SPECIAL ARTICLE

Procedural Volume and Outcomes for Transcatheter Aortic-Valve Replacement

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ABSTRACT

BACKGROUND

During the introduction of transcatheter aortic-valve replacement (TAVR) in the United States, requirements regarding procedural volume were mandated by the Centers for Medicare and Medicaid Services as a condition of reimbursement. A better understanding of the relationship between hospital volume of TAVR procedures and patient outcomes could inform policy decisions.

METHODS

We analyzed data from the Transcatheter Valve Therapy Registry regarding procedural volumes and outcomes from 2015 through 2017. The primary analyses examined the association between hospital procedural volume as a continuous variable and risk-adjusted mortality at 30 days after transfemoral TAVR. Secondary analysis included risk-adjusted mortality according to quartile of hospital procedural volume. A sensitivity analysis was performed after exclusion of the first 12 months of transfemoral TAVR procedures at each hospital.

RESULTS

Of 113,662 TAVR procedures performed at 555 hospitals by 2960 operators, 96,256 (84.7%) involved a transfemoral approach. There was a significant inverse association between annualized volume of transfemoral TAVR procedures and mortality. Adjusted 30-day mortality was higher and more variable at hospitals in the lowest-volume quartile (3.19%; 95% confidence interval [CI], 2.78 to 3.67) than at hospitals in the highest-volume quartile (2.66%; 95% CI, 2.48 to 2.85) (odds ratio, 1.21; P=0.02). The difference in adjusted mortality between a mean annualized volume of 27 procedures in the lowest-volume quartile and 143 procedures in the highest-volume quartile was a relative reduction of 19.45% (95% CI, 8.63 to 30.26). After the exclusion of the first 12 months of TAVR procedures at each hospital, 30-day mortality remained higher in the lowest-volume quartile than in the highest-volume quartile (3.10% vs. 2.61%; odds ratio, 1.19; 95% CI, 1.01 to 1.40).

CONCLUSIONS

An inverse volume–mortality association was observed for transfemoral TAVR procedures from 2015 through 2017. Mortality at 30 days was higher and more variable at hospitals with a low procedural volume than at hospitals with a high procedural volume. (Funded by the American College of Cardiology Foundation National Cardiovascular Data Registry and the Society of Thoracic Surgeons.)

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Transcatheter aortic-valve replacement (TAVR) was approved in 2011 in the United States. As a condition of reimbursement, the Centers for Medicare and Medicaid Services (CMS) requires TAVR programs to perform a minimum of 20 TAVR procedures per year or 40 over a period of 2 years.[1] Although other cardiovascular[2-4] and cardiac surgical[5] procedures have shown an association between procedural volume and outcomes, no data were available to document a TAVR volume–outcome relationship at the time that CMS established the policy.

Carroll et al. subsequently found a TAVR volume–outcome association in the United States.[6] Since then, outcomes have improved with better technology and techniques, and indications for TAVR have expanded to include intermediate-risk patients. A recent analysis questioned whether there is a volume–outcome association for balloon-expandable TAVR.[7]

The purpose of this study was to update the analysis by Carroll et al. The objectives were to examine the association between hospital or operator volume of TAVR procedures and 30-day unadjusted and risk-adjusted outcomes, to determine the effect of hospital "start-up" period and assess whether volume–outcome associations persist after the first 6 months and 12 months of TAVR experience at a hospital, and to assess whether patient characteristics and hospital characteristics differ according to hospital procedural volume.

Methods

Study Population

CMS coverage requires hospitals to submit in-hospital, 30-day, and 1-year data for patients receiving a commercially approved TAVR device to the Society of Thoracic Surgeons (STS)–American College of Cardiology (ACC) Transcatheter Valve Therapy (TVT) Registry. Standardized data elements[8] and quality checks are implemented by the National Cardiovascular Data Registry and Duke Clinical Research Institute (DCRI). Participating sites are randomly selected for yearly independent audits. Institutional review boards at Chesapeake Research Review and Duke University approved this study and granted a waiver of informed consent.

All TAVR procedures that were performed between January 1, 2015, and December 31, 2017, were included in the analysis to represent TAVR performed with the latest devices in high-risk and intermediate-risk patients.[9,10] The primary population comprised patients undergoing transfemoral TAVR for symptomatic severe aortic stenosis. The secondary population of interest comprised patients undergoing nontransfemoral access TAVR.

Site-reported hospital characteristics included U.S. Census region, facility type, teaching status, rurality, and number of certified beds (see the Supplementary Appendix, available with the full text of this article at NEJM.org). Patient and procedure characteristics were defined according to the TVT Registry data dictionary.[11] Annualized hospital or operator procedural volume was calculated as the total number of TAVR procedures performed at a hospital or by an operator from January 1, 2015, through December 31, 2017, divided by the number of months between the first and last cases by that hospital or operator during the study period, and then multiplied by 12. This allowed for calculation of procedural volumes for both established and new TAVR operators or hospitals, even if they did not meet CMS requirements regarding procedural volume. If two operators were present during TAVR, each operator was given credit for the case.

Outcomes

The primary outcome was risk-adjusted mortality at 30 days. Secondary outcomes included a 30-day composite complication outcome (stroke, moderate or severe paravalvular leak, major vascular access-site complications or Valve Academic Research Consortium major or life-threatening or disabling bleeding, or acute kidney injury) and outcomes for each component of the composite outcome (see the Supplementary Appendix).

