Tese de Doutorado

ESCORES DE RISCO DE NEFROPATIA INDUZIDA PELO CONTRASTE COMO PREDITORES DO DESENVOLVIMENTO DE DESFECHOS ADVERSOS EM PACIENTES SUBMETIDOS À INTERVENÇÃO CORONARIANA PERCUTÂNEA

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DEDICATÓRIA

Ao meu pai, de quem herdei esta linda profissão
e espero sempre herdar o caráter; À minha mãe,
de quem herdei todo amor que tenho; À Lauren,
por me mostrar a beleza da vida, todos os dias.

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“Mesmo que a rota da minha vida me conduza
à uma estrela, nem por isso fui dispensado a
percorrer os caminhos do mundo”
(José Saramago)

SUMÁRIO

LISTA DE ABREVIATURAS

ACEF – Age, Creatinine and Ejection Fraction (score)

AKIN – Acute Kidney Injury Network

ARB – Aldosterone Receptor Blocker

CI-AKI – Contrast-Induced Acute Kidney Injury

CKD – Chronic Kidney Disease

IAMCSST – Infarto Agudo do Miocárdio com Supradesnível do segmento ST

ICP – Intervenção Coronariana Percutânea

LV – Left Ventricle

MACE – Major Adverse Cardiovascular Events

MDRD – Modification of Diet in Renal Disease

MI – Myocardial Infarction

NIC – Nefropatia Induzida pelo Contraste

NO – Nitric Oxide

PCI – Percutaneous Coronary Intervention

STEMI – ST Elevation Myocardial Infarction

TAVR – TransAortic Valve Replacement

RESUMO

Nefropatia induzida pelo contraste (NIC) não é um evento incomum após a exposição à contraste e afeta cerca de 1-2% dos pacientes em procedimentos de imagem radiológica geral. A incidência de NIC é ainda maior entre os pacientes submetidos à intervenção coronária percutânea (ICP) e varia de 3% a 19% de acordo com o perfil de risco do paciente. A NIC está associada ao aumento da morbidade, da mortalidade, do tempo de permanência hospitalar e dos custos de saúde, e porque não há tratamento direcionado após o desenvolvimento, identificar pacientes de alto risco e prevenir a ocorrência é a pedra angular para evitar resultados adversos após a ICP.

Vários modelos de predição do desenvolvimento de NIC foram criados usando definições discrepantes do desfecho. O escore ACEF (Age, Creatinine and Ejection Fraction) é um modelo de risco simples desenvolvido para predizer a mortalidade em pacientes submetidos à cirurgia de revascularização miocárdica eletiva, sendo mais tarde validado em pacientes submetidos à ICP. O objetivo deste trabalho é determinar se este simples modelo de risco de mortalidade é capaz de prever também NIC, já que estas duas condições têm fatores de risco em comum, em pacientes submetidos à ICP primária.

ABSTRACT

Contrast-induced acute kidney injury (CI-AKI) is not an uncommon event after contrast media exposure, and affects around 1-2% of the patients in general radiological imaging procedures. CI-AKI incidence is even higher among patients undergoing percutaneous coronary intervention (PCI), and ranges from 3% to 19% according to the patient`s risk profile. CI-AKI is associated with increased morbidity, mortality, hospital length-of-stay and healthcare costs, and because there is no targeted treatment after it develops, identifying high risk patients and preventing its occurrence is the cornerstone to avoid adverse outcomes after PCI.

Several prediction models of CI-AKI development were created using discrepant definitions of this outcome. ACEF (Age, Creatinine and Ejection Fraction) score is a simple risk model developed to predict mortality in patients undergoing elective myocardial revascularization, and later validated in patients undergoing PCI. The objective of this study is to determine whether this simple model of mortality risk is able to predict CI-AKI, since these two conditions have common risk factors, in patients submitted to primary PCI.

ARTIGO DE REVISÃO – BASE TEÓRICA

CONTRAST-INDUCED ACUTE KIDNEY INJURY

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INTRODUCTION

Contrast-induced acute kidney injury (CI-AKI) is not an uncommon event after contrast media exposure, and affects around 1-2% of the patients in general radiological imaging procedures (1). CI-AKI incidence is even higher among patients undergoing percutaneous coronary intervention (PCI), and ranges from 3% to 19% according to the patient`s risk profile (2-4). CI-AKI is associated with increased morbidity, mortality, hospital length-of-stay and healthcare costs (4), and because there is no targeted treatment after it develops, identifying high risk patients and preventing its occurrence is the cornerstone to avoid adverse outcomes after PCI.

Figure 1. Contrast-induced acute kidney injury highlights

DEFINITION
A rise of 0.3mg/Dl or 50% in 48-72h post-procedure creatinine compared to baseline.
PATHOPHYSIOLOGY
Afferent vasoconstriction and direct tubular damage.
RISK FACTORS
Related to previous kidney dysfunction, impaired kidney perfusion and nephrotoxicity.
CLINICAL IMPLICATIONS
Increased risk of bleeding, dialysis, stroke, myocardial infarction and mortality.
PREVENTION
Identify high risk patients, avoid high volume of contrast, hydration protocols, avoid concomitant nephrotoxic agents.

