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Articolo originale

Original article

Molecular epidemiology of methicillin-resistant *Staphylococcus aureus* from bacteraemia in northern Italy

Epidemiologia molecolare di batteriemie da Staphylococcus aureus *meticillino-resistente in nord-Italia*

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INTRODUCTION

High level glycopeptide resistance in *Staphylococcus aureus* (GRSA) due to acquisition of the *vanA* operon from enterococci is rare and, thus far, uniquely associated with MRSA belonging to CC5 [1].
Strains with reduced susceptibility to glycopeptides, including glycopeptide intermediate *S. aureus* (GISA) and heterogenous glycopeptide intermediate *S. aureus* (hGISA) are more common and found worldwide with varying frequencies [2].
According to the European Antimicrobial Resistance Surveillance Network (EARS-Net) data of 2010, the percentage of MRSA from invasive isolates was 36.8% in Italy and 26% in Bolzano (http://ecdc.europa.eu/). Previously, 66 invasive MRSA isolates collected in 2005-06 from 19 laboratories throughout Italy were characterised by *spa* typing, 5 of which originated from Bolzano [3]. In view of the scarcity of molecular typing data regarding invasive MRSA isolates in Italy, we carried out a retrospective molecular epidemiological survey of 81 blood MRSA isolates collected over a 9 year period (2002-10) in the Province of Bolzano, Northern Italy.

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MATERIALS AND METHODS

Study isolates and susceptibility testing

A total of 81 first, non-duplicate MRSA bacteraemia isolates (corresponding to about 30% of the total isolates collected from 2002 to 2010) were randomly selected for study [(specifically: 2002 (n=2), 2003 (n=1), 2004 (n=1), 2005 (n=2), 2006 (n=13), 2007 (n=15), 2008 (n=5), 2009 (n=24), 2010 (n=18)]). The isolates originated from the Province of Bolzano, Northern Italy, which has a population of 500,000 and 7 public hospitals: Bolzano, Merano, Bressanone, Brunico, Silandro, Vipiteno and San Candido. The study was approved by the Ethics Committee of the Bolzano Hospital. The isolates were identified according to morphological features, a latex agglutination test (Slidex®Staph Plus, bioMérieux, Marcy l'Étoile, France) and Vitek 2 system (bioMérieux). MICs for chloramphenicol and fosfomycin were determined with an automated microdilution system (Wider, Soria Melguzio, Madrid, Spain). MICs for ciprofloxacin, clindamycin, daptomycin, erythromycin, fusidic acid, gentamicin, linezolid, moxifloxacin,

mupirocin, oxacillin, quinupristin/dalfopristin, rifampicin, teicoplanin, tetracycline and vancomycin were determined by agar dilution, according to British Society for Antimicrobial Chemotherapy (BSAC) method [4]. Tigecycline MICs were determined by Etest (bioMérieux, Marcy l'Étoile, France) on Mueller Hinton 2 plates (SCLAVO, Siena, Italy). Results were interpreted according to EUCAST guidelines, except for mupirocin (BSAC breakpoints were used), and glycopeptides (analysed according to EUCAST and CLSI guidelines [5]). For between-method comparison of MICs for vancomycin and teicoplanin, glycopeptide MICs were also determined with Etest (bioMérieux), with Vitek 2 using the AST-P580 card and with the Wider system using the Gram-Positives panel WIDER MIC GRAM POS. REV.2 (Soria Melguizo, Madrid, Spain). All isolates were tested for inducible clindamycin resistance by Vitek 2 and D-zone test (http://www.eucast.org/) and were screened for heteroresistance to vancomycin and teicoplanin by the Macro Etest and with Etest glycopeptide resistance detection (GRD) according to the manufacturer's protocol (bioMérieux); a positive screening test was defined as positive by at least one of the two methods. Confirmation of the hGISA phenotype was performed by the vancomycin population analysis profile - area under the curve (PAP-AUC) method [6] plus teicoplanin population analysis [6]. Teicoplanin population analysis profiles were determined as for vancomycin PAP-AUC with 1, 2, 4, 6 and 8 mg/L teicoplanin. Frequencies of hGISA isolates were compared with the two-tailed Fisher's exact test (MedCalc® version 7.3.0.1).

