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TRANSPLANT INFECTIOUS DISEASE

BRIEF COMMUNICATION

Vancomycin-resistant *Enterococcus* outbreak in a pre- and post-cardiothoracic transplant population: Impact of discontinuing multidrug-resistant organism surveillance during the coronavirus disease 2019 pandemic

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Abstract

Introduction: Many institutions suspended surveillance and contact precautions for multidrug-resistant organisms (MDROs) at the outset of the coronavirus disease 2019 (COVID-19) pandemic due to a lack of resources. Once our institution reinstated surveillance in September 2020, a vancomycin-resistant *Enterococcus* (VRE) *faecium* outbreak was detected in the cardiothoracic transplant units, a population in which we had not previously detected outbreaks.

Methods: An outbreak investigation was conducted using pulsed-field gel electrophoresis for strain typing and electronic medical record review to determine the clinical characteristics of involved patients. The infection prevention (IP) team convened a multidisciplinary process improvement team comprised of IP, cardiothoracic transplant nursing and medical leadership, environmental services, and the microbiology laboratory.

Abbreviations: COVID-19, coronavirus disease 2019; CTICU, cardiothoracic transplant intensive care unit; CTSDU, cardiothoracic transplant stepdown unit; ECMO, extracorporeal membrane oxygenation; EMR, electronic medical record; EVS, environmental services; Heme/Onc/SCT, hematologic/oncologic/stem cell transplant; ICU, intensive care unit; IP, infection prevention; IRB, Institutional Review Board; LOS, length of stay; LVAD, left ventricular assist device; MDRO, multidrug-resistant organism; MICU, medical intensive care unit; MPIT, multidisciplinary process improvement team; PFGE, pulsed-field gel electrophoresis; PPE, personal protective equipment; SOT, solid organ transplant; VAD, ventricular assist device; VRE, vancomycin-resistant *Enterococcus*; VSE, vancomycin-susceptible *enterococci*; VV ECMO, veno-venous extracorporeal membrane oxygenation.

Results: Between December 2020 and March 2021, the outbreak involved thirteen patients in the cardiothoracic transplant units, four index cases, and nine transmissions. Of the 13, seven (54%) were on the transplant service, including heart and lung transplant recipients, patients with ventricular assist devices, and a patient on extracorporeal membrane oxygenation as a bridge to lung transplantation. Four of 13 (31%) developed a clinical infection.

Discussion: Cardiothoracic surgery/transplant patients may have a similar risk for VRE-associated morbidity as abdominal solid organ transplant and stem cell transplant patients, highlighting the need for aggressive outbreak management when VRE transmission is detected. Our experience demonstrates an unintended consequence of discontinuing MDRO surveillance in this population and highlights a need for education, monitoring, and reinforcement of foundational infection prevention measures to ensure optimal outcomes.

KEYWORDS
VRE outbreak, COVID-19 pandemic, heart transplant, lung transplant, ventricular assist device, extracorporeal membrane oxygenation

1 | INTRODUCTION

Due to anticipated personnel, personal protective equipment (PPE), and testing shortages, many institutions suspended multidrug-resistant organism (MDRO) surveillance early in the coronavirus disease 2019 (COVID-19) pandemic.[1–3] At our institution, surveillance and contact precautions for vancomycin-resistant *Enterococcus faecium* (VRE) were suspended for all but the hematologic/oncologic/stem cell transplant (Heme/Onc/SCT) and abdominal solid organ transplant (SOT) populations, where we had previously detected outbreaks. In September 2020, we reinstituted VRE surveillance and contact precautions in the medical intensive care unit (MICU), the cardiothoracic transplant intensive care unit (CTICU), and the cardiothoracic transplant stepdown unit (CTSDU).

The CTICU and CTSDU house cardiac, thoracic, and vascular surgical patients including heart and lung transplant recipients, and patients requiring advanced heart/lung failure circulatory support, namely ventricular assist devices (VADs) and extracorporeal membrane oxygenation (ECMO) as a bridge to lung transplantation. During the pandemic, patients with severe COVID-19 lung injury had extended stays for ventilator and ECMO support in these units. This was a significant change in the patient population on these units, resulting in a longer length of stay (LOS) for certain patients compared to pre-pandemic. We had not previously detected VRE outbreaks in this population at our institution, and existing literature primarily describes VRE-associated morbidity in the Heme/Onc/SCT and abdominal SOT populations.[4,5] VRE outbreaks in the cardiothoracic transplant population have not been prominently featured in the literature.

