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ORIGINAL ARTICLE

# Evaluation of rapid polymerase chain reaction-based organism identification of gram-positive cocci for patients with a single positive blood culture

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**Abstract**
For patients with a single-positive blood culture growing gram-positive cocci, organism identification can provide supportive information for differentiating contamination from infection. We investigated the effect of a rapid blood culture identification panel (BCID) on vancomycin-prescribing patterns and patient outcomes for single positive blood culture (PBC) growing gram-positive cocci. Adult patients with single-positive blood culture growing gram-positive cocci with conventional organism identification (pre-BCID) were compared with organism identification by BCID (post-BCID). Antimicrobial Stewardship Program (ASP) review of PBC was performed in both study groups. Vancomycin prescribing patterns were studied. Secondary endpoints were the incidence of nephrotoxicity, length of stay (LOS), readmission rate, mortality, and hospital costs. A total of 188 patients (86 pre-BCID, 102 post-BCID) were included. Organism identification was known 21 h sooner in the post-BCID group ($P < 0.001$). Coagulase-negative staphylococci were the most commonly isolated organisms (73%). In patients where vancomycin was deemed unnecessary ($n = 133$), vancomycin use (51% pre-BCID vs 36% post-BCID; $P = 0.09$) and time from culture positivity to vancomycin discontinuation (1.5 vs. 1.7 days; $P = 0.92$) did not differ between groups. We found no differences in the development of nephrotoxicity, LOS, readmission, mortality, or hospital costs. Earlier identification of single positive blood culture growing gram-positive cocci did not significantly influence prescribing patterns of vancomycin. However, baseline antimicrobial stewardship review of single positive blood culture growing gram-positive cocci may have lessened the opportunity for detectable differences. Larger studies, accounting for the impact of ASP intervention, should be performed to determine the value of each individual component.

**Keywords** Rapid diagnostics · Gram-positive cocci · Stewardship · Contaminant

**Electronic supplementary material** The online version of this article (https://doi.org/10.1007/s10096-019-03574-3) contains supplementary material, which is available to authorized users.

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## Introduction

Determining the clinical significance of a single positive blood culture with gram-positive cocci (GPC) can be challenging, often dependent on organism characteristics and the clinical presentation of the patient [1]. From a diagnostic standpoint, organism identification can provide supportive information for differentiating contamination from a true bloodstream infection in patients with a single-positive blood culture with GPC. Whereby, once the identity of the GPC organism is known, clinicians can tailor antibiotic therapy and order any necessary laboratory tests to optimize patient outcomes. Coagulase-negative staphylococci (CoNS), a group of commensal bacteria of the skin, are the GPC most often isolated from blood cultures. However, only 22–36% of blood cultures that grow CoNS are determined to be clinically significant and frequently represent contamination from the patient's skin

[2–4]. Despite this fact, it is our experience that a large proportion of patients with contaminated blood cultures frequently receive vancomycin therapy [5]. *Staphylococcus aureus* bacteremia, on the other hand, is associated with significant morbidity and mortality, and the growth of *S. aureus* in a blood culture is universally regarded as a clinically relevant finding [6]. The uncertainty of organism identity for single positive blood culture with GPC prompts empirical prescribing of vancomycin in most medical centers due to high rates of methicillin resistance among staphylococcal species [6]. Each day of antibiotic therapy increases the risk of an antibiotic-associated adverse event occurrence [7]. For example, vancomycin adverse events include rash (due to red man syndrome or true vancomycin sensitivity), infusion-related reactions, nephrotoxicity, and ototoxicity.

Recently, rapid diagnostic testing (RDT) has been shown to enhance the management of patients with bloodstream infections, significantly decreasing time to effective therapy, mortality, and length of stay as shown in a meta-analysis of 31 studies including nearly 6000 patients [8]. However, the impact of RDTs on reducing exposure to unnecessary or inappropriate antibiotics for contaminated blood cultures and the subsequent impact on patient care is less clearly defined and understudied [9]. The objectives of this study were to analyze vancomycin prescribing patterns and describe patient outcomes following rapid PCR-based organism identification of a single positive blood culture with GPC, which frequently represents contamination, compared with conventional organism identification.

