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Clinical Studies

Influence of GeneXpert MRSA/SA test implementation on clinical outcomes of *Staphylococcus aureus* bacteremia — a before–after retrospective study

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ABSTRACT

Use of GeneXpert MRSA/SA in diagnostic algorithms of *Staphylococcus aureus* bacteremia may influence both patients' clinical outcomes and antibiotic stewardship. We evaluated these outcomes in a retrospective cohort before (1/6/2015–31/5/2016) and after (1/6/2016–31/8/2017) the introduction of the test in adult patients with Gram-positive cocci in clusters in blood cultures. We included 254 patients (125 preintervention, 129 postintervention). No significant difference in 30-day mortality or clinical success was demonstrated between periods. Appropriate antibiotic therapy rates were significantly higher in the postintervention group, and vancomycin use was significantly reduced (80.6% vs 53.6%, $P < 0.01$; 2.3±0.38 vs 2.98±1.02 defined daily doses/100 patient days, $P = 0.026$, respectively). Appropriate beta-lactam use was also significantly higher (56.7% postintervention vs 23.1% preintervention, $P < 0.01$). Use of GeneXpert MRSA/SA test has a positive effect on antibiotic stewardship measures, though it has no significant effect on clinical outcomes including mortality in this fatal infection.

1. Introduction

Staphylococcus aureus (SA) is a leading cause of bacteremia. Increased frequency of invasive surgery, use of intravascular devices, and immunosuppression have led to a sharp increase in the incidence of *Staphylococcus aureus* bacteremia (SAB) in recent years, carrying 30-day mortality of 20–40% (Holland et al., 2014; Khatib and Sharma, 2013; van Hal et al., 2012; Yahav et al., 2016). In the US, annual incidence of methicillin-resistant *S. aureus* (MRSA) invasive infections has been reported to be 27.7/100,000 in Caucasians (van Hal et al., 2012).

Several studies have demonstrated inappropriate empirical therapy as a risk factor for mortality in SAB (Bassetti et al., 2012; Paul et al., 2010). As a consequence, many centers use vancomycin as empirical treatment in cases of suspected staphylococcal bacteremia. Nevertheless, vancomycin has been demonstrated to be inferior to beta-lactams as both empirical and definitive treatment for methicillin-sensitive *S. aureus* (MSSA) bacteremia (Schweizer et al., 2011; Wong et al., 2016).

Due the aforementioned importance of optimal early antibiotic therapy, rapid molecular identification methods were introduced into the diagnostic algorithm of SAB in recent years. These methods' impact on clinical outcomes is not thoroughly evaluated in clinical studies to date (Kothari et al., 2014).

Previous studies have focused on the role of rapid molecular tests in antibiotic stewardship, demonstrating prevention of unnecessary vancomycin use, early stop of unnecessary vancomycin, and early administration of beta-lactams for MSSA bacteremia (Aitken et al., 2015; Bauer et al., 2010; Davies et al., 2012; Wong et al., 2012).

None of these studies have comprehensively evaluated all clinical outcomes relevant for treatment of SAB, including mortality, treatment success, and optimal antibiotic therapy. We aimed to perform a study addressing all the above outcomes before and after the introduction of GeneXpert MRSA /SA test in our institution.

2. Methods

2.1. Study design

This was a retrospective, uncontrolled before–after study conducted in a 900-bed tertiary center in Israel. The study was approved by the local ethical committee.

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Adult patients hospitalized with SAB were included between 1 June 2015 through 31 May 2016 (before the introduction of GeneXpert MRSA/SA test for clinical use) and between 1 June 2016 through 31 August 2017 (after the introduction of the test). Patients from all hospital departments excluding intensive care unit (ICU) and with any source of bacteremia were included. Each patient was included once. Polymicrobial cultures were excluded, and so were patients who died at the day of culture collection. The reason for excluding ICU patients was limited access to medical files.

