Published in final edited form as:

Can J Cardiol. 2018 December ; 34(12): 1648–1654. doi:10.1016/j.cjca.2018.10.002.

The Value of Claims-based Non-Traditional Risk Factors in Predicting Long-term Mortality after MitraClip

Harun Kundi, MD, Jeffrey J. Popma, MD, Linda R. Valsdottir, MS, Changyu Shen, PhD, Kamil F. Faridi, MD, Duane S. Pinto, MD, and Robert W. Yeh, MD, MSc

From the Richard A. and Susan F. Smith Center for Outcomes Research in Cardiology, Beth Israel Deaconess Medical Center

Abstract

Background: We sought to identify non-traditional risk factors coded in administrative claims data and evaluate their ability to improve prediction of long-term mortality in patients undergoing percutaneous mitral valve repair.

Methods: Patients undergoing transcatheter mitral valve repair using MitraClip between September 28, 2010 and September 30, 2015 were identified among Medicare fee-for-service beneficiaries. We used nested Cox regression models to identify claims codes predictive of long-term mortality. Four groups of variables were introduced sequentially: cardiac and non-cardiac risk factors, presentation characteristics, and non-traditional risk factors.

Results: A total of 3,782 patients from 280 clinical sites received treatment with MitraClip over the study period. During the follow-up period, 1,114 (29.5%) patients died with a median follow-up time period of 13.6 (9.6–17.3) months. The discrimination of a model to predict long-term mortality including only cardiac risk factors was 0.58 (0.55–0.60). Model discrimination improved with the addition of non-cardiac risk factors ($c=0.63$, 0.61–0.65; integrated discrimination improvement [IDI]=0.038, $p<0.001$), and with the subsequent addition of presentation characteristics ($c=0.67$, 0.65–0.69; IDI=0.033, $p<0.001$ compared to the second model). Finally, the addition of non-traditional risk factors significantly improved model discrimination ($c=0.70$, 0.68–0.72; IDI=0.019, $p<0.001$, compared to the third model).

Conclusions: Risk prediction models which include non-traditional risk factors as identified in claims data can be used to more accurately predict long-term mortality risk in MitraClip patients.

Brief Summary

The current study shows that the inclusion of non-traditional risk factors as identified in Medicare beneficiaries significantly improved the prediction of long-term mortality in MitraClip patients.

Corresponding Author: Robert W. Yeh, MD MSc. *Address for correspondence:* Richard A. and Susan F. Smith Center for Outcomes Research in Cardiology, Beth Israel Deaconess Medical Center, 375 Longwood Ave, Fourth Floor, Boston, MA 02215; Phone: 617-632-7653; Fax: 617-632-7698; ryeh@bidmc.harvard.edu.

Publisher's Disclaimer: This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

CONFLICT OF INTEREST STATEMENT: The following authors have no conflicts of interest to declare: HK, JJP, LRV, KFF and CS.

These claims-based non-traditional risk factors may allow for enhanced mortality prediction in the absence of prospectively collected data.

Keywords

Administrative data; Integrated Discrimination Improvement; Long-term mortality; Non-traditional risk factors; MitraClip

INTRODUCTION

Mitral valve regurgitation is one of the most common types of valvular disease in the United States (US), especially in the older population, with a prevalence of more than 10% ¹. While surgical mitral valve replacement remains the gold standard therapy for symptomatic severe mitral valve regurgitation, half of affected patients cannot undergo a surgical procedure due to reduced left ventricular ejection fraction, co-morbidities or otherwise high surgical risk ^{2, 3}. Transcatheter percutaneous edge-to-edge mitral valve repair, also known as MitraClip (Abbott, Menlo Park, CA, US) therapy, has been developed to treat patients with symptomatic severe mitral valve regurgitation who cannot undergo surgical valve replacement. Patients with this condition who are at high surgical risk have similar survival benefit after MitraClip compared to surgically treated patients, with both groups experiencing a survival benefit when compared to those undergoing medical treatment alone ⁴. More recently, MitraClip resulted in a lower rate of hospitalization for heart failure and lower all-cause mortality within 2-years of follow-up than medical therapy alone in patients with heart failure ⁵.

