ORIGINAL ARTICLE

Clinical outcomes of intestinal transplant recipients colonized with multidrug-resistant organisms: a retrospective study

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SUMMARY

Rates of multidrug-resistant organisms (MDRO) colonization among intestinal transplant (ITx) recipients have not been reported. Colonization rates with vancomycin-resistant *Enterococcus* (VRE), carbapenem-resistant Gram-negative bacteria (CR-GNB), and methicillin-resistant *Staphylococcus aureus* (MRSA) were obtained retrospectively in adults undergoing ITx (isolated or multivisceral) from 1/2009 to 12/2015. We assessed for VRE, CR-GNB, and MRSA bacteremia during the first year post-transplant for patients colonized with VRE, CR-GNB, and MRSA, respectively, and for those who were not colonized. We evaluated whether the number of hospitalization days and one year post-transplant survival were different in MDRO-colonized patients. Forty-five ITx recipients were identified. Twenty-eight (62%) were colonized with MDRO [VRE in 22 (50%) patients, MRSA in seven (16%), and CR-GNB in six (15%)]. VRE and CR-GNB-colonized patients were more likely to develop VRE and CR-GNB bacteremia, respectively, than noncolonized patients [8/22 (36%) vs. 1/23 (4%), and 4/6 (67%) vs. 2/39 (5%), $P < 0.05$ for both]. There was no difference in one-year survival between MDRO-colonized and noncolonized patients. However, survival was lower among MDRO-colonized patients who developed VRE, CR-GNB, or MRSA bacteremia ($P < 0.001$). MDRO colonization was common among our ITx recipients. VRE and CR-GNB bacteremia was more common among colonized patients, and survival was lower among MDRO-colonized patients who developed bacteremia.

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Key words

bacteremia, intestinal transplant, multidrug-resistant organisms colonization, survival

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Introduction

Intestinal transplantation (ITx) is an acceptable therapeutic modality for irreversible intestinal failure. However, it is performed by very few transplant centers. Of a total of 653,111 solid organ transplants (SOT) performed in United States between 1998 and 2015, only 2,658 (0.4%) were ITx [1].

Infections are very common after ITx. Silva *el al* reported an incidence of 2.81 episodes per 1000 transplant days in 87 ITx recipients. Of the nonopportunistic infections, 121 (60%) were bacterial (57%: Gram-negative, 31%: Gram-positive, and 12%: others). Bloodstream infection was seen in 72 (34%) of the cases [2].

Infections due to multidrug-resistant organisms (MDRO) have become very common and are

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considered a substantial threat to the public health worldwide [3]. These infections are difficult to treat due to the paucity of effective antimicrobials, as well as the toxicity and cost of second-line agents that treat some of these infections [3]. SOT recipients colonized with MDRO are at a higher risk for developing an infection with the same organisms that they are colonized with, as it was demonstrated in a meta-analysis that showed that patients colonized with methicillin-resistant *Staphylococcus aureus* (MRSA) and vancomycin-resistant *Enterococcus* (VRE) were 5.5 times and 6.7 times more likely to develop MRSA and VRE infections, respectively, post-liver transplant, respectively [4]. Twenty-two (39%) SOT recipients who had carbapenem-resistant Gram-negative bacteria (CR-GNB) colonization or infection prior to transplant developed CR-GNB infection post-transplant [5]. In another study, 20 (49%) of CR-*Klebsiella pneumoniae*-colonized liver transplant recipients developed *Klebsiella pneumoniae* infection (bloodstream infection in 18 and pneumonia in two patients) [6].

The MDRO colonization data in patients undergoing ITx is scarce. In this study, we evaluated colonization rates and clinical outcomes among ITx recipients.