On June 1, 2016, the intervention was introduced. The traditional processing of blood cultures in our laboratory before the intervention was done with an automated Bactec FX system. After the system detects a positive blood culture and broadcasts a sound signal, a Gram stain is prepared. In case of Gram-positive cocci in clusters (GPCC), the sending department is reported on the results by phone, and final identification of bacteria is done classically by standard methods of testing (DNAse test, Pastorex Staph-Plus, Sanofi Pasteur, Guildford, UK). BBL CHROMagar *Staph aureus*/BBL CHROMagar MRSA II (Biplate) (Hylabs, Israel) and cefoxitin/oxacillin discs (Oxoid; Thermo Scientific, UK) screen tests are used to test for methicillin resistance phenotypically in our lab. In any case of uncertainty, E-test for oxacillin and cefoxitin is conducted. In addition, all isolates are sent to a national reference lab for confirmation and determination of mecA, PVL, and spa type. Methicillin resistance is determined according the established Clinical and Laboratories Standards Institute (CLSI) guidelines for disk-diffusion susceptibility testing (cefoxitin disk, 30 μg) (Clinical and Laboratory Standards Institute (CLSI) CaLSI, 2015).

Since June 2016, the GeneXpert assay was performed directly on every positive blood culture specimens that were determined by Gram stain as GPCC. The sending department is reported on the positive Gram stain by phone as accepted but also receives a report on the GeneXpert's results electronically within 1 h of the telephonic report.

The GeneXpert system performs a qualitative in vitro test to detect *S. aureus* DNA directly from positive blood cultures. This is performed using automated real-time polymerase chain reaction (PCR) to amplify MRSA/SA specific DNA targets and fluorogenic target-specific hybridization probes for the real-time detection of the amplified DNA. The primers and probes of the test detect sequences for the staphylococcal protein A (spa), the mecA gene, and the staphylococcal cassette chromosome (SCCmec) (Donnio et al., 2005; Rossney et al., 2008; Spencer et al., 2011).

During the study period, no other changes in the management of SAB or in antimicrobial stewardship interventions were done; local instructions for use of vancomycin were not changed; infectious diseases consultants were not replaced. Positive blood cultures for Gram-positive cocci in clusters were reported to the departments by the lab 24 h a day in both periods, and GeneXpert was performed 24 h a day during the second period. Due to high MRSA bacteremia rates in our center (~40% of SAB) (Yahav et al., 2016), local empirical therapy for suspected staphylococcal bacteremia was vancomycin throughout the study periods. We also assumed no changes in the characteristics of hospitalized patients in our center between the before and after periods.

2.2. Data collection

The study population was retrieved from the computerized data system of the microbiology laboratory. Medical files of all patients meeting inclusion criteria were analyzed. The following data were collected for each patient, including baseline patient characteristics (age; sex; antibiotic allergies; Charlson comorbidity score); infection characteristics (PITT bacteremia score at infection presentation); department at which cultures were taken (ICU, medical, or surgical); source of bacteremia as defined by the investigator; oxacillin resistance; and antibiotic therapy (type of antibiotics and duration of each antibiotics thought the infection).

2.3. Outcomes and definitions

The following outcomes were compared between the 2 time periods evaluated in the study (before and after the intervention). The primary outcome was all-cause 30-day mortality. Secondary outcomes included all-cause 7-day mortality; success at day 7 and day 90; appropriate beta-lactam antibiotics for MSSA cases in patients nonallergic to beta-lactams within 24 h from blood cultures collection; appropriate MRSA coverage within 24 h from blood cultures collection; total use of vancomycin, measured in defined daily dose (DDD) per 100 hospital days; and length of hospital stay.

2.3.1. Definitions

- Success at day 7: survival, resolution of fever, stable/improved PITT bacteremia score, and clearance of blood cultures with no microbiologically confirmed failure up to 90 days (Harris et al., 2017).
- Success at 90 days: survival and no microbiologically confirmed failure (Harris et al., 2017).
- Appropriate beta-lactam for MSSA: we used two definitions — a stricter definition including only first-generation cephalosporins or antistaphylococcal penicillins, and a permissive definition including first- to third-generation cephalosporins (excluding ceftazidime), antistaphylococcal penicillins, beta-lactam/beta-lactamase inhibitors or carbapenems.
- Appropriate MRSA coverage was considered vancomycin, daptomycin, or linezolid.

