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ORIGINAL PAPER

# A selected screening programme was less effective in the detection of methicillin-resistant *Staphylococcus aureus* colonisation in an orthopaedic unit

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**Abstract**
*Purpose* Our unit has used a selective screening policy for methicillin-resistant *Staphylococcus aureus* (MRSA) colonisation using standard chromogenic growth media, based upon risk stratification. The aim of this study was to examine the effectiveness of this selective screening policy.
*Methods* A cohort of 429 patients was assessed for their risk status for MRSA colonisation using both rapid polymerase chain reaction (PCR) swabs and traditional culture and sensitivity analysis. The sensitivity, specificity, positive predictive values and negative predictive values of the traditional selective approach were calculated compared to universal rapid screening.
*Results* One hundred eighteen patients were considered high risk and would traditionally be further screened with standard culture of swabs. The prevalence of MRSA was 15/429 (3.5 %). The sensitivity of selective screening was 53 % identifying eight of 15 cases. The false-negative rate was therefore 47 % and seven would have been missed. PCR results were available within four to six hours, whereas culture results were only available at 24 hours for the media showing no growth and not until 72 hours for positive MRSA cases.
*Conclusions* We now advocate universal screening prior to, or on admission, using this rapid PCR test, as we consider this identifies MRSA colonisation more effectively and facilitates "ring-fencing" of orthopaedic beds.

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## Introduction

Methicillin-resistant *Staphylococcus aureus* (MRSA) can lead to considerable morbidity and mortality in orthopaedic patients. The death rate from MRSA bacteraemia is double that of methicillin-sensitive *Staphylococcus aureus* (MSSA) [1]. The complication rate and cost of periprosthetic joint infection with MRSA is considerably higher compared to MSSA [2]. Patients receiving orthopaedic implants are most vulnerable, given the potential for biofilm formation and long-term morbidity [3, 4]. Yet, worryingly, the incidence of MRSA in orthopaedic departments has increased [5]. Measures taken to prevent MRSA infection include screening to detect colonisation, isolation, treatment of colonisation and antibiotic stewardship [6, 7]. Biant et al. reduced overall infection rates for MRSA by the introduction of ring-fencing, essentially segregating patients based upon risk status [8]. Ring-fencing of beds, and a "search and destroy" policy of universal screening and isolation has been credited with producing very low rates of MRSA in the Netherlands [9, 10]. However, ring-fencing of beds can often be difficult to achieve in clinical practice because of the competing pressures of infection control and targets for emergency department (ED) waiting times coupled with bed shortages. Screening for MRSA is recommended in high-risk areas such as intensive care and orthopaedics [11]. Screening can either be universal for all admissions or on a selective basis in patients with known risk factors for MRSA carriage and infection. Selective screening may be as effective, but more cost-effective than universal screening [12–14]. This has been questioned with another study

demonstrating an overall cost benefit if only four MRSA infections per year were prevented [15, 16]. The cost-effectiveness of universal screening "break-even" point depends on the local prevalence of MRSA [17]. Risk factors for MRSA carriage in the elderly include age over 80 years and recent hospitalisation and open wounds and sores [18, 19]. It has also been demonstrated that universal screening may be more effective in the emergency admission category as these patients generally have more risk factors for MRSA carriage [20, 21].

The aim of this study was to evaluate the effectiveness of a selective screening policy with traditional chromogenic culture of swabs from high-risk patients, compared to a universal screening policy with a rapid molecular detection (polymerase chain reaction, PCR) methodology.

## Patients and methods

As this was an evaluation of an accepted procedure and comparison with a gold standard the study design was classed as audit and not subject to Research Ethics Committee approval at our institution.

Over a two-month period, 429 consecutive admissions to the orthopaedic unit were screened for MRSA. Of the patients, 191/429 (44 %) were male and 238/429 (56 %) were female. This study was classed as audit as screening for MRSA status is a routine part of perioperative care for orthopaedic patients. This was an assessment of the performance of our selective screening protocol against a gold standard of universal screening.

The MRSA was based on reported risk factors for MRSA colonisation [13, 18, 19, 22–24]. Risk stratification consisted of nursing staff assessment of the following risk factors via a pro forma collected on admission or in the pre-assessment clinic:

1. Admission to hospital in the previous 12 months
2. Transfer from another hospital
3. Transfer from a residential care or nursing institution
4. Contact with someone with MRSA
5. A previous diagnosis of MRSA

Risk stratification was carried out by nursing staff at the pre-assessment visit for elective patients or on admission for trauma patients. This risk status was independently determined by the authors from retrospective review of the patient's electronic patient record and microbiology results in the laboratory system. On initial assessment 118 patients were considered high risk. Of 242 elective patients, 82 (34 %) were considered high risk at assessment (Table 1). Of 187 trauma admissions, 26 (14 %) were considered high risk. On retrospective review it was found that 58 (49 %) of those in the high-risk group had been wrongly classified and similarly 57 (18 %) of 311 in the low-risk group were wrongly classified. Therefore the overall error rate in determining risk was 115 (37 %) of 429. On reclassification there were therefore 117 high-risk patients and 312 low-risk patients. The patients were analysed on an intention to treat basis that was based on the initial risk assessment.

