PNA FISH for Hospital Acquired Enterococcal Bacteremia: Delivering Earlier Effective Antimicrobial Therapy

Graeme N. Forrest,¹* Mary-Claire Roghmann,² Latoya S. Toombs,³ Jennifer K. Johnson,⁴
Elizabeth Weekes,³ Durry P. Lincalis,⁴ Richard A. Venezia.⁴

Performed at University of Maryland Medical Center, 22 S. Greene St, Baltimore, Md, 21224.

From the ¹Division of Infectious Diseases, University of Maryland School of Medicine, Baltimore, MD, USA, ²Department of Epidemiology and Preventive Medicine, University of Maryland School of Medicine, Baltimore, MD, USA. ³University of Maryland Medical Center, Department of Pharmacy, Baltimore, MD, USA, and the Department of Pathology ⁴University of Maryland School of Medicine

Corresponding author: Graeme N. Forrest, M.B.B.S.
Division of Infectious Diseases
Department of Medicine
University of Maryland
20 Penn Street, Room S403B
Baltimore, MD  21201
Phone: 410-706-5680
Fax: 410-706-8700
E-mail: gforrest@medicine.umaryland.edu

Key words: Enterococcus faecalis, vancomycin resistant Enterococcus faecium, Rapid diagnostic testing, linezolid

Running head: PNA FISH for Enterococcal Bacteremia

Footnote: L.S. Toombs now at Washington Hospital Medical Center, Washington D.C.
E. Weekes now at Rocky Mountain Poison and Drug Center, Denver, Co.
Abstract:

**Background:** Hospital acquired vancomycin resistant enterococcal (VRE) bacteremia has been associated with increased hospital costs, length of stay and mortality. The *Enterococcus faecalis* and other enterococci (EFOE) peptide nucleic acid fluorescent in-situ hybridization (PNA FISH) test is a multicolor probe that identifies *E. faecalis* from other enterococcal species within 3 hours directly from blood cultures demonstrating Gram positive cocci in pairs and chains (GPCPC).

**Method:** A quasi-experimental study was performed over two consecutive years beginning in 2005 identifying GPCPC by conventional microbiological methods and in 2006 adding PNA FISH with a treatment algorithm developed by the antimicrobial team (AMT). Primary outcome assessed was time from blood culture draw to the implementation of effective antimicrobial therapy before and after PNA FISH. Severity of illness, patient location and empiric antimicrobial therapy were measured.

**Results:** A total of 224 patients with hospital acquired enterococcal bacteremia were evaluated with 129 in the pre-intervention period and 95 in the PNA FISH period. PNA FISH identified *E. faecalis* 3 days earlier than conventional cultures (1.1 vs. 4.1 days, p<0.001). PNA FISH identified *E. faecium* a median 2.3 days earlier (1.1 vs. 3.4 days, p<0.001) and was associated with statistically significant reductions in time to initiating effective therapy (1.3 vs. 3.1 days, p<0.001) and decreased 30 day mortality (26% vs. 45%, p=0.04).

**Conclusion:** EFOE PNA FISH test in conjunction with an AMT treatment algorithm and resulted in earlier initiation of appropriate empiric antimicrobial therapy for patients with hospital acquired *E. faecium* bacteremia.
Introduction

Enterococcal bacteremia is the fourth most common cause of hospital acquired bacteremia within the United States and the fifth most common in Europe from the SENTRY antimicrobial surveillance program. The predominant enterococcal species that cause these infections are Enterococcus faecalis and Enterococcus faecium. Vancomycin resistant enterococci (VRE) have emerged as a major problem and has progressively increased over the last decade. The most recent surveillance data from SENTRY showed E. faecium resistance to vancomycin had increased from 40% to 61% in 2002, while the Surveillance and Control of Pathogens of Epidemiologic Importance (SCOPEI), also found 40% VR E. faecium in 2002. At many tertiary care medical centers, E. faecium is approaching nearly 100% vancomycin resistance. In contrast, E. faecalis has maintained susceptibility to ampicillin with a relatively small increase in vancomycin resistance.