3. Statistical methods

Categorical variables were compared using the χ^2 test; continuous variables were compared by the *t* test (for normal distribution) or the Mann–Whitney *U* test (for other distributions). *P* value of 0.05 was used to determine statistical significance. Multivariable analysis of risk factors for 30-day mortality was conducted introducing period (before or after intervention) as a predicting variable. Analyses were performed using the Statistical Package for the Social Sciences (SPSS Inc., Chicago, IL).

4. Results

During the entire study period, 254 patients were included: 125 in the preintervention period (i.e., before the implementation of the GeneXpert MRSA/SA test, 1/6/2015–31/5/2016) and 129 in the postintervention period (1/6/2016–31/8/2017). No discrepancies between GeneXpert results and routine susceptibility testing as described above were demonstrated during the study period.

4.1. Baseline patient and infection characteristics

Baseline characteristics of patients according to study period are elaborated in Table 1. No significant difference was found between baseline patients' characteristics including age, gender, functional capacity, and department of hospitalization. Charlson comorbidity score was significantly lower in the postintervention period [median 0, interquartile range (IQR) 0–2 versus median 1 IQR 0–3.5 in the preintervention group, $P = 0.021$, though the score was low in both groups] (Table 1). Regarding the infection characteristics, no significant differences between study periods were noticed for place of acquisition and severity of presentation as measured by septic shock at presentation and the PITT bacteremia score. In both groups, MSSA was the main cause of bacteremia, though MRSA was more common in the preintervention group (47/125, 37.6% compared with 32/129, 24.8% in the postintervention group) (Table 1).

Table 1
Baseline patient and infection characteristics according to study group.

Variable	Preintervention (n = 125 patients)	Postintervention (n = 129 patients)	P value
Patient characteristics			
Age	69 (60–81.5)	74 (61–84)	0.283
Gender: female	50 (40.0)	48 (37.2)	0.648
Functional capacity: independent	51/124 (41.1)	58/127 (45.7)	0.659
Department of hospitalization:			0.842
Medical	102 (81.6)	104 (80.6)	
Surgical	23 (18.4)	25 (19.4)	
Charlson comorbidity score	1 (0–3.5)	0 (0–2)	0.021
Infection characteristics			
Type of SA			0.028
MSSA	78 (62.4)	97 (75.2)	
MRSA	47 (37.6)	32 (24.8)	
Place of acquisition of infection: community	63 (50.4)	72 (55.8)	0.387
Septic shock at presentation	6 (4.8)	6 (4.7)	0.955
PITT bacteremia score	0 (0–2)	0 (0–1)	0.113
Temperature at presentation	38.2 (37.2–39.1)	38.3 (37.3–39.1)	0.488

Categorical variables are presented as number (percentage); continuous variables are presented as median (interquartile range).
SA = *S. aureus*; MSSA = methicillin-sensitive *S. aureus*; MRSA = methicillin-resistant *S. aureus*.

Table 2
Outcomes.1a, 2

Outcome	Preintervention (n = 125 patients)	Postintervention (n = 129 patients)	P value
All-cause 30-day mortality			
Total	41 (32.8)	43 (33.3)	0.928
MSSA	24/78 (30.8)	32/97 (33.0)	0.754
MRSA	17/47 (36.2)	11/32 (34.4)	0.870
All-cause 7-day mortality			
Total	21 (16.8)	21 (16.3)	0.911
MSSA	11/78 (14.1)	15/97 (15.5)	0.801
MRSA	10/47 (21.3)	6/32 (18.8)	0.784
Success day 7			
Total	78 (62.4)	91 (70.5)	0.169
MSSA	51/78 (65.4)	68/97 (70.1)	0.506
MRSA	27/47 (57.4)	23/32 (71.9)	0.162
Success day 90			
Total	73 (58.4)	78 (60.5)	0.738
MSSA	49/78 (62.8)	61/97 (62.9)	0.993
MRSA	24/47 (51.1)	17/32 (53.1)	0.857
Appropriate empirical within 24 h: all[a]			
Total	67 (53.6)	104 (80.6)	<**0.01**
MSSA	45/78 (57.7)	81/97 (83.5)	<**0.01**
MRSA	22/47 (46.8)	23/32 (71.9)	**0.027**
Appropriate empirical within 24 h: specific[b]			
Total	40 (32.0)	78 (60.5)	<**0.01**
MSSA	18/78 (23.1)	55/97 (56.7)	<**0.01**
MRSA	22/47 (46.8)	23/32 (71.9)	**0.027**
Length of hospital stay (median (IQR))	19 (10.5–37)	17 (11–28.5)	0.388
Vancomycin consumption (DDD per 100 hospital days) (mean (SD))	2.98 (1.02)	2.30 (0.38)	**0.026**

