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Accurate of RCRI and MFI-5 scores as predictors of mortality and adverse outcomes after thoracic endovascular aortic repair (TEVAR)

Tomás Martins Mendes Calisto

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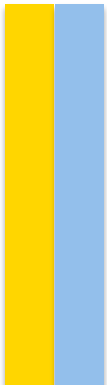

INSTITUTO DE **CIÊNCIAS BIOMÉDICAS ABEL SALAZAR**

Accurate of RCRI and MFI-5 scores as predictors of mortality and adverse outcomes after thoracic endovascular aortic repair (TEVAR)

Dissertação de candidatura ao grau de Mestre em Medicina, submetida ao Instituto de Ciências Biomédicas Abel Salazar, Universidade do Porto.

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Dedicatória

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Resumo

Introdução: A reparação endovascular da aorta torácica (TEVAR) apresenta benefícios significativos, mas permanece associada a uma morbimortalidade substancial. Embora o *Revised Cardiac Risk Index* (RCRI) e o *Modified Frailty Index 5* (MFI-5) estejam validados como preditores de desfechos pós-operatórios adversos noutros contextos cirúrgicos, a sua utilidade em candidatos a TEVAR ainda não foi avaliada. Este estudo avalia a capacidade preditiva do RCRI e do MFI-5 na previsão da morbimortalidade pós-operatória em doentes submetidos a TEVAR.

Materiais e Métodos: Foi realizada uma análise retrospetiva de doentes submetidos a TEVAR entre janeiro de 2010 e dezembro de 2024. Os critérios de exclusão incluíram: seguimento inferior a um ano; dados insuficientes para o cálculo dos scores, intervenções aórticas prévias e patologias aórticas de etiologia traumática, neoplásica ou trombótica. A morbilidade pós-operatória foi quantificada através do *Comprehensive Complication Index* (CCI). Para cada doente, foram calculados os scores RCRI, MFI-5 e CCI. Foram analisadas associações com eventos cardíacos adversos *major* (*major adverse cardiac events*, MACE) no primeiro ano e a performance preditiva foi avaliada através da área sob a curva (AUC) ROC (*receiver operating characteristic*) para MACE, morbilidade grave (CCI > 26,2) e mortalidade aos 30 dias e ao fim de um ano.

Resultados: Numa amostra de 76 doentes (76.3% do sexo masculino; idade média 76,0 ± 13,4 anos), diversos fatores foram significativamente associados ($p < 0,05$) a MACE no primeiro ano, incluindo história de alcoolismo, cardiopatia estrutural, presença de patologia aórtica sintomática, intervenção de caráter urgente, presença de rotura aórtica, bem como a ocorrência de choque ou complicações da ferida no pós-operatório. Por outro lado, verificou-se que doentes com autonomia funcional completa e aqueles sob antiagregação plaquetária, apresentaram um menor risco de MACE no primeiro ano. O MFI-5 apresentou valor preditivo limitado para mortalidade aos 30 dias (AUC = 0,66) contrariamente ao RCRI, sem valor preditivo. Adicionalmente, os scores não demonstraram capacidade preditiva para MACE aos 30 dias, bem como para MACE, mortalidade e morbilidade grave primeiro ano (todos com AUC < 0,6).

Conclusão: Nesta amostra, apesar destes scores demonstrarem ser fracos preditores da morbimortalidade pós-operatória, o MFI-5 parece ser superior ao RCRI. Estes resultados reforçam a necessidade de investigação adicional, de modo a superar as limitações do estudo, com o objetivo de validar, otimizar ou desenvolver ferramentas de estratificação do risco, especificamente adaptadas a esta população, podendo as associações encontradas neste estudo, ou outros fatores preditivos, a identificar em futuras análises exploratórias ser muito úteis para esta finalidade.

Palavras-chave (MeSH): TEVAR; Aneurisma da Aorta Torácica; Previsão do Risco de Morbimortalidade

Abstract

Introduction: Thoracic endovascular aortic repair (TEVAR) offers significant benefits but remains associated with substantial morbidity and mortality. Although the Revised Cardiac Risk Index (RCRI) and the Modified Frailty Index-5 (MFI-5) are validated predictors of adverse postoperative outcomes in other surgical contexts, their utility in TEVAR patients has not yet been assessed. This study evaluates the predictive accuracy of RCRI and MFI-5 for postoperative morbidity and mortality in patients undergoing TEVAR.

Materials and Methods: A retrospective analysis was conducted on patients who underwent TEVAR between January 2010 and December 2024. Exclusion criteria included follow-up of less than one-year, insufficient data for score calculation, prior aortic interventions, and aortic disease of traumatic, neoplastic, or thrombotic etiology. Postoperative morbidity was quantified using the Comprehensive Complication Index (CCI). RCRI, MFI-5, and CCI scores were calculated for each patient. Associations with major adverse cardiac events (MACE) within one year were analyzed and the predictive performance of the two scores was assessed through the analysis of the area under the receiver operating characteristic (ROC) curve (AUC) for 30-day and 1-year mortality, MACE, and severe morbidity (defined as CCI > 26.2).

Results: In a cohort of 76 patients (76.3% male; mean age 76,0 ± 13.4 years), several factors were significantly associated ($p < 0.05$) with 1-year MACE, including history of alcoholism or structural heart disease, presence of symptomatic aortic disease, an urgent/emergent intervention, aortic rupture, and postoperative wound complications or shock. Conversely, patients with full functional autonomy and those with undertaken antiplatelet agents, shown a smaller risk of MACE. MFI-5 demonstrated a limited predictive accuracy for 30-days mortality with an AUC of 0.66, contrary to RCRI, without any predictive value for this outcome. Additionally, both scores didn't show any predictive capacity for 30-days MACE and one-year MACE, mortality and severe morbidity (all with AUC < 0.60).

Conclusion: In this cohort, despite both scores had exhibited poor predictive value for postoperative morbidity and mortality, the MFI-5 seems superior to the RCRI. These findings emphasize the necessity for further research, with the ultimate goal of validate, optimize or develop a simple and effective risk stratification tool that can be used to aid preoperative risk stratification on this patient's population. The founded associations, or other possible predictive factors, to identify in future exploratory analysis can be very useful to achieve this endpoint.

Keywords (MeSH): TEVAR; Thoracic Aortic Aneurysm; Morbimortality Risk Prediction

List of abbreviations

ACC: American College of Cardiology

ACS NSQIP: American College of Surgeons National Surgical Quality Improvement Program

AHA: American Heart Association

ASA: American Society of Anesthesiologist's

ATOM: Assessment of Thoracic Endografting Operative Mortality

AUC: Area under the curve

CCI: Comprehensive Complication Index

COPD: Chronic obstructive pulmonary disease

EVAR: Endovascular Aneurysm Repair

H-CCI: High Comprehensive Complication Index

IBM SPSS: International Business Machines - Statistical Package for the Social Sciences