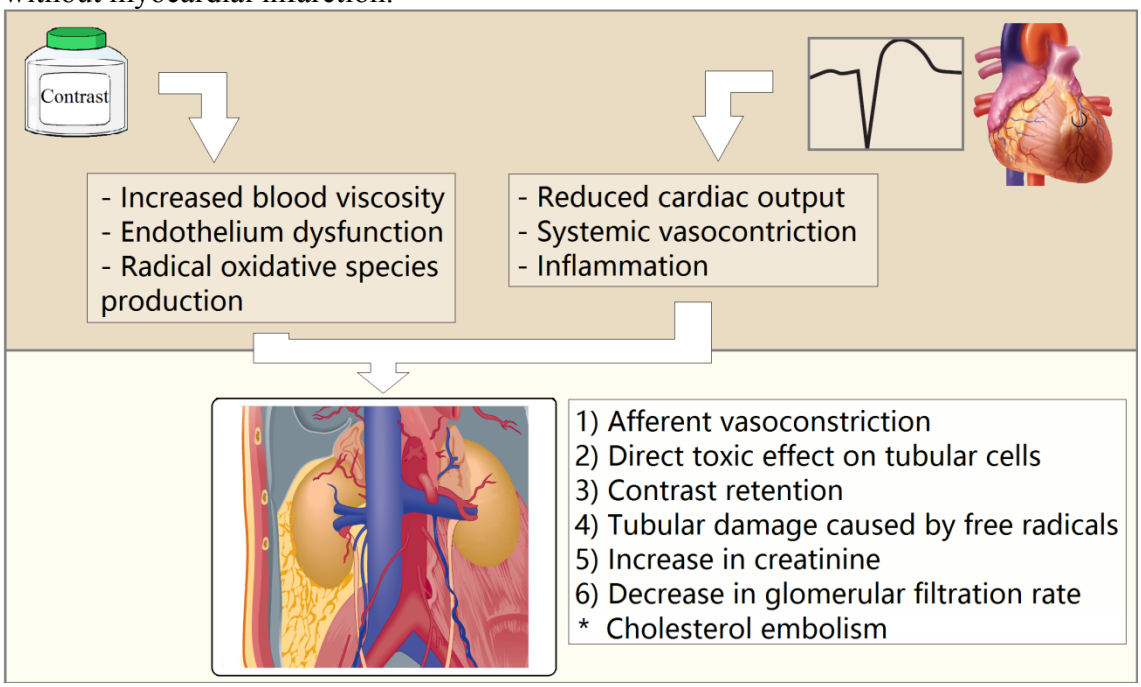
PATHOPHISIOLOGY

Iodinated contrast media are water soluble carbon-based benzene rings used in interventional radiology in order to obtain vessel and chamber imaging. By raising blood viscosity, it causes both a direct toxic effect on renal tubular cells, as well as the production of reactive oxygen species (5, 6). When iodinated contrast is injected into the systemic arterial circuit, there is a transient endothelium-dependent vasodilation mediated by release of nitric oxide (NO), followed by arteriolar vasoconstriction, lasting from seconds to hours. NO causes a release of reactive oxygen species, leading to a reduction in PO2 and increased vascular reactivity to various vasoconstrictors such as norepinephrine, angiotensin II, endothelin and adenosine. The reduction in renal blood flow causes impaired oxygenation to the outer medulla, resulting in ischemia and apoptosis of the tubular cells. Because there is no glomerular injury, hematuria is not

present. Oliguria is also not expected in CI-AKI. Subclinical kidney injury occurs in virtually every patient exposed to iodinated contrast; however, because there is a robust tubular repair capability in healthy subjects, clinically relevant CI-AKI only occurs in predisposed patients who are unable to rapidly repair tubular damage.

A less common cause of kidney injury after PCI is cholesterol embolism. Because the kidneys receive 25% of cardiac output, microshowers of atheroembolic material may deposit into the renal tissue after PCI. Cholesterol embolization syndrome (affecting different organs) occurs in up to 1.4% of patients undergoing cardiac catheterization (7). However, a series of autopsies in patients who died within six months after arteriographic procedures showed that subclinical embolization can be seen in up to 30% of cases (8).

Figure 2. Pathophysiology of Contrast-induced acute kidney injury in patient with and/or without myocardial infarction.



DEFINITION / DIAGNOSIS

The most contemporary CI-AKI definition is a rise of 0.3 mg/Dl or 50% in 48-72h post-procedure creatinine compared to baseline values. The amount of increase in post-procedure creatinine, however, has been controversial. Definitions range from a more restrictive (i.e. an increase > 1.0 mg/dl in creatinine above baseline) to a more sensitive criteria (i.e. an increase of creatinine > 25% above baseline), which leads to a wide variation in its incidence (2% in restrictive (9) and 12.3% in sensitive criteria (10)) and short- and long-term prognostic value after CI-AKI development. Harjai at al. (11) compared different definitions of CI-AKI, and found that a more restrictive criteria fails to identify a large amount of patients with smaller increases in creatinine, leading to underestimation of the incidence of CI-AKI and failing to predict adverse events. In this study, a rise in serum creatinine ≥ 0.5 mg/dl and/or ≥25% within 72 hours after PCI was predictive of 6-month MACE and all-cause mortality after PCI. Although several studies used the latter definition (12, 13), growing data suggested that CI-AKI identification could be improved.

In 2007, the Acute Kidney Injury Network (AKIN) proposed a novel CI-AKI definition in order to standardize AKI assessment and classification in everyday clinical practice as well as in research conditions (14). CI-AKI was defined as a rise of 48-72h post-procedure creatinine higher than 0.3 mg/Dl or 50% compared to baseline. The absolute criteria for the diagnosis of CI-AKI were based on the emerging knowledge that even small variations in creatinine levels are associated with higher morbidity and mortality rates. Centola et al have confirmed that AKIN definition provides a better accuracy in predicting long-term mortality compared to a rise in serum creatinine ≥ 0.5 mg/dl and/or ≥25% within 72 hours after PCI (15). Using a definition that correlates

better with hard outcomes seems reasonable, since reducing CI-AKI may potentially reduce these outcomes.

EPIDEMIOLOGY

The incidence of CI-AKI is highly variable in literature. It depends on procedure type, clinical presentation (i.e. primary vs. elective PCI), population`s characteristics and CI-AKI definition which, as commented above, is not uniform.

In hospitalized patients, contrast media exposure after radiological imaging procedures is related to the development of acute kidney injury in approximately 1% of the cases (1). According to the USA National Cardiovascular Data Registry, 7.1% of the 985,737 patients who underwent elective and urgent PCI developed CI-AKI (AKIN definition), and 3,005 (0.3%) required new dialysis (16). While CI-AKI complicated 4.4% of the elective cases, it was seen in 7.9% of patients after overall acute coronary syndromes, in 10.9% of overall patients after STEMI and in 36.9% of CKD patients presenting with STEMI. In an Italian registry, the incidence of CI-AKI was 14% in patients hospitalized with acute coronary syndromes (17); the same authors had previously found an incidence of 19% using a different CI-AKI definition (2).

Table 1. Contrast-induced acute kidney injury risk according to glomerular filtration rate.

Glomerular filtration rate – Ml/min	CI-AKI risk – %
> 60	5.2
60 – 45	8.0
45 – 30	12.9
< 30	26.6

RISK FACTORS

The risk factors for CI-AKI are mainly related to previous kidney dysfunction, current nephrotoxicity and potential kidney mal perfusion, and can be classified into modifiable and non-modifiable risk factors (Table 2). Patients with **pre-existing kidney** disease are unable to rapidly correct tubular damage, potentially leading to CI-AKI. CI-AKI risk is directly related to baseline glomerular filtration rate (Table 1) (16). **Age** is a risk due to natural loss of tubular function, but also because of more difficult vascular access requiring greater amount of contrast, presence of multivessel disease, and comorbidities. Patients with **diabetes** also have kidney dysfunction more commonly, as well as a higher risk of vascular disease. **Anemia** leads to reduced kidney perfusion, as well as cardiac risk factors such as **heart failure**, **cardiogenic shock** and use of **intra-aortic balloon pump**. **Acute coronary syndromes** increase the risk of CI-AKI due to a multifactorial mechanism, including kidney damage by inflammatory cytokines and kidney hypoperfusion. Use of other **nephrotoxic medications** such as nonsteroidal anti-inflammatory drugs also increases the risk of CI-AKI.

