10. Madias JE. Cerebral blood flow in Takotsubo syndrome: is it specific for the disease. *Circ J* 2014;78:775.
11. Suzuki H, Matsumoto Y, Shimokawa H. Cerebral blood flow in takotsubo syndrome: is it specific for the disease. *Circ J* 2014;78:776.
12. Hiestand T, Hänggi J, Klein C, Topka MS, Jaguszewski M, Ghadri JR, Luscher TF, Jäncke L, Templin C. Takotsubo syndrome associated with structural brain alterations of the limbic system. *J Am Coll Cardiol* 2018;71:809–811.
13. Templin C, Hänggi J, Klein C, Topka MS, Hiestand T, Levinson RA, Jurisic S, Lüscher TF, Ghadri JR, Jäncke L. Altered limbic and autonomic processing supports brain-heart axis in Takotsubo syndrome. *Eur Heart J* 2019. pii: ehz068. https://doi.org/10.1093/eurheartj/ehz068. [Epub ahead of print].
14. Xu B, Williams PD, Brown M, Macisaac A. Takotsubo cardiomyopathy: does recurrence tend to occur in a previously unaffected ventricular wall region. *Circulation* 2014;129:e339–e340.
15. Sestini S, Pestelli F, Leoncini M, Bellandi F, Mazzeo C, Mansi L, Carrio I, Castagnoli A. The natural history of Takotsubo syndrome: a two-year follow-up study with myocardial sympathetic and perfusion G-SPECT imaging. *Eur J Nucl Med Mol Imaging* 2017;44:267–283.

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Characteristics, Outcomes, and Predictors of Significant Pericardial Complications in Patients who Underwent Transcatheter Aortic Valve Implantation

Large pericardial effusion and cardiac tamponade are known periprocedural complications of Transcatheter Aortic Valve Implantation (TAVR).[1,2] Pericardial complications have also been associated with increased morbidity and mortality in patients who underwent permanent pacemaker insertion and percutaneous coronary intervention.[2–4] This study describes characteristics, outcomes, and predictors of patients who develop significant pericardial complications related to TAVR.

For our analysis, we included all patients who underwent TAVR (ICD 9 DM 35.05 and 35.06) in the National Inpatient Sample database from 2012 to 2014. We excluded those patients who underwent other procedures that might cause pericardial complications. Our primary outcome of interest was significant pericardial complication, defined as a composite of cardiac tamponade (ICD 9 DM 42.33), pericardiocentesis (ICD 9 DM 37.0), or pericardial window (ICD 9 DM 37.12). We performed multivariable regression analysis on predictors of significant pericardial complications.

Between 2012 and 2014, 41,025 patients underwent TAVR. After exclusions, 34,820 were included in our

Table
Baseline characteristics and inhospital outcomes of patients with significant pericardial complications versus those without

Variables	Significant pericardial complication N = 465 (%)	No significant pericardial complication N = 34,355 (%)	p value
Age	82.9 ± 8.5	81.1 ± 8.5	<0.001
Female	340 (73.1)	16385 (47.7)	<0.001
Caucasian versus other race	370 (85.1)	27985 (87.7)	0.46
Hypertension	365 (78.5)	27450 (79.9)	0.75
Diabetes mellitus	110 (23.7)	11820 (34.4)	0.035
Congestive heart failure	30 (6.5)	4045 (11.8)	0.11
Chronic pulmonary disease	130 (28)	11575 (33.7)	0.227
Renal failure	165 (35.5)	12120 (35.3)	0.966
Obesity	55 (11.8)	4820 (14)	0.531
Anemia	130 (28)	9020 (26.3)	0.701
Coagulopathy	160 (34.4)	8090 (23.5)	0.015
Liver disease	<11*	880 (2.6)	0.805
Weight loss or underweight	65(14.0)	1665(4.8)	<0.001
Chronic malnutrition	35(7.5)	900(2.6)	0.003
Fluid and electrolyte imbalance	180(38.7)	8895(25.9)	.005
Coronary artery disease	255 (54.8)	24395 (71)	0.001
History of tobacco use	105 (22.6)	9745 (28.4)	0.211
History of PCI	55 (11.8)	6595 (19.2)	0.057
History of CABG	30 (6.5)	7990 (23.3)	<0.001
History of valve replacement	<11*	495 (1.4)	.227
Cardiac implantable electronic devices	20 (4.3)	5185 (15.1)	0.004
Teaching hospital	400 (86)	30470 (88.7)	0.452
Rural hospital	<11*	265 (0.8)	0.713
Elective versus non-elective admission	355 (76.3)	26785 (78)	0.676
Transapical TAVR	65 (14.0)	6430 (18.7)	0.266
Cardiac arrest	75 (16.1)	930 (2.7)	<0.001
Cardiogenic shock	40 (8.6)	910 (2.6)	<0.001
Respiratory failure	180 (38.7)	7015 (20.4)	<0.001
Acute renal failure	115 (24.7)	5935 (17.3)	0.063
Hemorrhage	40 (8.6)	1390 (4)	0.019
Acute renal failure+hemodialysis	20 (4.3)	550 (1.6)	0.04
Discharge to skilled nursing facility	170 (36.6)	9825 (28.6)	0.085
Mortality	115 (24.7)	1130 (3.3)	<0.001
Length of hospital stay (days) (IQR)	9(0−20)	6(2−10)	<0.001

PCI = Percutaneous coronary intervention: CABG = Coronary artery bypass grafting

analysis. Of these, 465 (1.3%) developed significant pericardial complications. Patients with significant pericardial complications were more likely to develop in-hospital complications including all-cause mortality. Female [OR 2.29, 95% CI 1.46−3.6; p <0.001] and coagulopathy [OR 1.6, 95% CI 1.05−2.46; p = 0.031] were associated with higher rates of significant pericardial complications, while a history of coronary artery bypass grafting (CABG) [OR 0.39, 95% CI 0.16−0.92; p = 0.033] or cardiovascular implantable electronic device (CIED) implantation [OR 0.32, 95% CI 0.11 −0.88; p = 0.028] was associated with a lower odds for significant pericardial complications. Significant pericardial complications were also independently associated with >7-fold higher odds for mortality [OR 4.91, 95% CI 2.56−9.43, p <0.001].

