Bacterial infections after liver transplantation and the role of oral selective digestive decontamination: a retrospective cohort study

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Bacterial Infections After Liver Transplantation and the Role of Oral Selective Digestive Decontamination: A Retrospective Cohort Study

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ABSTRACT

Background. Bacterial infections are common after liver transplantation (LT) and cause serious morbidity and mortality. In our center, prolonged selective digestive decontamination (SDD) is the standard of care, which may lead to a reduced number and severity of bacterial infections. The aim of the current study was to investigate bacterial infection rates, the causative pathogens, localization, and the possible influence of SDD within the first year after LT.

Methods. A retrospective single-center cohort study was performed. Patients within their first year after LT between 2012 and 2017 were included. Patients received SDD for 3 weeks immediately after LT. The type of infection, bacterial subtype, CSI classification, severity, and potential interventions were recorded.

Results. One hundred eighty-six patients were included in the study. Seventy-eight patients (41.9%) had a bacterial infection within the first year after LT. The most common types of infection were cholangitis (25.8%) and secondary infected abdominal fluid collections (25.3%). The most common bacteria were Gram-positive enterococcal- (36.5%) and Gram-negative enterobacterial species (34.2%). 35.5% of the infections occurred within the first month after LT, mainly caused by Gram-positive bacteria (76.7%).

Conclusions. Cholangitis and infected abdominal fluid are the most common types of infection within one year after LT, mainly caused by enterococcal- and enterobacterial species. Within the first month after LT, infections were mostly caused by Gram-positive bacteria, which could be a consequence of protocol use of SDD. The results can be used for the choice of empirical antibiotic therapy based on the most common types of bacteria and the time frame after LT.

LIVER transplantation (LT) can be a lifesaving treatment for patients with end-stage liver disease with a one- and five-year survival rate of 90% and 80%, respectively [1]. One of the challenges after LT is the handling of infections. A previous study estimates that 80% of the patients will suffer from at least one infection within the first year after LT [2]. These infections lead to significant morbidity and mortality [3]. Risk factors for post-transplant infections are well-defined but often multifactorial and difficult to manage [4].

Up to 70% of post-transplant infections are caused by bacteria, and of these bacterial infections, 40% have an onset within the first month after LT [5−7]. Half of these early infections are from abdominal origin (hepatic abscesses, cholangitis, infected fluid collections, or peritonitis), followed by septicemia (34%), pulmonary infections (31%), and wound problems (10%) [3,6,7]. Intra-abdominal infections are associated with transplant failure and re-transplantation [5,8].

Infections in LT patients can be less symptomatic due to the use of immunosuppression, which can cause a diagnostic delay, potentially leading to a more serious course of infection [4,7].

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During and on the first day after LT, the use of prophylactic antibiotics is considered as standard of care in most centers [9,10]. Earlier studies suggested that the use of oral selective digestive decontamination (SDD) directly after LT may be beneficial; this was based on the finding that up to 67% of early post-transplant bacterial infections are caused by Gram-negative bacteria [3,11]. On the other hand, SDD may lead to antibiotic resistance in Gram-positive bacteria [4,11]. In the overall intensive care unit (ICU) population, Gram-negative bacterial infections and mortality can be reduced using SDD [12]. However, previous systematic reviews are inconclusive regarding the beneficial effect of protocol SDD usage after LT [13,14].

In our transplant center, prophylaxis with SDD for a period of 3 weeks immediately after LT has been the standard of care since 1994. This retrospective study investigated infections and bacterial species within the first year after LT in a single center using protocol SDD.

MATERIALS AND METHODS

Patients and Study Design

We performed a single-center, retrospective cohort study. All adult patients who underwent their first orthotopic LT between 2012 and 2017 at the Leiden University Medical Center were included. Patients with previous or concomitant organ transplantation were excluded.

Immunosuppressive therapy was initiated according to protocol, with basiliximab induction and postoperative treatment with calcineurin-inhibitors (mostly tacrolimus) and prednisolone, in some cases combined with mycophenolate mofetil, sirolimus, or everolimus.

The standard antibiotic prophylaxis for LT consisted of intravenous cefazolin, penicillin, metronidazole, and gentamicin from the start of the operation until 24 hours postoperatively. The prophylaxis could be adapted in case of allergies or in case of bacterial colonization with resistance to certain antibiotics.

