TAVR and Cancer: Machine Learning-Augmented Propensity Score Mortality and Cost Analysis in Over 30 Million Patients

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Abstract

Introduction: Cardiovascular disease (CVD) and cancer are the top mortality causes globally, yet little is known about how the diagnosis of cancer affects treatment options in patients with hemodynamically compromising aortic stenosis (AS). Patients with cancer often are excluded from aortic valve replacement (AVR) trials including both trials with transcatheter AVR (TAVR) and surgical AVR (SAVR). This study looks at how cancer may influence treatment options, and assess the outcome of cancer patients who undergo surgical or TAVR intervention. Additionally, we sought to quantitate and compare both clinical and cost outcomes for cancer and non-cancer patients.

Methods: This population-based case-control study uses the most recent year available National Inpatient Sample (NIS (2016) from the United States Department of Health and Human Services' Agency for Healthcare Research and Quality (AHRQ). Machine learning augmented propensity score adjusted multivariable regression was conducted based on the likelihood of undergoing TAVR versus MM and TAVR versus SAVR with model optimization supported by backward propagation neural network machine learning.

Results: Of the 30,195,722 total hospital admissions, 39,254 (0.13%) TAVRs were performed, with significantly fewer performed in cancer versus non-cancer patients even in those of comparable age and mortality risk (23.82% versus 76.18%, $p<0.001$) despite having similar mortality. Multivariable regression in cancer patients demonstrated that mortality was similar for TAVR, MM, and SAVR, though LOS and cost was significantly lower for TAVR versus MM and comparable for TAVR versus SAVR. Patients with prostate cancer constituted the largest primary malignancy among TAVR patients including those with metastatic disease. There were no significant race or geographic disparities for TAVR mortality.

Discussion: Comparison of aortic valve intervention in cancer patients with those without co-existing malignancy suggests that intervention is underutilized in the cancer population. This study suggests that as cancer patients including those with metastasis have similar clinical outcomes, patients who are symptomatic and those with higher risk aortic valve lesions should be offered the benefit of intervention. Modern techniques have reduced intervention-related adverse events, provided improved quality of life, and appear to be cost effective; these advantages should not be denied to patients on the basis of co-existing malignancy.

1. Introduction

Cardiovascular disease (CVD) and cancer remain the top causes mortality in developed countries.[1] Aortic stenosis (AS) is prevalent in age-comparable groups to the same extent as in the general population, yet little is known about how the treatment of AS in cancer patients differs from those without cancer. Furthermore, patients with malignancy are often excluded from aortic valve replacement (AVR) trials, making direct outcome comparisons problematic.[2] As interventional strategies evolved to include transcatheter aortic valve repair (TAVR) the lack of information on selection of patients, as well as the

outcome statistics have been lacking. Transcatheter AVR initially emerged as the main treatment option for patients with severe AS who are at high risk for surgery.[3] More recently, evidence extended the indication to intermediate and low-risk patients.[4,5,6] When compared with surgical aortic valve repair (SAVR), TAVR is cost-effective for high-risk patients and offers considerable cost savings for the group of intermediate risk patients.[7,8,9] Single center experience suggests that both SAVR[9] and transcatheter (TAVR) versus medical management (MM) improve survival with an incremental survival advantage of up to 36 months.[10] These trends underscore the increasing evidence that TAVR versus surgical AVR (SAVR) patients have comparable mortality, stroke, and rehospitalization rates at one and two years for high, intermediate and now low surgical risk patients.[11] Lower cost derived from reduced length of stay (LOS) in the index hospitalization as well as less costly follow-up surveillance decreased lifetime costs by $8000-$10,000 while improving overall quality of live and quality-adjusted survival.

The number of TAVR patients has increased substantially, especially in older patients; the extent to which cancer patients have benefitted from this change is less clear, but as older patients are more likely to be afflicted with cancer, one would expect that some TAVR procedures to have been undertaken in such patients. Initial non-randomized studies with small sample sizes showed comparable 30-day results, but 1-year mortality in cancer patients receiving TAVR are lower, possibly related to factors associated with the underlying malignancy or its treatment.[12,13]

The present study was therefore undertaken to compare cancer and non-cancer patients undergoing TAVR and the clinical and cost outcomes of these patients relative to MM and SAVR. We further sought to compare non-cancer versus cancer patients who under TAVR to estimate the extent of underutilization of TAVR in the cancer population.

