CONCISE COMMUNICATION

Epidemiologic Review of Veterans Health Administration Patients with Isolation of Nontuberculous Mycobacteria after Cardiopulmonary Bypass Procedures

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We evaluated the isolation of postoperative nontuberculous mycobacteria (NTM) associated with heater-cooler devices (HCDs) used during cardiopulmonary bypass (CPB) surgery in the Veterans Health Administration from January 1, 2010, to December 31, 2016. In more than 38,000 CPB procedures, NTM was isolated in 111 patients; 1 *Mycobacterium chimaera* mediastinitis case and 1 respiratory isolate were found.

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In October 2015, the US Centers for Disease Control and Prevention (CDC) and the US Food and Drug Administration (FDA) issued communications regarding the association between nontuberculous mycobacteria (NTM) infections and heater-cooler devices (HCDs) used during cardiopulmonary bypass (CPB) procedures.[1,2] At some facilities, *Mycobacterium chimaera*, an NTM species within the *Mycobacterium avium* complex (MAC), was linked to infections associated with HCD use.[3,4] HCDs were allegedly contaminated with *M. chimaera* during manufacturing, and more than 70 people worldwide became infected, with significant morbidity and mortality.[5] Although *M. chimaera*, most often associated with the LivaNova PLC (formerly Sorin Group Deutschland GmbH) Stöckert 3T HCD, is the most prevalent organism causing infection, other NTM species were associated with that HCD model, as well as other HCD brands.[6] We conducted a review to identify and characterize NTM isolates in veterans who underwent CPB procedures.

The Department of Veterans Affairs (VA) databases were queried for (1) CPB procedures using *International Classification of Diseases, Ninth and Tenth Revision, Clinical Modification and Procedure Coding System* (ICD-9-CM and ICD-10-PCS) codes 39.61 and 5A1221Z; (2) NTM isolates recovered from any anatomic site characterized by standard microbiologic methods; and (3) ethambutol (EMB) outpatient orders between January 1, 2010, and December 31, 2016. Moreover, VA and non-VA procedures were included, while only VA microbiologic and pharmacy data were extracted. Data were merged to compile the cohort of patients with CPB procedures and NTM isolated after the procedure. The HCD manufacturers were determined for VA medical centers performing CPB procedures. Health records of patients with NTM isolated from any source after CPB procedure were reviewed for procedure details, risk factors, and presence of infection. We reviewed records of all patients with *M. chimaera* isolated to identify any with CPB procedures not captured in our ICD code query. Additionally, standard and mycobacterial blood culture orders were extracted for the study period.

More than 38,000 CPB procedures were performed in 37,950 patients, and 25,564 NTM isolates among 11,921 unique patients were identified. A total of 33,763 outpatient EMB prescriptions were identified among 4,724 patients (Figure 1 and Supplementary Table 1). The median number of procedures performed at 41 VA facilities was 770 (range, 72–2,050), with 10 facilities performing 40% of all CPBs and non-VA facilities accounting for 8,347 (22%) procedures. Of 41 VA facilities, 30 (73%) used the Stöckert 3T HCD, most of which were manufactured in 2014 or earlier. The manufacturers of HCDs at the remaining 11 facilities included Cincinnati Sub-Zero (5 sites), Terumo (3 sites, including 2 also using Stöckert 3T), CardioQuip and Medtronic (2 sites each), and Maquet (1 site). Of patients undergoing CPB procedures, 3,222 (8%) had 9,190 blood cultures ordered, and 237 (1%) patients had 319 mycobacterial blood cultures ordered anytime postoperatively, with 68% of mycobacterial blood cultures ordered in the last quarter of 2016. Of 41 facilities, 23 contributed samples.