Pre-procedural risk assessment can help physicians select patients who will most likely benefit from the procedure and facilitate shared decision making with patients. Clinical risk prediction models for mortality after MitraClip have been developed using traditional risk scoring systems, such as the Society for Thoracic Surgery Predicted Risk of Mortality (STS-PROM) ⁶, logistic EuroSCORE ⁷ and clinical risk predictors ^{8–15}. However, these risk prediction models do not include nontraditional risk factors. Furthermore, the potential for improvement by adding non-traditional risk factors to those traditionally incorporated remains unclear ¹⁶. In this study, we sought to identify non-traditional risk factors in claims data and measure their potential to improve the prediction of long-term mortality after MitraClip using data from the Centers for Medicare and Medicaid Services (CMS) Medicare Provider Analysis and Review (MedPAR) files.

METHODS

Study Population

The CMS MedPAR files include administrative billing claims for all hospitalizations of Medicare fee-for-service beneficiaries, and have been used to study national patterns of procedure utilization in the US ^{17–21}. We identified MitraClip patients with a principal International Classification of Diseases, 9th revision, Clinical Modification (ICD-9-CM) procedure code “3597” between September 27, 2010, and September 30, 2015.

Risk factors

A total of 38 cardiac and non-cardiac covariates, presentation risk factors, and non-traditional risk factors were defined as possible factors for all-cause mortality after MitraClip procedures based on our clinical knowledge and prior studies^{8, 22–24}. Age, sex, chronic heart failure, diabetes mellitus, smoking, coronary artery disease without revascularization, prior myocardial infarction, prior percutaneous coronary intervention, prior valvular surgery, prior coronary artery bypass graft surgery, peripheral vascular disease, atrial fibrillation, left and right bundle branch blocks, cerebrovascular disease, and endocarditis were defined as cardiac risk factors. Other comorbidities such as chronic kidney, liver and obstructive pulmonary diseases, anemia, obesity, and hypothyroidism were defined as non-cardiac risk factors. Procedural risk factors included emergency or urgent admission at index procedure, and admission with shock at index procedure.

A series of administrative claims codes were used to identify potential non-traditional risk factors after MitraClip procedures²⁴. In order to examine the prognostic importance of non-traditional risk factors often omitted from risk adjustment, we classified a subgroup of variables including neuropsychiatric disorders, rheumatological disorders, venous and lymphatic disease and infectious diseases as non-traditional risk factors. These codes include those for the following diagnoses: neurotic disorders and other nonpsychotic mental disorders, organic psychotic conditions, hereditary and degenerative diseases of the central nervous system, other psychoses, open wound of lower limb, arthropathies and related disorders, pneumonia and influenza, other bacterial diseases, diseases of veins and lymphatics, other diseases of the urinary system, ill-defined and unknown causes of morbidity and mortality, and contusion with intact skin surface (Supplementary Table 1).

All covariates were ascertained using secondary diagnosis codes that were coded as “present on admission” during the index hospitalization, as well as from principal and secondary diagnosis codes from all hospitalizations in the year prior to the date of admission for the index procedure (Supplementary Table 1).

Outcome

The outcome in this study was all-cause long-term mortality, determined through linkage of the MedPAR files to the CMS denominator file, which includes information on a patient’s vital status. Time to death was calculated as the time between the date of procedure and the date of death. Patients were censored if they were no longer enrolled in Medicare according to the denominator file on or before December 31, 2015, the last date of the analysis.