VRE bacteremia has been associated with increased mortality, longer hospital length of stay and higher health care costs. In a large meta-analysis on the outcomes of VRE infections, Salgado and Farr postulated that one of the reasons for the increased mortality in these patients was delayed effective antimicrobial therapy towards VRE. Patients at greatest risk for VRE are most likely to be critically ill, be solid organ transplant recipients, prolonged neutropenia and/or spent prolonged time periods within the hospital. Early appropriate antimicrobial therapy has been demonstrated to improve patient outcomes in the ICU setting which is clearly a high risk setting for VRE infection.

Peptide nucleic acid fluorescent in-situ hybridization (PNA FISH) probes are DNA mimics where a sugar-phosphate backbone of DNA is replaced with a non-charged peptide backbone. This allows the probes to target individual species-specific targets on the 16S
ribosomal RNA within living bacteria. There are presently 3 commercially available FDA approved probes for *Staphylococcus aureus*, *Candida albicans* and for *Enterococcus* species. The *E. faecalis* and other enterococci (EFOE) PNA FISH probe (AdvanDx, Inc., Woburn, Ma) is unique in that it is a multicolor probe that is applied to drop of blood from a positive blood culture that has Gram positive cocci in pairs and chains (GPCPC) and results can be obtained in about 2 ½ hours. Typical results include green fluorescence for *E. faecalis*, red for other *Enterococcus* species including *E. faecium* and no color if not an *Enterococcus* (e.g. a *Streptococcus* species). PNA FISH is easier to perform than a Gram-stain and importantly, retains cellular morphology to assist in the identification of the organism under the fluorescent microscope.

Given this information, we can prescribe more appropriate directed therapy to patients with hospital acquired enterococcal bacteremia and potentially decrease the delay in appropriate therapy to patients. The University of Maryland Medical Center microbiology laboratory has performed PNA FISH testing since 2004 and introduced the EFOE PNA FISH test in 2006. The reporting of results was incorporated into the hospital’s Antimicrobial Management Team (AMT), which consists of a full-time infectious disease pharmacist and 25% Infectious Disease physician effort. This successful synergy between the AMT and PNA FISH has previously been reported from our institution showing cost savings and reduction in length of stay. Here we present the impact of implementing the EFOE PNA FISH test on the clinical care of patients with hospital acquired enterococcal bacteremia.

**Methods**
Study Design: This was a quasi-experimental study (1 group, pre-test, post test design) performed at the University of Maryland Medical Center (UMMC) over two years (2005-2006). The University of Maryland Institutional Review Board approved this study.

Setting and Patients: The UMMC is a ~600 bed inner-city tertiary care teaching hospital which includes 130 intensive care unit (ICU) beds, the Marlene and Stewart Greenebaum Cancer Center and a large solid organ transplant program. All patients with hospital acquired bacteremia due to *E. faecium* or *E. faecalis* during the study period were included as study subjects. Hospital acquired bacteremia was defined as either occurring greater than 72 hours after admission. This included the length of stay from transfer from another hospital setting. The AMT did not make interventions in patients with Streptococcal infections as these are often community acquired, present with admitting cultures, occur more often and are frequently covered by many classes of antibiotics and would consume too much of the AMT time with minimal changes to antibiotic therapy. Only the first episode of enterococcal bacteremia per patient per admission was included. The following patient groups were excluded from the study analysis: pediatric patients and R. Adams Cowley Shock Trauma Center patients (because these patient groups are not evaluated by the hospital’s Anti-Microbial Team [AMT]), patients who died in either group before the culture was positive (because the AMT were unable to intervene), or patients with documented endocarditis based on modified Duke criteria (because the developed treatment algorithm did not apply). Surveillance for VRE with perirectal cultures was standard practice on all patients on the day of admission to an ICU or the Cancer center and then performed weekly during both pre and post-intervention periods. VRE alerts were present in the chart for current and prior VRE colonization and patients appropriately isolated. A prior VRE culture in both time periods warranted early linezolid therapy.
Laboratory: Blood cultures were drawn per standard hospital policy from 2 separate sites and collected in blood culture bottles (BacTAlert, Becton Dickinson, MD, USA). The cultures were placed in a continuous automated detection incubator (BacT/Alert). When GPCPC were identified by Gram staining signal-positive blood cultures, they were plated onto standard growth media as per standard laboratory protocol. These results were called to the treating physician as per normal policy. When there was growth on the plates, enterococci were identified (catalase negative, alpha or non-haemolytic colonies) using catalase detection with 3% $\text{H}_2\text{O}_2$ and PYR positive. (Hardy Diagnostics, Santa Maria, Ca).\textsuperscript{3,4} Subspecies identification was performed using VITEK 2 (bioMerieux, Marcy l'Etoile, France) and susceptibilities were performed using disc-diffusion assay following the Clinical and Laboratory Standards Institute (CLSI) protocols.\textsuperscript{4}