Statistical Analysis

As per the statistical analysis plan (included in the Supplementary Appendix), annualized hospital volume of TAVR procedures was analyzed both as a continuous variable and as a categorical variable (in quartiles). Quartiles were chosen to ensure an adequate number of hospitals in each volume category and to protect hospital identity. Descriptive, unadjusted 30-day outcomes according to quartile of annualized hospital procedural volume are provided in Table S1 in the Supplementary Appendix. Categorical variables are presented as frequencies and percentages. Continu-

ous variables are summarized as medians with interquartile ranges. There was no prespecified plan to adjust for multiple comparisons. Except for the primary analyses, results are reported with 95% confidence intervals without P values. A P value of less than 0.05 was considered to indicate statistical significance; 95% confidence intervals were not adjusted for multiple comparisons, and inferences drawn from them may not be reproducible.

The primary prespecified analysis examined the association between hospital procedural volume as a continuous variable and risk-adjusted 30-day mortality. Generalized linear mixed models were developed to assess hospital TAVR volume–outcome relationships. Marginal estimates are reported.[12] Restricted cubic splines were used to explore potential nonlinear relationships between continuous case volume and outcomes (see the Supplementary Appendix). Relationships were plotted as curves for annualized hospital procedural volume versus outcome. A three-level (patients, operators, and hospitals) hierarchical structure was adopted with the use of random intercepts with a covariance matrix that accounted for interhospital variability and interoperator variability nested within sites, to reflect clustering of TAVR outcomes.

Analyses were repeated after adjustment of outcomes for relevant covariates (see the Supplementary Appendix). Covariates for adjusted models were derived from the expert consensus list considered for the TVT Registry in-hospital risk model[13] plus operator case number. Operator case number was included as a covariate to account for operator "learning curve" while we assessed volume–outcome relationship at the hospital level. Interaction terms for year of procedure performance and patient risk (see the Supplementary Appendix) were included initially in the hospital-level model, and there was a prespecified plan to remove these variables if no interaction was found. All risk factors for each outcome were first combined into a single risk score before construction of the hierarchical model.[14] To create this score, we performed an ordinary logistic-regression model and used predicted log odds of the outcome. The risk score was then added as a single independent variable in the subsequent hierarchical model. Missing covariate data were handled with single imputation (see the Supplementary Appendix). Data on death within 30 days were missing for 7858 patients (8.2%), and data on the 30-day composite outcome were missing for 12,773 (13.3%) (Table S1 in the Supplementary Appendix). Missing outcome data were handled by inverse probability weighting to increase the weight of patients who were most like those with missing follow-up data (see the Supplementary Appendix).[15] A post hoc secondary analysis of the unadjusted and adjusted relationship between annualized operator procedural volume and outcomes was performed by means of the methods described above. For transfemoral TAVR, we prespecified multiple sensitivity analyses to allow for hospital "start-up" by excluding procedures within 6 months and 12 months after the date of the first TAVR procedure at the hospital.

The relative difference in adjusted risk of outcome was calculated as follows: [(risk of outcome with annualized procedural volume of x) − (risk of outcome with annualized procedural volume of y)] / (risk of outcome with annualized procedural volume of x). The delta method was used to calculate 95% confidence intervals for relative risk and for the difference in the adjusted risk of an outcome between an annualized procedural volume of x and a volume of y.[16] All analyses were performed at DCRI with the use of SAS software, version 9.4 (SAS Institute), and R software, version 3.4.2 (R Foundation for Statistical Computing).

RESULTS

HOSPITAL AND OPERATOR PROCEDURAL VOLUMES

Between January 1, 2015, and December 31, 2017, a total of 113,662 TAVR procedures with commercially approved devices were performed at 555 hospitals by 2960 operators (Fig. S1 in the Supplementary Appendix). The main analysis population included 96,256 transfemoral TAVR procedures performed at 554 sites by 2935 operators. The spectrum of annualized hospital and operator volumes of transfemoral TAVR procedures is shown in Figure 1. The median annualized hospital procedural volume was 54 (interquartile range, 36 to 86) and operator procedural volume was 27 (interquartile range, 17 to 43).

HOSPITAL CHARACTERISTICS ACCORDING TO QUARTILE OF PROCEDURAL VOLUME

The majority of hospitals that performed TAVR were urban (Table 1). A greater percentage of hospitals in the lowest-volume quartile than in the

