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Abstract

Universal surveillance upon patient admission is important in reducing the transmission of methicillin-resistant Staphylococcus aureus (MRSA) and associated disease in hospitals. High costs for the health care system in conjunction with MRSA have promoted the development of rapid screening methods to detect MRSA carriers. This study compared two real-time PCR methods, the BD GeneOhm MRSA assay (BDGO) and the Xpert MRSA assay, with broth-enriched culture to define their performance characteristics and rapidity in an area with low MRSA prevalence. In total, 414 swabs from the nose and 389 swabs from the groin from 425 patients were tested. Of those 425 patients, 378 had swabs from both the nose and groin in parallel. Two hundred thirty-one and 194 patients were randomly assigned to the BDGO group and the Xpert MRSA group, respectively. In general, sensitivity, specificity, and negative predictive value (NPV) were high for the BDGO (100%, 98.5%, and 100%, respectively) and the Xpert MRSA (100%, 98.2%, and 100%, respectively), irrespective of whether or not nasal and inguinal specimens were considered alone or combined. In contrast, the positive predictive value (PPV) was lower: before the resolution of discrepant results, the PPVs for nasal and inguinal specimens alone and combined were 87.5%, 86.7%, and 82.4% for the BDGO and 91.7%, 66.7%, and 92.9% for the Xpert MRSA, respectively. After the resolution of discrepant results, PPVs were 93.8%, 93.3% and 94.1% for the BDGO and 91.7%, 88.9% and 92.9% for the Xpert MRSA, respectively. With the BDGO, 4 of 16 carriers were each identified by nasal or inguinal swabs alone, whereas in the Xpert MRSA group, 4 of 13 carriers were exclusively identified by nasal swabs and 2 of 13 were identified by inguinal swabs alone. Both PCR methods showed no significant difference in the number of discrepant results (odds ratio, 0.70 [P = 0.789]), but specimens from wounds and other body sites (axilla, vagina, and throat) produced discrepancies more often than nasal and groin specimens (odds ratios, 4.724 [P = 0.058] and 12.163 [P < 0.001], respectively). The facts that no false-negative PCR results were detected and increased PPVs were found after the resolution of discrepant results point to PCR as the actual gold standard. Since both sensitivity and NPV were exceptionally high for PCR, backup cultures may, therefore, be unnecessary in an area with low prevalence and with a preemptive isolation strategy but may still be useful for PCR-positive specimens because of the lower PPV for both methods and the possibility of susceptibility testing. The median time for analysis, including extraction, hands-on time, and actual PCR was 2 h 20 min for the Xpert MRSA versus 5 h 40 min for the BDGO. Concerning reporting time, including administration and specimen collection, the Xpert MRSA was faster than the BDGO (7 h 50 min versus 17 h).
Detection of MRSA in Specimens from Various Body Sites: Performance Characteristics of the BD GeneOhm™ MRSA Assay, the Xpert™ MRSA Assay and Broth-Enriched Culture in a Low-Prevalence Area

