

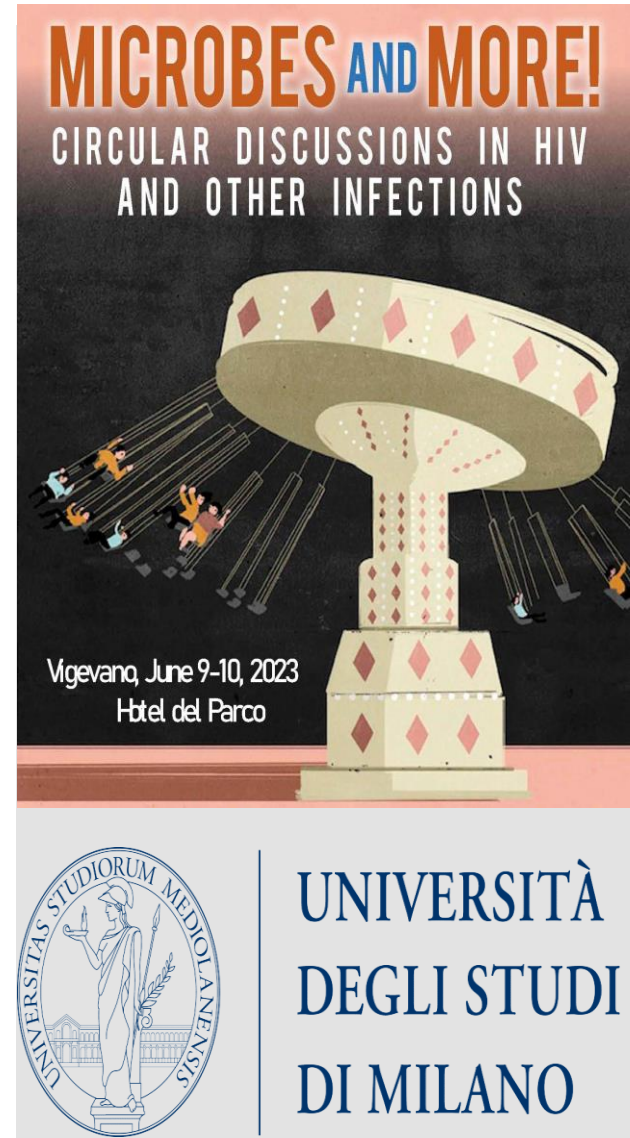
The PerSAB Study: risk factors associated with *S. aureus* persistent bacteremia, a preliminary analysis

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Rational of the study

- *S. aureus* bacteremia (SAB) is a high mortality condition (20-40%) with a high rate of morbidity due to its potential dissemination
- Persistent bacteremia is defined by the presence of positive follow-up blood cultures (FU-BC) after 48 hours from the start of a active antibiotic therapy, with a incidence estimated between 9 and 36%
- Mortality risk raises everyday of positive FU-BC with a cut-off of 48 hours as the limit to the higher incrementation of mortality
- Some risk factors for persistent SAB, in literature, have been identified but its determinants are still not completely known

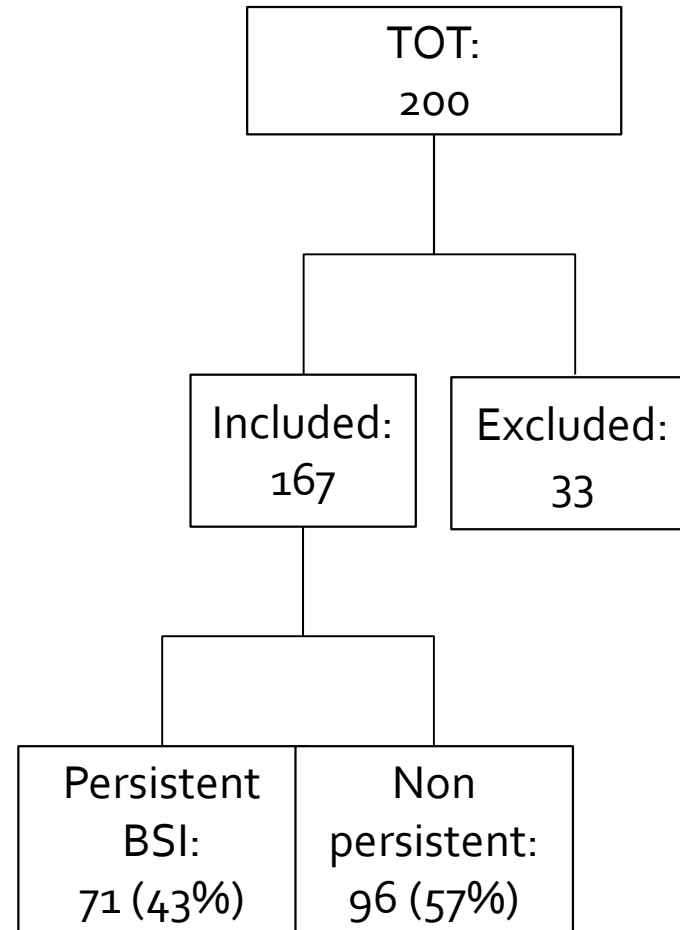
Aims

- To assess prevalence of SAB and persistent SAB
- To assess all-causes in-hospital mortality according to non-persistent and persistent SAB
- To assess risk factors associated with persistent SAB

Material and methods

- Retrospective monocentric study
- Inclusion criteria: all patients with SAB, age ≥ 18 y.o.; for statistical analysis: FU-BC at 48 hours, survival at 48h from SAB onset
- All patients with SAB, from January 1st 2019 to December 31st 2021
- Collection of demographic, clinical, microbiological and of outcomes datas from hospital's digital records
- Statistical analysis (Chi square for nominal variables, Mann-Whitney or Student t test test for numerical variables and logistic regression for dicotomic numeric variables)
- Predictive factors for persistent SAB have been investigated by fitting a logistic regression analysis

Inclusion



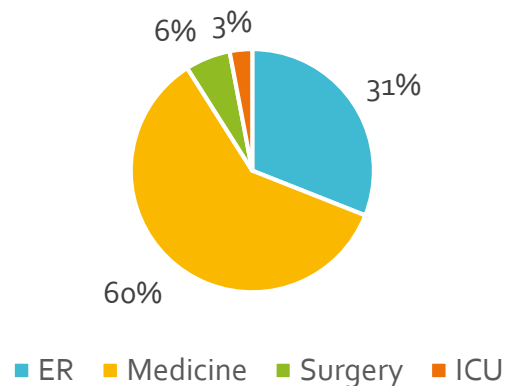
Demographic

	Overall (200)	Persistent (71)	Non persistent (96)	p
Age Median (IQR)	74 (59-83)	69 (56-80)	75 (59-82)	0.191
Gender M n (%)	119 (59.5%)	56 (58.33%)	46 (64.79%)	0.398
Hospitalization days Median (IQR)	24 (14-38)	28 (16-45)	26 (19-41)	0.349
Charlson Median (IQR)	6 (5-8)	6 (4-8)	6 (5-8)	0.897
Ward:				
- ER	62 (31%)	22 (31%)	31 (32%)	0.858
- Medicine	120 (60%)	43 (61%)	54 (56%)	0.577
- Surgery	11 (5.5%)	4 (6%)	7 (7%)	0.670
- ICU n (%)	7 (3.5%)	2 (2%)	4 (5%)	0.645

