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Research Article

Surgical versus Interventional Mitral Valve Repair: Analysis of 1,100 Propensity Score-Matched Patients

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Objective. We aimed to investigate outcomes in transcatheter versus surgical mitral valve repair in patients with secondary mitral regurgitation (MR) by leveraging a global, multi-institutional federated network database. *Methods*. Using validated ICD-10 and CPT codes, the TriNetX Analytics Research Data Network (a global federated database of electronic health records from 58 healthcare organizations) was queried to identify patients diagnosed with chronic, severe, ischemic MR and undergoing either transcatheter mitral valve repair (TMVr) or surgical mitral valve repair (SMVr) between January 1, 2015 and December 31, 2020. To adjust for baseline differences, 1 : 1 propensity score matching was performed via logistic regression using the nearest-neighbor approach and matching for 29 covariates including demographics, comorbidities, surgical history, preoperative medications, left ventricular function and heart failure status. We compared 1- and 3-year mortality rates and 1- and 3-year mitral valve reoperation rates in the matched cohorts using Kaplan-Meier estimates and adjusted Cox proportional hazards models. *Results*. A total of 2,352 patients met inclusion criteria (1,392 in the surgical mitral valve repair group and 960 in the TMVr group). After 1 : 1 propensity score matching, a total of 550 patients undergoing surgical mitral valve repair (SMVr) were compared to 550 patients undergoing TMVr. All characteristics were adequately matched between the cohorts (standardized mean difference <0.1). At 1- and 3-years respectively, mortality rate was 13.4% and 20.7% for surgical patients and 19.8% and 40.3% for TMVr patients. When compared to TMVr, patients undergoing SMVr were significantly less likely to face mortality at 3 years (HR: 0.42, 95% CI: 0.31–0.56, $p < 0.0001$). At 1- and 3-years respectively, mitral valve reoperation was 2.2%, and 2.4% for surgical patients and 6.6% and 7.8% for TMVr patients. When compared to TMVr, patients undergoing SMVr were significantly less likely to undergo mitral valve reintervention at 3 years (HR: 0.29, 95% CI: 0.14–0.58, $p = 0.0002$). *Conclusion*. In a real-world, propensity score matching analysis of a large cohort of patients with chronic ischemic MR, surgical mitral valve repair had significantly better survival rates and significantly lower reintervention rates at 1- and 3-years compared to TMVr.

1. Introduction

What the best treatment for secondary mitral regurgitation (MR) is remains debated. Surgical randomized controlled trials (RCTs) comparing mitral valve replacement to mitral valve repair are in favor for the replacement of the mitral valve in patients with secondary MR [1]. In that frame, adequately powered, randomized controlled trials comparing outcomes of transcatheter mitral valve repair (TMVr) versus surgical mitral valve repair (SMVr) are currently lacking. The results of the only RCT comparing mitral valve surgery versus TMVr [2] were in favor of a surgical approach in terms of freedom from mitral valve reintervention and recurrent MR. Unfortunately, the trial was limited by the inclusion of patients with both primary and secondary MR, as well as by the different surgical approaches which also included mitral valve replacement.

Nevertheless, the 2020 ACC/AHA valve guidelines provided a class 2a recommendation for the use of TMVr in patients with chronic, severe, secondary MR related to left ventricular systolic dysfunction who remain symptomatic after optimization of guidelines-directed medical therapy (GDMT) and have proper anatomy [3]. The recommendation for TMVr in these patients is predominantly a byproduct of the conflicting results between the MITRA-FR [4] and the COAPT [5] trials. The COAPT trial showed improvement in survival, hospitalization, symptoms, and quality of life in patients with persistent symptoms despite optimization of GDMT, whereas the MITRA-FR trial was not able to demonstrate a difference in reducing the composite endpoint of death or hospitalization as compared with medical therapy. Although both studies included different patient populations (which is most likely responsible for the different results), both studies compared TMVr with medical therapy. Accordingly, it remains unclear which interventional approach (TMVr or SMVr) is superior in the treatment of secondary mitral regurgitation.