All patients received SDD during a period of 3 weeks after transplantation, with the first dose given immediately before LT. SDD consisted of a combination of oral norfloxacin, amphotericin B, and polymyxin/neomycin. In addition, intubated patients received orabase (2% gentamicin/colistin/vancomycin) and intravenous cefotaxime for a period of 4 days.

Because of the retrospective nature of the study with existing data and the consent of patients to use the data, the institutional review board waived the need for further consent. This study complied with the latest version of the Declaration of Helsinki. The data will be made available on request.

Evaluations and Definitions

Patient characteristics like age, sex, LT indication, Model for End-Stage Liver Disease score, type of donor organ, ischemia times, operation duration, hospitalization time, and microbiological results for all proven bacterial infections within the first year after LT were extracted from electronic patient records and the transplant database.

The criteria for clinically significant bacterial infections (CSI), according to the Centers for Disease Control and Prevention, were used to define clinically significant bacterial infections [15]. All infections with a positive culture and who met the CSI criteria were included. The associated bacterial species were recorded, along with the type of infection, antibiotic treatment, potential intervention, and clinical outcome. Clinical suspicions of an infection without a positive culture were not included.

Regarding the type of infection, a distinction was made between an infected abdominal collection and infected ascites. Ascites was considered as diffuse abdominal fluid, whereas an abdominal collection had to be clearly localized. Biliary peritonitis was defined by any abdominal fluid collection with proven high bilirubin levels. A positive blood culture without any overt localized infection was called bacteremia. Any complications related to the infection were scored according to the Clavien-Dindo classification [16].

Endpoints

The primary endpoint of the study was infection type and bacterial species. Secondary endpoints were intervention type, infection-related complications, re-transplantation, one-year mortality, and the incidence of infection related to time after LT. Four different time periods were defined: LT <1 month, 1 to 3 months after LT, 4 to 6 months after LT, and 7 to 12 months after LT.

Statistical Analysis

Categorical data were reported as frequencies (percentages), and continuous data were reported as mean with SD. All data were collected and analyzed by SPSS Statistics 25 (IBM SPSS, Inc).

RESULTS

Patients

Between 2012 and 2017, 205 patients underwent LT in our center. Nineteen patients were excluded based on the defined criteria: 12 patients with a combined kidney−liver transplantation, 4 auxiliary liver transplantations, 2 living −related liver transplantations, and 1 patient with a previous stem cell transplantation.

All other 186 patients were included in this study. Patient characteristics are shown in Table 1. Most patients were male (71.5%), with a median age of 57 years. One hundred seventy-one patients (92%) underwent their first LT, and 15 patients (8%) were re-transplanted due to graft failure. The most common underlying liver disease was hepatocellular carcinoma (37.4%), followed by cholangiopathies (22.5%) and alcoholic liver disease (15.1%). The 2 different donor types, donation after brain death and donation after circulatory death, were relatively evenly distributed: 52.2% vs 47.8%, respectively.

Endpoints

Primary endpoints. Within the first year of LT, 78 patients (41.9%) developed 186 bacterial infections. The most common type of infection was cholangitis (n = 48; 25.8%), followed by infected abdominal collections (n = 47; 25.3%) and urinary tract infections (n = 23; 12.4%). Most of these infections were caused by Gram-positive *Enterococcus* species (*Enterococcus faecium* 25.3%, *Enterococcus faecalis* 11.2%) and Gram-

Table 1. Baseline-Characteristics

	Total patients (n = 186)
Male, n (%)	133 (71.5%)
Age, y, median (spread)	57 (19-72)
Donation after Brain Death, n (%)	97 (52.2%)
Donation after Circulatory Death, n (%)	89 (47.8%)
MELD-score (Matched MELD), median (spread)	24 (6-40)
MELD-score (Lab MELD), median (spread)	13 (6-40)
Underlying liver disease	
Viral hepatitis (HBV, HCV), n (%)	5 (2.6%)
Hepatocellular carcinoma, n (%)	69 (37.4%)
Cholangiopathies (PSC, PBC, ITBL, CCA), n (%)	42 (22.5%)
Auto-immune hepatitis, n (%)	7 (3.7%)
Post-alcoholic liver disease, n (%)	28 (15.1%)
Metabolic disorders (NASH, Wilson, A1ATD), n (%)	11 (5.9%)
Vascular liver disease (Budd-Chiari, HAT), n (%)	6 (3.2%)
Acute liver failure or ACLF, n (%)	9 (4.9%)
Others, n (%)	8 (4.2%)
Ischemia times	
Donor warm ischemia time, min, median (range)	14 (6-174)
Cold ischemia time, min, median (range)	527 (270-1089)
Warm ischemia time, min, median (range)	35 (18-102)
Operation duration, min, median (range)	315 (153-590)
Hospitalization duration, d, median (range)	14 (6-174)