Patients and methods

Study population

This is a single-center retrospective study that was conducted at Jackson Memorial-Miami Transplant Institute, a 1558-licensed bed tertiary care teaching hospital in Miami, Florida. Our study was approved by the Institutional Review Board of University of Miami. The objectives of this study were to evaluate the MDRO colonization rates among ITx recipients and to determine whether MDRO colonization had an impact on clinical outcomes. All adult patients who underwent ITx (isolated and multivisceral) between 1/2009 and 12/2015 were evaluated. Typically, a multivisceral transplant includes stomach, pancreaticoduodenal region, small bowel, liver with or without the colon and spleen; the liver is spared in modified multivisceral transplants. The perioperative prophylactic antibiotic protocol at our institution during the study period included cefepime 2 g IV every 12 h, metronidazole 500 mg IV every 8 h and vancomycin 10 mg/Kg IV every 12 h for three days. Levofloxacin 500 mg IV every 24 h was recommended instead of cefepime for patients with documented penicillin allergy. The immunosuppressive protocol included antithymocte globulin 3 mg/Kg on days 0 and 2, rituximab 375 mg/m^2 on day 1, methylprednisolone 500 mg IV on days 0, 1, and 2, and 20 mg IV on day 3. On 3/2013, the protocol was changed to antithymocte globulin 2 mg/Kg on days 0, 2, 4, and 8 and rituximab 150 mg/m^2 on day 1 for all ITx recipients. In addition, multivisceral transplant recipients received methylprednisolone 500 mg IV on day 0, 250 mg on days 1, 2, and 3, and modified multivisceral and isolated transplant recipients received methylprednisolone 500 mg IV on days 0, 1, 2, and 3, 250 mg IV on day 4, and basiliximab 40 mg IV every four weeks started on day 14 for three doses. A postoperative gut decontamination protocol was used for those patients who underwent ITx prior to 3/2013. It consisted in administering 15 ml of sterile water mixed with polymyxin B 125,000 IU, gentamicin 20 mg and amphotericin B 12.5 mg every 6 h until tolerating enteral or oral feeds.

MDRO colonization

Patients were considered colonized with MDRO if they had at least one positive surveillance culture for VRE, MRSA, or CR-GNB within six months from transplant. Our hospital protocol includes weekly surveillance in all the intensive care units (ICU) from the date of admission (which could precede the date of transplant). Rectal swabs were obtained to detect VRE colonization, nasal swabs to detect MRSA, and rectal and/or respiratory specimens (only for patients on mechanical ventilation) to detect CR-GNB colonization. The CR-GNB included were Enterobacteriaceae, *Pseudomonas,* and *Acinetobacter* species. Carbapenem resistance was determined by VITEK 2. From 2009 to 2010, modified Hodge test was used to confirm CR-GNB for those Enterobacteriaceae isolates with meropenem minimum inhibitory concentration (MIC) of 2–4 μg/ml. From 2011 on, modified Hodge test was no longer required as the MIC susceptibility breakpoints were lowered. The susceptibility breakpoints for meropenem MIC were lowered from <4 μg/ml to < 2 μg/ml in 2012 for *P. aeruginosa* and in 2014 for *Acinetobacter spp*. No molecular testing was used to detect VRE, CR-GNB, or MRSA during the study period. We evaluated whether there were any differences in the number of patients screened and number of specimens collected per patient to detect VRE, MRSA, and CR-GNB colonization. In addition, we determined the onset of colonization after ITx for those who initially had negative surveillance cultures. No outbreaks were detected for any of the pathogens of interest during the study period.

General characteristics

We assessed whether there were any differences in demographics (gender and age), underlying intestinal disease, type of ITx, antibiotic exposure, and hospitalizations within three months prior to transplant, and length of primary hospitalization and ICU stay after transplantation between patients colonized with MDRO and those who were not colonized.

Clinical outcomes during the first year post-transplant

We evaluated for VRE, CR-GNB, and MRSA bacteremia during the first year post-transplant for those patients colonized with VRE, CR-GNB, and MRSA, respectively, and for those who were not. In addition, we determined the rates of acute cellular rejection (grade II or grade III) and graft-versus-host disease (GVHD), and number of hospitalizations days and hospital readmissions within a year after transplant, and one year post-transplant survival between patients colonized with MDRO and those who were not colonized. The presence of central venous catheters was investigated for those who developed bacteremia. The location of the patients at the onset of bacteremia and bacteremia sources were also evaluated. It was considered community onset if admitted ≤ 48 h from blood cultures collection. The cases of rejection and GVHD were identified by reviewing all the biopsies results. The histological criteria for the identification of acute cellular rejection used in our Institution came from the results of the pathology workshop at the VIII International Small Bowel Transplant Symposium [7].