Differently than TMVr, surgical mitral valve intervention received a 2a indication only in patients undergoing concomitant coronary artery bypass grafting, and in this patients population the mitral valve was recommended to be replaced rather than repaired (2b recommendation).

In this frame, high-powered and well-controlled studies directly comparing survival and freedom from reoperation in TMVr versus SMVr in patients with secondary MR are lacking. We aimed to investigate these outcomes in a large study population of more than 1,000 matched patients by leveraging a global, multi-institutional federated network database.

2. Methods

2.1. Study Design and Data Source. This study was a retrospective cohort study with data sourced from the TriNetX Analytics Research Network, Cambridge MA (TriNetX). TriNetX is a global federated database containing electronic health records from over 80 million patients from 58 healthcare organizations (community and academic hospital centers, and physician networks) worldwide; however, we use data exclusively from the United States. Detailed descriptions of the TriNetX network have previously been published [6, 7]. The network database complies with the Health Insurance Portability and Accountability Act (HIPAA), a United States national law which protects the integrity and confidentiality of health information. As such, data for research purposes are available without the need for institutional review board approval only in aggregate, fully-deidentified form. Furthermore, the TriNetX platform uses standardized coding systems like International Classification of Diseases, Tenth Revision (ICD-10) and Current Procedural Terminology (CPT) to index data including patient demographics, vital signs, medications, lab results, diagnoses, and procedures. Within the TriNetX network database, internal validity is maintained in real-time by monitoring temporal data trends, and several external validation studies were performed using TriNetX data which confirmed its reliability as a source for retrospective studies.

2.2. Sample. We searched the TriNetX database for patients ≥18 years with ischemic mitral valve regurgitation between 1 January 2015 and 31 December 2020 who exclusively underwent either surgical mitral valve repair (CPT: 33425, 33426, 33427) or transcatheter mitral valve repair, TMVr (CPT: 33418, 0345T). Since there is univocal ICD-10 code for the diagnosis of "ischemic mitral regurgitation," we queried the database for patients who had nonrheumatic mitral insufficiency (I34.0) who had a previously documented diagnosis of chronic ischemic heart disease (I25). We elected to exclude patients with acute myocardial infarction or papillary muscle rupture in the periprocedural period, as mitral valve regurgitation is an acute onset impairing outcomes in this specific patient population. Additionally, we excluded patients who underwent mitral valve replacement and transcatheter mitral valve implantation, as the indications and outcomes of these are considerably different than in valve repair and are outside the scope of this paper.

2.3. Outcomes. Selected baseline characteristics were identified and matched for by propensity score matching (please see "statistical analysis"). The primary outcomes were mortality and mitral valve reintervention (i.e., open repair, replacement and transcatheter procedures) at 1- and 3-postoperative years from the index procedure.

2.4. Statistical Analysis. Categorical variables are presented as percentage of the total cohort and were compared using the chi-squared test; continuous variables are presented as mean ± standard deviation and were comparedwith the Student's *t*-test. After initial database querying and generation of cohorts, we performed 1 : 1 propensity score matching to control for differences in preoperative characteristics between cohorts. More specifically we matched for 29 unique variables including demographics, preoperative comorbidities, surgical history, use of cardiovascular medications, anti-platelet medications, anticoagulants, preoperative B-type natriuretic peptide, and preoperative left ventricular ejection fraction (Table 1) using logistic regression and the nearest-neighbor approach with a caliper of 0.1 pooled standard deviations. The proportionality assumption was assessed using the Schoenfeld residuals. Furthermore, Kaplan-Meier survival analyses with log-rank test, and corresponding Cox proportional hazards models were generated to 1- and 3-year cumulative incidence of outcomes of interest. All the estimates (and corresponding Kaplan-Meier curves) were therefore converted into failure rates. All statistical analyses were performed using the TriNetX Analytics platform (Cambridge, MA) which leverages R v. 3.2–12 and SAS v. 9.4 to perform statistical tests. Of note, the *R Survival library* uses a robust (sandwich) estimator of variance, which produces conservative estimates of standard errors and minimizes bias. Unless otherwise stated, statistical significance was set to a two-tailed p value of 0.05.

Table 1: Patients' characteristics before and after propensity score matching.