## Methods

### Study design

This single-center, pre-post quasi-experimental study was performed at a 709 bed academic medical center in the Southeastern USA. The study was approved by the local Institutional Review Board. Patients were evaluated for study inclusion by querying the institution's database for positive blood cultures. All adult (≥ 18 years of age) patients with a single positive blood culture showing GPC (of any morphology) on Gram stain between 1 August and 31 October of the years 2012 and 2014 were included in the study, unless they met any exclusion criterion. Only the first positive culture for each patient was included during the study period; any subsequent admission with a positive blood culture for GPC was excluded. Patients who had expired or were placed on hospice care prior to blood culture positivity, those who had been transferred from an outside hospital and had a history of a previously positive blood culture of the same organism, those with polymicrobial bacteremia or more than one positive blood culture in a 24-h period, and those who were not admitted to the hospital were excluded from the study. Once patients were identified, information was collected by investigators using REDCap electronic data capture tools [10]. Patients with a single positive blood culture from August through October of 2012, prior to the implementation of the blood culture identification technology (pre-BCID), were compared with patients with a single positive blood culture from August through October of 2014 (post-BCID). The FilmArray BCID (BioFire Diagnostics, LLC, Salt Lake City, UT) analysis was performed on all index-positive blood cultures beginning on 1 December 2013. Both time periods had antimicrobial stewardship intervention.

### Interventions

ASP interventions were performed throughout the study period, which included a review of positive blood cultures by a team member (ID physician or ID pharmacist) using real-time alerts provided by SafetySurveillor (Premier, Inc., Charlotte, NC), a web-based infection tracking and antimicrobial utilization tool. During the pre-BCID time period, an ASP member reviewed the Gram stain results of the positive blood culture, assessed for adequate coverage (generally recommending vancomycin therapy until species identification is determined), and recommended therapy modification as appropriate following organism identification by conventional methods. The BCID can identify *Staphylococcus* spp., *S. aureus*, *Streptococcus* spp., *S. agalactiae*, *S. pyogenes*, *S. pneumoniae*, *Enterococcus* spp., *Listeria monocytogenes*, as well 10 Gram-negative organisms, 5 *Candida* spp., and 4 antibiotic resistance genes, *mecA*, *vanA* and *vanB* (*vanA/B*), and $bla_{KPC}$, within 1 h directly from positive blood culture bottles [11]. During the post-BCID period, the BCID results were used by the ASP to assess the appropriateness of therapy based on the institution's pathogen-specific treatment algorithms according to organism identification, which were posted on the hospital intranet (see supplementary file). The ASP recommended changes to antimicrobial therapy, if needed, to the primary care team (Monday through Friday from 0800 hours to 1700 hours). For results occurring outside these working hours, ASP interventions were made the following working day, if necessary.

It was the standard of care to draw two sets (a set contains one aerobic and one anaerobic) of blood cultures at our facility during both study periods. Blood cultures were performed during the pre-BCID period using BacT/Alert standard aerobic, standard anaerobic, Fan Plus aerobic, and Fan Plus anaerobic blood culture bottles (bioMérieux, Durham, NC) and during the post-BCID period using Bactec Plus aerobic/F and Plus anaerobic/F bottles (BD Diagnostic Systems, Sparks, MD). During both study periods, aliquots from bottles that gave positive signals were Gram stained and subcultured for organism identification by conventional methods. During pre-BCID period, the results of the Gram stain were communicated by laboratory personnel to nursing staff via telephone within 1 h of the blood culture being identified as positive. During the post-BCID procedure, laboratory personnel would wait for both the Gram stain and the BCID result to be available and would then communicate to the nursing staff via telephone within 2 h of blood culture being identified as positive. The ASP was notified of positive blood cultures only through SafetySurveillor, and the data were updated and monitored in real time. Results were posted to the electronic medical records once verbal notification was received. No templated comments or clinical interpretations of the results were provided at the time of reporting. Single positive blood cultures for any CoNS were reported as "Staphylococcus species coagulase negative (undifferentiated)" and susceptibilities were not performed or reported. Identification and susceptibility testing were performed using conventional phenotypic methods and a MicroScan WalkAway system (Beckman Coulter, Inc., Brea, CA). No other rapid identification techniques were in place except for those used for identification of *S. aureus* (direct tube coagulase testing and plating to methicillin-resistant *S. aureus* [MRSA] chromogenic medium) at the time of BCID implementation. The microbiology laboratory was staffed 24 h a day, 7 days a week throughout the study.