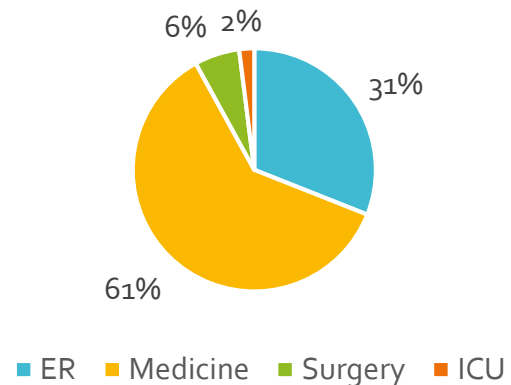
Patients characteristic

	Overall	Persistent	Non persistent	p
Origin: N (%)				
- Primary	86 (43%)	28 (39%)	39 (41%)	0.88
- Pulmonary	12 (6%)	2 (3%)	7 (7%)	0.22
- PVC-CVC	68 (34%)	31 (44%)	32 (34%)	0.17
- ABSSI	17 (9%)	6 (8%)	8 (8%)	0.98
- Bone	10 (5%)	4 (6%)	5 (5%)	0.90
- Non skin Abscess	6 (3%)	0	4 (4%)	
Endovascular devices N (%)	41 (21%)	19 (27%)	16 (17%)	0.12
Dyalisis	22 (11%)	12 (17%)	9 (10%)	0.16
Orthopedic devices N (%)	11 (5.5%)	3 (4%)	6 (6%)	0.56