Once MDRO surveillance was reinstituted, we quickly detected a VRE outbreak involving both the CTICU and CTSDU. This study describes the outbreak, the infection control measures implemented, and the lessons learned from the pandemic-prompted discontinuation of MDRO surveillance in the cardiothoracic transplant population.

2 | METHODS

2.1 | The institution

Northwestern Memorial Hospital is a 943-bed academic medical center in Chicago, IL. The Northwestern University Institutional Review Board (IRB) reviewed this study and deemed it exempt from IRB review.

2.2 | MDRO surveillance

Prior to the pandemic, the Heme/Onc/SCT, abdominal SOT, CTSDU, and all adult intensive care units (ICUs) conducted VRE surveillance rectal swabs upon admission and weekly. VRE surveillance was suspended in all areas except Heme/Onc/SCT and abdominal SOT units in March 2020 due to an anticipated shortage of resources. VRE surveillance was reinstituted in September 2020 in populations deemed at higher risk for VRE colonization and infection including the CTICU, CTSDU, and MICU.

2.3 | VRE culturing

VRE surveillance screening was performed using VACC Media (Thermo Fischer Scientific, Lenexa, KS). All isolate identifications were performed using the Vitek MS system (bioMérieux, Balmes-les-Grottes,

France). Vancomycin resistance was confirmed using Kirby-Bauer disc diffusion or the Vitek 2 system according to Clinical and Laboratory Standards Institute guidelines.

2.4 | Pulsed-field gel electrophoresis typing

Pulsed-field gel electrophoresis (PFGE) was performed according to previously published methodologies.[6] Genomic preparations were digested and run on the Chef Mapper System (BioRad, Hercules, CA) for 18.5 h, with switch times of 1.0 and 12.0 s. Sma1 restriction enzyme was used to digest the genomic DNA (New England Biolabs, Ipswich, MA). Genetic similarities of intra-patient isolates were determined by visual inspections of DNA banding patterns using the criteria of Tenover et al.[7] with isolates having three or fewer differing bands labeled as closely related, those with four to six differing bands possibly related, and those with more than six differing bands genetically distinct. VRE isolates are routinely identified from surveillance screening and clinical cultures within three days of specimen collection. Strain typing results within one to two weeks of culturing.

2.5 | VRE management

Every patient admitted to the CTICU and CTSDU is screened for VRE upon admission. If the culture is positive, contact isolation precautions require a gown and gloves to be worn when inside the room; if negative, a best practice advisory populates in the electronic medical record (EMR) prompting an order for a weekly screen. All patient rooms in both units are single rooms with a single toilet.

2.6 | Definitions

VRE colonization was defined as a positive culture from a rectal specimen, and VRE infection as a positive culture from any non-rectal specimen. An outbreak was defined as three or more patients with VRE isolated from clinical or surveillance rectal samples whose epidemiology indicated shared time, space, and/or healthcare providers and whose PFGE strain types were related.[7] An index case was defined as: (1) the first patient with a particular PFGE type or (2) a patient who did not share time and space with the first patient with the same strain type but did with a subsequently positive patient. A PFGE strain type was designated an outbreak strain type when three or more transmissions were attributed to the same strain type. Outbreak resolution was defined as four consecutive weeks without a VRE transmission from both units.

2.7 | Outbreak investigation

Clinical characteristics determined through EMR review included demographics, LOS prior to VRE detection, COVID-19 disease, admitting service, VRE risk factors, VRE colonization versus infection, and adverse outcomes from VRE infection. The infection prevention (IP) team convened a multidisciplinary process improvement team (MPIT) comprised of IP, CTICU and CTSDU clinical leadership, Environmental Services (EVS), and the microbiology laboratory.

