cases. All cases with a minimal follow-up of at least 30 days after transplantation were included in the analysis. To understand the impact of an HIV infection on the occurrence of ID events, we matched a comparison group of people without HIV: we first identified all STCS participants who underwent a kidney transplantation at the age of 18 or older, with a follow-up of at least 30 days after transplantation. Further, we removed all PWH from this population (the participants already matched with the SHCS, as well as 4 individuals with HIV but not registered in the SHCS). We then matched a control group with a 1:3 ratio based on age at transplantation, sex, and calendar year of transplantation.

Definitions

Sex was defined as biological sex assigned at birth and categorised as male or female. Ethnicity was grouped into Caucasian, African, or Asian. Age was reported as a continuous variable in Table 1, and was included as a categorical variable (<45, 45–65, >65) in the statistical model (see section Statistical Analysis). The HIV transmission group was defined as the most likely source of HIV transmission (sexual transmission, intravenous drug use, or other) reported by the participant. Follow-up time was defined as the time between transplantation and the last recorded information (follow-up visit) within the STCS. Body mass index (BMI) was defined as kg/m^2 and categorised into <18.5, 18.5–25, and >25. CD4 count was defined as CD4+T cell count in cells/mm^3 blood, with CD4 nadir defined as the minimum of all recorded CD4 counts of a participant. Viral suppression was defined as a documented HIV viral load of less than 400 copies/mL. CMV risk constellation was defined as high risk for the serological constellation of CMV IgG donor+/recipient–, intermediate risk for the serological constellation of CMV IgG donor+/recipient+or donor–/recipient+, and low risk constellation for the serological constellation of CMV IgG donor–/recipient–. Categories of induction immunosuppression were administration of basiliximab, thymoglobulin/anti-thymocyte globulin (ATG), or none. Reason for transplantation was grouped into diabetes mellitus (DM) nephropathy, glomerulonephritis, hypertensive/renovascular, polycystic kidney disease, or other (including HIV nephropathy, congenital, interstitial nephritis) for the statistical analysis. Renal replacement therapy was categorised into hemodialysis, peritoneal dialysis, and no dialysis. Donor type was categorised into living (living related, living unrelated) and deceased (donation after brain death (DBD) and donation after cardiocirculatory death (DCD)).

Statistical analysis

We used R Studio (version 4.3.1) for all analyses and visualisation of the timeline for ID events. The observation time starts at the day of transplantation until the last follow-up information. The matched control group was generated by randomly choosing three patients from the potential control group (i.e., HIV-uninfected, same sex, same transplantation year, difference in age at transplantation being less than 3 years) using the R function *sample*. The rate of ID events in the group of PWH and the matched control group was compared using the rate-ratio test (*rateratio.test*). The distribution of pathogens and infection sites was compared using Fisher's exact test. Further, the Anderson-Gill counting process was used to model the occurrence of multiple ID events over time [10, 11]. We compared whether HIV is an independent risk factor for the occurrence of ID events, after adjusting the model for sex, age, year of transplantation, as well as ethnicity, BMI, type of induction immunosuppressive treatment, reason for transplantation, and donor type.

Results

Study population

We identified 24 PWH who received a K-Tx in Switzerland since 2008 (Table 1), all of whom were included in our study population, i.e., were 18 years or older at the time of transplantation and were followed for at least 30 days after transplantation. Most patients were male (83.3%) and of white ethnicity (54.2%). The median age at transplantation was 48.5 years (IQR=43.8–54.8). The main reasons for transplantation were HIV nephropathy (5, 20.8%) and diabetic nephropathy (5, 20.8%). Basiliximab was the main induction immunosuppression chosen (91.7%), followed by ATG (18.8%). The median CD4