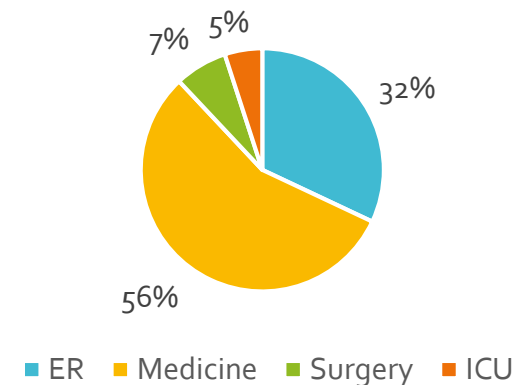
Ward: overall



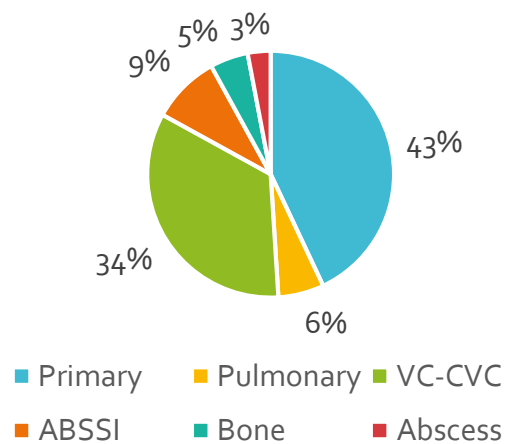
Ward: persistent



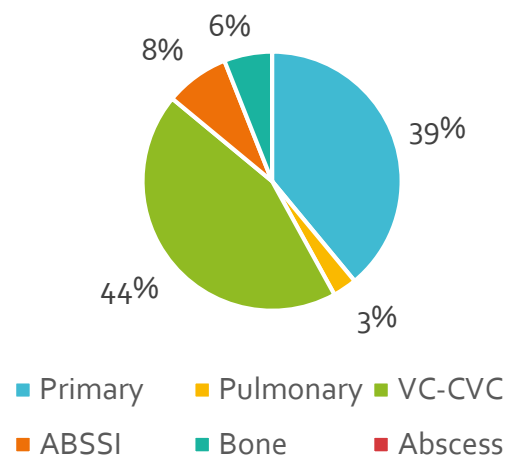
Ward: non-persistent



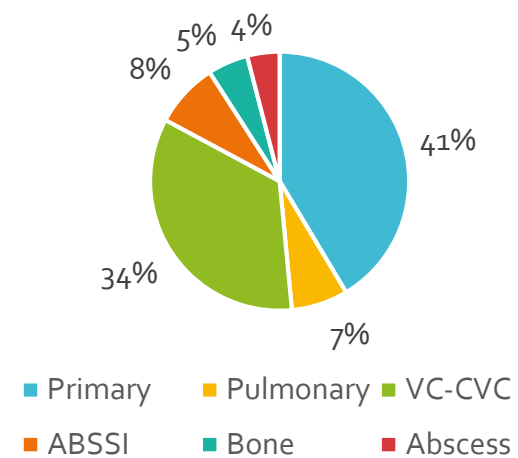
Origin: overall



Origin: persistent

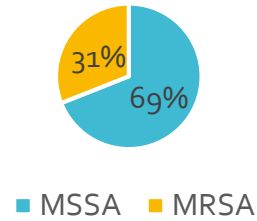


Origin: non-persistent

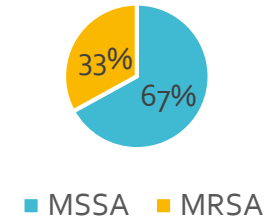


Blood cultures characteristics

Pathogen: overall

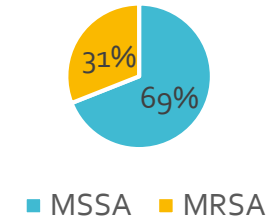


Pathogen: non-pers

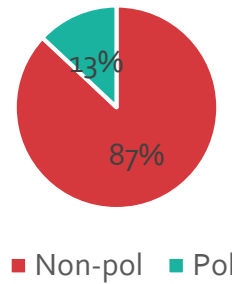


Pathogen: pers

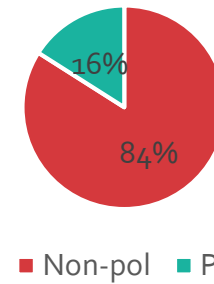
p=0.749



Polimicrobic: overall

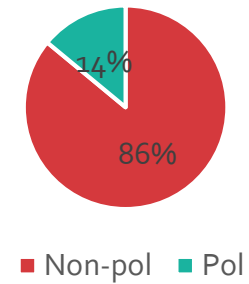


Polimicrobic: non-pers

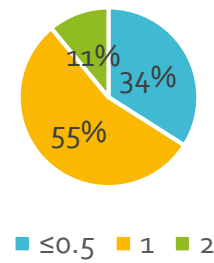


Polimicrobic: persistent

