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Real-World Evaluation of the Impact of Implementation of the Virtuo Blood Culture System in a Tertiary Care Hospital

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ABSTRACT The bioMérieux BacT/Alert Virtuo blood culture system used in combination with resin-containing media may enhance the growth of microorganisms. Our objective was to assess the impact of transitioning to the Virtuo system in comparison to the VersaTREK blood culture system at a tertiary care medical center. We retrospectively reviewed all blood cultures performed at a 1,250-bed academic medical center between January and December 2018 (VersaTREK) and January and December 2019 (Virtuo). Blood culture positivity rates and contamination rates were compared before and after Virtuo implementation. Of 101,438 blood cultures performed during the study period, 48,839 (48.1%) were processed preimplementation and 52,599 (51.9%) postimplementation. The blood culture positivity rate increased from 8.1% preimplementation to 11.7% postimplementation \((P < 0.001)\). Staphylococcus aureus was the most frequently isolated species in both time periods and had a higher recovery rate postimplementation (1.5% of all blood cultures obtained preimplementation versus 3.4% postimplementation; \(P < 0.001\)). A higher recovery rate in the postimplementation period was also noted for coagulase-negative staphylococci (1.9% preimplementation versus 2.7% postimplementation; \(P < 0.001\)), as well as modest but statistically significant changes for Escherichia coli (0.8% versus 1.0%; \(P < 0.001\)), Klebsiella pneumoniae (0.4% versus 0.5%; \(P = 0.005\)), and Candida albicans (0.1% versus 0.2%; \(P = 0.038\)). The inpatient blood culture contamination rate was higher postimplementation (1.5% preimplementation versus 1.9% postimplementation; \(P < 0.001\)). The Virtuo blood culture system was associated with a higher observed proportion of positive blood cultures than the VersaTREK system. Future studies are needed to assess whether an increased rate of positive blood cultures is associated with changes in clinical outcomes.

KEYWORDS blood culture, Virtuo, bloodstream infections

Bloodstream infections (BSI) are a major cause of morbidity and mortality in the hospital and community (1, 2). Identification of BSI and the responsible pathogens is crucial for prompt initiation of appropriate antibiotic therapy (3, 4), which can lead to improved patient outcomes (5). Blood cultures are the standard method for detection of BSI caused by bacteria and fungi, and numerous changes in recent years have been made to blood culture media and culture incubation/growth detection systems to improve organism recovery and decrease the time to microorganism detection.

The BacT/Alert Virtuo (bioMérieux, Durham, NC) system is a closed microbial detection system for blood cultures that utilizes automated loading and unloading of blood culture bottles to improve temperature stability during the incubation period, improving time to microbial detection. The system uses colorimetric technology to detect pH changes caused by carbon dioxide produced by microorganisms during metabolism. Furthermore, the blood culture medium formulations include added supplements and peptones as well as polymeric resins that bind antibiotics, possibly improving microorganism recovery. Virtuo has been compared to the BacT/Alert 3D system (bioMérieux,
Durham, NC) using clinical samples with equivalent recovery but shorter time to positivity (6, 7).

The VersaTREK system (TREK Diagnostic Systems, Cleveland, OH) is a microbial detection system that has been commercially available since 2003. The VersaTREK system uses an external pressure sensor to measure pressure changes in the sample bottle which can happen due to consumption and production of gases by microorganisms (i.e., oxygen, nitrogen, hydrogen, etc.). This system uses blood culture bottles with highly enriched Redox medium and a 1:9 blood-to-broth dilution to neutralize the effects of inhibitory substances that may be present in the specimen. Using clinical samples, the VersaTREK system detected more streptococci and enterococci than the BacT/Alert 3D system, and in samples from patients with prior antibiotic use, it detected more microorganisms overall (8). However, there has not been a comparison study evaluating both the Virtuo and VersaTREK blood culture systems in clinical operation.

Our objective was to assess the impact of transitioning from the VersaTREK blood culture system to the Virtuo system at a large academic medical center. Our results may help understand changes in detection rate that happen when new blood culture systems are implemented in hospitals, as a difference can potentially translate into differences in observed persistent BSI and rate of blood culture contamination.

**MATERIALS AND METHODS**

**Setting and study design.** We performed a retrospective cohort study of all blood cultures performed between 1 January 2018 and 31 December 2019 at Barnes-Jewish Hospital (BJH), a 1,250-bed academic medical center located in St. Louis, MO, USA. The Virtuo blood culture system was adopted for use for all blood cultures processed in the clinical microbiology laboratory on 14 January 2019.

