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Epidemiology, clinical characteristics, and outcome of infective endocarditis due to *Abiotrophia* and *Granulicatella* in a Tertiary Hospital in China, 2015–2023: a retrospective study

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Abstract

Background Abiotrophia (ABI) and *Granulicatella* (GRA) are rare causative pathogens in infective endocarditis (IE). This study aims to describe the epidemiology, clinical characteristics, and outcome of ABI/GRA-IE. The main features of ABI/GRA-IE were compared with Viridans group streptococci (VGS) IE.

Methods From January 2015 to December 2023, a total of 1531 definite IE in Zhongshan Hospital, Fudan University, Shanghai, China were retrospectively enrolled in this study. Clinical and laboratory data were collected.

Results Forty-five ABI/GRA-IE cases were identified, representing 2.9% of all IE cases in Zhongshan Hospital between 2015 and 2023, compared to 20.1% of VGS-IE. ABI and GRA IE shared similar clinical characteristics. Congenital valvulopathy was reported in 21 (46.7%) ABI/GRA-IE and 85 (28.8%) VGS-IE ($P=0.025$). Pulmonary valve was more frequently affected in ABI/GRA-IE (6 [13.3%]) than VGS-IE (7 [2.4%]) ($P=0.002$). Congestive heart failure was observed in 30 (66.7%) ABI/GRA-IE and 103 (34.9%) VGS-IE ($P<0.001$). Systemic embolization excluding central nervous system (CNS) occurred in 13 (28.9%) ABI/GRA-IE and 39 (13.2%) VGS-IE ($P=0.012$). In-hospital mortality was reported as 4.4% in ABI/GRA-IE and 3.7% in VGS-IE ($P=0.854$).

Conclusion GRA/ABI-IE was approximately one-seventh as prevalent as VGS-IE. Congestive heart failure and systemic embolization (excluding CNS) were more frequent in GRA/ABI-IE compared to VGS-IE. Mortality of ABI/GRA-IE in this study was comparable to that of VGS-IE and lower than previously reported results.

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Keywords *Abiotrophia*, *Granulicatella*, Infective endocarditis, Viridans group streptococci, Nutritionally variant streptococci

Background

Abiotrophia (ABI) and *Granulicatella* (GRA) are fastidious gram-positive cocci previously described as nutritionally variant streptococci (NVS) because they grow as satellite colonies around other microorganisms or in complex media containing sulfhydryl compounds, such as cysteine or pyridoxal hydrochloride. NVS include one *Abiotrophia* species (*Abiotrophia defective*) and three *Granulicatella* species (*Granulicatella adiacens*, *Granulicatella elegans* and *Granulicatella balaenopterae*) [1]. They are part of the normal oral cavity, urogenital, and intestinal flora, and an important cause of bacteremia and infective endocarditis (IE) [2–5].

IE is a life-threatening disease with high mortality [6–8]. IE due to ABI and GRA represents around 1–3% of all IE, typically presenting with a subacute course [2, 9]. However, epidemiology, clinical characteristics, and outcome of ABI/GRA related IE remain poorly studied.

The largest case series of IE due to ABI or GRA for a single institution was reported [2]. In this single center study, periannular complication were more common in ABI/GRA-IE and overall mortality was low. The largest multicenter prospective cohort study of ABI/GRA-IE was recently published and clinical features of ABI/GRA-IE were compared with Viridans group streptococci (VGS) IE [10]. In this study, patients with ABI/GRA-IE were younger, had similar clinical features and rates of surgery and better prognosis than VGS-IE. However, most of the reported cases of ABI/GRA-IE were from Europe, America, or Australia. Data from Asian patients were lacking.

Here, we retrospectively reviewed all the IE cases admitted to Zhongshan Hospital, Fudan University, Shanghai, China from 2015 to 2023 and identified 45 ABI/GRA-IE. Epidemiology, clinical characteristics, and outcome of ABI/GRA-IE were described and compared with those of VGS-IE.

Methods

Patients

We retrospectively searched the electronic medical history retrieval system in Zhongshan Hospital, Fudan University, Shanghai, from January 2015 to December 2023, using the term "infective endocarditis". Zhongshan Hospital is a 3000-bed, tertiary-level university hospital and a cardiac surgery center in China.