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ABSTRACT

Universal surveillance upon patient admission is important in reducing transmission of methicillin-resistant *Staphylococcus aureus* (MRSA) and associated disease in hospitals. High cost for the health care system in conjunction with MRSA has promoted the development of rapid screening methods to detect MRSA carriers. This study aimed at comparing two real-time PCR methods, the BD GeneOhm™ MRSA assay (BDGO) and the Xpert™ MRSA assay, with broth-enriched culture to define their performance characteristics and rapidity in a low-prevalence area of MRSA. In total, 414 swabs from nose and 389 swabs from groin were tested from 425 patients. Of those 425 patients 378 had swabs from both nose and groin in parallel. 231 and 194 patients were randomly assigned to the BDGO group and Xpert™ MRSA group, respectively. In general, sensitivity, specificity and negative predictive value (NPV) were high for the BDGO (100%, 98.5% and 100%, respectively) and the Xpert™ MRSA (100%, 98.2% and 100%, respectively), irrespective of whether or not nasal and inguinal specimens were considered alone or combined. In contrast, the positive predictive value (PPV) was lower: Before resolution of discrepant results the PPV for nasal and inguinal specimens alone and combined was 87.5%, 86.7 and 82.4% for the BDGO and 91.7, 66.7 and 92.9 for the Xpert MRSA™, respectively. After resolution of discrepant results the PPV was 93.8%, 93.3 and 94.1% for the BDGO and 91.7, 88.9 and 92.9 for the Xpert MRSA™, respectively. With the BDGO 4 of 16 carriers were each identified by nasal or inguinal swabs alone, whereas in the Xpert MRSA™ group 4 of 13 carriers were exclusively identified by nasal swabs and 2 of 13 were identified by inguinal swabs alone. Both PCR methods showed no significant difference in the number of discrepant results (Odds ratio 0.70, p = 0.789), but specimens from wounds and other body sites (axilla, vagina, throat) produced discrepancies more often if compared to nasal and groin specimens (Odds ratios 4.724, p = 0.058, and 12.163, p < 0.001, respectively). The fact that no false-negative PCR results were detected...
and an increased PPV after resolution of discrepant results point to PCR as the actual gold standard. Since both sensitivity and NPV were exceptionally high for PCR, backup cultures may, therefore, be unnecessary in a low-prevalence area with a pre-emptive isolation strategy, but may still be useful for PCR-positive specimens because of the lower PPV for both methods and the possibility of susceptibility testing. Median time for analysis including extraction, hands-on time and actual PCR was 2 h 20 min for the Xpert MRSA versus 5 h 40 min for the BDGO, respectively. Concerning reporting time including administration and specimen collection the Xpert™ MRSA was faster than the BDGO (7 h 50 min versus 17 h).

INTRODUCTION

Methicillin-resistant *Staphylococcus aureus* (MRSA) strains have become a major concern for health care systems. Prevention of MRSA spreading has, therefore, become a main goal in the past decade, and active screening programs have been established worldwide (4, 26). If compared to infections caused by methicillin-susceptible *S. aureus* (MSSA) the organism causes severe infections with increased morbidity, mortality, and prolonged hospitalization (9, 17). Contrary to countries facing a high prevalence of MRSA like the USA and Japan, prevalence in Switzerland has remained low to date (5, 13, 21, 31). In most parts of our country prevalence rates between 4 and 7% are observed (19). Apart from spreading in the hospital environment MRSA carriage in our community as well as other countries seems to be more prevalent than previously assumed (30, 31, 36).

To facilitate rapid detection of colonized patients real-time PCR assays have been developed. The first method to directly detect MRSA from clinical specimens was developed by Huletsky et al. (20). The principle of this method is used in two commercially available tests, *i)* the BD-GeneOhm-MRSA assay (BDGO) (BD-GeneOhm, San Diego, CA), and *ii)* the Xpert™ MRSA assay (Cepheid, Inc., Sunnyvale, CA).
Recent studies have shown that universal admission surveillance for MRSA was associated with a reduction in MRSA disease (18, 27). Likewise, Cunningham et al. have reported a reduction in MRSA transmissions in a critical care unit. The authors attributed these findings, at least partially, to the availability of rapid PCR screening tests, apart from other measures like improved hygiene measures (10). PCR screening methods are cost-efficient, especially in a low-prevalence area where high-risk patients are subjected to pre-emptive contact isolation (6). Our facility is a 1,000-bed tertiary care teaching hospital with a known low prevalence (<5%) for MRSA colonization of patients, and follows a surveillance policy similar to that of the University Hospital of Berne, Switzerland (6). As reported in other studies this means pre-emptive isolation on admission of all patients who i) came from or had travelled to countries with known high prevalence rates for MRSA; ii) were transferred from long-term care facilities; iii) were transferred from another health care facility; iv) were hospitalized within the previous 6 months; and/or v) had a history of MRSA colonization or infection (6, 8, 23). As soon as PCR is negative for MRSA patient isolation is stopped. Under these circumstances, a rapid screening method with a high NPV is desirable, because the bulk of cost emerge mainly from non-colonized patients being unnecessarily isolated. In this study, we aimed at comparing two real-time PCR methods, the BDGO and Xpert™ MRSA assays, with broth-enriched culture to assess their performance characteristics and rapidity in a low-prevalence area for MRSA.

