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A review of recommendations for infective endocarditis prevention in patients undergoing transcatheter aortic valve implantation

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Short running title: Infection control recommendations for TAVI

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Abstract

Infective endocarditis (IE) after transcatheter aortic valve implantation (TAVI) is a new disease entity. The rate of IE after TAVI is like that after surgical aortic valve replacement, but mortality and prevalence of *Enterococcus* spp. as causing pathogens are significantly higher. Guidelines on infection prevention measures before TAVI procedures are currently lacking. We performed a structured review of the available data to provide interim recommendations based on guidelines to prevent infections issued by the World Health Organisation as well as guidelines by professional societies from Europe and the United States. Such interim recommendations based on expert opinions are likely justified until large randomized trials provide the strong evidence for infection control in TAVI, because IE after TAVI is often related to the TAVI procedure itself and the mortality rate is high. Antibiotic prophylaxis should be adapted from an intravenous cephalosporin to e.g. amoxicillin/clavulanic acid to cover enterococci. In addition, infection control should follow operating room standards as far as reasonable, even if the evidence for this recommendation is very low. These recommendations are endorsed by the International Society for Cardiovascular Infectious Diseases (ISCVID).

Classification

Miscellaneous; No complication

Abbreviations

CDC: Centres for Disease Control & Prevention

CI: confidence interval

HEPA: high-efficiency particulate air

IE: infective endocarditis

IV: intravenous

OR: operating room

SAVR: surgical aortic valve replacement

TAVI: transcatheter aortic valve implantation

VRE: vancomycin-resistant enterococci

WHO: World Health Organisation

Introduction

Since the first-in-man implantation in 2002, transcatheter aortic valve implantation (TAVI) rapidly evolved to a standard procedure in the treatment of aortic valve stenosis. Initially, only elderly patients with multiple comorbidities at high-risk for surgical aortic valve replacement (SAVR) were treated with TAVI (1). Subsequently, TAVI was proven to be at least as effective as SAVR in intermediate and low risk patients, thereby increasing the number of patients undergoing TAVI (2, 3).

Infective endocarditis (IE) after TAVI was first reported in 2010 (4). The annual incidence varies between 0.2-3.4% in retrospective analyses and cohort studies, while a large international registry reported an incidence of 1.1% per person-year (95% CI 1.1-1.4), which is comparable with rates of IE after SAVR, despite larger wound surface and longer surgical procedure (1, 2, 5-11). However, due to the allocation of older patients with multiple comorbidities for TAVI, IE after TAVI is associated with a relevant impact on healthcare costs, morbidity and mortality. In-hospital and one-year mortality in IE after TAVI has been reported to be as high as 30-40% and up to 66%, respectively, which exceeds the rate of mortality in IE following SAVR (5, 8, 11-14). As TAVI is employed by using different access routes, relevant differences in the pathogen spectrum were reported when compared with IE after SAVR. In addition, the presence of multiple comorbidities, the higher age and the frequent healthcare contacts of patients with a TAVI prosthesis probably also contribute to the different pathogen spectrum (8, 15). Compared to native and prosthetic valve IE, where the most common pathogens are *Staphylococcus* spp. (more than 50%), followed by *Streptococcus* spp. (30%) and *Enterococcus* spp. (10%), IE after TAVI is dominantly caused by *Enterococcus* spp. in 25-30%, specifically in early infections within the first year of implantation, followed as well by *Staphylococcus* and *Streptococcus* spp. as causing pathogens (**Table 1)** (5-9, 12, 16, 17).

The World Health Organization (WHO) and professional societies, including the European Society of Cardiology, issued guidelines for the prevention of IE after SAVR (18-20). In contrast, similar published guidelines on infection prevention measures before a TAVI procedure are currently lacking. Cardiac surgery is generally performed in a well-designed operating room (OR) with highly filtrated

air, or sophisticated laminar air flow systems, with limited access for healthcare workers, standard surgical gowns and drapes, and well-trained OR nurses; standards that are currently not well defined for TAVI procedures. Therefore, we performed a structured review of the currently available data to provide interim recommendations for TAVI procedures. These recommendations are issued as interim recommendations since large randomized controlled clinical trials are lacking; observational studies may face serious bias since clinical practices vary widely between hospitals and countries. However, interim recommendations may be even more helpful in situations of uncertainty and harmonizing will allow for a more structured approach – such as is done in registries – to prevent procedure-associated infections including IE.

