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Rapid Detection of *Staphylococcus aureus* and Methicillin-Resistant *S. aureus* in Atopic Dermatitis by Using the BD Max StaphSR Assay

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Eczematous lesions of atopic dermatitis (AD) patients are known to be a source of *Staphylococcus aureus* (SA) transmission and might be a reservoir for community-associated methicillin-resistant SA (MRSA). The BD Max StaphSR (BD-SR) is a fully automated, multiplex real-time PCR assay for the direct detection and differentiation of SA and MRSA from nasal swab samples. We evaluated the detection rates of SA and MRSA from skin lesions of outpatients with AD using the BD-SR assay, and determined the usefulness of the BD-SR assay. A total of 244 skin swab samples (skin lesions of 213 outpatients with AD and normal skin of 31 healthy controls) were tested directly by using the BD-SR assay. Of the 213 samples from patients with AD, 69 (32.4%) were positive for SA, 6 (8.7%) of which were positive for MRSA. Only 1 (3.2%) of 31 samples from healthy controls was positive for SA. The BD-SR assay is effective for the rapid detection of SA and MRSA from skin swab samples, which can provide important information for managing patients with AD and preventing the spread of MRSA.

Key Words: Atopic dermatitis, *Staphylococcus aureus*, Methicillin-resistant *Staphylococcus aureus*, BD Max StaphSR

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Atopic dermatitis (AD) is a chronic, relapsing inflammatory skin disease that affects 10–20% of children and 2% of adults [1]. *Staphylococcus aureus* (SA) is highly prevalent among patients with AD, and skin colonization by SA may contribute to the onset or aggravation of AD lesions [2]. SA is a gram-positive bacterium that naturally colonizes the surface of the skin. Methicillin-resistant *S. aureus* (MRSA) are strains of SA that have acquired mechanisms of resistance against β-lactam antibiotics. Methicillin resistance in *Staphylococcus* species is most often due to production of an altered penicillin-binding protein known as PBP2a, a product of the *mecA* gene [3]. MRSA is an important cause of community-associated (CA) and healthcare-associated infections [4]. Eczematous lesions of AD patients are known to be a source of SA transmission, and might be a favorable reservoir for CA-MRSA [5]. Therefore, the rapid detection and differentiation of SA and MRSA are important for managing patients with AD and preventing the spread of MRSA.

The BD Max StaphSR (BD-SR) system (BD Diagnostics, Sparks, MD, USA) is a fully automated, multiplex real-time PCR assay for the direct detection and differentiation of SA and MRSA from nasal swab samples. The test uses three DNA targets: staphylococcal cassette chromosome *mec* (SCC*mec*)-*orfX* right-extremity junction (MREJ), thermostable nuclease of SA (*nuc*), and methicillin resistance (*mecA/mecC*). Detection of MREJ and *mecA/mecC* is required for the result "MRSA", while detection of *nuc* or MREJ without *mecA/mecC* is interpreted as "positive for SA" (Table 1). Compared with the traditional culture method, the BD-SR assay has excellent sensitivity (96.4% and 94.3%) and specificity (93.6% and 97.7%) for detecting SA and MRSA, respectively, in nares samples [6]. The BD-SR assay provided

Table 1. Results and suggested interpretations of skin swab samples from patients with AD and healthy controls using the BD Max Staph-SR assay

Results displayed		Targets*				AD	Control
SA	MRSA	MREJ	*nuc*	*mecA/mecC*		(N=213)	(N=31)
Pos	**Pos**	D	D or ND	D	MRSA	6	-
Pos	Neg	ND	D	ND	MSSA	27	1
Pos	Neg	ND	D	D	Mixed MSSA & MRnonSA	33	-
Pos	Neg	D	D or ND	ND	SA empty-cassette variant	3	-
Neg	Neg	ND	ND	D	MRnonSA	43	7
Neg	Neg	ND	ND	ND	nonSA & nonMRSA	101	23

*The positive Ct value ranges for MREJ, *nuc*, and *mecA/mecC* were 25.8–38.6, 23.5–38.6, and 24.5–39.4, respectively. The detection rate of SA was significantly higher in patients with AD than that in controls ($P=0.0008$).
Abbreviations: AD, atopic dermatitis; D, detected; MRnonSA, methicillin-resistant non–*Staphylococcus aureus*; MRSA, methicillin-resistant *Staphylococcus aureus*; MSSA, methicillin-susceptible *Staphylococcus aureus*; ND, not detected; Neg, negative; nonMRSA, non–methicillin-resistant *Staphylococcus aureus*; nonMSSA, non–methicillin-susceptible *Staphylococcus aureus*; Pos, positive; SA, *Staphylococcus aureus*; SA empty-cassette variant, *Staphylococcus aureus* carrying a genetic element lacking *mecA*.

rapid results within 2 hr. By contrast, conventional identification and antimicrobial susceptibility testing based on phenotypic characteristics take up to 72 hr.