ICBAS: Instituto de Ciências Biomédicas Abel Salazar

ITR: Laboratory for Integrative and Translational Research in Population Health

MACE: Major adverse cardiac events

MFI-5: Modified 5-Item Frailty Index

MOTHER: Medtronic Thoracic Endovascular Registry

OSA: Obstructive sleep apnea

PAU: Penetrating aortic ulcer

RCRI: Revised Cardiac Risk Score

ROC: Receiving operating characteristic

SD: Standard deviation

TEVAR: Thoracic endovascular aortic repair

ULSSA: Unidade Local de Saúde de Santo António

UMIB: Unidade Multidisciplinar de Investigação Biomédica

wC: Weighted complication

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Introduction

Thoracic aortic pathology represents a significant public health concern, encompassing a broad spectrum of conditions including aneurysmal disease, dissection, traumatic injury, penetrating aortic ulcers (PAUs), and intramural hematomas. These entities may occur independently or concomitantly, presenting with diverse clinical manifestations and varying degrees of severity. In the absence of appropriate treatment, these pathologies are associated with highly catastrophic outcomes, and its prevalence is significant. Aneurysmal disease, for instance, has a reported age and sex adjusted incidence of approximately 5 to 10 cases per 100,000 inhabitants, with evidence suggesting an increasing trend.[1; 2]

This condition is associated with substantial mortality. Historical data from McNamara and Presler (1977) indicate that, among untreated patients, approximately 40% die from aneurysmal rupture and 32% from other cardiovascular causes, with a mean survival of less than three years following diagnosis.[3]

Pseudoaneurysms are less frequent than true aneurysms and are typically the result of iatrogenic or traumatic injury. They arise from a disruption of the arterial wall that is contained solely by the adventitia or adjacent tissues, lacking the involvement of all three layers of the aortic wall present in true aneurysms. They are also associated with a higher risk of rupture.[4; 5]

The estimated incidence of other aortic diseases is approximately 2 to 3.5 cases per 100,000 inhabitants for aortic dissection, 2.1 for PAUs, 1.2 for intramural hematomas, and approximately 1% for traumatic aortic injuries.[6; 7; 8; 9]

Despite their relatively low incidence, these conditions are characterized by a high lethality. Type A aortic dissections, involving the ascending aorta, carry a mortality rate approaching 50%, whereas type B dissections, occurring distal to the origin of the left subclavian artery, are associated with a 30-day mortality rate of approximately 13.9%.[7; 10]

PAUs, particularly those located in the ascending aorta, present a substantial risk of progression to dissection or rupture. Intervention is recommended in symptomatic patients or in cases with high-risk morphological features.[2] Intramural hematomas similarly exhibit a high propensity for progression to overt dissection.[7] In cases of traumatic aortic injury, overall mortality is approximately 20%, but may be significantly higher in the presence of severe vascular disruption.[9]

According to the 2022 American College of Cardiology/American Heart Association (ACC/AHA) Guidelines for the Diagnosis and Management of Aortic Disease, major risk factors for these conditions include advanced age,

degenerative changes in the aortic wall, hypertension, atherosclerosis (and related comorbidities). Systemic inflammatory disorders such as Behçet's disease, giant cell arteritis, and Takayasu arteritis, as well as infectious aortitis (bacterial or fungal), can also contribute to disease pathogenesis. Additionally, a strong association exists with family history and genetic conditions, including Marfan syndrome, Ehlers-Danlos syndrome, Loeys-Dietz syndrome, Turner syndrome, and congenital anomalies such as bicuspid aortic valve.[1]

Thoracic endovascular aortic repair (TEVAR)

TEVAR marked a paradigm shift in the management of thoracic aortic pathology. Its introduction enabled the minimally invasive treatment of various thoracic aortic conditions that would otherwise require conventional open surgery, typically involving thoracotomy, aortic cross-clamping, and left heart bypass. Consequently, TEVAR has been associated with significant reductions in perioperative morbidity and mortality, lower complication rates, shorter hospital stays, and faster postoperative recovery compared to traditional surgical approaches.[11; 12; 13]
These advantages make TEVAR particularly beneficial for older patients and those with elevated surgical risk who may not tolerate open surgery.[14; 15]

Current indications for TEVAR include thoracic aortic aneurysms, particularly those that are symptomatic, rapidly enlarging, or ruptured, as well as aortic dissections, traumatic aortic injuries, and intramural hematomas.[2; 11; 12; 16]

Despite its advantages, TEVAR remains a major surgical procedure associated with considerable operative risk and potential long-term complications. It is not suitable for all patients, as it requires favorable anatomy for prosthesis deployment. Additionally, the frequent occurrence of endoleaks necessitates lifelong postoperative surveillance and appears to be associated with a higher rate of reintervention, which may constitute a significant disadvantage for some patients.[11; 17; 18; 19]

The most common complication of TEVAR is the development of endoleaks. According to data from the Society for Vascular Surgery, endoleaks may occur in up to 30% of patients within the first year following the procedure, contributing to a reintervention rate of approximately 6% within the same period. In the context of aortic dissection, the reintervention rate increases to 12.8%. These findings suggest that, despite favorable early outcomes, endograft failure over the short to long term is common.[20]

Cardiovascular complications, such as myocardial infarction and stroke, significantly contribute to postoperative morbidity, occurring in up to 10.2% of patients within 90 days post-procedure.[14] Neurological complications are also concerning, with reported incidences of stroke ranging from 1.2% to 3.1%, spinal cord ischemia in 3.1%, and paraplegia occurring in approximately 1.2% of cases.[21; 22; 23]

Given requirement for intravenous contrast and substantial hemodynamic changes during TEVAR, renal complications, particularly contrast-induced nephropathy, are relatively common, though underreported in the literature.[24] Access site complications and general hospital-related adverse events, including respiratory complications, deep vein thrombosis, and pulmonary embolism, may also occur.

Thirty-day mortality rates range from 1.7% to 7.63%, while one-year mortality is approximately 8.1%, with a five-year survival rate around 49%. Leading causes of death include aortic rupture, neurological injury, renal failure, and cardiac insufficiency. However, these outcomes are strongly influenced by the patient's baseline clinical status, age, and procedural characteristics, which may vary substantially depending on the indication, anatomical location, extent of disease, number, type, and size of endografts used, and the need for adjunctive procedures such as debranching.[21; 22; 23]

Risk stratification for TEVAR patient's

In patients undergoing TEVAR, accurate risk stratification is essential and should be approached in an individualized and systematic manner, carefully weighing the risks and benefits of the procedure.

Such stratification facilitates evidence-based shared decision making between physicians and patients, by enabling more transparent discussions regarding potential risks and benefits, ensuring realistic expectations, and promoting an active participation of patients in treatment decisions. Furthermore, it allows for improved patient selection by identifying those most likely to benefit from the intervention while also recognizing those who may require intensified perioperative optimization and monitoring. This ultimately contributes to a more efficient allocation of resources, reduces unnecessary interventions, and avoids procedures that may impose additional suffering without clear benefit.[25; 26]

Several preoperative risk prediction models have been used in multiple clinical contexts as simple tools to assist this complex decision-making process. These models correlate various patient-specific variables with the likelihood of adverse outcomes, supporting a more objective risk stratification where clinical judgment alone may be insufficient.[27]

Several specific risk scores have been proposed for assessing perioperative risk in TEVAR candidates.