Risk factors for IE after TAVI

Independent associations for the risk of IE after TAVI were male gender, younger age as well as comorbidities including chronic kidney disease and diabetes mellitus (8, 10). Severe paravalvular aortic regurgitation, redo-procedures (including TAVI in a prior TAVI), a low TAVI implantation, that interferes with mitral valve closure and generates turbulences, high transvalvular gradients (>50 mmHg) as well as vascular access site complications were identified as procedure-related risk factors for IE after TAVI (7-9).

Guidelines for prevention of surgical site infection have been published by the WHO, Centers for Disease Control & Prevention (CDC) and professional medical societies (18, 21). They include a detailed description on the type of preparation of the surgical site using disinfectants, timing of antimicrobial prophylaxis and recommendations for the environment where SAVR is performed (18). The outbreak of *Mycobacterium chimaera* has recently challenged current cardiac theatre ventilation requirements since the pathogen was transmitted by the airborne route to the newly implanted heart valve (22). Among patients undergoing TAVI, *Enterococcus* spp. belong to the three most commonly isolated pathogens during IE (5-9, 12, 16, 17). The high prevalence of *Enterococcus* spp. might be explained by differences in the bacterial colonization between the chest for SAVR and the groin for TAVI, as currently more than 90% of TAVI procedures are employed using the femoral vascular

access (23, 24). However, the high enterococcal prevalence might also be due to the higher patient age and the presence of multiple comorbidities, predisposing to frequent healthcare contacts with antibiotic exposure leading to a change of the normal microbiological flora (8, 15). The current recommendation for antibiotic prophylaxis for TAVI has been adapted from SAVR routine and includes a cephalosporin focusing on the coverage of the most common pathogens in surgical site infection after cardiac surgery, namely *Staphylococcus* spp. However, cephalosporins are inherently not active against *Enterococcus* spp., which belong to the most commonly isolated pathogens from IE after TAVI (25). In addition, many TAVI procedures are performed in catheterization laboratories, outside of OR with clear requirements as for OR standards. Non-surgical staff (nurses and physicians) might not have necessarily being specifically trained for the higher risk for contamination during the procedure, as is well known from SAVR. Periprocedural inguinal skin disinfection hence might follow requirement for diagnostic cardiac procedures, possibly not to be sufficient for a long-term implant. In fact, the level of asepsis is more demanding in implant surgery, than e.g. in abdominal surgery. Alcoholic compounds with chlorhexidine or povidone-iodine are most effective, but these compounds may also be used without alcohol: The exposure time without alcohol increases to up to 10 minutes to be fully effective, a time, difficult to follow in a busy catheter laboratory and even worse in cases of emergencies. Ventilation does not appear to play a major role, since similar rates of IE are reported, irrespective whether TAVI was performed in a hybrid OR or in a catheterization laboratory (8, 12).

Interim infection control recommendations for the TAVI procedure

Infection control recommendations adapted from the OR should basically be followed, since IE complications are fatal in up to 40%, with the early period after the procedure being specifically at risk for infection. Implementation of these measures should be supervised e.g. by using a check list issued by WHO (**Table 2**) (19).

Infrastructure: Interventions are preferably performed in either designated catheter laboratories or hybrid OR, as available, lacking substantial evidence for the higher standards of an OR (8, 12). Standards for OR ventilation requirement differ from country to country, and industry standards also

have been applied, but 6 air changes per hour may be reasonable: Today, Cleanroom Standards - ISO 14644-1 with ISO class < 7, may be useful, but high-efficiency particulate air (HEPA) filter (Type HEPA13) have not been shown to decrease infection rate and therefore cannot be recommended at large. Traffic in the intervention rooms should be kept to a minimum, doors closed and noise reduced (26). The exposure time to ambient air of the unpacked TAVI prosthesis should be minimally short to avoid contamination, therefore, unpacking is recommended only immediately before the valve is inserted. Whenever possible an exposure time below 15 minutes should be targeted, extrapolated from data generated from orthopaedic surgery and animal experiments (27). Airborne pathogens can result in contamination of the valve, as observed during open heart surgery with *M. chimaera*, where the pathogen originated from the ventilator of the computer of the heater-cooler system (22).