MATERIALS AND METHODS

Patients and Clinical Specimens. This study was conducted prospectively over a period of 12 months at the Luzerner Kantonsspital (LUKS) from August 2007 to August 2008. Swabs from nose, groin, wound, axilla, vagina, and throat were collected on admission according to the LUKS policy for MRSA screening for patients with a high risk for MRSA carriage. High-
risk patients were individuals who (i) came from or had travelled to countries with known high prevalence rates for MRSA; (ii) were transferred from long-term care facilities; (iii) were transferred from another health care facility; (iv) were hospitalized within the previous 6 months; and/or (v) had a history of MRSA colonization or infection. Double-swabs were transported in Copan Transystem Liquid Stuart (Copan Italia S.p.A., Brescia, Italy) and stored at room temperature. If further processing of the swabs was not possible on the same day, swabs were stored overnight at 4°C. Patient samples were then randomly assigned to be tested with either the BDGO or the Xpert™ MRSA assay.

**BD-GeneOhm-MRSA™ assay (BDGO).** Swabs were transferred to the sample reagent buffer and processed for cell lysis and DNA extraction according to the manufacturer’s recommendations. Lysed specimen (2.8 µl) was added to the PCR tubes containing 25 µl of the reconstituted master mix. PCR was performed with the Smart Cycler® II instrument (Cepheid, Sunnyvale, CA). Positive and negative controls were included in each run. In case of inhibition the sample was briefly frozen to remove inhibitors and the run repeated. If a sample was still inhibited after freezing-thawing the lysed specimen was diluted 1:20 with sample reagent buffer and the run repeated. The BDGO is both FDA approved in the US and CE approved in Europe for nasal specimens exclusively. Since there are instructions of the manufacturer for nasal swabs only, specimens from body sites other than the nares were treated as were the nasal ones.

**Xpert™ MRSA assay.** According to the instructions of the manufacturer swabs were transferred into extraction buffer vials and mixed to remove bacteria from the swab. Again, nasal specimens only are FDA and CE approved. Specimens from body sites other than the nares were treated the same way as nasal ones.

**Detection of MRSA by culture.** In parallel to PCR, the second part of the double swab was transferred into enrichment broth (1 ml; Tryptic Soy Broth [Becton Dickinson, Franklin...
Lakes, NJ supplemented with 7.5% NaCl) and incubated for 24 h in ambient air at 35° C. Subcultures were done on chromogenic agar medium (Chrom ID™ MRSA Agar, bioMérieux, Marcy l’Etoile/France) at 35° C in ambient air. Plates were read after 24 and 48 h of incubation, respectively. Blue colonies were tested by the Staphaurex Plus test (Remel Europe Ltd., Dartford, Kent/UK). Presence of MRSA was confirmed by the Vitek 2 System (bioMérieux; GP colorimetric identification card; software version 04.03). Susceptibility testing for confirmation of methicillin resistance was done by the disk diffusion method with 30-µg cefoxitin disks (bioMérieux) according to the guidelines of the Clinical Laboratory Standards Institute (CLSI) (7).

**Calculation of inhibition rates.** Initial inhibition rates were recorded for both test systems. For the BDGO inhibition rates were recalculated after freezing-thawing and after freezing-thawing/diluting the sample 1:20 with sample reagent buffer, respectively. For the Xpert™ MRSA assay repeating a test was not possible.