Molecular characterisation of study isolates

DNA sequence-based typing of the staphylococcal protein A (*spa*) gene repeat region [7] and multi-locus sequence typing (MLST) [8] were performed as described previously [7, 8]. MLST and *spa* typing were carried out on an ABI Genetic Analyser capillary platform 3130XL (Applied Biosystems, CA, USA) and the data analysed using BioNumerics (Sint-Martens-Latem, Belgium) and by comparison with online databases (http://www.ridom.de/, http://www.mlst.net/). Pulsed–field gel electrophoresis (PFGE) following macrorestriction of chromosomal DNA with *Sma*I PFGE was performed as described previously [9]. Data were analysed using BioNumerics via the unweighted-pair group method (1% optimization and 1.9% position tolerance). Staphylococcal chromosome cassette *mec* (SCC*mec*) typing and SCC*mec* IV subtyping was performed using multiplex PCR [10,11]; *mecA* and *ccr* complex typing was also carried out [10-12]. Multiplex PCRs were used to detect 14 *S. aureus* toxin genes encoding enterotoxins A-E and G-J, exfoliatins A, B and D, toxic shock syndrome toxin-1 and Panton-Valentine leucocidin (PVL) [13]. Multiplex PCR was used for accessory gene regulator (*agr*) typing [14]; for the single isolate not typeable using this method, alternative primers were used [14, 15].

RESULTS

Patient data

Among the 81 patients with MRSA bacteremia the median age was 77 years (range 41-94 years); 64% were male. The isolates were mainly collected from Bolzano (63; 78%) and Merano (11; 13.5%); the remainder were from hospitals in the same Province distant not more than 80 km from Bolzano: Bressanone, Brunico, Silandro and Vipiteno. All patients were hospitalized, including Geriatrics (20%), Internal Medicine (20%), Pneumology (7%), Intensive care Units (6%), Nephrology/Hemodialysis (6%), Vascular surgery (5%), Neurosurgery (4%) and Cardiology (4%); the remaining 28% were from various other hospital departments.

Antimicrobial susceptibilities

All isolates were susceptible to quinupristin/dalfopristin (MIC_{90} = 1 mg/L) and fusidic acid (MIC_{90} = 0.5 mg/L). Susceptibilities were as follows: trimethoprim/sulfamethoxazole (95%, MIC_{90} ≤ 10 mg/L), mupirocin (95%, MIC_{90} ≤ 4 mg/L), fosfomycin (95%, MIC_{90} ≤32 mg/L), rifampicin (94%, MIC_{90} ≤ 0.03 mg/L), chloramphenicol (85%, MIC_{50} ≤8 mg/L; MIC_{90} >8 mg/L), tetracycline (94%, MIC_{90} = 1 mg/L), gentamicin (57%, MIC_{50} ≤ 0.5 mg/L; MIC_{90} > 128 mg/L), ciprofloxacin (5%, MIC_{50} and MIC_{90} > 8 mg/L), moxifloxacin (5%, MIC_{50} and MIC_{90} = 8 mg/L), erythromycin (25%, MIC_{50} and MIC_{90} > 16 mg/L), clindamycin (62%, MIC_{50} ≤ 0.25 mg/L; MIC_{90} >8 mg/L). One isolate had low level mupirocin resistance (MIC 8-256 mg/L) and two had high level resistance (MIC >256 mg/L). All isolates (37%) resistant to erythromycin but susceptible to clindamycin had dissociated clindamycin resistance, the Vitek 2 test and the D-test showed 100% concordant results.

Table 1 - MIC distribution for vancomycin, teicoplanin, daptomycin, linezolid and tigecycline of 81 MRSA from blood cultures.

	MIC mg/L							
Antibiotic (no. of isolates)	*0.06*	*0.12*	*0.25*	*0.5*	*1*	*2*	*4*	*8*
Vancomycin								
hGISA (18)						18		
GISA (2)							2	
GSSA (58)					8	53		
Teicoplanin								
hGISA (18)					1	2	13	2
GISA (2)							1	1
GSSA (58)					53	7		1
Daptomycin				41	40			
Linezolid						52	29	
Tigecycline	8	49	23	1				

Vancomycin, teicoplanin, daptomycin and linezolid were tested with using the BSAC agar dilution method and tigecycline by Etest. Numbers corresponding to MIC_{90} values are in bold. hGISA confirmed by PAP-AUC.