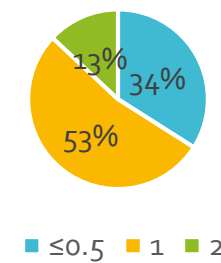
p=0.783



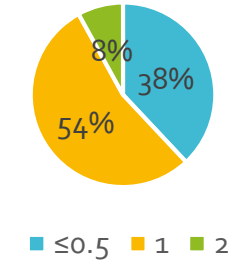
MIC vanco: over



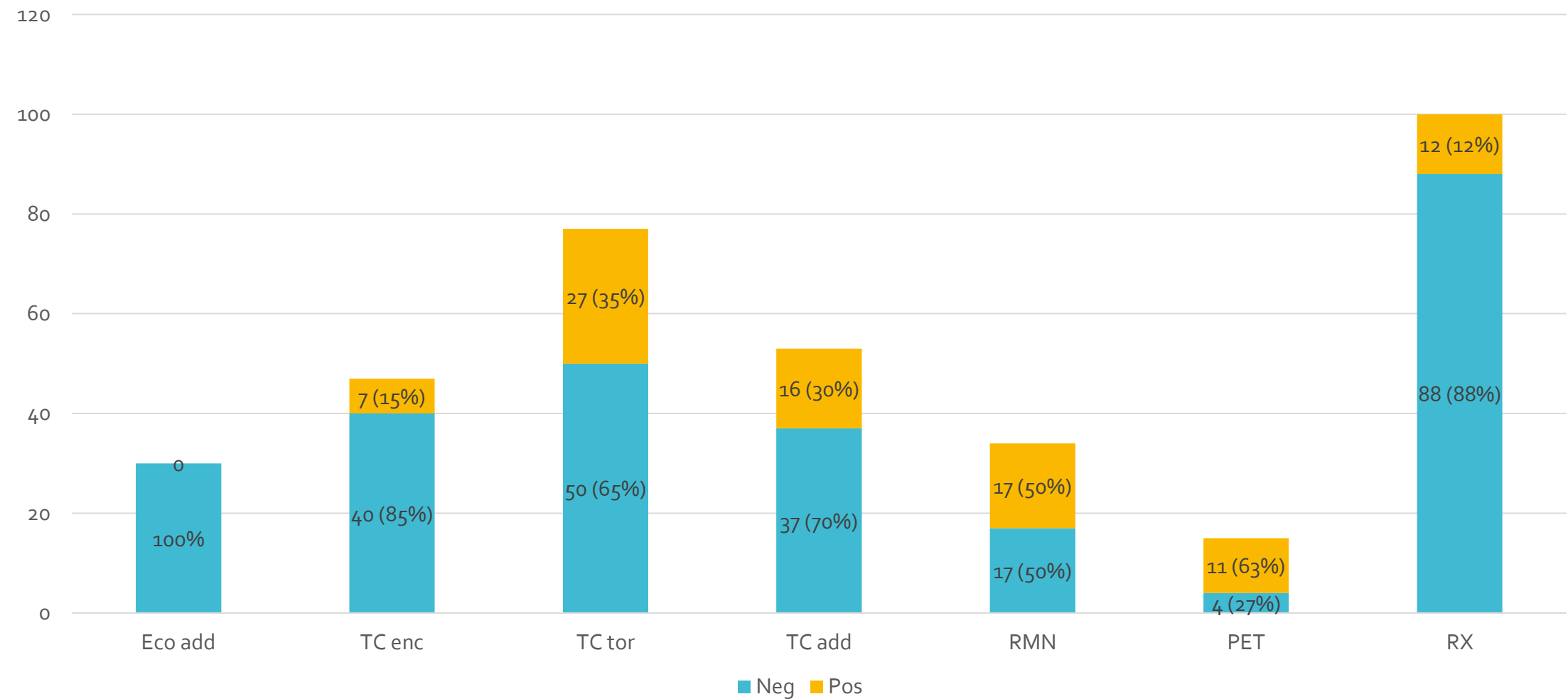
MIC vanco: non-pers



MIC vanco: pers



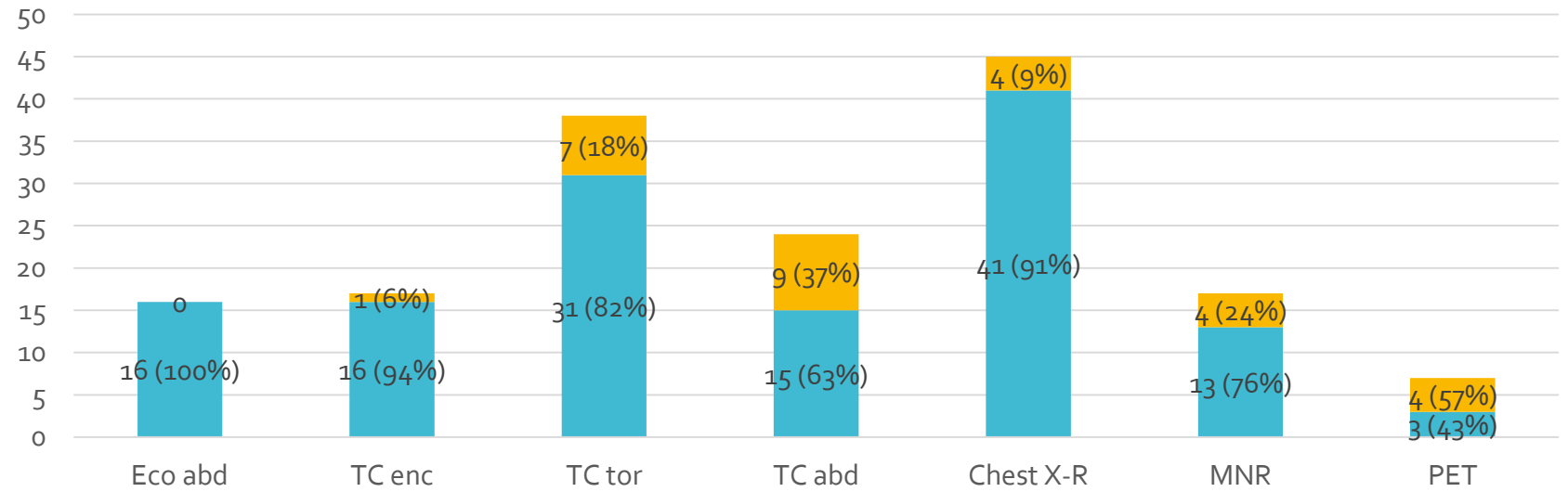
Imaging: overall





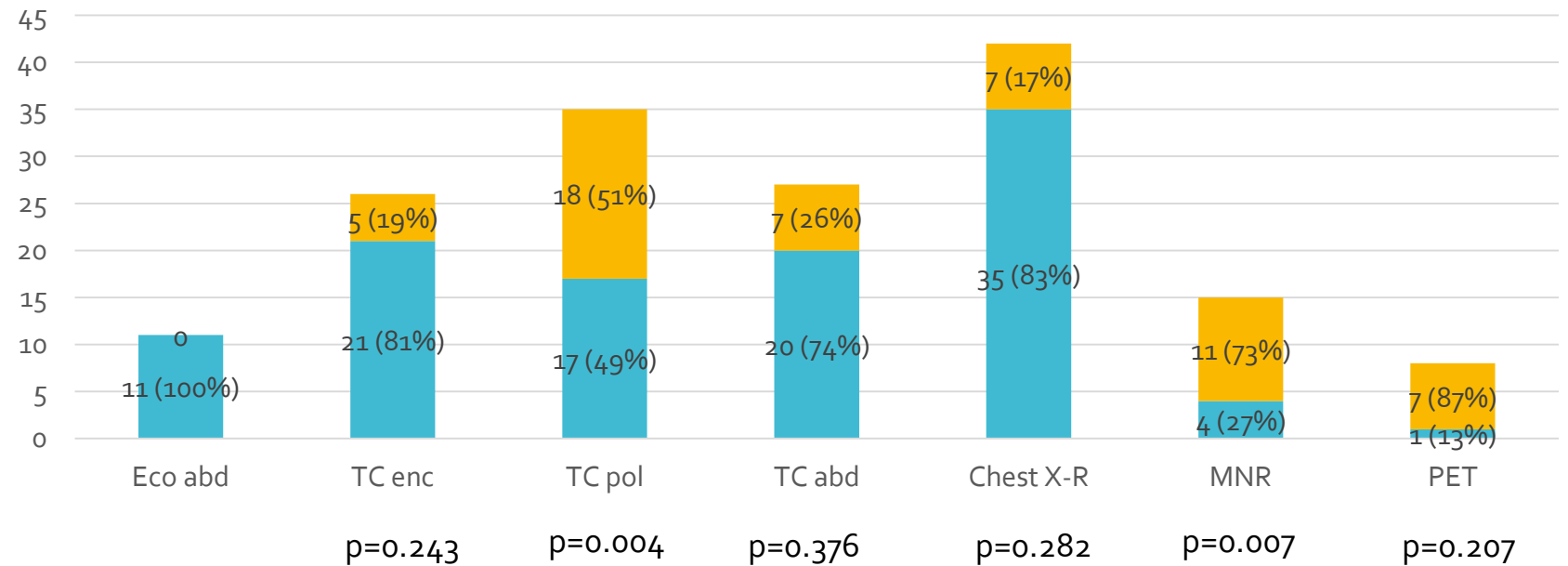
Imaging: non-persistent

Neg Pos



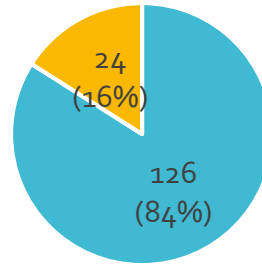
Imaging: persistent

Neg Pos



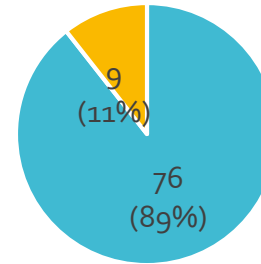
Ecocardiography

EcoTT: overall



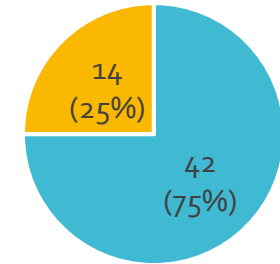
■ Neg ■ Pos

EcoTT: non-pers



■ Neg ■ Pos

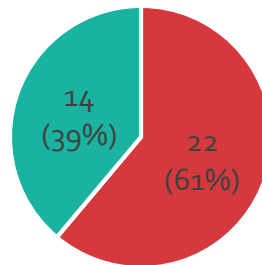
EcoTT: pers



■ Neg ■ Pos

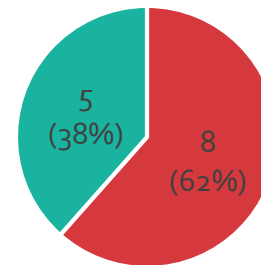
p=0.027

EcoTE: overall



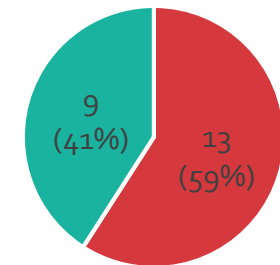
■ Neg ■ Pos