Table 1 Demographic and clinical information about the study population

		People with HIV	Control group
		N **= 24**	***N*** **= 72**
Age at transplantation	median (IQR)	48.5 (43.8–54.8)	49 (43.0–56.0)
Sex	male, n (%)	20 (83.3%)	61 (84.7%)
	female, n (%)	4 (16.7%)	11 (15.3%)
STCS centre	Centre A, n (%)	8 (33.3%)	12 (16.7%)
	Centre B, n (%)	5 (20.8%)	23 (31.9%)
	Centre C, n (%)	4 (16.7%)	10 (13.9%)
	Centre D, n (%)	3 (12.5%)	8 (11.1%)
	Centre E, n (%)	3 (12.5%)	14 (19.4%)
	Centre F, n (%)	1 (4.2%)	5 (6.9%)
Ethnicity	Caucasian, n (%)	13 (54.2%)	62 (86.1%)
	African, n (%)	10 (41.7%)	2 (2.8%)
	Asian, n (%)	1 (4.2%)	7 (9.7%)
HIV transmission risk group	Sexual contacts	17 (70.8%)	-
	Intravenous drug use	6 (24%)	-
	Unknown/Inconclusive	1 (4.2%)	-
Year of transplantation	year, median (IQR)	2016.5 (2015–2018)	2016 (2015–2018)
Follow-up time	years, median (IQR)	5.5 (4.0–7.0)	5.0 (3.0–6.2)
Median BMI at K-Tx	median (IQR)	23.8 (22.1–25.9)	24.7 (22.6–27.9)
Reason for transplantation	Diabetes Mellitus nephropathy, n (%)	5 (20.8%)	13 (18.1%)
	HIV nephropathy, n (%)	5 (20.8%)	0 (0%)
	Hypertensive/ renovascular, n (%)	3 (12.5%)	11 (15.3%)
	Glomerulonephritis, n (%)	3 (12.5%)	17 (23.6%)
	Polycystic kidney disease, n (%)	2 (8.3%)	9 (12.5%)
	Congenital	0 (0%)	3 (4.2%)
	Interstitial nephritis, n (%)	1 (4.2%)	2 (2.8%)
	Other/Unknown, n (%)	5 (20.8%)	17 (23.6%)
Renal replacement therapy	Hemodialysis, n (%)	22 (91.7%)	53 (73.6%)
	Peritoneal dialysis, n (%)	2 (8.3%)	10 (13.9%)
	None, n (%)	0 (0%)	9 (12.5%)
Donor type	DBD, n (%)	17 (70.8%)	38 (52.8%)
	Living related, n (%)	2 (8.3%)	13 (18.1%)
	Living unrelated, n (%)	2 (8.3%)	13 (18.1%)
	DCD, n (%)	3 (12.5%)	8 (11.1%)
CMV risk constellation	High risk (Donor CMV+/Recipient CMV-)	1 (4.2%)	11 (14.9%)
	Intermediate risk (Donor CMV+/Recipient CMV + or Donor CMV-/Recipient CMV+)	20 (83.3%)	49 (66.2%)
	Low risk (Donor CMV-, Recipient CMV-)	3 (12.5%)	14 (18.9%)
Induction immunosuppression	Basiliximab, n (%)	22 (91.7%)	49 (68.1%)
	Thymoglobulin/ATG, n (%)	6 (18.8%)	26 (36.1%)
Maintenance immunosuppression	Glucocorticoid	24 (100%)	71 (98.6%)
	MMF or EC-MPS	23 (95.8%)	72 (100%)
	Tacrolimus-containing regimen	19 (79.2%)	64 (88.9%)
	Cyclosporine A-containing regimen	3 (12.5%)	8 (11.1%)
	mTor inhibitor-containing regimen	1 (4.2%)	0 (0%)
CD4 nadir	Median (IQR)	108 (44–153)	-
CD4 prior to transplantation	Median (IQR)	385 (294–531)	-
HIV viral load prior to transplantation	Suppressed, n (%)	20 (83.3%)	-
	Unknown, n (%)	4 (16.7%)	-

Table 1 (continued)

