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Unnecessary Routine Use of Mycobacterial Cultures in Patients With Periprosthetic Joint Infections

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Accurate diagnosis ensures appropriate therapy of periprosthetic joint infection (PJI). Since mycobacterial PJI is rare, routine testing is inappropriate. We reviewed hip and knee PJI at our institution over 28 months. Mycobacterial cultures were routinely sent with rare positivity. Mycobacterial cultures should be sent only when there is clinical suspicion.

Keywords. mycobacterial cultures; prosthetic joint infection.

Practice-based guidelines were developed to address variability in medical diagnosis and treatment [1]. Choosing appropriate tests requires a thorough history and understanding of pretest probability. Compliance with guidelines is not universal [2].

Most cases of periprosthetic joint infection (PJI) are caused by bacteria. Less than 1% are caused by fungi and, rarely, by zoonotic organisms or mycobacteria [3–6]. Culture-negative PJI (CNPJI) accounts for about 15% of cases [3–7]. Guidelines published by the Infectious Diseases Society of America (IDSA) and the American Academy of Orthopedic Surgeons (AAOS) direct workup for patients with possible PJI [8, 9], including recommendations for preoperative arthrocentesis and collection of multiple intraoperative specimens for bacterial culture.

Since mycobacterial PJI is unusual, routine mycobacterial cultures are not cost effective [10]. AAOS cites a lack of evidence supporting routine mycobacterial cultures and recommends submitting only bacterial cultures from intraoperative specimens along with bacterial culture of sonicate from explanted hardware [8]. IDSA guidelines do not mention routine tissue culture for mycobacteria but specifically state that culture of sonicate fluid is not validated for mycobacteria and should not be routinely ordered [9].

The aim of this study was to assess the frequency of mycobacterial testing from operating room (OR) specimens of patients with known or suspected PJI.

METHODS

Eligible subjects were identified through the Yale Center for Clinical Investigation Joint Data Analytics Team database using specific *International Classification of Diseases, Tenth Revision* codes for PJI hips and knees.

We retrospectively reviewed charts of 97 patients admitted to Yale New Haven Hospital from 1 September 2017 through 31 December 2019, and meeting criteria for first PJI of the hip or knee. We reviewed OR cultures from all procedures in patients diagnosed with PJI over the course of the study period. We included patients with evidence of infection after primary or revision arthroplasty. Revision arthroplasty could have been done for management of prosthesis failure or reimplantation of a new joint following appropriate treatment of PJI (second stage of a 2-stage procedure). Patients with prior history of PJI, those with PJI managed exclusively as outpatients, and those who had surgery at another institution were excluded.

Abstracted variables included demographics, surgical procedures, tissue cultures submitted (ie, bacterial, mycobacterial, fungal), and number of intraoperative cultures.

PJI was defined using IDSA criteria [9]. CNPJI was diagnosed based on the following criteria: purulence surrounding the prosthesis at surgery, histopathologic evidence of acute inflammation, or cutaneous sinus tract communicating with the prosthesis with negative aerobic and anaerobic cultures [7].

Costs were calculated using variable supply and variable labor estimates as determined by the Yale New Haven Hospital Microbiology Department (personal communication).

All charts were reviewed by 2 authors. Statistical analyses were conducted using SAS Studio (3.8) software. Demographic and clinical characteristics of the sample were summarized using appropriate descriptive statistics.

Ethical Consideration and Patient Consent Statement

This research was approved by the Yale University Institutional Review Board Human Investigation Committee. No patient consent was required. None of the authors have any relevant disclosures.

Table 1. Summary of Mycobacterial Cultures (N = 97)

Culture	No. (%)
Mycobacterial cultures sent[a]	91/97 (93.4)
Mycobacteria isolated[b]	1/91 (1.1)
Preoperative evidence of infection	56/91 (61.5)
Pathogenic organism isolated on prior culture	50/56 (89.3)
Presumptive hematogenous seeding of joint	5/56 (8.9)
Positive Synovasure	1/56 (1.8)
Revision arthroplasty (stage 2 of 2) performed	29/97 (29.9)
Mycobacterial cultures sent[c]	21/29 (72.4)
Revision arthroplasty for prosthesis failure performed	22/97 (22.7)
Mycobacterial cultures sent	16/22 (72.7)
Culture-negative PJI	4/97 (4.1)
Mycobacterial cultures sent	3/4 (75.0)

Abbreviation: PJI, periprosthetic joint infection.