3 | RESULTS

3.1 | VRE surveillance and outbreak investigation

Once VRE surveillance was reinstituted in the CTICU and CTSDU, screening compliance rates reached pre-pandemic levels (95% and 80%, respectively) within six weeks. There was a subsequent increase in VRE colonization and infection rates (Figure 1A). The VRE colonization rates in the CTICU and CTSDU pre-pandemic in the calendar year 2019 were 103.3 and 48.9 cases per 10 000 patient-days, respectively. The VRE infection rates in the CTICU and CTSDU in the same time period were 4.7 cases per 10 000 patient-days and 0. The VRE infection rates in CTICU and CTSDU while surveillance was suspended between March and September 2020 were 9.4 and 4.2 cases per 10 000 patient-days, respectively. In comparison, the colonization rates in CTICU and CTSDU during the study period were 157.5 and 91.4 cases per 10 000 patient-days, respectively. The VRE infection rates in the CTICU and CTSDU during the study period were 26.2 and 9.5 cases per 10 000 patient-days, respectively. Between December 2020 and March 2021, the outbreak involved 13 patients, four index cases, and nine transmissions (Figure 1B). Six transmissions occurred in CTICU, and three in CTSDU. Of the 13, seven (54%) were on the transplant service: post-heart transplant ($n = 2$), post-lung transplant ($n = 2$), left ventricular assist device ($n = 2$), and ECMO as bridge to lung transplantation ($n = 1$) (Table 1). The remaining six were post-surgical patients without advanced heart/lung failure circulatory support. All 13 initially had VRE rectal colonization. Four (31%) developed clinical infection: one transplant evaluation, two cardiac surgery, and one vascular surgery, as follows: (1) VRE bacteremia and intraabdominal abscess, (2) infected abdominal wound and sacral decubitus ulcer, (3) VRE bacteremia and infected leg stump, and (4) mediastinal wound infection. All four required surgical debridement. Of these four, three expired due to factors unrelated to their VRE infection. Notable VRE risk factors in this cohort included hemodialysis (46%), cardiothoracic surgery (77%), a central venous catheter (92%) and urinary catheter (54%) placement, and prior vancomycin and cephalosporin use (100%). Two (15%) patients had prior COVID-19 infection and extended LOS in the CTICU for 36 and 62 days, respectively. The average LOS for cardiac surgery patients in the CTICU and CTSDU is 17.6 and 8.5 days, respectively. Similarly, the average LOS for thoracic surgery patients in the CTICU and CTSDU is 33.4 days and 7.9 days, respectively. The outbreak was comprised of two distinct PFGE strain types.

3.2 | Outbreak interventions

The MPIT convened on March 16, 2021, consisting of key stakeholders from IP, CTICU, CTSDU clinical leadership, EVS, and microbiology