Contrast media is nephrotoxic, thus the risk of CI-AKI is dose-related. However, CI-AKI is unlikely in patients receiving less than 100 ml of volume (18). Increasing complexity of coronary intervention leads to higher volumes of contrast, leading to increased risk of CI-AKI. The role of **contrast osmolality** in the development of CI-AKI has been suggested by trials comparing low and high-osmolar agents. A metanalysis of 31 of these trials showed that, only in patients with pre-existing kidney disease, CI-AKI was significantly higher in patients using high-osmolar contrast (19). The advent of iso-osmolar contrast media was further promising, but a systematic review of 17 trials with 1365 high risk patients showed that the risk of CI-AKI was similar with iso and low-

osmolar agents (20). In the same study, the incidence of CI-AKI with iohexol (low-osmolar) was higher than both iopamidol (low-osmolar) and iodixanol (iso-osmolar), while there was no difference between the latter two agents. This shows that, although osmolality might play a key role in kidney damage, other factors such as ionicity and viscosity are also involved.

Table 2. Risk factors for development of contrast-induced acute kidney injury.

Non-modifiable	Age Heart Failure Diabetes mellitus Acute coronary syndromes Pre-existing kidney disease
Modifiable	Anemia Contrast volume Contrast osmolality* Cardiogenic shock Nephrotoxic medications

* Iso-osmolar and low-osmolar contrast appear to reduce the risk of contrast nephropathy.

CLINICAL IMPLICATIONS

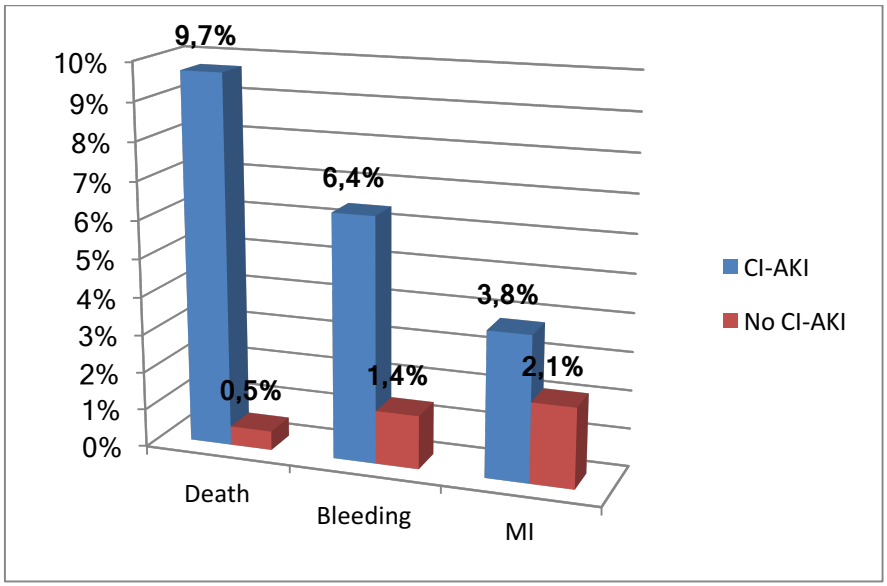
The most common manifestation of CI-AKI is an asymptomatic transient decline in renal function, which starts within 24 hours of procedure, peaks in 3 to 5 days and returns to baseline within up to 14 days. Oliguric acute renal failure leading to volume overload and hyperkalemia may require hemodialysis, but and only a minority will require permanent dialysis or kidney transplantation.

CI-AKI is associated with higher rates of access-site complications, including bleeding, hematoma and pseudo-aneurysms (4). Non-cardiac complications, such as

stroke, pulmonary embolism and gastrointestinal hemorrhage are also more common. The length of hospital stay in patients with CI-AKI is in average 8.3 days or approximately 1.5 times longer than that in patients without CI-AKI (2, 21). Acute renal failure requiring dialysis after percutaneous coronary intervention is a particularly serious complication associated with 27% in-hospital mortality (22). The in-hospital rate of MI is around 4% in patients who develop CI-AKI, compared with 2% in patients in whom it does not. The rates of MI are even higher (7.9%) in patients who require dialysis (16).

Both in-hospital and long term mortality are higher in patients who develop CI-AKI. These finding are consistent throughout the literature, with a follow-up to as long as five years (4, 12, 16, 23, 24). However, because of all the data available are based in observational studies, researchers have recently questioned the true impact of CI-AKI in hard outcomes, suggesting that it is only a marker of high risk patients who developed clinical events despite of CI-AKI (21, 25). Acute kidney injury is strongly associated with important risk factors for mortality, such as preexisting CKD, diabetes, LV dysfunction and markers of more aggressive atherosclerosis (i.e. cerebrovascular disease). Also, it is curious to see how a transient decrease in GFR, with total recovery within a few days, can be associated with such an increase in mortality. On the other hand, it is possible that acute tubular injury triggers clinical events in other organs and with mechanisms still not understood. Yet, it is of great importance trying to anticipate CI-AKI while this doubt remains unsolved. Defining the association of AKI with an adverse long-term prognosis identifies a high-risk cohort that warrants aggressive secondary prevention and monitoring.

Figure 3. Risk of death, bleeding and myocardial infarction (MI) in patients with and without contrast-induced acute kidney injury (CI-AKI). Adapted from Tsai TT et al, JACC Cardiovasc Interv 2014; 7: 1-9.



TREATMENT

Identifying high risk patients

There is no specific treatment after CI-AKI develops. Thus, the main strategy to avoid it lies in prevention, and identifying patients at high risk is essential. Multiple prediction models have been created in different populations and using discrepant CI-AKI definitions (9, 13, 26-29). Given the distinct clinical characteristics of each population, these models perform well where they were developed, but may not predict CI-AKI equally in different scenarios. Mehran`s score (13) is one of the most commonly used prediction models and includes eight variables (hypotension, intra-aortic balloon pump, congestive heart failure, chronic kidney disease, diabetes, age >75 years, anemia, and volume of contrast) with a cumulative score dividing patients from low (7.5%) to

very high risk (57.3%) of developing CI-AKI. When compared to another widely used risk model in a population from northwest USA undergoing elective or urgent PCI, Mehran score was more accurate with a greater area under the curve to predict CI-AKI (30). When compared to ACEF-MDRD score in a population from southern Brazil undergoing primary PCI, Mehran score was less accurate to predict CI-AKIN (31). Ideally, every population should have their own risk prediction tool.