**Resolution of discrepant results.** Specimens showing discrepant results for the BDGO and Xpert MRSA assays and culture were further analyzed. In case of PCR-positive but culture-negative results from one body site and concordantly positive results of specimens from another body site of the same patient at the same time, PCR results were regarded as true-positives (TP).

**Data analysis of PCR results.** Specificity, PPV, and NPV were calculated for the BDGO and the Xpert™ MRSA assay compared to culture as the gold standard before and after resolution of discrepant results. Confidence intervals were calculated according to the Wilson’s method (1), odds ratios were calculated for the frequency of discrepant results with culture comparing both PCR based methods in general as well as different types of specimens with nasal specimens as the Food and drugs administration (FDA) approved reference by logistic regression adjusted for clustering.
Calculation of turnaround times. Transport time (collecting to arrival at the laboratory) and laboratory turnaround time (arrival of specimen to reporting of either PCR or culture results) were recorded electronically in hours and minutes for each specimen and the median was calculated. Reporting time (sampling to reporting of results) was calculated as the sum of transport and laboratory turnover times.

Software. All calculations were done with the MS Excel Software (Microsoft, Redmond, WA) and the Stata software (StataCorp LP, College Station, TX). Results of the analysis with p-values < 5% were considered statistically significant.

RESULTS

In total, 414 swabs from nose and 389 swabs from groin were tested from 425 patients. Of those 425 patients 378 had swabs from both nose and groin in parallel. 231 and 194 patients were randomly assigned to the BDGO group and Xpert™ MRSA group, respectively.

In the BDGO group 8 of 13 initially inhibited specimens could eventually be included in the data analysis, because results became available after a freezing/thawing step. The remaining 5 specimens could be included after a freezing/thawing step plus a 1:20 dilution step of the extracted DNA. Specimens from 7 of 194 patients in the Xpert™ MRSA group were excluded from the study due to persistent PCR inhibition.

Initial inhibition rates with swabs from nose and groin were comparably low in the BDGO group (1.7% and 1.3%, respectively) and the Xpert™ MRSA group (1.6% and 1.7%, respectively). For wound specimens the Xpert™ MRSA showed distinctly lower initial inhibition rates than the BDGO (0 and 6.2%, respectively). Repeat PCRs were possible with the BDGO samples and the inhibition rate dropped to 0 after a freezing/thawing step, followed by a 1:20 dilution step of the lysate.
Performance characteristics of the BDGO and Xpert MRSA™ were calculated for each specimen type separately as well as for nose and groin specimens combined before and after resolution of discrepant results (Table 2) using broth-enriched culture as the gold standard (Table 1). No significant differences in the performance of the two PCR methods were observed. Sensitivity, specificity and negative predictive value (NPV) of the BDGO was high already before resolution of discrepant results (100%, 98.5% and 100%, respectively) irrespective of body sites considered alone or combined. The same was true for the Xpert MRSA™ with a sensitivity, specificity and NPV of 100%, 98.2% and 100%, respectively. After resolution of discrepancies sensitivity, specificity and negative predictive value marginally changed to 100%, 99.5%, and 100% for the BDGO and 100%, 99.4%, and 100% for the Xpert MRSA™, respectively. In contrast, the positive predictive value (PPV) was lower: Before resolution of discrepant results the PPV for nasal specimens was 87.5% and 91.7% for the BDGO and Xpert MRSA™, respectively. After resolution of discrepant results the PPV for nasal specimens rose to 93.8% for the BDGO and remained 91.7% for the Xpert MRSA™. For specimens from the groin the PPV was only 86.7% and 66.7% before resolution of discrepant results and rose to 93.3% and 88.9% after resolution of discrepant results for the BDGO and Xpert MRSA™, respectively. Combining specimens from nose and groin resulted in a PPV of 82.4% and 92.9% before resolution of discrepancies and 94.1% and 92.9% after resolution of discrepancies for the BDGO and Xpert MRSA™, respectively.