Patients: An elective TAVI procedure should be postponed if the patient suffers from an active even remote source of infection, e.g. urosepsis, pneumonia or venous catheter infection, since remote infections are a risk factor for infection of any device to be implanted (28). Patient preparation includes whole body showering preferably with chlorhexidine soap before the intervention. We suggest to inform the patient on the option of decolonization from *Staphylococcus aureus* with nasal mupirocin ointment for 5 days, based on recommendations from WHO for SAVR, if the patient is known to be a *S. aureus* carrier or has a body mass index >30 kg/m2 and suffers from diabetes mellitus (19, 29). Clipping instead of shaving should be used, if hair removal is considered necessary (19). Periinterventional skin disinfection should be performed according to surgical standards with three applications of an alcohol-based disinfectant with a remanent supplement such as chlorhexidine or povidone-iodine following the manufacturer's recommendation. Since *Enterococcus* spp. dominate in IE after TAVI, the commonly recommended antibiotic prophylaxis with an intravenous (IV) cephalosporin (cefazolin or cefuroxime) fails to cover for one of the most common pathogen in IE after TAVI, therefore antimicrobial prophylaxis should be switched to an antibiotic covering enterococci, e.g. IV amoxicillin/clavulanic acid 2.2 grams (single dose) 0-120 minutes (preferably 0-60 minutes) before intervention (18). In cases where the TAVI procedure takes longer than two hours, a second dose of IV amoxicillin/clavulanic acid 2.2 grams should be administered (25). Intravenous

vancomycin (15 mg/kg) or teicoplanin (9-12 mg/kg) are alternatives if the patient is known to be allergic to penicillin or colonized with penicillin-resistant *Enterococcus* spp. or methicillin-resistant *S. aureus*. Vancomycin should be infused slowly and preferably 2 hours prior to intervention to reach high enough tissue drug levels at the time of arterial puncture and to avoid the "red-man-syndrome" (30). When using a glycopeptide in settings with a high prevalence of methicillin-resistant staphylococci, a first- or second-generation cephalosporin (e.g. cefazolin 2 grams or cefuroxime 1.5 grams) is preferably added. If vancomycin-resistant enterococci (VRE) are highly prevalent, IV daptomycin (≥ 10 mg/kg) is one option or teicoplanin in case of VRE VanB.

Staff: All staff members having contact with either the sterile operation/intervention field or being directly involved in crimping the TAVI prosthesis must perform surgical hand hygiene, wear sterile gowns and gloves in addition to a surgical hood and mask, recommendations taken from OR guidelines although they lack strong evidence. All health care professionals handling the TAVI prosthesis preferably change to a new pair of sterile gloves before having contact with it since gloves can get rapidly contaminated in 10-30% either during surgery when preparing the vascular access or while unpacking the TAVI prosthesis.

In addition, every patient should be instructed about personal measures to prevent IE after TAVI, including the compliance with strict dental hygiene and with non-specific prevention measures such as no self-medication with antibiotics in case of fever, the renouncement of piercing and tattooing and the timely limitation of intravascular catheters. Furthermore, patients with a TAVI prosthesis should receive an endocarditis prophylaxis document describing prophylactic antibiotic use in different medical interventions such as dental, gastrointestinal, urogenital and infected skin interventions (20).

Conclusion

IE after TAVI is a new disease entity which is associated with high rates of morbidity and mortality. The rate of IE after TAVI is like that after SAVR, but *Enterococcus* spp. are three times more

common in IE after TAVI. Therefore, antibiotic prophylaxis prior to inserting TAVI should be changed from an IV cephalosporin to e.g. IV amoxicillin/clavulanic acid or an alternative if patient is allergic or colonized with resistant pathogens. Prosthetic heart valves, including TAVI, are most likely contaminated during the procedure, therefore, prevention should follow OR recommendations as far as reasonable, even if the evidence for this recommendation is very low. The high mortality in IE after TAVI likely justifies interim recommendations for implanting TAVI based on expert opinions until large randomized trials provide the strong evidence for infection control in TAVI.