A1ATD, alfa-1 antitrypsin deficiency; ACLF, acute on chronic liver failure; CCA, cholangiocarcinoma; HAT, hepatic artery thrombosis; HBV, hepatitis B virus; HCV, hepatitis C virus; ITBL, ischemic type biliary lesions; MELD, Model for End-Stage Liver Disease; NASH, non-alcoholic steatohepatitis; PBC, primary biliary cholangitis; PSC, primary sclerosing cholangitis.

Table 2. Bacterial Infections Within the First Year of LT (n = 186)

Characteristics	Total
No. of patients with an infection	78 (41.9%)
DBD recipients with an infection	42 (53.8%)
DCD recipients with an infection	36 (46.2%)
One-year overall mortality	16 (8.6%)
No. of retransplantation within 1 year	11 (5.9%)
Infection type	
Cholangitis	48 (25.8%)
Infected abdominal fluid collection	47 (25.3%)
Urinary tract infection	23 (12.4%)
Infected ascites	17 (9.1%)
Pneumonia	14 (7.5%)
Biliary peritonitis	14 (7.5%)
Wound infection	10 (5.4%)
Bacteremia	4 (2.2%)
Gastro-enteritis	4 (2.2%)
Central line associated infection	3 (1.6%)
Pancreatitis	2 (1.1 %)
Bacterial species	
Enterococcus species	36.5%
Enterococcus faecium	77 (25.3%)
Enterococcus faecalis	34 (11.2%)
Enterobacterial species	34.2%
Escherichia coli	34 (11.2%)
Klebsiella pneumoniae	23 (7.6%)
Others	(29.3%)

Data are expressed as n (%).
DBD, donation after brain death; DCD, donation after circulatory death; LT, liver transplantation.

negative enterobacterial species (*Escherichia coli* 11.2%, *Klebsiella pneumoniae* 7.6%).

Most of the complications were graded as grade 2 (44%) or 3A (40%), according to the Clavien-Dindo classification. All primary endpoints are presented in Table 2.

Secondary endpoints. The one-year survival rate of this group was 91.4%. Eleven patients (5.9%) were re-transplanted within the first year after LT.

35.5% of infections occurred within the first month of LT (period 1), 25.8% between the first and third month (period 2), 24.7% between the fourth and sixth month (period 3) and 14% between 7 and 12 months after LT (period 4).

Infected abdominal fluid collections (24.2%) and ascites (22.7%) were the most common type of infection during period 1. Most infections during this time frame were caused by Gram-positive bacteria (76.7%), especially *Enterococcus* species (49%). Infected abdominal fluid collections were also frequently seen (17.4-33.3%) during the second, third, and fourth periods, along with cholangitis (33.3-46.2%). Most of the infections during these time frames were caused by Gram-positive (enterococcus) species (22.9-37.2%) and Gram-negative (enterobacterial) species (35.2-52.1%). Overall, Gram-positive bacterial infections were frequently seen shortly after LT, whereas most of the later infections within the first year of LT were caused by Gram-negative bacteria. All types of infection, intervention types, and severity scores per time frame are presented in Table 3. The associated bacterial species are presented in Table 4. An overview of all bacterial species specified for different types of infection can be found in Table 5.

DISCUSSION

In this retrospective study, we evaluated bacterial infections within the first year of LT, localization, the associated bacterial species, and the possible influence of prolonged SDD prophylaxis.