## Outcomes

The primary objective was to analyze vancomycin prescribing patterns following rapid organism identification with BCID plus ASP intervention versus conventional organism identification methods with ASP intervention. The primary objective endpoints included vancomycin use and the time elapsed between blood culture positivity and vancomycin discontinuation. Patients were further divided into four categories for analysis:

i. Pre-BCID patients with warranted vancomycin therapy
ii. Post-BCID patients with warranted vancomycin therapy
iii. Pre-BCID patients for whom vancomycin therapy was deemed unnecessary
iv. Post-BCID patients for whom vancomycin therapy was deemed unnecessary

Any patients with a single positive blood culture of methicillin-resistant *S. aureus* (MRSA), *Enterococcus* spp. (vancomycin-susceptible and *vanA/B* not detected), or *S. pneumoniae* were categorized into the warranted vancomycin group, as bacteremia with these organisms justifies the continuation of vancomycin therapy. Additionally, patient with a single positive blood culture of CoNS and the presence of any of the following were categorized as warranting vancomycin therapy; fever (≥ 39.0 °C within 48 h before or on the day of first positive blood culture collection), neutropenia, or a presumed infectious source for CoNS. As the clinical significant of CoNS is thought to be higher in patients exhibiting these clinical parameters, vancomycin was deemed warranted [3]. All other patients with a single positive blood culture of some other GPC (eg., methicillin-susceptible *S. aureus*) were categorized into one of the unnecessary vancomycin therapy groups, as these patients likely had blood culture contaminants or should have been treated with a more appropriate antibiotic other than vancomycin. To account for the influence that concomitant infections might have had on vancomycin prescribing patterns, we performed a subgroup analysis of patients without concomitant infections. Concomitant infections were determined by documentation in the medical record (eg, pneumonia, intraabdominal infection), and culture from the concurrent infection site grew at least one organism that was not isolated from blood. Severity of illness (Pitt bacteremia score) and comorbidities (Charlson comorbidity index) were recorded for each patient [12, 13].

For the secondary objective, clinical endpoints included development of acute kidney injury (AKI), in-hospital all-cause mortality, 30-day all-cause readmission, hospital length of stay (LOS) following blood culture positivity, and overall patient-specific hospital costs. All-cause mortality was defined as death resulting from any cause at the end of hospitalization. Patients who died during their hospital admission were not included in the LOS analysis.

AKI was defined as meeting any RIFLE (risk, injury, failure, loss, end stage renal disease) criteria as follows: risk, a rise in creatinine by 1.5 times baseline or a decrease in glomerular filtration rate (GFR) by 25%; injury, a rise in creatinine of 2 times baseline or a decrease in the GFR by 50%; and failure, a rise in creatinine by 3 times baseline or a GFR decrease by 75% [14]. Patients were excluded from the AKI analysis if their baseline serum creatinine was > 1.5 mg/dL, or if they required renal replacement therapy at the time of blood culture collection. Receipts of concomitant nephrotoxins (aminoglycosides, amphotericin B, angiotensin-converting enzyme inhibitors, angiotensin II receptor blockers, diuretics, IV contrast) were recorded. Neutropenia (± 48 h of initial positive blood culture collection) was defined as absolute neutrophil count of less than 1500 neutrophils/mm$^3$. Immunosuppressive therapy data represent active systemic chemotherapy, tacrolimus, mycophenolate mofetil, azathioprine, cyclosporine (or equivalent) for more than 7 days, or a systemic steroid for more than 10 days the previous month. Time to effective therapy (for vancomycin warranted group) was defined as the elapsed time in hours between the index culture positivity time and receipt of the initial dose of an antibiotic shown to exhibit activity against the patient-specific isolate based on the in vitro susceptibility results (antibiotics with intermediate susceptibility were considered to be ineffective). All costs were adjusted for inflation and converted to 2014 dollars, according to the consumer price index inflation calculator provided by the United States Department of Labor, Bureau of Labor Statistics (http://www.bls.gov/data/inflation_calculator.htm).

## Statistical analysis

Statistical comparisons were performed between study groups with student *t* test or Mann-Whitney *U* test for continuous variables, where appropriate. Dichotomous variables were compared using the chi-square test or Fisher's exact test. All statistical analyses were performed using Stata statistical software v12.0 (Stata Corp LP, TX). A *P* value of $\leq 0.05$ (two-tailed test) was considered statistically significant.

