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Staphylococcus aureus strains sustain their high-virulent phenotype during native endocarditis

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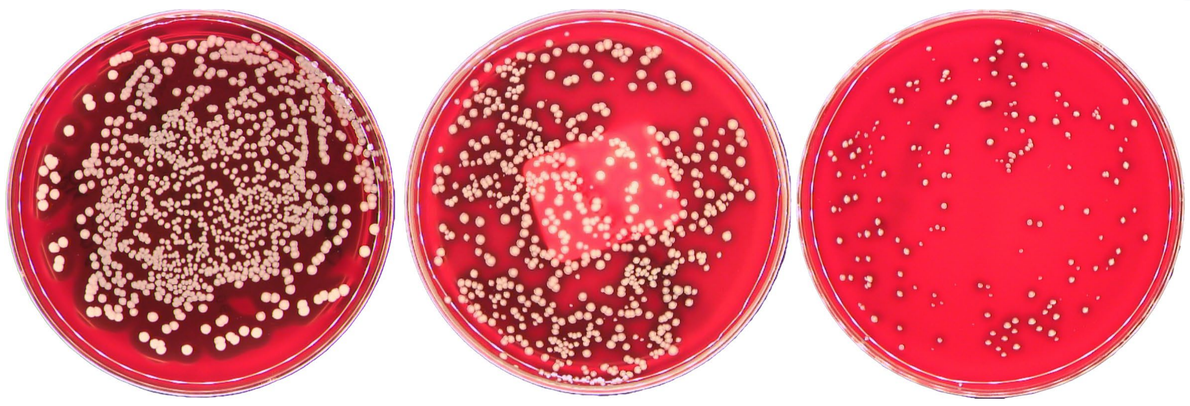
BACKGROUND

Staphylococcus aureus endocarditis is a severe infection associated with the rapid destruction of heart valves and tissue. Although the processes of adaptation in bone and joint infections that lead to the formation of small colony variants (SCVs) are well documented, data on adaptation in endocarditis remains limited. Our study aimed to analyse the virulence and adaptation of *S. aureus* isolates from heart valves, compared to primary blood culture isolates, in patients with endocarditis.

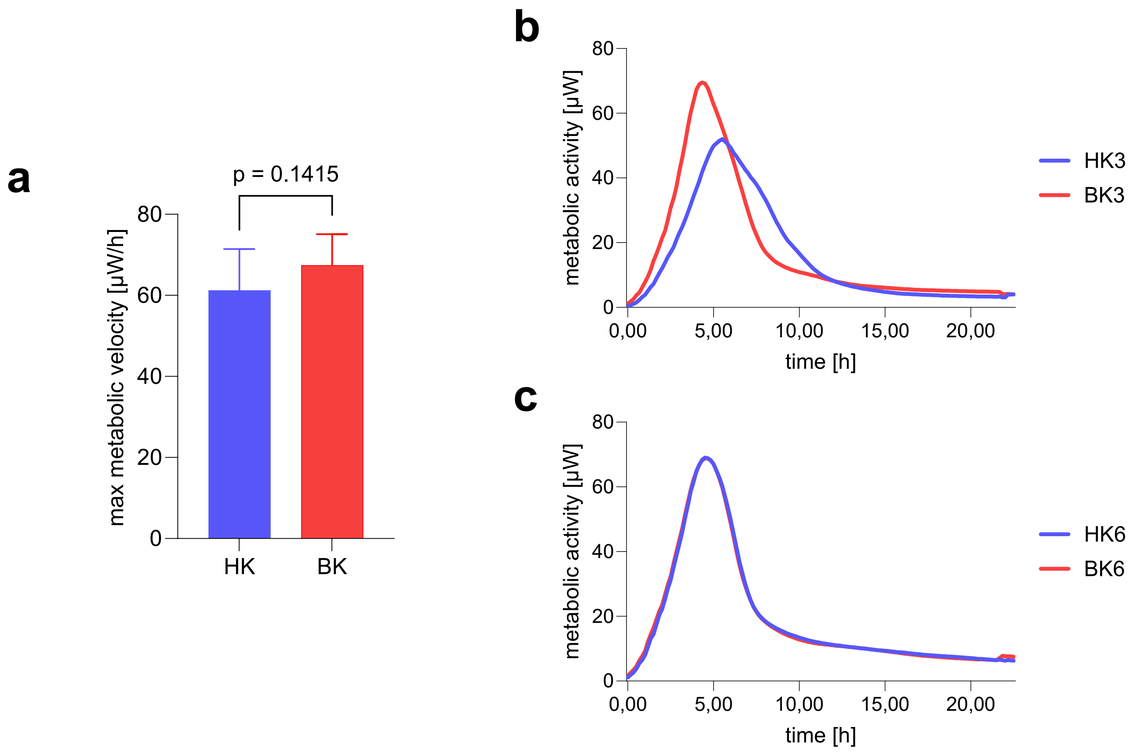
METHODS

We collected pairs of *S. aureus* strains obtained from valve tissue and blood cultures from ten patients undergoing valve surgery. We analysed these strain pairs extensively using molecular and phenotypic methods to measure endothelial cell invasion, cytotoxicity, biofilm production and metabolic activity, in order to detect early bacterial adaptation during the endocarditis infection process. Additionally, we screened the phenotypes of 15 *S. aureus* isolates that were plated directly from heart valve specimens, in order to determine the abundance of SCVs, and we compared these results with those obtained from samples of deep-seated tissue infections and bloodstream infections.

