Smoking and TAVR
J. James Edelman, MBBS(Hons), PhD; Vinod H. Thourani, MD

Smoking has long been associated with early onset and rapid progression of cardiovascular disease. Degenerative aortic stenosis (AS) is caused by mechanical and inflammatory factors; early in the disease it shares some similar pathological pathways to atherosclerosis where mechanical damage and endothelial injury is followed by lipid deposition, inflammatory cell infiltration, fibrosis, and calcification. Smoking is a dose-dependent risk factor for AS and has been associated with an increased rate of its progression. Smoking is also a cause of various comorbidities that increase the risk of treatment for aortic valve disease.

In this issue of the *Journal of the American Heart Association (JAH)*, Qintar and colleagues use the Society of Thoracic Surgeons/American College of Cardiology Transcatheter Valve Therapies Registry to describe differences in smokers and nonsmokers undergoing transcatheter aortic valve replacement (TAVR) for aortic stenosis (AS). The results of the current analysis are important and offer new insights into this population of patients. Smokers were younger and had a higher burden of both cardiovascular and noncardiovascular disease. While they had lower Society of Thoracic Surgeons predicted risk of mortality scores, smokers had other significant factors associated with surgical risk not captured by their Society of Thoracic Surgeons score (eg, a porcelain aorta). Moreover, smokers were more likely to require alternative, nontransfemoral TAVR access, because of increased peripheral artery disease. Although in-hospital mortality was not lower in nonsmokers in the unadjusted analysis, it was lower in the adjusted analysis. Surprisingly, the higher mortality in smokers at 1 year was no longer significant once adjustments were made for baseline characteristics. The authors suggest that the younger age of smokers helps give them a survival advantage in the periprocedural period, but in the long term this advantage is eroded by smoking’s associated comorbidities.

There remains concern about the impact of smoking on the potential for accelerated valve degeneration or increased rate of hypo-attenuated leaflet thickening. Smoking has been associated with a prothrombotic state because of impairment of fibrinolysis, which may influence the rate of hypo-attenuated leaflet thickening; however, there was no difference in the rate of smoking history in patients with and without hypo-attenuated leaflet thickening in 2 TAVR registries. Interestingly, in the current study, there is a small increase in early postoperative gradient in smokers, despite lower preoperative baseline left ventricular ejection fraction. Longer-term echocardiographic data in smokers who continue to smoke post-TAVR will be critical to ascertain whether this modifiable risk factor leads to accelerated structural valve deterioration.

This current analysis is the largest of its type evaluating the impact of smoking and TAVR performed to date, and the results broadly support those of 2 recently published smaller series. The concept of the “smokers’ paradox” has been reported in myocardial infarction, where smokers had lower mortality rates after ST-segment–elevation myocardial infarction. Though this result is mostly driven by their younger age at the time of event, other potential mechanisms included increased responsiveness of smokers to antiplatelet medications by induction of various cytochrome P450 enzymes. While smoking has not led to increased mortality in surgical aortic valve replacement, it does likely contribute to increased pulmonary complications and long-term mortality.

The benefits of smoking cessation in the months before pulmonary resection, but not other types of surgery, have been demonstrated. There remain many outstanding questions regarding the impact of preoperative smoking on patients with severe AS. This analysis does not clarify the reason why smokers undergoing TAVR presented at a younger age. Does smoking cause an earlier presentation of AS or were smokers less likely to be accepted for surgical intervention and treated by TAVR? It is likely that both mechanisms contribute to the younger age of smokers undergoing TAVR. The current
analysis does not report the rate of vascular complications in either group, which may be expected to be higher in smokers because of the increased proportion of patients with peripheral artery disease. There are no data as to whether smokers are less likely to have nonthoracic alternative access options, such as transcaval, subclavian, or carotid TAVR. Lastly, the importance (and efficacy) of smoking cessation strategies before and after TAVR, and their influence on long-term structural valve deterioration, remain unclear.

The Heart Team must recognize the importance of smoking as a risk factor for long-term prognosis after TAVR. The impact of smoking cessation strategies before and/or after TAVR has not been investigated, but may become more relevant once TAVR is approved for low-risk patients who are expected to live longer than the cohort of patients reported in this analysis of the Society of Thoracic Surgeons/American College of Cardiology Transcatheter Valve Therapies Registry.

Disclosures

Dr Thourani is an advisor and performs research for Abbott Vascular, Boston Scientific, Edwards Lifesciences, Gore Vascular, and JenaValve. Dr Edelman has no disclosures to report.