# Results

## Patients

There were 335 unique patients with a positive blood culture with gram-positive cocci on Gram stain that were screened for the study (Fig. 1). After 147 patients were excluded, 188 (86 pre-BCID, 102 post-BCID) remained in the evaluation. Baseline characteristics and pre-existing conditions were comparable between pre-BCID and post-BCID groups (Table 1). Post-BCID patients had higher Charlson comorbidity scores (5.0 versus 4.0; $P = 0.04$) and more concomitant infections (53% versus 37%; $P = 0.03$) than the Pre-BCID group. Pitt bacteremia score, rates of ICU admission, and presumed source of infection were comparable between groups (Tables 1 and 2).

## Microbiology

The arrangement of Gram-positive cocci was most commonly clusters (69%), followed by chains (9%) and pairs (5%). No arrangement was reported in 17% of Gram-positive cocci. There were similar proportions of organisms isolated in each group (Table 1). Coagulase-negative staphylococci were the most commonly isolated organisms in the study (73%), of which 135/138 (98%) were deemed contaminants. Mean time to blood culture positivity from blood culture collection was similar between groups (25.4 h in the pre-BCID group versus 27.4 h in the post-BCID group, $P = 0.30$). There were a similar number of positive blood culture results that occurred during ASP working hours between groups (46.5% pre-BCID vs 42.1% post-BCID, $P = 0.55$). Time to organism identification from blood culture collection was known an average of 21 h sooner in the post-BCID group (46.9 versus 26.3 h, $P < 0.001$).

## Antibiotic utilization

In the total population, vancomycin use (52% in the pre-BCID group versus 41% in the post-BCID group, $P = 0.13$) and median time from culture positivity to vancomycin discontinuation (1.4 [0.6–3.9] versus 1.9 days [0.1–5.0], $P = 0.30$) were

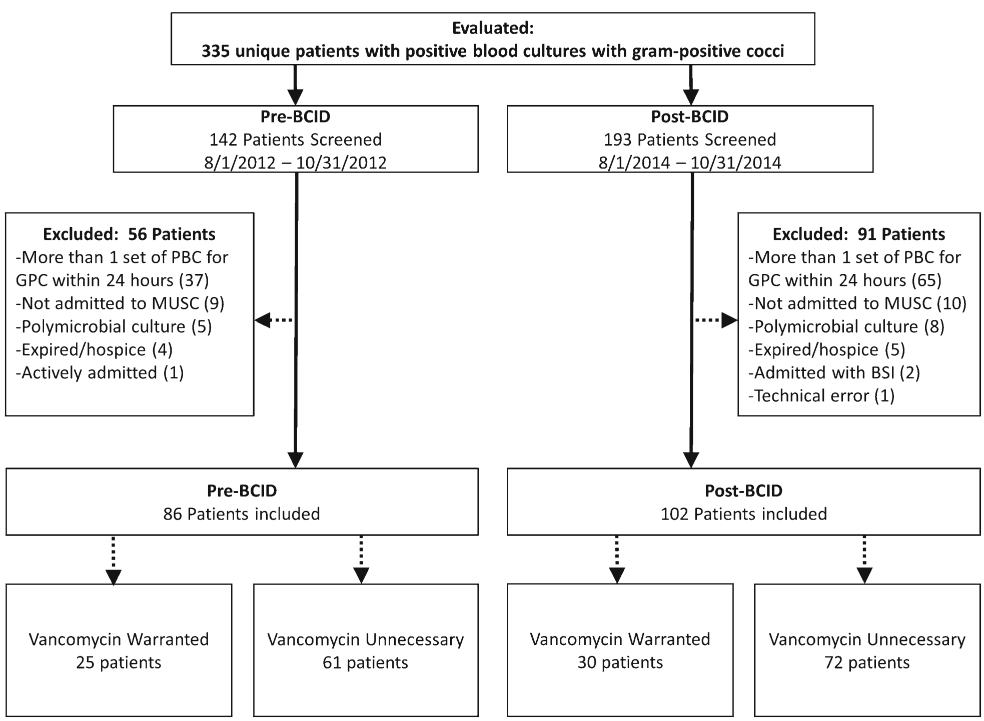


**Fig. 1** Flowchart of study participants. BCID, blood culture identification panel; GPC, gram-positive cocci. One patient remained actively admitted to hospital at the time of data collection and was excluded due to inability to determine multiple endpoints