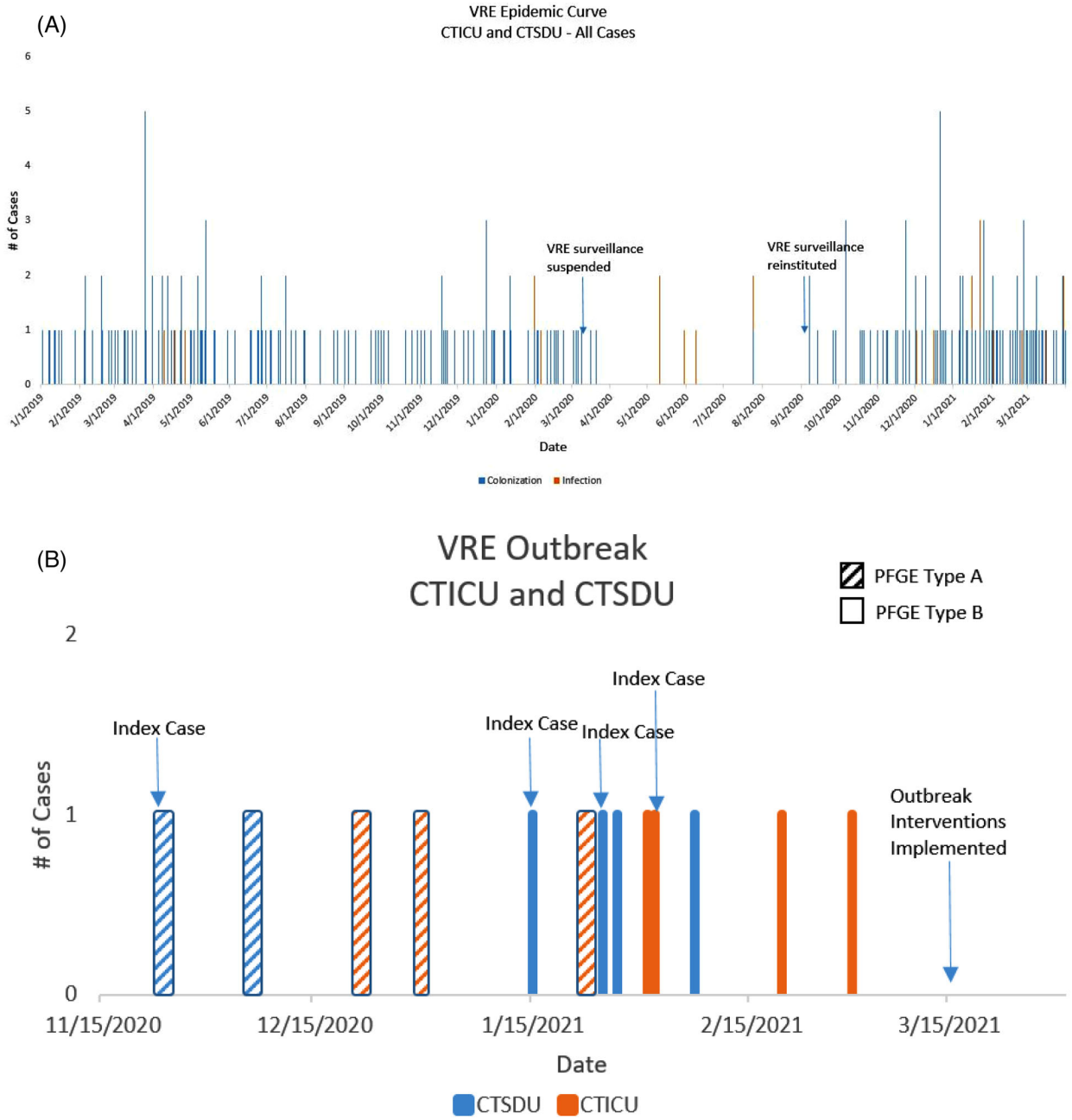

FIGURE 1 (A) All vancomycin-resistant Enterococcus (VRE) cases from January 2019 through the end of the study period (March 2021). (B) The epidemic curve during the study period

laboratory. The MPIT met weekly to review outbreak data and recommendations and disseminated findings to all relevant stakeholders.

MPIT action items including education regarding outbreak epidemiology, hand hygiene, PPE, and environmental cleanliness were organized by task and responsible party. Daily interventional hand hygiene and PPE compliance audits were performed by IP and unit leadership. CTICU improved from 56% to 80% hand hygiene compliance and CTSDU from 75% to 85% after four weeks. VRE rectal swab screening was tracked to ensure compliance. Efforts to determine environmental bioburden after room discharge using the 3M™ Clean-Trace™ Luminometer LX25 (Saint Paul, MN), and cleaning of shared patient equipment with PDI Super Sani-Cloth Germicidal Disposable Wipes (Woodcliff Lake, NJ) were enhanced. Clinical leadership ensured only essential personnel entered rooms of VRE-positive patients with a maximum of four team members during daily rounding. Medical, nursing, and advanced practice provider leadership owned an accountability plan to address repeated noncompliance. CTICU and CTSDU leadership collaborated with IP to implement sustainable IP measures, particularly around the ECMO population with extended LOS. Stricter cleaning and disinfection schedules were implemented for ECMO machines (Cardiohelp system, Wayne, NJ) and heater-cooler devices (CardioQuip MCH-1000, College Station, TX) in adherence with the manufacturers' instructions for use. The outbreak was resolved on April 14, 2021, after four weeks.

TABLE 1 Characteristics and outcomes of the 13 patients involved in the outbreak

Demographics	
Age in years, median (IQR)	67 (55,73)
Sex at birth	
Male	10 (77)
Race and ethnicity	
White/Not Hispanic or Latino	9 (69)
Black or African American/Not Hispanic or Latino	2 (15)
Other/Not Hispanic or Latino	1 (8)
White/Declined	1 (8)
COVID-19 disease status	
Prior history	2 (15)
Diabetes Mellitus, Type I	0 (0)
Diabetes Mellitus, Type II	5 (38)
Hemodialysis	6 (46)
Hospitalizations within prior 90 days	5 (38)
Length of Stay (days)	
Total length of stay at the hospital, median (IQR)	45 (33,81)
Length of stay at the hospital prior to VRE detection, median (IQR)	24 (16,36)
Total length of stay in CTICU, median (IQR)	13 (10,32)
Length of stay in CTICU prior to VRE detection, median (IQR)	12 (8,16)
Total length of stay in CTSDU, median (IQR)	11 (7,16)
Length of stay in CTSDU prior to VRE detection, median (IQR)	4 (2,9)
Admitting Service	
Cardiac Surgery	7 (54)
OHT recipient	2 (29)
OHT + kidney recipient	1 (50)
LVAD patient	1 (14)
Pre-kidney transplant patient	2 (29)
Thoracic Surgery	4 (31)
BOLT recipient	2 (50)
VV ECMO patient	1 (25)
Pre-lung + kidney transplant patient	1 (100)
Cardiology/Heart Failure	1 (8)
LVAD patient	1 (100)
Vascular Surgery	1 (8)
Antibiotic Exposure	
Antibiotic use within prior 90 days	13 (100)
Vancomycin use	13 (100)
Cephalosporin use	13 (100)
Indwelling Medical Devices	
Central venous catheter	12 (92)
Urinary catheter	7 (54)