ICD10	Characteristic	Before matching			After matching		
		Open repair ($N = 1392$) %	TMVr ($N = 960$) %	SMD	Open repair ($N = 550$) %	TMVr ($N = 550$) %	SMD
	Demographics						
	Age, mean ± SD	66.6 ± 11.1	76.1 ± 9.7	0.921	72.1 ± 9.1	72.6 ± 10.1	0.052
	Male	69.04%	63.13%	0.125	64.73%	66.55%	0.038
	Comorbidities						
I10-I16	Hypertensive diseases	74.71%	85.63%	0.276	82.36%	82.73%	0.010
I50	Heart failure	62.07%	84.79%	0.532	78%	76.91%	0.026
I50.2	Systolic heart failure	34.84%	55%	0.414	48%	45.82%	0.044
I50.4	Combined systolic and diastolic heart failure	17.46%	32.92%	0.362	28.18%	27.27%	0.020
I48	Atrial fibrillation and flutter	49.50%	64.17%	0.299	58.73%	58.91%	0.004
I49	Other cardiac arrhythmias	30.32%	43.85%	0.283	38%	37.82%	0.004
I05-I09	Chronic rheumatic heart diseases	46.98%	57.40%	0.210	53.46%	52.73%	0.015
I26-I28	Pulmonary heart disease and diseases of pulmonary circulation	31.83%	49.38%	0.363	42.91%	41.09%	0.037
I42	Cardiomyopathy	26.44%	39.27%	0.276	35.46%	36%	0.011
I38	Endocarditis, valve unspecified	12.07%	16.25%	0.120	11.82%	11.82%	0.000
I33	Acute and subacute endocarditis	5.75%	1.56%	0.224	1.82%	2.18%	0.026
I60-I69	Cerebrovascular diseases	29.89%	38.75%	0.188	35.46%	34.55%	0.019
E00-E89	Endocrine, nutritional and metabolic diseases	80.10%	90%	0.280	87.64%	87.27%	0.011
J00-J99	Diseases of the respiratory system	64.22%	70.31%	0.130	69.27%	70%	0.016
N00-N99	Diseases of the genitourinary system	53.02%	71.77%	0.395	64.55%	66.36%	0.038
K00-K95	Diseases of the digestive system	54.02%	66.25%	0.252	61.64%	62%	0.007
D50-D89	Hematologic and immunologic diseases	51.94%	58.96%	0.142	57.09%	56.18%	0.018
G00-G99	Diseases of the nervous system	46.41%	57.71%	0.228	53.27%	52.55%	0.015
C00-D49	Neoplasms	22.34%	35.52%	0.294	28.73%	29.46%	0.016
A00-B99	Certain infectious and parasitic diseases	24.50%	32.40%	0.176	25.82%	27.82%	0.045
F01-F99	Psychiatric and neurodevelopmental disorders	43.25%	43.75%	0.010	44.73%	43.46%	0.026
	Medications						
	Cardiovascular medications*	93.10%	95.63%	0.110	93.27%	94.55%	0.053
	Antiplatelets†	74.21%	82.60%	0.205	80%	80%	0.000
	Anticoagulants‡	74.35%	77.60%	0.076	76.73%	78%	0.030
	Previous surgeries						
	Surgical procedures on the cardiovascular system	56.18%	72.40%	0.343	65.82%	66.36%	0.012
	Preoperative labs & imaging						
	Natriuretic peptide B [mass/volume] ± SD	1830 ± 4440.9	2019.4 ± 6133.7	0.035	1934.5 ± 5083.6	2570.7 ± 8005.2	0.095
	Left ventricular ejection fraction, % ± SD	45.7 ± 18.0%	44.6 ± 16.6%	0.061	42.3 ± 17.5%	44.2 ± 16.5%	0.111