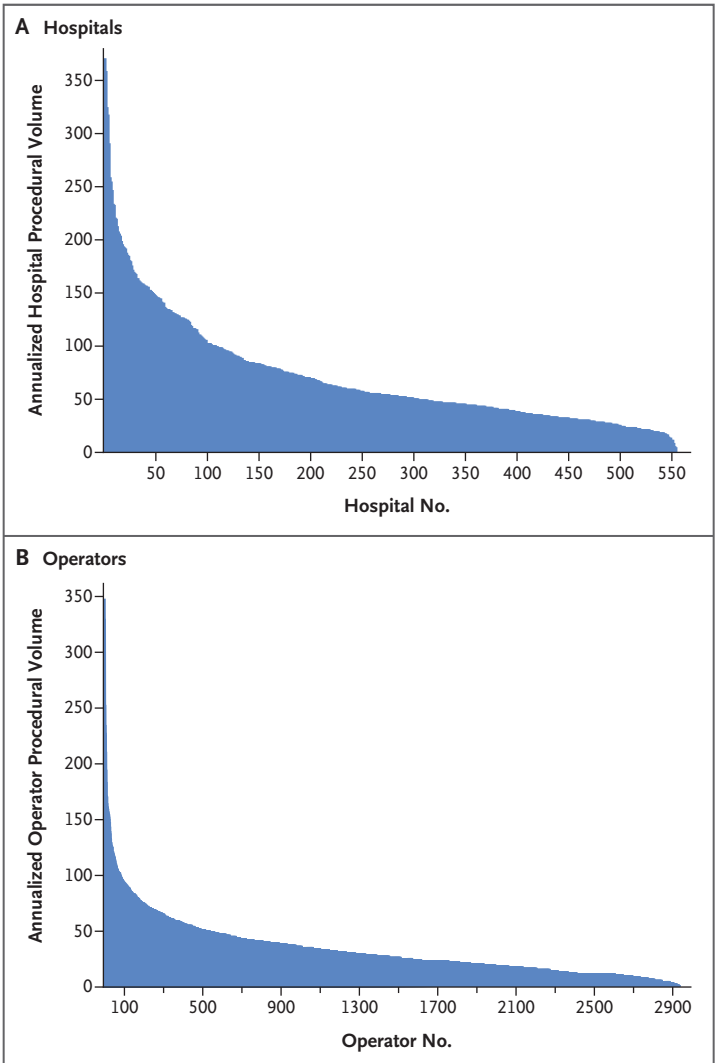

Figure 1. Annualized Hospital and Operator Volume of Transfemoral Transcatheter Aortic-Valve Replacement (TAVR) Procedures.

Shown are histogram distributions for 96,256 transfemoral TAVR procedures performed at 554 hospitals (Panel A) by 2935 operators (Panel B).

highest-volume quartile were rural (13.6% vs. 2.9%) or suburban (30.7% vs. 22.3%), private or community hospitals (90.7% vs. 64.0%), and located in the western United States or the Midwest.

PATIENT AND PROCEDURAL CHARACTERISTICS ACCORDING TO HOSPITAL QUARTILE

There were no clinically significant differences in sex or age between quartiles, but a higher percentage of patients treated at hospitals in the lowest-volume quartile than in the highest-volume quartile were black or Hispanic (12.1% vs. 7.8%) (Table 2). However, of the 8031 black or Hispanic patients who underwent TAVR, the majority (6194) were treated at hospitals in the two highest-volume quartiles.

Heart-team classification showed a greater proportion of inoperable or extreme-risk patients and high-risk patients with increasing quartile of procedural volume. The median STS Predicted Risk of Mortality (PROM) score (which estimates each patient's risk of death within 30 days after isolated aortic-valve replacement, with scores of 0 to 100%) ranged from 5.2% in the lowest-volume quartile to 5.5% in the highest-volume quartile. The use of surgical cutdown for femoral access was more common in the lowest-volume quartile than in the highest-volume quartile (26.7% vs. 9.1%), as was the use of general anesthesia (81.1% vs. 54.8%).

HOSPITAL PROCEDURAL VOLUME AND OUTCOMES

There was a significant nonlinear association between mortality (unadjusted and adjusted) and annualized hospital volume of transfemoral TAVR procedures. The difference in adjusted mortality between a mean annualized volume of 27 procedures in the lowest-volume quartile and 143 procedures in the highest-volume quartile was a relative reduction of 19.45% (95% confidence interval [CI], 8.63 to 30.26) (Fig. 2A and 2C). Adjusted 30-day mortality was higher and more variable in the lowest-volume quartile (3.19%; 95% CI, 2.78 to 3.67) than in the highest-volume quartile (2.66%; 95% CI, 2.48 to 2.85) (odds ratio, 1.21; P=0.02) (Table S2 in the Supplementary Appendix). Only seven hospitals performed at least 250 cases per year. There was no significant interaction between the volume–mortality relationship and year of procedure or patient risk. Observed individual hospital mortality and modeled confidence intervals in Figure 2A show a wide variation in hospitals with low procedural volumes.

SENSITIVITY ANALYSIS EXCLUDING HOSPITAL START-UP PERIOD

In a sensitivity analysis that excluded data from the first 6 months of TAVR performance at each hospital, adjusted 30-day mortality remained higher in the lowest-volume quartile (3.19%; 95% CI, 2.77 to 3.68) than in the highest-volume quartile (2.63%; 95% CI, 2.45 to 2.82) (odds ratio, 1.22; 95% CI, 1.04 to 1.43) (Fig. S2 and Table S2 in the Supplementary Appendix). After exclusion of the

Table 1. Hospital Characteristics According to Quartile of Annualized Volume of Transfemoral TAVR Procedures.*