For instance, Hu et al. described the TEVAR Mortality Risk Score (2017) for predicting 30-days mortality following TEVAR. This model incorporates variables such as patient age, urgency of intervention, American Society of Anesthesiologists (ASA) classification, need for blood transfusions,

preoperative creatinine and leukocyte counts. However, its predictive value for perioperative morbidity has not been evaluated and was only internally validated study, so its clinical utilization remains limited.[22]

The TEVAR Mortality Risk Calculator, derived from the Vascular Quality Initiative database, is another score incorporating predictors such as age, coronary artery disease, prior carotid revascularization, ASA classification, urgency of intervention, and the proximal landing zone. This model demonstrated strong predictive accuracy for 30-day mortality in patients undergoing TEVAR for descending thoracic aortic aneurysms.[25]

Another example is the Assessment of Thoracic Endografting Operative Mortality (ATOM) score that was developed using data from the American College of Surgeons National Surgical Quality Improvement Program (ACS NSQIP). It includes risk factors such as age, sex, functional status, procedural urgency, selected comorbidities, and preoperative albumin and hematocrit levels. This score has demonstrated effectiveness in predicting operative mortality.[28] From the same database, the Frailty-Based Risk Score was developed, with a focus on frailty markers and procedural complexity. It demonstrates a good predictive performance regarding 30-days mortality and major systemic complications in patients with descending thoracic aortic aneurysms after TEVAR, and incorporates variables such as functional dependence, pulmonary disease, thoracoabdominal extent of aortic pathology, need for iliac access, and landing zone characteristics.[26]

Additionally, the Mid-Term All-Cause Mortality Risk Score, derived from the Medtronic Thoracic Endovascular Registry (MOTHER) database, has demonstrated strong predictive capacity for mid-term mortality following elective TEVAR in patients with descending thoracic aortic aneurysms. It includes factors such as age, smoking status, renal disease, cerebrovascular disease, number of endografts used, and maximum aneurysm diameter.[27]

Despite the availability of these risk scores, most are specific to a single underlying pathology leading to TEVAR and often require highly specific procedural data. Furthermore, although some have undergone internal validation, external validation across diverse populations and clinical settings is frequently absent, as seen with the ATOM score and the TEVAR Mortality Risk Calculator.[25; 28]

Additionally, most of these models primarily assess short-term outcomes, such as 30-day mortality, leaving a substantial gap in the literature regarding their ability to predict medium- and long-term outcomes. Patient-centered metrics such as quality of life, functional status, and morbidity burden, which are crucial considerations in treatment decisions, are often overlooked.[27; 29]

The Revised Cardiac Risk Index (RCRI) and Modified Frailty Index-5 (MFI-5)

The RCRI, developed by Lee et al. in 1999[30], is a well-established tool for assessing the risk of postoperative cardiac events. The score includes the risk of the type of surgery, history of ischemic heart disease, cerebrovascular disease, congestive heart failure, pre-operative treatment with insulin and serum creatinine levels higher then 2 mg/dL. It ranges from 0 to 6 points, with higher scores indicating a greater risk of major adverse cardiac events (MACE), including mortality, cardiac arrest and various cardiovascular or cerebrovascular events. It has been validated across multiple surgical contexts, including vascular procedures. Current guidelines from the ACC/AHA recommend its use for cardiovascular risk stratification in non-cardiac surgeries. To this date, no studies have evaluated its applicability specifically in TEVAR patients.[30; 31; 32; 33]

A substantial proportion of complications following this procedure have a cardiovascular nature.[14] In this context, the RCRI remains a highly recommended tool for predicting perioperative cardiac risk in non-cardiac surgery, indicating significant potential utility in the TEVAR population.[32] However, studies by Danielle M. Gualandro et al. (2017) and J. Fronczek et al. (2019) suggest that, in other vascular surgeries, the RCRI may underestimate complication risk, and the same could happen in these patient group.[34; 35; 36]

The MFI-5[37] is another score, derived from the ACS NSQIP database, assesses patient frailty and has demonstrated strong predictive value for postoperative complications across various surgical specialties. Several studies have validated its effectiveness in predicting 30-day mortality, prolonged hospitalizations and readmissions, making it particularly useful for evaluating frailty in elderly surgical patients. The score includes variables such as the functional status on the activities of daily living, the history of chronic pulmonary obstructive disease (COPD) or pneumonia, diabetes, arterial hypertension requiring treatment, and congestive heart failure.[37; 38]

The MFI-5, by specifically assessing frailty, may offer superior discriminatory capacity for MACE and mortality prediction. Moreover, this score has demonstrated efficacy in forecasting hospital resource utilization, which is valuable for postoperative planning and resource optimization.[26; 38]

Compared to the previously discussed models, the RCRI and MFI-5 offer several advantages, particularly their broad applicability. Both scores are widely used and validated across a range of non-cardiac surgeries, including multiple vascular procedures, making them versatile tools for perioperative risk stratification in diverse patient populations. Additionally, these models are intuitive, easy to calculate and require only a small number of variables, making them practical for routine clinical application.[32] Although no studies have assessed the performance of RCRI and MFI-5 specifically in TEVAR patients, comparative analysis in individuals undergoing endovascular

abdominal aortic repair, another endovascular procedure, indicate that the MFI-5 may outperform the RCRI in predicting MACE.[39] This may happen cause, frailty markers can strongly predict major adverse events after TEVAR as suggested by Harris et al.[26]

Based on this background, the present study aims to evaluate the predictive accuracy of the RCRI and MFI-5 in a cohort of patients undergoing TEVAR, focusing on postoperative adverse outcomes such as mortality, MACE, and overall morbidity.

Materials and methods

Sample and data collection

This study was designed as retrospective cohort study. Data were obtained through a review of the electronic medical records from the *Unidade Local de Saúde de Santo António* (ULSSA) in Porto, Portugal. All patients who underwent TEVAR at this healthcare unit between January 2010 and December 2024 were identified through the surgical intervention registry. Demographic, characteristics of the aortic pathology, procedural details and postoperative outcomes, including mortality, complications, and duration of hospitalization were extracted from patient's clinical records. Exclusion criteria included: absence of at least one year of follow-up, a prior aortic instrumentation, traumatic, neoplastic or thrombotic etiology of aortic pathology motivating the intervention and insufficient data for score calculation.

The primary outcome was the occurrence of MACE, defined as composite of death, cardiac arrest, non-fatal acute coronary syndrome, stroke, or acute heart failure. Additionally, isolated mortality and the morbidity were evaluated and considered secondary outcomes. These adverse outcomes were assessed at 30 days and one year after the intervention.

This study was reviewed and approved by the Ethics Committee of the ULSSA, and the *Instituto de Ciências Biomédicas Abel Salazar* (ICBAS) of Porto University. The study adheres to the ethical principles outlined in the Declaration of Helsinki [local reference: 2024.307(244-CAC/278-CE)].

Data analysis

For each patient, the RCRI and the MFI-5 were computed. These scores were determined by summing the points assigned to each of their respective parameters, with each parameter contributing either with 1 point (if present) or 0 points (if absent). Tables I and II outline the parameters included in each scoring model.[30; 37] To quantify postoperative morbidity burden over the first year, the Comprehensive Complication Index (CCI), originally described by Slankamenac et al. was used. This index is a continuous scale ranging from 0 (no complications) to 100 (death), providing a single numeric value encompassing all postoperative complications and their severity.[40] The CCI is derived from the Clavien-Dindo classification, a standardized system for categorizing postoperative complications based on severity and the required therapeutic interventions for management.[41; 42]

For each patient, the first year CCI was calculated, assigning a Clavien-Dindo classification grade to each recorded complication, following the criteria listed in Table III. Each Clavien-Dindo grade corresponds to a specific complication weight (wC), also detailed in Table III.[40]

The cumulative wC values for all complications occurring within the first postoperative year were summed and the CCI was computed as half the square root of this total. A threshold higher than 26.2 was categorized as "High Comprehensive complication Index" (H-CCI), since on the literature this value has been correlated with moderate/severe postoperative complications, prolonged hospitalizations, increased costs, and reduced long-term survival, representing a significant morbidity burden.[40] (Table IV).