ICD-10: international classification of diseases tenth edition, TMVr: transcatheter mitral valve repair, SMD: standardized mean difference, SD: standard deviation. *Cardiovascular medications represents a composite code in TriNetX which include beta blockers, calcium channel blockers, diuretics, ACE inhibitors, ARBs, direct renin inhibitors, sacubitril, hydralazine, clonidine, methyldopa, minoxidil, angiotensin II inhibitors, alpha blockers, milrinone, bosentan, cilostazol, ivabradine, nitroglycerine, isosorbide, antilipemics (including statins, fibrates, cholesterol binding resins, PCSK9 inhibitors), antiarrhythmics, and digoxin. †Antiplatelet medications represents a composite code in TriNetX which includes aspirin, clopidogrel, prasugrel, ticagrelor, cangrelor, and dipyridamole. ‡Anticoagulants represents a composite code in TriNetX which includes warfarin, heparin, low-molecular-weight-heparin, direct factor Xa inhibitors, and direct thrombin inhibitors.

3. Results

3.1. Baseline Characteristics. Before matching, our cohorts consisted of 1,392 SMVr and 960 TMVr patients across 30 healthcare organizations in the United States. TMVr patients tended to be older (76.1 ± 9.7 vs. 66.6 ± 1.11 years; $p < 0.001$; SMD = 0.921) and were more likely to have several cardiovascular and non-cardiovascular comorbidities (see Table 1). SMVr was more common amongst male patients (69.0% vs. 63.1%; $p = 0.003$, SMD: 0.125). After propensity score matching, baseline characteristics were comparable between cohorts (standardized mean difference <0.1) and 550 open repair patients were compared to a corresponding cohort 550 TMVr patients.

3.2. Mortality. In the unmatched analysis, mortality rate was 11.9% in SMVr patients versus 22.7% in TMVr patients (HR: 0.512; 95% CI: 0.418–0.626; log-rank $p < 0.0001$) at 1 postoperative year. Mortality rate at 3 years postoperatively remained significantly lower in SMVr patients: 18.6% vs. 44.8%; HR: 0.382; 95% CI: 0.33–0.45; $p < 0.0001$.

In the matched analysis, mortality rate in SMVr patients was 13.4% versus 19.8% in TMVr (HR: 0.69; 95% CI: 0.50–0.94; log-rank $p = 0.018$) at 1 postoperative year. Mortality rate at 3 years postoperatively remained significantly lower in SMVr patients: 20.7% vs. 40.3%; HR: 0.53; 95% CI: 0.41–0.67; $p < 0.001$. See Figures 1 and 2.

3.3. Mitral Valve Reintervention. In the unmatched analysis, 1-year mitral valve reintervention rate was 0.8% in initial SMVr patients and 4.8% in initial TMVr patients, representing a statistically significant difference (log-rank $p < 0.0001$; HR: 0.152; 95% CI: 0.075–0.309). Similarly, at 3 postoperative years, reintervention rate remained lower in SMVr patients (1.1% vs. 6.4%; $p < 0.0001$; HR: 0.158; 95% CI: 0.085–0.293).

In the matched analysis, 1-year reintervention rate on the mitral valve was 2.2% in initial SMVr patients and 6.6% in initial TMVr patients, representing a statistically significant difference (log-rank $p = 0.006$; HR: 0.32; 95% CI: 0.16–0.64). Similarly, at 3 postoperative years, reintervention rate remained lower in SMVr patients (2.4% vs. 7.8%; $p = 0.002$; HR: 31; 95% CI: 0.16–0.60). Reintervention is further outlined in Figures 1 and 2.

4. Discussion

In March 2019, the Food and Drug Administration has approved MitraClip for the treatment of secondary mitral regurgitation as a result of the COAPT trial [8], and the 2020 ACC/AHA valve guidelines have provided a Class 2A recommendation for TMVr in patients with severe, secondary mitral regurgitation who remain symptomatic after optimization of guidelines-directed medical therapy [3]. In this frame, the number of transcatheter mitral valve procedure performed in the United States has been steadily growing over time, both in general and in particular for each subtype of mitral regurgitation [9].

Our study is the first in its nature to probe clinical outcomes in patients of any ages with ischemic mitral regurgitation undergoing SMVr versus TMVr after propensity score matching: we uniquely gathered real-world data from >50 institutions across the United States by leveraging the TriNetX Analytics Research Data Network. The role of this dataset has been recently started to be validated in the cardiac surgery literature [7, 10] and the online, continuously updated, interactive platform of the data network allowed us to query data from 80 million electronic medical records and design a propensity score matching model accounting for an extensive number of variables. As such, we were able to demonstrate that SMVr in ischemic mitral regurgitation holds both a survival advantage as well as lower hazards of reoperation at short- and mid-term compared to TMVr.