		People with HIV	Control group
		N = 24	*N* = 72
ART at transplantation	Integrase inhibitors		-
	- Dolutegravir, n (%)	11 (45.8%)	
	- Raltegravir, n (%)	8 (33.3%)	
	Protease inhibitors		-
	- Lopinavir, n (%)	3 (12.5%)	
	- Atazanavir, n (%)	1 (4.2%)	
	- Darunavir, n (%)	1 (4.2%)	
	Non-Nucleoside reverse transcriptase inhibitors		
	- Etravirine, n (%)	3 (12.5%)	
	- Efavirenz, n (%)	2 (8.3%)	
	Nucleoside reverse transcriptase inhibitors		
	- Lamivudine, n (%)	19 (79.2%)	
	- Abacavir, n (%)	13 (54,2%)	
	- Other, n (%)	7 (29.2%)	
	CCR5-antagonist		
	- Maraviroc, n (%)	1 (4.2%)	

STCS: Swiss Transplant Cohort Study, IQR: interquartile range, DBD: donation after brain death, DCD: donation after cardiocirculatory death, ATG: Anti-thymocyte globulin, MMF: Mycophenolate mofetil, EC-MPS: Enteric-coated mycophenolate sodium, ART antiretroviral therapy

cell count prior to transplantation was 385 cells/mm^3 blood (IQR = 294–531) and all participants with an HIV RNA measurement available before transplantation (20, 83.3%) were virally suppressed. Similarly, all participants with HIV RNA measurements available post-transplant were virally suppressed (20, 83.3%), with 8 (33.3%) participants experiencing episodes of viral blips during follow-up. Most participants were on a dolutegravir-based (9, 37.5%) or raltegravir-based (8, 33.3%) antiretroviral therapy at the time of K-Tx, with 6 (25.0%) participants changing treatment within the first-year post-transplant. Strategies for routine anti-infective prophylactic strategies after K-Tx have been reported elsewhere and were not different for PWH [12]. Briefly, all transplant centres prescribed trimethoprim/sulfamethoxazole (80/400 mg) every day for 6 to 12 months, there was no routine antifungal prophylaxis. For CMV prevention, the strategy varied by risk constellation: in high risk constellation, all centres applied a prophylactic strategy with administration of valganciclovir; in intermediate-risk constellation, 4 of 6 centres applied a preemptive approach, whereas 2 of 6 centres applied a prophylactic strategy with administration of valganciclovir, and in low-risk constellation, 5 of 6 centres applied a preemptive approach and 1 of 6 centres a prophylactic approach with administration of valacyclovir The median follow-up duration after transplantation was 5.5 years (range: 129 days to 13.2 years). Two patients died during follow-up, one patient due to severe sepsis due to extended-spectrum beta-lactamase-producing *Escherichia coli*; the other patient due to an unknown reason.

Infectious disease events

Overall, 57 ID events were reported for 17 (70.8%) patients: 22 (38.6%) viral infections (HIV not counted), 18 (31.6%) bacterial, 16 (28.1%) probable infections and one probable fungal infection (see Fig. 1). The time to first ID event was 154 days (IQR = 42–1511 days), and was in most cases a viral infection (8 cases), followed by bacterial infections in 5 cases. Hospitalisation was required for 21 (36.8%) ID events in 9 patients, mainly due to bacterial infections (11 cases). The most common bacterial pathogen was *Escherichia coli* (8, 44.4%), of which 6 events required hospitalisation, see Table 2. The most common viral infection was severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) (7, 31.8%) with 2 hospitalisations, followed by rhinovirus infection (3, 13.6%). Most ID events affected the respiratory tract (25, 43.9%), followed by the urinary tract (13, 22.8%), which was also the most frequent infection site requiring hospitalisation. Of note, even after excluding the 7 SARS-CoV-2 infections, the respiratory tract was still the most affected infection site (18 of 50 ID events, 36.0%), followed by urinary tract (13 of 50 ID events, 26.0%). Only 8 (14.3%) of the ID events classified as potentially opportunistic infections (varicella zoster virus (n = 2), herpes simplex virus (n = 2), cytomegalovirus (n = 1), BK virus (BKPyV) (n = 1), *Candida albicans* (n = 1), nontuberculous mycobacteria (n = 1)). These potentially opportunistic infections were observed after a median of 396 days (IQR = 250–827) after transplantation. Affected patients had a median CD4 count of 346 cells/mm^3 blood (IQR = 178–476).