Characteristic	Overall (N=554)	Quartile 1: 5–36 Procedures/Yr (N=140)	Quartile 2: 37–54 Procedures/Yr (N=138)	Quartile 3: 55–85 Procedures/Yr (N=137)	Quartile 4: 86–371 Procedures/Yr (N=139)
Location of facility (%)					
Urban	63.9	55.7	60.1	65.0	74.8
Suburban	26.7	30.7	29.0	24.8	22.3
Rural	9.4	13.6	10.9	10.2	2.9
Type of facility (%)					
Private or community	80.7	90.7	90.6	77.4	64.0
University	18.4	8.6	8.7	22.6	33.8
Government	0.9	0.7	0.7	0.0	2.2
Teaching hospital (%)	57.8	43.6	51.4	59.9	76.3
Region (%)					
Northeast	17.7	7.9	15.9	19.0	28.1
West	21.5	23.6	23.2	19.7	19.4
Midwest	23.5	24.3	26.8	21.2	21.6
South	36.8	42.9	33.3	40.1	30.9
Missing data	0.5	1.4	0.7	0.0	0.0
No. of certified beds†					
Median	459.0	395.0	402.0	522.0	623.0
IQR	333.0–637.0	296.5–477.5	296.0–547.0	374.0–653.0	438.0–819.0
No. of nontransfemoral TAVR procedures/yr					
Median	4	1	3	5	11
IQR	1–8	0–2	1–5	3–8	7–16
No. of valve-in-valve TAVR procedures/yr					
Median	3	1	2	4	9
IQR	1–6	0–2	1–3	2–5	5–12

* Percentages may not total 100 because of rounding. IQR denotes interquartile range, and TAVR transcatheter aortic-valve replacement.
† A "certified" bed is a bed in a health care facility approved by authorities for use by patients on a permanent basis and that a governing body deems to have sufficient staffing to support its unqualified use.

first 12 months of TAVR performance, adjusted 30-day mortality was 3.10% (95% CI, 2.68 to 3.58) in the lowest-volume quartile and 2.61% (95% CI, 2.43 to 2.81) in the highest-volume quartile (odds ratio, 1.19; 95% CI, 1.01 to 1.40) (Fig. 3, and Table S2 in the Supplementary Appendix).

There was no association between annualized hospital procedural volume and the 30-day composite complication outcome, both adjusted and unadjusted, or its nonfatal components, except for the outcome of major vascular complications or major bleeding (Figs. S3 and S4 in the Supplementary Appendix). The adjusted percentage of patients who had major vascular complications or major bleeding was 10.03% (95% CI, 8.99 to 11.18) at hospitals in the lowest-volume quartile, as compared with 8.21% (95% CI, 7.58 to 8.89) at hospitals in the highest-volume quartile (odds ratio, 1.25; 95% CI, 1.08 to 1.45).

OPERATOR PROCEDURAL VOLUME AND OUTCOMES

There was a nonlinear association between mortality (unadjusted and adjusted) and annualized operator volume of transfemoral TAVR procedures. The difference in adjusted mortality between a mean annualized volume of 11 procedures in the

Table 2. Patient Characteristics According to Quartile of Annualized Hospital Volume of Transfemoral TAVR Procedures.*

Characteristic	Overall: 554 Hospitals (N=96,256)	Quartile 1: 140 Hospitals with 5–36 Procedures/Yr (N=6827)	Quartile 2: 138 Hospitals with 37–54 Procedures/Yr (N=13,753)	Quartile 3: 137 Hospitals with 55–85 Procedures/Yr (N=22,799)	Quartile 4: 139 Hospitals with 86–371 Procedures/Yr (N=52,877)
Age — yr					
Median	82	82	82	82	82
IQR	76–87	76–87	76–87	76–87	76–87
Female sex — no. (%)	44,889 (46.6)	3188 (46.7)	6,348 (46.2)	10,652 (46.7)	24,701 (46.7)
Race or ethnic group — no. (%)†					
White	86,300 (89.7)	5908 (86.5)	12,591 (91.6)	20,350 (89.3)	47,451 (89.7)
Black	3,622 (3.8)	365 (5.3)	450 (3.3)	975 (4.3)	1,832 (3.5)
Hispanic	4,409 (4.6)	458 (6.7)	564 (4.1)	1,099 (4.8)	2,288 (4.3)
Other	1,925 (2.0)	96 (1.4)	148 (1.1)	375 (1.6)	1,306 (2.5)
Previous stroke — no. (%)	10,859 (11.3)	798 (11.7)	1,568 (11.4)	2,709 (11.9)	5,784 (10.9)
Dialysis — no. (%)	3,793 (3.9)	299 (4.4)	517 (3.8)	892 (3.9)	2,085 (3.9)
Moderate or severe COPD — no. (%)	21,523 (22.4)	1706 (25.0)	3,155 (22.9)	5,333 (23.4)	11,329 (21.4)
Atrial fibrillation or flutter — no. (%)	37,163 (38.6)	2410 (35.3)	5,201 (37.8)	8,793 (38.6)	20,759 (39.3)
Time on 5-m walk test of >6 sec or inability to walk — no. (%)	61,686 (64.1)	4595 (67.3)	8,958 (65.1)	15,393 (67.5)	32,740 (61.9)
STS-PROM score‡					
Median — %	5.4	5.2	5.3	5.4	5.5
IQR — %	3.5–8.5	3.5–8.1	3.5–8.2	3.6–8.3	3.5–8.6
Distribution					
<8%	69,602 (72.3)	5095 (74.6)	10,191 (74.1)	16,688 (73.2)	37,628 (71.2)
8–15%	19,928 (20.7)	1289 (18.9)	2,733 (19.9)	4,673 (20.5)	11,233 (21.2)
>15%	6,710 (7.0)	443 (6.5)	826 (6.0)	1,432 (6.3)	4,009 (7.6)
Missing data	16 (0.0)	0	3 (0.0)	6 (0.0)	7 (0.0)
Operator reason for procedure — no. (%)§					
Inoperable or extreme risk	13,944 (14.5)	804 (11.8)	1,842 (13.4)	3,864 (16.9)	7,434 (14.1)
High risk	58,860 (61.1)	4024 (58.9)	7,800 (56.7)	13,251 (58.1)	33,785 (63.9)
Intermediate risk	21,840 (22.7)	1859 (27.2)	3,788 (27.5)	5,286 (23.2)	10,907 (20.6)
Low risk	1,450 (1.5)	135 (2.0)	297 (2.2)	367 (1.6)	651 (1.2)
Missing data	162 (0.2)	5 (0.1)	26 (0.2)	31 (0.1)	100 (0.2)