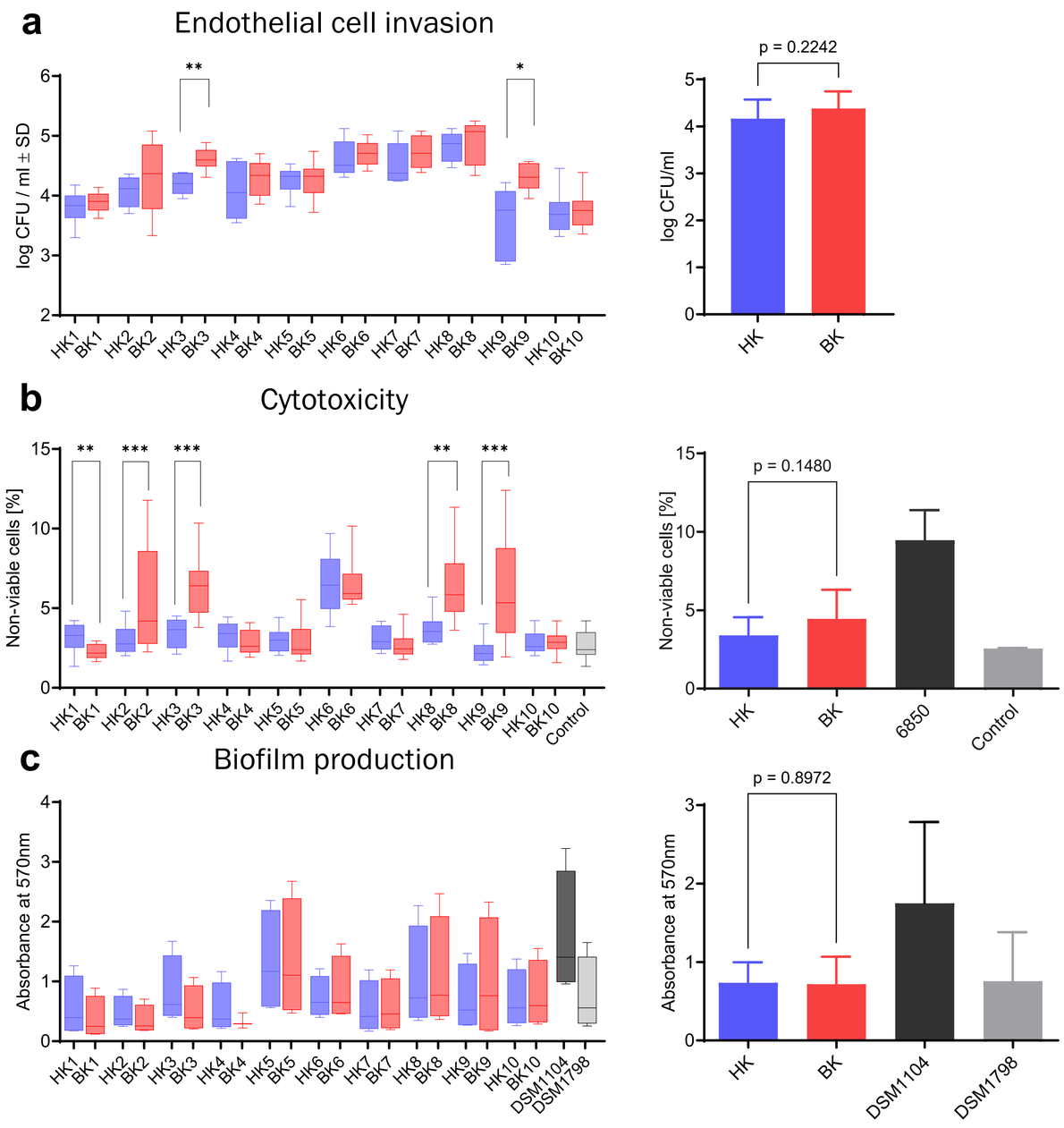
RESULTS



No SCVs could be found in the bacteraemia samples (left), whereas the samples from deep-seated tissue infections (right) showed an abundance of SCVs (median 19.2%, IQR 14.8–28.6%). Valve samples (middle) had a significantly lower prevalence of SCV (median 6.8%, IQR 0.0–10.5%; p < 0.0001, Mann–Whitney U test). All identified SCVs were unstable and reverted to the wild type after one subculture.



Maximum metabolic activity, as measured by biocalorimetry, did not differ significantly between *S. aureus* strains isolated from heart valves (HK) and blood culture (BK) (a). Only one strain pair, isolated from patient 3 who had a cardiac device-associated endocarditis, showed a reduced metabolic activity in the valve isolate (b). Nine out of ten pairs displayed no difference at all, as illustrated by the example of patient 6 (c).



Phenotypic characterisation of the 10 endocarditis strain pairs showed no significant differences in grouped analysis of cell invasion (a) and cytotoxicity (b) using EA.hy926 cells, as well as biofilm production (c). The valve isolate from patient 3, which showed reduced metabolic activity, also showed lower cytotoxicity and endothelial cell invasion capacity than its counterpart isolated from the bloodstream.

Whole-genome sequencing revealed no significant differences in virulence genes between the two strains isolated from different sample sites of the same patient, confirming that the strains identified in *S. aureus* endocarditis in blood and valve cultures are genetically identical.

CONCLUSION

S. aureus mostly remains in a highly virulent state when infecting heart valves, which may explain the severe tissue destruction usually observed in acute endocarditis. Constant exposure to the hostile blood environment, with its strong vascular immune defenses during endocarditis, may inhibit bacterial adaptation processes and keep the bacteria in a metabolically active and antibiotic-susceptible state. Foreign material like cardiac devices and long-term persistence, as seen in bone infections, may promote bacterial adaptation.

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