Data were analyzed using the version 29 of IBM SPSS Statistics 2019 for Mac. A descriptive analysis of dataset was performed. Categorical variables are presented as the absolute number of observed cases alongside their corresponding frequencies, while continuous variables are reported as means, followed by their respective standard deviations. The Student's t-test, Chi-square test, and Fisher's exact test were applied to identify potential associations between selected variables and the occurrence of MACE within the first year. This outcome was chosen due to its comprehensiveness, as it encompasses both mortality and severe cardiovascular complications. Statistically significant was considered for $p < 0.05$.

When these analyses were performed the case counts are also displayed by the occurrence of 1-year MACE. When a statistically significant association was identified, Phi (for 2x2 tables) and Cramer's V (for bigger tables) coefficients were calculated. These coefficients are association measures for categorical variables, ranging from -1 to 1. Its absolute value corresponds to the strength of the association: Very weak, < 0.10; Weak, 0.10-0.30; Moderate, 0.30-0.50; Strong, ≥ 0.50.

To assess the ability of the RCRI and MFI-5 to predict perioperative morbidity and mortality, receiver operating characteristic (ROC) curves were generated for multiple outcomes, including 30-days and one-year MACE occurrence, isolated mortality, and first-year CCI. The area under the curve (AUC) was used to determine predictive accuracy. Based on AUC values, the predictive capacity of the model was classified as follows: Excellent, between 0.90-1.00; Good, between 0.80-0.90; Reasonable, between 0.70-0.80; Poor, between 0.60-0.70; No predictive capacity if < 0.60.

Results

Demographics and Comorbidities (Table V)

A total of 100 patients underwent TEVAR at the ULSSA between January 2010 and December 2024. After applying the exclusion criteria, 76 patients were included in the final analysis. The mean age of the sample was 76.0 ± 13.5 years, with 76.3% being male. Most patients were fully autonomous in their daily activities.

Regarding lifestyle habits and comorbidities, a high prevalence of smoking (61.8%) was observed among patients. In this study cohort, the most prevalent comorbidities were dyslipidemia (69.7%) and arterial hypertension (75.0%) followed by COPD (25.0%) and ischemic heart disease (21.1%). Additionally, several other conditions were frequently observed, including type 2 diabetes mellitus (17.1%), chronic kidney disease (14.5%), cerebrovascular disease (14.5%) and peripheral arterial disease (13.2%). These findings underscore the substantial burden of cardiovascular disease within this patient population.

In alignment with the high prevalence of cardiovascular disease and associated risk factors in this cohort, the most prescribed pharmacological therapies included antihypertensive (65.8%) and lipid-lowering agents (59.2%). These were followed by antiplatelet agents (38.2%), and anticoagulants (18.4%), with antidiabetic drugs (oral antidiabetic drugs: 17.6%; insulin: 2.6%) being the least commonly prescribed among them.

Some rare risk factors in aortic pathology, namely autoimmune diseases (7.9%) such as Sjögren's syndrome, connective tissue disorders (2.6%) such as Marfan syndrome, and chronic infections (11.8%) such as syphilis were observed in a notable subset of the cohort.

Additionally, 7.9% of patients have a past history of malignancy, with the majority of them (66.7%) being bladder cancer.

Aortic Disease and Procedural Details (Table VI)

Regarding the aortic pathology, most patients were asymptomatic (67.1%) with an incidental diagnosis. Aneurysmal and pseudo aneurysmal disease were the most frequent (65.8% and 9.2%, respectively), followed by penetrating aortic ulcers (PAUs) (25.0%), dissection (17.1%), and rupture (5.3%).
The most common proximal landing zone of endograft deployment was Ishimaru zone 4, with progressively lower utilization in more proximal aortic segments. Debranching procedures were undertaken in 50.0% of patients, predominantly involving the supra-aortic trunks (39.5%), such as carotid-subclavian bypass, followed by visceral debranching (13.2%), with 3.9% doing both. The use of fenestrated endografts and concomitant endovascular aneurysm repair (EVAR) was less frequent, observed in 9.2% and 13.2% of cases, respectively. Among the interventions performed, 75.0% were elective.

Postoperative Morbidity and Mortality (Table VII)

During hospitalization, five patients died before discharge. Among the surviving patients, the length of hospital stay varied considerably, with a mean duration of 22.5 ± 41.3 days (Range: 1 – 302 days).

The most frequently reported complications during hospitalization included the need for red blood cell transfusion (21.1%), followed by shock and nosocomial infections (13.2% each). Acute kidney injury (2.8%) and arterial access-related complications, such as thrombosis (2.6%), rupture (2.6%) or wound complications (2.6%) were observed less frequently.

By 30 days post-procedure, six patients (7.9%) had died, and MACE were recorded in eight cases (10.5%). At the one-year follow-up, 21 patients had died, resulting in an overall one-year mortality rate of 27.6%, with MACE occurring in 23 patients (30.3%).

The mean CCI of the entire sample was 40.2 ± 41.2, and 55.3% had a H-CCI, reflecting a substantial burden of morbidity following the intervention. These values remained high even when considering only the 1-year survivors (n=55), with a mean CCI of 17.4 ± 20.8, and a 45.5% occurrence of H-CCI in this subgroup.

The most common procedure-related complication observed was endoleak occurrence, affecting 60.0% of patients. In contrast, ischemic events, including spinal cord ischemia (5.3%), stroke (1.3%), acute myocardial infarction (1.3%) and member ischemia (2.6%) were considerably less frequent. Among patients who underwent debranching procedures (n=38), 52.6% experienced complications directly associated with these interventions.

Variables associated with MACE occurrence after one year (Table V to VII)

The presence of symptomatic disease exhibited a strong association (Phi = 0.507) with one-year MACE occurrence.

Several additional variables were found to have weak associations with this outcome, including the occurrence of postoperative shock (Phi = 0.282), history of alcoholism (Phi = 0.266), wound-related complications after the surgery (Phi = 0.266), the urgent or emergent character of the procedure (Phi = 0.255), presence of aortic rupture (Phi = 0.250) and history of structural cardiac disease (Phi = 0.229).

A complete autonomy in daily activities and the use of antiplatelet agents had a weak association to a reduced incidence of MACE at one year (Phi = -0.250 and -0.229, respectively).

RCRI and MFI-5 and its capacity to predict adverse outcomes

The mean RCRI and MFI-5 scores in the sample were 2.1 ± 0.9 and 1.5 ± 0.9 points, respectively (Table VIII).

There were no patients with a RCRI score of 6 and only one with a score of 5, in fact, the majority (71.9%) of the patients had a RCRI score inferior to 3. The same happened with the MFI-5, there were no patients with a score of 5, only one with a 4 score and the majority (88.1%) with scores of 2 or less, indicating a population with low frailty (Table VIII).

Both RCRI and MFI-5 scores exhibited no predictive capacity on this population for the occurrence of MACE at the two timepoints analyzed, with AUC of 0.56 and 0.54, respectively, at 30-days, and AUC of 0.47 and 0.54, respectively, at 1 year. The same happened with its predictive capacity of one-year H-CCI with AUC of 0.48 and 0.53, respectively.
Neither RCRI with an AUC of 0.52 and 0.43 at 30 days and one year, respectively nor the MFI-5 with an AUC of 0.58 at one-year exhibit any predictive accuracy for the mortality occurrence. On the other hand, at 30 days, the MFI-5 shown some predictive, but low ability to predict the mortality on the sample with an AUC of 0.66. In general, the AUC values seemed higher for the MFI-5 score despite the analyzed outcome (Figures 1 to 5).