2. Methods

2.1. Study design

This is the first known nationally representative population-based case-control study comparing TAVR, SAVR, and MM clinical and cost outcomes among all hospitalized patients (with and without malignancy and within individual primary malignancies), and the first to apply a machine learning-augmented propensity score adjusted multivariable regression methodology for such a cardio-oncology study. It uses the most recent year available (2016) from the NIS, the latest year of available data, to allow optimal generalizability to current practice. The data was available from The United States Department of Health and Human Services' Agency for Healthcare Research and Quality (AHRQ). Study inclusion criteria were 2016 hospitalizations of adults 18 years of age or older with documented mortality and malignancy presence or absence. This study using de-identified data was performed in accordance with the Declaration of Helsinki and did not require Institutional Review Board approval. The National Inpatient Sample (NIS) discharge weights were utilized to calculate national estimates, allowing optimal generalizability to current practice.

Subjects undergoing PCI were identified by the ICD-10 procedure codes of 02RF37H (“Replace of Aort Valve with Autol Sub, Transap, Perc Approach”), 02RF37Z (“Replacement of Aortic Valve with Autol Sub, Perc Approach”), 02RF38H (“Replace Aort Valve w Zooplastic, Transap, Perc”), 02RF38Z (“Replacement of Aortic Valve with Zooplastic, Perc Approach”), 02RF3JZ (“Replacement of Aortic Valve with Synth Sub, Perc Approach”), 02RF3KH (“Replace Aort Valve w Nonaut Sub, Transap, Perc”), 02RF3KZ (“Replacement of Aortic Valve with Nonaut Sub, Perc Approach”), 02RF47Z (“Replacement of Aort Valve with Autol Sub, Perc Endo Approach”), 02RF48Z (“Replace of Aort Valve with Zooplastic, Perc Endo Approach”), 02RF4JZ (“Replacement of Aort Valve with Synth Sub, Perc Endo Approach”), and 02RF4KZ (“Replace of Aort Valve with Nonaut Sub, Perc Endo Approach”). ICD-10 codes were also used to identify demographics, comorbidities, and outcomes. HCUP tools such as the Clinical Classification Software, which had been used prior to the NIS 2016 dataset for such purposes as classifying cancer (e.g., by primary type, current versus historical), were not used in this study because they were found by HCUP as a beta version to be unreliable when applied to the 2016 dataset’s ICD-10 data.

2.2. Clinical outcomes

The clinical outcomes compared the cancer population with similar patients who did not have cancer. Secondary assessed outcomes included mortality, post-procedure pacemaker implantation, total direct cost, and outcome racial and geographic disparities. The associations assessed included these outcomes and the following predictors: TAVR versus MM and TAVR versus SAVR (additionally by cancer versus non-cancer overall, by metastatic disease within cancer patients, by active versus prior malignancy within cancer patients, by solid versus hematological malignancies overall within cancer and by specific primary malignancy types, within thrombocytopenic patients, and within radiation patients particularly mediastinal). Propensity score matching was utilized to reduce bias and unequal distribution of treatment between patients with and without cancer, particularly in the assessment of TAVR versus MM (considering the absence of aortic stenosis severity documented in the data) given the clinical importance of this assessment, the paucity of data on this comparison in cancer versus non-cancer patients, and the typical exclusion of cancer patients from TAVR and SAVR randomized trials (and thus in current medical practice a possible tendency away from providing non-medical intervention for cancer patients leaving the majority of such patients to be managed medically).