Management

Principles of management include minimization of the total amount of contrast (i.e. biplane coronary angiography, "staged" procedures, avoid ventriculography) and routine use of hydration protocols before contrast exposure, with or without sodium bicarbonate (32). Volume expansion inhibits the renin-angiotensin system, dilutes the contrast media, and protects against reactive oxygen species (33). Administration of iso or low-osmolar rather than high-osmolar contrast media is also recommended (20), as well as avoiding use of concomitant nephrotoxic agents.

Hydration is the cornerstone for prevention of CI-AKI, by increasing renal flow, reducing the contraction of renal vessels and diluting direct nephrotoxic agents. Only intravenous hydration with isotonic sodium chloride is uniformly accepted in clinical practice, with consistent evidence of its effectiveness in reducing CI-AKI (34-36). Although there is a recent paper questioning the true impact of hydration in preventing CI-AKI (37), the patients in this study had very low risk for developing CI-AKI, therefore risk reduction could not be seen. In such patients, oral hydration is at least as effective as IV hydration (38).

Excessive hydration and volume overload, however, may be deleterious and increase CI-AKI risk (39). In order to guarantee an euvolemic state, hemodynamic-guided

hydration have been tested and proved to reduce CI-AKI incidence in patients with heart failure and/or chronic kidney disease. Central venous pressure (40) and left ventricular end diastolic pressure (41) were the strategies used to guide hydration.

Sodium bicarbonate hydration is at least as effective as sodium chloride volume expansion with the advantage of using less volume when volume overload is not desired (i.e. patients with heart failure). While sodium chloride protocols recommend an infusion of 1 ml/Kg body weight per hour 12 hours before and 12 hours after administration of the contrast agent, a widely used sodium bicarbonate protocol (42) consists of 3 ml/kg body weight for 1 hour before and 1 ml/Kg during contrast exposure and for 6 hours after the procedure. A metanalysis of 20 randomized trials showed that sodium bicarbonate is more effective than saline in preventing CI-AKI [OR 0.67 (0.47, 0.96)] in patients with pre-existing renal insufficiency, although it did not lower the risks of dialysis [OR 1.08 (0,52, 2.25)] and mortality [OR 0.69 (0.13, 1.32)] (43).

High volumes of crystalloid infusion with forced diuresis (RenalGuard system®) have been compared with sodium bicarbonate, and reduces the incidence of CI-AKI in high risk patients submitted to PCI and TAVR (44, 45). RenalGuard® measures and controls intravenous crystalloid volume with urine output, increasing the urine flow rate (>150 Ml/h) and reducing the toxic effect of contrast media. The device, however, is not widely available and its use was not popularized.

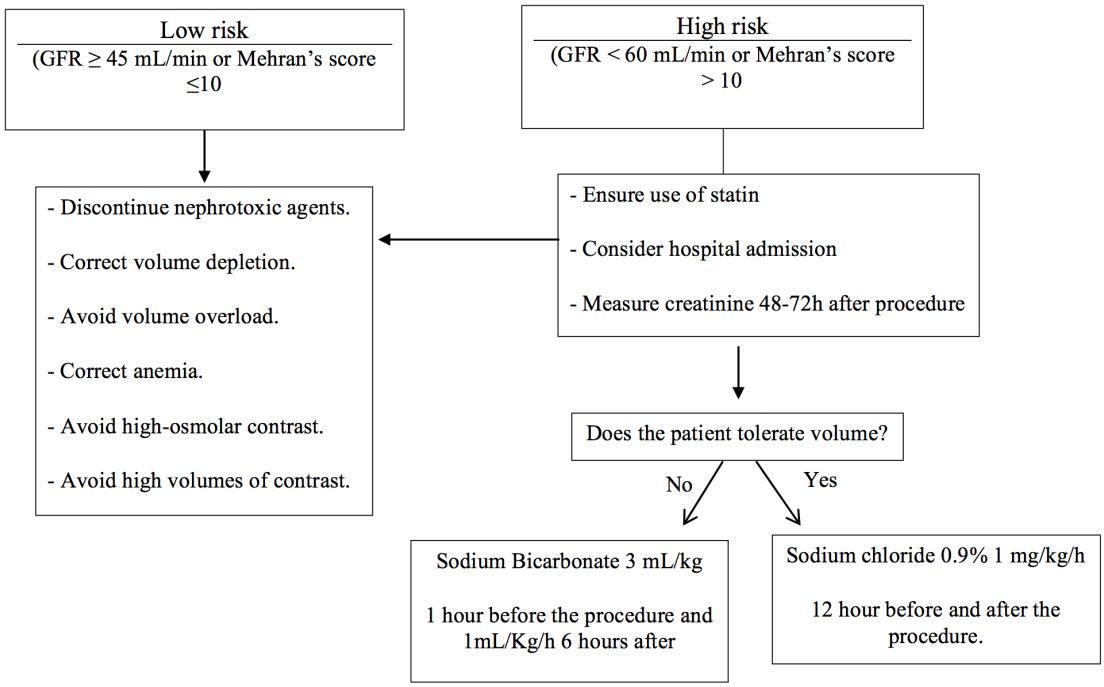
Statins are the only pharmacological intervention to date that consistently prevents CI-AKI, probably through pleiotropic effect of statins on inflammatory pathways, endothelial reactivity, and apoptosis. Statins reduce the incidence of CI-AKI irrespective of the presence of diabetes and CKD (46). However, one can argue that while reducing

the incidence of other cardiovascular outcomes that statins are known to reduce, CI-AKI incidence consequently decreases.

Other pharmacological therapy remains controversial. There has been small randomized trials showing benefit from agents such as theophylyne, trimetazidine, ascorbic acid and others (47-50); however, because of the small benefit and the inconsistent results in larger randomized trials, there is currently no conclusive evidence to use any of these medications broadly. Acetylcysteine is an illustrative example of a medication that performed well in small trials and even in a metanalysis (51), but failed to reduce CI-AKI risk in a well-designed large randomized trial of 2308 patients (47).