**Table 1** Demographics and characteristics

| Demographics | Pre-BCID ($n = 86$) | Post-BCID ($n = 102$) | *P* |
|---|---|---|---|
| Age, years, mean ± SD | 56 ± 18 | 57 ± 17 | 0.77 |
| Male | 46 (54) | 47 (46) | 0.31 |
| Preexisting conditions | | | |
| HIV/AIDS | 0 (0) | 4 (4) | 0.13 |
| Solid organ malignancy | 12 (14) | 19 (19) | 0.39 |
| Hematologic malignancy | 4 (5) | 3 (3) | 0.54 |
| Chronic lung disease | 17 (20) | 27 (27) | 0.28 |
| Cardiovascular disease | 31 (36) | 38 (37) | 0.86 |
| Cerebrovascular disease | 22 (26) | 20 (20) | 0.33 |
| Diabetes mellitus | 35 (41) | 48 (47) | 0.38 |
| Receipt of renal replacement therapy | 4 (5) | 8 (8) | 0.37 |
| Receipt of total parenteral nutrition | 3 (4) | 3 (3) | 0.83 |
| Liver disease | 11 (13) | 20 (20) | 0.21 |
| Presumed source of infection | | | |
| Contamination | 71 (83) | 79 (78) | 0.47 |
| Unidentified | 2 (2) | 7 (7) | 0.18 |
| Skin or skin-structure related | 3 (4) | 6 (6) | 0.51 |
| Urine | 4 (5) | 2 (2) | 0.41 |
| Respiratory | 3 (4) | 3 (3) | 1.00 |
| Catheter-related | 1 (1) | 2 (2) | 0.59 |
| Other | 2 (2) | 1 (1) | 0.59 |
| Intra-abdominal | 0 (0) | 2 (2) | 0.50 |
| Clinical features | | | |
| ID consult obtained | 14 (16) | 23 (23) | 0.28 |
| Community-associated (< 48 h onset) | 58 (67) | 63 (62) | 0.42 |
| Hospital-associated (> 48 h onset) | 28 (33) | 39 (38) | 0.42 |
| Infecting organism | | | |
| *Enterococcus* spp. (vancomycin-susceptible) | 2 (2.3) | 6 (5.9) | 0.29 |
| *Enterococcus* spp. (vancomycin-resistant) | 0 | 1 (1.0) | 1.00 |
| *Micrococcus* spp. | 2 (2.3) | 2 (2.0) | 1.00 |
| Methicillin-susceptible *Staphylococcus aureus* | 4 (4.7) | 9 (8.9) | 0.39 |
| Methicillin-resistant *Staphylococcus aureus* | 5 (5.8) | 1 (1.0) | 0.09 |
| *Staphylococcus not aureus spp.* (i.e., CoNS) | 66 (76.7) | 72 (70.6) | 0.41 |
| *Streptococcus agalactiae* | 2 (2.3) | 1 (1.0) | 0.59 |
| *Streptococcus pyogenes* | 1 (1.2) | 1 (1.0) | 1.00 |
| *Streptococcus pneumoniae* | 1 (1.2) | 1 (1.0) | 1.00 |
| *Streptococcus* spp. (other species) | 3 (3.5) | 9 (8.9) | 0.23 |

Data are presented as number (%) of patients unless specified otherwise. Other infection sources were: 1 pacemaker pocket infection, 1 pacemaker lead infection, and 1 wound infection adjacent to spinal hardware. CoNS, coagulase-negative staphylococci; HIV/AIDS, Human immunodeficiency virus infection and acquired immune deficiency syndrome; ID, infectious diseases

not different between pre-BCID and post-BCID groups. There were similar proportions of patients in each group which warranted vancomycin therapy (29% versus 29%, $P = 0.96$). Of the patients who warranted vancomycin therapy ($n = 55$), there was no difference in time to appropriate therapy between groups (3.9 versus 0.9 h). In patients for whom vancomycin was deemed unnecessary ($n = 133$), vancomycin use (51% pre-BCID versus 36% post-BCID, $P = 0.09$), and time from culture positivity to vancomycin discontinuation (1.5 vs. 1.7 days; $P = 0.92$) did not reach statistical significance. Among patients who received unnecessary vancomycin therapy after blood culture positivity, a higher percentage (12/26, 46%) had vancomycin discontinued within 24 h of blood culture positivity in the post-BCID group than the pre-BCID group (10/31, 32%), but this finding was not statistically significant ($P = 0.28$). One-time doses of vancomycin were