[a] For MSSA: first- to third-generation cephalosporins (excluding ceftazidime), antistaphylococcal penicillins, beta-lactam/beta-lactamase inhibitors or carbapenems.
[2] For MSSA: first-generation cephalosporins or antistaphylococcal penicillins.

4.2. Outcomes

4.2.1. Mortality

No significant difference in 30-day or 7-day all-cause mortality was demonstrated between study periods (30 day mortality: 41/125, 32.8% in the preintervention group versus 43/129, 33.3% in the postintervention group, $P = 0.928$). These nonsignificant differences were kept when analyzing separately patients with MSSA and MRSA bacteremia (Table 2).

4.2.2. Success

No significant difference in success rate at day 7 was demonstrated between the postintervention and preintervention periods (91/129, 70.5% vs 78/125, 62.4%, $P = 0.169$). Nonsignificantly higher rates of positive blood cultures at day 7 were documented in the preintervention group (11/125, 8.8% positive cultures at day 7 preintervention vs 4/129, 3.1% postintervention, $P = 0.065$). No significant difference in the other components of this outcome was demonstrated. In addition, no significant difference between study periods was demonstrated for the outcome of success at day 90 (Table 2).

4.2.3. Appropriate antibiotic therapy

Appropriate antibiotic therapy within 24 h of culture collection was significantly more commonly administered in the postintervention period (104/129, 80.6% vs 67/125, 53.6%, $P < 0.01$). This significant difference was demonstrated for both MRSA (23/32, 71.9% vs 22/47, 46.8%, $P = 0.027$) and MSSA (81/97, 83.5% vs 45/78, 57.7%, $P < 0.01$ when appropriate defined as any beta-lactam; 55/97, 56.7% vs 18/78, 23.1% when appropriate defined as first-generation cephalosporins or antistaphylococcal penicillins only) (Table 2).

4.2.4. Other outcomes

Length of hospitalization was nonsignificantly shorter in the postintervention period (median 17, IQR 11–28.5 days vs 19, IQR 10.5–37.0, $P = 0.388$).

Vancomycin consumption was significantly reduced in the postintervention period (2.3±0.38 vs 2.98±1.02 DDD/100 patient days, $P = 0.026$) (Table 2).

4.3. Predictors of 30 day mortality: univariable analysis and multivariable analysis

Variables significantly associated with 30-day all-cause mortality in univariable analysis included age, functional capacity, Charlson comorbidity score, acquisition of infection outside the community, admission to medical ward, and higher PITT bacteremia score. The period of time (pre- or postintervention) was not statistically significantly associated with 30-day morality (Table 3). Factors remaining significant in the multivariable analysis were age, Charlson comorbidity score, place of acquisition, admission to medical ward, and PITT bacteremia score. Time period (pre- or postintervention) was introduced into the multivariable analysis and was found to be not significantly associated with mortality (odds ratio 1.232, 95% confidence interval 0.632–2.404, $P = 0.54$) (Table 4).

5. Discussion

We evaluated the clinical impact of GeneXpert MRSA/SA test in a retrospective before–after study including 254 patients. The use of the test was demonstrated to significantly improve rates of appropriate antibiotic therapy for both MSSA and MRSA and significantly reduce vancomycin consumption. Use of the test was not significantly associated with reduced mortality or clinical success or shortening of hospital stay in our cohort. Nonsignificantly lower rate of repeated positive blood cultures on day 7 was demonstrated in the postintervention period.