Statistical analyses

Chi-square and Fisher's exact tests were used as appropriate to assess bivariate associations between categorical variables; Student's *t*-test or Mann–Whitney test were used to compare continuous variables between groups, depending on normality of the distributions. A *P*-value <0.05 was considered significant.

Results

MDRO colonization

Number of patients screened and specimens obtained, and colonization rates

A total of 45 consecutive adult ITx patients were evaluated (Table 1). There were no differences in the number of patients screened for VRE [44(98%)] and for CR-GNB [40 (89%), $P = 0.20$] and MRSA [43 (96%), $P > 0.99$], and there were no differences either in the mean number of specimens obtained per patient to screen for VRE [4.9 ± 3.8] and for CR-GNB [4.2 ± 4.5, $P = 0.46$] and MRSA [5.6 ± 4.6, $P = 0.40$]. More patients were screened at the time of transplant for VRE [40 (89%)] than for CR-GNB [29 (64%), $P = 0.01$], but there was no difference for VRE and MRSA [41 (91%), $P > 0.99$].

Twenty-eight (62%) patients were colonized with MDRO [VRE in 22 (50%), MRSA in 7(16%), and CR-GNB in six (15%) patients]. Seven (16%) were colonized with more than one organism (VRE/CR-GNB and VRE/MRSA in three patients each and CR-GNB/MRSA in one). The species of the *Enterococcus* colonizers were not reported as part of our hospital protocol. The CR-GNB colonizers were *Pseudomonas aeruginosa* (three patients), *Klebsiella pneumoniae* (two patients), and *Acinetobacter baumannii* (one patient). *P. aeruginosa* was detected by respiratory culture in one patient and by rectal culture in the other two patients (no respiratory culture obtained in one of them). *K. pneumoniae* was detected by rectal and respiratory culture in one patient and by rectal culture in the other (no respiratory culture obtained), and *A. baumannii* was detected by rectal and respiratory cultures.

Timing of MDRO colonization with respect to ITx

Eight (36%) and five (71%) of the patients that screened positive for VRE and MRSA were already colonized by the time of transplant. In contrast, none of those who screened positive for CR-GNB were colonized at the time of ITx. Post-transplant colonization with VRE, CR-GNB, and MRSA, occurred in 14 (64%), six (100%), and two (29%) patients, respectively. Among those patients with post-transplant colonization, the median time from ITx to first positive surveillance culture for VRE, CR-GNB, and MRSA was 73.5 (range: 12–177), 56.5 (24–131), and 95.5 (62–129) days, respectively.

General characteristics

There were no differences in gender, age, underlying intestinal disorders and type of ITx between patients who were colonized with MDRO and those who were not (Table 1). There were no differences in antibiotic exposure within three months prior to ITx between MDRO-colonized and noncolonized patients. However,

Table 1. General characteristics.