**Table 1** Comparison of cases of MRSA colonisation identified by selective, risk-stratified screening versus universal PCR testing

| | MRSA positive ($n$=15) | MRSA negative ($n$=414) | Total ($n$=429) |
|---|---|---|---|
| Risk stratification | | | |
| High risk | 8 | 110 | 118 |
| Low risk | 7 | 304 | 311 |
| Total | 15 | 414 | |

The gold standard for determination of MRSA colonisation was considered to be universal PCR testing; this was carried out on all admissions and formal culture for MRSA was performed on patients considered high risk according to the unit protocol. The PCR assay was performed as described by Renwick et al., [25]. Briefly, samples and controls were extracted using the NucliSENS® easyMAG™ system (bioMérieux, Basingstoke, UK). Lysis buffer contained phocine herpesvirus (PhHV) for the internal control. Saline suspensions were pretreated with Proteinase K (QIAGEN Ltd., Crawley, UK) and were extracted according to the manufacturer's instructions. The PCR was performed in a volume of 25 μl, consisting of 10 μl extracted nucleic acid, 2.5 units HotStarTaq DNA Polymerase, 200 μM of each dNTP, 1.5 mM $MgCl_2$ (final concentration 5 mM) (QIAGEN Ltd., Crawley, UK), 0.5 μM each SCC*mec* primer, 0.35 μM SCC*mec* probe, 0.3 μM each of the forward and reverse PhHV primer and 0.05 μM PhHV probe. Amplification, detection and analysis were performed in an ABI 7500 real-time PCR system (Applied Biosystems, Warrington, UK). Culture was performed using the Medical Wire Transwab® with plain medium and charcoal medium (Medical Wire & Equipment, Wiltshire, UK). The same specimen was used for standard culture and for PCR. These swabs were plated onto Brilliance™ Chromogenic MRSA agar (Oxoid, Basingstoke, UK) for 18 h at 37 °C. Latex agglutination test for *S. aureus* surface antigens was carried out (Pastorex®, Biostat, Stockport, UK) on pure colonies followed by DNAse test (DNAse plate, Oxoid, Basingstoke, UK). For new MRSA positives antibiotic susceptibility was determined by VITEK (bioMérieux, Basingstoke, UK) and E-tests for cefoxitin resistance and oxacillin resistance. Latex agglutination test for penicillin-binding protein (PBP2', Oxoid, Basingstoke, UK) was also performed on certain specimens. All PCR results were available within four to six hours. Negative culture

results were available at 24 hours. Positive culture results were available in the five patients cultured positive at 72 hours. Samples that tested positive for MRSA only on PCR testing were evaluated by sequencing or by culture of the nutrient broth from the PCR testing. High-risk patients underwent three site swabs (nose, throat and groin) for culture-based MRSA screening and PCR. The remaining patients had three site swabs for PCR only.

The prevalence of MRSA in the study group, according to the PCR gold standard, was 15/429 (3.5 %). Patients with MRSA colonisation who were scheduled to have elective surgery had their procedure delayed until repeat screening was clear. They were treated with chlorhexidine body wash for bathing, chlorhexidine mouthwash and mupirocin nasal ointment for one week. Where patients were admitted as an emergency, they were isolated and treated with the protocol above.

## Results

The sensitivity of the selective screening approach was 53 % (Table 2). It failed to identify 7 (47 %) of 15 patients who were colonised with MRSA. The rate of MRSA in the high-risk group was 6.8 % and was 2 % in the low-risk group. In the high-risk group, eight patients were identified as colonised with MRSA by PCR testing. Direct culture was positive in five (63 %) of the eight cases. In the remaining three, MRSA colonisation was confirmed by sequencing for SCC*mec* and *mecA*. Although culture was not available in the low-risk patients, stored nutrient broth used for enrichment culture grew MRSA from six of the seven low-risk patients and sequencing confirmed the presence of the SCC*mec* and *mecA* gene in the remaining patient.

Of the 15 patients that had PCR-positive samples, 13 had positive nose swabs, five had positive throat swabs and three had positive groin swabs. Nose swabs were negative in two patients who were positive in one site only, throat and groin respectively. Two patients were positive in all three sites and two others were positive in both nose and throat. Nine patients had MRSA isolated from nose swabs alone.