The diagnosis of IE was made according to the modified Duke criteria [11]. Only definite IE cases were included in this study. All the patients admitted to Zhongshan Hospital were asked on admission whether they agreed to sign the informed consent of biological sample donation and agreed that the donated samples and related information could be used for all medical research. Only patients who had signed the informed consent of biological sample donation were included in this study. The exclusion criteria in this study were patients whose demographic information, clinical presentations, etiological tests, laboratory and echocardiography examinations, complications, treatments, and outcomes were incompletely recorded, not including etiologically unknown IE. As for the etiologically unknown IEs in this study, etiological tests such as blood culture or valve culture were conducted and turned negative, and culture results were precisely recorded in the medical history. A total of 1591 definite IE patients were screened, including 60 patients with incomplete medical history records and 1531 enrolled in this study. Demographic information, medical history, clinical presentations, laboratory and echocardiography examinations, complications, treatments, and outcomes were documented.

Definition

Patients were identified with congestive heart failure if at least one of the following conditions were met: (1) N-terminal pro-B type natriuretic peptide (NT-proBNP) on admission higher than 1500 pg/mL; (2) cardiac function of III or IV class evaluated with New York Heart Association (NYHA) classification; (3) echocardiogram on admission identifying reduced cardiac activity. Duration of symptoms referred to the period from onset until admission. Follow-up time referred to the period from admission until the last follow-up. Cumulative mortality included the period from admission until the last follow-up.

Culture

Blood samples (8–10 mL) of IE patients were injected into aerobic, anaerobic, and fungal blood culture bottles [BD BACTECTM, Becton, Dickinson, and Co. (BD), Franklin Lakes, NJ, USA] and then loaded into an automated continuous monitoring system (BD BACTECTM, BD) for 7 days. For the patients who received cardiac surgery, valve homogenates after surgery were cultured onto blood agar plates, chocolate agar plates, and fungal chromogenic plates for 14 days. If the culture showed growth of microbes, strain identification was conducted by VITEK MALDI-TOF mass spectrometry (bioMérieux, Craponne, France).

In vitro susceptibility assays

The minimal inhibitory concentrations (MICs) of penicillin were determined by the epsilometer test (E-test). The Kirby-Bauer disc diffusion method was used to determine in vitro susceptibility of clindamycin, linezolid, cefepime, ceftriaxone, levofloxacin, vancomycin, and erythromycin.

Statistical analysis

For continuous variables, data were expressed as median (interquartile range, IQR) if they followed a non-normal distribution and comparative analysis between the two groups was conducted by the Mann-Whitney *U* test. For discrete variables, comparative analysis between the two groups was conducted by the Chi-square test. Data analysis was performed with the statistical software SPSS version 21.0 (IBM Corp., Armonk, NY, USA). All tests were two-tailed, and statistical significance was considered at $P<0.05$.

Results

Cases identified

From January 2015 to December 2023, a total of 1591 definite IE patients were admitted to Zhongshan Hospital, Fudan University, Shanghai, China, including 60 patients with incomplete medical history records. Among the remaining 1531 IE cases, 307 (20.1%) were caused by VGS, 45 (2.9%) by ABI/GRA, 534 (34.9%) by other pathogens, and 645 (42.1%) by unknown pathogens, as shown in Fig. 1. Among the 307 VGS-IE cases, 12 patients lost follow-up. Clinical and laboratory data of the remaining 295 VGS-IE cases were used in the final analysis. Among the 45 ABI/GRA-IE cases, no patient lost follow-up. Nineteen (1.2%) cases were due to ABI and 26 (1.7%) cases were due to GRA.

Abiotrophia and Granulicatella infective endocarditis

The demographic characteristics, baseline comorbidities, underlying cardiopathy, clinical and echocardiographic findings, complications, and outcomes of ABI and GRA IE were summarized in Table 1. As the characteristics mentioned above and outcomes were similar between ABI and GRA IE, they were analyzed together