PNA FISH testing for Enterococcus species was batched and performed twice a day (8 AM and 3PM) using manufacturers instructions during 2006.\textsuperscript{8,32} After identification of GPCPC from blood culture, a drop of blood is placed on a slide and the probe is added, the slide is then placed in a water bath for 90 minutes, washed for 30 minutes and read under a fluorescent microscope.\textsuperscript{8,32} Green fluorescence indicates \textit{E. faecalis} while red fluorescence indicates other \textit{Enterococcus} species including \textit{E. faecium}. PNA FISH results were called to the physician with follow up by the AMT. Final cultures were compared to the PNA FISH results.

Intervention: The study subjects were derived from two consecutive time periods. During 2005, \textit{E. faecium} and \textit{E. faecalis} were identified using standard microbiologic methods and AMT action on antimicrobial therapy was directed by clinical factors and final susceptibility results. During 2006, \textit{E. faecium} and \textit{E. faecalis} were identified using the PNA FISH and standard microbiological methods. The AMT intervened at the time of the PNA FISH results to direct antimicrobial therapy.
Based on our antibiograms from 2004, 100% of our *E. faecalis* organisms were ampicillin susceptible and 90% were vancomycin susceptible. Of our other *Enterococcus* species, 99% were *E. faecium*. None of the *E. faecium* were ampicillin susceptible based on CLSI standards and only 15% were vancomycin susceptible. With this data, the AMT developed a treatment algorithm shown in Figure 1. The AMT discussed the PNA FISH results daily, including weekends, with the treating physician who then determined whether a change in therapy was necessary. Prior VRE colonization and VRE surveillance cultures were also taken into consideration during the entire study period. The treatment algorithm had preferred therapies with ampicillin for *E. faecalis* (vancomycin when penicillin allergic) and linezolid for *E. faecium* and if not an *Enterococcus* species, then penicillin or ceftriaxone (vancomycin could be added if meningitis or febrile neutropenia). High dose daptomycin was considered as an alternative to linezolid when necessary with vancomycin resistant *E. faecium*. Because enterococcal bacteremia is frequently associated with other organisms, especially Gram-negative bacteria, piperacillin/tazobactam or imipenem/cilastatin could be utilized in place of ampicillin, as both these antibiotic have adequate *E. faecalis* activity. Ampicillin susceptibility was used as a marker for imipenem/cilastatin and piperacillin/tazobactam susceptibility. All central lines were removed after documentation of enterococcal bacteremia.

**Data Collection:** We collected the following information on study subjects via chart review: age, sex, length of stay (LOS); central line status, APACHE II score at time of blood culture, serum chemistry, complete blood count, hospital location (all at onset of bacteremia); time from report of Gram-stain to final enterococcal susceptibilities, other organisms in the blood culture, initial antimicrobial therapy, time to change antimicrobial therapy to appropriate therapy after report of GCPC and survival status at 30 days. Neutropenia was defined as having an absolute neutrophil...
count less than 500 cells at onset of bacteremia. The prospective intervention group also included time from Gram Stain to PNA FISH report and accuracy of PNA FISH result to final culture.

Appropriate antimicrobial therapy was defined as the receipt of an antibiotic with activity against the cultured Enterococci. Time to appropriate therapy was from the time the blood culture was drawn to the time of receipt of appropriate therapy. We assessed whether the selected empiric therapy had coverage of all organisms from the blood culture based on their final susceptibilities. Mortality was all cause mortality and was determined at 30 days after the first positive blood culture.