Univariable and multivariable analyses of risk factors for mortality did not find the time period (before/after the introduction of the test) to be associated with mortality; rather, nonmodifiable variables predicted mortality (age, medical ward hospitalization, higher PITT bacteremia score and Charlson comorbidity score, and place of acquisition of infection).

Table 3
Predictors of 30-day mortality: univariable analysis.

Variable	Survived ($n = 170$ patients)	Died ($n = 84$ patients)	*P* value
Group:			0.928
Preintervention	84 (49.4)	41 (48.8)	
Postintervention	86 (50.6)	43 (51.2)	
Bacterial type:			0.589
MSSA	119 (70.0)	56 (66.7)	
MRSA	51 (30.0)	28 (33.3)	
Gender: female	61 (35.9)	37 (44.0)	0.209
Functional capacity: nonindependent	82 (48.2)	60 (71.4)	<**0.01**
Department of hospitalization: medical	127 (74.7)	79 (94.0)	<**0.01**
Place of acquisition: noncommunity	66 (38.8)	53 (63.1)	<**0.01**
Inappropriate empirical therapy within 24 h	54 (31.8)	29 (34.8)	0.659
Age	65.5 (57.8–78.0)	82 (69.8–89.0)	<**0.01**
Charlson comorbidity score	0 (0–2)	2 (0–6)	**0.001**
PITT bacteremia score	0 (0–1)	1 (0–2.8)	<**0.01**

Several studies have previously evaluated the performance of rapid diagnostic tests for Gram-positive cocci in clusters in bloodstream infections compared with routine microbiological methods. Most of the studies evaluated adequacy of antibiotic therapy, and some assessed clinical outcomes, mainly mortality, with variable results. The largest study included 664 pre-PCR and 570 post-PCR patients and demonstrated, similar to our findings, improved initiation of optimal antibiotics in MSSA bacteremia and reduced unnecessary vancomycin use. Clinical outcomes, however, were not evaluated in this study (Na et al., 2016). Bauer et al. conducted a before–after study evaluating the use of GeneXpert MRSA/SA in 156 patients with SAB. They reported a trend toward shorter length of stay in the post-PCR period, without a significant difference in mortality (Bauer et al., 2010). Ly et al. demonstrated significantly reduced mortality among 226 patients evaluated using PNA-FISH for Gram-positive cocci in clusters bacteremia. They showed a reduction in antimicrobial use and a trend toward reduced length of stay (Ly et al., 2008). Emonet et al. demonstrated no significant effect on mortality, need for ICU, and septic complications using real-time PCR versus conventional microbiology in a randomized clinical study including 89 patients (Emonet et al., 2016). In another before–after study, adequacy of the empirical antibacterial therapy was similar between pre- and post-MALDI-TOF use periods (Romero-Gómez et al., 2017). Recently, Eby et al. demonstrated reduced 30-day mortality using combination of nucleic acid microarray testing with direct infectious diseases physician notification for management of SA bacteremia (Eby et al., 2018). The latter intervention of notification of an infectious diseases physician with immediate consultation following may be a strategy to further improve antibiotic prescribing in addition to the real-time laboratory testing.

None of the previous studies have demonstrated our finding of reduced positive repeated cultures on day 7.

Table 4
Predictors of 30 day mortality: multivariable analysis.

Variable	Odds ratio (95% confidence interval)	*P* value
Group (pre- or postintervention)	1.232 (0.632–2.404)	0.540
Age	1.071 (1.041–1.101)	<0.01
Department: medical	3.683 (1.106–12.264)	0.034
PITT bacteremia score	1.542 (1.232–1.930)	<0.01
Place of acquisition: noncommunity	3.538 (1.750–7.154)	<0.01
Charlson comorbidity score	1.170 (1.054–1.298)	0.003

Odds ratio > 1 associated with increased risk of mortality.

