Nearly all clinical isolates of group B Streptococcus (GBS) are Streptococcus agalactiae, which causes neonatal pneumonia, sepsis, meningitis, and invasive diseases in the elderly and in people with underlying conditions. GBS is occasionally isolated from the vagina or the intestinal canal of people without any disease symptoms (1). As all clinical isolates of GBS are uniformly susceptible to β-lactams, including penicillins, penicillins are often used as the first-line drugs for the prevention and treatment of infections caused by GBS (2,3). However, our previous studies of clinical isolates in Japan have shown the emergence and high prevalence of group B streptococci with reduced penicillin susceptibility (PRGBS) harboring amino acid substitutions in the penicillin-binding protein 2X (4–6). Moreover, PRGBS tends to be non-susceptible to macrolides and fluoroquinolones (7). Therefore, in cases of infections with multidrug-resistant PRGBS, the drug choice would be very limited.

Daptomycin is a relatively new cyclic lipopeptide antibiotic approved for the treatment of infections with methicillin-resistant Staphylococcus aureus (MRSA) in 2011. It is also expected to be effective for the treatment of daptomycin-susceptible gram-positive bacterial infections, including vancomycin-resistant Enterococcus (VRE) and GBS infections. However, some clinical isolates of S. aureus and Enterococcus faecalis have reportedly acquired daptomycin resistance (8). In our previous study, although the minimum inhibitory concentrations (MICs) of daptomycin for nearly all clinical GBS isolates were below the susceptible breakpoint settled by the Clinical and Laboratory Standards Institute (CLSI), the MIC for one clinical GBS isolate was above the breakpoint (3,9). This finding suggests the possibility of unrecognized occurrences and spreading of daptomycin-non-susceptible clinical GBS isolates in Japan. Therefore, this study aimed to investigate daptomycin susceptibility among 1,046 clinical GBS isolates that were recovered after the approval of daptomycin in Japan. MICs of daptomycin for the 1,046 clinical isolates were determined by the microdilution method recommended by the CLSI. The MIC range was 0.12–1 µg/mL, and the MIC$_{50}$ and MIC$_{90}$ were 0.5 µg/mL and 1 µg/mL, respectively. All the GBS isolates evaluated in this study were susceptible to daptomycin. Therefore, at present, daptomycin might be considered as a new option to treat GBS infections, especially multidrug-resistant PRGBS infections.
Daptomycin is produced by *Streptomyces roseosporus*. Although the detailed mode of antibacterial action is still under investigation, most studies suggest that daptomycin is a membrane-targeting antibiotic. In support of this hypothesis, daptomycin resistance in *S. aureus*, *E. faecium*, and *E. faecalis* has been linked with changes in membrane structure. The development of daptomycin resistance in *S. aureus* is mainly caused by mutations in *mprF*, leading to an increase in lysylphosphatidyl-glycerol (LysPG) in the outer leaflet of the cytoplasmic membrane, thus protecting *S. aureus* against daptomycin (10–12). However, according to sequence data in GenBank, *S. agalactiae* does not harbor *mprF* and its homologue. Therefore, although we previously detected one daptomycin non-susceptible clinical isolate of *S. agalactiae* (9), *S. agalactiae* cannot acquire daptomycin resistance through the *mprF* mutation, similar to *S. aureus*.

Daptomycin is used for the treatment of infections caused by gram-positive pathogens, including MRSA and VRE infections. In Japan, VRE infections are relatively rare and MRSA infections are usually treated with vancomycin; thus, the use of daptomycin for the treatment of VRE and MRSA infections is relatively limited. In addition, daptomycin is rarely used to treat GBS infections. The above reasons may explain why we did not detect daptomycin non-susceptible GBS isolates. Due to a high fitness cost, such isolates may only survive under selection pressures that seem to not be present in Japan currently.

Although daptomycin is not administered for the treatment of pneumonia or meningitis, specimens for this study contained many respiratory specimens. In some cases, novel drug-resistant bacteria were isolated from specimens of infections for which the drug was not applied. We also analyzed clinical isolates from respiratory specimens, among others, for which daptomycin was not applied.

As mentioned above, *S. aureus* is one of the major species that acquired daptomycin resistance, mainly through mutations in *mprF*. However, some clinical isolates of *S. aureus* acquired daptomycin resistance through *mprF*-unrelated changes (13,14). Therefore, while *S. agalactiae* does not harbor *mprF*, when daptomycin is used frequently in the future, daptomycin non-susceptible clinical GBS isolates can be expected to appear more regularly. We have previously reported that the MIC range, MIC₅₀, and MIC₉₀ of daptomycin are 0.25–1 µg/mL, 0.5 µg/mL, and 1 µg/mL, respectively, for 74 PRGBS, and 0.25–2 µg/mL, 1 µg/mL, and 1 µg/
mL, respectively, for 80 penicillin-susceptible GBS (9). As the antibacterial activity of daptomycin may be inhibited by pulmonary surfactants, and it does not permeate the blood–cerebrospinal fluid barrier well, daptomycin is not an optimal drug for the treatment of pneumonia and meningitis. Given that daptomycin non-susceptible clinical GBS isolates were not detected in this study, daptomycin may be a new treatment option for GBS infections, especially multidrug-resistant PRGBS infections.

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Conflict of interest None to declare.

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