[a]Of the patients who did not have intraoperative mycobacterial cultures sent (n = 6), half had a preoperative aspirate with evidence of bacterial infection.

[b]The sole positive mycobacterial culture was deemed a contaminant by the treating physicians.

[c]Mycobacterial cultures were sent at the time of revision arthroplasty after causative organism(s) had already been identified, hardware had been removed, and culture-directed antibiotics had been prescribed.

RESULTS

Ninety-seven patients were included in the study, with mean age of 69.0 (± 13.4) years (range, 35–97 years). The sample was divided relatively equally by sex (n = 48 male; n = 49 female). Most subjects were White (79.6%) and non-Hispanic (95.9%).

Overall, 256 surgical procedures were performed during the study period, ranging from 1 to 10 procedures per patient (median, 2). Intraoperative specimens were always sent for bacterial culture and routinely for mycobacterial culture. Of 97 patients, 91 (93.4%) had ≥1 OR specimens submitted for mycobacterial culture. Overall, a total of 556 mycobacterial cultures were sent.

Table 1 shows the distribution of mycobacterial cultures. Among 29 patients undergoing revision arthroplasty following hardware removal and culture-directed antibiotics, 21 (72.4%) still had mycobacterial cultures sent at time of reimplantation, even though a causative organism(s) had already been identified. Ninety OR specimens were sent for acid-fast bacilli (AFB) culture from these 21 patients (range, 1–8; median 2). Among the 4 patients with CNPJI, 3 had mycobacterial cultures at the time of revision. Twenty-two patients had revision arthroplasty for failure of the prosthesis as their index procedure. Sixteen (72.7%) had mycobacterial cultures sent, though concern for infection was documented in only 3 (18.8%).

Among 91 patients who had mycobacterial cultures sent, 56 (61.5%) had preoperative evidence of infection (2 fungal and 54 bacterial). In these patients, diagnosis was based on clinical impression of PJI with bacteremia and presumptive seeding of the joint (5 patients), positive Synovasure for *Staphylococcus* species (1 patient), and prior OR cultures with isolation of pathogenic organism (50 patients). Of the 6 patients who had no intraoperative AFB cultures sent, 3 had a preoperative aspirate with evidence of bacterial infection. Only 1 patient in our study had mycobacteria isolated (*Mycobacterium avium* complex [MAC]).
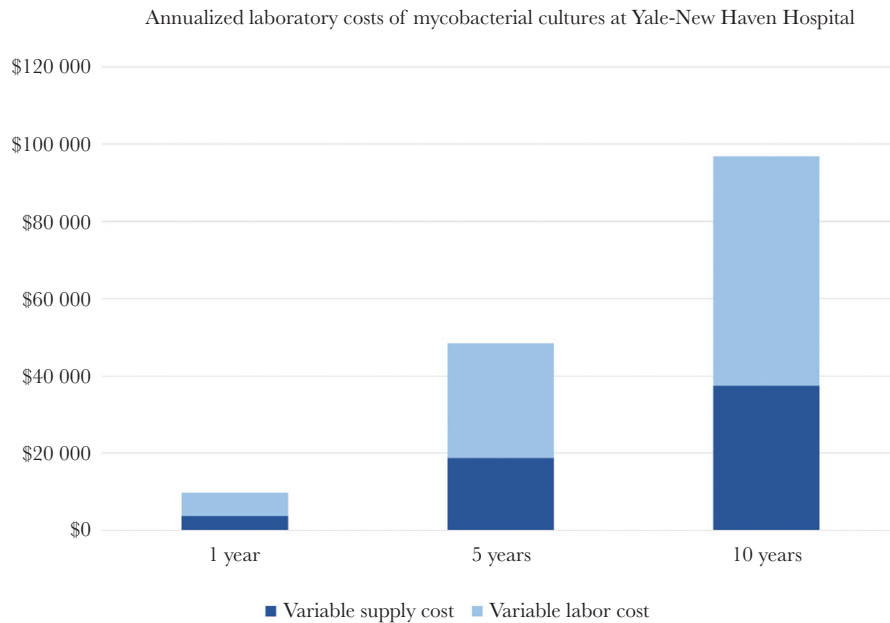
Cost Analysis

Laboratory costs are assessed using variable supply and labor values. Variable supply represents estimated minimum cost of raw materials while variable labor represents time required for the technologist to perform an assay. At Yale New Haven Hospital in 2021, mycobacterial cultures had variable supply costs of $15.72 and variable labor expenditure of 49.85 minutes/test. Over the course of the study period, cost of mycobacterial cultures was $8740.32 and consumed 462 hours of technologist time. By discontinuing routine mycobacterial cultures, we estimate a modest variable supply cost savings of $18 730 over 5 years but a substantial (990 hours) savings in technologist time without sacrificing quality of care (Figure 1).