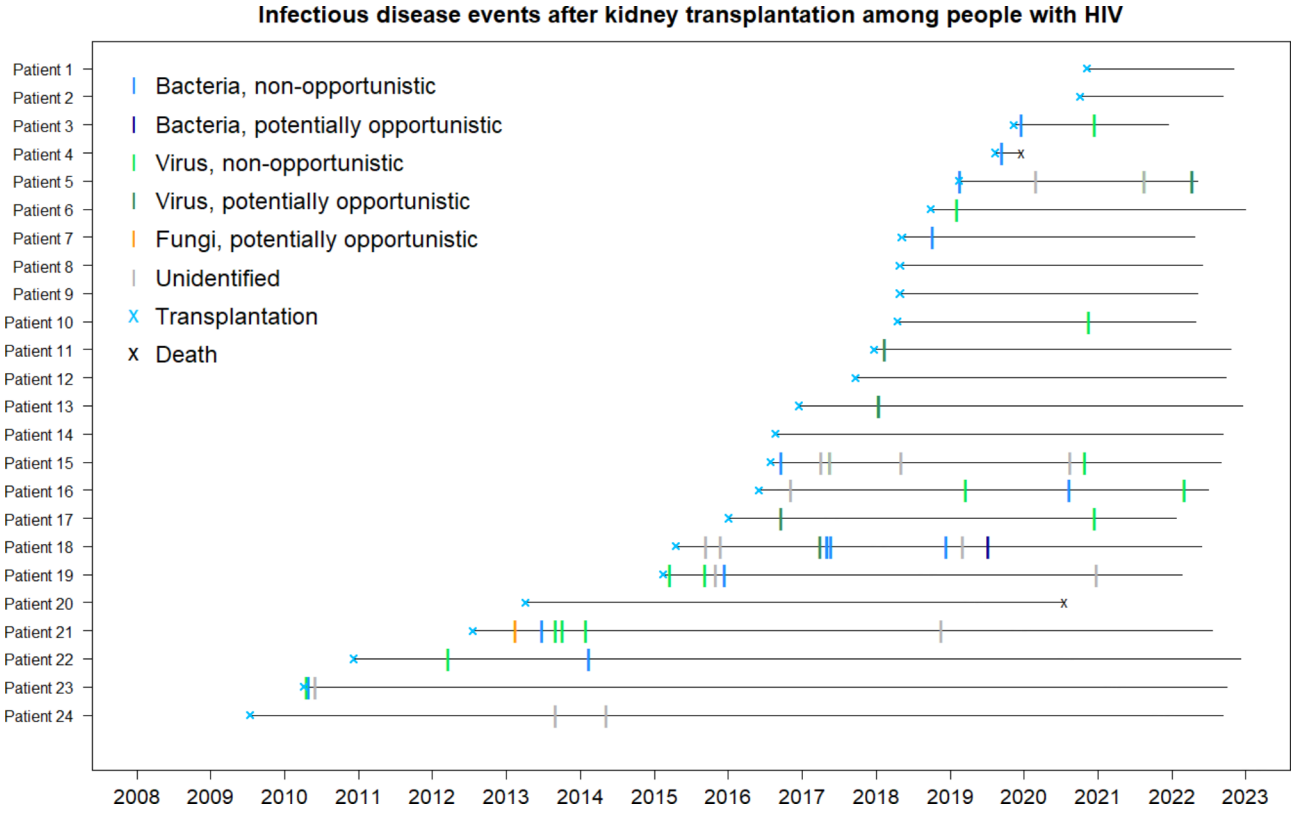

Fig. 1 Timeline of people with HIV receiving a kidney transplantation. Blue cross indicates the transplantation, the vertical lines indicate the occurrence of infectious disease events. Horizontal lines indicate the time of follow-up, black cross indicates death