Variables	MDRO-colonized N° 28(%)	Non-MDRO-colonized N° 17(%)	*P*-value
Gender (female)	18 (64)	8 (47)	0.26
Mean age (years)	43.9 ± 11	45 ± 15	0.78
Underlying Intestinal disorder			
Short gut resulted from prior surgery	12 (43)	6 (35)	0.62
Ischemic	9 (32)	7 (41)	0.54
Tumor	5 (18)	3 (18)	>0.99
Dysmotility	2 (7)	1 (6)	>0.99
Type of intestinal transplant			
Multivisceral	11 (39)	11 (65)*	0.10
Isolated	10 (36)	5 (29)†	0.66
Modified multivisceral	7 (25)	1 (6)	0.13
Recent antibiotics	11 (39)	5 (29)	0.50
Vancomycin	9 (32)	3 (18)	0.49
3rd or 4th generation cephalosporin	6 (21)‡	1 (6)§	0.23
Carbapenems	1 (4)¶	1 (6)**	>0.99
Extended-spectrum penicillin	4 (14)††	3 (18)‡‡	>0.99
Aztreonam	0	0	>0.99
Tigecycline	0	0	>0.99
Quinolones	3 (11)§§	2 (12)¶¶	>0.99
Days of antibiotics	9.9 ± 8.6	17.8 ± 13.8	0.19
≥ 2 antibiotic classes	7 (25)	4 (24)	>0.99
Recent hospitalizations	22 (79)	8 (47)	0.03
Length of primary hospitalization	56.7 ± 40.9	53.1 ± 60	0.81
Length of ICU stay	15.6 ± 22.5	14.3 ± 15.8	0.85

MDRO, multidrug-resistant organisms; ICU, intensive care unit.

*Three patients had a kidney transplant performed at the same time.

†One patient had the intestinal transplant for the second time.

‡Five patients received cefepime and one ceftriaxone.

§Received ceftriaxone and cefepime.

¶Received meropenem and ertapenem.

**Received only meropenem.

††Three received piperacillin–tazobactam and one received ampicillin-sulbactam.

‡‡Two received piperacillin–tazobactam and one received ampicillin-sulbactam.

§§Three received levofloxacin.

¶¶One received levofloxacin and the other patient received levofloxacin and ciprofloxacin.

colonized patients were more likely to have been hospitalized within three months prior to transplant [22 (79%) vs. 8 (47%), $P = 0.03$] (Table 1). There were no differences in length of primary hospitalization and ICU stay after transplantation between both groups (Table 1). Five colonized and six noncolonized patients died during their primary hospitalization after transplantation. They died at days 2, 10, 58, 82, and 187, and 1 (three patients), 75, 79, and 130, respectively. Note that three patients in the noncolonization group were not included in the ICU stay analysis as they were not admitted to the ICU (they died in the operative room).

Clinical outcomes during the first year post-transplant

VRE, CR-GNB, and MRSA bacteremia

VRE and CR-GNB bacteremia were more frequent among those patients colonized with VRE and CR-GNB, respectively, compared to those who were not [VRE: 8/22 (36%) vs. non-VRE: 1/23 (4%), $P = 0.009$, and CR-GNB: 4/6 (67%) vs. non-CR-GNB: 2/39 (5%), $P = 0.001$]. All the cases of VRE bacteremia were due to *E. faecium* (Table 2). CR-GNB bacteremia in the CR-GNB-colonized patients was only due to the bacteria they were colonized with except for the patient

colonized with *A. baumannii* who had *A. baumannii* and *A. iwoffii* bacteremia (Table 2). The ICU was the most common location at the onset of bacteremia, all patients but one had central venous catheters at the time of bacteremia, and the source of bacteremia was unclear in seven of the cases, due to central line-associated bloodstream infection (CLABSI) in four, bowel ischemia in two and due to peritonitis, urinary tract infection and septic arthritis in one case each (Table 2). The median time from colonization to VRE and CR-GNB bacteremia were 61 days (range: 4–101) and 64.5 days (36–93), respectively.

The rates of VRE and CR-GNB bacteremia were not different between patients who received postoperative gut decontamination and the older immunosuppressive protocol and those who received the newer immunosuppressive protocol [5/14 (36%) vs. 4/31 (13%), $P = 0.11$ and 3/14 (21%) vs. 3/31 (10%), $P = 0.36$], respectively.

Acute cellular rejection and GVHD

There was no difference in acute cellular rejection (grade II or III) between patients colonized with MDRO and those who were not [8 (29%) vs. 2 (12%), $P = 0.28$]. Three patients had grade II and five patients had grade III rejection among the MDRO-colonized patients, and one patient had grade II and one had grade III rejection among the noncolonized patients. There was no difference either in the rates of GVHD between MDRO-colonized and not colonized patients [6 (21%) vs. 4 (24%), $P > 0.99$].