ACE inhibitors and ARB`s may increase the incidence of CI-AKI and should be avoided (52). By reducing intra-glomerular pressure due to efferent glomerular arteriolar dilation, they may cause loss of ability to raise intra-glomerular pressure in order to maintain glomerular filtration and forward flow of urine through the proximal tubules and the remainder of the nephron.

Figure 4. Proposed management of contrast-induced acute kidney injury according to baseline risk factors



CONCLUSION

CI-AKI is a common complication in invasive cardiology, and even more common in patients with STEMI. The lack of effective treatment strategies once CI-AKI develops in conjunction with the demonstrated long-term risks associated with the development of CI-AKI makes identification of high risk patients and targeted implementation of CI-AKI preventative strategies as the best contemporary approach to avoid harm effects associated with CI-AKI.

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JUSTIFICATIVA DE PESQUISA

Nefropatia induzida por contraste (NIC) é um evento comum após a intervenção coronariana percutânea (ICP), e está associada a um aumento de morbidade, mortalidade, do tempo de permanência hospitalar e dos custos de saúde. Estudos recentes têm questionado o verdadeiro impacto da NIC nos desfechos duros, sugerindo que é apenas um marcador de pacientes de alto risco que desenvolverão eventos clínicos apesar da NIC. No entanto, é de grande importância tentar antecipar a NIC enquanto esta dúvida permanece sem solução. A incidência de NIC é em torno de 1-2% na população geral, e varia de 3% a 14% entre os pacientes submetidos à ICP.

Várias definições de NIC já foram propostas ao longo dos anos, e a mais contemporânea é um aumento da creatinina 48-72h pós-procedimento superior a 0,3 mg/Dl ou 50% em relação à creatinina basal. Para ser bem caracterizada e relatada nos ensaios, uma definição NIC padrão deve ser utilizada, e a AKIN (acute kidney injury network) propôs essa padronização com a definição acima. Esta definição proporciona uma melhor precisão na predição de mortalidade em longo prazo do que um aumento da creatinina sérica superior a 0,5 mg/dl e/ou 25% dentro de 72 horas após à ICP.

Atualmente, a principal estratégia para evitar a NIC reside na sua prevenção, já que, uma vez estabelecida, apenas cuidados de suporte podem ser oferecidos até que a função renal se resolva. Raramente, a hemodiálise pode ser necessária, transitoriamente ou mesmo permanentemente. A terapia farmacológica permanece controversa e as únicas recomendações bem estabelecidas são: identificar pacientes de alto risco, evitar uso excessivo de contraste, uso rotineiro de protocolos de hidratação antes e após exposição ao contraste e administração de meios de contraste que não sejam de alta osmolalidade.

Para identificar pacientes de alto risco, vários modelos de predição do

desenvolvimento de NIC foram criados usando definições discrepantes de desfechos. Dadas as diferentes características clínicas de cada população, não é possível que um modelo de risco sozinho preveja eventos igualmente em diferentes cenários. Brown et al, por exemplo, validaram um modelo após uma coorte da National Veterans Health Administration, com todas as suas características e peculiaridades. Nosso grupo comparou dois modelos de risco diferentes em uma população do noroeste dos EUA submetidos à ICP eletiva ou urgente. Idealmente, cada população deve ter sua ferramenta de previsão de risco.

O escore ACEF (Age, Creatinine and Ejection Fraction) é um modelo de risco simples desenvolvido para predizer a mortalidade em pacientes submetidos à cirurgia de revascularização miocárdica eletiva, com uma precisão preditiva similar ou até melhor que escores mais complexos de predição de eventos. Este modelo foi mais tarde validado em pacientes submetidos à ICP tanto na doença arterial coronariana estável quanto na instável para estratificar o risco de mortalidade e infarto do miocárdio. O uso da taxa de filtração glomerular como uma variável semi-contínua (taxa de filtração glomerular) ao invés de creatinina sérica melhora a precisão preditiva do escore ACEF em pacientes submetidos à ICP (escore ACEF-MDRD).

HIPÓTESES

O escore ACEF-MDRD é capaz de prever NIC em pacientes submetidos à ICP primária tão bem quando um modelo validado e bem conhecido, porém de maneira mais simples e prática.

OBJETIVOS

Objetivo principal

Determinar se um modelo de risco de mortalidade fácil de usar (ACEF-MDRD) é capaz de prever a NIC em pacientes submetidos à ICP primária e supera modelos validados e bem conhecidos desenvolvidos exclusivamente para prever NIC, utilizando uma definição de NIC consensual.

Objetivos secundários

Identificar, entre os modelos de predição de risco de NIC existentes, aquele que apresenta melhor desempenho para identificação de pacientes com mais alto risco de desenvolver esta complicação.

PRIMEIRO ARTIGO ORIGINAL

Comparison of two risk models in predicting the incidence of contrast-induced nephropathy after percutaneous coronary intervention

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ABSTRACT

OBJECTIVES: We sought to compare two contrast-induced nephropathy (CIN) risk prediction models in a validation cohort using a consensus definition.

BACKGROUND: Contrast-induced nephropathy (CIN) is independently associated with mortality following percutaneous coronary intervention (PCI). Multiple prediction models for the development of CIN have been published using heterogeneous outcome definitions.

METHODS: We analyzed 5,540 patients who underwent PCI from January 2005 to June 2012 at a single academic medical center. The primary outcome was development of CIN, defined as an increase in serum creatinine of ≥0.5 mg/dl or a relative increase of ≥25% from baseline. Receiver operator characteristic (ROC) curves were used to evaluate the discriminatory power of Mehran and WBH prediction models.

RESULTS: The mean age of our cohort was 68 ± 12 years. The mean baseline creatinine was 1.2 ± 0.53 mg/dl (eGFR 73 ± 27 ml/min). The mean contrast volume used was 212 ± 92 ml. CIN occurred in 436 patients (7.9%). The Mehran risk score demonstrated better discrimination than the William Beaumont Hospital (WBH) risk score to predict the occurrence of CIN (c statistic: 0.82 vs 0.73, respectively). Mortality at 30 days was approximately eight times higher among patients with CIN as compared to those without (14.7% vs 1.8% $p < 0.01$).

CONCLUSION: In an independent validation cohort, the Mehran risk model demonstrates greater discriminatory power than the WBH model in predicting the incidence of CIN. Mortality was significantly higher in patients who developed CIN after PCI.