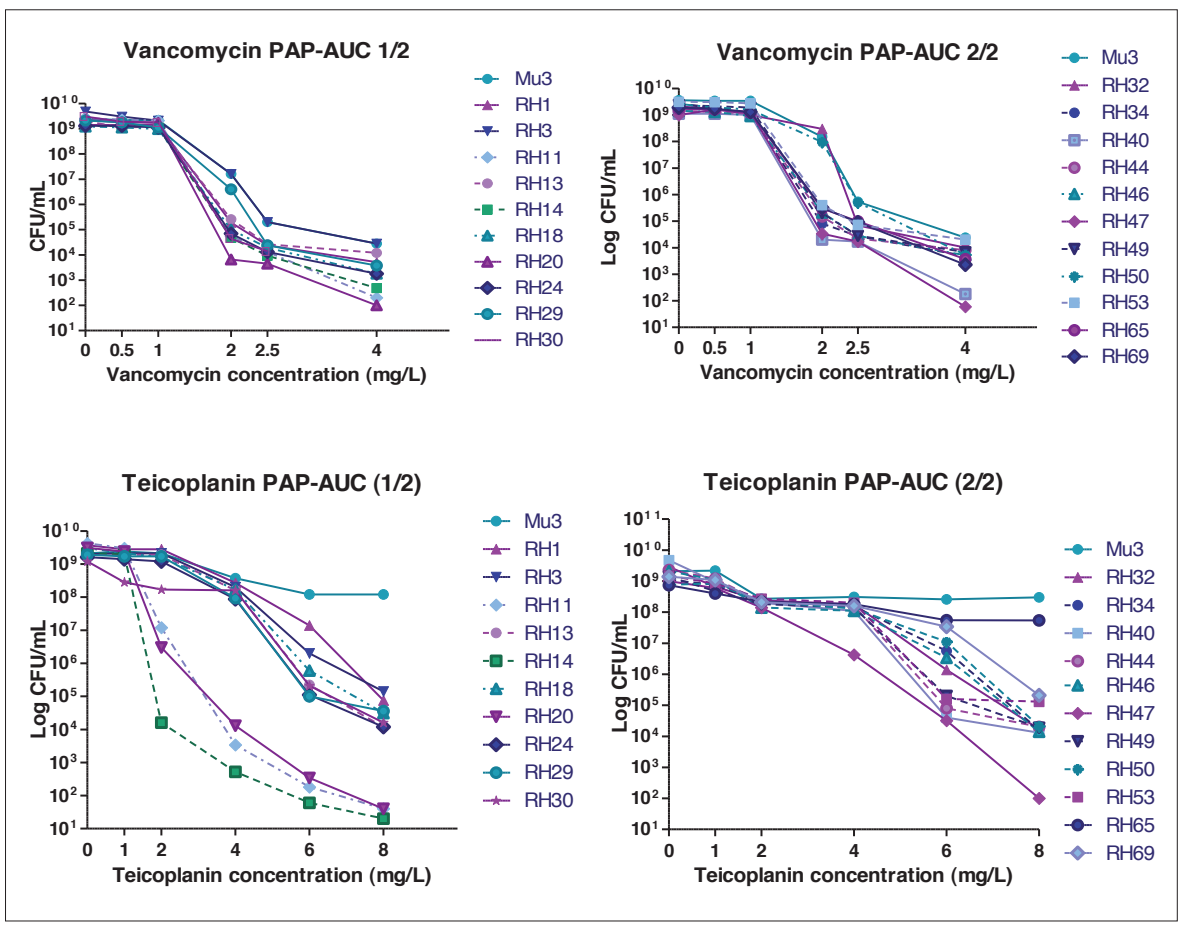

Figure 1 - Vancomycin (upper figure) and teicoplanin (lower figure) PAP-AUCs for all 21 screening positive hGISA strains. Strain Mu3 was used as hGISA control.

Table 2 - Molecular typing and results of hGISA/GISA screening.