* In addition to patients with missing data that are shown in the table, the number and percentage of patients with missing data were as follows: sex, 12 (0.0%); previous stroke, 216 (0.2%); dialysis, 214 (0.2%); moderate or severe chronic obstructive pulmonary disease (COPD), 679 (0.7%); atrial fibrillation or flutter, 277 (0.3%); and walking speed or ability, 13,055 (13.6%). Percentages may not total 100 because of rounding.

† Race and ethnic group were reported by the patient or family and were grouped into four mutually exclusive categories: non-Hispanic white, non-Hispanic black, Hispanic, and other.

‡ The Society of Thoracic Surgeons (STS) Predicted Risk of Mortality (PROM) (STS-PROM) score predicts the risk of death within 30 days after isolated aortic-valve replacement. The theoretical range of the score is 0 to 100%.

§ The level of risk was assessed by the heart team. Inoperable or extreme-risk patients could not undergo surgical aortic-valve replacement, had coexisting conditions, or were debilitated. High-risk patients had a predicted risk of death within 30 days after the procedure of at least 8% according to the risk model developed by the STS. Intermediate-risk patients had a predicted risk of death within 30 days of 4 to 7% according to the risk model developed by the STS. Low-risk patients had a predicted risk of death within 30 days of less than 4% according to the risk model developed by the STS.

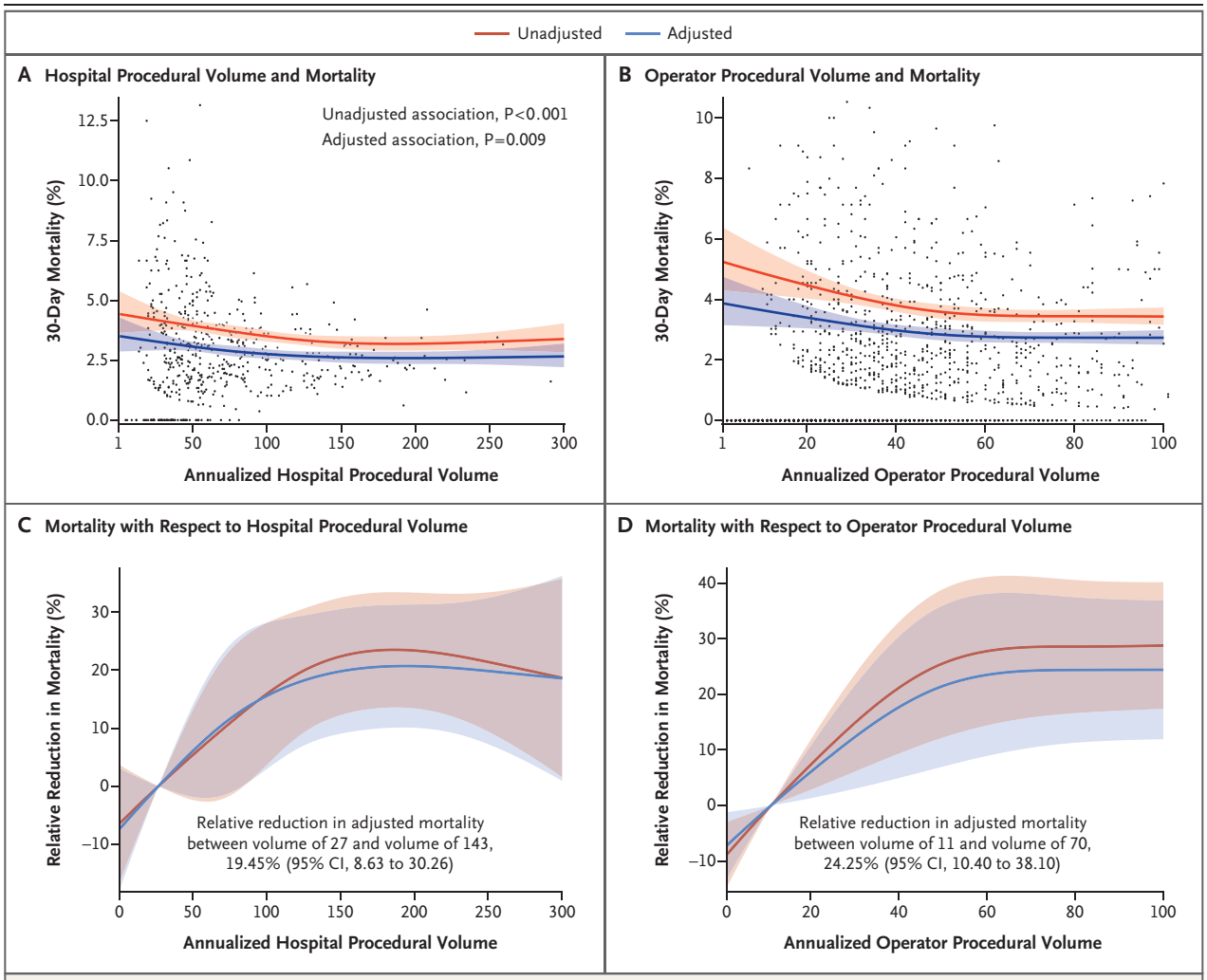

Figure 2. Relationship between Procedural Volume and Mortality.