**Table 2** Clinical features

| Characteristic | Total population | | | Vancomycin warranted | | | Vancomycin unnecessary | | |
|---|---|---|---|---|---|---|---|---|---|
| | Pre-BCID (n = 86) | Post-BCID (n = 102) | *P* | Pre-BCID (*n* = 25) | Post-BCID (*n* = 30) | *P* | Pre-BCID (*n* = 61) | Post-BCID (*n* = 72) | *P* |
| Immunosuppressed secondary to therapy[a] | 13 (15) | 17 (17) | 0.77 | 3 (12) | 4 (13) | 0.88 | 10 (16) | 13 (18) | 0.80 |
| Absolute neutrophil count < 1500 cells/μL | 3 (4) | 2 (2.0) | 0.52 | 2 (8) | 0 (0.0) | 0.12 | 1 (1.6) | 2 (2.8) | 0.66 |
| Charlson comorbidity index, median (IQR) | 4 (2–6) | 5 (3–8) | 0.04 | 3 (1–5) | 4 (2–6) | 0.21 | 5 (3–7) | 6 (4–8) | 0.08 |
| Pitt bacteremia score, median (IQR) | 0 (0–2) | 1 (0–3) | 0.12 | 1 (1–2) | 1 (1–4) | 0.28 | 0 (0–2) | 0 (0–2) | 0.18 |
| ICU admission, any | 27 (31) | 44 (43) | 0.10 | 12 (48) | 16 (53) | 0.69 | 15 (25) | 28 (39) | 0.08 |
| ICU admission ± 48 h of blood culture | 13 (15) | 25 (25) | 0.11 | 6 (24) | 10 (33) | 0.45 | 7 (12) | 15 (21) | 0.15 |
| Concomitant infection | 32 (37) | 54 (53) | 0.03 | 7 (28) | 15 (50) | 0.10 | 25 (41) | 39 (54) | 0.13 |

Data are presented as number (%) unless otherwise specified. [a] Immunosuppressive therapy including active systemic chemotherapy, tacrolimus, mycophenolate mofetil, azathioprine, cyclosporine, (or equivalent), for more than 7 days or a systemic steroid for more than 10 days the previous month. *BCID* blood culture identification panel; *ICU* intensive care unit; *IQR* interquartile range

comparable between groups (28% pre-BCID vs. 29% post-BCID group). The findings were unchanged after excluding patients with documented infection or CoNS with neutropenia or fever (Table 3). Of the 71 patients (40 pre-BCID and 31 post-BCID) who were categorized into the unnecessary vancomycin group that were not initiated on vancomycin before blood culture positivity, 55% in the pre-BCID and 39% in the post-BCID were treated with vancomycin ($P = 0.27$). Forty-nine of these patients did not have concomitant infections, with 45% in pre-BCID and 30% in the post-BCID group being treated with vancomycin.

### Clinical and economic outcomes

Clinical and economic data are shown in Table 4. Incidence of acute kidney injury, as defined by the RIFLE criteria, in the post-BCID group (14%) was similar to the pre-BCID group (13%). Exposure to concomitant nephrotoxins did not differ between groups. There was no difference in LOS, 30-day hospital readmission, all-cause mortality, and total hospital costs between groups (Table 4). When exploring these outcomes accounting for the necessity of vancomycin therapy, only 30-day hospital readmission was significantly reduced in the unnecessary vancomycin post-BCID group (23% versus 9%, $P = 0.03$).

## Discussion

Contaminated blood cultures are a clinically significant problem leading to unnecessary antibiotic exposures and laboratory tests, extended hospital stays, and increased healthcare costs [15, 16]. Information pertinent to determining the significance of a single positive blood culture may include the identity of the organism isolated, the number of blood cultures obtained, and clinical parameters of the patient. Traditionally, organism identification is not known until 24–48 h after Gram stain findings. Rapid molecular diagnostics panels for blood cultures can identify microorganisms earlier than previously used conventional systems, and as soon as 1 h after blood culture positivity and Gram stain results, and therefore providing clinicians the opportunity to discontinue unnecessary antibiotics earlier in a patient's hospitalization, a key facet of effective antimicrobial stewardship practices [17].