Taking swabs from nose and groin resulted in a higher detection rate of MRSA carriers: In the BDGO group with specimens from nose and groin 4 of 16 carriers were each identified by nasal or inguinal swabs alone, whereas 8 carriers showed positive PCR results for both body sites. In the Xpert MRSA™ group with specimens from nose and groin 4 of 13 carriers were
exclusively identified by nasal swabs and 2 of 13 were identified by inguinal swabs alone, whereas 7 carriers showed positive PCR results for both body sites.

Additionally, the probability of producing discrepant results was analyzed by logistic regression adjusted for clustering to compare both PCR methods as well as different body sites. If both PCR tests were compared independent of the body site there was no difference in the probability of producing discrepant results with culture (Odds ratio 0.70, p = 0.789, 95%).

To compare the body sites nasal specimens were chosen as the comparator as they are widely accepted and approved by the FDA. In addition to specimens from the groin (n = 389) other body sites were included into the analysis (wounds [n = 99], axilla [n = 24], throat [n = 11], and vagina [n = 3]). If body sites were compared regarding the probability of discrepant results (in our case for PCR-positive and culture-negative results [FP] only) significant differences were detected independent of the PCR method: Specimens from groin only tended to produce discrepant results more often compared to nasal specimens (Odds ratio 1.09, p = 0.001), while specimens from wounds and various other body sites (axilla, vagina, throat) exhibited a distinct higher probability of discrepant results (Odds ratios 4.724, p = 0.058, and 12.163, p < 0.001, respectively).

Turnaround times for the BDGO and Xpert™ MRSA are shown in Table 3. Transport time was the same for both assays, but reporting times of the PCR methods differed: the Xpert™ MRSA revealed a reporting time of 7 h 50 min and thus, provided results 9 h and 10 min earlier than the BDGO to the clinicians.

**DISCUSSION**

Several recent studies have aimed at comparing the BDGO and Xpert™ MRSA assays in high-prevalence countries (22, 28, 33-35). In our study, not only did we aim at comparing classical performance parameters like sensitivity, specificity, PPV, and NPV in a low-
prevalence area, but also analyzed the likelihood of discrepant PCR and culture results for specimens from body sites other than the nares. In addition, we assessed the rapidity by which the respective results became available.

Both PCR assays had comparable sensitivities, specificities, PPVs, and NPVs, similar to what has been observed by others (2, 11, 22, 25, 32, 34). Notably, the sensitivity of the BDGO in this study was found to be higher (100% vs. 84.3%) than in our previous study (23). This may possibly be attributed to the use of Amies gel agar in the previous study instead of liquid Stuart’s medium as used in the current one. Use of an agar-based medium may compromise the elution process of staphylococcal organisms.

Most recently, Kelly et al. (22) reported that sampling more than one single body site with pooled swabs from nose and groin resulted in a higher detection rate of colonization by PCR screening assays in a high-prevalence area (2, 14, 22, 24), while sensitivity and PPV (ranging from 84.8% to 87% and from 76.5 to 80%, respectively) were relatively low. Our results support those findings inasmuch as the detection rate of MRSA carriers was increased by 25% (4 of 16 carriers) and 15.4% (2 of 13 carriers) with the BDGO and Xpert MRSA™, respectively, if swabs from groin were added to those from the nares. Sensitivity, specificity, PPV and NPV of combined swabs equalled the performance values of swabs from a single body site. Thus, an advantage of pooling specimens from nose and groin are lower cost for MRSA screenings along with an even enhanced detection rate of MRSA carriers. However, for specific decolonization procedures additional testing will be necessary to determine the sites actually colonized relativizing cost savings from pooling.