In both females and the elderly, it has been suggested that a thinner myocardial wall leaves these patients more vulnerable to pericardial injury.[5,4,5] In contrast, a history of CABG has been reported to be associated with lower incidence of significant pericardial complications in patients who underwent noncoronary procedures such as device implantation.[3,5] This is likely due to pericardial inflammation and subsequent fibrosis, postcardiotomy.[3,5] This study also reports an association of CIED in situ with a lower incidence of significant pericardial complications in a TAVR cohort. Rapid pacing with implanted CIEDs is not currently routine practice, therefore, it does not follow that CIEDs are in any way cardio-protective, but rather that many significant pericardial complications may be due to requisite temporary pacemaker insertion. Nonetheless, operators should pay particularly close attention during insertion or manipulation of temporary pacemaker wires during TAVR procedures.

The National Inpatient Sample (NIS) database includes limitations inherent to retrospective database analysis. The inability to review procedural details limits our ability to ascertain exact clinical circumstances in any single case. We exercised due diligence to exclude patients who may have suffered significant pericardial complications from other causes, and present only patients who most likely developed significant pericardial complications due to their TAVR procedure. Our results do not extend to patients who experienced major procedural complication resulting in surgical aortic valve replacement or those who required permanent pacemaker implantation (Table).

In this observational study describing characteristics and predictors of significant pericardial complications in patients who underwent TAVR, we found that (1) significant pericardial complications were not uncommon, ranging 1.2% −1.5% in the 3 years studied. (2) These complications were associated with markedly increased morbidity and mortality. (3) Presence of CIED and a history of CABG were associated with lower odds for these complications while female and a history of coagulopathy were associated with higher odds.

Disclosures

The authors have no conflicts of interest to disclose.

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1. Beohar N, Kirtane AJ, Blackstone E, Waksman R, Holmes D, Minha S, Alli O, Suri RM, Svensson LG, Leon M, Kodali S. Trends in complications and outcomes of patients undergoing transfemoral transcatheter aortic valve replacement: experience from the PARTNER continued access registry. *JACC Cardiovasc Interv* 2016;9:355–363.
2. Sabaté M, Cánovas S, García E, Hernández Antolín R, Maroto L, Hernández JM, Alonso Briales JH, Muñoz García AJ, Gutiérrez-Ibañes E, Rodríguez-Roda J. In-hospital and mid-term predictors of mortality after transcatheter aortic valve implantation: data from the TAVI National Registry 2010−2011. *Rev Esp Cardiol* 2013;66:949–958. Available at: http://www.sciencedirect.com/science/article/pii/S1885585713002405.
3. Moazzami K, Dolmatova E, Kothari N, Mazza V, Klapholz M, Waller AH. Trends in cardiac tamponade among recipients of permanent pacemakers in the United States: from 2008 to 2012. *JACC Clin Electrophysiol* 2017;3:41–46. Available at: https://doi.org/10.1016/j.jacep.2016.05.009.
4. Kinnaird T, Kwok CS, Kontopantelis E, Ossei-Gerning N, Ludman P, Belder M De, Anderson R, Mamas MA. Incidence, determinants, and outcomes of coronary perforation during percutaneous coronary intervention in the United Kingdom Between 2006 and 2013. *Circ Cardiovasc Interv* 2016;9:1–8.
5. Hsu JC, Varosy PD, Bao H, Dewland TA, Curtis JP, Marcus GM. Cardiac perforation from implantable cardioverter-defibrillator lead placement : insights from the National Cardiovascular Data Registry. *Circ Cardiovasc Qual Outcomes* 2013;6:582–590.

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Prognosis is Different than Treatment Effect

We have concerns with the publication, "Relation of Obesity to Outcomes of Hospitalizations for Atrial Fibrillation"[1] (AF). We found it to be another example in which the rules of logic are ignored to produce findings that appear paradoxical and surprising, but are really predictable and mundane. This analysis and others like it misinterpret associations seen in observational evidence, and ultimately serve as a source of confusion to those aiming to practice evidence-based medicine.

Agarwal et al[1] analyzed a nationwide sample of patients who were hospitalized with AF and found that those who were obese had better outcomes than those who were not obese. Because obesity is a known risk factor for AF, the authors convey a sense of surprise in the findings, describing them as "paradoxical." The findings are not paradoxical. There are many things that cause AF. Obesity is just one cause. Patients included in this study who were not obese must have had another cause for the condition. And those who have non−obesity-related causes for AF (e.g., systolic and diastolic heart failure, valvular heart disease, uncontrolled hypertension, chronic obstructive lung disease, aging-related frailty, and so on) did worse. Thus, in relative terms, patients who had the condition caused merely by obesity appear to do better.

Prognosis (i.e., prediction) is different than treatment effect. A clinician can see a patient drive up to the clinic in a new $75,000 Tesla and predict that the patient will live longer than another patient who arrives to clinic through less wealthy means. It does not