Statistical analysis: The primary objective of this study was to determine if the EFOE PNA FISH test would lead to the earlier initiation of appropriate antimicrobial therapy for patients with E. faecium and E. faecalis bacteremia. The secondary objective was to determine the effect of PNA FISH on survival and hospital length of stay. We initially described the study population using proportions for categorical variables and medians for continuous variables. Because the intervention was likely to have a greater effect in patients with E. faecium bacteremia as compared to E. faecalis bacteremia, we stratified our results by enterococcal species. We compared categorical variables using chi-squared analysis or Fisher exact test (if appropriate) and continuous variables using t-test in the pre- and post intervention period stratified by enterococcal species. Survival curves of time to effective antibiotic therapy were compared by Log Rank test. Data analysis was performed using SPSS version 15 (SPSS, Chicago, Ill). All tests were two-tailed with the level of statistical significance was set with a p-value <0.05.

Results:

Description of Study population: Overall there were 650 patients with blood cultures positive for gram positive cocci in pairs or chains. All blood cultures positive for gram positive cocci in pairs
during 2006 had the PNA-FISH test in the laboratory. From these 271 patients had hospital
acquired \textit{E. faecium} or \textit{E. faecalis} bacteremia during the study period with 50 patients (23
patients had a repeat episode of enterococcal bacteremia, 10 died before the blood culture turned
positive, 7 were from pediatrics and Shock Trauma and 7 had endocarditis) and 379 had a
\textit{Streptococcal} species and were excluded from analysis. Thus 224 patients were included with
129 patients in the pre-intervention period and 95 patients in post-intervention period. The EFOE
PNA FISH test identified all 48 \textit{E. faecalis} organisms and 44 OE organisms which all were \textit{E.
faecium} by probe and confirmed by culture in the post-intervention group and identified 3
patients with both \textit{E. faecalis} and \textit{E. faecium} in the same blood culture.

The study population had a median age of 56 years (range 19-90) with 118 (53%) being
of male sex. There were 100 of 224 patients (45%) present in an intensive care unit (ICU) at the
onset of their enterococcal bacteremia and 40 (18%) were located in the cancer center; 203
(91%) had central venous access. The median APACHE II score at baseline was 14 (range 3-28),
and white cell count at index blood culture was 9 X 10^3 cells/dL. All \textit{E. faecalis} isolates were
ampicillin susceptible; however, only 100 of 112 (89%) were vancomycin susceptible. In
contrast, no \textit{E. faecium} isolates were ampicillin susceptible and only 13 (11.6%) isolates were
vancomycin susceptible. The overall length of stay prior to developing an enterococcal
bacteremia was a median of 9 days (range 0-123) and the median length of stay after a positive
culture was 11 days (range 1-175) with an overall 30 day mortality of 24%. The EFOE PNA
FISH test was performed on 95 patients (42%). The time to get the final microbiology report
from the blood culture draw took a median of 3.7 days (range 2.0 – 9.8) with all 224 patients,
while the time to get the PNA FISH report after the blood culture in those patients took a median
of 1.1 days (range 0.5-3.5).
Comparing Pre- and post PNA-FISH Intervention: Obtaining species level identification was 2.6 days quicker with PNA FISH compared to conventional culture reporting (p<0.001, t-test). The effect of PNA FISH on antibiotic selection and clinical outcomes with *E. faecalis* and OE separately offers more information.

There were 112 individual episodes of *E. faecalis* bacteremia evaluated with 64 in the pre-intervention and 48 in the intervention period. (Table 1) The clinical characteristics between the 2 groups were similar with a slightly greater severity of illness within the PNA FISH group (APACHE II score, 14 vs. 12, p=0.08). The reporting of PNA FISH for *E. faecalis* was 3 days earlier than conventional cultures (1.1 vs. 4 days, p<0.001); however, most patients received empiric effective antimicrobial therapy (99% vs. 96%, p=0.4). There was no difference in mortality between the groups (13% vs. 10%, p=0.73).

There were a total of 112 episodes of non-*E. faecalis* bacteremia. All were *E. faecium* except one *E. avium* which was in the pre-intervention period. There were 65 patients in the pre-intervention and 47 patients in the intervention period. Demographics were similar with a trend towards more patients with neutropenia from the cancer center in the intervention group (20% vs. 36%, p=0.06). Over 75% of patients with *E. faecium* bacteremia were from either the ICU or neutropenic. The median length of stay until onset of bacteremia between the groups was similar (12 vs. 14 days, p=0.7). The reporting of *E. faecium* with the PNA FISH test was a median 2.3 days earlier than with conventional reporting (p<0.001, t-test). Initial empiric antimicrobial therapy was inadequate in 53 of 65 (82%) in the pre-intervention group 41 of 47 (87%) in the intervention group (p=0.4, chi-sq). However, as seen in figure 2, there was a significant difference with the time it took for the intervention group receiving appropriate therapy
compared to the pre-intervention group (p<0.001, log rank test). There was also lower mortality in the intervention group (26% vs. 45%, p=0.04) though no difference in length of stay.