No. (%) of isolates (Total=81)	*agr-type*	*MLST-clonal complex*	*MLST-type*	*spa-type*	*SCC mec-type*[a,b]	*Toxin gene profile*[c]	*Antibiotic resistance profile*[d]	*hGISA/GISA total isolates*[e] *(% isolates)*
13 (16%)	2	CC5	ST228	t041	I (1B)	*sea*, *seg*, *sei* (10); *sea* (3)	cip, ery, clin, gen (12); cip, ery, clin, gen, rif (1)	13/13 (100%)
3 (4%)	2	CC5	ST228	t001	I (1B)[f]	*sea*, *seg*, *sei* (2), *sea* (1)	cip, ery, clin, gen (3)	2/3
1	2	CC5	ST228	t013	I (1B)	*sea*	cip, ery, clin, gen	1/1
1	2	CC5	ST111[g]	t892	I (1B)	*sea*, *seg*, *sei*	cip, ery, clin, gen	1/1
1	2	CC5	ST111[g]	t3786	I (1B)	*sea*	cip, ery, clin, gen	1/1
1	2	CC5	ST111[g]	t10870	I (1B)	*sea*, *seg*, *sei*	cip, ery, clin, gen	1/1
1	2	CC5	ST5	t242	II (2A)	*sed*, *seg*, *sei*, *sej*	cip, ery, clin, rif	
5 (6%)	2	CC5	ST225	t003	II (2A)	*sed*, *seg*, *sei*, *sej*	cip, ery, clin (4); cip, ery, clin, rif (1)	
1	2	CC5	ST225 (CC5)	t014	II (2A)	*sed*, *seg*, *sei*, *sej*	cip, ery, clin	
45 (55%)	1	CC8	ST8	t008	IVc (2B)[h]	*sea*, *sed*, *sej* (39); *sea* (4); *sed*, *sej* (2)	cip, ery, clin (18); cip (11); cip, ery, clin, gen (9); cip, gen (4), cip, gen, tet (2); cip, ery, clin, gen, rif (1)	1/45 (2%)
1	1	CC8	ST8	t400	IVc (2B)	*sea*, *sed*, *sej*	cip, ery, clin	
1	1	CC8	ST72	t3092	V (5C)	*seg*, *sei*	gen, sxt	
1	1	CC8	ST239	t037	III (3A-ccrC)		cip, ery, clin, gen, tet, rif, sxt	
3 (4%)	1	CC22	ST22	t515	IVh (2B)	*seg*, *sei*	cip, ery, clin (3)	
1	1	CC45	ST45	t015	IVa (2B)	*sea*, *sec*, *seg*, *sei*	All susceptible	
1	1	CC398	ST398	t011	V (5C)		tet	
1	3	CC1	ST1	t127	IVa (2B)	*seh*	ery, clin, gen, tet	

[a]Milheiriço et al. [10, 11]; [b]Kondo et al. [12]; [c]Staphylococcal enterotoxin genes *sea, sed, seg, sei, sej*, Panton-Valentine leucocidin genes, *pvl*; [d]ciprofloxacin (cip); erythromycin (ery); clindamycin (clin), comprising dissociated clindamycin resistance; gen (gentamicin); tetracycline (tet); rifampicin (rif); sxt (trimethoprim/sulfamethoxazole); [e]hGISA confirmed by PAP-AUC; [f]one isolate with shorter than expected fragment for mecA-IS1272 [12]; [g]single locus variant of ST228; [h]one isolate had *ccr* types 2 and 4.

MIC distributions for vancomycin, teicoplanin, daptomycin, linezolid and tigecycline are shown in table 1. Two isolates were GISA with vancomycin MICs of 4 mg/L and teicoplanin MICs of 4 mg/L and 8 mg/L, respectively. Twenty-one (26%) of the remaining isolates were positive in at least one of the screening tests for hGISA, no significant difference was found for the percentage of isolates with vancomycin MICs of 2 mg/L (100% for hGISA by screening methods vs. 86% for GSSA; p=0.10) but a significantly higher proportion of hGISA (by screening methods) had teicoplanin MICs >2 mg/L (71%) compared with GSSA (17%) (p=0.0001).

Repeating the Etest MICs for the hGISA strains (by the screening tests) after several passages (Wootton M, Cardiff, UK; data not shown) led generally to a lowered MIC for vancomycin and teicoplanin by 0.5 mg/L compared with the first determination (Aschbacher R, Bolzano, Italy; data used in this paper).