In total, 111 patients had 209 NTM isolated after 112 CPB procedures. Most NTM were respiratory MAC isolates. Table 1 shows characteristics of patients undergoing CPB and NTM isolates. Mean age was 66 years (range, 34–89), and 96% were male. The median time between CPB and the first NTM isolate was 546 days (range, 2–2,440). Of 13 patients with NTM isolated from a wound, tissue, or blood, 7 had infections not related to CPB: 3 foot ulcers, 2 skin infections, 1 spinal infection, and 1 abdominal abscess. Furthermore, 6 patients had NTM-associated mediastinitis: 1 with *M. chimaera*, 4 with *M. fortuitum* complex, and 1 with *M. chelonae/abscessus*. These 6 surgeries (5 coronary artery bypass graft (CABG) and 1 mitral valve replacement) were performed on separate dates at 5 different facilities. Stöckert 3T HCDs were used in 4 of 5 cases, a Terumo HCD was used in 1 case. The CPB procedure with culture for *M. chimaera* was performed at a non-VA hospital, and the HCD model was not available. Neither isolates nor devices were available for further testing. In addition, 2 patients with *M. fortuitum* mediastinitis had surgeries at the same facility, 19 months apart. Of 6 NTM mediastinitis patients, 5 had 2 or more time-related surgical risk factors longer than median times recorded for the 111 patient cohort (ie, operating room time, surgery duration, CPB time, aortic cross clamp time at 400, 304,118 and 85 minutes, respectively).

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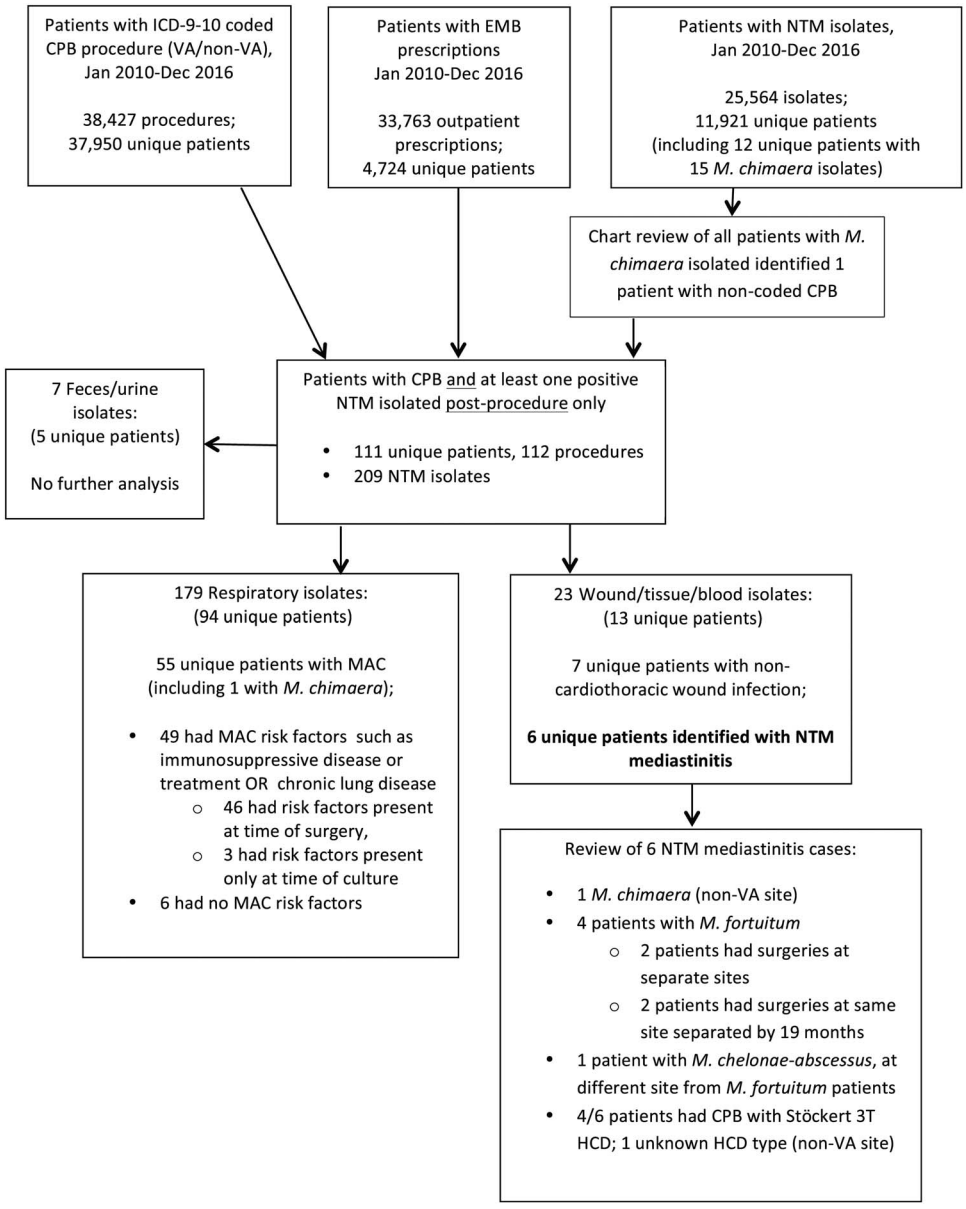