Discussion

Demographics and preoperative morbidity

The demographic characteristics of the cohort—marked by a predominance of male patients, a mean age of 76 years, and a high prevalence of cardiovascular diseases and associated risk factors, including hypertension, dyslipidemia, ischemic heart disease and cerebrovascular disease —are consistent with the established epidemiology of aortic aneurysmal disease population, where a high burden of this conditions was expected.[1] This condition was the most common underlying pathology leading to TEVAR. Additionally, the substantial prevalence of COPD within the cohort is likely attributed to the high proportion of current or former smokers.

Postoperative morbimortality

The mean CCI was notably high (40.2 ± 41.2), with 55.3% of cases classified as having a H-CCI, indicating substantial perioperative morbidity and mortality risks. Even among surviving patients, 45.5% exhibited H-CCI, further reflecting the procedural burden. Within the first-year post-procedure, approximately one-quarter of patients developed endoleaks, and 21.1% required reintervention at the first year following the procedure. These findings highlight that, despite minimally invasive approach, TEVAR remains associated with significant morbidity and procedural failure rates.[1] This consideration is particularly critical for moderate and high-risk patients, where, under certain circumstances, the risks of intervene may surpass the benefits, demanding a careful assessment of the risk-benefit ratio.[26] However, it remains unclear whether the observed morbidity primarily stems from the TEVAR procedure itself or reflects the natural progression of underlying aortic disease. It is likely that both factors contribute to postoperative outcomes.

Although the incidence of complications in this cohort appears to be higher than those reported in the literature—particularly concerning mortality, reintervention rates, endoleaks, stroke, and spinal cord ischemia—direct comparisons should be interpreted with caution.[14; 20; 21; 22; 23] No formal statistical analysis was performed to determine whether these observed differences are attributable to chance. Additionally, there are variations from the previous studies, including differences in urgency status, underlying pathology, that may account for these discrepancies. Therefore, further studies employing alternative methodological approaches would be necessary to enable an adequate comparison. Nonetheless, the present findings serve as a valuable reference point for ongoing monitoring and evaluation of TEVAR-related outcomes within our center.

Variables associated with one-year MACE

The strongest association found between the collected variables, and the one-year MACE was the presence of symptomatic disease. Symptoms typically

manifest as chest or back pain, ranging from sharp and intense, as observed in dissections, to more prolonged and less severe presentations characteristic of indolent pathologies. These symptoms result from nociceptor activation due to injury to the aortic wall layers, and are frequently linked to acute, life-threatening conditions such as dissections or penetrating ulcers. Additionally, dissections may lead to ischemic symptoms resulting from collateral artery occlusion.[1]

Shock symptoms often develop due to blood loss in cases of rupture. Extensive pathology such as large aneurysms can lead compression of adjacent structures, including the trachea, esophagus, or recurrent laryngeal nerve, possibly resulting in dyspnea, dysphagia, or hoarseness. Thus, symptomatic presentations typically indicate severe disease that necessitates immediate intervention or extensive pathology with mass effect, both of which inherently increase the likelihood of treatment failure and complications.[1]

This explains the strong association observed between symptomatic disease and MACE, along with additional, albeit weaker associations with urgent or emergent interventions, aortic rupture, and postoperative shock. These factors are closely interrelated, for instance, aortic rupture frequently leads to hemodynamic instability, requiring urgent surgical intervention. This, in turn, increases the risk of postoperative shock and subsequent cardiovascular complications or mortality, further contributing to MACE-occurrence.[1] Additionally, asymptomatic patients typically present without acute complications and benefit from enhanced surgical risk control and preoperative health optimization, leading to better outcomes.[16]

Further research is needed to determine which specific symptom types most reliably predict adverse events, enabling a more effective incorporation of clinical presentation into prognostic models. This deeper understanding of symptomatology and its association with postoperative complications could enhance risk stratification, improve decision-making, and optimize patient outcomes.

Structural heart disease, which includes valvular disorders and cardiomyopathies, can impair functional cardiovascular reserve and exacerbate hemodynamic stress during TEVAR, particularly in urgent cases where preoperative optimization is not feasible. Additionally, TEVAR may contribute to increased aortic stiffness, triggering cardiac processes such as left ventricular hypertrophy and diastolic dysfunction. These physiological changes can be particularly detrimental in patients with compromised cardiovascular reserve due to pre-existing structural heart disease, potentially leading to worse outcomes and explaining its association with one-year MACE occurrence.[43; 44; 45]

Several hypotheses may explain the weak association between high alcohol consumption and increased occurrence of MACE. Alcohol is known to contribute to hepatic dysfunction, potentially leading to alcoholic liver disease

and cirrhosis. The impact of hepatic dysfunction is bidirectional—it can induce coagulopathy, increasing bleeding risk and the need for transfusions, or promote a hypercoagulable state that predisposes thrombus formation, thereby increasing MACE occurrence.[46] However, no independent association between liver disease and MACE was found in this study.

A small protective effect over one-year-MACE was observed in patients with full independence in daily activities, a key component of the MFI-5 that helps assess frailty and overall health status. Autonomous individuals tend to follow postoperative recommendations more effectively and maintain an active lifestyle, which reduces the risk of adverse outcomes. Additionally, greater functional capacity enhances resilience to physiological stressors associated with major surgical interventions. These findings could explain the apparent better performance of the MFI-5 over the RCRI in predict postoperative morbimortality.[26; 38]

Antiplatelet therapy was associated with a lower risk of one-year-MACE. This can be explained primarily by its capacity in reducing thromboembolic events, despite the potential for increased bleeding risk. This effect is especially significant in patients with underlying cardiovascular disease, where effective thrombotic risk management contributes to better clinical results. In a population with a high cardiovascular burden, antiplatelet therapy may help mitigate the risk of events such as myocardial infarction, particularly in high-risk individuals.[47]

In fact, a holistic evaluation of patients undergoing TEVAR is imperative. The procedure's success is determined not only by appropriate preoperative patient selection, characteristics of the underlying aortic pathology, and technical expertise, but also by effective management of modifiable risk factors. Cardiovascular risk factors, notably, are key contributors to the development of systemic complications such as atherosclerosis, which impacts multiple organ systems beyond the aorta and remains a major driver of morbidity and mortality in these patients like is suggested on the literature and verified in this cohort.[14; 21; 48]

Predictive accuracy of adverse outcomes by RCRI and MFI-5

The findings suggest that, neither the RCRI nor the MFI-5 demonstrated reliable predictive capability for the intended outcomes—namely, MACE, morbidity and all-cause mortality—within this population.[30; 37] Nonetheless, the MFI-5 seems to be superior to RCRI on its predictive capacity with higher AUC values for the majority of analyzed outcomes. The MFI-5 exhibited some predictive capacity for 30-days mortality, albeit with limited accuracy. This may be attributed to the inclusion of functional status as key component of the MFI-5, which was found to be associated with one-year MACE in this study, unlike other elements within these scoring systems. These results align with previous studies by Gualandro et al. (2017) and Fronczek et al. (2019), which raised concerns regarding the potential underestimation of postoperative risk by the

RCRI in vascular surgery and the ones that suggest that MFI-5 is superior in the vascular surgery context. [26; 34; 36; 38]

Limitations and future research

A key limitation of this study is its small sample size, drawn from a single tertiary center with a low volume of TEVAR cases, which may restrict external validation and generalizability. Additionally, its retrospective and observational design, and the presence of a big heterogenicity cohort, that encompasses patients with a wide range of indications, different urgency levels, and multiple thoracic aortic pathologies, often associated with concomitant procedures such as debranching. This heterogeneity introduces the potential for statistical variability or outliers that could influence the findings and generate conclusion bias. In fact, the analyzed patients were previously selected to undergo TEVAR, and this selection may have excluded beforehand the frailest patients or those with a higher morbidity burden, generating a pre-selection bias in the sample. The mean RCRI score, although substantial (>1), fell within the lower half of the scoring range, while the mean MFI-5 score indicated low frailty, further supporting the presence of pre-selection bias.