Analysis Cohort

Continuous variables are presented as means and standard deviations and categorical variables are presented as counts and percentages. Covariates were compared between surviving and non-surviving patients using chi square statistics and t-tests. Kaplan-Meier plots were created to plot time to death, stratified by the number of non-traditional risk factors included. The log-rank test was used to compare the survival distributions of each group. Subsequently, nested multivariable Cox regression incorporating random hospital effects was performed using four sequential models to determine the incremental

improvement in prediction of long-term mortality with the addition of four sets of covariates. Each sequential model added variables associated with 1) cardiac risk factors, 2) non-cardiac risk factors, 3) presentation risk factors, and 4) non-traditional risk factors. Harrell's c-statistic was used to assess model discrimination, with improvement in discrimination assessed by the change in the c-statistic and the DeLong test²⁵. Integrated discrimination improvement (IDI) was also used to assess discrimination Improvement²⁶. Gronnesby and Borgan goodness-of-fit test was used for the objective assessment of calibration in the entire cohort²⁷. In addition, the effect modifications of age and sex were assessed by including interaction terms between any of the presence of non-traditional risk factors. All statistical analyses were performed in STATA software version 15.0 (Stata Corporation, College Station, TX) using a two-tailed p-value of <0.05 for significance.

RESULTS

In total, 3,782 patients from 280 clinical sites underwent a MitraClip procedure over the study period. The baseline characteristics of patients based on survival status are shown in Table 1. A total of 2,086 (55.2%) were men and the mean age was 79.4 ± 9.3 years. A total of 1,644 (43.5%) patients had at least one coded non-traditional risk factor. Neurotic disorders (15.2%) and arthropathies and related disorders (14.2%) were the most common diagnoses designated as non-traditional risk factors.

Mortality

A total of 1,114 (29.5%) patients died within the study period, with a median follow-up of 13.6 (IQR: 9.6–17.3) months. The all-cause mortality rate was 2.2% in-hospital, and rose to 4.5% at 30-days, 23.1% at 1-year, 30.0% at 2-years, and 43.6% at 3-years after MitraClip. Kaplan–Meier curves showing overall mortality up to 3 years after MitraClip, stratified by number of non-traditional risk factors, are shown in Figure 1. Compared to the reference group (without non-traditional risk factors), the hazard ratio (HR) for 3-year mortality was 1.166 (95% confidence interval [CI]: 1.020–1.332; $p = 0.023$) when one non-traditional risk factor was incorporated, and 1.552 (95% CI: 1.308–1.842; $p < 0.001$) when 32 non-traditional risk factors were incorporated.

Discrimination Improvement

In nested models, while the discrimination of the first model including only cardiac risk factors was 0.58 (0.55–0.60), the addition of non-cardiac risk factors in the second model resulted in a discrimination of 0.63 (0.61–0.65) (IDI=0.038; $p < 0.001$). The discrimination of the third model which added presentation characteristics was 0.67 (0.65–0.69) (IDI=0.033; $p < 0.001$ compared to the second model). Finally, the fourth model which included non-traditional risk factors had a discrimination of 0.70 (0.68–0.72) (IDI=0.019; $p < 0.001$ compared to the third model). Comparisons of c-statistics as assessed by the DeLong test were statistically significant for each model (Model 2 vs Model 1, $p < 0.001$; Model 3 vs Model 2, $p < 0.001$; Model 4 vs Model 3, $p = 0.029$) (Table 2).

Model Covariates

Hazard ratios for each of 18 final covariates from nested multivariable Cox regression analysis are presented in Table 3. The covariates that were most strongly associated with increased long-term mortality were chronic heart failure (HR: 1.709, $p < 0.001$) and atrial fibrillation (HR: 1.300, $p < 0.001$) among cardiac risk factors; liver disease (HR: 1.948, $p < 0.001$) and dialysis (HR: 1.696, $p < 0.001$) among non-cardiac risk factors; admission with shock at index (HR: 2.460, $p < 0.001$) among presentation risk factors; and other bacterial diseases (HR: 2.530, $p < 0.001$) among non-traditional risk factors. The Gronnesby and Borgan goodness-of-fit test with 10 subgroups was found to have a p value of 0.251 with $\chi^2_{10} = 11.37$. There was no effect modification by age ($p = 0.128$) and sex ($p = 0.755$) between any of the presence of non-traditional risk factors.