EcoTE: non-pers



■ Neg ■ Pos

EcoTE: pers

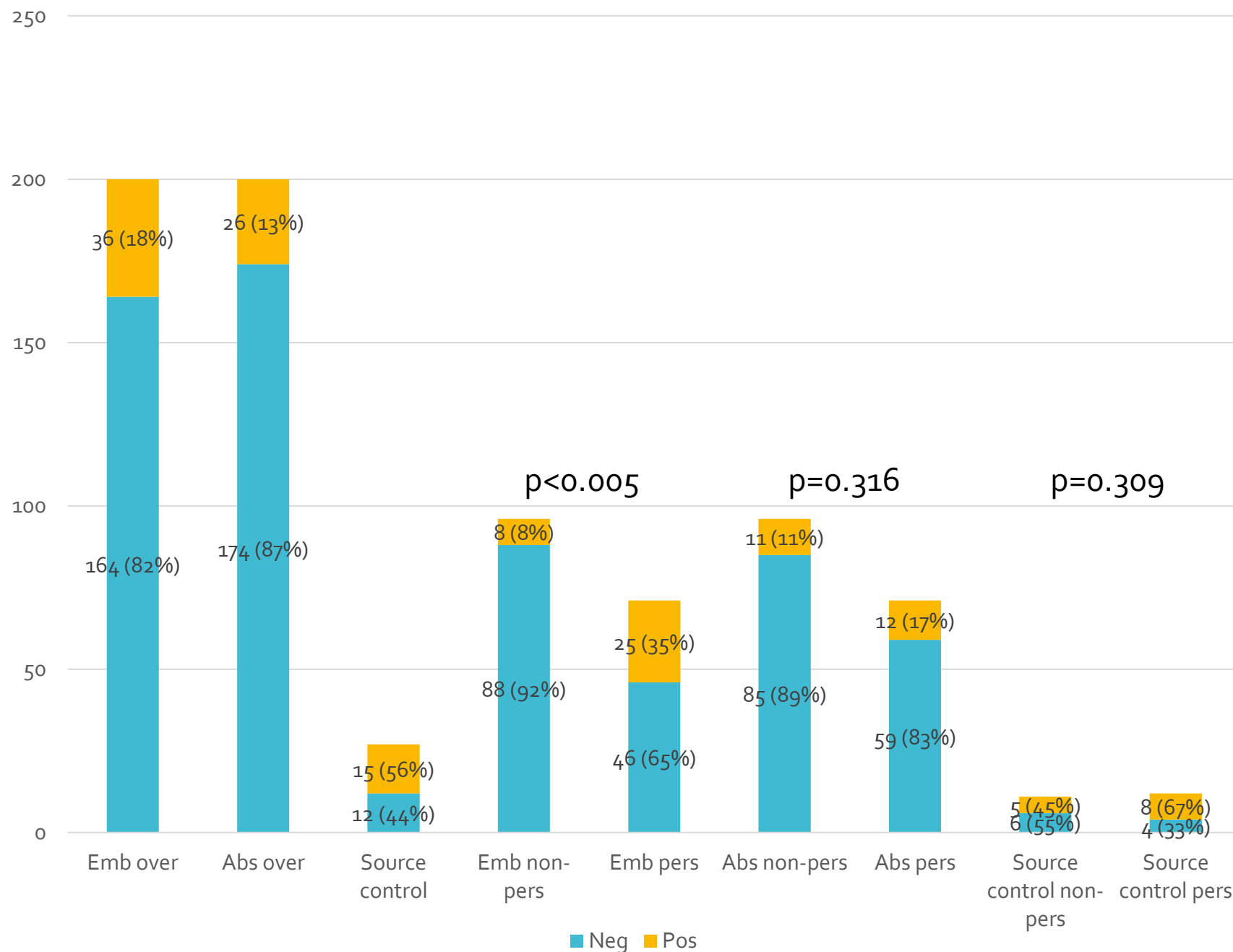


■ Neg ■ Pos

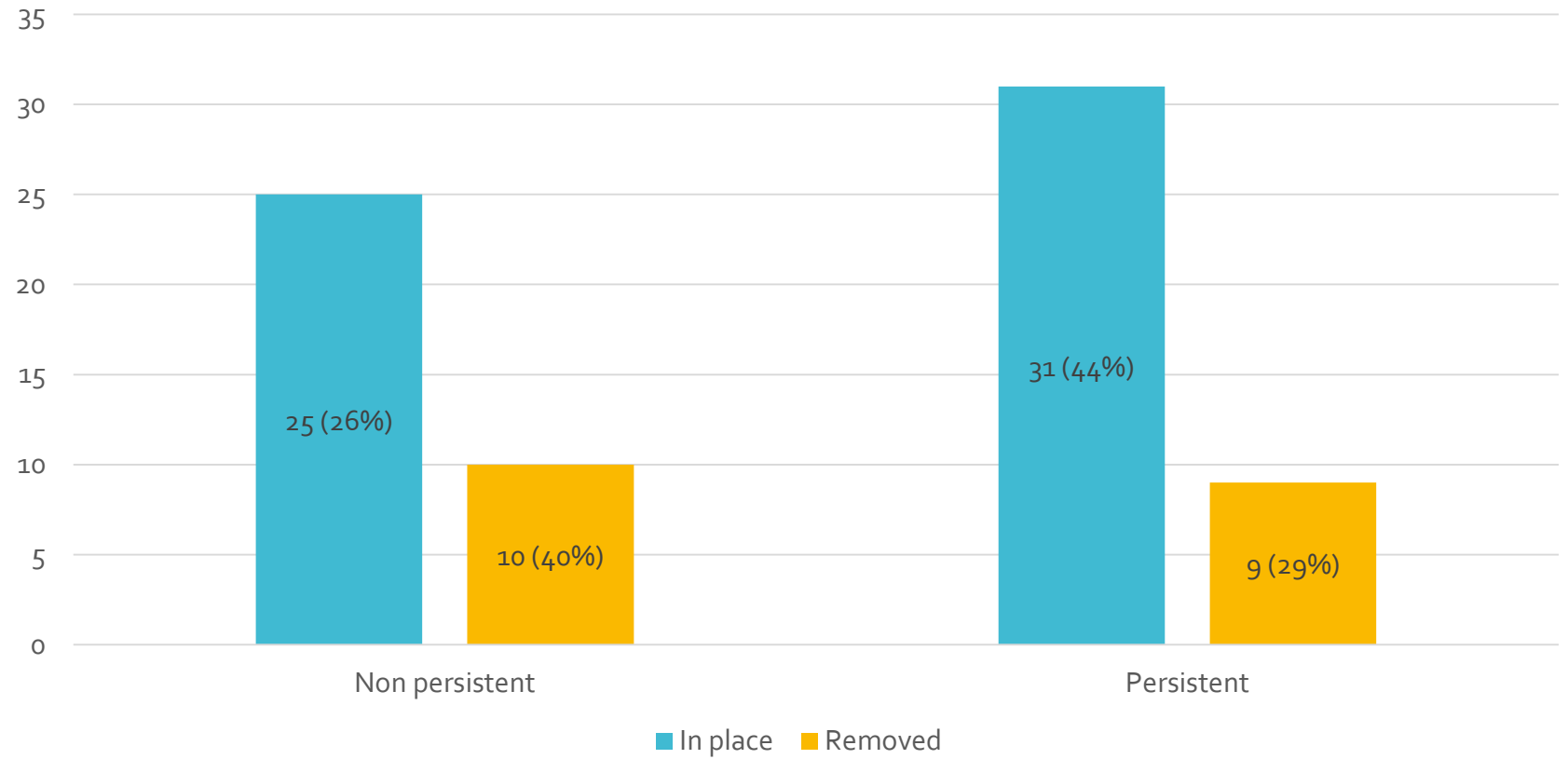
p=0.886

Secondary localization

Secondary localization

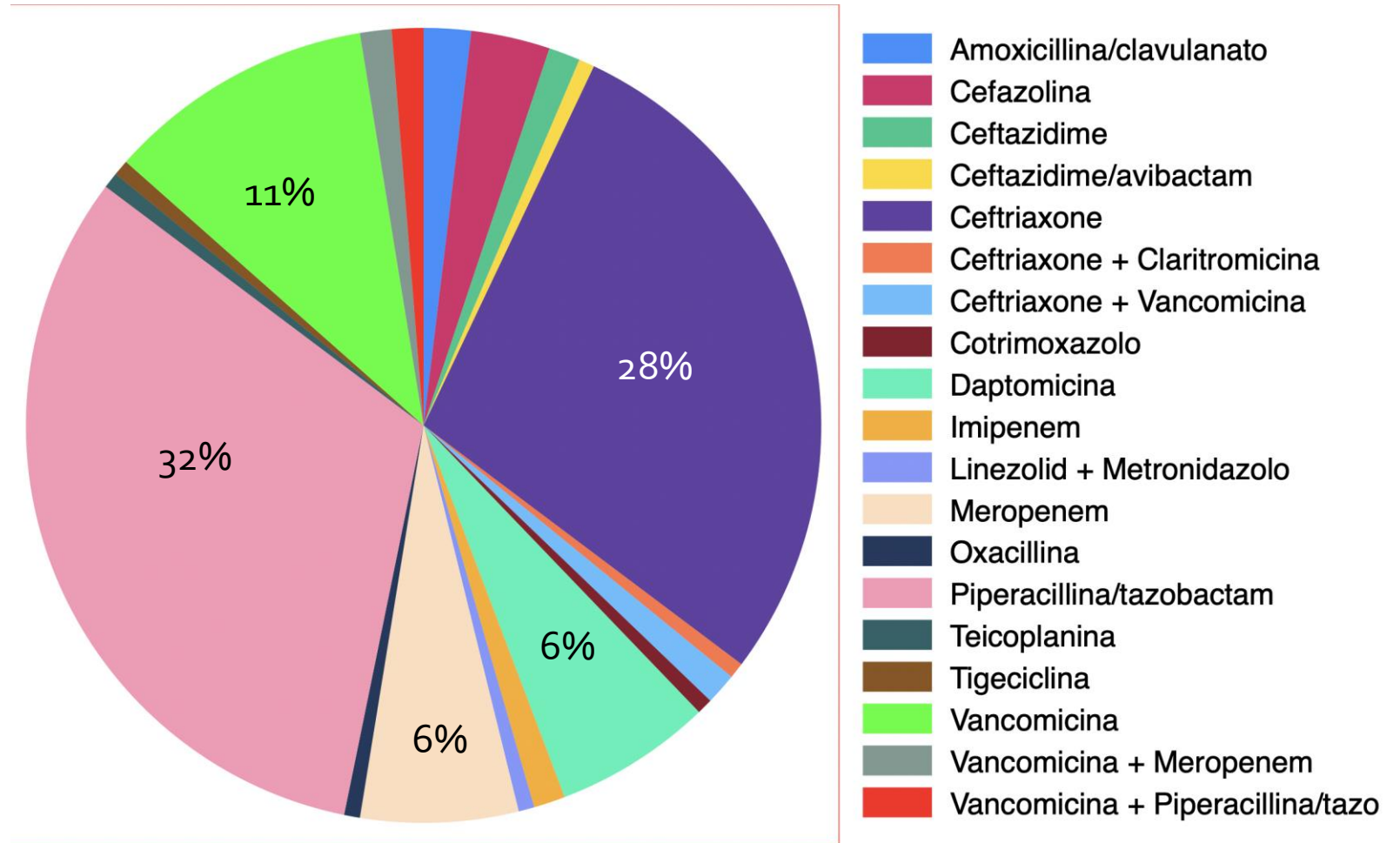


CVC



OR 2.16 (present vs not present), 95%C.I.: 1.12 – 4.17, p=0.022

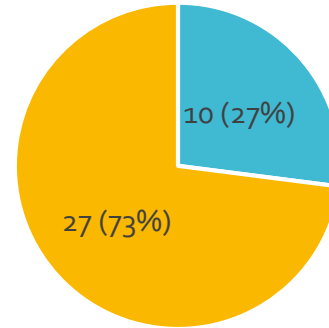
Empiric Therapy



Empiric Therapy

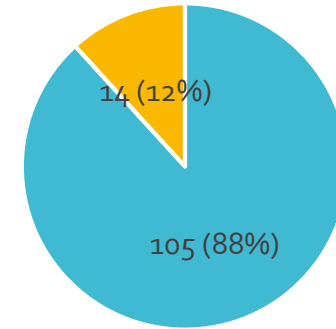
Adequacy of empiric treatment

Inadequate empiric therapy



■ MSSA ■ MRSA

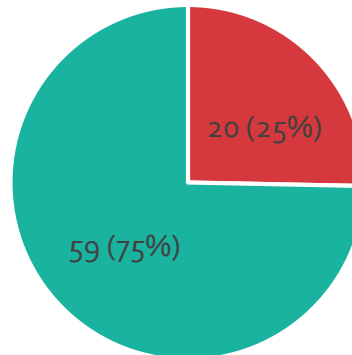
Adequate empiric therapy



■ MSSA ■ MRSA

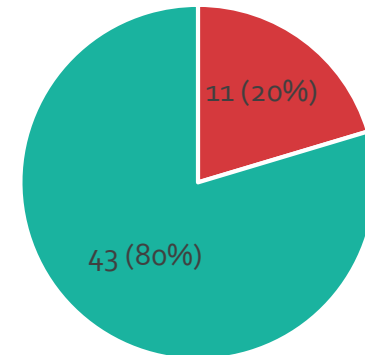
$p < 0.005$

Non persistent



■ Inadequate ■ Adequate

Persistent

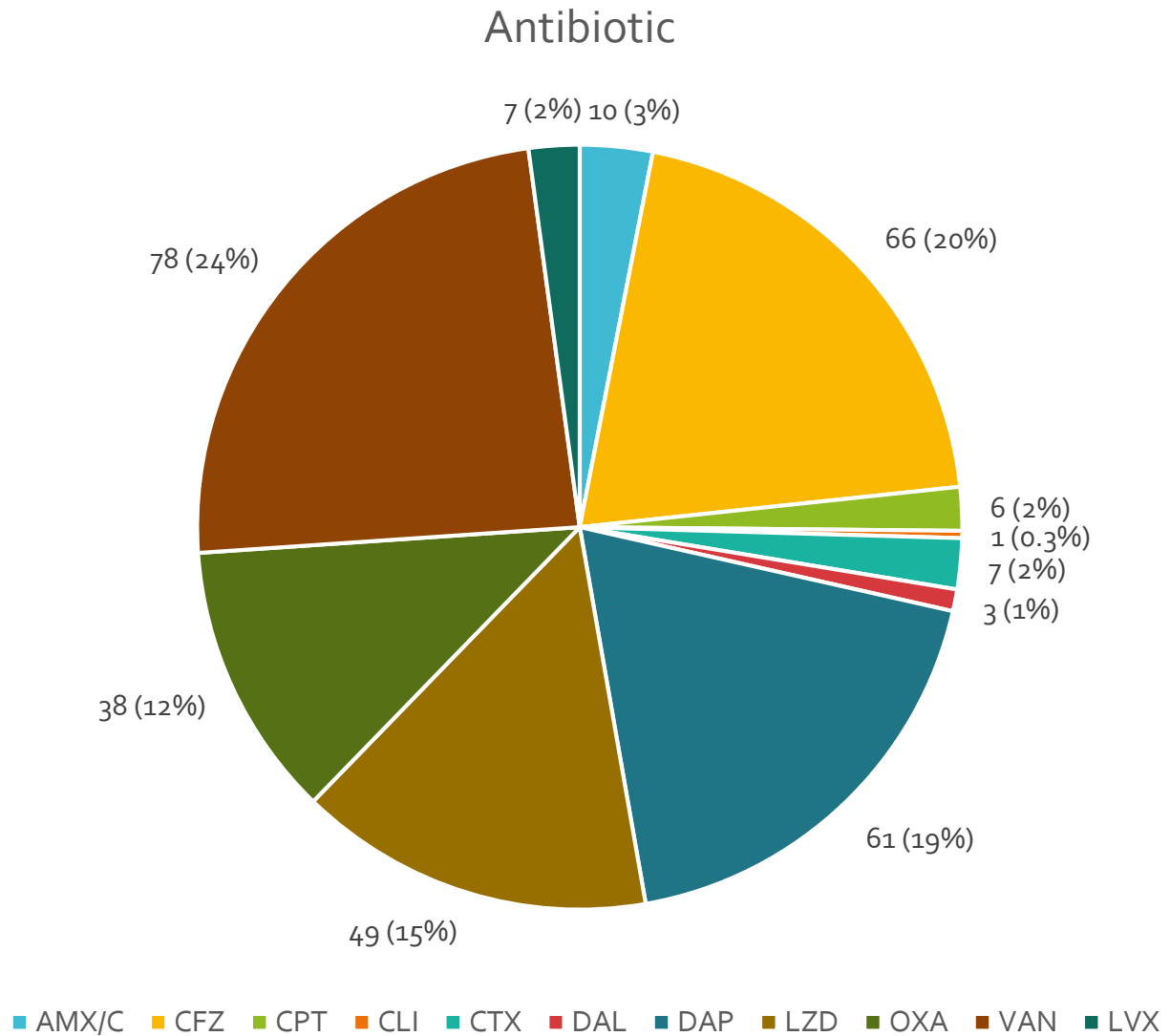


■ Inadequate ■ Adequate