In 41.9% of the patients, at least one infection developed within the first year after LT. Most of these infections (33.5%) occurred within the first month after LT, and most of these were infected abdominal collections (24.2%) or infected ascites (22.7%). This finding aligns with previous studies and is related to the recent major surgery and strong immunosuppression directly after LT [6,7]. Most infections occurring between 4 and 12 months after LT were caused by cholangitis. This can be explained by the frequent occurrence of post-transplant cholangiopathy with the occurrence of ischemic-type biliary lesions, usually with non-anastomotic biliary strictures, which become clinically manifest typically during this time frame and is more frequent in livers from donation after cardiac death (which were received by 46% of our population) [5].

Gram-positive *Enterococcus* species and Gram-negative enterobacterial species were responsible for the majority of

Table 3. Bacterial Infections Per Time Frame

Characteristics	Period 1	Period 2	Period 3	Period 4
No. of patients with infection	45	31	28	17
Infections per period, n (%)	66 (35.5 %)	48 (25.8%)	46 (24.7%)	26 (14%)
1 infection	32	19	19	11
2 infections	8	7	4	3
3 infections	3	5	2	3
4 infections	1	0	2	0
5 infections	1	0	1	0
Infection type				
Cholangitis, n (%)	3 (4.5%)	16 (33.3%)	17 (37%)	12 (46.2%)
Infected abdominal fluid collection, n (%)	16 (24.2%)	16 (33.3%)	8 (17.4%)	7 (27%)
Urinary tract infection, n (%)	5 (7.6%)	8 (16.7%)	8 (17.4%)	2 (7.7%)
Infected ascites, n (%)	15 (22.7%)	1 (2.1%)	0 (0%)	1 (3.8%)
Pneumonia, n (%)	8 (12.1%)	1 (2.1%)	4 (8.7%)	1 (3.8%)
Wound infection, n (%)	6 (9.1%)	1 (2.1%)	3 (6.5%)	0 (0%)
Biliary peritonitis, n (%)	8 (12.1%)	5 (10.4%)	0 (0%)	1 (3.8%)
Bacteremia, n (%)	3 (4.5%)	0 (0%)	1 (2.2 %)	0 (0%)
Central line infection, n (%)	1 (1.5%)	0 (0%)	1 (2.2%)	1 (3.8%)
Pancreatitis, n (%)	1 (1.5%)	0 (0%)	1 (2.2%)	0 (0%)
Gastro-enteritis, n (%)	0 (0%)	0 (0%)	3 (6.5%)	1 (3.8%)
Antibiotic treatment, n (%)	62 (34.3%)	47 (26%)	46 (25.4%)	26 (14.4%)
Intervention				
ERCP, n (%)	2 (5.1%)	6 (18.8%)	5 (19.2%)	3 (20%)
Drainage, n (%)	17 (43.6%)	14 (43.8%)	5 (19.2%)	7 (46.7%)
Surgery, n (%)	12 (30.8%)	3 (9.4%)	0 (0%)	0 (0%)
ICU-admission, n (%)	1 (2.6%)	4 (12.5%)	4 (15.4%)	0 (0%)
PTCD, n (%)	0 (0%)	3 (9.4%)	9 (34.6%)	4 (26.7%)
Wound revision, n (%)	6 (15.4%)	1 (3.1%)	2 (7.7%)	0 (0%)
Bronchoalveolar lavage, n (%)	1 (2.6%)	1 (3.1%)	1 (3.8%)	1 (6.7%)
Severity				
Clavien–Dindo score I, n (%)	4 (6.1%)	1 (2.1%)	0 (0%)	0 (0%)
Clavien–Dindo score II, n (%)	31 (47%)	17 (35.4%)	22 (47.8%)	11 (42.3%)
Clavien–Dindo score IIIA, n (%)	18 (27.3%)	23 (48%)	19 (41.3%)	14 (53.8%)
Clavien–Dindo score IIIB, n (%)	13 (19.7%)	2 (4.2%)	0 (0%)	0 (0%)
Clavien–Dindo score IV, n (%)	0 (0%)	5 (10.4%)	4 (8.7%)	0 (0%)
Clavien–Dindo score V, n (%)	0 (0%)	0 (0%)	1 (2.2%)	1 (3.8%)

Period 1: < 1month, Period 2: 1-3 months, Period 3: 4-6 months, Period 4: 7-12 months.
ERCP, endoscopic retrograde cholangiopancreatography; ICU, intensive care unit; PTCD, percutaneous biliary drainage.

infections within the first year of LT. Notably, 76.7% of the early infections (within the first month of LT) were caused by Gram-positive bacteria vs 23.3% by Gram-negative bacteria. This is probably the result of standard postoperative SDD prophylaxis and differs from an earlier report, which demonstrated a higher (67%) cumulative incidence of Gram-negative infections in the early phase after LT [3]. An important finding was that the majority of the enterococcal infections were caused by *E. faecium*, which is usually resistant to amoxicillin. This has consequences for the empirical treatment of infections.