Comparison to the matched control group

The matched control group ($N=72$) was selected among 3156 eligible control patients, i.e., age at transplantation of at least 18 years and minimum follow-up after transplantation of at least 30 days (45 potential controls were removed due to the last criterion). The incidence rate of all ID events among PWH was 0.41 (95%-confidence interval (CI): 0.30–0.52) events per person-year of follow-up and did not significantly differ to the rate of ID events in the matched control group (0.48 (95%-CI: 0.41–0.55) ID events per person-year of follow-up, rate-ratio test p value: 0.32). Restricting to ID events requiring hospitalisation, the same rates were observed for PWH and the matched control group, i.e., 0.15 per person-year of follow-up (95%-CI for PWH: 0.09–0.22, 95%-CI for control population: 0.11–0.19). Similarly, the Anderson-Gill counting process did not identify HIV as an independent risk factor for recurrent ID events (adjusted hazard ratio=0.94, 95%-CI: 0.46–1.91, p value=0.9). Compared to the matched control group, the fraction of viral infections was slightly higher for PWH (38.6% versus 33.5%) and the fraction of bacterial infections smaller (31.6% versus 43.7%). However, the observed difference in the distribution of bacterial, viral, and fungal pathogens was not statistically significant ($p=0.45$). Having a closer look at the pathogen types, *Klebsiella* spp. was the second most frequent bacterial pathogen but was not reported in the group of PWH. For viral infections, while SARS-CoV-2 was the most frequent pathogen type in both groups, BKPyV was the second most frequent pathogen type in the matched control group (12.5%), but only occurred in one PWH. Although very small numbers, the occurrence of potentially opportunistic infections was not increased among PWH (0.06 ID events per person-year follow-up in both groups, 95%-CI for PWH: 0.02–0.10, 95%-CI for control population: 0.04–0.09). In the matched control group, urinary tract infections (30.4%) were most common (compared to 19.4% among PWH), followed by 29.3% respiratory tract infections (compared to 37.3% among PWH). This difference in the distribution of infection sites was however not statistically significant ($p=0.45$).

Discussion

In this study, we provide a comprehensive description of a representative sample of PWH receiving K-Tx in Switzerland in the years 2008 until 2022. Using the strength of two nation-wide longitudinal prospective cohort studies, one enrolling people receiving solid organ transplantations and one enrolling PWH, we were able to provide a detailed description of infectious complications post-transplant (recorded in the STCS) as well as HIV-specific

Table 2 Pathogen types and infections site of all infectious disease events reported for people with HIV receiving a kidney transplantation. Potentially opportunistic infections are indicated with *

Pathogens		***N*** **= 57 (All ID events)**	***N*** **= 21 (hospitalisation required)**
Bacteria		18	11
	Escherichia coli	8 (44.4%)	6 (54.5%)
	Haemophilus influenzae	2 (11.1%)	
	Enterococcus spp.	1 (5.6%)	
	Other *Enterobacterales*	1 (5.6%)	
	Clostridioides difficile	1 (5.6%)	1 (9.0%)
	Streptococcus spp.	1 (5.6%)	1 (9.0%)
	Coagulase negative staphylococci	1 (5.6%)	
	Other non-enteric Gram-negative bacteria	1 (5.6%)	1 (9.0%)
	Mycobacteria other than tuberculosis*	1 (5.6%)	1 (9.0%)
	Campylobacter spp.	1 (5.6%)	1 (9.0%)
Viruses		**22**	**4**
	SARS-CoV-2	7 (31.8%)	2 (50%)
	Rhinovirus	3 (13.6%)	
	Herpes simplex virus*	2 (9.1%)	1 (25%)
	Varicella zoster virus*	2 (9.1%)	1 (25%)
	Influenza	2 (9.1%)	
	Cytomegalovirus*	1 (4.5%)	
	BKPyV*	1 (4.5%)	
	Picornavirus	1 (4.5%)	
	Norovirus	1 (4.5%)	
	Respiratory syncytial virus	1 (4.5%)	
	Other, not specified	1 (4.5%)	
Fungi		1	
	*Candida albicans**	1 (100%)	
Probable infections without identification of causative pathogens	-	16	6
Infection Sites	Respiratory tract	25 (43.9%)	5 (23.8%)
	Urinary tract	13 (22.8%)	7 (33.3%)
	Blood	7 (12.3%)	5 (23.8%)
	Gastrointestinal tract	8 (14.0%%)	5 (23.8%)
	Mucocutaneous	7 (12.3%)	3 (14.3%)
	Other	5 (8.8%)	2 (9.5%)
	Eye	2 (3.5%)	2 (9.5%)