2.3. Statistical analysis

Descriptive statistics and bivariable analysis by mortality were performed for the overall sample. Independent sample t-test was conducted to assess means and Wilcoxon rank sum tests for medians for continuous variables. Pearson's chi square test or Fisher's exact test were conducted to assess proportions for categorical variables. Multivariable regression was then conducted for the primary outcome of in-patient mortality and the secondary outcomes of length of stay (LOS, in days) and total direct cost (also adjusting for LOS); sub-group analysis within TAVR subjects of the above outcomes were also conducted to assess possible race and geographic disparities. Propensity scores based on the likelihood of undergoing TAVR versus MM and TAVR versus SAVR were also calculated and used to

further adjust the final regression models that also controlled for age, race, income, metastases, and mortality risk (as calculated by the NIS using the DRGs). The selection of variables in the final regression models were determined by the clinically and/or statistically significant variables identified in bivariable analysis and/or the existing literature, with selection also augmented by forward and backward stepwise regression. To optimize the likelihood of robust, validated, and replicable results, the performance of the final regression models was first assessed by backward propagation neural network machine learning by accuracy and root mean squared error (RMSE) to ensure they were comparable based on an integrated hybrid methodology of traditional statistics reinforced by machine learning.[14,15] The following diagnostics were conducted also to optimize performance of the final regression models: Hosmer-Lemeshow's goodness-of-fit test, Akaike's and Schwarz's Bayesian information criteria, correlation matrix, AUC, tolerance, variance inflation factor, specification error, and multicollinearity. 95% confidence intervals (CIs) were reported for the final regression results with statistical significance determined by a two-tailed p-value of <0.05. This has been demonstrated in recent studies. STATA 14.2 (STATACorp, College Station, Texas, USA) was used for statistical analysis, and Java 9 (Oracle, Redwood Chores, California, USA) was used for machine learning analysis.

3. Results

3.1. Descriptive statistics & bivariable analysis

Of the 30,195,722 total hospital admissions in 2016 during the United States,3%) underwent TAVR and 69,450 (0.23%) underwent SAVR, and 661,286 (2.19%) died among all hospitalized adults nationally in 2016. Among cancer patients (Table 1), TAVR patients compared to both MM and SAVR patients were more likely to be older and have non-private insurance, diabetes, hypertension, congestive heart failure, and chronic kidney disease stage 3-5 (all p<0.001). TAVR versus MM and SAVR patients had the lowest mortality (respectively, 1.43% versus 3.99% versus 3.24%, all p<0.001) and median length of stay in days (respectively, 4.59 [standard deviation {SD} 4.56] versus 5.45 [6.34] versus 9.10 [7.09], all p<0.001).

Among TAVR subjects, 23.53% were done in cancer patients and 0.67% in those with metastatic cancer. In sub-group analysis among patients 65 years of age and older and elevated mortality risk (moderate, major, and extreme but not minor as calculated by the NIS according to DRGs), still significantly fewer TAVR procedures were done in cancer versus non-cancer patients (23.82% versus 76.18%, p<0.001). Yet mortality was comparable among cancer and non-cancer patients undergoing TAVR (1.43% versus 1.98%, p=0.118), including in the similar above sub-group of patients of comparable age and mortality risk (1.57% versus 1.96%, p=0.297). The leading primary malignancies in which TAVR was done included: prostate (23.06%), skin (16.71%), breast (15.34%), bladder (7.88%), colon (6.45%), with the leading malignancies among SAVR subjects being similar including prostate (26.69%), skin (21.77%), breast (13.32%), bladder (5.54%), and colon (5.15%).

Among TAVR performing hospitals, the mean number of procedures annually was 29.94 (SD 21.00) with the tertiles being 1-17, 18-36, and 37-112. In sub-group analysis among cancer patients, descriptive

statistics and bivariable analysis by aortic stenosis treatment modality are provided in Table 1.

3.2. TAVR versus MM

TAVR versus MM patients were significantly older (80.28 years [SD 8.32] versus 57.46 [SD 20.34; p<0.001), and less likely to be female (45.78% versus 58.22%, p<0.001), non-white (13.53% versus 32.26%, p<0.001), and die inpatient (1.85% versus 2.19%, p=0.039), while being more likely to have a longer LOS (mean 5.16 days [SD 6.04] versus 4.72 [SD 6.33], p<0.001), higher cost (mean USD $216,458.70 [SD 136,223.5] versus $49,903.50 [81,963.57], p<0.001).