Our study is one of the largest evaluating the use of GeneXpert MRSA/SA in clinical practice. Another advantage is the comprehensiveness of outcomes assessed, including both clinical outcomes significant for the patient and outcomes relevant for antimicrobial stewardship. Reduced vancomycin use could not be explained by reduction in MRSA or *Staphylococcus* coagulase-negative infection rates (which were steady over 2012 to 2018 in our center, with mean bloodstream infections per year 33±6 and 411±37, respectively). Limitations include the retrospective uncontrolled before–after design (with no control group) and the performance in a single center. Data on source of bacteremia were not extracted due to technical difficulties. In addition, we do not have data specifically on the appropriateness of empirical therapy of SAB during the years previous to the study in order to exclude the possibility of a prolonged trend of improvement in empirical therapy possibly started prior to the intervention. However, we have generally noticed an increase in inappropriateness of empirical therapy for bacteremia in our center during the years (from 33.5% in 2003–2004 to 55.9% in 2010–2011), so we have no reason to assume improvement in empirical coverage of SAB regardless of the intervention examined (Daitch et al., 2018).

Appropriate empirical therapy for SAB has been previously associated with improved survival. In addition, beta-lactams have been demonstrated to be superior to vancomycin for MSSA bacteremia (Kothari et al., 2014). Nevertheless, our finding of improved coverage for MSSA was not associated with improved survival. This may be explained by the fact that ICU patients were not included in our cohort or by the limited sample size.

The finding of reduced vancomycin use during the postintervention period had no other obvious explanation other than the introduction of GeneXpert MRSA/SA test. No changes in the infectious diseases or infection control teams or guidelines were conducted during the study's period. The reduced use of vancomycin may be associated with avoidance of unnecessary adverse events, reduced cost, and less resistance development (Na et al., 2016).

In summary, we found the use of GeneXpert MRSA/SA test in Gram-positive cocci in clusters bacteremia to be associated with improved rate of appropriate therapy for both MSSA and MRSA and reduced total vancomycin use. Mortality rates and clinical success rates were not significantly changed following the introduction of the test.

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Conflict of interest

All authors declare none.

Ethical approval

This study was approved by the local ethical committee of Rabin Medical Center.

Informed consent

Retrospective study.

References

Aitken SL, Hemmige VS, Koo HL, Vuong NN, Lasco TM, Garey KW. Real-world performance of a microarray-based rapid diagnostic for Gram-positive bloodstream infections and potential utility for antimicrobial stewardship. Diagn Microbiol Infect Dis 2015;81(1):4–8.

Bassetti M, Trecarichi EM, Mesini A, Spanu T, Giacobbe DR, Rossi M, et al. Risk factors and mortality of healthcare-associated and community-acquired Staphylococcus aureus bacteraemia. Clin Microbiol Infect 2012;18(9):862–9.

Bauer KA, West JE, Balada-Llasat JM, Pancholi P, Stevenson KB, Goff DA. An antimicrobial stewardship program's impact with rapid polymerase chain reaction methicillin-