DISCUSSION

Among patients with PJI, mycobacterial cultures should only be sent in select circumstances, such as patients receiving immunosuppressive therapy and those with CNPJI or failure to respond to antibacterial therapy [3, 4, 10, 11]. In addition, patients with PJI and epidemiologic risk factors for tuberculosis should have specimens sent for mycobacterial culture [12]. A history of trauma, corticosteroid injection, and certain environmental exposures (example: hot tub exposures or gardening) may be considered as risk factors for mycobacterial infection. Mycobacterial cultures are also appropriate in patients with evidence of granulomatous inflammation on histology. Last, given the poor sensitivity of mycobacterial culture from synovial fluid, when mycobacterial infection is suspected, molecular diagnostics may be more appropriate than culture, further challenging the role of routine mycobacterial culture [13].

Given the overall rarity of mycobacterial PJI, Wadey et al proposed an algorithm to guide use of mycobacterial cultures, which resulted in an 80% decrease in unnecessary mycobacterial cultures [10]. Routine AFB cultures, especially in patients where a pathogen has already been isolated, is not an appropriate use of limited resources. This is especially true in the midst of the current coronavirus disease 2019 pandemic, where technician time could be better directed. Mycobacterial cultures can take up limited Biosafety Level 3 space and are labor intensive, since solid media plates are held for 6 weeks and are checked manually by the technologist on a weekly basis [14]. A better use of resources is to identify patients at risk for mycobacterial infections and target them for AFB cultures [15, 16]

Assessing the cost of failure to diagnose a mycobacterial PJI is difficult. Romanò et al [17] attempted to address indirect costs of a missed diagnosis, but their analysis was limited by small sample size (20 patients) and was not conducted in the United States, limiting generalizability. Berbari et al [7] reviewed 60 episodes of CNPJI over 10 years and none had mycobacteria

Annualized laboratory costs of mycobacterial cultures at Yale-New Haven Hospital

Figure 1. Annualized laboratory costs of mycobacterial cultures at Yale New Haven Hospital. Variable supply represents estimated minimum cost of raw materials necessary for performing an assay. Variable labor represents estimated minimum hands-on time required of a technologist to perform an assay. At Yale New Haven Hospital in 2021, mycobacterial cultures had variable supply costs of $15.72. Variable labor costs were based on an assumed labor expenditure of 49.85 minutes per test and microbiology technologist salary of $30/hour (mean of the national range). The annualized projections at 5 and 10 years were not adjusted for inflation or technologist salary increase over time.

isolated. In a retrospective study of 2116 episodes of PJI over 22 years by Marculescu et al [15], 0.3% were caused by *M tuberculosis*. Nontuberculous mycobacteria such as *M fortuitum*, *M chelonei*, and *M avium-intracellulare* complex (MAC) were rarely isolated [4–6, 11] In this review article, 1 case of MAC PJI was described in the setting of advanced human immunodeficiency virus disease and known disseminated mycobacterial infection [18]. Eid at al reviewed all cases of rapidly growing mycobacteria causing PJI at Mayo Clinic over 38 years and found only 9 episodes (8 patients) [5].

We had only 1 positive mycobacterial culture in our study (MAC), which was deemed a contaminant by the treating physicians. In addition, among the 4 patients in our study with CNPJI where mycobacterial cultures would be expected to have the most utility, it was sent in only 3 patients.

Our cost calculations are likely underestimates, given that none of these variables account for compounded opportunity costs in lost technologist effort toward onboarding new technologies, validating new assays, and training staff, all of which can bring additional revenue and improve patient care. Given the current national shortage of microbiology technologists [19], many hospital laboratories are understaffed, and it would be helpful to reallocate technologist effort for other laboratory testing. Some hospital microbiology laboratories cannot perform AFB testing in-house, and send-out testing may carry additional costs that we have not included in our analysis. Wadey et al estimated a cost to their healthcare system of more than $66 000 to identify 1 patient with mycobacterial PJI [10]

In summary, we found that routine cultures for mycobacteria in patients with PJI are routinely sent, which does not reflect high-value care. This practice may be cultural within the OR environment rather than representing best practice guidelines of major societies, so reeducation of surgeons, OR nurses, and staff will be needed to modify this practice. Use of an algorithm to guide selection of cultures is recommended.

Notes

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