In fully adjusted analysis for all hospitalized adults, TAVR compared to MM significantly reduced mortality (OR 0.52, 95%CI 0.43-0.63; p<0.001) and non-home discharge (OR 0.84, 95%CI 0.84-0.85; p<0.001) overall, and non-significantly reduced mortality for cancer patients (OR 0.71, 95%CI 0.45-1.11; p=0.133) and more so for metastatic cancer patients (OR 0.29, 95%CI 0.04-2.20; p=0.233), while significantly reducing cancer patients' LOS (beta days -0.72, 95%CI -1.04- -0.40; p<0.001) and cost (beta USD $-5,186, 95% CI -8,627.01- -1,745.08; p=0.003) (Table 2). In stratified analysis, there was no significant association with mortality between TAVR versus MM for cancer patients with active versus prior malignancy, solid versus non-solid malignancies, thrombocytopenia versus not, or radiation versus non-radiation.

Assessing primary malignancies separately, there was no significant association with mortality between TAVR versus MM for cancer patients with the top five above primary malignancies. TAVR versus MM did significantly reduce costs for those with skin cancer (beta $-11,175.68, 95%CI -18,134.07- -4,217.30; p=0.002) and breast (beta $-14,012.76, 95%CI -21,054.98- -6,970.53; p<0.001) while significantly raising it for those with bladder cancer (beta $11,974.51, 95% CI 1,545.01-22,404.01; p=0.024) (Figure 1).

3.3. TAVR versus SAVR

TAVR versus SAVR patients were significantly older (mean 80.28 years [SD 8.32] versus 66.40 [SD 12.62], p<0.001) and more likely to be female (45.78% versus 33.05%, p<0.001) and less likely to be non-white (13.53% versus 17.58%, p<0.001), die (1.85% versus 3.31%, p<0.001), and be discharged non-home (44.93% versus 64.84%, p<0.001). TAVR versus SAVR patients also had lower LOS (mean 5.16 [SD 6.04] versus 10.19 [SD 9.51], p<0.001) and cost (mean USD $216,458.70 [SD 136,223.5] versus $242,302.10 [SD 232,242.80], p<0.001).

TAVR versus SAVR for cancer patients non-significantly decreased mortality (OR 0.76, 95%CI 0.43-1.32; p=0.326) and non-home discharge (OR 0.89, 95%CI 0.76-1.05; p=0.172), but increased LOS (beta 0.35, 95%CI -0.20-0.89, p=0.214) and costs (beta USD $10,725.28, -575.25-22,025.82; p=0.063). There was no significant association with mortality, LOS, nor cost between TAVR versus SAVR for cancer patients with the top five above primary malignancies. In stratified analysis, there was no significant association with mortality between TAVR versus SAVR for cancer patients with active versus prior malignancy, solid versus non-solid malignancies, thrombocytopenia versus not, or radiation versus non-radiation.

3.4. TAVR procedural volume

TAVR procedural volume did not significantly impact mortality or LOS, but compared to the lowest tertile, the second tertile significantly decreased costs (beta $-10,498.49, 95%CI -16,575.01- -4,421.97; p=0.001) while the third tertile significantly increased costs (beta $11,742.95, 95%CI 5,455.22-18,030.68; p<0.001).

Among all TAVR subjects, there were no significant race or geographic disparities for mortality; there were significantly different LOS by geographic region relative to New England: West North Central (beta -1.26, -1.95- -0.57; p<0.001), Mountain (beta -1.07, 95%CI -1.79- -0.35; p=0.004), and Pacific (beta -0.72, 95%CI -1.31- -0.14; p=0.016). All regions had significantly increased costs relative to New England with the most expensive regions being the Pacific (beta $120,651.20, 95%CI 108,823.80-132,478.50; p<0.001), Mountain (beta $91,538.29, 95%CI 77,089.44-105,987.10; p<0.001), and Mid-Atlantic (beta $86,865.73, 95%CI 75,686.65-98,044.80; p<0.001). Among TAVR subjects who also have cancer, there were no significant race or geographic disparities for mortality; all geographic regions had significantly lower LOS relative to New England with the lowest LOS being for Mountain (beta -2.19, 95%CI -3.38- -1.01; p<0.001), West North Central (beta -2.01, 95%CI -3.14- -0.89; p<0.001), and West South Central (beta -2.00, 95%CI -3.05- -0.94; p<0.001). Yet all regions had significantly greater costs relative to New England with the greatest being: Pacific (beta $120,414.30, 95%CI 99,695.70-141.132.80; p<0.001), Mid Atlantic (beta $94,020.50, 95%CI 74,543.15-113,497.80; p<0.001), and Mountain (beta $80,620.67, 95%CI 51,101.14-107,140.20; p<0.001).

