

Identification of risk factors for long-term persistence of linezolid resistant enterococci – experiences from a tertiary care centre

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Introduction

Linezolid-resistant enterococci (LRE) have raised concern worldwide due to their increased detection in healthcare settings. Infections are often preceded by colonisations and intensified infection prevention and control strategies are established to minimize spreading. As specific eradication strategies are lacking, these precautions are often continued until spontaneous clearance occurs. However, LRE may persist over long periods of time. Here, we aim at identifying factors determining a prolonged colonisation.

Methods

Patients that were admitted on an intensive care unit, oncological or infectious disease ward at a tertiary care hospital were screened for LRE via rectal swab during a one year study period. Patients colonized for more than ten weeks were defined as long-term carriers. LRE-isolates were subjected to whole genome sequencing and compared using a core genome Multilocus Sequencing Typing (cgMLST) approach. Demographic and clinical risk factors of admitted patients were recorded.

Results

In the study period, 77 patients colonized with LRE (59 LR *E. faecium*, 18 LR *E. faecalis*) were identified. Of these, 30 (39%) were female. The median age was 65 years (range 23-90 years). For 46 patients, follow-up samples were available to determine LRE persistence (colonisation >10 weeks) or clearance (colonisation <10 weeks). Of all patients, 7 (15%) were LRE long-term carriers whereas spontaneous LRE clearance was observed in 39 patients (85%). Multivariate analysis of risk factors in the LRE persistence vs. LRE clearance group exhibit that duration of hospitalization was the only factor significantly increased in LRE-persistent patients (p=0.02). Other clinical or demographic factors did not differ significantly between both groups. Assessment of genetic relatedness of detected LRE revealed 12 clusters comprising 1-12 genotypes of LR *E. faecium* and 4 clusters comprising 2 genotypes of LR *E. faecalis*.

Table 1: Linezolid resistance mechanisms detected in *E. faecium* (Efm; n=42) and *E. faecalis* (Efs; n=11) isolates, University Hospital Würzburg, 2020.

Characteristic	LRE-persistence	LRE-clearance	p-value*
Sex (male)	5 (71%)	23 (59%)	0.33
Age [years]	58 (32-77)	62 (23-83)	0.78
Haemato-oncological disease	3 (43%)	21 (54%)	0.07
Immunodeficiency	5 (71%)	31 (79%)	0.53
Antibiotic treatment	6 (86%)	29 (74%)	0.31
Liver dysfunction	3 (43%)	7 (18%)	0.18
Kidney dysfunction	5 (71%)	16 (41%)	0.20
Admission from another hospital	1 (14%)	8 (21%)	0.30
Hospitalization on an ICU	2 (28%)	15 (38%)	0.13
Duration of hospitalization [days]	110 (28-225)	53 (5-213)	0.02

* multivariate analysis

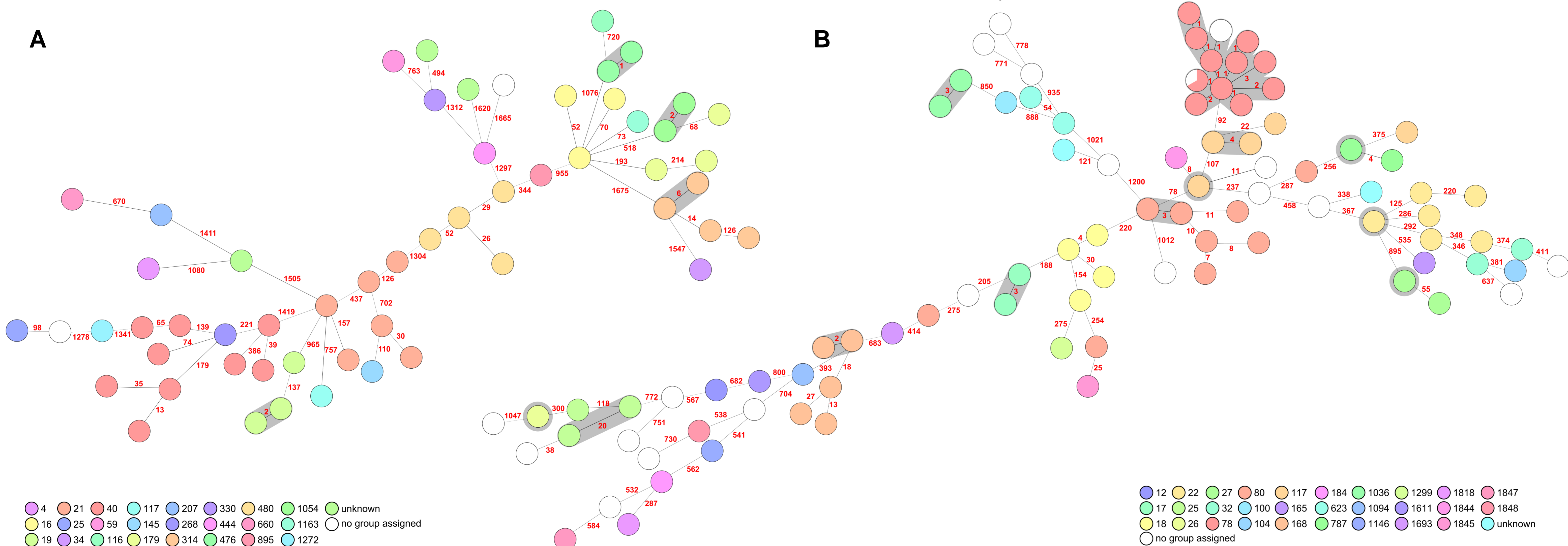


Figure 1: Minimum spanning tree of LRE isolates. (A) cgMLST of LR *E. faecalis* isolates show 4 clusters (grey) comprising 2 genotypes. (B) cgMLST of LR *E. faecium* isolates revealed 12 clusters (grey) comprising 1-12 genotypes. Red numbers indicate allelic differences. Colored dots illustrate different MLST sequence types.

Summary

First results of our study suggest that persistence of LRE colonisation is potentially overestimated. Long-term-colonisation is favoured by patient associated risk factors, whereby duration of hospitalization plays a relevant role. Genetically, the LRE isolates of this study show a high diversity, revealing that LRE are rather acquired due to antibiotic treatment than by pathogen transmission.