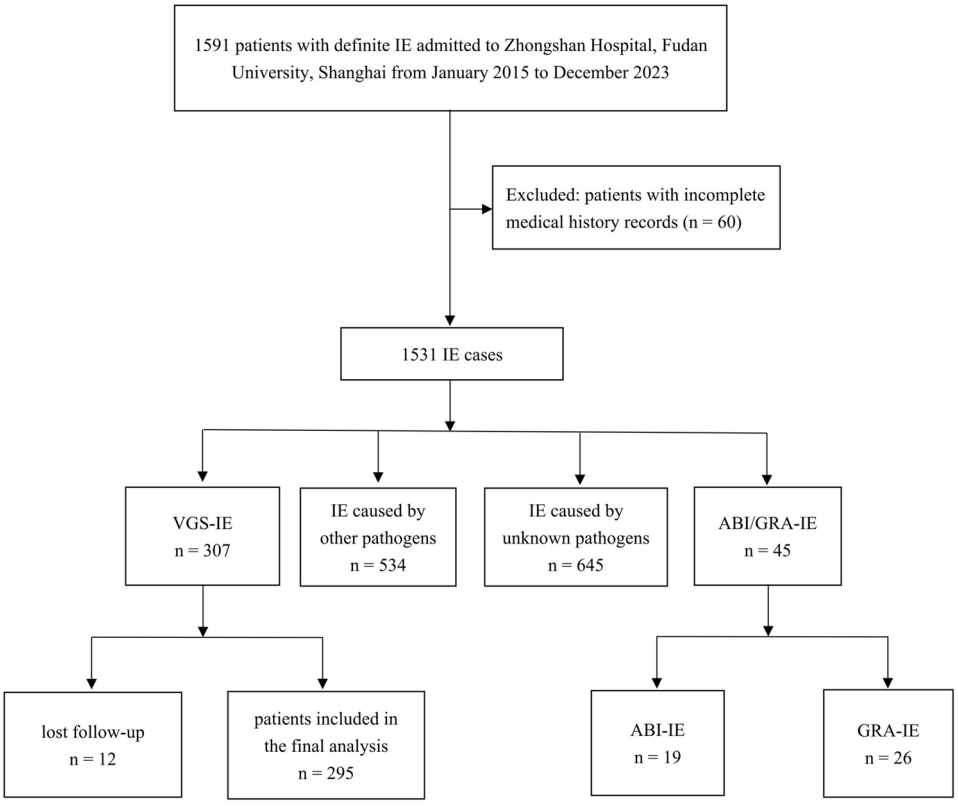

Fig. 1 Flowchart of patient inclusion. A total of 1591 definite IE patients were screened from January 2015 to December 2023 in Zhongshan Hospital, Fudan University, Shanghai, China. Sixty patients with incomplete medical history records were excluded. Among the remaining 1531 IE cases, 307 (20.1%) were caused by VGS, 45 (2.9%) by ABI/GRA, 534 (34.9%) by other pathogens, and 645 (42.1%) by unknown pathogens. Among the 45 ABI/GRA-IE cases, 19 (1.2%) were due to ABI and 26 (1.7%) were due to GRA *Abbreviations* ABI, *Abiotrophia*; GRA, *Granulicatella*; IE, infective endocarditis; VGS, Viridans group streptococci

Table 1 Comparative characteristics of *Abiotrophia* and *Granulicatella* Infective Endocarditis cases

Characteristics	Abiotrophia spp (*n* = 19)	Granulicatella spp[a] (*n* = 26)	*P* Value
Demographic			
Age, y, median (IQR)	51 (41, 59.5)	45.5 (40, 58.8)	0.573
Sex, male	13 (68.4%)	21 (80.8%)	0.548
Place of Acquisition:			
Community	19 (100.0%)	26 (100.0%)	N/A
Nosocomial	0 (0.0%)	0 (0.0%)	
Type of IE			
NVE	18 (94.7%)	24 (92.3%)	0.778
PVE	1 (5.3%)	2 (7.7%)	
CIED	0 (0.0%)	0 (0.0%)	
Underlying condition			
Diabetes mellitus	0 (0.0%)	5 (19.2%)	0.122
Hypertension	4 (21.1%)	6 (23.1%)	0.840
Other	6 (31.6%)[b]	2 (7.7%)[c]	0.094
Underlying cardiopathy			
Previous IE	0 (0.0%)	0 (0.0%)	N/A
Congenital valvulopathy	7 (36.8%)	14 (53.8%)	0.408
Previous cardiac surgery	1 (5.3%)	2 (7.7%)	0.778
Mitral prolapse	2 (10.5%)	0 (0.0%)	0.337
Rheumatic valvulopathy	2 (10.5%)	1 (3.8%)	0.778
Hypertrophic cardiomyopathy	1 (5.3%)	1 (3.8%)	0.614
Medical history			
History of trauma or invasive dental procedures	1 (5.3%)	1 (3.8%)	0.614
Injection drug use	0 (0.0%)	0 (0.0%)	N/A
Clinical presentation			
Duration of symptoms[d], d, median (IQR)	30 (14.5, 60)	60 (30, 97.5)	0.098
Fever	13 (68.4%)	16 (61.5%)	0.872
Splenomegaly	7 (36.8%)	7 (26.9%)	0.701
Chest tightness	15 (78.9%)	17 (65.4%)	0.510
Valves affected			
Mitral	12 (63.2%)	18 (69.2%)	0.915
Aortic	10 (52.6%)	15 (57.7%)	0.973
Tricuspid	2 (10.5%)	2 (7.7%)	0.841
Pulmonary	2 (10.5%)	4 (15.4%)	0.976
Complications			
Paravalvular Complications			
Perforation	7 (36.8%)	12 (46.2%)	0.750
Abscess	2 (10.5%)	5 (19.2%)	0.704
Prosthetic paravalvular dehiscence	0 (0.0%)	0 (0.0%)	N/A
Congestive heart failure	14 (73.7%)	16 (61.5%)	0.594
CNS involvement	8 (42.1%)	6 (23.1%)	0.300
Systemic emboli (excluding CNS)	4 (21.1%)	9 (34.6%)	0.510
Outcomes			
Follow-up time[e], d, median (IQR)	360 (110, 1066)	360 (180, 1370)	0.572
In-hospital cardiac surgery	16 (84.2%)	26 (100.0%)	0.136

