INPLASY

INPLASY2023120069

doi: 10.37766/inplasy2023.12.0069

Received: 18 December 2023

Published: 18 December 2023

Diagnostic Value of BHI-V4 for Heterogeneous and Vancomycin-Intermediate Staphylococcus aureus Isolates

Cheng, X[1]; Zhou, JT[2]; Yuan, F[3]; Ma, JX[4]; Guo, SL[5]; Su, JR[6].

Corresponding author:
Jianrong Su

youyi_lab@163.com

Author Affiliation:
Clinical Laboratory Center, Beijing Friendship Hospital, Capital Medical University.

ADMINISTRATIVE INFORMATION

Support - National Key R&D Program of China (2021YFC2301004).

Review Stage at time of this submission - Completed but not published.

Conflicts of interest - None declared.

INPLASY registration number: INPLASY2023120069

Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 18 December 2023 and was last updated on 18 December 2023.

INTRODUCTION

Review question / Objective P: Heterogeneous and vancomycin-intermediate Staphylococcus aureus Isolates(hVISA/VISA); I: Brain-heart infusion agar supplemented with 4 μg/mL of vancomycin (BHI-V4) ; C: Population analysis profiling with area under the curve (PAP-AUC);O: Accuracy of dignosis about BHI-V4 (sensitivity, specificity, etc.) for hVISA/VISA;S: Systematic review and meta-analysis.

Rationale The "gold standard" for hVISA/ VISA detection is population analysis profiling with area under the curve (PAP-AUC). However, this method is time-consuming and labor-intensive, making it unsuitable for routine clinical use.
The routine screening for hVISA/VISA is mainly conducted through phenotypic analysis using BHIA with different glycopeptides. Numerous studies made extensive use of BHI-V4 due to its affordability and ease of use. However, the diagnostic value of this screening plate remains unclear. To the best of our knowledge, there is few meta-analysis available regarding the screening methods for hVISA/VISA in English journals. As a result, it becomes necessary to summarize the reported findings, assess the available data, and attempt to identify research gaps that need to be filled.

Condition being studied Staphylococcus aureus presents a significant threat to human health as it capable of causing a wide range spectrum of infections from minor skin conditions to life-threatening diseases, particularly in healthcare settings. According to a survey conducted in 2019, Staphylococcus aureus ranked first in global mortality rates among 33 bacterial pathogens. This bacterium has developed resistance to multiple antibiotics, making it difficult to treat and increasing the risk of severe and prolonged infections. Initially, vancomycin was considered the last resort for treating multidrug-resistant Staphylococcus aureus (MRSA). However, the subsequent discovery of hVISA/VISA has posed

new challenges in the clinical treatment of these pathogens. Studies have shown that VISA/hVISA was associated with persistent infection, treatment failure, and prolonged hospital stays.

VISA/hVISA and vancomycin-resistant Staphylococcus aureus (VRSA) are collectively known as vancomycin-insensitive Staphylococcus aureus. In clinical practice, VRSA is rare, while VISA/hVISA is more commonly encountered. However, the main challenge for VISA/hVISA lies in its identification. hVISA consists of subpopulations with a frequency of 10-4-10-6, exhibiting varying levels of vancomycin-intermediate resistance. Standard antimicrobial susceptibility testing methods, such as the broth microdilution method (BMD) and agar dilution method (AD), utilize a two-fold dilution system, which may mistakenly classify hVISA as vancomycin-sensitive Staphylococcus aureus (VSSA). In addition, the disk diffusion method is not recommended by CLSI as a screening method for vancomycin resistance due to the slow diffusion of vancomycin in the culture medium. Different methods commonly used for detecting the minimum inhibitory concentration (MIC) of vancomycin also show variations.