Of the 21 hGISA screening positive isolates vancomycin PAP-AUCs confirmed 4 as hGISA with a further 10 isolates close to the cut off criteria for hGISA (Figure 1). Teicoplanin PAP-AUCs classified a further 4 isolates as hGISA (RH30, RH34, RH40, RH47). Teicoplanin PAP-AUCs for isolates with vancomycin PAP-AUC ratios near the cut off criteria (RH1, RH13, RH24 etc) clearly showed a distinct resistance profile. Therefore, 21% (18/81) of the isolates were considered as hGISA and 2.5% (2/81) as GISA. Of the 18 PAP-AUC confirmed hGISA, all except one (RH30) belonged to the ST111-ST228 group; three isolates (RH11, RH14, RH20; all t008) were classed as susceptible by both PAPs.

Vancomycin and teicoplanin MICs obtained by Etest and BSAC agar dilution were generally one and two dilutions higher compared to automatic systems; Wider and Vitek 2,. Essential agreement (±1 dilution) for vancomycin of the BSAC agar dilution method with Etest (100%) or Wider (97%) were higher than with Vitek 2 (55%) as was the essential agreement for teicoplanin of the BSAC reference method with Etest (97%) and Wider (91%) compared with Vitek 2 (68%).

Genotypic characteristics

The overall results are shown in table 2. A total of 17 different *spa* types were identified, with two major genotypes (t008 and t041) accounting for 72% of the isolates. MLST was performed on three representative *spa* type t008 isolates with differing toxin and antibiotic resistance profiles, plus one representative of all other *spa* types. The isolates comprised mainly MLST clonal complexes CC8 (59%) and CC5 (33%), with sporadic isolates belonging to CC1, CC22, CC45 and CC398. A significant difference in the frequency of hGISA (based on PAP-AUC) and GISA phenotypes between the two major *spa* types was apparent (p<0.001): all t041 displayed the hGISA or GISA phenotype compared with only 2% of t008 strains.

Sixteen *spa* t008 isolates with varying antimicrobial phenotypes and toxin gene profiles plus the single *spa* t400 isolate (a single *spa* repeat deletion variant of t008) were compared by PFGE. Thirteen, including the t400 isolate, had indistinguishable banding profiles representing a major cluster; the remaining four showed ≥84% similarity with this group (data not shown). One *spa* type t008 isolate harboured SCC*mec* type IVc [10, 11] but *ccrA2-ccrB* (primers 2- c) and *ccrA4-ccrB4* (primers 4.2- 4.2) were identified in multiplex and simplex PCRs [12]; 851 bp of the *ccrA2-ccrB* and 1173 bp of the *ccrA4-ccrB4* fragments were sequenced and showed 100% homology with Genbank sequences AB266532 and HM030720 respectively.

One tetracycline resistant isolate from a bronchial aspirate collected in 2009 from the Vipiteno Hospital was included in the study for comparison with the ST398 bacteraemia isolate recovered two weeks later from the same hospital; it had an identical antibiotype and genotype with *agr* type 1, *spa* type t011, SCC*mec*V, it was negative for all tested toxin genes and resistant only to tetracycline. No significant changes in single genotypes were observed during the study period and all isolates were PVL-negative.

DISCUSSION

A previous study of hospital acquired MRSA (HA-MRSA) from different specimen types in Italy showed ST228-MRSA-I (the Southern German/Italian clone) was dominant (57%) during 2000-07, followed by ST22-MRSA-IV (UK-EMRSA-15) and ST8-MRSA-IV [16]. Similarly, of 56 mainly HA-MRSA isolates collected from different specimen types in Bolzano during 2005-06, t008 was the most common lineage (33 isolates; corresponding to ST8-MRSA-IV), followed by t041 (11 isolates) and t001 (5 isolates), both belonging to ST228-MRSA-I [17]. A European study in 2005-06 of invasive MRSA from

19 laboratories, including 66 from Italy, showed the prevalent *spa*-types in Italy were t041 (35.3%), t008 (28.4%) and t001 (13.4%); three isolates from Bolzano were included in the study (one t008 and two t041) but were not included in the present study; all except one European isolates were PVL-negative [3].

In this study, molecular analyses of 81 blood culture isolates randomly collected in 2002-10 in the Province of Bolzano indicated two major MLST clonal complexes were predominant (CC8, 59% and CC5, 33%), with single isolates belonging to CC1, CC22, CC45 and CC398.