Table 1 (continued)

Characteristics	Abiotrophia spp (*n* = 19)	Granulicatella spp[a] (*n* = 26)	*P* Value
In-hospital death	1 (5.3%)	1 (3.8%)	0.614
Cumulative mortality[f]	1 (5.3%)	1 (3.8%)	0.614

Data are presented as No. (%) of patients

Abbreviations: CIED, cardiovascular implantable electronic device; CNS, central nervous system; IE, infective endocarditis; IQR, interquartile range; N/A, not available; NVE, native valve endocarditis; PVE, prosthetic valve endocarditis

[a]Twenty-two *Granulicatella adiacens* and 4 *Granulicatella elegans*

[b]Two patients with malignant tumor, 1 with hepatitis B virus infection, 1 with renal insufficiency, and 2 under immunosuppressive therapy

[c]Two with hepatitis B virus infection

[d]From onset until admission

[e]From admission until the last follow-up

[f]From admission until the last follow-up

and compared with VGS-IE. The detailed clinical and microbiological characteristics of ABI/GRA-IE patients are provided in Additional file 1. Detailed complications, treatment, and outcome of ABI/GRA-IE cases are provided in Additional file 2.

Demographic features, type of infective endocarditis, comorbidities and underlying cardiopathy

Table 2 summarized the demographic characteristics, baseline comorbidities, underlying cardiopathy, clinical and echocardiographic findings, complications, and outcomes of ABI/GRA-IE and VGS-IE. The median age in the ABI/GRA-IE was 48 years (IQR, 40, 59) and 51 (IQR, 37.5, 60) in the VGS-IE group ($P=0.832$). Most of the cases were male in both groups, 34 (75.6%) in ABI/GRA-IE and 220 (74.6%) in VGS-IE ($P=0.965$). All the cases were community acquired in both groups. Most of the cases were native valve endocarditis (NVE) in both groups, 42 (93.3%) in ABI/GRA-IE and 274 (92.9%) in VGS-IE ($P=0.839$). Baseline comorbidities including diabetes mellitus, hypertension, malignant tumor, hepatitis B virus infection, renal insufficiency, and immunosuppression were similar in both groups. Congenital valvulopathy was more frequent among ABI/GRA-IE (21 [46.7%]) than VGS-IE (85 [28.8%]) ($P=0.025$).

Clinical presentation and echocardiographic findings

Fever was less frequent among ABI/GRA-IE (29 [64.4%]) than VGS-IE (233 [79.0%]) ($P=0.048$). Splenomegaly was more frequent among ABI/GRA-IE (14 [31.1%]) than VGS-IE (37 [12.5%]) ($P=0.002$). More chest tightness was presented in ABI/GRA-IE (32 [71.1%]) than VGS-IE (142 [48.1%]) ($P=0.007$). Pulmonary valve was more frequently affected in ABI/GRA-IE (6 [13.3%]) than VGS-IE (7 [2.4%]) ($P=0.002$).