Discussion:

This study used the EFOE PNA FISH test in a clinical setting and showed its ability to more rapidly identify *Enterococcal* species than conventional culture. In addition for *E. faecium* bacteremia, its use reduced the time to effective antimicrobial therapy. PNA FISH was accurate (sensitivity, specificity, positive and negative predictive value were 100%) and significantly faster by almost 3 days in identifying the *Enterococcus* species when compared to standard microbiologic methods. Identification of enterococci by standard methods is often prolonged because they are often part of mixed bacteremia with other organisms. By implementing the test with a treatment algorithm and incorporating it into the AMT responsibilities, we reduced the time to effective antibiotic therapy for those with *E. faecium* bacteremia. We did not see the same benefits of PNA FISH with *E. faecalis* bacteremia which reflects the fact that, in our analysis, all of these infections received effective empiric antibiotic therapy prior to culture information. We also observed improved survival during the PNA FISH intervention period for those with *E. faecium* bacteremia; however, we did not detect a difference in length of stay which may reflect the severity of illness of the study population. Vergis *et al* and Lodise *et al* in separate studies showed that up to 80% of patients with VRE bacteremia had received ineffective therapy. In addition, Vergis *et al* demonstrated that among patients with monomicrobial enterococcal bacteremia, receipt of effective antimicrobial therapy within 48 hours of the blood culture independently predicted survival (OR for death, 0.21 [CI,0.06 to 0.80]; P < 0.02). These authors have suggested that delays in appropriate therapy may be associated with increased mortality. Early initiation of linezolid therapy could impact outcomes in patients with VRE
bacteremia. Our results are consistent with these and other studies. Taken together they show that earlier identification of *E. faecium* is important for initiating earlier effective therapy and this may improve survival in patients with hospital acquired *E. faecium* bacteremia.\(^{14,22,40}\)

An alternative to rapid microbiological testing would be to use a risk based approach to empirically treat patients with linezolid at “high-risk” for VRE bacteremia before or after identification of GPCPC by the laboratory. The high risk patients could be patients with prolonged ICU admission, neutropenia or liver transplantation with VRE colonization based on surveillance cultures or prior colonization. The presence of VRE colonization has been strongly associated with subsequent VRE bacteremia.\(^{22,37,39}\) However VRE screening is limited in its ability to detect VRE colonization prior to bacteremia and has been an asset in controlling spread. Garbutt et al showed less than 20% of patients were positive for VRE before index blood culture and Zaas et al had 10 out 24 (42%) patients had developed VRE bacteremia up to 24 hours before identification of colonization.\(^{12,39}\) Our center tracks a prior history of VRE colonization or infection and performed admission and weekly perirectal surveillance cultures for VRE in the ICUs and cancer center. These practices were in place and available to clinicians and the AMT during the entire study period. Thus the decrease in time to effective therapy and perhaps the mortality difference was due to the use of the PNA-FISH test and the AMT algorithm. We believe that risk factors can be helpful in making empiric antibiotic decisions; however, they are a supplement rather than a substitute for more rapid microbiological testing. We believe that the PNA-FISH test is a relatively easy to implement, positive step towards more rapid microbiological testing.

The conclusions of this study are limited by its non-randomized design. Because of its uncontrolled before-after quasi-experimental design, there may have been other unmeasured
factors which changed during the intervention period which could account for our results. However there were no differences between the pre- and post intervention groups in baseline characteristics including severity of illness and the AMT was active during both time periods. 

The conclusions of this study are also limited by the generalizability of this test and the AMT intervention to other medical centers. We have experienced laboratory staff accustomed to performing the test; however, the test is technically easy to perform. Our intervention required an active AMT that could implement a simple treatment algorithm and the treatment algorithm was based on high rates of VRE among our *E. faecium*. The majority of the decrease in time to effective therapy was driven by more rapid treatment of VRE with linezolid. Development and use of a test which could rapidly identify vancomycin resistance would remove the need for the treatment algorithm.