FIGURE 1. Review process for patients with cardiopulmonary bypass and nontuberculous mycobacteria isolated 2010–2016. Immunosuppressive disease defined as HIV/AIDS, lymphoma; immunosuppressive treatment defined as corticosteroids, or agents prescribed for autoimmune diseases, or cancer. Abbreviations: CPB, cardiopulmonary bypass; EMB, ethambutol; NTM, non-tuberculous mycobacteria; MAC, *Mycobacterium avium* complex; HCD, heater-cooler device.

Of 6 mediastinitis patients, 5 had diabetes mellitus. All 6 received targeted antimicrobial therapy and recovered. *Mycobacterium chimaera* was isolated in 2 additional patients who underwent prior surgical procedures at non-VA hospitals. In 1 case, CPB was performed during a CABG procedure 8 months prior to *M. chimaera* isolation from sputum in a patient with chronic obstructive pulmonary disease, without evidence of respiratory infection. The second patient had *M. chimaera* isolated from blood after endovascular repair of ruptured abdominal aorta, with subsequent infected endograft leading to death despite antimicrobial treatment and debridement. In this surgery, CPB was not utilized. Neither *M. chimaera* isolate was available for further testing.

Mycobacterium chimaera mediastinitis was identified in a patient whose CPB procedure was performed at a non-VA hospital and for whom treatment is ongoing. We cannot exclude HCDs as a source in the *M. fortuitum* and *M. chelonae/abscessus* sternal wound infections identified in our review. These organisms were reported in 1 FDA medical device report associated with the Stöckert 3T[6] and are rarely associated with

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TABLE 1. Characteristics of Patients Undergoing Cardiopulmonary Bypass (CPB) and Their Nontuberculous Mycobacteria (NTM) Isolates, 2010–2016

Procedure location (n = 112 procedures)	No. (%)
VA facility	89 (79)
Non-VA facility	23 (21)
Predisposing condition (n = 111 patients)	No. (%)
Diabetes mellitus[a]	44 (40%)
Immunosuppressive disease[b]	6 (5%)
Immunosuppressive treatment[c]	13 (12%)
Surgical risk factors (n = 112 procedures)	Min, median (range)
Time in operating room (n = 90)	400 (260–1050)
Surgery duration (n = 89)	304 (169–665)
Cardiopulmonary bypass time (n = 93)	118 (47–371)
Aortic cross clamp time (n = 82)	85 (31–217)
Nontuberculous mycobacteria recovered (n = 209)	No. of isolates
Avium/intracellulare complex (MAC)	107
Gordonae	30
Chelonae/abscessus	22
Fortuitum	20
Unspeciated	8
Simiae	5
Mucogenicum	3
Chimaera	3
Farcinogenes/senegalense	2
Boletti, Bovis, Immunogenum, Kansasii, Kubicae, Scrofulaceum, Smegmatis, Szulgai, Xenopi	1 each
Culture site (n = 209)	No. of isolates
Respiratory	179
Wound/tissue/blood	23
Feces/urine	7

[a]Determined by presence of *International Classification of Diseases, Ninth and Tenth Revision, Clinical Modification and Procedure Coding System* (ICD-9-CM and ICD-10-PCS) diagnosis code.

[b]Immunosuppressive disease (eg, HIV/AIDS, lymphoma) present in chart documentation.