Panel A shows the relationship between annualized hospital volume of transfemoral TAVR procedures and 30-day mortality, with specific estimates (black dots) for all 554 hospitals completing at least 1 TAVR procedure from 2015 through 2017. Panel B shows the relationship between annualized operator volume of transfemoral TAVR procedures and 30-day mortality, with specific estimates (black dots) for all 2935 operators completing at least 1 TAVR procedure from 2015 through 2017. Panel C shows the relative difference (expressed as a reduction) in 30-day mortality with respect to hospital procedural volume, with data for all hospitals completing at least 1 transfemoral TAVR procedure from 2015 through 2017. The mean procedural volume was 27 in the lowest-volume quartile and 143 in the highest-volume quartile. Panel D shows the relative difference (expressed as a reduction) in 30-day mortality with respect to operator procedural volume, with data for all operators completing at least 1 transfemoral TAVR procedure from 2015 through 2017. The mean procedural volume was 11 in the lowest-volume quartile and 70 in the highest-volume quartile. The shaded areas indicate 95% confidence intervals.

lowest-volume quartile and 70 procedures in the highest-volume quartile was a relative reduction of 24.25% (95% CI, 10.40 to 38.10) (Fig. 2B and 2D). Adjusted 30-day mortality was 3.54% (95% CI, 2.59 to 4.84) in the lowest-volume quartile and 2.84% (95% CI, 2.68 to 3.01) in the highest-volume quartile (odds ratio, 1.26; 95% CI, 0.91 to 1.75) (Table S2 in the Supplementary Appendix). Only 200 operators performed at least 75 cases per year.

NONTRANSFEMORAL TAVR

There were 8644 nontransfemoral TAVR cases at 486 sites (Fig. S5 in the Supplementary Appendix). There was a nonlinear relationship between volume of nontransfemoral TAVR procedures and mortality (unadjusted and adjusted), with adjusted 30-day mortality of 10.13% (95% CI, 7.76 to 13.11) in the lowest-volume quartile and 6.40% (95% CI, 5.56 to 7.35) in the highest-volume quartile (odds

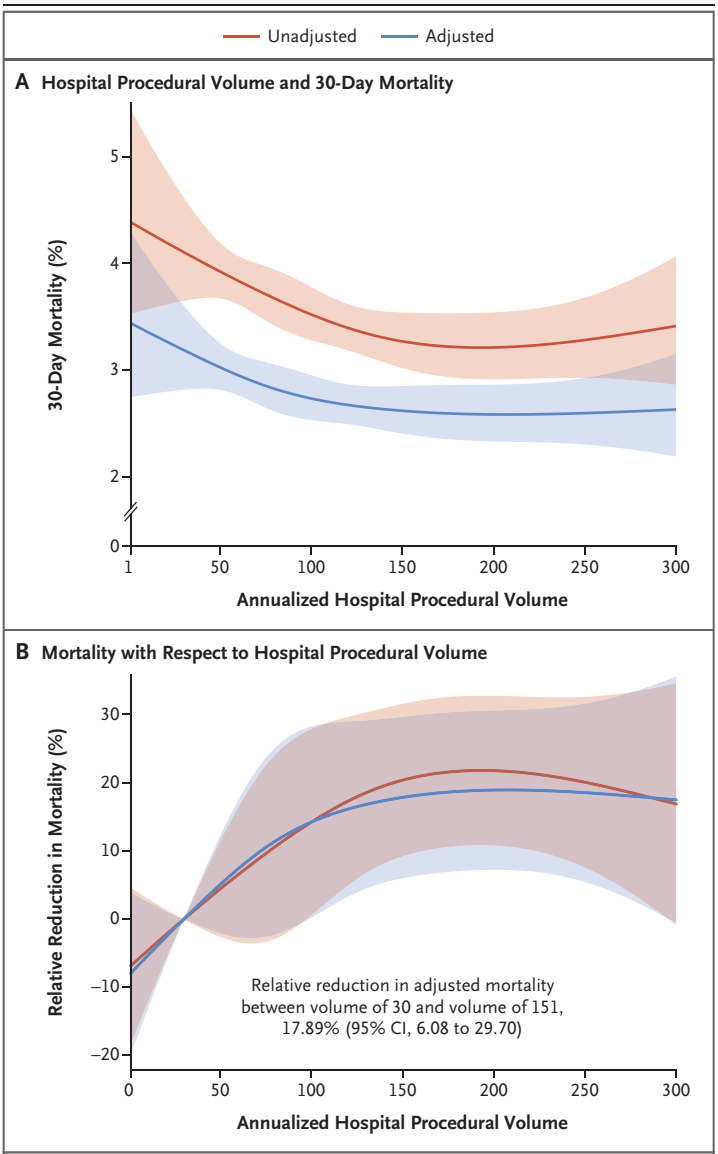

Figure 3. Sensitivity Analysis Excluding 12-Month Start-up Period at Each Hospital.