Preimplementation, the hospital used the VersaTREK blood culture system (TREK Diagnostic Systems, Cleveland, OH). We divided our study into two periods: before implementation (1 January 2018 to 13 January 2019) and after implementation (14 January 2019 to 31 December 2019) of the new system. All blood culture specimens obtained at BJH locations (i.e., inpatient areas, emergency department [ED], and outpatient areas) were included. Aerobic and anaerobic blood culture bottles from a blood draw were considered a single blood culture for purposes of analysis and were identified using the BJH medical informatics database. The study was approved by the Washington University School of Medicine Institutional Review Board with a waiver of informed consent.

**Blood culture systems.** The blood culture media used for the VersaTREK blood culture system were VersaTREK Redox 1 (aerobic) and Redox 2 (anaerobic) standard bottles, which are made of glass and were transported manually via courier to the laboratory. As mentioned above, the Redox 1 and Redox 2 media utilize a 1:9 blood-broth dilution to neutralize the effects of inhibitory substances that may be present in the specimen. Once the blood culture bottles were manually inserted into the VersaTREK instrument and incubated at 35°C, an external pressure sensor automatically screened for culture positivity at regular intervals by detection of pressure changes in the blood culture bottles caused by gas consumption or produced during microbial metabolism. The Virtuo blood culture system was paired with FA Plus (aerobic) and FN Plus (anaerobic) blood culture bottles, and the bottles were routinely transported to the laboratory from inpatient units and the emergency department using the pneumatic tube system. These bottles have polymeric resins that reduce the concentration of inhibitors and antibiotics that may be present in the blood. Carbon dioxide produced by microorganisms during metabolism diffuses to a wafer in the bottom of the bottle that is sensitive to pH (color change). The Virtuo instrument incubates bottles at 37°C, scans the bottles at regular intervals to detect this color change, and signals positive when a threshold is met. For both blood culture systems, bottles were incubated for up to 5 days or until they signaled positive on the instrument.

Positive bottles were processed according to laboratory standard operating procedures during both time periods, as explained elsewhere (9). Briefly, when blood cultures signaled positive, a Gram stain was prepared and the bottles were subcultured to solid medium for additional workup, including identification using matrix-assisted laser desorption ionization–time of flight mass spectrometry (MALDI-TOF MS) (Bruker Biotyper instrument; Bruker Daltonics).

**Study outcomes and statistical analysis.** Our primary endpoints were proportion of positive blood cultures, contamination rate, and time from blood culture collection to arrival at the laboratory. Contaminated blood cultures were defined as a single blood culture positive with a skin commensal organism within a 3-day period. Common commensal organisms included those in the National Health Safety Network (NHSN) organism list, including coagulase-negative staphylococci (CoNS), Bacillus spp., coryneforms, Cutibacterium spp., viridans group streptococci, and Micrococcus spp. (10).

Continuous variables were expressed as medians with interquartile ranges, as appropriate, and assessed using the Mann-Whitney U test. Categorical variables were presented as absolute numbers, and frequencies and were compared using a chi-square test or Fisher’s exact test, as appropriate. Microorganisms isolated from $\geq$100 blood cultures during the entire study period were analyzed for comparison between the pre- and postimplementation period. Temporal changes in the daily blood culture positivity rate during the study period was assessed using autoregressive integrated moving average models.
average (ARIMA) analysis. Segmented linear regression analyses were performed to assess changes in the inpatient areas and ED contamination rates during the pre- and postintervention periods. Two-sided P values of <0.05 were considered statistically significant. Analyses was performed with SAS version 9.3 software (SAS Institute Inc., Cary, NC).

RESULTS

Blood culture collection and overall positivity rate. We analyzed 101,438 blood cultures obtained throughout the study period: 48,839 (48.1%) were collected preimplementation using the VersaTREK system from 16,054 unique patient encounters, and 52,599 (51.9%) were obtained postimplementation using the Virtuo system from 15,900 unique patient encounters. Most blood cultures were collected in inpatient areas (n = 72,968 [71.9%]), followed by the ED (n = 20,809 [20.5%]) and non-ED outpatient areas (n = 7,661 [7.6%]). Preimplementation, 3,971 (8.1%) blood cultures were positive for growth of microorganisms, compared to 6,132 (11.7%) cultures postimplementation (P < 0.001). Differences in the positivity rate in the pre- versus postimplementation period were observed in inpatient areas (7.1% versus 11.4%; P < 0.001) but not in the ED (12.7% versus 13.4%; P = 0.137) or non-ED outpatient areas (8.3% versus 8.5%; P = 0.794). Furthermore, the median daily positivity rate was lower in the preimplementation period than the postimplementation period (7.8% versus 11.5%; P < 0.001) (Fig. 1). A decreased median time from collection until arrival at the laboratory was seen postimplementation (2.0 h pre- versus 0.8 h postimplementation; P < 0.001), and this difference was similar in the ED (2.1 versus 0.5 h postimplementation; P < 0.001), non-ED outpatient areas (1.8 versus 1.1 h postimplementation; P < 0.001) and inpatient areas (2.0 versus 0.8 h postimplementation; P < 0.001).