**Table 2** Sensitivity and specificity along with other parameters of selective screening

| | Worst case |
|---|---|
| Sensitivity | 53 % |
| Specificity | 73 % |
| False-negative rate | 47 % |
| False-positive rate | 27 % |
| Positive predictive value (PPV) | 6.8 % |
| Negative predictive value (NPV) | 98 % |

## Discussion

The prevalence rate of 3.5 % colonisation of MRSA in patients admitted to the musculoskeletal service is equivalent to other UK rates [26, 27] and lower than other centres, which have reported rates of MRSA colonisation in elective patients as high as 27 % [28]. There was an inappropriate classification of low-risk patients demonstrated in 18 % of cases, i.e. 18 % of patients classified as low risk were in fact high risk, indicating that the current screening of high-risk patients alone would lead to a substantial percentage of MRSA-positive patients in the low-risk group being missed. The reasons for inappropriate classification include the failure to detect one or more of the risk factors during initial admission or assessment. The causes for this include unfamiliarity with the pro forma and "paperwork overload" at the time of admission. Staff were educated through written and oral techniques when the protocol was introduced; however, staff turnover and the possibility of absence coverage by staff from outwith the unit meant that some staff may have been unfamiliar with its use. The results suggest that other units using a selective screening policy would be at a similar risk of misallocation of cases. Although a redesigned pro forma and further staff education may improve this error rate, we believe that the potential cost-effectiveness and clinical efficacy of universal screening recommend its future adoption. Use of such a protocol removes the need for potentially complex decision-making.

Overall approximately 50 % of the MRSA-positive cases were missed using purely the selective screening policy. This is in keeping with the findings of Thyagarajan et al. who noted that more than 50 % colonised patients came from home [27]. These findings indicate that selective screening is highly inaccurate and support the introduction of universal MRSA screening for admissions to orthopaedic and trauma units.

Universal screening of patients could have increased the laboratory workload but this was offset by simplified admission criteria for screening, which reduced incorrect sampling. The rapid automated real-time PCR facilitated comprehensive screening of all patients for MRSA. The majority of results which were negative for MRSA were available within 4 h with the real-time PCR. All of the samples could be stored in nutrient broth at 4 °C, and antibiotic susceptibility tests could be carried out for patients requiring treatment for MRSA infection. It has been reported that molecular tests were too costly for universal screening [29]; however, the consumable cost for this in-house assay was £3 compared to £20 for some commercial options. Labour costs were not calculated for the traditional culture method and the PCR assay but automation does release staff time for other laboratory duties.

Previous studies have suggested that nasal swabs were sufficient as screening swabs and may reduce cost, whereas the additional throat and perineal wound swabs increased the sensitivity, but increased the costs. However, this study

demonstrated that emphasis on nasal swabs as screening samples would miss MRSA-positive patients. In addition, the use of nasal swabs can compromise sensitivity as patients may have transient carriage. We therefore advocate the continued use of throat and perineal testing as well as nose swabs.

In accordance with the unit policy culture results were available for high-risk patients as well as the PCR results. This enabled us to compare the two tests directly in a subset expected to have a significant number of positive results. The real-time PCR generated rapid results compared to chromogenic media. In addition the PCR assay was highly sensitive and detected more MRSA-positive isolates as shown by the three samples, which were direct culture negative but confirmed to be MRSA by sequencing for SCC*mec* and *mecA* gene. As a result of detecting MRSA with this more sensitive technique, the management of these patients was adjusted to that of other MRSA-positive patients in order to reduce their risk of developing invasive infections. Although the chromogenic media delivered results fast enough for those screened in the pre-admission clinic, our results suggest that the increased sensitivity of the PCR may justify using PCR only, provided that the cost of the PCR was reduced to that of the chromogenic media with an increased volume of testing.

A strength of this study was the consecutive prospective application of this protocol for a large number of patients. This has reduced the potential for a type II error due to the relatively low rate of colonisation in this population. We reassessed all patients retrospectively to assess their risk stratification. Through the use of a computerised electronic patient record we were able to assess each patient retrospectively.

In summary, the selective screening policy missed half of the MRSA-positive cases, which supports the case for the introduction of a universal screening policy. Secondly, the cost-effective PCR technique for MRSA screening used in this study was at least equivalent to culture in sensitivity, but had the advantage of providing rapid results within four hours. This rapid result can enable the orthopaedic community to achieve ring-fencing in the face of competing pressures to fill empty beds with patients of unknown MRSA status.

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**Conflict of interest** The authors declare that they have no conflict of interest.

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