In vitro susceptibility and antimicrobial therapy

In vitro susceptibility results were available in 12 ABI-IE and 12 GRA-IE (9 *G. adiacens* and 3 *G. elegans*) cases (1 strain in each case), as summarized in Tables 3 and Fig. 2. Eight (66.7%) ABI strains and 9 (75.0%) GRA strains were sensitive to penicillin. All the 24 ABI/GRA strains were susceptible to vancomycin and linezolid. The antimicrobial susceptibility information of the other 21 ABI/GRA-IE cases was lost during data migration, as the electronic medical history retrieval system in Zhongshan Hospital had several updates and even replacements from 2015 to 2023.

Vancomycin as monotherapy were used in 21 ABI/GRA-IE cases. Twenty ABI/GRA-IE patients were treated with combination antimicrobial therapy (β-lactam plus quinolone, β-lactam plus aminoglycoside, vancomycin plus β-lactam, or other antibiotics).

Complications

Paravalvular complications including perforation, abscess and prosthetic paravalvular dehiscence were similar between ABI/GRA-IE and VGS-IE, as shown in Table 2. More congestive heart failure was observed in patients with ABI/GRA-IE (30 [66.7%]) than VGS-IE (103 [34.9%]) ($P<0.001$). Central nervous system (CNS) involvement was comparable in both groups while systemic embolization (excluding CNS) was more frequent among ABI/GRA-IE (13 [28.9%]) than VGS-IE (39 [13.2%]) ($P=0.012$).

Outcome

Follow-up time was longer in the ABI/GRA-IE group. The median follow-up time in ABI/GRA-IE was 360 days (IQR, 157.5, 1297.5) and 270 days (IQR, 90, 670) in VGS-IE ($P=0.020$). Forty-two (93.3%) patients with ABI/GRA-IE and 270 (91.5%) patients with VGS-IE received cardiac surgery during hospitalization ($P=0.905$). In-hospital death was reported as 4.4% in ABI/GRA-IE and 3.7% in VGS-IE ($P=0.854$). Cumulative mortality was 4.4% in ABI/GRA-IE and 4.1% in VGS-IE ($P=0.776$).

Table 2 Comparative characteristics of *Abiotrophia* and *Granulicatella*, *and* Viridans Group Streptococci Infective Endocarditis Cases

Characteristics	Viridans group streptococci[a] (*n* = 295)	Abiotrophia and Granulicatella spp (*n* = 45)	*P* Value
Demographic			
Age, y, median (IQR)	51 (37.5, 60)	48 (40, 59)	0.832
Sex, male	220 (74.6%)	34 (75.6%)	0.965
Place of Acquisition:			
Community	295 (100.0%)	45 (100.0%)	N/A
Nosocomial	0 (0.0%)	0 (0.0%)	N/A
Type of IE			
NVE	274 (92.9%)	42 (93.3%)	0.839
PVE	21 (7.1%)	3 (6.7%)	
CIED	0 (0.0%)	0 (0.0%)	
Underlying condition			
Diabetes mellitus	43 (14.6%)	5 (11.1%)	0.695
Hypertension	57 (19.3%)	10 (22.2%)	0.799
Other	23 (7.8%)[b]	8 (17.8%)[c]	0.059
Underlying cardiopathy			
Previous IE	5 (1.7%)	0 (0.0%)	0.830
Congenital valvulopathy	85 (28.8%)	21 (46.7%)	0.025
Previous cardiac surgery	21 (7.1%)	3 (6.7%)	0.840
Mitral prolapse	19 (6.4%)	2 (4.4%)	0.853
Rheumatic valvulopathy	12 (4.1%)	3 (6.7%)	0.688
Hypertrophic cardiomyopathy	2 (0.7%)	2 (4.4%)	0.150
Medical history			
History of trauma or invasive dental procedures	17 (5.8%)	2 (4.4%)	0.992
Injection drug use	0 (0.0%)	0 (0.0%)	N/A
Clinical presentation			
Duration of symptoms[d], d, median (IQR)	60 (30, 90)	45 (20, 90)	0.0713
Fever	233 (79.0%)	29 (64.4%)	0.048
Splenomegaly	37 (12.5%)	14 (31.1%)	0.002
Chest tightness	142 (48.1%)	32 (71.1%)	0.007
Valves affected			
Mitral	179 (60.7%)	30 (66.7%)	0.546
Aortic	146 (49.5%)	25 (55.6%)	0.550
Tricuspid	11 (3.7%)	4 (8.9%)	0.238
Pulmonary	7 (2.4%)	6 (13.3%)	0.002
Complications			
Paravalvular Complications			
Perforation	91 (30.8%)	19 (42.2%)	0.178
Abscess	22 (7.5%)	7 (15.6%)	0.127
Prosthetic paravalvular dehiscence	3 (1.0%)	0 (0.0%)	0.860
Congestive heart failure	103 (34.9%)	30 (66.7%)	< 0.001
CNS involvement	73 (24.7%)	14 (31.1%)	0.467
Systemic emboli (excluding CNS)	39 (13.2%)	13 (28.9%)	0.012
Outcomes			
Follow-up time[e], d, median (IQR)	270 (90, 670)	360 (157.5, 1297.5)	0.020
In-hospital cardiac surgery	270 (91.5%)	42 (93.3%)	0.905