Number of hospitalization days and hospital readmissions within a year post-transplant and one year post-transplant survival

There was a trend toward more hospitalizations days within a year after ITx among those who were colonized with MDRO compared to those who were not (122.9 ± 68.2 vs. 79.6 ± 72.4 days, $P = 0.05$). MDRO-colonized patients were more likely to be readmitted during the first year post-transplant compared to those who were not. However, it did not reach statistical significance (4.6 ± 3.1 vs. 3.2 ± 2, $P = 0.18$). Please note that the five colonized and six noncolonized patients who died during the primary hospitalization were not included in this analysis. There was no difference in one-year survival between patients colonized with MDRO and those who were not [16 (57%) vs. 11 (65%), $P = 0.62$]. However, survival was lower among MDRO-colonized patients who developed bacteremia due to VRE, CR-GNB, or MRSA compared to colonized patients who did not, [2/11(18%) vs. 15/17(88%), $P < 0.001$].

Discussion

To the best of our knowledge, this is the first study to report rates of colonization with MDRO in ITx recipients. It is concerning that more than 60% of our screened patients were colonized with either VRE, MRSA, or CR-GNB. VRE was the most commonly isolated organism, colonizing half of our patients. In addition, the rates of MDRO colonization found in this population may be an underestimate as outpatients or hospitalized patients outside of the intensive care units were not screened (all ITx recipients are immediately hospitalized in the surgical intensive care unit post-transplant for three days or longer as needed). For the purpose of this study, we only included VRE, MRSA, and CR-GNB as MDRO. We did not consider other MDRO such as extended-spectrum beta-lactamases (ESBL)-producing organisms as our infection control program does not screen for those. In our institution (inpatient setting, including intensive care units), 77% of the *E. faecium* isolates in 2010 and 69% in 2014 were VRE, 53% of the *S. aureus* isolates in 2010 and 48% in 2014 were MRSA, and 1% and 3% of the *K. pneumoniae*, 14% and 15% of the *P. aeruginosa,* and 52% and 40% of the *A. baumannii* isolates were carbapenem-resistant in 2010 and 2014, respectively [data not published].

Consistent with prior reports in nontransplant patients [6], our study showed that recent hospitalization is a risk factor for MDRO colonization. Recent antibiotic exposure is another known risk factor [8–10]. However, it was not demonstrated in our study likely due to its small size.

We observed that VRE and CR-GNB-colonized patients were more likely to develop VRE and CR-GNB bacteremia, respectively, compared to patients who were not colonized with these bacteria. These findings are consistent with previous reports [4–6]. VRE colonization leading to infection is less frequent in kidney transplant recipients [11]. The source of bacteremia was unclear in seven (44%) of the cases. Gut translocation could have been a possible source in some of them. Four of the cases were due to CLABSI meeting the National Healthcare Safety Network definition [12]. Our hospital policy in CLABSI prevention during the study period consisted in hand hygiene by washing hands for a minimum of 15 seconds or using an

Table 2. Bacteremia due to VRE, CR-GNB, and MRSA in colonized and noncolonized patients