DISCUSSION

In the present study, we used administrative codes to identify cardiac, non-cardiac, and presentation characteristics of patients as well as non-traditional risk factors in patients who underwent MitraClip. More than 40% of MitraClip patients had at least one code associated with non-traditional risk factors, and inclusion of these codes alongside traditional risk factors in our model improved the prediction of long-term mortality in patients undergoing MitraClip procedures. Furthermore, our results demonstrate that long-term mortality gradually increases with an increasing number of non-traditional risk factors. These findings highlight the important role of assessing non-traditional risk factors in determining outcomes following MitraClip procedures.

The collection of prospective information is time-consuming and potentially not always feasible. In addition, registries may misrepresent some non-traditional risk factors by not including all hospitals, and defining risk factors according to one point in time. We demonstrated that incorporating claims-based non-traditional risk factors into risk prediction models significantly improved the discrimination of long-term mortality. Because detailed assessments of these markers may be difficult to conduct in the routine course of care, the retrospective identification of such non-traditional risk factors using data collected in administrative claims data may help to define patient risk, understand long-term patient outcomes, and improve patient selection. Additionally, inclusion of these markers that are likely not available in most clinical studies may improve the performance of risk models used in retrospective analyses, including those used to benchmark hospital performance or in comparative effectiveness research. Risk prediction models have become particularly important in the assessment and reporting of hospital quality with the current growing emphasis on public reporting of outcomes for certain procedures. Importantly, our predictors were developed accounting for natural clustering in the data by hospital, and can be used for assessments of hospital quality at the site level.

Use of claims data may offer advantages over other methods of collecting information regarding patient risk. Claims data are widely available, and are less costly to collect than prospective registry data. As such, they may offer some advantages over other methods of collecting information regarding patient risk. They also can provide a comprehensive interpretation of a patient's interactions with the healthcare system, and can be linked to

external data sources. Perhaps the main advantage of claims data is its extensive coverage of large, representative populations²⁸. Although we do not have all the necessary variables to calculate traditional surgical risk scores such as the STS-PROM or logistic EuroSCORE, our final model derived from MedPAR data had good discrimination (c-statistic = 0.70). There is a lack of specific tools for risk stratification in MitraClip patients. To predict 1-year mortality, a recent study⁸ showed that the logistic EuroSCORE and STS-PROM, derived from surgical series, was fairly modest with a c-statistic of 0.61 and 0.55, respectively, in patients undergoing MitraClip implantation. Therefore, a novel risk prediction model including our non-traditional risk factors may be useful for the stratification of mortality and other outcomes including complications in patients who undergo MitraClip implantation.

Several limitations exist in the current study. First, indications and criteria for patient selection and success rates for MitraClip procedures are not available. Second, administrative coding may misclassify some comorbidities and complications compared with prospective data collection using standard clinical trial definitions. Third, some commonly used risk factors such as physical performance tests, cognitive testing, and phenotypic scales, as well as other potentially informative variables such as durable medical equipment use, are not available in the dataset. We are not able to estimate surgical traditional risk score such as the such as the STS PROM or logistic EuroSCORE because the dataset did not have necessary variables to calculate them. We did not have information on all patients younger than 65 years of age who might have undergone MitraClip procedures in the US, and those patients < 65 who were included in the study may not be representative of younger patients overall. Finally, while this study evaluated long-term mortality, it should be noted that other post-procedural outcomes such as symptom improvement and overall quality of life are also important to this patient population. This data was not available in the present dataset, but future studies might evaluate how non-traditional risk factors may be related to these endpoints.