References

1. Ambrose JA, Barua RS. The pathophysiology of cigarette smoking and cardiovascular disease: an update. J Am Coll Cardiol. 2004;43:1731–1737.
2. Dweck MR, Boon NA, Newby DE. Calcific aortic stenosis. J Am Coll Cardiol. 2012;60:1854–1863.
3. Mohler ER III. Are atherosclerotic processes involved in aortic-valve calcification? Lancet. 2000;356:524–525.
4. Palta S, Pai AM, Gill KS, Pai RG. New insights into the progression of aortic stenosis: implications for secondary prevention. Circulation. 2000;101:2497–2502.
5. Larsson SC, Wolk A, Back M. Alcohol consumption, cigarette smoking and incidence of aortic valve stenosis. Int Med J. 2017;282:332–339.
6. Qintar M, Li Z, Vemulapalli S, Chhatriwalla AK, Baron SJ, Kosinski AS, Saxon JT, Spertus JA, Cohen DJ, Arnold SV. Association of smoking status with long-term mortality and health status after transcatheter aortic valve replacement: insights from the Society of Thoracic Surgeons/American College of Cardiology Transcatheter Valve Therapy Registry. J Am Heart Assoc. 2019;8:e011766. DOI: 10.1161/JAHA.118.011766.
7. Edelman JJ, Reddel CJ, Kritharides L, Bannon PG, Fraser IF, Curnow JL, Vallenty MP. Natural history of hypercoagulability in patients undergoing coronary revascularization and effect of preoperative myocardial infarction. J Thorac Cardiovasc Surg. 2014;148:536–543.
8. Makkar RR, Fontana G, Jilaihawi H, Chakravarty T, Kofoed KF, de Backer O, Asch FM, Ruiz CE, Olsen NT, Trento A, Friedman J, Beman D, Cheng W, Kashif M, Jelin V, Kilger CA, Guo H, Pichard AD, Weissman NJ, Kapadia S, Manasse E, Bhat DL, Leon MB, Sondergaard L. Possible subclinical leaflet thrombosis in bioprosthetic aortic valves. N Engl J Med. 2015;373:2015–2024.
9. Abawi M, Van Gils L, Agostoni P, Van Mieghem NM, Kooistra NHM, van Dongen CS, van Jaarsveld RC, de Jaegere PPT, Doevendans PAFM, Stella PR. Impact of baseline cigarette smoking status on clinical outcome after transcatheter aortic valve replacement. Catheter Cardiovasc Interv. 2019. Available at: https://onlinelibrary.wiley.com/doi/abs/10.1002/ccd.28175. Accessed August 13, 2019.
10. Agarwal M, Agrawal S, Garg L, Reed GL, Kouzam RN, Ibebuogu UN. Impact of smoking in patients undergoing transcatheter aortic valve replacement. Ann Transl Med. 2018;6:2.
11. Gupta T, Kolte D, Khera S, Harikrishnan P, Mujib M, Aronow WS, Jain D, Ahmen A, Cooper HA, Frishman WH, Bhatt DL, Fonarow GC, Panza JA. Smoker’s paradox in patients with ST-segment elevation myocardial infarction undergoing primary percutaneous coronary intervention. J Am Heart Assoc. 2016;5:e003370. DOI: 10.1161/JAHA.116.003370.
12. Yousuf A-M, Arafat T, Bulatova NR, Al-Zumyli R. Smoking behaviour modulates pharmacokinetics of orally administered clopidogrel. J Clin Pharm Ther. 2008;33:439–449.
13. Sharabiani MTA, Fiorentino F, Angelini GD, Patel NN. Long-term survival after surgical aortic valve replacement among patients over 65 years of age. Open Heart. 2016;3:e000338. DOI: 10.1136/openhrt-2015-000338.
14. Saxena A, Shan L, Dinh DT, Smith JA, Sharedy GC, Reid CM, Newcombe AE. Impact of smoking status on early and late outcomes after isolated aortic valve replacement surgery. J Heart Valve Dis. 2013;22:184–191.
15. Saxena A, Shan L, Dinh D, Reid C, Smith J, Sharady G, Newcomb A. Impact of smoking status on outcomes after concomitant aortic valve replacement and coronary artery bypass graft surgery. Thorac Cardiovasc Surg. 2014;62:052–059.
16. Myers K, Hajek P, Hinds C, McRobbie H. Stopping smoking shortly before surgery and postoperative complications: a systematic review and meta-analysis. Arch Intern Med. 2011;171:983–989.
17. Fukui M, Suzuki K, Matsunaga T, Oh S, Takamochi K. Importance of smoking cessation on surgical outcome in primary lung cancer. Ann Thorac Surg. 2019;107:1005–1009.

Key Words: Editorials • smoking • transcatheter aortic valve implantation