Table 2 (continued)

Characteristics	Viridans group streptococci[a] (*n* = 295)	Abiotrophia and Granulicatella spp (*n* = 45)	*P* Value
In-hospital death	11 (3.7%)	2 (4.4%)	0.854
Cumulative mortality[f]	12 (4.1%)	2 (4.4%)	0.776

Data are presented as No. (%) of patients

Abbreviations: CIED, cardiovascular implantable electronic device; CNS, central nervous system; IE, infective endocarditis; IQR, interquartile range; N/A, not available; NVE, native valve endocarditis; PVE, prosthetic valve endocarditis

[a]The streptococcal isolates were identified at the species level in 252 cases (85.4%): mitis group, 180 isolates (61 *S. oralis*; 50 *S. sanguinis*; 46 *S. gordonii*; 15 *S. mitis*; 6 *S. crista*; 1 *S. parasanguinis*; 1 *S. infantarius*); mutans group, 14 isolates (14 *S. mutans*); anginosus group, 38 isolates (30 *S. anginosus*; 5 *S. intermedius*; 3 *S. constellatus*); salivarius group, 8 isolates (8 *S. salivarius*); bovis group, 12 isolates (12 *S. gallolyticus*)

[b]Ten patients with malignant tumor, 9 with hepatitis B virus infection, 2 with renal insufficiency, and 2 under immunosuppressive therapy

[c]Two patients with malignant tumor, 3 with hepatitis B virus infection, 1 with renal insufficiency, and 2 under immunosuppressive therapy

[d]From onset until admission

[e]From admission until the last follow-up

[f]From admission until the last follow-up

Table 3 In vitro susceptibility results in *Abiotrophia* and *Granulicatella* Infective Endocarditis cases

Genus	Species	Patient Number	Peni	Da	Lzd	Fep	Ctx	Lev	Van	E
Abiotrophia	*Abiotrophia defectiva*	P1	S	S	S	S	S	S	S	R
(*n* = 12)	*A. defectiva*	P2	I	S	S	S	S	S	S	S
	A. defectiva	P3	S	S	S	S	S	S	S	S
	A. defectiva	P8	S	S	S	R	R	S	S	S
	A. defectiva	P9	R	S	S	R	R	S	S	R
	A. defectiva	P11	I	R	S	I	I	S	S	R
	A. defectiva	P12	S	R	S	S	S	S	S	R
	A. defectiva	P13	S	R	S	S	S	S	S	R
	A. defectiva	P15	I	R	S	S	S	R	S	R
	A. defectiva	P18	S	S	S	S	S	S	S	R
	A. defectiva	P19	S	S	S	S	S	S	S	R
	A. defectiva	P32	I	S	S	S	S	S	S	S
Granulicatella	*Granulicatella adiacens*	P4	S	S	S	S	S	S	S	S
(*n* = 12)	*G. adiacens*	P5	S	S	S	S	S	S	S	S
	G. adiacens	P6	S	S	S	S	S	S	S	S
	G. adiacens	P10	I	R	S	R	R	R	S	R
	Granulicatella elegans	P14	S	S	S	S	S	S	S	R
	G. adiacens	P16	S	S	S	S	I	S	S	S
	G. elegans	P17	S	S	S	S	S	S	S	I
	G. adiacens	P23	I	S	S	S	S	S	S	S
	G. adiacens	P24	R	S	S	R	R	S	S	R
	G. elegans	P25	S	R	S	S	S	S	S	R
	G. adiacens	P29	S	R	S	S	S	S	S	R
	G. adiacens	P38	S	S	S	S	S	S	S	S

Abbreviations Ctx, ceftriaxone; Da, clindamycin; E, erythromycin; Fep, cefepime; Lev, levofloxacin; Lzd, linezolid; Peni, penicillin; Van, vancomycin