The results of this study indicate that earlier identification of single positive blood cultures with GPC did not significantly influence prescribing patterns of vancomycin; with no change in vancomycin use and time from culture positivity to vancomycin discontinuation when compared with a historical control group without RDTs. Furthermore, the implementation of rapid organism identification did not reduce clinical and economic burden of likely blood culture contaminants in this study. These findings may be expected, as the value of BCID on reducing vancomycin use likely is found in vancomycin avoidance or earlier discontinuation. For patients who did not have empiric vancomycin started before blood culture positivity, the BCID may be beneficial for avoiding the initiation of vancomycin in the first place. Vancomycin is frequently administered to patients before a blood culture detects microorganism growth, likely for suspicion of infection due to the clinical presentation of the patient. Therefore, vancomycin avoidance is unlikely to be realized in this situation. Vancomycin is often started empirically to cover for multiple possible sources of infection, and the results of the BCID may not impact discontinuation results, as providers may be waiting for further culture information to result. As many patients had concomitant infections and the number of patients who were not empirically treated with vancomycin before blood culture positivity was low, this may explain the lack of difference in vancomycin utilization between the groups. To further explore some of our findings, we analyzed outcomes among patients for which vancomycin therapy was unnecessary (i.e., contaminants and pathogens susceptible to narrower spectrum antimicrobials) and patients that did not have concomitant infections. The majority of these patients had contaminated blood cultures with coagulase-negative staphylococci. Earlier organism identification in this subset of patients should provide antimicrobial stewardship programs with opportunities to minimize the duration of unnecessary vancomycin. While there was less vancomycin use and an increased proportion of patients who received a one-time dose of vancomycin in this subset of the post-BCID group, no statistical differences were observed compared with the pre-BCID group. A higher percentage of patients had vancomycin discontinued within 24 h of blood culture positivity in the post-BCID group than the pre-BCID group, but this finding was also not statistically significant. Among patients without concomitant infections who did not warrant vancomycin therapy, vancomycin use and frequency of one-time doses were improved in the post-BCID group (Table 3), but not to a significant extent.

It is possible that the baseline antimicrobial stewardship review of positive blood cultures that was present in both groups lessened the opportunity for detectable improvements in the post-BCID group in this analysis [18]. Three other studies on the impact of RDTs for blood culture contaminants have found significant reductions of inappropriate antimicrobial prescribing [19–21]. The duration of vancomycin administration for blood culture contaminants ranged from 2.4 to 3.9 days in the pre-RDT groups, and were reduced by 1.2 to 2.6 days to a duration of 1.1 to 1.6 days of vancomycin for the post-RDT group in these studies. Two of the three studies also observed meaningful reductions in length of stay and hospitals costs [19, 21]. These findings are starkly different from the findings of our study. However, only one of these three studies had established ASP review of positive blood cultures in the pre-RDT group, but all three involved ASP review in the post-RDT. The mean duration of vancomycin therapy in our pre-BCID group was 1.4 days, highlighting the impact ASP intervention on positive blood cultures can have on minimizing inappropriate antibiotic exposure even in the absence of RDTs. Therefore, the lack of improvement in vancomycin prescribing patterns in the post-BCID group may be a result of judicious use of vancomycin in the pre-BCID group. Unfortunately, whether antimicrobial changes were made by ASP or independently by the treatment team were not consistently documented across all study periods, nor were they part of our study design, so we were not able to evaluate these endpoints. Additionally, ASP review and intervention did not occur 24 h a day. It is possible that having ASP intervene around the clock may have reduced unnecessary vancomycin use, and should be explored in future studies. However, as most of these interventions are related to non-urgent antimicrobial de-escalation, overnight staffing of the ASP may not be cost-effective. The relatively brief and comparable duration of vancomycin therapy in each of our study groups may also explain the similar rates of nephrotoxicity. Overall, clinical and economic outcomes remained largely unchanged in the unnecessary vancomycin analysis of our study, except that fewer patients in the post-BCID were readmitted to the hospital within 30 days compared with the pre-BCID group. Whether this finding is attributed to the BCID technology is uncertain. Of note, this study was a crude analysis that did not attempt to adjust for confounding, and the results should be interpreted as such.

