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Focus on MRSA/SA SSTI Assay Failure in Prosthetic Joint Infections: 213 Consecutive Patients Later

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In prosthetic joint infection (PJI) cases (1), rapid detection of methicillin-resistant staphylococci (MRS) is the key to avoiding the use of broad-spectrum antimicrobials such as vancomycin. Indeed, vancomycin use is associated with a risk of renal impairment, a lesser efficacy against methicillin-susceptible strains compared with beta-lactams (2), and a negative ecological impact. In these regards, the Xpert MRSA/SA SSTI assay (Cepheid, Sunnyvale, CA, USA) appears as a potentially useful tool. It enables the detection of the genetic support of methicillin resistance, the *mecA* gene, directly in intraoperative samples (IOS) in less than 1 h (3). In our center, the test has been routinely used for the last 4 years in order to stop the anti-MRS antibiotic early in those patients managed for PJI and having a negative result for the detection of the *mecA* gene in surgical samples. For each patient, three IOS were taken to perform both standard culture and molecular testing before any antimicrobial therapy. These three samples were also kept for prolonged culture (15 days) in Rosenow's enrichment broth (4, 5). The criteria for a microbiological infection were the same coagulase-negative *Staphylococcus* (CoNS) species related to the same antimicrobial pattern found in culture in at least two samples and/or an *S. aureus* strain found in culture in at least one sample. Methicillin susceptibility was assessed by using Vitek2 AST cards (bioMérieux, Marcy l'Etoile, France). Oxacillin and cefoxitin results issued from the automated system were interpreted according to the Comité de l'antibiogramme de la Société Française de Microbiologie recommendations (http://www.sfm-microbiologie.org). A cefoxitin disk was also used in the case of a discrepancy.

Among the 213 consecutive patients studied (118 with hip, 82 with knee, and 13 with shoulder prostheses), culture was correlated with the molecular detection of MRS in 186 cases (87.3%). The overall sensitivity (Se), specificity (Sp), positive predictive value (PPV), and negative predictive value (NPV) were 56, 93, 58, and 92%, respectively. Xpert failed to detect a resistant strain in 14 (6.6%) of 213 patients who were examined carefully owing to a high risk of clinical failure. Eight of these false-negative patients were positive for a single methicillin-resistant (MR) coagulase-negative *Staphylococcus* (MRCoNS) strain, in either standard or enriched medium, which could be considered contamination. The six remaining cases were positive by culture for an MRCoNS strain (patients 1 to 5) or MRSA (methicillin-resistant *Staphylococcus aureus*) (patient 6) PJI (Table 1). Xpert failed to diagnose one patient (patient 1) because of late amplification (cycle threshold [C_T], 39.1) interpreted as negative by the software. Two other patients (no. 3 and 5) had polymicrobial infections. Patients 2, 4, and 6 were infected with MRSE (MR *Staphylococcus epidermidis*) and MRSA small-colony

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TABLE 1 Characteristics of six patients negative for *mecA* detection

Patient no., sex, and culture medium	Result (no. of days to positive culture)			*mecA* detection (C_T)
	IOS 1	IOS 2	IOS 3	
1, M				
Standard	MRSE (3)	Sterile	Sterile	Negative (39.1)
Enriched broth	MRSE (3)	MRSE (3)	MRSE (3)	
2, F				
Standard	Sterile	Sterile	Sterile	Negative (0)
Enriched broth	MRSE (4)	MRSE (4)	Sterile	
3, M				
Standard	MS[a] *Staphylococcus pettenkoferi* (4)	Sterile	MS *Staphylococcus pettenkoferi* + MR *Staphylococcus capitis* (4)	Negative (0)
Enriched broth	MR *Staphylococcus hominis* (2)	MS *Staphylococcus caprae* + MR *Staphylococcus capitis* (2)	MS *Staphylococcus caprae* + *Bacillus simplex* (2)	
4, F				
Standard	Sterile	MRSE (5)	Sterile	Negative (0)
Enriched broth	Sterile	MRSE (5)	MRSE (6)	
5, F				
Standard	Sterile	MRSE (2)	*Lactobacillus rhamnosus* (5)	Negative (0)
Enriched broth	*Lactobacillus rhamnosus* (3)	MRSE (2)	*Lactobacillus rhamnosus* (3)	
6, M				
Standard	Sterile	Sterile	MRSA (4)	Negative (0)
Enriched broth	MRSA (5)	MRSA (6)	MRSA (4)	

[a]MS, methicillin susceptible.

variants, respectively. None of these false-negative patients had a microbiological relapse. In the light of these data, the sensitivity, specificity, PPV, and NPV moved to 75, 93, 58, and 97%, respectively.

Xpert is an easy-to-use PCR method that has been turned away from in favor of bone and joint infection diagnosis and rapid antimicrobial adjustment. High performance of the test was described in osteoarticular infections (3) and chronic PJI (5), but this was recently outweighed by poor sensitivity results (36%) in cases of MRCoNS infection (6). These points were examined here in an extended cohort of 213 patients. A focus on false-negative cases revealed different kinds of risk factors, such as (i) MRCoNS infections, (ii) a high C_T value related to a low inoculum concentration, (iii) polymicrobial infections, and (iv) small-colony variant infections. Furthermore, a comparison of PCR and culture results was made, but culture remains an imperfect gold standard that must be interpreted according to the patient's medical history (e.g., 8/14 contaminations).

In conclusion, our results confirm the high NPV of Xpert, which makes it a useful tool in an attempt to reduce vancomycin use in PJI.

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REFERENCES

1. Zimmerli W, Trampuz A, Ochsner PE. 2004. Prosthetic-joint infections. N Engl J Med 351:1645–1654. https://doi.org/10.1056/NEJMra040181.
2. Kim SH, Kim KH, Kim HB, Kim NJ, Kim EC, Oh M, Choe KW. 2008. Outcome of vancomycin treatment in patients with methicillin-susceptible *Staphylococcus aureus* bacteremia. Antimicrob Agents Chemother 52:192–197. https://doi.org/10.1128/AAC.00700-07.
3. Dubouix-Bourandy A, de Ladoucette A, Pietri V, Mehdi N, Benzaquen D, Guinand R, Gandois JM. 2011. Direct detection of *Staphylococcus* osteoarticular infections by use of Xpert MRSA/SA SSTI real-time PCR. J Clin Microbiol 49:4225–4230. https://doi.org/10.1128/JCM.00334-11.
4. Senneville E, Savage C, Nallet I, Yazdanpanah Y, Giraud F, Migaud H,

Dubreuil L, Courcol R, Mouton Y. 2006. Improved aero-anaerobe recovery from infected prosthetic joint samples taken from 72 patients and collected intraoperatively in Rosenow's broth. Acta Orthop 77:120–124. https://doi.org/10.1080/17453670610045795.

5. Titécat M, Loïez C, Senneville E, Wallet F, Dezèque H, Legout L, Migaud H, Courcol RJ. 2012. Evaluation of rapid *mecA* gene detection versus standard culture in staphylococcal chronic prosthetic joint infections. Diagn Microbiol Infect Dis 73:318–321. https://doi.org/10.1016/j.diagmicrobio.2012.04.011.
6. Lourtet-Hascoët J, Bicart-See A, Félicé MP, Giordano G, Bonnet E. 2015. Is Xpert MRSA/SA SSTI real-time PCR a reliable tool for fast detection of methicillin-resistant coagulase-negative staphylococci in periprosthetic joint infections? Diagn Microbiol Infect Dis 83:59–62. https://doi.org/10.1016/j.diagmicrobio.2015.04.009.