The aim of this study was to determine the detection rates of SA and MRSA from skin lesions of outpatients with AD using the BD-SR assay, and to evaluate the usefulness of the BD-SR assay for the direct detection of SA and MRSA from skin swab samples. This study was approved by the Institutional Review Board of the Chung-Ang University Hospital. Informed consent was obtained from all subjects.

Samples were obtained from the skin lesions of 213 outpatients with AD and the normal skin (antecubital area) of 31 healthy controls between January 2011 and February 2013 at Chung-Ang University Hospital, Seoul, Korea. The BD-SR assay was performed according to the manufacturer's instructions. Although the BD-SR assay displays the results of SA and MRSA, we obtained the Ct values for further analysis. Statistical analysis was performed by chi-square test or Fisher's exact test using Statcalc (Epi Info Version 3.5.1, Centers for Disease Control and Prevention, Atlanta, GA, USA). $P<0.05$ was considered statistically significant.

A total of 244 skin swab samples were tested directly by using the BD-SR assay. Of the 213 samples from patients with AD, 69 (32.4%) were positive for SA, six (8.7%) of which were positive for MRSA. Only one (3.2%) of 31 samples from healthy controls was positive for SA (methicillin-susceptible SA [MSSA]) (Table 1). The detection rate of SA was significantly higher in patients with AD than in controls ($P=0.0008$). The incidence of MRSA in SA isolated from AD skin lesions has been reported to range from 0% to 30% [5, 7, 8]. In this study, MRSA was detected only in AD skin lesions. Topical use of antibiotics for the treatment of AD skin lesions is common and has advantages over systemic therapy. However, the frequent and repeated use of topical antibiotics promotes the development of resistant strains. It has been suggested that CA-MRSA can be easily controlled with oral cephalosporin [9]. CA-MRSA infections tend to manifest as skin infections, and the rate of CA-MRSA infections is continuously increasing. Given that eczematous lesions in AD might be a reservoir for CA-MRSA, the rapid detection of SA and MRSA is needed to manage patients with AD and prevent the spread of MRSA [4, 5].

In this study, we obtained the Ct values of three targets using BD-SR software, and evaluated its potential for the differentiation of MSSA, mixed MSSA and MRnonSA, SA empty-cassette variant, and MRnonSA (Table 1). Because the samples were skin swabs, the presence of *mecA/mecC* in MRnonSA can be regarded as methicillin-resistant coagulase-negative staphylococci. The positive Ct value ranges for MREJ, *nuc*, and *mecA/mecC* were 25.8–38.6, 23.5–38.6, and 24.5–39.4, respectively.

Most available molecular assays for methicillin resistance in *Staphylococcus* species target *mecA* or SCC*mec*, a mobile genetic element that caries *mecA* [3]. The presence of an SCC element that does not contain the *mecA* gene might indicate the loss of this gene [10]. SA isolates with SCC*mec* lacking *mecA* (SA empty-cassette variant) can be misidentified as MRSA by assays that do not specifically target *mecA* [6, 11]. False-positive results can lead to inappropriate patient care (i.e., the empirical use of glycopeptide compounds instead of β-lactam antibiotics, and unnecessary expenses related to infection control practices) [10, 11]. In addition, MRSA strains with the newly

discovered methicillin resistance gene (*mecC*) cannot be detected by assays that do not detect *mecC*. These false-negative results can lead to the uncontrolled transmission of undetected MRSA [6]. Thus, use of the BD-SR assay can decrease the number of false-positive results caused by an SA empty-cassette variant, and can detect MRSA strains harboring *mecC* [6, 11]. Recently, Mendes *et al* [11] reported that 7.1% (64/900) of MSSA isolates showed results compatible with the SA empty-cassette variant. In the present study, 4.8% (3/63) of MSSA samples from patients with AD were interpreted as an SA empty-cassette variant.

The BD-SR assay was developed for the detection of SA and MRSA from nasal swab samples [6]. Recently, several studies have shown that the BD-SR assay can be used for the rapid detection of SA, MSSA, and MRSA in positive blood culture broths [12-14]. To our knowledge, this is the first study to investigate the detection rates of SA and MRSA from skin lesions of patients with AD using the BD-SR assay. However, this study has a limitation in that the results of the BD-SR assay were not compared with those of conventional culture.

In conclusion, the BD-SR assay, a direct multiplex real-time PCR assay, is effective for the rapid detection of SA and MRSA, which can provide important information on managing patients with AD and preventing the spread of MRSA. Further studies incorporating conventional culture methods and larger sample sizes are needed to validate these results using the BD-SR assay.

Authors' Disclosures of Potential Conflicts of Interest

No potential conflicts of interest relevant to this article were reported.

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