As pointed out by Conterno et al. screening patients by PCR was more costly than screening them with cultural methods despite an extended period of isolation associated with culture (8). However, 37% of cost could be attributed to the high rate (41.4%) of patients isolated because of false-positive results that resulted from a low PPV (65%) of the used IDI-
MRSA assay (now BDGO). On the one hand, PCR-positive, culture-negative results may be attributed to high colonization rates, e.g. in wounds infected with MSSA containing SCCmec-like elements without a functional mecA gene which are inserted in the same integration site as SCCmec and reportedly may result in true false-positive PCR results (12, 15), or, on the other hand, lower colonization rates of other body sites below the detection limit of culture (28, 29). For one single discrepant result with the Xpert MRSA™ (Table 2, patient 4) we found no possible explanation: Neither could MRSA be detected in other specimens of the same patient (pointing to an actually true-positive PCR result) nor could MSSA be cultured from this specimen (pointing to a true false-positive PCR result). Interestingly, Staphylococcus sciuri was isolated from culture and identified by biochemical and 16S rRNA gene homology analysis. Hence, PCR was considered false-positive after resolution of discrepancies. The reason for the positive PCR result remains unclear. Work is in progress to further characterize this strain. However, S. sciuri is a rarely isolated species in humans and may bias our results as this specimen was the only false-positive after resolution of discrepancies with the Xpert MRSA™. Thus, the actual PPV of the Xpert MRSA™ in routine use may even be higher than reported in this study. Results of Wolk et al. (34) for nasal specimens parallel those of our study using various specimen types. This study and our own results (no false-negative PCRs, sensitivity of 100%) suggest that the low PPV of PCR assays may result from the higher sensitivity of PCR assays compared to culture, i.e., PCR is the likely new gold standard. Our results support those findings inasmuch as 3 of 7 specimens with PCR-positive culture-negative results went along with positive parallel specimens of the same patient at the same time, pointing to true-positive PCRs and false-negative cultures which resulted in an increased PPV (Tables 1 and 2). Furthermore, our data show that discrepant results for both PCR methods – exclusively FP - occurred significantly more frequent with swabs from body sites other than the nares and groin, and, therefore, contribute
to a low PPV. This may be due to lower MRSA colonization rates and, therefore, lower pre-
test probability of sites like throat, axilla or vagina compared to the nares (3, 24). Although it
has been recommended to include at least throat specimens for optimal sensitivity our results
indicate that a sensitivity of 100% can be achieved with nasal and inguinal swabs alone (24).
Thus, testing of body sites other than the nares and groin may be dispensable.

Another disadvantage of swabs from body sites other than the nares and groin may be the
higher inhibition rates (1 of 17 swabs and 2 of 22 swabs from other body sites compared to
only 7 of 414 and 6 of 389 for nose and groin swabs for BDGO and Xpert MRSA,
respectively). With specimens from wounds 4 of 65 invalid results were observed with the
BDGO, while with the Xpert™ MRSA none were seen (0 of 34). The number of finally
invalid results due to inhibition for nose and groin specimens was comparably low for both
PCR assays (1.3 to 1.7% and 1.5 to 1.6% for the BDGO and Xpert™ MRSA, respectively).
For the nose and groin swabs analyzed by the BDGO this is well in line with previous reports
(2, 11, 23, 32). Initial inhibition rates of the BDGO can be reduced by a freezing/thawing step
of the DNA extract (12, 22, 37) or be even completely overcome by an additional dilution
step (23, 37). If, however, persistent PCR inhibition is observed for a specimen it seems
reasonable to do cultures and keep the patient isolated until results become available. In the
case of the Xpert™ MRSA our inhibition/invalid rates are far below the values generally
observed, ranging from 4% (28) for nasal swabs up to 20.9% (22) for nose and groin swabs
combined. These high rates may be due to the formation of crystals in the cartridges (22).
Therefore, prewarming of the reagents prior to repeating the test has been suggested, a
strategy which, however, will increase cost (22). Since we have stored the reagents at 4°C and
did not pre-warm them prior to use, the reason for our lower inhibition rates remains
unexplained.
In addition to the classical performance characteristics a short reporting time for MRSA detection is crucial to reduce both rate of nosocomial MRSA transmission and number of patient isolation days (4, 16, 26). Primarily, reporting time depends on turnaround time in the laboratory, including \(i\) collection time for the specimens in the laboratory to use the PCR mastermix to its full capacity (for the BDGO only); \(ii\) preanalytic steps; and \(iii\) the time needed to perform the assay. The BDGO is available for batched, single-use mastermix vials for as many as 6 specimens plus two controls. In this case collection time in the laboratory is an important parameter. If used in a hospital with a low prevalence of MRSA carriers there will be a limited number of screening tests. For financial reasons laboratories will try to accumulate specimens up to 6 tests before performing the assay. As a consequence, results may be delayed. Conversely, the Xpert™ MRSA cartridges may be used for one single specimen at any time, and, therefore, such limitations do not apply for this method.