There are other rapid tests available for the identification of enterococci. At present, there are several polymerase chain reaction (PCR) tests that can screen patients as carriers of VRE infection which could mark these patients to begin early VRE therapy at the start of their infections. These PCR tests are performed off swabs, but with the technology evolving they may become available for use with blood cultures in the near future. In fact, Peters *et al* have performed real-time PCR directly of blood on ICU patients for *E. faecalis* with a sensitivity of 73% and specificity of 96%. We believe that rapid testing with the ability to identify antibiotic susceptibility would be superior to the PNA-FISH test with AMT algorithm.

In conclusion, use of the EFOE PNA FISH test in conjunction with a treatment algorithm lead to earlier identification of the *Enterococcus* species for patients with hospital acquired enterococcal bacteremia and the earlier initiation of effective antimicrobial therapy for patients with hospital acquired *E. faecium* bacteremia. Earlier appropriate therapy may decrease in
hospital mortality for those patients. Further evaluation in a prospective interventional trial is needed to determine the benefit of rapid identification of antibiotic resistant pathogens such as VRE in hospitalized patients.

Acknowledgements:

Results from this study were presented at the 44th Infectious Diseases Society of America Meeting [Abstract 131], Toronto, Canada, October 12-15, 2006.

Potential conflicts of interest:

GNF has received research funding, speaking honoraria from AdvanDx, Cubist Pharmaceuticals, Inc. and Pfizer Inc. MR has received research funding from 3M and Merck. RAV and JKJ has received speaking honoraria from AdvanDx.

Financial support: None

Study design and manuscript preparation:

All authors were involved in data analysis as well as manuscript preparation.
Reference List


Figure 1:

Antibiotic treatment algorithm utilized by the antimicrobial team with results from the

*Enterococcus faecalis* and other enterococci PNA FISH test.
Figure 1.

Gram-positive Cocci Pairs and Chains

- FISH Green (E. faecalis)
  - Ampicillin\(^a\)

- FISH Red (Other enterococci)
  - Linezolid\(^b\)

- No Color (Streptococcus sp.)
  - Penicillin/Ceftriaxone\(^c\)

Footnote:

a) Vancomycin could be substituted for Penicillin allergic.

b) High dose daptomycin could be substituted if unable to take linezolid.

c) Vancomycin could be added when febrile neutropenia or suspected meningitis.

Other enterococci = usually E. faecium with > 90% vancomycin resistant.
Figure 2:

Graph showing the significant decrease in time to initiating effective therapy with using PNA FISH reporting versus standard microbiological reporting with *Enterococcus faecium*. (p<0.001, log rank test)
Figure 2: Time to Effective Therapy for *E. faecium* Patients

Proportion of population not receiving effective therapy

Total time in days from blood culture draw to effective Therapy

PNA FISH Use
- After PNA FISH
- Before PNA FISH
Table 1: Characteristics of unique patients with *E. faecalis* and *E. faecium* bacteremia pre and post implementation of PNA FISH test