CONCLUSIONS

We found that adding administrative claims-based non-traditional risk factors improve prediction of long-term mortality in patients following MitraClip. Use of claims data may be informative for future clinical studies and could be utilized in clinical care and procedural planning for patients being considered for MitraClip procedures.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

ACKNOWLEDGEMENTS:

FUNDING:

Members of the study team are supported by funding from the National Heart, Lung, and Blood Institute (1F32HL1407-11[J.B.S.], R01HS024520-01[C.S.] and 1R01HL136708-01[R.W.Y.]).

Dr. Popma reports grants from Medtronic, Abbott Vascular, and Direct Flow Medical and personal fees from Boston Scientific, Cordis, and Direct Flow Medical, outside the submitted work. Dr. Yeh reports investigator-

initiated grant funding from Abiomed, grant support from Boston Scientific, and consulting from Abbott, Medtronic, and Teleflex, outside the submitted work.

REFERENCES

1. Nkomo VT, Gardin JM, Skelton TN, Gottdiener JS, Scott CG, Enriquez-Sarano M. Burden of valvular heart diseases: a population-based study. *The Lancet* 2006;368:1005–1011.
2. Iung B, Baron G, Butchart EG, et al. A prospective survey of patients with valvular heart disease in Europe: The Euro Heart Survey on Valvular Heart Disease. *European heart journal* 2003;24:1231–1243. [PubMed: 12831818]
3. Bolling SF, Li S, O'Brien SM, Brennan JM, Prager RL, Gammie JS. Predictors of mitral valve repair: clinical and surgeon factors. *The Annals of thoracic surgery* 2010;90:1904–1912. [PubMed: 21095334]
4. Swaans MJ, Bakker AL, Alipour A, et al. Survival of transcatheter mitral valve repair compared with surgical and conservative treatment in high-surgical-risk patients. *JACC: Cardiovascular Interventions* 2014;7:875–881. [PubMed: 25147032]
5. Stone GW, Lindenfeld J, Abraham WT, et al. Transcatheter Mitral-Valve Repair in Patients with Heart Failure. *New England Journal of Medicine* 2018 doi:10.1056/NEJMoa1806640
6. O'Brien SM, Shahian DM, Filardo G, et al. The Society of Thoracic Surgeons 2008 cardiac surgery risk models: part 2—isolated valve surgery. *The Annals of thoracic surgery* 2009;88:S23–S42. [PubMed: 19559823]
7. Nashef SA, Roques F, Michel P, et al. European system for cardiac operative risk evaluation (Euro SCORE). *European journal of cardio-thoracic surgery* 1999;16:9–13. [PubMed: 10456395]
8. Buccheri S, Capodanno D, Barbanti M, et al. A risk model for prediction of 1-year mortality in patients undergoing MitraClip implantation. *American Journal of Cardiology* 2017;119:1443–1449. [PubMed: 28274574]
9. Triantafyllis AS, Kortlandt F, Bakker AL, et al. Long-term survival and preprocedural predictors of mortality in high surgical risk patients undergoing percutaneous mitral valve repair. *Catheterization and Cardiovascular Interventions* 2016;87:467–475. [PubMed: 26268819]
10. Adamo M, Capodanno D, Cannata S, et al. Comparison of three contemporary surgical scores for predicting all-cause mortality of patients undergoing percutaneous mitral valve repair with the MitraClip system (from the multicenter GRASP-IT registry). *American Journal of Cardiology* 2015;115:107–112. [PubMed: 25456878]
11. Paranskaya L, D'Ancona G, Bozdog-Turan I, et al. Early and mid-term outcomes of percutaneous mitral valve repair with the MitraClip®: comparative analysis of different EuroSCORE strata. *EuroIntervention: journal of EuroPCR in collaboration with the Working Group on Interventional Cardiology of the European Society of Cardiology* 2012;8:571–578.
12. Toggweiler S, Zuber M, Sürder D, et al. Two-year outcomes after percutaneous mitral valve repair with the MitraClip system: durability of the procedure and predictors of outcome. *Open Heart* 2014;1:e000056. [PubMed: 25332799]
13. Puls M, Lubos E, Boekstegers P, et al. One-year outcomes and predictors of mortality after MitraClip therapy in contemporary clinical practice: results from the German transcatheter mitral valve interventions registry. *European heart journal* 2015;37:703–712. [PubMed: 26614824]
14. Reichenspurner H, Schillinger W, Baldus S, et al. Clinical outcomes through 12 months in patients with degenerative mitral regurgitation treated with the MitraClip® device in the ACCESS-Europe Phase I trial. *European Journal of Cardio-thoracic Surgery* 2013;44:e280–e288. [PubMed: 23864216]
15. Glower DD, Kar S, Trento A, et al. Percutaneous mitral valve repair for mitral regurgitation in high-risk patients: results of the EVEREST II study. *Journal of the American College of Cardiology* 2014;64:172–181. [PubMed: 25011722]
16. Nishimura RA, Otto CM, Bonow RO, et al. 2014 AHA/ACC Guideline for the Management of Patients With Valvular Heart Disease: Executive Summary. *Circulation* 2014;129:2440–2492. [PubMed: 24589852]