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References

1. Mack MJ, Leon MB, Smith CR, Miller DC, Moses JW, Tuzcu EM, Webb JG, Douglas PS, Anderson WN, Blackstone EH, Kodali SK, Makkar RR, Fontana GP, Kapadia S, Bavaria J, Hahn RT, Thourani VH, Babaliaros V, Pichard A, Herrmann HC, Brown DL, Williams M, Akin J, Davidson MJ, Svensson LG, investigators Pt. 5-year outcomes of transcatheter aortic valve replacement or surgical aortic valve replacement for high surgical risk patients with aortic stenosis (PARTNER 1): a randomised controlled trial. *Lancet*. 2015;385:2477-84.

2. Leon MB, Smith CR, Mack MJ, Makkar RR, Svensson LG, Kodali SK, Thourani VH, Tuzcu EM, Miller DC, Herrmann HC, Doshi D, Cohen DJ, Pichard AD, Kapadia S, Dewey T, Babaliaros V, Szeto WY, Williams MR, Kereiakes D, Zajarias A, Greason KL, Whisenant BK, Hodson RW, Moses JW, Trento A, Brown DL, Fearon WF, Pibarot P, Hahn RT, Jaber WA, Anderson WN, Alu MC, Webb JG, Investigators P. Transcatheter or surgical aortic valve replacement in intermediate-risk patients. *N Engl J Med*. 2016;374:1609-20.

3. Mack MJ, Leon MB, Thourani VH, Makkar R, Kodali SK, Russo M, Kapadia SR, Malaisrie SC, Cohen DJ, Pibarot P, Leipsic J, Hahn RT, Blanke P, Williams MR, McCabe JM, Brown DL, Babaliaros V, Goldman S, Szeto WY, Genereux P, Pershad A, Pocock SJ, Alu MC, Webb JG, Smith CR, Investigators P, the PI. Transcatheter aortic valve replacement with a balloon-expandable valve in low-risk patients. *N Engl J Med*. 2019;380:1695-705.

4. Carnero-Alcazar M, Maroto Castellanos LC, Carnicer JC, Rodriguez Hernandez JE. Transapical aortic valve prosthetic endocarditis. *Interact Cardiovasc Thorac Surg*. 2010;11:252-3.

5. Pericas JM, Llopis J, Cervera C, Sacanella E, Falces C, Andrea R, Garcia de la Maria C, Ninot S, Vidal B, Almela M, Pare JC, Sabate M, Moreno A, Marco F, Mestres CA, Miro JM, Hospital Clinic Endocarditis Study G. Infective endocarditis in patients with an implanted

transcatheter aortic valve: Clinical characteristics and outcome of a new entity. *J Infect*. 2015;70:565-76.

6. Latib A, Naim C, De Bonis M, Sinning JM, Maisano F, Barbanti M, Parolari A, Lorusso R, Testa L, Actis Dato GM, Miceli A, Sponga S, Rosato F, De Vincentiis C, Werner N, Fiorina C, Bartorelli A, Di Gregorio O, Casilli F, Muratori M, Alamanni F, Glauber M, Livi U, Nickenig G, Tamburino C, Alfieri O, Colombo A. TAVR-associated prosthetic valve infective endocarditis: results of a large, multicenter registry. *J Am Coll Cardiol*. 2014;64:2176-8.

7. Olsen NT, De Backer O, Thyregod HG, Vejlstrup N, Bundgaard H, Sondergaard L, Ihlemann N. Prosthetic valve endocarditis after transcatheter aortic valve implantation. *Circ Cardiovasc Interv*. 2015;8:1-9.

8. Regueiro A, Linke A, Latib A, Ihlemann N, Urena M, Walther T, Husser O, Herrmann HC, Nombela-Franco L, Cheema AN, Le Breton H, Stortecky S, Kapadia S, Bartorelli AL, Sinning JM, Amat-Santos I, Munoz-Garcia A, Lerakis S, Gutierrez-Ibanes E, Abdel-Wahab M, Tchetche D, Testa L, Eltchaninoff H, Livi U, Castillo JC, Jilaihawi H, Webb JG, Barbanti M, Kodali S, de Brito FS, Jr., Ribeiro HB, Miceli A, Fiorina C, Dato GM, Rosato F, Serra V, Masson JB, Wijeysundera HC, Mangione JA, Ferreira MC, Lima VC, Carvalho LA, Abizaid A, Marino MA, Esteves V, Andrea JC, Giannini F, Messika-Zeitoun D, Himbert D, Kim WK, Pellegrini C, Auffret V, Nietlispach F, Pilgrim T, Durand E, Lisko J, Makkar RR, Lemos PA, Leon MB, Puri R, San Roman A, Vahanian A, Sondergaard L, Mangner N, Rodes-Cabau J. Association between transcatheter aortic valve replacement and subsequent infective endocarditis and in-hospital death. *JAMA*. 2016;316:1083-92.