METHODS

Search strategy Relevant studies on VISA and hVISA published from inception to October 2023 were searched in PubMed, Cochrane Library using the following keywords: 'vancomycin-intermediate Staphylococcus aureus'; 'VISA'; 'heterogeneous vancomycin-intermediate Staphylococcus aureus'; 'hVISA'; 'Staphylococcus aureus with reduced susceptibilities to vancomycin'; 'VNSA'; 'glycopeptide-intermediate Staphylococcus aureus'; 'GISA'; 'heterogeneous glycopeptide-intermediate Staphylococcus aureus'; 'hGISA'. Figure 1 performs the search strategy outlined following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. The systematic search conducted was not restricted to any specific study or publication type to ensure a thorough evaluation of the literature. Relevant studies on VISA and hVISA published from inception to October 2023 were searched in PubMed, Cochrane Library.

Participant or population Heterogeneous and vancomycin-intermediate Staphylococcus aureus Isolates(hVISA/VISA).

Intervention Brain-heart infusion agar supplemented with 4 μg/mL of vancomycin (BHI-V4).

Comparator Population analysis profiling with area under the curve (PAP-AUC).

Study designs to be included The primary study design is a systematic review, which involves a comprehensive and structured analysis of existing research literature on the topic. Additionally, a meta-analysis is incorporated, enabling the quantitative synthesis of data from multiple studies to provide a more robust and statistically supported assessment of the BHI-V4' effectiveness.

Eligibility criteria Original studies that met the following criteria were included: (1) all experiments including BHI-V4 screening (The standard inoculum concentration and volume are 0.5McFarland and 10ul, respectively); (2) published papers; (3) reference method was PAP-AUC; (4) The indicators of true positive (TP), false positive (FP), false negative (FN), and true negative (TN) needed for the combined effect value could be derived directly or indirectly using the original study's data.Exclusion criteria included: (1) review, brief report, case report, letter, comment, or conference paper; (2) duplicate publications; (3) unable to retrieve full text; (4) non-English publications; (5) unable to obtain the TP, FP, FN, TN, and other data directly or indirectly, or the data is incorrect; (6) without PAP-AUC.

Information sources PubMed and Cochrane Library.

Main outcome(s) Accuracy of dignosis about BHI-V4 (sensitivity, specificity, etc.) for hVISA/VISAdiagnosis of hVISA/VISA.

Quality assessment / Risk of bias analysis Two reviewers (X.C and J.Z.) conducted a quality assessment for each study using the QUADAS-2 tool, which is a method for evaluating the quality of diagnostic studies. Review Manager 5.4 was utilized for data visualization in the quality assessment.

Strategy of data synthesis STATA17.0 (MP) was utilized for statistical analysis. The effect sizes of diagnostic accuracy were pooled, which included sensitivity, specificity, diagnostic odds ratio (DOR), negative likelihood ratio, and positive likelihood ratio with their associated 95% confidence intervals (95%CIs). The summary receiver operating characteristic (SROC) curves were employed to compute the AUC of the integrated model. The threshold heterogeneity of the included studies was assessed using Spearman's correlation coefficient, and non-threshold

heterogeneity was assessed using Cochran's Q and I2 values. A random effects model was employed to integrate the data if the I2 value was greater than 50% or P<0.05 which indicated significant heterogeneity. When the I2 value was 50% or P≥0.05, a fixed effect model was chosen. Deek's funnel plot was used to examine the publication bias of the included studies. A P<0.05 was deemed statistically significant.

Subgroup analysis None.

Sensitivity analysis All calculations were conducted with a 95% confidence level, employing a continuity correction of 0.5 when applicable.

Country(ies) involved China.

Keywords hVISA;VISA; BHI-V4; Diagnostic value; Systematic review; Meta-analysis.

Contributions of each author

Author 1 - Xin Cheng.
Email: 15735537628@163.com
Author 2 - Juntong Zhou.
Email: z_juntong@163.com
Author 3 - Fan Yuan.
Email: yuanfferic@163.com
Author 4 - Jingxin Ma.
Email: majingxin225@163.com
Author 5 - Shuilong Guo.
Email: youyi_friendship@163.com
Author 6 - Jianrong Su.
Email: youyi_lab@163.com