Bacteremia	Susceptibility profile	Colonizer	# days (colonization-bacteremia)	Onset	Venous catheters (# lumens)	Source
VRE (*Enterococcus faecium*)	S to LZD and DAP	VRE	N/A*,†	ICU	IJ (4)	Unclear
VRE (*E. faecium*)	S to LZD and DAP	VRE	21	Floor	PICC (3)	CLABSI
VRE (*E. faecium*)	S to LZD and DAP	VRE	66	Floor	Port-a-cath (1), PICC (3)	Unclear
VRE (*E. faecium*)	S to LZD and DAP	VRE	9	ICU	PICC (2), Hickman‡	Unclear
VRE (*E. faecium*)	S to LZD§	VRE	101	Community	PICC‡	CLABSI
VRE (*E. faecium*)	S to LZD, R to DAP [MIC 8 μg/ml]	VRE	61	ICU	PICC (2)	Unclear
VRE (*E. faecium*)	S to LZD and DAP	VRE	82	Community	IJ (2)	Unclear
VRE (*E. faecium*)	S to LZD, R to DAP [MIC 8 μg/mL]	VRE	4	ICU	IJ and PICC‡	Bowel ischemia
VRE (*E. faecium*)	S to LZD, R to DAP [MIC 6 μg/mL]	Not colonized	N/A	ICU	PICC (2), IJ (3)	Unclear
Acinetobacter baumannii	S to CST	*A. baumannii*	93	Floor	Hickman‡	UTI
Pseudomonas aeruginosa	S to CST, GEN, TOB, AMI	*P. aeruginosa*	N/A*,¶	ICU	IJ (3)	CLABSI
Klebsiella pneumoniae	S to AMI**	*K. pneumoniae*	N/A*,††	ICU	PICC (1), IJ (4)	Peritonitis
K. pneumoniae	S to CST, GEN	*K. pneumoniae*	36	ICU	IJ‡	CLABSI
K. pneumoniae	S to AMI**	Not colonized	N/A	ICU	PICC and Femoral‡	Septic hip arthritis
K. pneumoniae	S to AMI, GEN**	Not colonized	N/A	Community	None	Bowel ischemia
MRSA	S to LZD/DAP not reported	MRSA	297	Outside hospital	IJ‡	Unclear

VRE, vancomycin-resistant *Enterococcus*; CR-GNB, carbapenem-resistant Gram-negative bacteria; MRSA, methicillin-resistant *Staphylococcus aureus*; S, susceptible; LZD, linezolid; DAP, daptomycin; N/A, not applicable; ICU, intensive care unit; IJ, internal jugular; PICC, peripherally inserted central catheter, CLABSI, central line-associated bloodstream infection; R, resistant; MIC, minimum inhibitory concentration; CST, colistin, GEN, gentamicin, TOB, tobramycin; AMI, amikacin.

*Bacteremia prior colonization.

†Not screened for VRE during the preceding two months.

‡Unclear number of lumens.

§DAP susceptible not checked.

¶Not screened for CR-GNB during the preceding two months.

**CST susceptibility not checked.

††Rectal screening negative five days prior bacteremia.

alcohol-based waterless hand cleaner and rubbing hands until dry, maximal barrier precautions by having the operator and assistants wearing cap, mask, sterile gown, and gloves and the patient covered from head to toe with a sterile drape, with a small opening for the site of insertion, optimal catheter site selection (the subclavian line site was preferred for nontunneled catheters), skin antisepsis with 2% chlorhexidine, and daily review of line necessity. In addition, all personnel who inserted/observed insertion of a central venous catheter were required to complete an online educational module.

Infections with MDRO are associated with poor outcomes in SOT recipients. Liver transplant candidates and recipients with VRE infections have an increased risk of death [13]. *S. aureus* infections were associated with a significant shorter survival in a study including small bowel and multivisceral transplant recipients [14]. 18% of SOT (mostly liver or intestinal) recipients with CR-*Klebsiella pneumoniae* bacteremia died of septic shock [15]. Our study showed lower one year post-transplant survival among those MDRO-colonized patients who developed bacteremia.

This study has limitations. Our data was generated in a relatively small cohort which could have prevented from achieving statistically significance in some of the analyses. Larger studies are also needed to analyze isolated and multivisceral transplant recipients separately as their mortality rates and risk for infection may be different. We did not collect infection data other than bacteremia so we probably underestimated the risk of infection following colonization. Prospective studies evaluating at all types of infections are needed. We reported the data from a single institution so our results may not apply to other institutions which may have different rates of MDRO, surgical techniques, immunosuppression and antimicrobial prophylaxis protocols. Despite these limitations, our observations provide novel insights into the rates of MDRO colonization and associated clinical outcomes among ITx recipients at one of the largest transplant centers performing ITx in the US.