4. Discussion

This is the first known nationally representative analysis of mortality and cost for cancer versus non-cancer patients (including by primary malignancy) by TAVR versus MM and TAVR versus SAVR, including the first to use a comprehensive machine learning-augmented propensity score analysis integrating traditional statistics and machine learning. It provides novel multi-center evidence that TAVR is preferentially performed less often in cancer versus non-cancer patients despite them having seemingly comparable risk profiles and mortality without significantly increased costs. TAVR when compared with MM in cancer patients produced comparable outcomes; however, TAVR patients had shorter lengths of stay and incurred less cost. Assessment of quality of life for cancer patients who underwent TAVR could not be assessed but would not be expected to be at significant variance with non-cancer patients. TAVR may have significant geographic disparities in both LOS and cost without mortality or racial disparities among cancer patients. The analysis further supports that these cost differences may be driven at least in part by particular primary malignancies, such as TAVR versus MM potentially reducing hospital costs for those with breast and skin cancers without significant differences by primary malignancy for TAVR versus SAVR.

This study thus provides novel, robust evidence that suggests TAVR's clinical and cost benefit may be extended to cancer patients not just for the treatment of AS to reduce CVD morbidity and mortality, but also to improve their functional status and allow the introduction of medications that impact cardiovascular function or reserve that might not be possible in the presence of hemodynamically

compromising AS. The study additionally provides the first known granular analysis by primary malignancy type and TAVR versus MM and TAVR versus SAVR in such a way that details where the overall cost differences in particular may be driven in a way that may alter pre-procedure management of such patients.

Prior studies suggest there may be increased mortality in TAVR for adults under 80 compared to older patients, or for those undergoing TAVR versus SAVR.[16] Additionally, TAVR versus SAVR are older and have a greater number of confounding comorbidities.[17,18] This study thus adds to this literature the novel finding that TAVR versus MM reduces LOS and cost but not mortality for cancer patients, but without any significant outcome differences for TAVR versus SAVR. Furthermore, this is the first NIS study of TAVR subjects that shows both overall and cancer-specific geographic disparities in LOS and cost, but no impact of outcomes by procedural volume.

The strengths of this study include its novel utilization of a nationally representative multi-center dataset to analyze among all adult hospitalized patients TAVR versus MM and specifically TAVR versus SAVR, which was a comprehensive analysis of multiple outcomes including a sub-group disparity analysis, and utilized a robust propensity score methodology augmented by a machine learning analysis (with implications for later more sophisticated and automated machine learning-based analysis with increasing amounts of data). The above analysis is thus novel even among other NIS studies by increasing the external validity and thus generalizability of the study by analyzing all adult hospitalizations to more finely hypothesize about the true association between TAVR and alternatives and clinical outcomes for cancer patients, while using a robust approach to optimize internal validity with a well-accepted study design that reduces bias and type I and II error through its large multi-center dataset and propensity score analysis.

The limitations of this study include its non-randomized study design and data limited to short-term outcomes without severity grading of AS or adequate grading of surgical risk, which the above strengths have sought to ameliorate as best as current best statistical practices allow. Future studies are required to confirm and expand these results including by primary malignancy type to ensure the best available data informs treatments for cardio-oncology patients to produce the best possible outcomes for them.