Despite the limitations, these results, in alignment with the existing literature, cannot support the use of MFI-5 or RCRI as reliable tools for preoperative risk stratification in TEVAR patients. This underscores the necessity for further research to surpass the encountered limitations, involving larger, multicentered cohorts with well-stratified subgroups and extended follow-up periods, enhancing validity by minimizing confounding factors. Additionally, exploratory analyses using binary logistic regression may help identify additional predictors of adverse outcomes, ultimately guiding the adaptation or development of a simple, intuitive, and effective risk stratification tool that can be validated for this patient population.

Conclusion

Despite the technical advancements and minimally invasive nature of TEVAR, which have broadened treatment options for a wider patient population, postoperative morbidity and mortality remain high, with substantial rates of failure and reintervention. The cardiovascular disease is a big contributor to this morbimortality, so its management is key to improve outcomes. In this context, the preoperative risk stratification is essential and can be complex and multifactorial. Some preoperative variables seem to have potential to aid this process, like a full functional status that seems to be related with better outcomes. Despite its wide use in multiple clinical scenarios there are no evidence to support the use of RCRI or the MFI-5 on the TEVAR candidates, and to this date there are no validated simple scores that can effectively be used in this context. These findings highlight the critical need for reliable preoperative risk stratification tools to support clinical decision-making and avoid interventions in patients for whom procedural risk outweighs potential benefits.

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Table I - Revised Cardiac Risk Index (Lee et al. 1999)[30]

REVISED CARDIAC RISK INDEX (0-6 POINTS)[30]	
High risk surgery (intraperitoneal; intrathoracic; supra-inguinal vascular)	1 Point
History of ischemic heart disease	1 Point
History of congestive heart failure	1 Point
History of cerebrovascular disease	1 Point
Pre-operative treatment with insulin	1 Point
Pre-operative creatinine >2 mg/dL	1 Point

Table II - Modified Frailty Index 5 (MFI-5; Subramaniam, S. et al. 2018)[37]

Modified Frailty Index 5 (0-5 points)[37]	
History of diabetes mellitus	1 Point
History of arterial hypertension requiring treatment	1 Point
History of congestive heart failure	1 Point
History of chronic pulmonary obstructive disease (COPD) or pneumonia	1 Point
Presence of a non-completely autonomous functional status	1 Point

Table III - Clavien-Dindo Classification of Surgical Complication Severity[41; 42]

Clavien-Dindo classification of surgical complication severity[41; 42]		
Grade	**Description**	**wC**
I	Deviation for the normal postoperative course without the need of surgical, endoscopic, radiological interventions or drugs other than: antiemetics, antipyretics, analgesics, diuretics and electrolytes and physiotherapy.	300
II	Need for pharmacologic treatment other than the referred in the class I, total parenteral nutrition or blood components	1750
III	Surgical, endoscopic or radiologic intervention needed	
IIIa	Intervention not under general anesthesia	2750
IIIb	Intervention under general anesthesia	4550
IV	Life threatening complication requiring intensive care management	
IVa	Single organ dysfunction	7200
IVb	Multiorgan dysfunction	8550
V	Death	Non applicable*

Table IV - Comprehensive Complication Index (CCI; Slankamenac, K. et al. 2013)[40]

Comprehensive Complication Index (CCI)[40]		
$CCI = (\sqrt{wC1 + wC2 \ldots + wCx})/2$ If any of the complications is a Clavien Dindo V, the CCI is automatically 100		
Value:		**Morbidity:**
< 26.2		"LOW CCI"
26.2 - 55	MODERATE	"High CCI" (H-CCI)
> 55	SEVERE	

Table V - Population demographics and pre-operatory morbidity and health status

	n/mean (%)/±SD	1y MACE	No 1y MACE	p	Phi/Cramer's V
Total	76	21	55		
Age (years)	76.0 ±13.5	70.1 ±13.4	68.0 ±13.6	0.536	
Sex (male)	58 (76.3%)	15 (71.4%)	43 (78.2%)	0.536	
Smoking	47 (61.8%)	12 (57.1%)	35 (63.6%)	0.602	
Alcoholism	2 (2.6%)	2 (9.5%)	0	**0.02**	0.266
Arterial hypertension	57 (75.0%)	13 (61.9%)	44 (80.0%)	0.130	
Anti-hypertensive drugs	50 (65.8%)	14 (66.7%)	36 (65.5%)	0.921	
Type 2 diabetes	13 (17.1%)	3 (14.3%)	10 (18.2%)	0.687	
Insulin therapy	2 (2.6%)	0	2 (3.6%)	0.376	
Oral anti-diabetics	13 (17.6%)	2 (10.5%)	11 (20.8%)	0,278	
Dyslipidemia	53 (69.7%)	13 (61.9%)	40 (72.7%)	0.358	
Lipid lowering therapy	45 (59.2%)	13 (61.9%)	32 (58.2%)	0.768	
Ischemic heart disease	16 (21.1%)	3 (14.3%)	13 (23.6%)	0.371	
Arrhythmic disease	9 (11.8%)	3 (14.3%)	6 (10.9%)	0.684	
Structural heart disease	9 (11.8%)	5 (23.8%)	4 (7.3%)	**0.046**	0.229
Chronic cardiac failure	10 (13.2%)	6 (28.6%)	4 (7.3%)	0.348	
Cerebrovascular disease	11 (14.5%)	3 (14.3%)	8 (14.5%)	0.977	
Peripheral artery disease	10 (13.2%)	3 (14.3%)	7 (12.7%)	0.857	
Previous pulmonary embolism	2 (2.6%)	0	2 (3.6%)	0.376	
Anti-coagulation drugs	14 (18.4%)	6 (28.6%)	8 (14.5%)	0.158	
Anti-platelet drugs	29 (38.2%)	4 (19.0%)	25 (45.5%)	**0.034**	-0.243
Chronic kidney disease	11 (14.5%)	5 (23.8%)	6 (10.9%)	0.153	
COPD	19 (25.0%)	6 (28.6%)	13 (23.6%)	0.657	
OSA	4 (5.3%)	0	4 (7.3%)	0.204	
Other respiratory diseases	5 (6.6%)	0	5 (9.1%)	0.153	
Chronic liver disease	6 (7.9%)	3 (14.3%)	3 (5.5%)	0.202	
Active oncologic disease	6 (7.9%)	0	6 (10.9%)	0.115	
Chronic infectious disease	9 (11.8%)	2 (9.5%)	7 (12.7%)	0.681	
Autoimmune disease	6 (7.9%)	2 (9.5%)	4 (7.3%)	0.745	
Genetic collagenous disease	2 (2.6%)	0	2 (3.6%)	0.376	
Completely autonomous	63 (82.9%)	14 (66.7%)	49 (89.1%)	**0.02**	-0.266
Hemoglobin (g/dL)	12.3 ± 2.4	11.5 ±2.0	12.5 ±2.5	0.087	
Serum creatinine (g/dL)	1.1 ±0.8	1.5 ±1.4	0.9 ±0.3	0.063	
C-reactive protein (g/dL)	46.5 ±79.6	55.3 ±68.7	43.5 ±83.5	0.569	