Prior studies have not assessed the impact of rapid molecular diagnostics in a population of patients with only a single positive blood cultures [9]. Our data indicate that in patients with a single positive blood culture of GPC, commonly receive antibiotics despite frequently being contamination even

**Table 3** Vancomycin prescribing patterns in patients without concomitant infections

| Characteristic | Total population | | | Vancomycin warranted | | | Vancomycin unnecessary | | |
|---|---|---|---|---|---|---|---|---|---|
| | Pre-BCID ($n = 54$) | Post-BCID ($n = 48$) | $P$ | Pre-BCID ($n = 18$) | Post-BCID ($n = 15$) | $P$ | Pre-BCID ($n = 36$) | Post-BCID ($n = 33$) | $P$ |
| Received vancomycin | 30 (56) | 26 (54) | 0.89 | 12 (67) | 10 (67) | 1.00 | 18 (50) | 16 (49) | 0.90 |
| Received one dose of vancomycin ($n = 56$) | 4 (7) | 7 (15) | 0.24 | 2 (11) | 1 (7) | 0.66 | 2 (6) | 6 (18) | 0.10 |
| Interval between blood culture positivity and vancomycin discontinuation, day, median (IQR) ($n = 43$) | 1.3 (0.4–2.0) | 1.7 (1.0–2.5) | 0.23 | 1.3 (0.6–2.5) | 1.7 (1.5–2.5) | 0.28 | 1.5 (0.6–2.5) | 1.6 (0.6–4.4) | 0.90 |

Data are presented as number (%) unless otherwise specified

**Table 4** Clinical and economic outcomes

| Characteristic | Total population | | | Vancomycin warranted | | | Vancomycin unnecessary | | |
|---|---|---|---|---|---|---|---|---|---|
| | Pre-BCID (*n* = 86) | Post-BCID (*n* = 102) | *P* | Pre-BCID (*n* = 25) | Post-BCID (*n* = 30) | *P* | Pre-BCID (*n* = 61) | Post-BCID (*n* = 72) | *P* |
| Development of acute kidney injury | 9 (13) | 9 (14) | 0.86 | 2 (10) | 4 (18) | 0.45 | 7 (14) | 5 (12) | 0.74 |
| Post culture length of stay, day, median (IQR)* | 6 (3–12) | 7 (3–16) | 0.07 | 8 (2–13) | 7 (4–20) | 0.75 | 4 (3–12) | 7 (3–16) | 0.05 |
| In-hospital mortality (all cause) | 6 (7) | 8 (8) | 0.83 | 2 (8) | 4 (13) | 0.53 | 4 (7) | 4 (6) | 0.81 |
| 30-day all cause hospital readmission* | 16 (20) | 10 (11) | 0.08 | 3 (13) | 4 (15) | 0.82 | 13 (23) | 6 (9) | 0.03 |
| Total hospital costs, $, median (IQR) | 17,769 (7514-56,100) | 26,206 (10,323-76,015) | 0.11 | 32,747 (9576-89,394) | 31,906 (15,076-108,663) | 0.76 | 12,866 (6271-41,447) | 25,312 (9756-67,476) | 0.09 |

Data are presented as number (%) unless otherwise specified. *IQR* interquartile range. *Analysis excludes patients with in-hospital mortality

with the RDTs and ASP intervention. This emphasizes the ongoing need for efforts to reduce blood culture contamination, such as blood diversion devices that divert and sequester the initial portion of blood that may contain contaminating skin cells and microbes. Use of these devices is clinically proven to dramatically reduce the number of blood cultures contaminants [22].

## Conclusion

In summary, our observations support that earlier organism identification of likely blood culture contaminants in conjunction with ASP intervention appears to limit the duration of unnecessary vancomycin therapy, but not in a significant manner compared with ASP intervention alone. The baseline ASP review of positive blood cultures and the small sample size lessening the opportunity for detectable differences between groups is possible but uncertain. Larger studies, accounting for the impact of ASP intervention, should be performed to determine the value of each individual component.

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## Compliance with ethical standards

**Conflict of interest** SHM is a current employee and shareholder of the Accelerate Diagnostics, Inc. All other authors report no conflicts of interest.

**Ethical approval** This study was approved by the local Institutional Review Board (IRB).

**Informed consent** A waiver of informed consent was granted by the IRB.

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