Malik et al. have performed a retrospective, observational evaluation of outcomes in octogenarians undergoing SMVr versus TMVr by leveraging the National Inpatient Sample database [11]. They demonstrated a 4-fold higher mortality rate in SMVr versus TMVr as well as an overall higher rate of cardiac, vascular, hemorrhagic, and respiratory complications. Even though the Authors performed propensity score matching between the two cohorts, they also stated not to have stratified results by the etiology and type of mitral regurgitation or to have matched for preoperative left ventricular function. Our group has previously elaborated on the limitations of the National Inpatient Sample data when used for outcome-based clinical research [12]. In a different setting, De Bonis et al. have reported their institutional mid-term results of TMVr versus surgical edge-to-edge repair in patients with severe left ventricular dysfunction and secondary mitral regurgitation [13]. They reported that residual (≥2+) MR at hospital discharge was significantly higher in the TMVr than in the surgical group (29% versus 7.6%, respectively; $p = 0.002$) and that at 4-year follow-up, freedom from MR ≥2+ was significantly higher in the surgical group than in the TMVr group (74.9% versus 51.4%, respectively; $p = 0.01$). Interestingly, the use of TMVr was identified as an independent predictor of recurrence of MR ≥2+ at multivariate analysis. Other studies have been published with neutral results, likely as a result of their limited sample sizes [14–17].

In this frame, our study showed a statistically significant lower reintervention rate as a surrogate marker for valvular function in the SMVr group compared to patients undergoing TVMr (2.4% vs. 7.8%, respectively; $p = 0.002$). This difference in reoperation rates are in line with the results of the EVEREST II (Endovascular Valve Edge-to-Edge Repair Study) RCT trial, which showed significantly higher rates for mitral valve reintervention and recurrent mitral valve regurgitation (3+ or 4+) in patients with TMVr compared to mitral valve surgery at 5 years.

Furthermore, both TMVr and SMVr showed a comparable 5-year mortality without underlying any statistically significant difference [18]. However, the conclusiveness of the EVEREST II trial is limited by the mixed population in terms of underlying mitral valve pathology (26% secondary MR) and different surgical treatment modalities (14% mitral valve replacement) [18, 19].