17. Krumholz HM, Lin Z, Drye EE, et al. An administrative claims measure suitable for profiling hospital performance based on 30-day all-cause readmission rates among patients with acute myocardial infarction. *Circulation: Cardiovascular Quality and Outcomes* 2011;4:243–252. [PubMed: 21406673]
18. Krumholz HM, Chen J, Wang Y, Radford MJ, Chen Y-T, Marciniak TA. Comparing AMI mortality among hospitals in patients 65 years of age and older. *Circulation* 1999;99:2986–2992. [PubMed: 10368115]
19. Schermerhorn ML, Buck DB, O'Malley AJ, et al. Long-term outcomes of abdominal aortic aneurysm in the Medicare population. *New England Journal of Medicine* 2015;373:328–338. [PubMed: 26200979]
20. Krumholz HM, Nuti SV, Downing NS, Normand S-LT, Wang Y. Mortality, hospitalizations, and expenditures for the Medicare population aged 65 years or older, 1999–2013. *Jama* 2015;314:355–365. [PubMed: 26219053]
21. Krumholz HM, Wang Y, Mattera JA, et al. An administrative claims model suitable for profiling hospital performance based on 30-day mortality rates among patients with heart failure. *Circulation* 2006;113:1693–1701. [PubMed: 16549636]
22. Metzke C, Matzik A-S, Scherner M, et al. Impact of frailty on outcomes in patients undergoing percutaneous mitral valve repair. *JACC: Cardiovascular Interventions* 2017;10:1920–1929. [PubMed: 28917516]
23. Faridi KF, Popma JJ, Strom JB, Shen C, Choi E, Yeh RW. Utilization, In-Hospital Mortality, and 30-Day Readmission After Percutaneous Mitral Valve Repair in the United States Shortly After Device Approval. *The American journal of cardiology* 2018;121:1365–1372. [PubMed: 29627105]
24. Kim DH, Schneeweiss S, Glynn RJ, Lipsitz LA, Rockwood K, Avorn J. Measuring Frailty in Medicare Data: Development and Validation of a Claims-Based Frailty Index. *The Journals of Gerontology: Series A* 2017.
25. DeLong ER, DeLong DM, Clarke-Pearson DL. Comparing the areas under two or more correlated receiver operating characteristic curves: a nonparametric approach. *Biometrics* 1988;44:837–845. [PubMed: 3203132]
26. Pencina MJ, D'Agostino RB, Vasan RS. Evaluating the added predictive ability of a new marker: from area under the ROC curve to reclassification and beyond. *Statistics in medicine* 2008;27:157–172. [PubMed: 17569110]
27. Grønnesby JK, Borgan Ø. A method for checking regression models in survival analysis based on the risk score. *Lifetime data analysis* 1996;2:315–328. [PubMed: 9384628]
28. Rumsfeld JS, Joynt KE, Maddox TM. Big data analytics to improve cardiovascular care: promise and challenges. *Nature reviews. Cardiology* 2016;13:350. [PubMed: 27009423]

Figure 1.