Table VI - Aortic pathology and TEVAR procedural details

	n (%)	1y MACE	No 1y MACE	p	Phi/Cramer's V
Total	76	21	55		
Aortic aneurysm	50 (65.8%)	11 (52.4%)	39 (70.9%)	0.128	
Aortic pseudoaneurysm	7 (9.2%)	2 (9.5%)	5 (9.1%)	0.953	
Aortic dissection	13 (17.1%)	6 (28.6%)	7 (12.7%)	0.101	
Aortic rupture	4 (5.3%)	3 (14.3%)	1 (1.8%)	**0.03**	0.250
PAU	19 (25.0%)	4 (19.0%)	15 (27.3%)	0.459	
Symptomatic disease	25 (32.9%)	15 (71.4%)	10 (18.2%)	**<0.001**	0.507
Urgent/emergent intervention	19 (25%)	9 (42.9%)	10 (18.2%)	**0.026**	0.255
Proximal landing zone:					
Zone 0	1 (1.3%)	0	1 (1.8%)	0.147	
Zone 1	9 (11.8%)	1 (4.8%)	8 (14.5%)	0.147	
Zone 2	14 (18.4%)	1 (4.8%)	13 (23.6%)	0.147	
Zone 3	21 (27.6%)	7 (33.3%)	14 (25.5%)	0.147	
Zone 4	31 (40.8%)	12 (57.1%)	19 (34.5%)	0.147	
Fenestrated endoprosthesis	7 (9.2%)	2 (9.5%)	5 (9.1%)	0.953	
Debranching procedure	38 (50.0%)	10 (47.6%)	28 (50.9%)	0.798	
EVAR (concomitant)	10 (13.2%)	3 (14.3%)	7 (12.7%)	0.257	
Surgical conversion	0	0	0		

Table VII - Post-operative outcomes

	n/mean (%)/±SD	1y MACE	No 1y MACE	p	Phi/Cramer's V
Total	76	21	55		
Hospitalization:					
Hemoglobin after 24h	10.9 ±1.9	10.6 ±1.5	11.0 ±2.1	0.397	
In-hospital death	5 (6.6%)				
Hospitalization time (days; n=71)	22.5 ±41.3	25.6 ±26.0	21.7 ±44.7	0.668	
Mortality and morbidity:					
30-day's mortality	6 (7.9%)				
1-year mortality	21 (27.6%)				
30-day's MACE	8 (10.5%)				
1-year MACE	23 (30.3%)				
1-year CCI:					
Global mean	40.2 ±41.2				
Total H-CCI	42 (55.3%)				
Alive patients mean (n=55)	17.4 ±20.8				
Alive patients with H-CCI (n=55)	25 (45.5%)				
Early complications:					
Shock	10 (13.2%)	6 (28.6%)	4 (7.3%)	**0.014**	0.282
Acute kidney injury	2 (2.8%)	1 (5.0%)	1 (1.9%)	0.473	
Transfusions required	16 (21.1%)	5 (23.8%)	11 (20.0%)	0.716	
Nosocomial infection	10 (13.2%)	4 (19.0%)	6 (10.9%)	0.348	
Access site complications:					
Thrombosis	2 (2.6%)	1 (4.8%)	1 (1.8%)	0.473	
Rupture	2 (2.6%)	1 (4.8%)	1 (1.8%)	0.473	
Wound complications	2 (2.6%)	2 (8.7%)	0	**0.020**	0.266
1-year complications:					
Endoleak	45 (60.0%)				
Prosthesis migration	1 (1.3%)				
Medullar ischemia	4 (5.3%)				
Member ischemia	2 (2.6%)				
Stroke	1 (1.3%)				
Acute myocardial infarction	1 (1.3%)				
Other ischemic events	2 (2.6%)				
Debranching complications (n=38)	20 (52.6%)				
Re-intervention	16 (21.1%)	7 (30.4%)	9 (17.0%)	0.105	

Table VIII - Calculated RCRI and MFI-5

Calculated RCRI and MFI-5 scores (N=76)			
RCRI mean ± SD	2.1 ± 0.9	**MFI-5 mean ± SD**	1.5 ± 0.9
Calculated RCRI, n (%)		**Calculated MFI-5, n (%)**	
0 Points	0	0 Points	9 (11.8%)
1 Points	21 (27.6%)	1 Points	33 (43.4%)
2 Points	34 (44.7%)	2 Points	25 (32.9%)
3 Points	15 (19.7%)	3 Points	8 (10.5%)
4 Points	5 (6.6%)	4 Points	1 (1.3%)
5 Points	1 (1.3%)	5 Points	0
6 Points	0		