5. Conclusions

This is the first known nationally representative comprehensive analysis of inpatient mortality and cost by cancer status (including primary malignancy type) and AS treatment modality (TAVR, SAVR, and MM). It utilizes a robust and novel traditional statistical approach of causal inference supported by machine learning to suggest the unique finding that TAVR's clinical, cost, and racially equitable advantages may be safely extended to cancer patients with not only cardiovascular net benefit (treating the primary problem of AS) but also oncological benefit (improving their functional status to potentially allow expanded cancer treatments).

6. Declarations

6.1. Ethical Approval and Consent to participate

Ethics approval and patient consent was deemed not required due to this study's dataset that consisted of the National Inpatient Sample de-identified administrative database.

6.2. Consent for publication

All authors consented to submission and if accepted then also publication of this manuscript.

6.3. Availability of data and materials

The data is available by purchase through the United States Agency for Healthcare Research and Quality (AHRQ) Healthcare Cost and Authorization Project (HCUP) Central Distributor (hcup-us.ahrq.gov).

6.4. Competing interests

The authors have no competing interests.

6.5. Funding

There is no funding for this study.

6.6. Authors' contributions

DJM created the study design and analyzed the data; DJM and LH drafted the manuscript; DJM, LH, PB, NP, JLM, MC, ZI, ME, KM, and CI interpreted the data, revised the manuscript, and consented to its publication.

6.7. Acknowledgements

There are no relevant acknowledgements.

6.8. Authors' information

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Tables

Table 1
Descriptive statistics and bivariable analysis by aortic stenosis treatment modality among cancer patients*

Variables	Sample	Treatment			P-value	
	N = 30,195,722	MM (n = 24,232,078 [80.25%])	TAVR (n = 40,265 [0.13%])	SAVR (n = 67,260 [0.22%])	TAVR versus MM	TAVR vs SAVR
Demographics, no. (%)						
Age, mean (SD)	68.70 (14.30)	68.67 (14.31)	81.00 (7.93)	71.52 (9.35)	**< 0.001**	**< 0.001**
Female	15,254,879 (50.52)	(50.54)	(40.2)	(32.61)	**< 0.001**	**< 0.001**
Race, nonwhite	7,132,230 (23.62)	(23.65)	(10.00)	(10.97)	**< 0.001**	0.349
Insurance, non-private	23,380,548 (77.43)	(77.4)	(93.23)	(79.23)	**< 0.001**	**< 0.001**
Medical history						
Diabetes	6247,495 (20.69)	(20.68)	(26.02)	(20.20)	**< 0.001**	**< 0.001**
Hypertension	19,790,276 (65.54)	(65.49)	(88.13)	(81.14)	**< 0.001**	**< 0.001**
Hyperlipidemia	11,869,938 (39.31)	(39.25)	(69.29)	(70.20)	**< 0.001**	0.546
Congestive heart failure	1,926,487 (6.38)	(6.33)	(34.3)	(12.95)	**< 0.001**	**< 0.001**
Smoking	332,153 (1.10)	(1.10)	(0.37)	(1.17)	**< 0.001**	**0.005**
Depression	3,895,248 (12.90)	(12.91)	(7.6)	(9.43)	**< 0.001**	**0.046**
Cirrhosis	742,815 (2.46)	(2.47)	(1.53)	(0.56)	**0.009**	**0.004**
CKD 3–5	4,055,285 (13.43)	(13.4)	(24.54)	(11.55)	**< 0.001**	**< 0.001**
Outcomes, median (range)						

*MM, medical management; TAVR, transcatheter aortic valve replacement; SAVR, surgical aortic valve replacement; bold = statistically significant; CKD, chronic kidney disease.

Variables	Sample	Treatment			P-value	
Mortality, no. (%)	1,201,790 (3.98)	(3.99)	(1.43)	(3.24)	**< 0.001**	**< 0.001**
Length of stay, days	5.46 (6.34)	5.45 (6.34)	4.59 (4.56)	9.10 (7.09)	**< 0.001**	**< 0.001**
Cost, dollars	60,612.22 (87,774.68)	60,002.30 (86,913.86)	210,106.90 (110,707.70)	219,202.30 (179,519.90)	**< 0.001**	0.065

*MM, medical management; TAVR, transcatheter aortic valve replacement; SAVR, surgical aortic valve replacement; bold = statistically significant; CKD, chronic kidney disease.