Kaplan-Meier mortality curves according to number of non-traditional risk factors

Table 1.
Characteristics of the study population stratified by vital status at the end of the study period

	Overall (n=3,782) (100%)	Alive (n=2,668) (70.5%)	Dead (n=1,114) (29.5%)	p-value
CARDIAC HISTORY				
Age, years (mean±SD)	79.4±9.3	79±9.2	80±9.7	0.47
Men, no. of pts (%)	2,086 (55.2)	1,431 (53.6)	7,703 (54.3)	0.004
Chronic heart failure, no. of pts (%)	2,940 (77.7)	2,007 (75.2)	933 (83.8)	<0.001
Diabetes mellitus, no. of pts (%)	948 (25.1)	641 (24.0)	307 (27.6)	0.022
Smoker, no. of pts (%)	1,203 (31.8)	858 (32.2)	345 (31.0)	0.47
Coronary artery disease without revascularization, no. of pts (%)	2,313 (61.2)	1,622 (60.8)	691 (62.0)	0.48
Prior myocardial infarction, no. of pts (%)	576 (15.2)	390 (14.6)	186 (16.7)	0.10
Prior percutaneous coronary intervention, no. of pts (%)	699 (18.5)	494 (18.5)	205 (18.4)	0.93
Prior valvular surgery, no. of pts (%)	306 (8.1)	196 (7.3)	110 (9.9)	0.009
Prior coronary artery bypass graft surgery, no. of pts (%)	1,030 (27.2)	717 (26.9)	313 (28.1)	0.44
Peripheral vascular disease, no. of pts (%)	148 (3.9)	108 (4.0)	40 (3.6)	0.51
Atrial fibrillation, no. of pts (%)	2,378 (62.9)	1,623 (60.8)	755 (67.8)	<0.001
Left bundle branch block, no. of pts (%)	83 (2.2)	60 (2.2)	23 (2.1)	0.72
Right bundle branch block, no. of pts (%)	62 (1.6)	39 (1.5)	23 (2.1)	0.18
Cerebrovascular disease, no. of pts (%)	237 (6.3)	169 (6.3)	68 (6.1)	0.79
Endocarditis, no. of pts (%)	12 (0.3)	6 (0.2)	6 (0.5)	0.12
NON-CARDIAC HISTORY				
Chronic kidney disease without dialysis, no. of pts (%)	1,480 (39.1)	901 (33.8)	579 (52.0)	<0.001
Renal dialysis, no. of pts (%)	92 (2.4)	50 (1.9)	42 (3.8)	<0.001
Liver disease, no. of pts (%)	179 (4.7)	50 (1.9)	88 (7.9)	<0.001
Chronic obstructive pulmonary disease, no. of pts (%)	1,023 (27.1)	704 (26.4)	319 (28.6)	0.16
Home O ₂ , no. of pts (%)	238 (6.3)	152 (5.7)	86 (7.7)	0.020
Hypothyroidism, no. of pts (%)	730 (19.3)	511 (19.2)	219 (19.7)	0.72
Obesity, no. of pts (%)	311 (8.2)	249 (9.3)	62 (5.6)	<0.001
Anemia, no. of pts (%)	1,383 (36.6)	893 (33.5)	490 (44.0)	<0.001