INTRODUCTION

Contrast-induced nephropathy (CIN) is a common complication after percutaneous coronary intervention (PCI). The incidence of CIN has been reported to be 1-2% in general population, and ranges from 3% to 14% among patients undergoing percutaneous coronary intervention (PCI) **(1-3)**. Several strategies have been tested in order to avoid CIN, but pharmacologic prophylaxis remains controversial. Efforts to decrease the incidence of CIN have focused on minimizing the use of contrast media as much as possible, ensuring adequate periprocedural hydration and reducing the nephrotoxicity of contrast media **(4).**

The cornerstone of CIN prevention is to avoid its occurrence. This is of particular importance because the development of this complication is associated with unfavorable outcomes, such as increased morbidity, mortality, long term renal impairment and prolonged hospitalization **(5, 6)**. In order to identify high risk patients, multiple prediction models for the development of CIN have been created using discrepant outcome definitions. In 2004, both Mehran **(7)** and William Beaumont Hospital`s (WBH) **(8)** prediction models were developed after analyzing thousands of patients undergoing PCI, and proposed immediate identification of high risk patients through accountable variables related to CIN development.

We sought to compare two CIN risk prediction models in a validation cohort using a consensus definition.

METHODS

Study Population

We analyzed 5,540 patients who underwent PCI at Brigham and Women's Hospital (BWH)

from January 2005 to June 2012. A prospective catheterization laboratory database, based on the American College of Cardiology–National Cardiovascular Data Registry definitions, was used to record clinical and procedural elements for each patient **(9)**. Patients had serum creatinine measured at baseline and 24-72h after procedure. The primary outcome was the development of CIN, defined as an increase in serum creatinine of ≥0.5 mg/dl or a relative increase of ≥25% from baseline **(10)**. Patients were prospectively followed up for the occurrence of death after 30 days of the baseline procedure. Patients who did not have data on all variables needed to calculate the risk scores were excluded from the study.

Cardiac Catheterization Protocol

PCI was performed according to standard guidelines. Unless contraindicated, all PCI patients received aspirin, clopidogrel, and weight-adjusted heparin therapy according to the standard American College of Cardiology/American Heart Association recommendations. There was a policy in place in the BWH catheterization laboratory to prehydrate every patient with an estimated glomerular filtration rate (eGFR) < 60cc/min with at least 500-1000cc of normal saline prior to the procedure, but adherence to this guideline was waived at the discretion of the operator. Periprocedural glycoprotein IIb/IIIa inhibitors and/or bivalirudin were used at the discretion of the treating physician. Anatomic landmarks were identified by preprocedure fluoroscopy, and vascular access was obtained through single-wall common femoral arterial puncture.

Clinical definitions

Chronic kidney disease was defined as baseline serum creatinine equal or greater than 1.5 mg/dl or an eGFR of 60 ml/min/1.73 m2 or less [10], based on the MDRD equation **(11)**. Anemia

was defined using World Health Organization criteria: baseline hematocrit value 39% (13g/dl hemoglobin) for men and 36% (12g/dl hemoglobin) for women **(12)**. Diabetes was defined using the criteria of the expert committee on the diagnosis and classification of diabetes mellitus, such as fasting plasma glucose ≥7.0 mmol/L (126 mg/dL) or 2-hour plasma glucose ≥11.1 mmol/L (200 mg/dL) **(13)**.

Risk scores

Mehran model (Table 1)

The definition of CIN was a raise of 0.5mg/dl or 25% in post procedure (24-72h) creatinine. Hypotension was defined as systolic blood pressure 80 mm Hg for at least 1 hour requiring inotropic support with medications or intra-aortic balloon pump (IABP) within 24 hours periprocedurally. Congestive heart failure was defined as New York Heart Association functional classification III/IV and/or history of pulmonary edema. Patients with pre-existing end-stage renal disease requiring dialysis and other contrast exposure within one week or less from the index procedure, patients treated with PCI for acute myocardial infarction, and patients in shock were excluded from the analysis. The Mehran score was calculated with 8 variables and its weighted integers. The sum of the integers was a total risk score for each patient, and patients were divided into 4 risk groups, according to their risk of developing CIN: low (lower than 5) – 7.5%; moderate (between 6 and 11) – 14%; high (between 11 and 15) – 26.1%; very high (higher than 16) – 57.3%.

WBH model (Table 2)

The definition of CIN was a raise of 1.0mg/dl in post procedure (24-72h) creatinine. Patients with any form of prior dialysis and those having in-hospital coronary artery bypass

grafting surgery were excluded from this analysis. The WBH score was calculated with 6 variables with weighted integers. The sum of the integers was a total risk score for each patient, and patients were divided into 4 risk groups, according to their risk of developing CIN: low (lower than 5) – 0.5%; moderate (between 5 and 7) – 5.5%; high (between 7 and 9) – 18%; very high (higher than 9) – 43%.

Statistical Analysis

All analysis was carried out using SPSS (Version 17.0, SPSS, Inc, Chicago, Ill) and SAS Statistical Analysis Software (SAS Institute Inc., Cary, NC). Continuous variables were reported as mean values. Patient groups were compared using Student *t* test (for normally distributed variable) or the Wilcoxon rank-sum test (for other variables) for continuous variables and χ^2 test or Fisher exact tests for categorical variables. *P* value was considered significant at <0.05.

Net reclassification index (NRI) was used to assess improvement in risk categories following the methodology in Pencina et al **(14)**. The integrated discrimination index (IDI) is a measure of the average sensitivity by the average of 1-specificity and therefore is closest to a measure of discrimination for these models. It is a measure that is not affected by the choice of risk categories. Receiver operator characteristic (ROC) curves were used to evaluate the discriminatory power of Mehran and WBH prediction models.

RESULTS

Of the 7940 patients with serum creatinine measured at baseline and 24-72h after the

procedure, 177 patients were excluded due to baseline end-stage renal disease undergoing dialysis prior to PCI and 1060 patients were excluded for not having hemoglobin pre procedure, one of the Mehran`s score variable. We ran a sensitivity analysis to determine if the missing hemoglobin interfered with the final result considering first all missing hemoglobin as non-anemic patients, and afterwards all missing hemoglobin as anemic patients. CIN percentages were similar for both groups. We had other 1163 losses due to random missing data. Documentation of the volume of prehydration was not complete in the medical record, and therefore cannot be included in the analysis.

The mean age of our cohort was 68 ± 12 years and 34% had diabetes. The mean baseline creatinine was 1.2 ± 0.99 mg/dl (eGFR 73 ± 25 ml/min). The index PCI was urgent in 68.2% of cases. The mean contrast volume used was 211 ± 94 ml. CIN occurred in 436 patients (7.9%). Baseline clinical and demographic information is shown in table 3.