The first major genotype (n=45; 55%), was related to the Lyon clone ST8-MRSA-IV [18], the most common lineage among invasive MRSA isolates in 2005-06 in France (48.6%) and the second most prevalent clone in Italy (28.4%) [3]; one identified as hGISA [3, 18]. One isolate had both *ccr* types 2 and 4, a combination described previously in a composite SCC*mec* IVa element [19].

The second major genotype (n=20; 25%) was ST228- and the single locus variant ST111-MRSA-I (*agr* type 2, *spa* t041 or related). Interestingly, t041 was the most common *spa* type in invasive MRSA isolates from 2005-06 in Italy (35.3%), being reported by 13 out of 19 laboratories and has been defined as the Northern Balkan/Adriatic cluster [3].

Five isolates (6%) were identified as genotype ST225-MRSA-II (*agr* type 2, *spa* t003 or related), also known as the Rhine Hesse MRSA clone [3].

Three isolates belonged to ST22-MRSA-IVh also known as EMRSA-15 clone, (*agr* type 1, *spa* t515); this *spa* type was identified previously in three of 66 invasive isolates collected during 2005-06 in Italy [3] and, although widely regarded as a highly successful HA-MRSA clone, it has been reported as a PVL negative community acquired MRSA (CA-MRSA) clone from different specimen types in Milan, Italy, in 2006-07 [3, 20].

One tetracycline resistant isolate in 2009 from the Vipiteno Hospital identified as ST398-MRSA-V (*agr* type 1, *spa* t011). An isolate from a bronchial aspirate with the same phenotypic and genotypic characteristics was collected two weeks later from a different patient in the same hospital, but no other isolate of this antibiotype has been identified subsequently in the same hospital. The ST398 livestock associated MRSA (LA-MRSA) has been reported colonizing pigs, cows and chickens with a capacity to spread to humans [21]. Tetracycline resistance is common among MRSA of different *spa* types and lineages from pigs, and has been associated with the use of tetracyclines in animal husbandry in some European countries [22, 23]. In Italy, ST398 MRSA have been implicated sporadically in invasive human bacteremic infections [24].

One tetracycline resistant isolate from the Geriatrics department of the Bolzano hospital was identified as ST1-MRSA-IVa (*agr* type 3, *spa* t127); an isolate with similar characteristics, but with SCC*mec* I, was also found previously in a blood isolate from Ferrara, Italy [3].

Single isolates were assigned to ST239-MRSA-III (*agr* type 1, *spa* t037, Brazilian/Hungarian clone), ST45-MRSA-IVa (*agr* type 1, *spa* t015, Berlin clone) and ST5-MRSA-II (*agr* type 2, *spa* t242), all lineages that have been found previously among MRSA bacteraemia isolates in Europe [3]. A single isolate was ST72-MRSA-V (*agr* type 1, *spa* t3092) [25]. This *spa* type has been found very occasionally among MRSA isolates from various European countries (http://spa.ridom.de/spa-t3092.shtml).

Vancomycin and teicoplanin MICs obtained by Etest and BSAC agar dilution were generally one or two dilutions higher than with the automatic systems Wider and Vitek 2, as already observed by other investigators [26], with Etest results more predictive of vancomycin treatment response compared to Vitek MICs [26, 27]. Tthe two GISA strains were not recognized by the automated systems (and only one of the two by Etest). The reduced vancomycin and teicoplanin MICs displayed by passaged hGISA isolates confirms the recognised instability of glycopeptide intermediate resistance. Two isolates were GISA; of the 19 hGISA screen positive isolates 18 (95%) were confirmed by either vancomycin or teicoplanin PAP-AUC. The majority (14; 78%) of the isolates were just under or close to the low level cut off for determining hGISA phenotype. These results correspond to slightly lower vancomycin and teicoplanin MICs and are probably attributable to instability of the resistance. Because this type of resistance is a continuum it is possible that the PAP-AUCs would increase given more time under a glycopeptides challenge. It can be argued though that they might still cause clinical treatment failure.