(Continues)

TABLE 1 (Continued)

Invasive Surgical Procedures	
Cardiothoracic surgery	10 (77)
Intraabdominal surgery	0 (0)
Colonization vs. Infection	
Colonization	13 (100)
Time between colonization and infection, median (IQR)	10 (5,22)
Infection[1]	4 (31)
VRE bacteremia	2 (50)
Wound infection	3 (75)
Intraabdominal infection	1 (25)
Surgical intervention	4 (100)
Death[2]	3 (75)

[1]A single patient may have had more than one listed outcome.
[2]The causes of death were attributed to factors other than VRE infection.
Abbreviations: BOLT, bilateral orthotopic lung transplant; IQR, interquartile range; LVAD, left ventricular assist device; OHT, orthotopic heart transplant; VV ECMO, veno-venous extracorporeal membrane oxygenation.

4 | DISCUSSION

VRE infection primarily occurs in previously colonized immunosuppressed patients.[8–11] Transplant recipients are at higher risk of colonization and infection due to frequent and extended contact with healthcare systems, chronic immunosuppression, and prolonged antibiotic exposure.[12] The SCT and abdominal SOT populations historically have the highest VRE infection rates with up to 32% of colonized patients subsequently developing an infection.[13–15] Limited literature exists detailing VRE colonization prevalence and associated morbidity in cardiothoracic transplant patients.[16] *Enterococcus spp.* is a frequent cause of VAD infections.[17,18] Patients with infected VADs may wait longer for transplantation, particularly those with *Enterococcus spp.* infective endocarditis.[19] *Enterococcus spp.* are frequent organisms involved in infections during ECMO, which may delay lung transplantation and contribute to early or late mortality for those cannulated post-transplantation.[20,21] Compared to bacteremia caused by vancomycin-susceptible *enterococci*, VRE bacteremia may increase LOS, mortality, and costs.[22,23]

Our experience with a complex cardiothoracic surgery/transplant population revealed that 31% of colonized patients developed an infection, suggesting a similar risk compared to Heme/Onc/SCT and abdominal SOT patients, highlighting the need for aggressive outbreak management. VRE outbreak measures have focused on rigorous hand hygiene, PPE compliance, and environmental cleaning. We found hand hygiene and PPE audits with real-time intervention and coaching to be effective. Forming a multidisciplinary team to establish expectations, interventions for noncompliance, and data dissemination to stakeholders helped rapidly control the outbreak. These interventions created a framework for sustainable infection control practices in this population.

Our experience highlights an unintended consequence of discontinuing MDRO surveillance in the cardiothoracic transplant population during the pandemic. This cohort was heavily predisposed to VRE risk factors, though it is interesting to note an outbreak in this population after reinstituting surveillance and not prior to the pandemic. Discontinuing VRE surveillance likely led to delayed recognition and possibly a larger outbreak than would have otherwise occurred. These units had not previously experienced a VRE outbreak at our institution; however, they were extraordinarily impacted during the pandemic with a population requiring mechanical support and lung transplantation.

Our patients requiring mechanical support due to COVID-19 acute respiratory distress syndrome and lung transplantation had complicated postoperative stays and prolonged LOS in the ICU.[24,25] ICU LOS is an independent risk factor for VRE acquisition in surgical patients.[26,27] Despite these units not having previously experienced VRE outbreaks, the pandemic-prompted shift in the patient population likely increased the risk for hospital-acquired VRE acquisition and subsequent transmissions.

This study has several limitations. Due to the small number of patients involved in the outbreak ($n = 13$), the rates in this study may not be a true reflection of this population as a whole. Additionally, VRE acquisition risk was likely increased by prolonged antibiotic exposure in the setting of critical illness and COVID-19, though the study did not assess the antibiotic burden in this population pre- and during the pandemic.

5 | CONCLUSION

Throughout the pandemic, many institutions experienced a rise in MDRO rates due to limited resources and deviations in infection control strategies.[1,28] The pandemic may have created a lapse in horizontal IP measures, emphasizing the importance of education, monitoring, and reinforcement of those principles to ensure optimal outcomes. Subsequent investigations of VRE colonization, infection, and

outbreaks in this population would shed additional light on the rates reflected in the study.

CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

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DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

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