Infections with Gram-negative bacteria are associated with a higher inflammatory response and more severe sepsis than with Gram-positive bacteria [17], even in immunocompetent patients. Despite this, the use of early postoperative SDD after LT is still under debate. SDD has been proven to reduce Gram-negative bacterial infections and mortality in the overall ICU population [12]. Despite this, 2 systematic reviews were unable to demonstrate an overall beneficial effect of standard SDD use in LT patients in terms of mortality or re-transplantation [13,14]. There is great heterogeneity between (small) randomized controlled trials [18–22], which all use different definitions of infection, SDD regimen, and primary outcome, thus making an overall judgment regarding the benefits of SDD difficult.

A shift toward more Gram-positive cultures with SDD administration after LT has been described elsewhere [11,18,21]. The duration of SDD treatment varies throughout the different studies, with starting times ranging from

Table 4. Bacterial Species Per Time Frame

Characteristics	Period 1	Period 2	Period 3	Period 4
Gram-positive species				
Enterococcus species	46 (49%)	35 (37.3%)	19 (27.9%)	11 (22.9%)
Enterococcus faecalis	13 (13.9%)	12 (12.8%)	3 (4.4%)	6 (12.5%)
Enterococcus faecium	33 (35.1%)	23 (24.5%)	16 (23.5%)	5 (10.4%)
Staphylococcus species	17 (18.1%)	5 (5.4%)	1 (1.5%)	5 (10.5%)
Staph. haemolyticus	6 (6.4%)	1 (1.1%)	0 (0%)	3 (6.3%)
Staph. epidermidis	9 (9.6%)	3 (3.2%)	1 (1.5%)	2 (4.2%)
Staph. hominis	2 (2.1%)	0 (0%)	0 (0%)	0 (0%)
Staph. aureus	0 (0%)	1 (1.1%)	0 (0%)	0 (0%)
MRSA	1 (1.1%)	0 (0%)	1 (1.5%)	0 (0%)
Streptococcus species	4 (4.3%)	3 (3.2%)	2 (2.9%)	2 (4.2%)
Streptococcus gordoni	2 (2.1%)	2 (2.1%)	0 (0%)	0 (0%)
Streptococcus mitis	1 (1.1%)	1 (1.1%)	2 (2.9%)	2 (4.2%)
Streptococcus oralis	1 (1.1%)	0 (0%)	0 (0%)	0 (0%)
Lactobacillus species	4 (4.2%)	4 (4.2%)	3 (4.4 %)	0 (0%)
Lactobacillus paracasei	2 (2.1%)	2 (2.1%)	1 (1.5%)	0 (0%)
Lactobacillus gasseri	2 (2.1%)	2 (2.1%)	2 (2.9%)	0 (0%)
Clostridioides difficile	0 (0%)	0 (0%)	2 (2.9%)	1 (2.1%)
Gram-negative species				
Enterobacter species	15 (16%)	33 (35.2%)	31 (45.6%)	25 (52.1%)
Klebsiella pneumoniae	2 (2.1%)	6 (6.4%)	10 (14.7%)	5 (10.4%)
Klebsiella oxytoca	1 (1.1%)	4 (4.3%)	2 (2.9%)	3 (6.3%)
Escherichia coli	6 (6.4%)	12 (12.8%)	9 (13.2%)	7 (14.6%)
Enterobacter cloacae	2 (2.1%)	6 (6.4%)	3 (4.4%)	4 (8.3%)
Citrobacter spp	0 (0%)	0 (0%)	3 (4.4%)	4 (8.3%)
Morganelli morgani	0 (0%)	1 (1.1%)	0 (0%)	0 (0%)
Serratia marcescens	3 (3.2%)	2 (2.1%)	1 (1.5%)	1 (2.1%)
Hafnia alvei	0 (0%)	2 (2.1%)	1 (1.5%)	1 (2.1%)
Proteus mirabilis	1 (1.1%)	0 (0%)	1 (1.5%)	0 (0%)
Campylobacter jejuni	0 (0%)	0 (0%)	1 (1.5%)	0 (0%)
Bacteroidales species	0 (0%)	3 (3.2%)	0 (0%)	0 (0%)
Prevotella species	0 (0%)	1 (1.1%)	0 (0%)	0 (0%)
Bacteroides fragilis	0 (0%)	2 (2.1%)	0 (0%)	0 (0%)
Mycobacterium tuberculosis	0 (0%)	0 (0%)	0 (0%)	1 (2.1%)
Stenotrophomonas maltophilia	1 (1.1%)	3 (3.2%)	5 (7.4%)	1 (2.1%)
Pseudomonas aeruginosa	6 (6.4%)	7 (7.4%)	2 (2.9%)	1 (2.1%)
Haemophiles influenza	0 (0%)	1 (1.1%)	2 (2.9%)	1 (2.1%)