9. Kolte D, Goldsweig A, Kennedy KF, Abbott JD, Gordon PC, Sellke FW, Ehsan A, Sodha N, Sharaf BL, Aronow HD. Comparison of incidence, predictors, and outcomes of early

infective endocarditis after transcatheter aortic valve implantation versus surgical aortic valve replacement in the United States. *Am J Cardiol*. 2018;122:2112-9.

10. Butt JH, Ihlemann N, De Backer O, Sondergaard L, Havers-Borgersen E, Gislason GH, Torp-Pedersen C, Kober L, Fosbol EL. Long-term risk of infective endocarditis after transcatheter aortic valve replacement. *J Am Coll Cardiol*. 2019;73:1646-55.

11. Moriyama N, Laakso T, Biancari F, Raivio P, Jalava MP, Jaakkola J, Dahlbacka S, Kinnunen EM, Juvonen T, Husso A, Niemela M, Ahvenvaara T, Tauriainen T, Virtanen M, Maaranen P, Eskola M, Rosato S, Makikallio T, Savontaus M, Valtola A, Anttila V, Airaksinen J, Laine M. Prosthetic valve endocarditis after transcatheter or surgical aortic valve replacement with a bioprosthesis: results from the FinnValve Registry. *EuroIntervention*. 2019.

12. Amat-Santos IJ, Messika-Zeitoun D, Eltchaninoff H, Kapadia S, Lerakis S, Cheema AN, Gutierrez-Ibanes E, Munoz-Garcia AJ, Pan M, Webb JG, Herrmann HC, Kodali S, Nombela-Franco L, Tamburino C, Jilaihawi H, Masson JB, de Brito FS, Jr., Ferreira MC, Lima VC, Mangione JA, Iung B, Vahanian A, Durand E, Tuzcu EM, Hayek SS, Angulo-Llanos R, Gomez-Doblas JJ, Castillo JC, Dvir D, Leon MB, Garcia E, Cobiella J, Vilacosta I, Barbanti M, R RM, Ribeiro HB, Urena M, Dumont E, Pibarot P, Lopez J, San Roman A, Rodes-Cabau J. Infective endocarditis after transcatheter aortic valve implantation: results from a large multicenter registry. *Circulation*. 2015;131:1566-74.

13. Mangner N, Leontyev S, Woitek FJ, Kiefer P, Haussig S, Binner C, Mende M, Schlotter F, Stachel G, Hollriegel R, Hommel J, Binner-Oussenek K, Misfeld M, Thiele H, Borger MA, Holzhey D, Linke A. Cardiac Surgery Compared With Antibiotics Only in Patients Developing Infective Endocarditis After Transcatheter Aortic Valve Replacement. *J Am Heart Assoc*. 2018;7:e010027.

14. Lalani T, Chu VH, Park LP, Cecchi E, Corey GR, Durante-Mangoni E, Fowler VG, Jr., Gordon D, Grossi P, Hannan M, Hoen B, Munoz P, Rizk H, Kanj SS, Selton-Suty C, Sexton DJ, Spelman D, Ravasio V, Tripodi MF, Wang A, International Collaboration on Endocarditis-Prospective Cohort Study I. In-hospital and 1-year mortality in patients undergoing early surgery for prosthetic valve endocarditis. *JAMA Intern Med*. 2013;173:1495-504.

15. Oliver L, Lavoute C, Giorgi R, Salaun E, Hubert S, Casalta JP, Gouriet F, Renard S, Saby L, Avierinos JF, Maysou LA, Riberi A, Grisoli D, Casalta AC, Collart F, Raoult D, Habib G. Infective endocarditis in octogenarians. *Heart*. 2017;103:1602-9.

16. Mangner N, Woitek F, Haussig S, Schlotter F, Stachel G, Hollriegel R, Wilde J, Lindner A, Holzhey D, Leontyev S, Mohr FW, Schuler G, Linke A. Incidence, predictors, and outcome of patients developing infective endocarditis following transfemoral transcatheter aortic valve replacement. *J Am Coll Cardiol*. 2016;67:2907-8.