clinical information (recorded in the SHCS). The main finding is that despite the potential detrimental effect of the chronic HIV infection on the immune system at the time of transplantation, PWH did not experience higher rates of infectious complications. The pathogen types and infection sites were mostly comparable, even when restricting to infections requiring hospitalisation or potentially opportunistic infections, respectively.

At the time of transplantation, the median CD4 cell count was 385 cells/mm^3 blood, reflecting a slightly impaired immune state. However, we did not see a higher frequency of potentially opportunistic infections when compared to the matched control group with likely higher CD4 cell counts (not measured for HIV-uninfected patients). All patients with documented HIV RNA measurement at the time of transplantation were virally suppressed, however, with few episodes of blips after the transplantation. The predominant antiretroviral therapies at the time of transplantation were integrase inhibitor-based regimens (dolutegravir- or raltegravir-based) with only a fourth of the patients switching the therapy after transplantation. These findings reflect the high efficacy and compatibility of immunosuppressive agents and integrase-inhibitor based HIV regimen, even in the case of highly comorbid patients.

In the present study, viral infections were the most common ID events in kidney transplant recipients with HIV. In the subset of ID events requiring hospitalisation, bacterial infections predominated. This finding is in line with prior studies reporting a large proportion of

bacterial infections among ID events requiring hospitalisation or even intensive care support of kidney transplant recipients with HIV [13, 14]. Stock et al. also found *E. coli* as the most frequently detected bacterium, just as we found [14]. The most common sites of infection were the respiratory tract, urinary tract, and bloodstream infections. Resembling to our findings, several studies confirmed that these sites were frequently affected by infections in kidney transplant recipients with HIV [13–15]. In kidney transplant recipients without HIV the urinary tract was the most common infection site, resembling to the findings of van Delden et al. [2]. Our dataset did not include information on the presence of urethral catheters, which represents a risk factor for urinary tract infections. Thus, we could not analyse if this difference was due to differences in urethral catheterisation between kidney transplant recipients with HIV and the control group.

In the comparison of causative pathogens, BKPyV infections were more frequent in the HIV-negative control group, the reasons for this difference being unclear. Among polyomaviruses, JC virus (JCPyV) infections with the clinical presentation of progressive multifocal leukoencephalopathy (PML) is most often seen in PWH [16], whereas BKPyV infections are of major relevance in K-Tx recipients and hematopoietic stem cell recipients. Few cases of BKPyV infections, including central nervous system manifestations such as encephalitis [17] or a PML mimicking disease [18] but also renal manifestations, have been described in PWH, especially with acquired immunodeficiency syndrome (AIDS) [19, 20]. A recent paper from McMullen et al. studying K-Tx in PWH reported four BKPyV infections among 25 kidney transplant recipients [21].

A survival benefit for PWH with end-stage renal disease who received a K-Tx has been previously reported [22]. Our findings argue against a fear of a potentially higher risk of infections in PWH. PWH with end-stage renal disease should be evaluated for K-Tx using the same criteria as for HIV-uninfected patients.