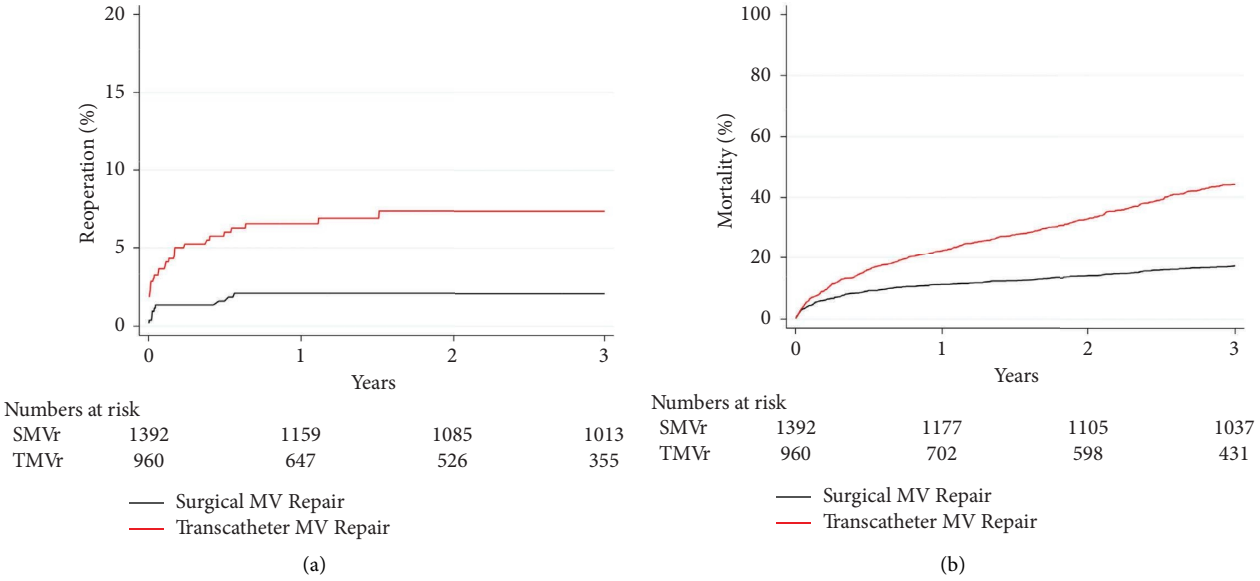

Figure 1: Failure rates in the unmatched cohorts: reoperation (a) and mortality (b).

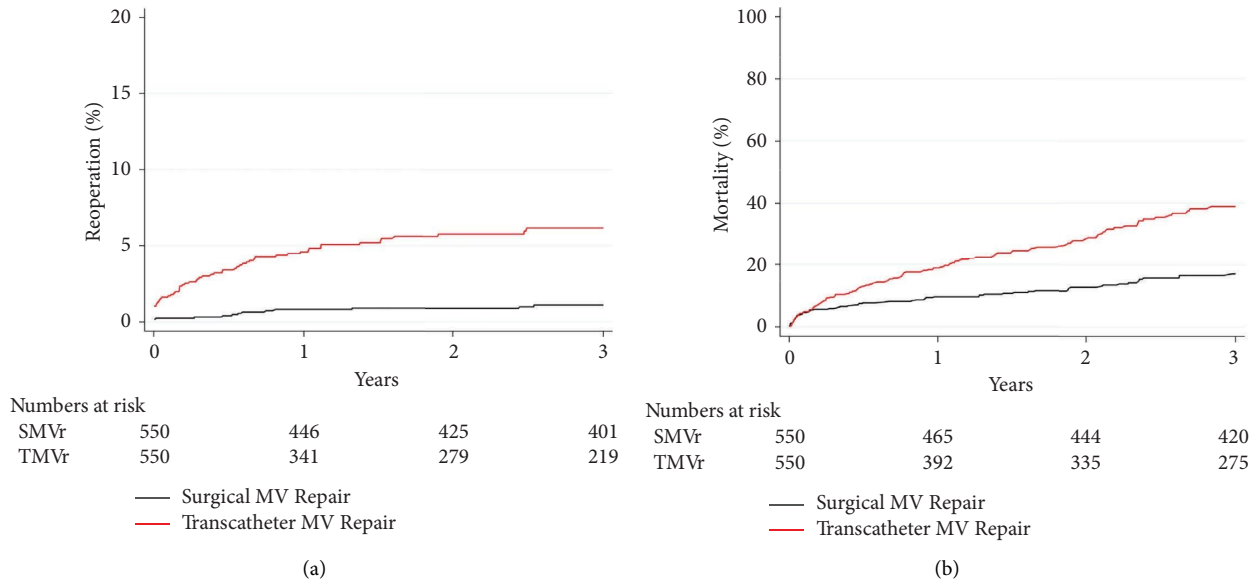

Figure 2: Failure rates in the matched cohorts: reoperation (a) and mortality (b).

Interestingly, Vinciguerra et al. have defined ischemic mitral regurgitation as a "multifaceted syndrome" [20] to underline the multiple components in its pathophysiology. From a mechanistic standpoint, the transcatheter option can only address the component of mitral regurgitation caused by lack of valvular leaflet coaptation–without the ability to fully address the mitral annular component or the underlying myocardial ischemia. Indeed, Cimino et al. have demonstrated that patients with more severely dilated left ventricles and mitral valve annulus, or higher pulmonary pressure values, have lower benefits from transcatheter options [21, 22].

4.1. Limitations. In spite of its solid methodology, with propensity score matching allowing to nullify confounding bias, our study have some limitations. First, its retrospective nature. Second, the classification of diseases and comorbidities based on available CPT and ICD-10 codes only. Third, the inability to access patients' electronic medical records at a granular level which would have allowed as to perform more advanced, stratified analysis. Finally, lack of data on the symptomatic classification of diseases and on center-level adherence to current guidelines.