Positivity rate of clinically significant organisms. *Staphylococcus aureus* was the most frequently isolated organism for both study periods, accounting for 2.4% of all blood cultures and 24.5% of positive blood cultures across the duration of the study. We detected a higher proportion of blood cultures positive for *S. aureus* postimplementation (716 [1.5%] pre- versus 1,764 [3.4%] postimplementation; P < 0.001) (Table 1). A higher proportion of blood cultures were also positive for CoNS in the postimplementation period (914 [1.9%] pre- versus 1,436 [2.7%] postimplementation; P < 0.001). We did not find a significant difference in the proportion of blood cultures positive for *Streptococcus* spp., *Enterococcus faecium, Enterococcus faecalis*, or *Bacillus* spp. (Table 1).

Among Gram-negative bacteria, postimplementation there was a higher recovery rate of *Escherichia coli* (384 [0.8%] pre- versus 534 [1.0%] postimplementation; P < 0.001) and *Klebsiella pneumoniae* (176 [0.4%] pre- versus 250 [0.5%] postimplementation; P = 0.005). No significant difference was noted for other *Enterobacteriales* or *Bacteroides fragilis* (Table 1).

Finally, the proportion of blood cultures which grew *Candida* spp. was significantly greater in the postimplementation period (160 [0.4%] pre- versus 286 [0.5%] postimplementation; P < 0.001), including the most commonly isolated species, *Candida albicans* (63 [0.1%] pre- versus 96 [0.2%] postimplementation; P = 0.038) and *Candida glabrata* (46 [0.1%] pre- versus 81 [0.2%] postimplementation; P = 0.009).
The overall contamination rate was higher postimplementation in the inpatient areas (1.5% pre- versus 1.9% postimplementation; \( P = 0.001 \)) and in the ED (3.6% pre- versus 4.2% postimplementation; \( P = 0.02 \)). During the postimplementation period, we detected an increase in the monthly percentage of contaminated blood cultures compared to the preimplementation period that was significant in inpatient areas (\( P = 0.009 \)) but not for the ED (\( P = 0.08 \)) (Fig. 2A and B).

DISCUSSION

Fast and accurate detection of BSI is crucial in order to choose and initiate appropriate antimicrobial therapy. Here, we evaluated the microbiological performance of Virtuo blood culture system after its implementation in a large academic medical center. We found that implementation of the FA and FN Plus media with the Virtuo system allowed faster transport of blood culture bottles to the microbiology laboratory (because the plastic bottles for this system could be sent through our pneumatic tube system) and a higher rate of organism recovery compared to the previous blood culture system. The increase in the proportion of positive blood cultures postimplementation was predominantly driven by a 2-fold increase in recovery of *Staphylococcus* spp.

No prior studies have compared the Virtuo and VersaTREK system using clinical samples; however, one prior study described similar detection rates between both systems, with the exception of increased detection of *Helicobacter cinaedi* by the VersaTREK system (11). This study included clinical cultures for VersaTREK and spiked blood culture bottles for Virtuo, which may explain the difference in results compared to our study. Virtuo has also been compared against other blood culture systems using clinical samples and simulated blood cultures (6, 7, 12–18). Using prospective clinical samples, the Virtuo had an overall positivity rate similar to that of BacT/Alert 3D using the same FA Plus and FN Plus media (6,