Table 4 presents the net reclassification index (NRI) and integrated discrimination index (IDI) results for the Mehran outcome and WBH outcomes separately. The NRI was used to assess improvement in categories. In this case, the categories are the risk categories named previously. For the Mehran outcome, for events and nonevents, the probability of events moving up (0.415 and 0.291) was higher than probability of events moving down (0.085 and 0.041). This NRI was statistically significant (p=0.043). However, the NRI for the WBH outcome shows that the probability of moving events and non-events up (0.019 and 0.031) was lower than the probability of moving events or non-events down (0.221 and 0.223). Thus, the NRI was not statistically significant (p=0.840). The IDI shows good discrimination for the Mehran classification (p=0.007) as compared to the WBH classification (p=0.191).

The Mehran risk score demonstrated better discrimination than the WBH risk score (c statistics 0.82 vs 0.73 respectively, figure 1). Mortality at 30 days was approximately eight times higher among patients with CIN as compared to those without (14.7% vs 1.8% $p < 0.01$).

DISCUSSION

Acute kidney injury (AKI) is a common event after PCI, and it is associated with higher morbidity, mortality, duration of hospital stay and healthcare costs **(1)**. However, it is still unknown if CIN is a direct cause of major events or if it is just a marker of high risk patients. The strength of association between CIN and mortality varies among different studies, and recent meta-analysis suggests that the relationship between CIN and subsequent clinical outcomes are substantially influenced by confounding factors **(15)**.

Presently, the main strategy to avoid CIN lies in its prevention, since once established, only supportive care is currently provided until renal function resolves; infrequently, hemodialysis may be required, either transiently or even permanently. Pharmacologic prophylaxis remains controversial, and the only well-established guideline recommendations are routine use of hydration protocols before contrast exposure and administration of low-osmolarity iodine contrast media **(16, 17)**. Studies of N-acetylcysteine **(18)**, sodium bicarbonate **(19)** and statins **(20)** have shown equivocal results, and there is currently no conclusive evidence to use any of these medications broadly. The RenalGuard system **(21, 22)** seems to have benefit over sodium bicarbonate and N-acetylcysteine, but further randomized studies are needed to confirm its efficacy. Other therapies such as hemofiltration, allopurinol, citrate, magnesium sulfate, ascorbic acid, theophylline, and dopamine-1-agonists have also been studied, but results were inconsistent

or had only small benefit **(23-28)**.

Regarding different CIN definitions in prior studies, the Mehran`s is more universally accepted, and we consider it more appropriate. Skelding et al **(29)** found that a creatinine raise of 0.5mg/dl or more had a better sensitivity predicting mortality as compared to an increase of 1.0 mg/dl, with a slight decrease in the discriminatory power. WBH`s study used a creatinine raise of 1.0 mg/dl or more, and consequently found a smaller incidence (2%) of CIN compared to Mehran`s (13.1%) and our dataset (7.9%). Although the mortality among patients who developed CIN in WBH dataset was impressive (21%, or twenty two times higher than patients without kidney injury), a significant raise of mortality in the present study (14.7 vs 1.8%, $P < 0.01$) using Mehran`s CIN definition shows that it is imperative to use a smaller cutoff value in order to identify not only patients at risk of CIN, but the ones at higher risk of mortality.

When we compared the two risk scores to predict occurrence of CIN, we found that the Mehran score is superior to WBH`s in this regard. The Mehran risk score is able to predict events better than the WBH risk score because of a higher probability of events when the risk score resulted in a higher risk classification than the probability of events moving down. Moreover, the NRI for the WBH was not statistically significant ($p<0.840$). It also appears to mirror the NRI results and shows good discrimination for the Mehran classification ($p<0.007$) as compared to the WBH classification ($p<0.191$).

There are a several postcatheterization CIN prediction models that have been developed after the publication of the Mehran and WBH models (29-34), each of them based on slightly differing patient populations. Brown et al (34) recently validated a model after a National Veterans Health Administration cohort, with all its features and peculiarities. We chose to compare the two major models above because they are simple to apply pre-procedure and widely used in clinical

practice. Ideally, each healthcare system should perform their own data analysis to validate the risk assessment model or tool they choose to implement in order ensure the best results in terms of individual patient prediction.

Study limitations

This was a retrospective analysis in which risk scores developed from an external population was applied. Although missing values of hemoglobin were common (13.3%), we ran a sensitivity analysis which demonstrated that the absence of these values did not represent a difference in Mehran score. Multiple imputation was not used. If we consider that the peak creatinine may occur up to 5 days after contrast administration, we may have underestimated CIN incidence. However, it`s known that 80% of CIN occurs in the first 24 hours.

CONCLUSION

The lack of effective treatment strategies once CIN develops in conjunction with the demonstrated long-term risks associated with the development of CIN makes identification of high risk patients and targeted implementation of CIN preventative strategies as the best contemporary approach approaches to avoiding morbidity associated with CIN. While several CIN prediction models have been developed and validated, there has been limited evidence to compare one prediction model with another. In an independent validation cohort, the Mehran risk model demonstrates greater discriminatory power than the WBH model in predicting the incidence of CIN.

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Table 1: Mehran contrast-induced nephropathy (CIN) score variables

Variables	Description	Wheighted Integer
Hypotension	SBD<80mmHg for 1h requiring inotropic support (medication/IABP)	5
IABP	Elective	5
CHF	NYHA III/IV or acute pulmonary edema admission	5
Age	> 75 years	4
Anemia	HT < 39%(M) or 36%(W)	3
Diabetes	Any type	3
Contrast media volume	each 100cc	1/each
CKD	60<GFR>40; 40<GFR>20; GFR<20	2; 4; 6

Table 2: William Beaumont Hospital`s contrast-induced nephropathy (CIN) score variables

Variables	Description	Weighted Integer
CKD	Cr>1.5 or eGFR<60 (MDRD)	2
IABP	yes/no	2
Urgency/Emergency	yes/no	2
Diabetes	yes/no	1
Heart Failure	yes/no	1
Hypertension	yes/no	1
Peripheral artery disease	yes/no	1
Contrast Volume	>260cc	1

Table 3: Demographic characteristics of patients overall, and divided between those who did and did not develop contrast induced nephropathy (CIN).