	Overall (n=3,782) (100%)	Alive (n=2,668) (70.5%)	Dead (n=1,114) (29.5%)	p-value
PRESENTATION AND PROCEDURAL CHARACTERISTICS				
Emergency or urgent admission at index procedure, no. of pts (%)	859 (22.7)	527 (19.8)	332 (29.8)	<0.001
Admission with shock at index procedure, no. of pts (%)	155 (4.1)	54 (2.0)	101 (9.1)	<0.001
NON-TRADITIONAL RISK FACTORS				
Neurotic disorders, and other nonpsychotic mental disorders, no. of pts (%)	576 (15.2)	426 (16.0)	150 (13.5)	0.051
Organic psychotic conditions, no. of pts (%)	40 (1.1)	24 (0.9)	6 (1.4)	0.14
Hereditary and degenerative diseases of the central nervous system, no. of pts (%)	123 (3.3)	94 (3.5)	29 (2.6)	0.15
Other psychoses, no. of pts (%)	40(1.1)	26 (1.0)	14(1.3)	0.44
Open wound of lower limb, no. of pts (%)	4 (0.1)	3 (0.1)	1 (0.1)	0.84
Arthropathies and related disorders, no. of pts (%)	536(14.2)	393 (14.7)	143 (12.8)	0.13
Pneumonia and influenza, no. of pts (%)	108 (2.9)	50 (1.9)	58 (5.2)	<0.001
Other bacterial diseases, no. of pts (%)	68 (1.8)	16 (0.6)	52 (4.7)	<0.001
Diseases of veins and lymphatics, no. of pts (%)	498 (13.2)	306 (11.5)	192 (17.2)	<0.001
Ill-defined and unknown causes of morbidity and mortality, no. of pts (%)	71(1.9)	50 (1.9)	21 (1.9)	0.98
Contusion with intact skin surface, no. of pts (%)	11 (0.3)	5 (0.5)	6 (0.5)	0.068

Table 2.

Comparison of the c-statistics in each model

Models	C-statistic (CI 95%)	IDI	IDI p-value	DeLong (p value)
Model 1 (cardiac risk factors)	0.58 (0.55–0.60)	-	-	-
Model 2 (adding non-cardiac risk factors)	0.63 (0.61–0.65)	0.038 *	<0.001 *	<0.001 *
Model 3 (adding presentation characteristics)	0.67 (0.65–0.69)	0.033 †	<0.001 †	<0.001 †
Model 4 (adding non-traditional risk factors)	0.70 (0.68–0.72)	0.019 ‡	<0.001 ‡	0.029 ‡

* Model 2 vs Model 1
† Model 3 vs Model 2
‡ Model 4 vs Model 3

Table 3.

Multivariable nested Cox regression results

	Adjusted Hazard Ratio	95% CI (lower-upper)	p-value
CARDIAC HISTORY			
Age, (by year)	1.007	1.001–1.014	0.037
Chronic heart failure	1.709	1.452–2.010	0.001
Atrial fibrillation	1.300	1.144–1.478	<0.001
Male	1.197	1.054–1.357	0.005
Prior valvular surgery	1.276	1.043–1.561	0.018
NON-CARDIAC HISTORY			
Chronic kidney disease without dialysis	1.555	1.337–1.810	<0.001
Dialysis	1.696	1.492–1.928	<0.001
Liver disease	1.948	1.556–2.439	<0.001
Chronic obstructive pulmonary disease	1.162	1.010–1.335	0.032
Home O ₂	1.316	1.040–1.660	0.020
Obesity	0.697	0.516–0.942	0.004
Anemia	1.170	1.032–1.326	0.014
PRESENTATION CHARACTERISTICS			
Emergency or urgent admission at index procedure	1.321	1.127–1.548	<0.001
Admission with shock at index procedure	2.460	2.101–2.649	<0.001
NON-TRADITIONAL RISK FACTORS			
Pneumonia and influenza	1.665	1.229–2.254	0.001
Other bacterial diseases	2.530	1.769–3.618	<0.001
Diseases of veins and lymphatics	1.387	1.153–1.668	<0.001
Contusion with intact skin surface	2.306	1.010–4.890	0.048