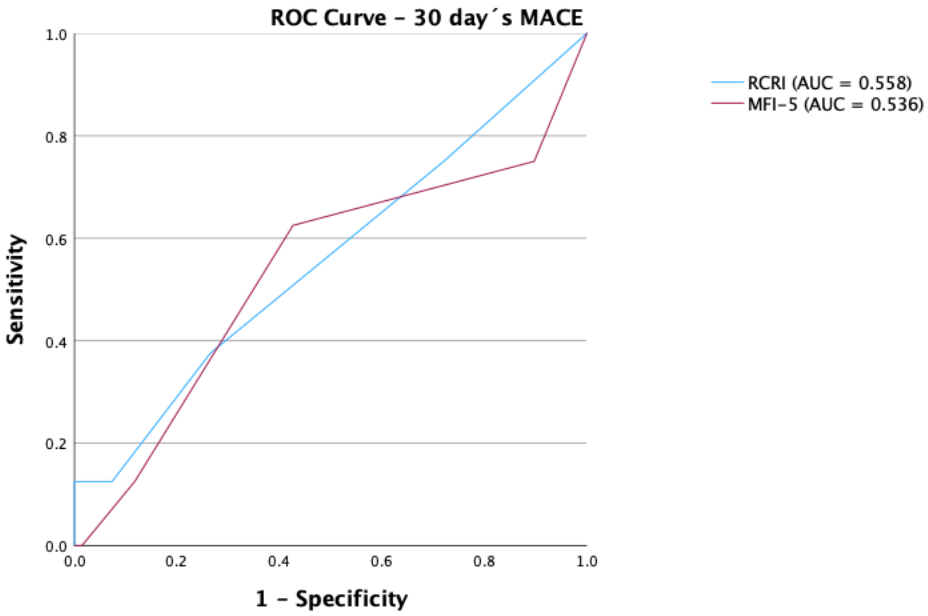

Figure 1: 30 day's MACE occurrence ROC curve

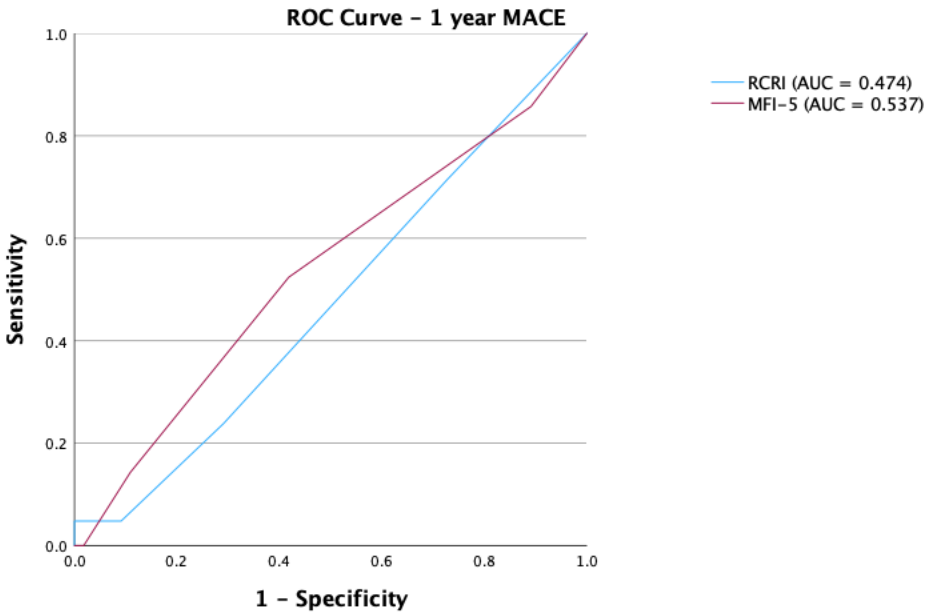

Figure 2: 1 year MACE occurrence ROC curve

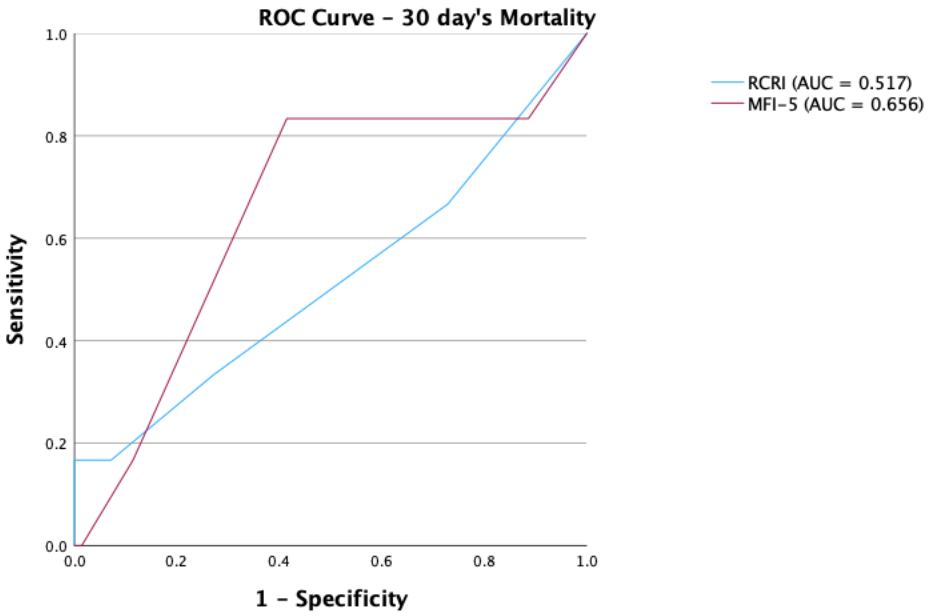

Figure 3: 30 day's mortality occurrence ROC curve

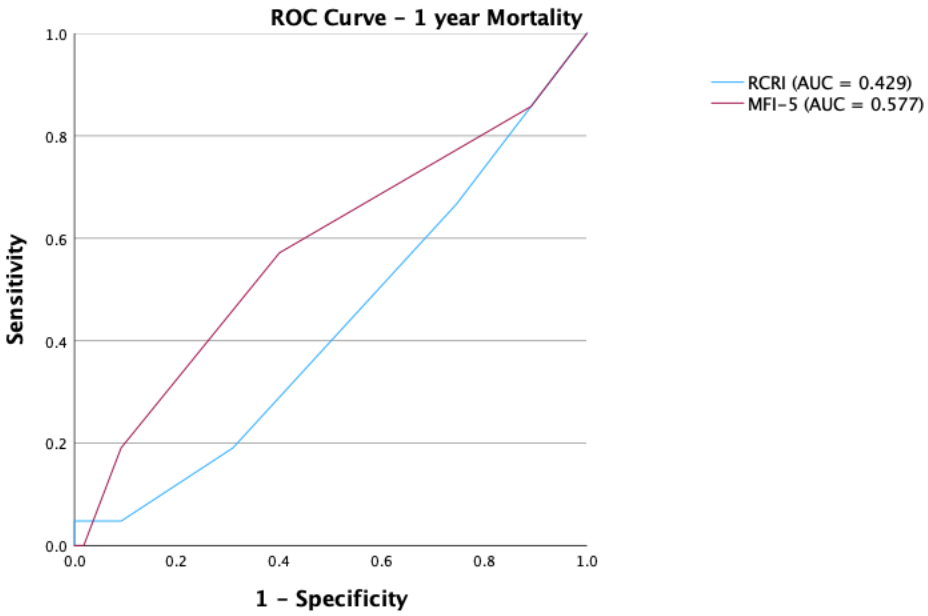

Figure 4: 1 year mortality occurrence ROC curve

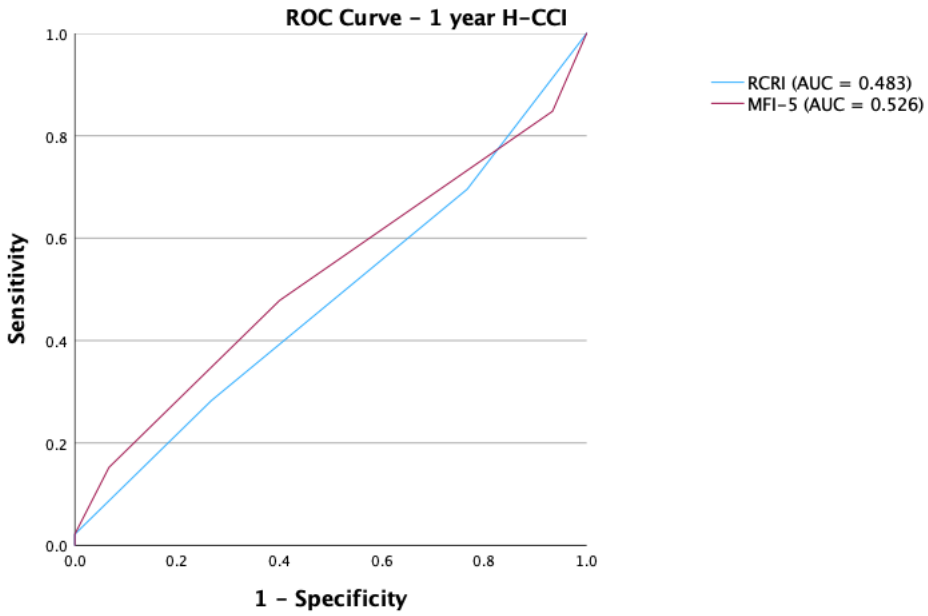

Figure 5: 1 year H-CCI occurrence ROC curve

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