Table 2
Propensity score adjusted multivariable regression of outcomes by aortic valve replacement versus medical management for cancer and non-cancer patients*

Variable	OR (95%CI; p-value)					
	Mortality		Cost (United States Dollars)		Length of stay (Days)	
Age by 10 years	TAVR vs MM	TAVR vs SAVR	TAVR vs MM	TAVR vs SAVR	TAVR vs MM	TAVR vs SAVR
Non-white race	**1.01 (1.01–1.01)**	1.00 (1.00-1.01)	**-43.90 (-47.04--40.76)**	-3.66 (-192.18-184.84)	**-0.02 (-0.02--0.02)**	**-0.06 (-0.07--0.05)**
Zip code income	**1.03 (1.02–1.04)**	0.98 (0.78–1.23)	**3,953.27 (3,833.21-4,073.34)**	**31,486.94 (25,653.33-37,320.55)**	**0.31 (0.30–0.32)**	**1.12 (0.84–1.40)**
1st quartile	Reference	Reference	Reference	Reference	Reference	Reference
2nd quartile	**0.96 (0.95–0.98)**	0.91 (0.71–1.16)	**2,120.83 (1,976.57-2,265.09)**	4,416.36 (-1,564.70–10,397.41)	**-0.13 (-0.15--0.12)**	-0.20 (-0.49-0.09)
3rd quartile	**0.92 (0.90–0.93)**	0.98 (0.77–1.25)	**5,372.67 (5,224.71-5,520.64)**	**16,506.95 (10,558.02-22,455.89)**	**-0.17 (-0.18--0.16)**	**-0.49 (-0.78--0.20)**
4th quartile	**0.93 (0.91–0.95)**	0.92 (0.71–1.19)	**9,909.08 (9,751.90–10,066.26)**	**31,220.53 (25,154.54-37,246.52)**	**-0.11 (-0.12--0.09)**	-0.25 (-0.54-0.04)
Procedure	**0.52 (0.43–0.63)**	0.90 (0.70–1.16)	**164,413 (162,704.90–166,121.10)**	**52,098.41 (46,359.88-57,836.93)**	-0.01 (-0.17-0.14)	**-3.85 (-4.13--3.58)**
Malignancy	**1.08 (1.06–1.10)**	1.07 (0.78–1.47)	**2,606.99 (2,441.96-2,772.02)**	-7,911.60 (-15,835.76–12.55)	**0.06 (0.05–0.08)**	**-0.89 (-1.27--0.51)**
Metastases	**1.95 (1.91-2.00)**	0.63 (0.15–2.70)	**-6,706.27 (-7,033.93--6,378.60)**	922.71 (-575.25-22,025.82)	**-0.31 (-0.34--0.28)**	0.86 (-0.81-2.54)
With Procedure	0.71 (0.45–1.11)	0.76 (0.43–1.32)	**-5,186.04 (-8,627.01--1,745.08)**	10,725.28 (-575.25-22,025.82)	**-0.72 (-1.04--0.40)**	0.35 (-0.20-0.89)
Mortality risk by DRG	**7.88 (7.81–7.96)**	10.74 (8.93–12.93)	**8,108.62 (8,042.55-8,174.68)**	**21,602.97 (18,898.19-24,307.74)**	**2.10 (2.09–2.10)**	**4.29 (4.18–4.41)**

*TAVR, transcatheter aortic valve replacement; MM, medical management; SAVR, surgical aortic valve replacement; DRG, Disease Related Group; bold = statistically significant.

Variable	OR (95%CI; p-value)		
	Mortality	Cost (United States Dollars)	Length of stay (Days)
Length of stay, days		7,514.37 (7,505.36-7,523.38)	14,544.34 (14,262.47-14,826.21)

*TAVR, transcatheter aortic valve replacement; MM, medical management; SAVR, surgical aortic valve replacement; DRG, Disease Related Group; bold = statistically significant.

