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Factors associated with vanA-positive vancomycin-susceptible Enterococcus faecium among patients with E. faecium bacteraemia

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Background: Vancomycin-variable enterococci (VVE) (i.e. vanA-positive enterococci susceptible to vancomycin) have been reported from Canada, the US, and Norway. Previous data show that they have the ability to revert into vancomycin-resistant enterococci (VRE) upon vancomycin exposure. However, the prevalence of VVE is unclear and clinical experience is limited.

Methods: We prospectively collected *Enterococcus faecium* blood isolates from patients hospitalized within the Toronto Invasive Bacterial Diseases Network (TIBDN) from 01/2015 to 06/2016. All isolates underwent PCR-testing for vanA/vanB. VVE and VRE isolates from 01/2012 to 12/2014 were retrospectively included. Chart reviews were performed on all VRE and VVE patients (first episodes) as well as on a random sample of patients with vanA/vanB-negative, vancomycin-susceptible enterococci (VSE). Variables associated with 30-day mortality in univariable logistic regression (p-value≤0.1) were entered into multivariable analysis (stepwise selection).

Results: Among vanA-positive isolates, 28/68 (41%) were VVE. We reviewed the charts of 25 VVE, 36 VRE and 79 VSE patients (Figure). Risk factors including comorbidities were similar across the three groups. VRE and VVE patients were more likely to have a catheter-related blood stream

infection (BSI) as source of bacteremia (56% and 44% vs 28% in VSE patients, p=0.01), whereas intra-abdominal infections were more common in VSE patients (51% vs 28% and 20% in VRE and VSE patients respectively, p=0.006). Pitt bacteremia score (OR 2.7), Charlson score (OR 1.3), and surgery/intervention to control the infection (OR 0.2) were independent predictors of 30-day mortality (Table). Among VVE patients, 17/25 (68%) received linezolid, daptomycin or tigecycline. 30-day mortality was non-significantly lower in this group (6/17, 35%) compared to those receiving vancomycin (5/8, 63%) (p=0.39). One VVE patient developed VRE bacteremia while on vancomycin.

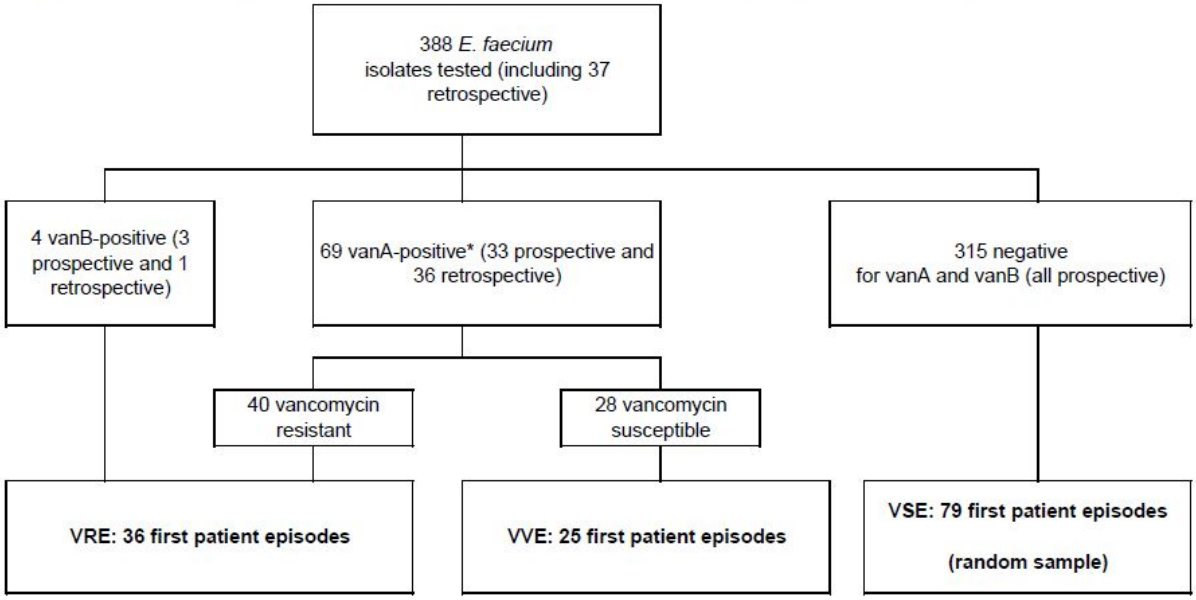
Conclusions: In this cohort, a considerable proportion of vanA-positive isolates were VVE. Although risk profiles were similar across patient groups, VRE and VVE patients more often presented with catheter-related BSI compared to VSE patients. 30-day mortality was influenced by underlying comorbidities, severity of illness and surgery/procedure to control the infection, but not by resistance status. Further studies have to evaluate the impact of type of antibiotic treatment on the outcome of VVE patients.

Table. Univariable and multivariable logistic regression analysis to assess 30-day mortality among patients with *E. faecium* bacteremia.

	Univariable		Multivariable	
	OR (95% CI)	**P-value**	**OR (95% CI)**	**P-value**
Resistance type				
VSE	Reference		non-significant	
VVE	1.9 (0.8-4.8)	0.08		
VRE	0.7 (0.3-1.8)	0.14		
Male	1.8 (0.8-3.8)	0.14		
Age	1.01 (0.99-1.03)	0.51		
Charlson score	1.2 (1.1-1.4)	**0.006**	1.3 (1.1-1.5)	**0.003**
Pitt bacteremia score	1.3 (1.1-1.5)	**0.002**	2.7 (1.2-6.2)	**0.02**
Bacteremia source				
Other	Reference			
Catheter-related BSI	0.6 (0.2-1.5)	0.15		
Intraabdominal	1.1 (0.4-2.7)	0.36		
Surgery/procedure	0.2 (0.0-1.4)	0.10	0.2 (0.0-0.8)	**0.03**
Polymicrobial infection	0.9 (0.4-2.0)	0.88		
Hours to effective therapy[1], /hour	1.00 (0.99-1.01)	0.72		

[1]Vancomycin considered effective against VVE

Figure. Flowsheet of prospectively (01/2015 to 06/2016) and retrospectively (01/2012 to 12/2014) collected *E. faecium* blood isolates



* Resistance test not available for 1 isolate