17. Slipczuk L, Codolosa JN, Davila CD, Romero-Corral A, Yun J, Pressman GS, Figueredo VM. Infective endocarditis epidemiology over five decades: a systematic review. *PLoS One*. 2013;8:1-17.

18. Allegranzi B, Zayed B, Bischoff P, Kubilay NZ, de Jonge S, de Vries F, Gomes SM, Gans S, Wallert ED, Wu X, Abbas M, Boermeester MA, Dellinger EP, Egger M, Gastmeier P, Guirao X, Ren J, Pittet D, Solomkin JS, Group WHOGD. New WHO recommendations on intraoperative and postoperative measures for surgical site infection prevention: an evidence-based global perspective. *Lancet Infect Dis*. 2016;16:e288-e303.

19. WHO. Global guidelines on the prevention of surgical site infection, from World Health Organisation. https://www.who.int/gpsc/ssi-prevention-guidelines/en2016 [

20. Habib G, Lancellotti P, Antunes MJ, Bongiorni MG, Casalta JP, Del Zotti F, Dulgheru R, El Khoury G, Erba PA, Iung B, Miro JM, Mulder BJ, Plonska-Gosciniak E, Price S, Roos-

Hesselink J, Snygg-Martin U, Thuny F, Tornos Mas P, Vilacosta I, Zamorano JL, Group ESCSD. 2015 ESC Guidelines for the management of infective endocarditis: The Task Force for the Management of Infective Endocarditis of the European Society of Cardiology (ESC). Endorsed by: European Association for Cardio-Thoracic Surgery (EACTS), the European Association of Nuclear Medicine (EANM). *Eur Heart J*. 2015;36:3075-128.

21. Berrios-Torres SI, Umscheid CA, Bratzler DW, Leas B, Stone EC, Kelz RR, Reinke CE, Morgan S, Solomkin JS, Mazuski JE, Dellinger EP, Itani KMF, Berbari EF, Segreti J, Parvizi J, Blanchard J, Allen G, Kluytmans J, Donlan R, Schecter WP, Healthcare Infection Control Practices Advisory C. Centers for Disease Control and Prevention guideline for the prevention of surgical site infection, 2017. *JAMA Surg*. 2017;152:784-91.

22. Kuehl R, Banderet F, Egli A, Keller PM, Frei R, Dobele T, Eckstein F, Widmer AF. Different types of heater-cooler units and their risk of transmission of Mycobacterium chimaera during open-heart surgery: Clues from device design. *Infect Control Hosp Epidemiol*. 2018;39:834-40.

23. Stortecky S, Franzone A, Heg D, Tueller D, Noble S, Pilgrim T, Jeger R, Toggweiler S, Ferrari E, Nietlispach F, Taramasso M, Maisano F, Grunenfelder J, Muller O, Huber C, Roffi M, Carrel T, Wenaweser P, Windecker S. Temporal trends in adoption and outcomes of transcatheter aortic valve implantation: a Swisstavi Registry analysis. *Eur Heart J Qual Care Clin Outcomes*. 2018:1-10.

24. Beezhold DW, Slaughter S, Hayden MK, Matushek M, Nathan C, Trenholme GM, Weinstein RA. Skin colonization with vancomycin-resistant enterococci among hospitalized patients with bacteremia. *Clin Infect Dis*. 1997;24:704-6.

25. Sommerstein R, Atkinson A, Kuster SP, Thurneysen M, Genoni M, Troillet N, Marschall J, Widmer AF, Swissnoso. Antimicrobial prophylaxis and the prevention of surgical site

infection in cardiac surgery: an analysis of 21 007 patients in Switzerland. *Eur J Cardiothorac Surg*. 2019:1-7.

26. Roth JA, Juchler F, Dangel M, Eckstein FS, Battegay M, Widmer AF. Frequent door openings during cardiac surgery are associated with increased risk for surgical site infection: A prospective observational study. *Clin Infect Dis*. 2018:1-5.

27. Dalstrom DJ, Venkatarayappa I, Manternach AL, Palcic MS, Heyse BA, Prayson MJ. Time-dependent contamination of opened sterile operating-room trays. *J Bone Joint Surg Am*. 2008;90:1022-5.