In contrast to the fully automated GeneXpert\textsuperscript{®} system another drawback of the BDGO affecting rapid availability of results is the higher complexity of the system due to the manual DNA extraction procedure. This will considerably increase the overall time for analysis (in our study 2 h 20 min for the Xpert MRSA versus 5 h 40 min for the BDGO, respectively). Our data, however, represent the situation in a low-prevalence area with low numbers of MRSA screening tests per day. As a consequence, this has considerably increased reporting time for the BDGO. Reporting time may decrease in high-prevalence areas where screening tests are performed more frequent, i.e., full BDGO batches are more rapidly achieved.

Altogether, reporting time for results by the Xpert™ MRSA in our setting was 9 hours shorter than for results generated by the BDGO. Since performance characteristics of both PCR assays were well comparable the Xpert™ MRSA may outplay the BDGO because of rapidity and associated cost savings for the hospitals at least if a pre-emptive isolation strategy is applied. In contrary, if considered per specimen Xpert™ MRSA disposables are more
expensive compared to the BDGO mastermix used to its full capacity. This holds, in particular, true for high-prevalence areas for MRSA where large numbers of screening tests are performed and, as a consequence, the BDGO mastermix will regularly be used up which results in lower laboratory cost.

From our study there are six major conclusions: (1) both PCR methods performed equally well regarding sensitivity, specificity, PPV, and NPV as well as the probability of producing discrepant results compared to culture. (2) Combining swabs from nose and groin increases the detection rate of MRSA carriers. (3) Taking swabs from body sites other than nares and groin may not be advisable because of higher inhibition rates and a significantly increased likelihood of discrepant results. (4) The NPV was exceptionally high (100%) for both PCR methods demonstrating that back up cultures are unnecessary if PCR is negative. For PCR-positive specimens back up cultures may, however, be useful because of the low PPV even after resolution of discrepancies. (5) The low PPV of both PCR methods might be due to PCR rather than culture being the actual gold standard. Culture in all likelihood produces false-negative results and, therefore, is not a true gold standard. (6) Concerning rapid availability of PCR results the Xpert™ MRSA was superior to the BDGO.

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REFERENCES


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<td>100 (97.4-99.9)</td>
<td>93.8 (71.7-98.9)</td>
</tr>
<tr>
<td></td>
<td>Xpert MRSA</td>
<td>186</td>
<td>11</td>
<td>1</td>
<td>174</td>
<td>0</td>
<td>100 (74.1-100)</td>
<td>99.4 (96.8-99.9)</td>
<td>91.7 (64.6-98.5)</td>
</tr>
<tr>
<td>Groin</td>
<td>BDGO</td>
<td>213</td>
<td>14</td>
<td>1</td>
<td>198</td>
<td>0</td>
<td>100 (78.5-100)</td>
<td>99.5 (97.2-99.9)</td>
<td>93.3 (70.2-98.8)</td>
</tr>
<tr>
<td></td>
<td>Xpert MRSA</td>
<td>176</td>
<td>8</td>
<td>1</td>
<td>167</td>
<td>0</td>
<td>100 (67.6-100)</td>
<td>99.4 (96.7-99.9)</td>
<td>88.9 (56.5-98.0)</td>
</tr>
<tr>
<td>Nose and groin combined</td>
<td>BDGO</td>
<td>210</td>
<td>16</td>
<td>1</td>
<td>193</td>
<td>0</td>
<td>100 (80.6-100)</td>
<td>99.5 (97.1-99.9)</td>
<td>94.1 (73.0-99.0)</td>
</tr>
<tr>
<td></td>
<td>Xpert MRSA</td>
<td>168</td>
<td>13</td>
<td>1</td>
<td>154</td>
<td>0</td>
<td>100 (77.2-100)</td>
<td>99.4 (96.4-99.9)</td>
<td>92.9 (68.5-98.7)</td>
</tr>
</tbody>
</table>