Data are expressed as n (%).
Period 1: < 1month, Period 2: 1-3 months, Period 3: 4-6 months, Period 4: 7-12 months.
MRSA, Methicillin-resistant *Staphylococcus aureus.*

admission on the LT waiting list until postoperative discharge from the ICU. The duration of SDD also differs between studies. In our center, we use a prolonged prophylaxis of 3 weeks, starting on the day of surgery. A beneficial effect of this prolonged prophylaxis remains unclear and needs further investigation, although there seems to be a trend of less severe infections during the first month of LT compared to after the first month in our study. Extension of prophylaxis with Gram-positive coverage could reduce early overall infection but could lead to antibiotic resistance or bacterial overgrowth (including *C. difficile*), which is already a concern in LT patients [5,7,11]. Another interesting finding of our study was the absence of occurrence of *Pneumocystis jirovecii* infections despite the use of double and even triple immunosuppressants.

This study was limited by its retrospective design and lack of randomization for demonstrating a beneficial effect of standard SDD use in LT patients. Possible other limitations of this study were the inclusion of multiple bacterial species in the same positive culture, thereby potentially analyzing non-pathogenic bacteria. Furthermore, patients with clinical signs of infection but without positive cultures have been excluded; this could have led to an underestimation of infections.

Table 5. Bacterial Species Per Infection Type

	T1*	T2†	T3‡	T4§	T5‖	T6¶	T7**	T8††	T9‡‡	T10§§	T11‖‖
Gram-positive species											
Enterococcus species	26 (28.9%)	42 (50%)	10 (33.3%)	6 (30%)	2 (11.8%)	8 (50%)	12 (52.2%)	2 (25%)	2 (40%)	1 (100%)	0 (0%)
Enterococcus faecalis	7 (7.9%)	13 (15.5%)	3 (10%)	0 (0%)	1 (5.9%)	3 (18.8%)	5 (21.7%)	1 (12.5%)	1 (20%)	0 (0%)	0 (0%)
Enterococcus faecium	19 (21.1%)	29 (34.5%)	7 (23.3%)	6 (30%)	1 (5.9%)	5 (31.3%)	7 (30.4%)	1 (12.5%)	1 (20%)	1 (100 %)	0 (0%)
Staphylococcus species	0 (0%)	3 (3.6%)	0 (0%)	3 (15%)	1 (5.9%)	1 (6.3%)	1 (4.3%)	1 (12.5%)	1 (20%)	0 (0%)	0 (0%)
Staph. haemolyticus	0 (0%)	3 (3.6%)	0 (0%)	2 (6.7%)	1 (5.9%)	0 (0%)	1 (4.3%)	1 (12.5%)	1 (20%)	0 (0%)	0 (0%)
Staph. hominis	0 (0%)	0 (0%)	0 (0%)	1 (3.3%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Staph. aureus	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (6.3%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
MRSA	1 (1.1%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (12.5%)	0 (0%)	0 (0%)	0 (0%)
Streptococcus species	3 (3.3%)	5 (6%)	0 (0%)	1 (3.3%)	0 (0%)	1 (6.3%)	1 (4.3%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Streptococcus gordoni	1 (1.1%)	4 (4.8%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Streptococcus mitis	2 (2.2%)	1 (1.2%)	0 (0%)	1 (3.3%)	0 (0%)	0 (0%)	1 (4.3%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Streptococcus oralis	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (6.3%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Lactobacillus species	0 (0%)	6 (7.1%)	0 (0%)	2 (6.7%)	1 (5.9%)	0 (0%)	1 (4.3%)	0 (0%)	1 (20%)	0 (0%)	0 (0%)