[c]Documentation of immunosuppressive treatment (eg, corticosteroids, agents prescribed for autoimmune diseases or cancer).

mediastinitis.[7] These cases were discussed with FDA investigators to ensure consideration in the larger NTM-HCD investigation. Currently, no definitive solution has been reached for potential NTM contamination of HCDs, and aggressive cleaning of contaminated HCDs apparently has not resolved the issue.[8]

Our analysis has some limitations. Scanned operative reports were not always available to allow us to extract surgical risk factors for the 23 CPB procedures performed at non-VA hospitals after which NTM was isolated from patients. Miscoding of CPB may have led to under- or overrepresentation of cases in our cohort. Due to potentially long incubation periods for *M. chimaera* infection, we may have missed infections when procedures took place late in our study period. Moreover, infections may have occurred in patients whose CPB procedures were performed in VHA but whose samples were cultured outside the VHA or were not cultured at all. Only 1% of patients undergoing CPB had mycobacterial blood cultures performed. Thus, cases of HCD-associated NTM infection may have been missed. Finally, not all VHA NTM isolates were identified to the species level.

It is unclear whether all VHA facilities or reference laboratories isolating MAC from clinical samples performed all microbiologic identification procedures to differentiate *M. intracellulare* from *M. chimaera*. In addition, recent data suggest that *M. chimaera*, when properly distinguished from *M. intracellulare*, can cause significant pulmonary disease.[9] We noted that *M. chimaera* was identified in VHA in 2016, so additional microbiologic methods may have been adopted at some VHA facilities and reference laboratories to inform future surveillance for association with HCDs. VHA implemented FDA-recommended HCD risk mitigation, notification of patients exposed to HCDs, and provider education about NTM infection recognition and culturing.

In summary, 1 *M. chimaera* mediastinitis case and 1 respiratory isolate were found in VHA patients whose CPB procedures were performed at non-VA hospitals. Whether other identified NTM infections are attributable to HCD use could not be determined. Undersampling and/or lack of NTM speciation or misidentification may have contributed to these findings.

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SUPPLEMENTARY MATERIAL

To view supplementary material for this article, please visit https:/doi.org/10.1017/ice.2017.148

REFERENCES

1. Non-tuberculous *Mycobacterium* (NTM) infections and heater-cooler devices interim practical guidance. Centers for Disease

Control and Prevention website. http://www.cdc.gov/HAI/pdfs/outbreaks/CDC-Notice-Heater-Cooler-Units-final-clean.pdf. Updated 2015. Accessed April 21, 2017.
2. Nontuberculous *Mycobacterium* infections associated with heater-cooler devices: FDA safety communication. US Food and Drug Administration website. http://www.fda.gov/MedicalDevices/Safety/AlertsandNotices/ucm466963.htm. Published 2015. Accessed April 21, 2017.
3. Sax H, Bloemberg G, Hasse B, et al. Prolonged outbreak of *Mycobacterium chimaera* infection after open-chest heart surgery. *Clin Infect Dis* 2015;61:67–75.
4. Sommerstein R, Rüegg C, Kohler P, Bloemberg G, Kuster SP, Sax H. Transmission of *Mycobacterium chimaera* from heater–cooler units during cardiac surgery despite an ultraclean air ventilation system. *Emerg Infect Dis* 2016;22:1008–1013.
5. Sommerstein R, Schreiber PW, Diekema DJ, et al. *Mycobacterium chimaera* outbreak associated with heater-cooler devices: piecing the puzzle together. *Infect Control Hosp Epidemiol* 2017;38:103–108.
6. FDA Presentation. Circulatory System Devices Panel of the Medical Devices Advisory Committee. U.S. Food and Drug Administration website. https://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/MedicalDevices/MedicalDevicesAdvisoryCommittee/CirculatorySystemDevicesPanel/UCM504026.pdf Published 2016. Accessed April 21, 2017.
7. Unai S, Miessau J, Karbowski P, Bajwa G, Hirose H. Sternal wound infection caused by *Mycobacterium chelonae*. *J Card Surg* 2013;28:687–692.
8. Schreiber PW, Kuster SP, Hasse B, et al. Reemergence of *Mycobacterium chimaera* in heater-cooler units despite intensified cleaning and disinfection protocol. *Emerg Infect Dis* 2016;22(10):1830–1833.
9. Moon SM, Kim SY, Jhun BW, et al. Clinical characteristics and treatment outcomes of pulmonary disease caused by *Mycobacterium chimaera*. *Diagn Microbiol Infect Dis* 2016;86:382–384.

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