In conclusion, MDRO, especially VRE, colonization was common among our ITx patients. VRE and CR-GNR bacteremia was more common among VRE and CR-GNB-colonized patients, respectively, and 1-year survival was lower among MDRO-colonized patients who developed bacteremia.

Authorship

JS: performed study design, data analysis/interpretation, drafting article, and critical revision of article. MIM, JFC and LMA: performed data analysis/interpretation and critical revision of article. RV and TB: performed critical revision of article.

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Conflict of interest

The authors of this manuscript have no conflict of interests to disclose.

REFERENCES

1. Organ procurement and transplantation Network. National Data. https://optn.transplant.hrsa.gov/data/view-data-reports/national-data/. Accessed on February 23, 2017
2. Silva JT, San-Juan R, Fernández-Caamaño B, *et al.* Infectious complications following small bowel transplantation. *Am J Transplant* 2016; **16**: 951.
3. Ventola CL. The antibiotic resistance crisis: part 1: causes and threats. 2015; **40**: 277.
4. Ziakas PD, Pliakos EE, Zervou FN, Knoll BM, Rice LB, Mylonakis E. MRSA and VRE colonization in solid organ transplantation: a meta-analysis of published studies. *Am J Transplant* 2014; **14**: 1887.
5. Huprikar S, Casner L, Pouch S, *et al.* Prior infection or colonization with carbapenem-resistant enterobacteriaceae is not an absolute contraindication for solid organ transplantation. *American Transplant Congress* 2016; [Abstract 161].
6. Giannella M, Bartoletti M, Morelli MC, *et al.* Risk factors for infection with carbapenem-resistant *Klebsiella pneumoniae* after liver transplantation: the importance of pre- and posttransplant colonization. *Am J Transplant* 2015; **15**: 1708.
7. Ruiz P, Bagni A, Brown R, *et al.* Histological criteria for the identification of acute cellular rejection in human small bowel allografts: results of the pathology workshop at the VIII International Small Bowel Transplant Symposium. *Transplant Proc* 2004; **36**: 335.
8. Nseir S, Grailles G, Soury-Lavergne A, Minacori F, Alves I, Durocher A. Accuracy of American Thoracic Society/Infectious Diseases Society of America criteria in predicting infection or colonization with multidrug-resistant bacteria at intensive-care unit admission. *Clin Microbiol Infect* 2010; **16**: 902.
9. Safdar N, Maki DG. The commonality of risk factors for nosocomial colonization and infection with antimicrobial-resistant Staphylococcus aureus, enterococcus, gram-negative bacilli, Clostridium

difficile, and Candida. *Ann Intern Med* 2002; **136**: 834.
10. Banach DB, Peaper DR, Fortune BE, Emre S, Dembry LM. The clinical and molecular epidemiology of pre-transplant vancomycin-resistant enterococci colonization among liver transplant recipients. *Clin Transplant* 2016; **30**: 306.
11. Bucheli E, Kralidis G, Boggian K, Swiss Transplant Cohort Study, *et al.* Impact of enterococcal colonization and infection in solid organ transplantation recipients from the Swiss transplant cohort study. *Transpl Infect Dis* 2014; **16**: 26.
12. The Centers for Disease Control and Prevention (CDC). National healthcare safety network. https://www.cdc.gov/nhsn/index.html. Accessed on April 21, 2017.
13. Russell DL, Flood A, Zaroda TE, *et al.* Outcomes of colonization with MRSA and VRE among liver transplant candidates and recipients. *Am J Transplant* 2008; **8**: 1737.
14. Florescu DF, Qiu F, Vivekanandan R, Mercer DF, Langnas AN, Kalil AC. Risk factors and outcomes of Staphylococcus aureus infections after small bowel and multivisceral transplantation. *Pediatr Infect Dis J* 2012; **31**: 25.
15. Clancy CJ, Chen L, Shields RK, *et al.* Epidemiology and molecular characterization of bacteremia due to carbapenem-resistant *Klebsiella pneumoniae* in transplant recipients. *Am J Transplant* 2013; **13**: 2619.