**TABLE 1** Comparative positivity rate of blood culture system by key organisms\(^a\)

<table>
<thead>
<tr>
<th>Microorganisms</th>
<th>Preimplementation(^b)</th>
<th>Postimplementation(^c)</th>
<th>( P ) value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Gram-positive bacteria</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Staphylococcus aureus</em></td>
<td>716 (1.5)</td>
<td>1,764 (3.4)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><em>Coagulase-negative staphylococci</em></td>
<td>914 (1.9)</td>
<td>1,436 (2.7)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><em>Staphylococcus epidermidis</em></td>
<td>304 (0.6)</td>
<td>578 (1.1)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><em>Viridans group streptococci</em></td>
<td>56 (0.1)</td>
<td>63 (0.1)</td>
<td>0.81</td>
</tr>
<tr>
<td><em>Streptococcus mitis group</em></td>
<td>73 (0.2)</td>
<td>76 (0.1)</td>
<td>0.90</td>
</tr>
<tr>
<td><em>Streptococcus pneumoniae</em></td>
<td>57 (0.1)</td>
<td>51 (0.1)</td>
<td>0.34</td>
</tr>
<tr>
<td><em>Enterococcus faecium</em></td>
<td>212 (0.4)</td>
<td>213 (0.4)</td>
<td>0.50</td>
</tr>
<tr>
<td><em>Enterococcus faecalis</em></td>
<td>165 (0.3)</td>
<td>182 (0.3)</td>
<td>0.97</td>
</tr>
<tr>
<td><em>Bacillus</em> spp.</td>
<td>58 (0.1)</td>
<td>49 (0.1)</td>
<td>0.22</td>
</tr>
<tr>
<td><strong>Gram-negative bacteria</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
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<td>384 (0.8)</td>
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<td>&lt;0.001</td>
</tr>
<tr>
<td><em>Klebsiella pneumoniae</em></td>
<td>176 (0.4)</td>
<td>250 (0.5)</td>
<td>0.005</td>
</tr>
<tr>
<td><em>Enterobacter cloacae</em></td>
<td>79 (0.2)</td>
<td>80 (0.2)</td>
<td>0.69</td>
</tr>
<tr>
<td><em>Proteus mirabilis</em></td>
<td>51 (0.1)</td>
<td>73 (0.1)</td>
<td>0.14</td>
</tr>
<tr>
<td><em>Pseudomonas aeruginosa</em></td>
<td>166 (0.3)</td>
<td>214 (0.4)</td>
<td>0.09</td>
</tr>
<tr>
<td><em>Bacteroides fragilis</em> group</td>
<td>57 (0.1)</td>
<td>59 (0.1)</td>
<td>0.83</td>
</tr>
<tr>
<td><strong>Fungi</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Candida</em> spp.</td>
<td>198 (0.4)</td>
<td>306 (0.6)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><em>Candida albicans</em></td>
<td>63 (0.1)</td>
<td>96 (0.2)</td>
<td>0.038</td>
</tr>
<tr>
<td><em>Candida glabrata</em></td>
<td>46 (0.1)</td>
<td>81 (0.2)</td>
<td>0.009</td>
</tr>
<tr>
<td><strong>Total positivity rate</strong></td>
<td>3,971 (8.1)</td>
<td>6,132 (11.7)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

\(^a\)Includes only microorganisms detected in 100 or more blood cultures during entire study period.

\(^b\)From 1 January 2018 to 13 January 2019.

\(^c\)From 14 January 2019 to 31 December 2019.

**Blood culture contamination rate.** The overall contamination rate was higher postimplementation in the inpatient areas (1.5% pre- versus 1.9% postimplementation; \( P < 0.001 \)) and in the ED (3.6% pre- versus 4.2% postimplementation; \( P = 0.02 \)). During the postimplementation period, we detected an increase in the monthly percentage of contaminated blood cultures compared to the preimplementation period that was significant in inpatient areas (\( P = 0.009 \)) but not for the ED (\( P = 0.08 \)) (Fig. 2A and B).

A. Inpatient areas.

B. Emergency Department.

FIG 2 Monthly blood culture contamination rate during the study period. Mean monthly contamination rates in the inpatient areas (A) and emergency department (B) in the pre- and postimplementation periods are shown. *, a significant difference was found for the inpatient areas but not for the emergency department using segmented linear regression analyses. †, the preimplementation period was from 1 January 2018 to 13 January 2019. ‡, the postimplementation period was from 14 January 2019 to 31 December 2019.

7, 12). The latter would explain the lack of difference, as the blood culture medium also plays a major role in microorganism recovery.