Strengths of the present study are the multi-centric design and the use of prospective, comprehensive data collection of two cohort studies. Both cohort studies share a large degree of representability for Switzerland. In particular, the STCS includes basic information on all solid organ transplantations in Switzerland since 2008, with a consent rate of 93% for reusing the information for research purposes [7]. Uniform definitions for ID events were applied for kidney transplant recipients with HIV and the control group of HIV-negative kidney transplant recipients, whereas prior studies often compared ID events between different cohorts likely lacking these uniform definitions. Further, all hospitals with transplant activity in Switzerland are part of the SHCS, most likely leading to a high coverage of PWH who received a donor organ in Switzerland. To the best of our knowledge, only 4 kidney transplant recipients with HIV since 2008 were missed in our analysis due to delayed or refused registration in the cohort studies. Hence, the major limitation of the present study is the limited total sample size of PWH who underwent a kidney transplantation in Switzerland. Most of kidney transplantations in recipients with HIV were performed in male recipients. Thus, the sample size for kidney transplantations in female recipients with HIV was much lower limiting the generalisability of our findings for this population. Similarly, our study focused on kidney transplantations in recipients with HIV, the transfer of our findings for other immune alterations present at the time of kidney transplant, e.g. due to a rheumatic disease, remains speculative. Furthermore, our analysis on potentially opportunistic infections likely overestimated the incidence of opportunistic infections, as our dataset did not include the granularity to adhere to the strict CDC definitions. However, we used uniform definitions for both, kidney transplant recipients with HIV and the matched control group, resulting in an identical bias.

Conclusion

Our findings strengthen the current guidelines of HIV not being a contraindication for transplantation. Evaluation of PWH for K-Tx seemed to differ from HIV-uninfected patients with end stage kidney disease, e.g. all PWH received renal replacement prior to K-Tx, whereas in the control group several pre-emptive K-Tx were performed. A harmonisation in evaluation strategies between PWH and HIV-uninfected patients should be considered. Further research and a higher sample size is needed to understand potentially yet unrevealed differences in ID events after transplantation in PWH compared to HIV-uninfected patients. Linkage of national transplantation registries and HIV cohorts are crucial to obtain these insights.

Abbreviations

AIDS	Acquired immunodeficiency syndrome
ART	Antiretroviral therapy
ATG	Anti-thymocyte globulin
DBD	Donation after brain death
DCD	Donation after cardiocirculatory death
EC-MPS	Enteric-coated mycophenolate sodium
HIV	Human immunodeficiency virus
ID	Infectious disease
IQR	Interquartile range
K-Tx	Kidney transplantation
MMF	Mycophenolate mofetil
PML	Progressive multifocal leukoencephalopathy
PWH	People with HIV
SARS-CoV-2	Severe acute respiratory syndrome coronavirus 2
SHCS	Swiss HIV Cohort Study
SOT	Solid organ transplant
STCS	Swiss Transplant Cohort Study

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Author contributions
KK, PWS, NJM and HFG designed the study. KK and PWS performed the analyses. KK and PWS drafted the first version of the manuscript. All authors contributed with requests concerning the data and commented on the manuscript. All authors have approved the final version of the manuscript.

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Data availability
The individual level datasets generated or analyzed during the current study do not fulfil the requirements for open data access: (1) The patient informed consent states that sharing data outside the studies is only permitted for specific studies on HIV infection and its complications, and to researchers who have signed an agreement detailing the use of the data and biological samples; and (2) the data is too dense and comprehensive to preserve patient privacy in persons living with HIV.According to the Swiss law, data cannot be shared if data subjects have not agreed or data is too sensitive to share. Investigators with a request for selected data should send a proposal to the respective SHCS address (www.shcs.ch/contact). The provision of data will be considered by the Scientific Board of the SHCS (and the Scientific Board of the STCS) and the study team and is subject to Swiss legal and ethical regulations, and is outlined in a material and data transfer agreement.

Declarations

Ethics approval and consent to participate
This project was approved by the responsible Ethics Committee (Kantonale Ethikkommission Zürich, Req. 2019 – 00248). The Swiss Transplant Cohort Study (STCS, www.stcs.ch, ClinicalTrials.gov Identifier: NCT01204944, first posted: September 17th 2010) was established in 2008 and was approved by the Ethic Committees of all participating institutions. The Swiss HIV Cohort Study was established in 1988 and approved by the Ethics Committees (SHCS, www.shcs.ch, Kantonale Ethikkommission Zürich, BASEC-Nr. 2023–02080). Written informed consent was obtained from all participants.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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