$p = 0.580$

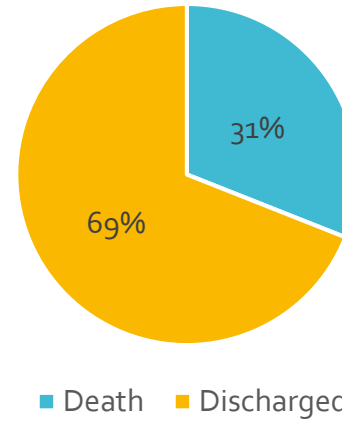
Targeted Therapy

Anti-Staphylococcus therapy

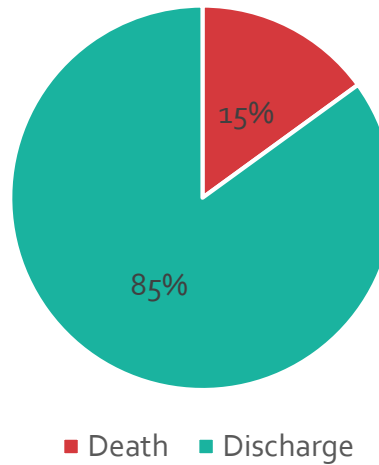


In-hospital mortality

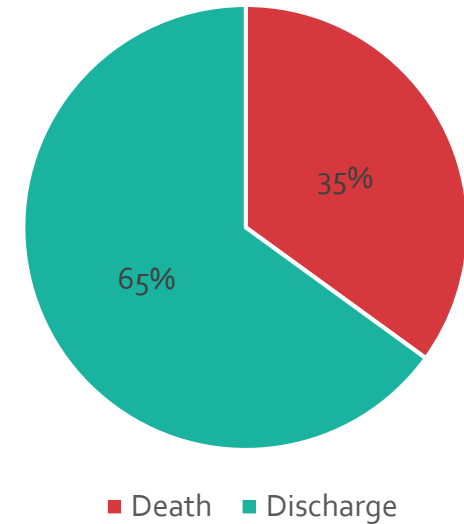
In hospital mortality: overall



In-hospital mortality: non-persistent



In-hospital mortality: persistent



O.R. 3.18 (persistent vs non persistent SAB) (C.I. 95%: 1.51-6.72), $p=0.002$

Factors associated with persistent SAB	OR	95%C.I.	p
Endovascular device	1.80	0.85 – 3.83	0.124
Dyalisis	1.94	0.77 – 4.90	0.159
Orthopedic device	0.65	0.16 – 2.71	0.559
Origin of BSI:			
- Primary	0.95	0.51 – 1.78	0.877
- Pulmonary	0.37	0.08 – 1.83	0.222
- Venous	1.55	0.82 – 2.92	0.174
- ABSSSI	1.02	0.34 – 3.07	0.978
- Bone	1.09	0.28 – 4.20	0.904
Presence of CVC	2.16	1.12 – 4.17	0.022
Removal of CVC in 72h	0.50	0.15 – 1.58	0.236
MRSA BSI	0.90	0.47 – 1.73	0.749
Polimicrobial BSI	0.89	0.37 – 2.11	0.783

Factors associated with persistent SAB	O.R.	95% I.C.	p
Positive ecoTT	2.81	1.12 – 7.05	0.027
Positive ecoTE	1.11	0.27 - 4.51	0.886
Diagnostic:			
- Positive enc CT	3.81	0.40 – 35.90	0.243
- Positive pul CT	4.69	1.63 – 13.46	0.004
- Positive abd CT	0.58	0.18 – 1.92	0.376
- Positive MNR	8.94	1.80 – 44.34	0.007
- Positive PET	5.25	0.40 – 68.95	0.207
- Positive chest X-ray	2.05	0.55 – 7.59	0.282
Embolization (at least one septic embolization):	5.98	2.50 – 14.30	<0.005
- Pulmonary	9.55	1.02 – 89.22	0.05
Abscess	1.57	0.65 – 3.80	0.316
Source control	2.4	0.44 – 12.98	0.309
Adequate empiric therapy	1.33	0.58 – 3.05	0.508