Discussion

ABI and GRA are relatively rare causative pathogens in IE [12–14]. However, there might be underestimation due to the special growth requirements of ABI/GRA. Prolonged incubation might allow for identification of these fastidious microorganisms and improve the positive rate of blood culture [15]. To our knowledge, this is the largest cohort study of ABI/GRA-IE for a single center. In our hospital, ABI and GRA related IE presented similar clinical characteristics and outcomes. ABI/GRA-IE was approximately 7 times less frequent than VGS-IE. Compared to VGS-IE, splenomegaly and chest tightness were more frequently found in the ABI/GRA-IE group while fever was less frequent. Pulmonary valve was more frequently affected in ABI/GRA-IE. Paravalvular complications were quite comparable in both groups while congestive heart failure and systemic emboli (excluding CNS) were more frequent in ABI/GRA-IE.

The aortic and mitral valves were reported to be the most commonly affected [2, 10, 14]. In our study, mitral valves were the most commonly affected (66.7%),

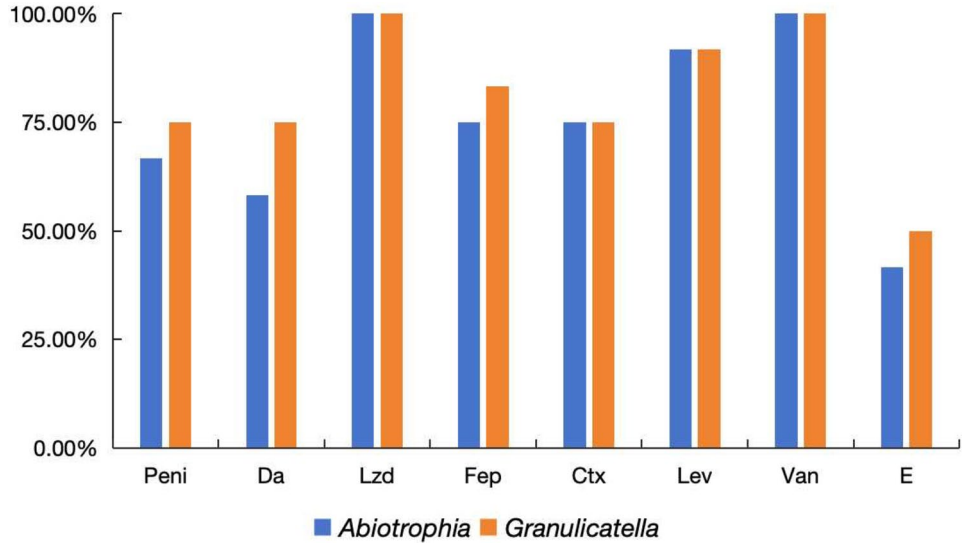

Fig. 2 In vitro susceptibility of 12 ABI-IE and 12 GRA-IE cases. For the 12 ABI-IE cases, eight (66.7%), 7 (58.3%), 12 (100.0%), 9 (75.0%), 9 (75.0%), 11 (91.7%), 12 (100.0%), and 5 (41.7%) were susceptible to penicillin, clindamycin, linezolid, cefepime, ceftriaxone, levofloxacin, vancomycin, and erythromycin, respectively. For the 12 GRA-IE cases, nine (75.0%), 9 (75%), 12 (100.0%), 10 (83.3%), 9 (75.0%), 11 (91.7%), 12 (100.0%), and 6 (50.0%) were susceptible to penicillin, clindamycin, linezolid, cefepime, ceftriaxone, levofloxacin, vancomycin, and erythromycin, respectively. *Abbreviations* ABI, *Abiotrophia*; Ctx, ceftriaxone; Da, clindamycin; E, erythromycin; Fep, cefepime; GRA, *Granulicatella*; IE, infective endocarditis; Lev, levofloxacin; Lzd, linezolid; Peni, penicillin; Van, vancomycin

followed by aortic valves (55.6%), pulmonary valves (13.3%), and tricuspid valves (8.9%), similar to previous studies.

In a previous study, the penicillin-non-susceptible rate of ABI and GRA was relatively high: 66.7% and 53.7% respectively [16]. However, in another study conducted by Téllez et al.., 84.6% of ABI and 90.9% of GRA strains were penicillin sensitive [2]. María A. Cañas et al.. observed reduced susceptibility to penicillin in both ABI and GRA, with zero of six (0%) and two of nine (22%) strains being completely susceptible, respectively [17]. Antimicrobial susceptibilities of ABI/GRA varied in different studies, partly due to limitations of sample size and regional diversities [1, 18, 19]. In our study, 66.7% of ABI strains and 75.0% of GRA strains were sensitive to penicillin.