resistant Staphylococcus aureus/S. aureus blood culture test in patients with S. aureus bacteremia. Clin Infect Dis 2010;51(9):1074–80.
Clinical and Laboratory Standards Institute (CLSI) CaLSI. M-100-S25. Performance Standards for Antimicrobial Susceptibility Testing; Twenty Fifth International Supplement; 2015. p. 25. [June 20 2017].
Daitch V, Akayzen Y, Abu-Ghanem Y, Eliakim-Raz N, Paul M, Leibovici L, et al. Secular trends in the appropriateness of empirical antibiotic treatment in patients with bacteremia: a comparison between three prospective cohorts. Eur J Clin Microbiol Infect Dis 2018;37(3):455–62.
Davies J, Gordon CL, Tong SY, Baird RW, Davis JS. Impact of results of a rapid Staphylococcus aureus diagnostic test on prescribing of antibiotics for patients with clustered Gram-positive cocci in blood cultures. J Clin Microbiol 2012;50(6):2056–8.
Donnio PY, Oliveira DC, Faria NA, Wilhelm N, Le Coustumier A, de Lencastre H. Partial excision of the chromosomal cassette containing the methicillin resistance determinant results in methicillin-susceptible Staphylococcus aureus. J Clin Microbiol 2005;43(8):4191–3.
Eby JC, Richey MM, Platts-Mills JA, Mathers AJ, Novicoff WM, Cox HL. A healthcare improvement intervention combining nucleic acid microarray testing with direct physician response for management of Staphylococcus aureus bacteremia. Clin Infect Dis 2018;66(1):64–71.
Emonet S, Charles PG, Harbarth S, Stewardson AJ, Renzi G, Uckay I, et al. Rapid molecular determination of methicillin resistance in staphylococcal bacteraemia improves early targeted antibiotic prescribing: a randomized clinical trial. Clin Microbiol Infect 2016;22(11):946.e9–946.e15.
Harris PN, McNamara JF, Lye DC, Davis JS, Bernard L, Cheng AC, et al. Proposed primary endpoints for use in clinical trials that compare treatment options for bloodstream infection in adults: a consensus definition. Clin Microbiol Infect 2017;23(8):533–41.
Holland TL, Arnold C, Fowler Jr VG. Clinical management of Staphylococcus aureus bacteremia: a review. JAMA 2014;312:1330–41.
Khatib R, Sharma M. Echocardiography is dispensable in uncomplicated Staphylococcus aureus bacteremia. Medicine (Baltimore) 2013;92:182–8.
Kothari A, Morgan M, Haake DA. Emerging technologies for rapid identification of bloodstream pathogens. Clin Infect Dis 2014;59(2):272–8.
Ly T, Gulia J, Pyrgos V, Waga M, Shoham S. Impact upon clinical outcomes of translation of PNA FISH-generated laboratory data from the clinical microbiology bench to bedside in real time. Ther Clin Risk Manag 2008;4(3):637–40.
Na SH, Kim CJ, Kim M, Park JS, Song KH, Choe PG, et al. Impact of the multiplex polymerase chain reaction in culture-positive samples on appropriate antibiotic use in patients with staphylococcal bacteremia. Diagn Microbiol Infect Dis 2016;84(4):353–7.
Paul M, Kariv G, Goldberg E, Raskin M, Shaked H, Hazzan R, et al. Importance of appropriate empirical antibiotic therapy for methicillin-resistant Staphylococcus aureus bacteraemia. J Antimicrob Chemother 2010;65(12):2658–65.
Romero-Gómez MP, Cendejas-Bueno E, García Rodriguez J, Mingorance J. Impact of rapid diagnosis of Staphylococcus aureus bacteremia from positive blood cultures on patient management. Eur J Clin Microbiol Infect Dis 2017;36(12):2469–73.
Rossney AS, Herra CM, Brennan GI, Morgan PM, O'Connell B. Evaluation of the Xpert methicillin-resistant Staphylococcus aureus (MRSA) assay using the GeneXpert real-time PCR platform for rapid detection of MRSA from screening specimens. J Clin Microbiol 2008;46(10):3285–90.
Schweizer ML, Furuno JP, Harris AD, Johnson JK, Shardell MD, McGregor JC, et al. Comparative effectiveness of nafcillin or cefazolin versus vancomycin in methicillin-susceptible Staphylococcus aureus bacteremia. BMC Infect Dis 2011;11:279–86.
Spencer David H, Sellenriek Patricia, Burnham Carey-Ann D. Validation and implementation of the GeneXpert MRSA/SA blood culture assay in a pediatric setting. Am J Clin Pathol 2011;136:690–4.
van Hal SJ, Jensen SO, Vaska VL, Espedido BA, Paterson DL, Gosbell IB, et al. Predictors of mortality in Staphylococcus aureus bacteremia. Clin Microbiol Rev 2012;25:362–86.
Wong JR, Bauer KA, Mangino JE, Goff DA. Antimicrobial stewardship pharmacist interventions for coagulase-negative staphylococci positive bloodcultures using rapid polymerase chain reaction. Ann Pharmacother 2012;46(11):1484–90.
Wong D, Wong T, Romney M, Leung V. Comparative effectiveness of β-lactam versus vancomycin empiric therapy in patients with methicillin-susceptible Staphylococcus aureus (MSSA) bacteremia. Ann Clin Microbiol Antimicrob 2016;15:27–35.
Yahav D, Shaked H, Goldberg E, Yassin S, Eliakim-Raz N, Paul M, et al. Time trends in Staphylococcus aureus bacteremia, 1988-2010, in a tertiary center with high methicillin resistance rates. Infection 2017;45(1):51–7.