5. Conclusion

Our analysis of real-world data including a large cohort of propensity score-matched patients with chronic ischemic MR, surgical mitral valve repair had significantly better survival rates and significantly lower reintervention rates at 1- and 3-years when compared to TMVr.

Data Availability

The data used in this study were collected from the TriNetX Network, which provided access to electronic medical records (diagnoses, procedures, medications, laboratory values, genomic information). TriNetX, LLC, is compliant with the Health Insurance Portability and Accountability Act (HIPAA), the US federal law which protects the privacy and security of healthcare data, and any additional data privacy regulations applicable to the contributing HCO. TriNetX is certified to the ISO 27001:2013 standard and maintains an Information Security Management System (ISMS) to ensure the protection of the healthcare data it has access to and to meet the requirements of the HIPAA Security Rule. Any data displayed on the TriNetX Platform in aggregate form, or any patient level data provided in a data set generated by the TriNetX Platform, only contain de-identified data as per the de-identification standard defined in Section §164.514(a) of the HIPAA Privacy Rule. The process by which the data are de-identified is attested to through a formal determination by a qualified expert as defined in Section §164.514(b)(1) of the HIPAA Privacy Rule.

Ethical Approval

Because this study used only de-identified patient records and did not involve the collection, use, or transmittal of individually identifiable data, this study was exempted from Institutional Review Board approval.

Disclosure

The study was performed as part of the employment of the Authors at Yale University School of Medicine.

Conflicts of Interest

Dr. Amabile receives consulting fees from JOMDD. Dr. Krane is a physician proctor and a member of the medical advisory board for JOMDD; Peter Duschek is a medical consultant for EVOTEC and Moderna and has received speakers' honoraria from Medtronic and Terumo. Dr. Geirsson receives consulting fees for being a member of the Medtronic Strategic Surgical Advisory Board and from Edwards Lifesciences. The authors declare that they have no conflicts of interest.

Authors' Contributions

Andrea Amabile and Brandon Muncan contributed equally to the study.

References

[1] D. Goldstein, A. J. Moskowitz, A. C. Gelijns et al., "Two-year outcomes of surgical treatment of severe ischemic mitral regurgitation," *New England Journal of Medicine*, vol. 374, no. 4, pp. 344–353, 2016.

[2] T. Feldman, E. Foster, D. D. Glower et al., "Percutaneous repair or surgery for mitral regurgitation," *New England Journal of Medicine*, vol. 364, no. 15, pp. 1395–1406, 2011.

[3] C. M. Otto, R. A. Nishimura, R. O. Bonow et al., "2020 ACC/AHA guideline for the management of patients with valvular heart disease: a report of the American college of cardiology/American heart association joint committee on clinical practice guidelines," *Circulation*, vol. 143, no. 5, pp. e72–e227, 2021.

[4] J. F. Obadia, D. Messika-Zeitoun, G. Leurent et al., "Percutaneous repair or medical treatment for secondary mitral regurgitation," *New England Journal of Medicine*, vol. 379, no. 24, pp. 2297–2306, 2018.

[5] G. W. Stone, J. Lindenfeld, W. T. Abraham et al., "Transcatheter mitral-valve repair in patients with heart failure," *New England Journal of Medicine*, vol. 379, no. 24, pp. 2307–2318, 2018.

[6] M. Taquet, J. R. Geddes, M. Husain, S. Luciano, and P. J. Harrison, "6-month neurological and psychiatric outcomes in 236 379 survivors of COVID-19: a retrospective cohort study using electronic health records," *The Lancet Psychiatry*, vol. 8, no. 5, pp. 416–427, 2021.

[7] V. Parcha, R. Kalra, A. M. Glenn et al., "Coronary artery bypass graft surgery outcomes in the United States: impact of the coronavirus disease 2019 (COVID-19) pandemic," *JTCVS Open*, vol. 6, pp. 132–143, 2021.