In our study, FA Plus (aerobic) and FN Plus (anaerobic) blood culture media were compared to the Redox 1 (aerobic) and Redox 2 (anaerobic) media used in the preimplementation period. FA Plus and FN Plus contain polymeric resins that adsorb antibiotics and have been shown to provide improved recovery compared to polymeric resin-free bottles (19, 20). Specifically, significantly more S. aureus and total microorganisms were recovered with FA Plus medium than with FA medium, while with the FN Plus bottles, more S. aureus, CoNS, and total microorganisms were recovered than with the FN bottles (19). Furthermore, in the presence of antibiotics, the FA Plus bottle had a higher overall recovery rate than Aerobic/F Plus media using the Bactec Plus system (BD Diagnostics, Sparks, MD) (20). In contrast, the Redox 1 and 2 media used by the VersaTREK system had more conflicting results than other blood culture media. An overall similar recovery rate was seen with Redox 1 and Redox 2 media compared to standard aerobic and anaerobic 3D media in the BacT/Alert 3D system, but with significantly more microorganisms recovered in samples from those receiving antimicrobial therapy by the Redox media (8). However, compared to the Bactec FX system using the Bactec Plus Aerobic/F and Bactec Plus Anaerobic/F media, Redox 1 and Redox 2 media had an overall reduced recovery rate (21). Unfortunately, in our analyses we could not compare positivity rates of aerobic and anaerobic bottles between systems because our medical informatics database did not include results by bottle type. However, the findings of these studies, in addition to our results, demonstrate a possible superiority in BSI recovery rate of the polymeric resin-containing FA Plus and FN Plus media compared to resin-free media such as Redox 1 and 2 media. The advantage
of resin-based medium is not completely explained by our study, but presumably these allow better inhibition of antibiotics (20), thus increasing the recovery rate of microorganisms in the index and subsequent repeat blood culture sets, as likely observed in the inpatient areas in our study.

In terms of specific microorganisms, we found a significant increase in *Staphylococcus* sp. recovery after the Virtuo system was implemented. *S. aureus* bacteremia is common and has high morbidity and mortality (22); thus, a higher recovery of *S. aureus* by Virtuo blood culture system can have important clinical implications. Furthermore, persistent recovery of *S. aureus* in subsequent blood cultures even after appropriate antibiotics could potentially impact management and should be studied further. Similarly, CoNS are common causes of nosocomial BSI but are also commonly considered contaminants (23). Differentiating contamination from true bacteremia is critical for management of patients and for hospital infection prevention measures. Our results indicate that CoNS was recovered more frequently postimplementation with the FA Plus and FN Plus media. These blood culture media have shown increased CoNS recovery compared to charcoal media (resin free) (19). The increased recovery rate of CoNS with Virtuo likely explains the increase in our blood culture contamination rate in the postimplementation period; however, whether this was associated with increased use of unnecessary antibiotics or tests is unknown.

Due to the small number of other microorganisms isolated in our study, including Gram-negative bacteria and *Candida* spp., as well as uncommon fastidious microorganisms, it is difficult to draw definitive conclusions regarding the relative performance of the Virtuo system and the blood culture media for recovering these organisms. Additional studies are warranted to confirm and further explore these observations.

There are several limitations to our study. First, this was a single-center study, and data may not be representative of other hospitals. However, our blood culture positivity rate (8.3% to 10.7%) and contamination rate (0.6% to 12.5%) are comparable to those in other clinical studies (7, 24, 25). The retrospective nature of our study and the pre- and postintervention comparison limit our ability to identify all potential factors influencing blood culture collection and positivity rate. For example, differences between our study periods in antimicrobial utilization trends, antimicrobial susceptibility patterns, and patient populations may have contributed to our results (26). Furthermore, when Virtuo was implemented and once an increase in the blood culture contamination rate was noted, education was provided to nursing staff on the new system and proper collection of blood cultures; however, no changes in blood culture collection practices were instituted between the two periods. Similarly, we found a similar number of blood culture orders per 1,000 patient-days pre- and postimplementation and no significant difference in the blood culture positivity rate in the preimplementation period (2018) compared to the year prior (January to December 2017; blood culture positivity rate, 8.3% in 2017 versus 8.1% in January to December 2018; *P* = 0.2). Furthermore, the proportion of critically ill patients was similar pre- and postimplementation, and no widespread educational interventions were performed to clinicians regarding indications for blood culture collection. Last, we did not determine whether the increase in the positivity rate was associated with changes in clinical outcomes, which would be the ultimate goal of newer blood cultures systems that increase detection of organisms in blood.

In summary, implementation of the Virtuo system with FA Plus and FN blood culture media resulted in a higher proportion of positive blood cultures across a large academic medical center, compared to the previous blood culture system, and this increase was primarily due to a higher recovery of *Staphylococcus* spp. A higher proportion of contaminated blood cultures was also seen. Taking the previous clinical data and our study findings, it is likely that the difference in performance is due to the medium formulation and the resins’ ability to inhibit antimicrobials from specimens, allowing growth in initial and subsequent blood cultures. When new blood culture systems are implemented, consideration should be given to changes in organism.
REFERENCES