Using the BSAC agar dilution method, 90% of our 81 blood MRSA isolates had vancomycin MICs >1 mg/L, 21% were hGISA by PAP-AUC and 2.5% were GISA. Poorer outcomes for vancomycin treatment of invasive MRSA infections with vancomycin MICs of 2 mg/L (MIC within the susceptible range of EUCAST and CLSI) and

especially of infections with GISA and hGISA are described but clinical implications of MRSA with reduced susceptibility to vancomycin remain controversial [2, 28]. In Italy genotype ST228-MRSA-I (*spa* types t041 and t001) has been associated with the hGISA and GISA phenotype, with 8 out of 24 (33%) *spa* t041 MRSA identified as hGISA and 1 as GISA [29]. Among our study isolates, 19/20 (95%) hGISA or GISA belonged to the ST111-ST228 group, including *spa* types t041, t001, t013, t892, t3786 and t10870. To conclude, in the North Italian Province of Bolzano several diverse lineages of MRSA with varying susceptibility profiles were identified causing bacteraemia, one of which (ST228 plus its single locus variant ST111) was strongly associated with an hGISA or GISA phenotype. This finding is of public health concern because of the association of hGISA and GISA phenotypes with glycopeptide treatment failure. A clinical study is required to ascertain the implication of these phenotypes in the ST111-ST228 genotype for the treatment of invasive infections.

Keywords: MRSA, GISA, hGISA, PAP-AUC, ST228.

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SUMMARY

Background. Vancomycin is frequently used in the treatment of methicillin-resistant *Staphylococcus aureus* (MRSA) bacteraemia; reduced susceptibility to vancomycin is therefore disturbing.
Methods. Molecular epidemiological analysis of 81 MRSA bacteraemia isolates collected during 2002-10 in the province of Bolzano, northern Italy was performed. MICs of a range of antimicrobials were determined by agar microdilution, screening for hGISA was by Macro-Etest and Etest GRD and confirmed by PAP-AUC with vancomycin and teicoplanin. All isolates were characterised by toxin gene profiling, *agr*, *spa*, and SCC*mec*-typing; MLST and PFGE were carried out on representative strains.
Results. The dominant clones identified were ST8-MRSA-IVc (55%) and ST228- and ST111-MRSA-I (25%); most of the latter two lineages (19/20; 95%) were GISA or PAP-AUC confirmed hGISA. One ST8-MRSA-IVc isolate harboured *ccr*A_2B_2 together with *ccr*A_4B_4. The remainder were diverse genotypically and belonged to MLST clonal complexes 1, 22, 45 and 398.
Conclusions. Diverse lineages of MRSA were identified as causing bacteraemia in a province in northern Italy. The association of a specific genotype with the hGISA and GISA phenotypes among representatives of the second most common lineage identified is of clinical concern.

RIASSUNTO

Background. *L'antibiotico vancomicina viene frequentemente usato nel trattamento delle batteriemie da* Staphylococcus aureus *meticillino-resistente (MRSA); la sensibilità ridotta nei suoi confronti risulta pertanto preoccupante.*
Metodi. *Un'analisi di epidemiologia molecolare è stata eseguita per 81 ceppi di MRSA isolati da batteriemie collezionate nel periodo 2002-10 in Provincia di Bolzano, Nord-Italia. Le MIC per il pannello di antibiotici selezionato sono state determinate tramite diluizione in agar e lo* screening *per hGISA é stato eseguito con Macro-Etest e Etest GRD; PAP-AUC basato su vancomicina e teicoplanina è stato scelto come test di conferma. Tutti gli isolati sono stati inoltre tipizzati per i geni produttori di tossine* agr, spa *e* SCCmec *e i ceppi più rappresentativi sottoposti a MLST e PFGE.*
Risultati. *ST8-MRSA-IVc (55%) assieme a ST228- e ST111-MRSA-I (25%) rappresenta il clone dominante; la quasi totalità delle ultime due linee (19/20; 95%) sono GISA o hGISA confermati con PAP-AUC. Un isolato ST8-MRSA-IVc contiene* ccrA_2B_2 *assieme a* ccrA_4B_4. *I rimanenti isolati sono genotipicamente diversi e appartengono ai complessi clonali 1, 22, 45 e 398.*
Conclusioni. *Diverse linee di MRSA sono state identificate come causa di batteriemia in Provincia provincia di Bolzano. L'associazione di un genotipo specifico con il fenotipo hGISA e GISA tra i ceppi della seconda linea per frequenza più rappresentati é clinicamente preoccupante.*

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