Colonization With Multiresistant Bacteria: Impact on Ventricular Assist Device Patients

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Background. **Although the effect of infections with multidrug-resistant bacteria (MDRB) in left ventricular assist device (LVAD) recipients is well characterized, the influence of perioperative colonization on the development of infections in this patient cohort remains unknown. The study evaluated the effect of MDRB colonization on patient outcomes after LVAD implantation.**

Methods. **We retrospectively analyzed the microbiological screening studies of nasal, throat, wound, and rectal swabs in 82 consecutive patients who received an LVAD at our center between 2010 and 2015. Four categories of MDRB were determined: methicillin-resistant *Staphylococcus aureus*, vancomycin-resistant *Enterococcus*, and Gram-negative bacterium resistant to three or four of four predefined pharmacologic categories of antibiotics. We also compared the long-term outcome of patients with and without colonization.**

Results. **There were 28 patients (34.1%) diagnosed as being colonized with at least 1 species of an MDRB. MDRB colonization was associated with the occurrence of fatal infections from any pathogen (MDRB positive, 63.2%; MDRB negative, 34.4%; $p = 0.04$) and fatal MDRB-specific infections (MDRB positive, 31.6%; MDRB negative, 6.3%; $p = 0.04$), significantly longer intensive care unit stay ($p < 0.0001$), and longer cumulative hospital stay ($p = 0.04$).**

Conclusions. **Our study demonstrates that the colonization with MDRB is a highly prevalent risk factor for infection-associated death in the vulnerable LVAD population. Routine screening for MDRB before and after LVAD implantation should be considered to identify high-risk individuals and facilitate effective prevention of infectious complications.**

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Long-term mechanical circulatory support with implantation of a left ventricular assist device (LVAD) is an established treatment for selected patients with advanced heart failure. This improves survival and quality of life compared with conventional therapy [1]. Device-associated adverse events are, however, a source of substantial morbidity and death. Among them, infections represent serious complications and are associated with prolonged hospitalizations, multisystem organ failure, and increased death and incremental costs. [2–4]. Eradication of infections is extremely challenging and often necessitates complex surgical therapy or even device exchange in addition to prolonged courses of antimicrobial therapy. Despite the significant reduction in observed rates after the introduction of the new generation of continuous-flow systems [5, 6], infections still remain a great concern as the duration of support extends and the patient profiles are changing in the era of destination therapy.

Previous studies identified Gram-positive cocci, particularly *Staphylococcus* and *Enterococcus* species, and Gram-negative rods, with a predominance of *Pseudomonas* species, as major culprits of LVAD-associated infections [2, 3, 7, 8]. Interestingly, an increased prevalence of multidrug-resistant bacteria (MDRB) was reported [9–11], which may further contribute to the complexity of treatment and negatively influence survival. Previous reports on other patient groups, such as transplant candidates, suggest a significant effect of MDRB colonization on the incidence of subsequent MDRB infections [12–16]. Although attention has been drawn to the strict adherence to aseptic techniques, driveline care, and the nutritional and metabolic status of the patients, the potential influence of colonization with MDRB on the development of infections in LVAD patients and their temporal relationship are unknown. The purpose of this study was to evaluate the prevalence of MDRB

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Abbreviations and Acronyms

CCM	= cardiac contractility modulation
COPD	= chronic obstructive pulmonary disease
CRT	= cardiac resynchronization therapy
ICD	= implantable cardioverter defibrillator
ICU	= intensive care unit
INTERMACS	= Interagency Registry for Mechanically Assisted Circulatory Support
LVAD	= left ventricular assist device
MDRB	= multidrug-resistant bacteria
3MRGN/4MRGN	= Gram-negative resistant to three or four of four categories of antibiotics
MRSA	= methicillin-resistant *Staphylococcus aureus*
NYHA	= New York Heart Association
PAP	= pulmonary artery pressure
PVR	= pulmonary vascular resistance
VRE	= vancomycin-resistant *Enterococcus*

colonization among LVAD recipients during the perioperative period and its association with infection-related death and all-cause death. We further investigated the association of the colonization status with intensive care unit (ICU) and hospital length of stay as well as the infection and hospitalization rates in the ensuing 12 months.

Patients and Methods

We retrospectively reviewed the LVAD database and digital reports of our heart failure clinic to identify consecutive adult patients who received an LVAD at our institution from January 2010 through April 2015. Patients were selected for LVAD implantation after an interdisciplinary evaluation of disease status and the preoperative diagnostic procedures were completed. All individuals received the continuous-flow HVAD (HeartWare, Framingham, MA). The Institutional Review Board approved the study.

Microbiological screening tests were conducted for all patients according to our institutional protocol, which complies with the national guidelines for prevention of MDRB colonization in medical and nursing facilities. Microbial cultures of nasal, throat, and rectal swabs were conducted within 24 hours of admission and repeated preoperatively, if implantation and admission were more than 2 weeks apart, to test for carriage of MDRB and provide antimicrobial susceptibility. Repeated sampling of all the above-mentioned sites and the driveline exit site was additionally performed during the postoperative stay at the ICU and on every subsequent internal ward change up to discharge or in clinician-determined intervals in case of a very long hospitalization. Thus, for every patient, at least two sets of microbiological screening data were available for analysis, one obtained preoperatively and one postoperatively. The following categories of MDRB were determined depending on the antibiotic resistance:

1. Methicillin-resistant *Staphylococcus aureus* (MRSA)
2. Vancomycin-resistant *Enterococcus* (VRE)
3. Multiresistant Gram-negative (MRGN) bacterium resistant to three of four predefined pharmacologic categories of antibiotics but susceptible to carbapenems (3MRGN)
4. MRGN bacterium resistant to all four categories of antibiotics or to three categories including carbapenems (4MRGN)

The four classes of antibiotics for the MRGN classification included acylureidopenicillins, third- and fourth-generation cephalosporins, fluoroquinolones, and carbapenems. Resistance was attributed based on the susceptibility to the representative antibiotic from each category; that is, piperacillin, ceftazidime or cefotaxime, ciprofloxacin, and imipenem or meropenem. In case of a positive result, in addition to basic hygienic measures, contact precautions (isolation, barrier nursing) were applied to prevent further contamination.

Infections were classified as LVAD-specific, LVAD-related, or non-LVAD, conforming with the consensus definitions proposed by the International Society for Heart and Lung Transplantation [17]. LVAD-specific infections include infections of the implanted device components or the tissues surrounding them; for example, pump infections, cannula infections, and driveline infections. LVAD-related infections refer to those that can also occur in non-LVAD patients and include infective endocarditis, blood stream infections, mediastinitis, and sternal wound infection, and non-LVAD infections refer to infections that are not related to the LVAD presence such as respiratory tract infections, *Clostridium difficile* infections, and urinary tract infections. An MDRB infection was diagnosed if an MDRB was isolated from the infection sites or blood. Hospitalizations concerned documented inpatient treatments for acute medical or surgical conditions after discharge from the index hospitalization.

Continuous variables are summarized as means (standard deviations), unless indicated otherwise, and categoric variables as counts (percentages). Continuous data were evaluated for normality of distribution using the Shapiro-Wilk test. The two-sided t test was used for comparison of continuous, normally distributed data, otherwise the Mann-Whitney U test was used. The χ^2 test and Fisher exact test were used for testing association between two categoric variables. Kaplan-Meier analysis was conducted to estimate survival for the different groups of patients, and the Cox proportional hazards regression analysis was implemented to test for possible covariate associations. Differences in survival distribution between groups were determined with the log-rank test. Patients were censored at the time of transplant, explantation for recovery, follow-up discontinuation, or by the