Lactobacilles paracasei	0 (0%)	2 (2.4%)	0 (0%)	1 (3.3%)	1 (5.9%)	0 (0%)	1 (4.3%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Lactobacilles gasseri	0 (0%)	4 (4.8%)	0 (0%)	1 (3.3%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (20%)	0 (0%)	0 (0%)
Clostridioides defficile	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	3 (75%)
Gram-negative species											
Enterobacterial species	49 (54.4%)	21 (25%)	16 (53.3%)	4 (20%)	3 (17.6%)	5 (31.3%)	5 (21.7%)	4 (80%)	0 (0%)	0 (0%)	1 (25%)
Klebsiella pneumonia	12 (13.3%)	3 (3.6%)	6 (20%)	0 (0%)	0 (0%)	1 (6.3%)	1 (4.3%)	1 (12.5%)	0 (0%)	0 (0%)	0 (0%)
Klebsiella oxytoca	3 (3.3%)	3 (3.6%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	2 (8.7%)	1 (12.5%)	0 (0%)	0 (0%)	0 (0%)
Escherichia coli	14 (15.6%)	8 (9.5%)	6 (20%)	2 (10%)	0 (0%)	3 (18.8%)	0 (0%)	1 (12.5%)	0 (0%)	0 (0%)	0 (0%)
Enterobacter cloacae	10 (11.1%)	3 (3.6%)	2 (6.7%)	2 (10%)	0 (0%)	0 (0%)	1 (4.3%)	1 (12.5%)	0 (0%)	0 (0%)	0 (0%)
Citobacter spp	6 (6.7%)	1 (1.2%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Morganelli morgani	0 (0%)	1 (1.2%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Serratia marcescens	0 (0%)	2 (2.4%)	1 (3.3%)	0 (0%)	3 (17.6%)	1 (6.3%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Hafnia alvei	3 (3.3%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (4.3%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Proteus mirabilis	1 (1.1%)	0 (0%)	1 (3.3%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Campylo bacter jejuni	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (25%)
Bacteroidales species	1 (1.1%)	1 (1.2%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Prevotella species	1 (1.1%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Bacteroides fragillis	0 (0%)	1 (1.2%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Mycobacterium tuberculosis	0 (0%)	1 (1.2%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Stenotrophomonas maltophilia	5 (5.6%)	3 (3.6%)	0 (0%)	0 (0%)	1 (5.9%)	0 (0%)	0 (0%)	0 (0%)	1 (20%)	0 (0%)	0 (0%)
Pseudomonas aeuroginosa	1 (1.1%)	2 (2.4%)	4 (13.3%)	1 (5%)	7 (41.2%)	1 (6.3%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Haemophilus influenza	1 (1.1%)	0 (0%)	0 (0%)	0 (0%)	1 (5.9%)	0 (0%)	2 (8.7%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)

Data are expressed as n (%).
MRSA, Methicillin-resistant *Staphylococcus aureus.*
* Cholangitis.
† Abdominal abscess.
‡ Urinary tract infection.
§ Infected fluid collection.
‖ Pneumonia.
¶ Wound infection.
** Biliary peritonitis.
†† Bacteremia.
‡‡ Catheter-related bloodstream infection.
§§ Pancreatitis.
‖‖ Gastroenteritis.

Nevertheless, this study gives an overview of bacterial infection types and their associated pathogens during the first year after LT in the context of prolonged postoperative administration of SDD prophylaxis. The follow-up time is significantly longer than in previous studies [18−22], thereby giving a more detailed insight into the course of post-LT infections. The results can be a guide for the design of future studies with SDD and may help in daily practice in LT patients. An example could be the use of a broader Gram-positive empirical treatment for infections in the early phase after LT in a center using SDD.

DECLARATION OF COMPETING INTEREST

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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