Multivariate for mortality	aOR	95% C.I.	p
Persistent SAB	1.65	0.69 – 3.97	0.263
Presence of CVC	1.18	0.48 – 2.90	0.710
I.E.	1.81	0.63 – 5.17	0.268
Embolization	1.49	0.53 – 4.15	0.448

Multivariate for persistent SAB	aOR	95% C.I.	p
MRSA	1.78	0.66 – 4.84	0.255
Age	1	0.97 – 1.02	0.918
Community acquired	0.89	0.42 – 1.89	0.760
Adequate empiric therapy	1.91	0.64 – 5.70	0.245
Charlson score	0.95	0.80 – 1.13	0.595
Dyalisis	1.59	0.55 – 4.59	0.394
Presence of endovascular device	2.20	0.94 – 5.10	0.068

Conclusions

- Prevalence of persistent SAB at San Paolo Hospital: 43%
- At univariate analysis persistent SAB associated risk factors: presence of a CVC, embolization, presence of I.E.; not confirmed at multivariate
- Persistent SAB is associated with a higher mortality risk

Limitations

- Small sample size (only 71 persistent SAB for the moment)
- Retrospective study

Bibliography

1. Chong, Y. P., Park, S. J., Kim, H. S., Kim, E. S., Kim, M. N., Park, K. H., Kim, S. H., Lee, S. O., Choi, S. H., Jeong, J. Y., Woo, J. H., & Kim, Y. S. (2013). Persistent staphylococcus aureus bacteremia: A prospective analysis of risk factors, outcomes, and microbiologic and genotypic characteristics of isolates. *Medicine (United States)*, 92(2), 98–108. <https://doi.org/10.1097/MD.0b013e318289ff1e>
2. Fowler, V. G., Olsen, M. K., Corey, ; G Ralph, Woods, C. W., Cabell, C. H., Reller, ; L Barth, Cheng, A. C., Dudley, T., & Oddone, E. Z. (n.d.). Clinical Identifiers of Complicated Staphylococcus aureus Bacteremia. <https://jamanetwork.com/>
3. Fowler, V. G., Sanders, L. L., Sexton, D. J., Kong, L., Marr, K. A., Gopal, A. K., Gottlieb, G., Mcclelland, R. S., & Corey, G. R. (n.d.). Outcome of Staphylococcus aureus Bacteremia According to Compliance with Recommendations of Infectious Diseases Specialists: Experience with 244 Patients. <https://academic.oup.com/cid/article/27/3/478/280719>
4. Guimaraes, A. O., Cao, Y., Hong, K., Mayba, O., Peck, M. C., Gutierrez, J., Ruffin, F., Carrasco-Triguero, M., Dinoso, J. B., Clemenzi-Allen, A., Koss, C. A., Maskarinec, S. A., Chambers, H. F., Fowler, V. G., Baruch, A., & Rosenberger, C. M. (2019). A prognostic model of persistent bacteremia and mortality in complicated Staphylococcus aureus bloodstream infection. *Clinical Infectious Diseases*, 68(9), 1502–1511. <https://doi.org/10.1093/cid/ciy739>
5. Hawkins, C., Huang, J., Jin, N., Noskin, G. A., Zembower, T. R., & Bolon, M. (n.d.). Persistent Staphylococcus aureus Bacteremia An Analysis of Risk Factors and Outcomes. <https://jamanetwork.com/>
6. Holland, T. L., Bayer, A. S., & Fowler, V. G. (2022). Persistent MRSA Bacteremia: Resetting the Clock for Optimal Management. *Clinical Infectious Diseases*. <https://doi.org/10.1093/cid/ciac364>
7. Kathib, R., Johnson, L. B., Fakih, M. G., Riederer, K., Khosrovaneh, A., Tabriz, M. S., Sharma, M., & Saeed, S. (2006). Persistence in staphylococcus aureus bacteremia: Incidence, characteristics of patients and outcome. *Scandinavian Journal of Infectious Diseases*, 38(1), 7–14. <https://doi.org/10.1080/00365540500372846>
8. Kathib, R., Johnson, L. B., Sharma, M., Fakih, M. G., Ganga, R., & Riederer, K. (2009). Persistent Staphylococcus aureus bacteremia: Incidence and outcome trends over time. *Scandinavian Journal of Infectious Diseases*, 41(1), 4–9. <https://doi.org/10.1080/00365540802441711>
9. Khuel, R., Morata, L., Boeing, C., Subirana, I., Seifert, H., Rieg, S., Kern, W. V., Kim, H. Bin, Kim, E. S., Liao, C. H., Tilley, R., Lopez-Cortés, L. E., Llewelyn, M. J., Fowler, V. G., Thwaites, G., Cisneros, J. M., Scarborough, M., Nsutebu, E., Gurgui Ferrer, M., ... Price, J. (2020). Defining persistent Staphylococcus aureus bacteraemia: secondary analysis of a prospective cohort study. *The Lancet Infectious Diseases*, 20(12), 1409–1417. [https://doi.org/10.1016/S1473-3099\(20\)30447-3](https://doi.org/10.1016/S1473-3099(20)30447-3)
10. Lee, Y. M., Chong, Y. P., Kim, M., Eom, Y., Kim, E. S., Kim, M., Park, K. H., Kim, S. H., Lee, S. O., Choi, S. H., Woo, J. H., & Kim, Y. S. (2020). Long-term methicillin-resistant Staphylococcus aureus bacteremia persisting for more than 2 weeks: risk factors and outcomes. *European Journal of Clinical Microbiology and Infectious Diseases*, 39(4), 773–781. <https://doi.org/10.1007/s10096-019-03795-6>
11. Minejima, E., Mai, N., Bui, N., Mert, M., Mack, W. J., She, R. C., Nieberg, P., Spellberg, B., & Wong-Beringer, A. (2020). Defining the Breakpoint Duration of Staphylococcus aureus Bacteremia Predictive of Poor Outcomes. *Clinical Infectious Diseases*, 70(4), 566–573. <https://doi.org/10.1093/cid/ciz257>
12. H. S., Lee, H. S., Park, M. J., Kim, K. H., Kim, B. K., Wi, Y. M., & Kim, J. M. (2013). Predictors and clinical outcomes of persistent methicillin-resistant Staphylococcus aureus bacteremia: A prospective observational study. *Korean Journal of Internal Medicine*, 28(6), 678–686.