In previous studies, in-hospital surgery was performed in 27-70% of ABI/GRA-IE [2, 10, 20, 21]. In our study, surgery was performed in 84.2% in ABI-IE and 100.0% in GRA-IE. The surgery rate in our study is quite high, which could partly be explained by the specific characteristics of our hospital. Zhongshan Hospital is a regional cardiac surgery center, and many patients have already received antibiotic treatment and evaluation before being admitted with indications for surgery. Etiological diagnosis of IE is interfered by previous antibiotic usage, which could partly explain the high portion of etiologically unknown IE (645 of 1531, 42.1%) in this study.

Mortality of ABI/GRA-IE varied from 2.1 to 25% in different previous studies [2, 10, 20]. Bouvet A. et al. reported the mortality as high as 17-20%. In our study, mortality of ABI/GRA-IE was 4.4%, comparable to that of VGS-IE (4.1%) and lower than previously reported results. Precise etiological diagnosis, targeted antibiotic treatment, and high-quality surgery might explain the improved outcomes. On the other hand, as we mentioned above, this study was conducted in a regional cardiac surgery center, and many patients had already received antibiotic treatment and evaluation before being admitted with indications for surgery. These patients were relatively mild and might have a better prognosis. This factor might also contribute to the low mortality of ABI/GRA-IE in this study.

There were some limitations in this study. This was retrospective study in a single center. Patient selection bias may have existed, and some clinical and laboratory data were not comprehensive. Antimicrobial susceptibilities were only available in 24 ABI/GRA-IE cases. In addition, due to the limitations of sample size, we did not construct a predictive model for the prognosis of ABI/GRA-IE.

Conclusions

ABI-IE and GRA-IE seem to have similar clinical characteristics. Patients with ABI/GRA-IE have comparable surgical rate and prognosis with VGS-IE patients, although congestive heart failure and systemic embolization (excluding CNS) were more frequently detected. Mortality of ABI/GRA-IE in this study was comparable to that of VGS-IE and lower than previously reported

results. These findings differ from previous reports and provide more understanding in ABI/GRA-IE.

Abbreviations

A. defective	Abiotrophia defective
ABI	Abiotrophia
Ak	Amikacin
Ao	Aortic
CIED	Cardiovascular implantable electronic device
CNS	Central nervous system
Ctx	Ceftriaxone
Da	Clindamycin
Dap	Daptomycin
E	Erythromycin
E-test	The epsilometer test
F	Female
Fep	Cefepime
Fos	Fosfomycin
G. adiacens	Granulicatella adiacens
G. elegans	Granulicatella elegans
Gen	Gentamicin
GRA	Granulicatella
HCM	Hypertrophic cardiomyopathy
IE	Infective endocarditis
IQR	Interquartile range
Lev	Levofloxacin
Lzd	Linezolid
M	Male
Mi	Mitral
MICs	Minimum inhibitory concentrations
MP	Mitral prolapse
Mxf	Moxifloxacin
N/A	Not available
NT-proBNP	N-terminal pro-B type natriuretic peptide
NVE	Native valve endocarditis
NVS	Nutritionally variant streptococci
NYHA	New York Heart Association
Peni	Penicillin
Pul	Pulmonary valve
PVE	Prosthetic valve endocarditis
PVS	Previous valve surgery
Rfp	Rifampicin
RHD	Rheumatic heart disease
Tri	Tricuspid valve
Van	Vancomycin
VGS	Viridans group streptococci

Supplementary Information

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Supplementary Material 1

Supplementary Material 2

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Author contributions

Contributions: (I) Conception and design: SC, JY; (II) Administrative support: LH, JP, CW, BH; (III) Provision of study materials or patients: SC, JY, CZ, YS, RB; (IV) Collection and assembly of data: SC, JY; (V) Data analysis and interpretation: SC, JY; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

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Data availability

The datasets used and/or analysed during the current study are available on request from Sishi Cai at cai.sishi@zs-hospital.sh.cn.

Declarations

Ethical approval

The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the Ethical Review Committee of Zhongshan Hospital, Fudan University, Shanghai, China (No. B2024-128R) and informed consent was taken from all the patients or the relatives.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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