28. Ban KA, Minei JP, Laronga C, Harbrecht BG, Jensen EH, Fry DE, Itani KM, Dellinger EP, Ko CY, Duane TM. American College of Surgeons and Surgical Infection Society: Surgical Site Infection Guidelines, 2016 Update. *J Am Coll Surg*. 2017;224:59-74.

29. Bode LG, Kluytmans JA, Wertheim HF, Bogaers D, Vandenbroucke-Grauls CM, Roosendaal R, Troelstra A, Box AT, Voss A, van der Tweel I, van Belkum A, Verbrugh HA, Vos MC. Preventing surgical-site infections in nasal carriers of Staphylococcus aureus. *N Engl J Med*. 2010;362:9-17.

30. Garey KW, Dao T, Chen H, Amrutkar P, Kumar N, Reiter M, Gentry LO. Timing of vancomycin prophylaxis for cardiac surgery patients and the risk of surgical site infections. *J Antimicrob Chemother*. 2006;58:645-50.

31. Bjursten H, Rasmussen M, Nozohoor S, Gotberg M, Olaison L, Ruck A, Ragnarsson S. Infective endocarditis after transcatheter aortic valve implantation: a nationwide study. *Eur Heart J*. 2019;40:3263-9.

Table 1: Microbiology of endocarditis after TAVI (in %) (5-9, 16, 31)

Pathogen	**Olsen n=18**	**Latib n=29**	**Pericas n=31**	**Amat-Santos n=53**	**Mangner n=55**	**Reguerio n=250**	**Kolte n=224**	**Bjursten n=103**
Enterococcus spp.	33	21	36	21	31	25	21	20
Staphylococcus aureus	22	14	6	21	38	23	22	22
Coagulase-negative staphylococci	11	17	19	24	9	17	8	7
Streptococcus spp.	33	14	13	6	4	7	30	34
Others*	1	34	26	28	18	28	19	17

*Including HACEK (*Haemophilus aphrophilus/paraphrophilus), Aggregatibacter actinomycetemcomitans, Cardiobacterium hominis, Eikenella corrodens, Kingella kingae*) and other gram-negative pathogens, *Cutibacterium* spp., *Corynebacterium* spp., *Lactobacillus* spp., *Candida* spp., polymicrobial infections, culture-negative infections

Table 2: Suggested infection control measures before TAVI procedure

Infrastructure	**Patient preparation**	**Staff**
Cardiac catheter laboratory or hybrid operating theatre	Shower with preferably chlorhexidine soap before the intervention If the patient is known to be a *S. aureus* carrier or has a body mass index >30 kg/m2 and suffers from diabetes mellitus, decolonization with nasal mupirocin ointment for 5 days may be considered	Surgical hand hygiene Sterile gown and gloves Surgical mask and hood
Clean room air	Hair removal with clipper before intervention if needed	Change gloves or remove outer gloves in "double gloving" before having contact with the unpacked TAVI prosthesis
Minimal traffic in cardiac catheter laboratory or hybrid operating theatre	Periinterventional skin disinfection according to surgical standards: Three applications of an alcohol-based disinfectant with a remanent supplement (e.g. chlorhexidine or povidone-iodine)	
Closed doors of cardiac catheter laboratory or hybrid operating theatre	Antimicrobial prophylaxis 0-120 minutes (preferably 0-60 minutes) before arterial puncture with a single dose[&] of e.g. IV amoxicillin/clavulanic acid[¥] 2.2 grams	
Minimal exposition time to ambient air of unpacked TAVI prosthesis [Ω]		

	Beta-lactam allergy or settings with a high prevalence of methicillin-resistant staphylococci [#]: single dose of IV vancomycin 15 mg/kg* or IV teicoplanin 9-12 mg/kg	

Abbreviation: IV, intravenous

[Ω] Whenever possible, an exposure time below 15 minutes should be targeted

[&] In case procedure takes longer than two hours, a second dose of IV amoxicillin/clavulanic acid 2.2 grams should be administered

[¥] Alternatively, single dose[&] of IV ampicillin/sulbactam 3 grams can be used

* Slow infusion time over one hour to avoid "red-man-syndrome", start two hours before intervention to reach high enough tissue drug levels at the time of TAVI

[#] When using a glycopeptide in settings with a high prevalence of methicillin-resistant staphylococci, a first- or second-generation cephalosporin (e.g. cefazolin 2 grams or cefuroxime 1.5 grams) is preferably added