[8] F. M. Asch, P. A. Grayburn, R. J. Siegel et al., "Echocardiographic outcomes after transcatheter leaflet approximation in patients with secondary mitral regurgitation: the COAPT trial," *Journal of the American College of Cardiology*, vol. 74, no. 24, pp. 2969–2979, 2019.

[9] M. Mack, J. D. Carroll, V. Thourani et al., "Transcatheter mitral valve therapy in the United States: a report from the STS/ACC tvt registry," *The Annals of Thoracic Surgery*, vol. 113, no. 1, pp. 337–365, 2022.

[10] B. Muncan, A. Amabile, A. P. Kalogeropoulos, A. Geirsson, and M. Krane, "Midterm outcomes of mitral valve repair versus replacement in elderly patients: a propensity score-matched analysis," *Journal of Cardiac Surgery*, vol. 37, no. 12, pp. 4391–4396, 2022.

[11] A. H. Malik, S. Zaid, S. Yandrapalli et al., "Trends and outcomes with transcatheter versus surgical mitral valve repair in patients ≥80 Years of age," *The American Journal of Cardiology*, vol. 125, no. 7, pp. 1083–1087, 2020.

[12] M. Mori, K. J. Brown, and A. Geirsson, "Understanding limitations of the national inpatient sample to facilitate its proper use," *JAMA Surg*, vol. 154, no. 9, pp. 881-882, 2019.

[13] M. De Bonis, M. Taramasso, E. Lapenna et al., "MitraClip therapy and surgical edge-to-edge repair in patients with severe left ventricular dysfunction and secondary mitral regurgitation: mid-term results of a single-centre experience," *European Journal of Cardio-Thoracic Surgery*, vol. 49, no. 1, pp. 255–262, 2016.

[14] T. Gyoten, S. Schenk, K. Rochor et al., "Outcome comparison of mitral valve surgery and MitraClip therapy in patients with severely reduced left ventricular dysfunction," *ESC Heart Failure*, vol. 7, no. 4, pp. 1781–1790, 2020.

[15] T. Okuno, F. Praz, M. Kassar et al., "Surgical versus transcatheter repair for secondary mitral regurgitation: a propensity score-matched cohorts comparison," *The Journal of Thoracic and Cardiovascular Surgery*, vol. 165, no. 6, pp. 2037–2046.e4, 2023.

[16] T. Ondrus, J. Bartunek, M. Vanderheyden et al., "Minimally invasive mitral valve repair for functional mitral regurgitation in severe heart failure: MitraClip versus minimally invasive surgical approach," *Interactive Cardiovascular and Thoracic Surgery*, vol. 23, no. 5, pp. 784–789, 2016.

[17] N. A. Oh, P. N. Kampaktsis, M. Gallo et al., "An updated meta-analysis of MitraClip versus surgery for mitral regurgitation," *Annals of Cardiothoracic Surgery*, vol. 10, no. 1, pp. 1–14, 2021.

[18] T. Feldman, S. Kar, S. Elmariah et al., "Randomized comparison of percutaneous repair and surgery for mitral regurgitation: 5-year results of EVEREST II," *Journal of the American College of Cardiology*, vol. 66, no. 25, pp. 2844–2854, 2015.

[19] L. Mauri, E. Foster, D. D. Glower et al., "4-year results of a randomized controlled trial of percutaneous repair versus surgery for mitral regurgitation," *Journal of the American College of Cardiology*, vol. 62, no. 4, pp. 317–328, 2013.

[20] M. Vinciguerra, F. Grigioni, S. Romiti et al., "Ischemic mitral regurgitation: a multifaceted syndrome with evolving therapies," *Biomedicines*, vol. 9, no. 5, p. 447, 2021.

[21] S. Cimino, V. Maestrini, D. Cantisani et al., "2D/3D echocardiographic determinants of left ventricular reverse remodelling after MitraClip implantation," *European Heart Journal- Cardiovascular Imaging*, vol. 20, no. 5, pp. 558–564, 2019.

[22] S. Cimino, V. Maestrini, D. Cantisani et al., "Mid-term repair durability after MitraClip implantation in patients with functional mitral regurgitation," *Journal of Cardiovascular Medicine*, vol. 20, no. 10, pp. 701–708, 2019.