Values were calculated before and after resolution of discrepancies for specimens from nose and groin alone and combined with corresponding 95% confidence intervals (CI). TP, true positive; TN, true negative; FP, false positive; FN, false negative; PPV, positive predictive value; NPV, negative predictive value.
### TABLE 2: Analysis of discrepant results of PCR based methods and culture

<table>
<thead>
<tr>
<th>PCR Method</th>
<th>Patient</th>
<th>Origins of specimens</th>
<th>Result, further analyses, and actions</th>
<th>Organisms cultured</th>
<th>Rating of PCR result before resolution</th>
<th>Rating of PCR result after resolution</th>
</tr>
</thead>
<tbody>
<tr>
<td>BDGO</td>
<td>1</td>
<td>nose</td>
<td>MRSA not detected in other specimens of the same patient</td>
<td>CoNS</td>
<td>FP</td>
<td>FP</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>inguina</td>
<td>MRSA confirmed in other specimens of same patient</td>
<td>MSSA</td>
<td>FP</td>
<td>FP</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>nose</td>
<td>MRSA confirmed in other specimens of same patient</td>
<td>none</td>
<td>FP</td>
<td>TP</td>
</tr>
<tr>
<td>Xpert MRSA</td>
<td>4</td>
<td>nose</td>
<td>MRSA not detected in other specimens of the same patient</td>
<td>CoNS</td>
<td>FP</td>
<td>FP</td>
</tr>
<tr>
<td></td>
<td>5</td>
<td>inguina</td>
<td>MRSA confirmed in other specimens of same patient</td>
<td>S. sciuri</td>
<td>FP</td>
<td>FP</td>
</tr>
</tbody>
</table>

MSSA, Methicillin susceptible *Staphylococcus aureus*; CoNS, coagulase negative staphylococci; TP, true positive; TN, true negative; FP, false positive; FN, false negative.
<table>
<thead>
<tr>
<th></th>
<th>Time for Transport</th>
<th>Time for Collection*</th>
<th>Time for Analysis*</th>
<th>Time to Reporting</th>
</tr>
</thead>
<tbody>
<tr>
<td>BDGO</td>
<td>4 h 25 min</td>
<td>6 h 55 min</td>
<td>5 h 40 min</td>
<td>17 h 00 min</td>
</tr>
<tr>
<td>Xpert MRSA</td>
<td>4 h 25 min</td>
<td>1 h 05 min</td>
<td>2 h 20 min</td>
<td>7 h 50 min</td>
</tr>
<tr>
<td>Culture</td>
<td>4 h 25 min</td>
<td>directly inoculated</td>
<td>54 h 30 min</td>
<td>68 h 50 min</td>
</tr>
</tbody>
</table>

* Transport time (collecting to arrival at the laboratory) and laboratory turnaround time (arrival to reporting of either PCR or culture results), the latter one being divided into time for specimen collection and time for running the assay. Reporting time (sampling to reporting of results) was calculated as the sum of transport and laboratory turnaround times. a) Collection includes administration and collection of specimens to utilize the mastermix to full capacity (BDGO only) b) Analysis includes DNA extraction and PCR.