Panel A shows the relationship between annualized hospital volume of transfemoral TAVR procedures and 30-day mortality, after exclusion of all procedures in the 12 months after the initial transfemoral TAVR procedure at each hospital. Panel B shows the relative difference (expressed as a reduction) in 30-day mortality with respect to hospital procedural volume, after exclusion of all procedures in the 12 months after the initial transfemoral TAVR procedure at each hospital. The mean procedural volume was 30 in the lowest-volume quartile and 151 in the highest-volume quartile. Data in the figure are for 88,592 procedures at 488 hospitals. The shaded areas indicate 95% confidence intervals.

ratio, 1.65; 95% CI, 1.20 to 2.27) (Fig. S5 and Table S2 in the Supplementary Appendix). Only 2 hospitals performed more than 50 cases per year. There was no association between procedural volume and the composite complication outcome.

DISCUSSION

Five new findings are presented in this analysis of a database of more than 100,000 TAVR procedures in a 3-year period in the United States. First, higher annualized hospital and operator procedural volumes were associated with significantly lower 30-day mortality. Second, there was substantial variability in mortality among low-volume programs. Third, the inverse relationship between procedural volume and mortality remained after the exclusion of patients from the 6-month and 12-month start-up period at each hospital. Fourth, nontransfemoral TAVR also showed an inverse relationship between procedural volume and mortality. Fifth, hospitals with a lower procedural volume were more likely to be located in rural areas than those with a higher volume, and they treated a greater proportion of black and Hispanic patients.

These results are from current practice in the United States and illustrate the major improvement in 30-day mortality with TAVR, from 7.5% in 2012[14] to a modeled rate that now approaches 2.5 to 3.0% in transfemoral TAVR. A previous study showed that higher TAVR case volumes were associated with lower in-hospital mortality and lower rates of vascular complications and bleeding.[6] However, intervening advancements in delivery-system size, valve design, national experience, and expansion of TAVR to intermediate-risk patients might be expected to blunt or eliminate any volume–outcome relationship. In addition, low-volume and new TAVR programs may especially benefit from extensive industry support in planning and performing TAVR. Yet in this comprehensive study, the absolute change in risk-adjusted mortality across the continuous spectrum of hospital procedural volume was significant and corresponded to a clinically relevant relative difference in mortality between the lowest and highest annualized procedural volume. Despite reductions in major vascular and bleeding complications over time,[17] we also observed a nonlinear inverse relationship between procedural volume and major bleeding or vascular complications. This is consistent with continued operator variation in vascular complications of percutaneous coronary intervention despite technology improvements.[18]

Hospitals in the lowest-volume quartile also had procedure characteristics that were different from those of hospitals in the highest-volume quartile, with greater use of femoral cutdown

(26.7% vs. 9.1%) and general anesthesia. This provides insight into the otherwise paradoxical finding that the rate of unplanned surgery or intervention for vascular complications was lower at hospitals in the lowest-volume quartile than at hospitals in the highest-volume quartile (2.6% vs. 3.4%).

We found persistent hospital and operator volume–mortality relationships even after accounting for operator learning curve in our models and a hospital start-up time of 6 months or 12 months in our sensitivity analyses. This finding suggests that the volume–mortality association is not simply related to operator learning or reasonable hospital start-up time. A recent analysis by Wassef et al. of international sites showed that both learning curve and annual case volume affect TAVR outcomes.[19]

Hospitals with greater volumes of TAVR procedures were also larger hospitals, and they performed more nontransfemoral forms of TAVR than smaller hospitals. Thus, they may have better outcomes from both more experience and the availability of other services that would be necessary to treat the coexisting conditions that are common in the population of patients undergoing TAVR. Non-TAVR services may be important because post-TAVR death is due to a combination of both cardiovascular and noncardiovascular causes.[20,21]

Observed mortality was highly variable for hospitals with lower procedural volumes (0 to >12.5%) and operators with lower procedural volumes (0 to >10%). This variability highlights the difficulties of performance estimation at low procedural volumes and suggests that some threshold volume may be needed to accurately measure outcomes.[22]

We found that hospitals in the lowest-volume quartile treat a greater proportion of potentially underserved racial or ethnic groups and patients in rural regions, although by absolute numbers the majority of these patients are treated at hospitals in the highest-volume quartile. This raises the key issue of measuring access to TAVR. The present study presents data on those receiving TAVR and does not address the number of patients who may benefit from TAVR but may not have access to care. There is a paucity of evidence characterizing access barriers and evaluating solutions in the complex U.S. health care system.

An updated TAVR National Coverage Determination (NCD) should promote and ensure a high quality of patient care. Currently, TAVR programs receive quarterly reports with national benchmarks, but there is no system for external review and assessment if corrective actions are needed. A transition from procedural volume to direct quality metrics is being proposed, but without an external certification or accreditation system an updated NCD may not have the intended effect. In addition, we think an updated NCD should include an effective mechanism to require hospitals to submit complete and accurate data for quality metrics to be valid.

This is a retrospective observational study and is therefore potentially subject to residual confounding. Our adjusted models incorporated a multitude of factors but did not assess patients' social factors or frailty, used outcome data to estimate patient risk score and assess the volume–outcome relationship, and did not consider variance in inverse probability weighting. Paravalvular leak was assessed by sites and not a core laboratory. The TVT Registry collects data only on commercially performed TAVR cases under the current CMS requirements regarding procedural volume. As a result, we probably underestimated the procedural volumes of hospitals enrolling patients into clinical trials, especially at centers with higher procedural volumes. We were not able to assess whether current CMS requirements reduced mortality after TAVR or whether continuing or removing the current thresholds would affect mortality.