Figures

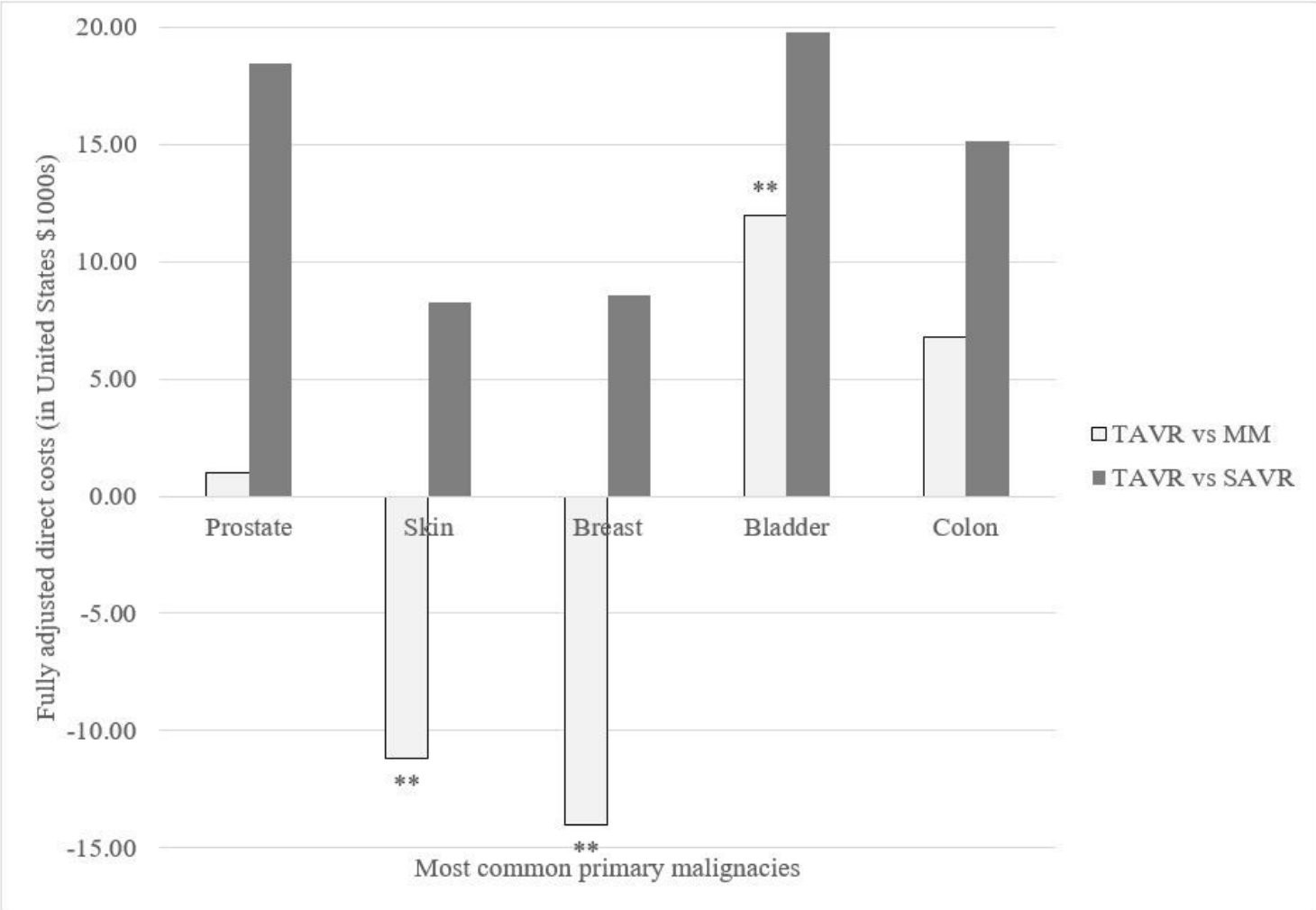

Figure 1

Propensity score adjusted multivariable regression of outcomes by aortic valve replacement versus medical management by primary malignancy* *Fully adjusted by age, sex, income, and metastases; **statistically significant; TAVR, transcatheter aortic valve replacement; MM, medical management; SAVR, surgical aortic valve replacement.