<table>
<thead>
<tr>
<th></th>
<th><em>E. faecalis</em></th>
<th>PNA FISH</th>
<th>p-value</th>
<th><em>E. faecium</em></th>
<th>PNA FISH</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Pre-PNA FISH</td>
<td>Pre-PNA FISH</td>
<td>PNA FISH</td>
<td>Pre-PNA FISH</td>
<td>Pre-PNA FISH</td>
<td>PNA FISH</td>
</tr>
<tr>
<td>n=64</td>
<td>n=65</td>
<td>n=48</td>
<td>n=47</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age, Median years (range)</td>
<td>53 (18-90)</td>
<td>60 (19-78)</td>
<td>0.2</td>
<td>54 (22-83)</td>
<td>53 (21-84)</td>
<td>0.5</td>
</tr>
<tr>
<td>Male Sex</td>
<td>29 (45%)</td>
<td>29 (60%)</td>
<td>0.11</td>
<td>37 (57%)</td>
<td>23 (49)</td>
<td>0.4</td>
</tr>
<tr>
<td>ICU at BC draw</td>
<td>28 (44%)</td>
<td>19 (40%)</td>
<td>0.66</td>
<td>33 (51%)</td>
<td>20 (41%)</td>
<td>0.39</td>
</tr>
<tr>
<td>Neutropenic at BC draw</td>
<td>6(9%)</td>
<td>2 (4%)</td>
<td>0.29</td>
<td>13 (20%)</td>
<td>17 (36%)</td>
<td>0.06</td>
</tr>
<tr>
<td>Central line at BC draw</td>
<td>57 (89%)</td>
<td>44 (92%)</td>
<td>0.65</td>
<td>59 (91%)</td>
<td>43 (91%)</td>
<td>0.9</td>
</tr>
<tr>
<td>Median LOS until BC draw (days)</td>
<td>5 (0-64)</td>
<td>2 (0-101)</td>
<td>0.68</td>
<td>12 (0-99)</td>
<td>14 (0-123)</td>
<td>0.72</td>
</tr>
<tr>
<td>LOS from BC to discharge (days)</td>
<td>9 (2-50)</td>
<td>10 (1-60)</td>
<td>0.304</td>
<td>13 (1-85)</td>
<td>14 (1-175)</td>
<td>0.44</td>
</tr>
<tr>
<td>Median WCC at BC draw (X10^3 cells/dL)</td>
<td>10.8 (0.1-38.3)</td>
<td>8.7 (1-47.3)</td>
<td>0.9</td>
<td>9.2 (0.1-40.5)</td>
<td>5.7 (0.1-31.7)</td>
<td>0.04*</td>
</tr>
<tr>
<td>Median APACHE II score at BC draw</td>
<td>12 (3-28)</td>
<td>14 (5-28)</td>
<td>0.08</td>
<td>16 (5-25)</td>
<td>16 (5-23)</td>
<td>0.9</td>
</tr>
<tr>
<td>Ampicillin Susceptible</td>
<td>64 (100%)</td>
<td>48 (100%)</td>
<td>1</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>1</td>
</tr>
<tr>
<td>Vancomycin Susceptible</td>
<td>57 (89%)</td>
<td>43 (90%)</td>
<td>0.93</td>
<td>11 (17%)</td>
<td>2 (4%)</td>
<td>0.04*</td>
</tr>
<tr>
<td>Other bacteria in same BC draw</td>
<td>41 (64%)</td>
<td>30 (63%)</td>
<td>0.87</td>
<td>22 (34%)</td>
<td>15 (34%)</td>
<td>0.9</td>
</tr>
<tr>
<td>Total time in days from BC drawn to final micro report</td>
<td>4 (2.4-9.8)</td>
<td>4.1 (2.3-8.5)</td>
<td>0.33</td>
<td>3.3 (2.0-8.6)</td>
<td>3.4 (2.5-7.1)</td>
<td>0.91</td>
</tr>
<tr>
<td>Total time in days from BC drawn to PNA FISH report</td>
<td>1.1 (0.5-3.3)</td>
<td>&lt;0.001*</td>
<td></td>
<td>1.1 (0.5-3.5)</td>
<td>&lt;0.001*</td>
<td></td>
</tr>
<tr>
<td>Total time in days from BC drawn to appropriate therapy</td>
<td>0 (0-5.3)</td>
<td>0.3 (0-6.5)</td>
<td>1</td>
<td>3.1 (0-9)</td>
<td>1.3 (0-4.3)</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Initial appropriate empiric therapy</td>
<td>63 (98%)</td>
<td>46 (96%)</td>
<td>0.4</td>
<td>12 (18%)</td>
<td>6 (13%)</td>
<td>0.42</td>
</tr>
<tr>
<td>Received appropriate therapy after final micro report</td>
<td>64 (100%)</td>
<td>48 (100%)</td>
<td>1</td>
<td>56 (86%)</td>
<td>46 (98%)</td>
<td>0.04*</td>
</tr>
<tr>
<td>30 day mortality</td>
<td>8 (13%)</td>
<td>5 (10%)</td>
<td>0.73</td>
<td>29 (45%)</td>
<td>12 (26%)</td>
<td>0.039*</td>
</tr>
</tbody>
</table>

Footnote: BC = blood culture, LOS = length of stay, WCC = white cell count, ICU = intensive care unit

* Significant values