A volume–mortality association persists in the United States for transfemoral TAVR, as well as TAVR using nontransfemoral approaches, despite improved patient selection, technology, and techniques as well as expansion of indications to intermediate-risk patients. Hospitals with lower procedural volumes have greater variability in outcomes than those with higher volumes. In addition, hospitals with lower procedural volumes are more likely to be rural, and they perform TAVR on a higher percentage of racial and ethnic minorities.

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REFERENCES

1. Centers for Medicare and Medicaid Services. Decision memo for transcatheter aortic valve replacement (TAVR). 2012 (https://www.cms.gov/medicare-coverage-database/details/nca-decision-memo.aspx?NCAId=257).
2. Jollis JG, Peterson ED, DeLong ER, et al. The relation between the volume of coronary angioplasty procedures at hospitals treating Medicare beneficiaries and short-term mortality. N Engl J Med 1994;331:1625-9.
3. Strom JB, Wimmer NJ, Wasfy JH, Kennedy K, Yeh RW. Association between operator procedure volume and patient outcomes in percutaneous coronary intervention: a systematic review and meta-analysis. Circ Cardiovasc Qual Outcomes 2014;7:560-6.
4. Jolly SS, Cairns J, Yusuf S, et al. Procedural volume and outcomes with radial or femoral access for coronary angiography and intervention. J Am Coll Cardiol 2014;63:954-63.
5. Birkmeyer JD, Siewers AE, Finlayson EVA, et al. Hospital volume and surgical mortality in the United States. N Engl J Med 2002;346:1128-37.
6. Carroll JD, Vemulapalli S, Dai D, et al. Procedural experience for transcatheter aortic valve replacement and relation to outcomes: the STS/ACC TVT Registry. J Am Coll Cardiol 2017;70:29-41.
7. Russo MJ, McCabe JM, Thourani VH, et al. Case volume and outcomes after TAVR with balloon-expandable prostheses: insights from TVT Registry. J Am Coll Cardiol 2019;73:427-40.
8. Kappetein AP, Head SJ, Généreux P, et al. Updated standardized endpoint definitions for transcatheter aortic valve implantation: the Valve Academic Research Consortium-2 consensus document. J Am Coll Cardiol 2012;60:1438-54.
9. Medtronic. Replacing aortic heart valves without open-heart surgery. 2019 (https://www.medtronic.com/us-en/about/news/corevalve-intermediate-risk.html).
10. FDA approves expanded indication for two transcatheter heart valves for patients at intermediate risk for death or complications associated with open-heart surgery. News release of the Food and Drug Administration, Silver Spring, MD, August 18, 2016 (https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm517281.htm.)
11. TVT Registry v2.0 coder's data dictionary. 2018 (https://www.ncdr.com/WebNCDR/docs/default-source/tvt-public-page-documents/tvt-registry-2_0_coderdatadictionary.pdf?sfvrsn=2).
12. Zeger SLL, Liang KY, Albert PS. Models for longitudinal data: a generalized estimating equation approach. Biometrics 1988;44:1049-60.
13. Edwards FH, Cohen DJ, O'Brien SM, et al. Development and validation of a risk prediction model for in-hospital mortality after transcatheter aortic valve replacement. JAMA Cardiol 2016;1:46-52.
14. Dimick JB, Ghaferi AA, Osborne NH, Ko CY, Hall BL. Reliability adjustment for reporting hospital outcomes with surgery. Ann Surg 2012;255:703-7.
15. Seaman SR, White IR. Review of inverse probability weighting for dealing with missing data. Stat Methods Med Res 2013;22:278-95.
16. Ver Hoef JM. Who invented the delta method? Am Stat 2012;66:124-7.
17. Grover FL, Vemulapalli S, Carroll JD, et al. 2016 Annual report of the Society of Thoracic Surgeons/American College of Cardiology Transcatheter Valve Therapy Registry. J Am Coll Cardiol 2017;69:1215-30.
18. Wimmer NJ, Secemsky EA, Mauri L, et al. Effectiveness of arterial closure devices for preventing complications with percutaneous coronary intervention: an instrumental variable analysis. Circ Cardiovasc Interv 2016;9(4):e003464.
19. Wassef AWA, Rodes-Cabau J, Liu Y, et al. The learning curve and annual procedure volume standards for optimum outcomes of transcatheter aortic valve replacement: findings from an international registry. JACC Cardiovasc Interv 2018;11:1669-79.
20. Urena M, Webb JG, Eltchaninoff H, et al. Late cardiac death in patients undergoing transcatheter aortic valve replacement: incidence and predictors of advanced heart failure and sudden cardiac death. J Am Coll Cardiol 2015;65:437-48.
21. Xiong TY, Liao YB, Zhao ZG, et al. Causes of death following transcatheter aortic valve replacement: a systematic review and meta-analysis. J Am Heart Assoc 2015;4(9):e002096.
22. Dehmer GJ, Brindis RG, Shahian DM, Mack MJ. Challenges of measuring and assuring quality for transcatheter aortic valve replacement. J Am Coll Cardiol 2019;73:336-9.