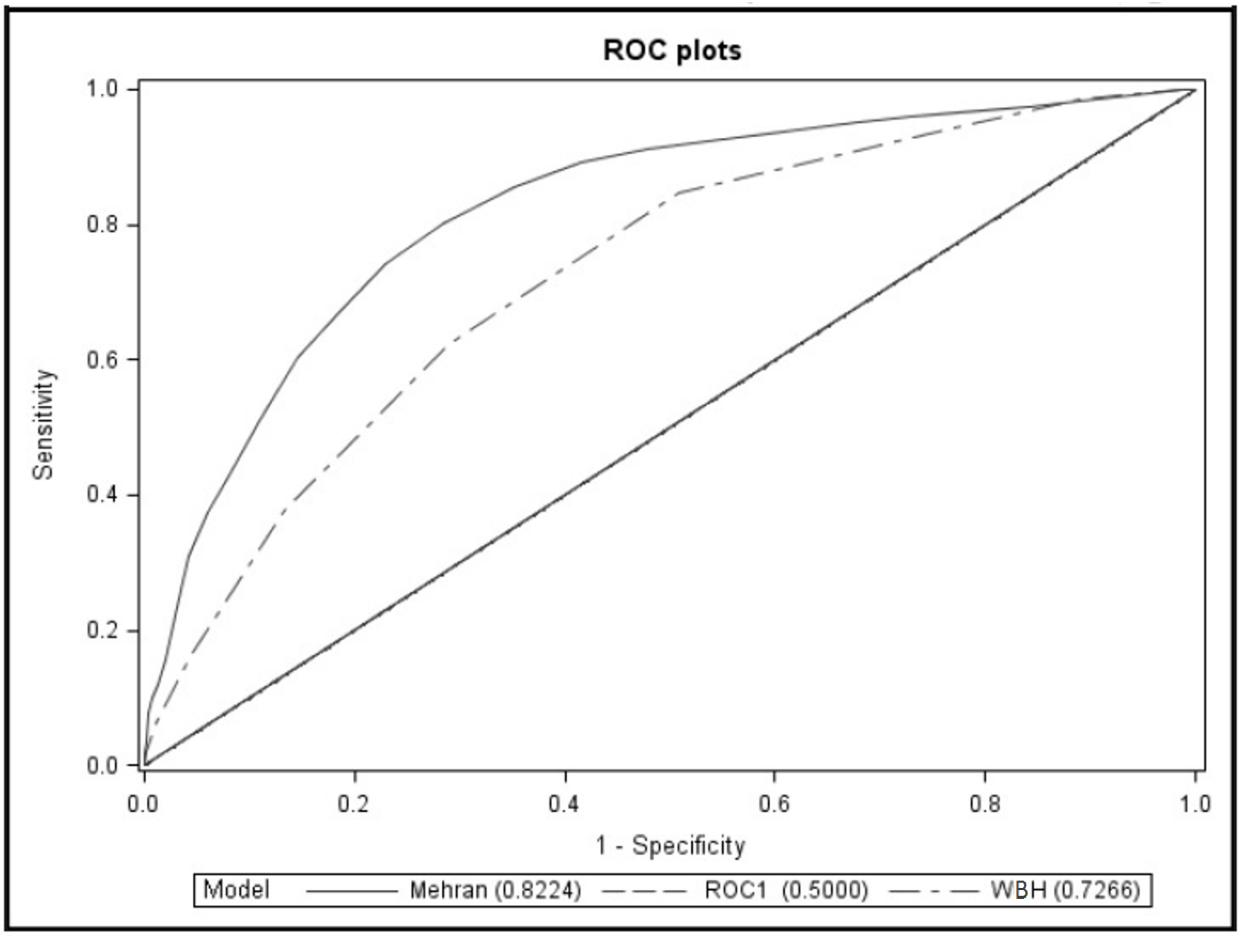
Variable	**Patients (n = 5,540)**	**CIN (n = 436)**	**No CIN(n = 5104)**	**p value**
Age (yrs) (mean +- SD)	68.0 ± 12.1	71.7 ± 11.8	67.4 ± 11.9	<0.001
Age > 75 yrs	29.9%	39.1%	29.1%	0.057
Male	69.9%	59.2%	70.8%	<0.001
Diabetes Mellitus	33.8%	52.6%	32.3%	<0.001
Hypertension	85.7%	88.9%	85.5%	0.023
Dyslipidemia	88.5%	88.6%	88.5%	0.983
Body Surface Area (m^2)	1.97 ± 0.25	1.91 ± 0.28	1.97 ± 0.25	<0.001
Smoking History	16.3%	18.8%	16.1%	0.097
Congestive Heart Failure	13.9%	37.5%	12%	<0.001
Cerebrovascular Disease	11.2%	16.9%	10.7%	<0.001
Peripheral Artery Disease	13.6%	28.5%	12.4%	<0.001
Previous CABG	19.7%	24.1%	19.1%	0.006
Previous PCI	31.1%	27.8%	31.4%	0.073

Hypotension	1.8%	8.7%	1.3%	<0.001
Intra-aortic Baloon Pump	2%	8.9%	1.4%	<0.001
Acute Coronary Syndrome	57.9%	77.6%	66.5%	<0.001
Urgency/Emergency	68.2%	89.4%	66.5%	<0.001
Baseline Creatinine	1.20 ± 0.99	1.25 ± 1.9	1.10 ± 0.8	0.177
Baseline eGFR (ml/min 1.73 m²)	73.3 ± 25.9	73.4 ± 38.6	75.6 ± 23.1	0.116
Baseline Hemoglobin	12.9 ± 1.9	12 ± 6.9	13 ± 2.1	<0.001
Contrast Volume	211 ± 94	230 ± 117	210 ± 91	<0.001

Table 4: Net reclassification index (NRI) and integrated discrimination index (IDI) results for Mehran and WBH outcomes.

Model	Probability up events	Probability down events	Probability up nonevents	Probability down nonevents	NRI p-value	IDI p-value
Mehran Outcome	0.415	0.085	0.291	0.041	0.080 0.043	0.085 0.007
WBH outcome	0.019	0.221	0.031	0.223	-0.010 0.840	0.071 0.191

Figure 1: Receiver operating characteristic (ROC) curve comparing Mehran and WBH contrast-induced nephropathy models



SEGUNDO ARTIGO ORIGINAL

Simplifying contrast-induced acute kidney injury prediction after primary percutaneous coronary intervention: the Age, Creatinine and Ejection Fraction score

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Short Title: Contrast-induced nephropathy prediction model

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ABSTRACT

BACKGROUND: Contrast-induced acute kidney injury (CI-AKI) is a common event after percutaneous coronary intervention (PCI). Presently, the main strategy to avoid CI-AKI lies in saline hydration, since to date none pharmacologic prophylaxis proved beneficial. Our aim was to determine if a low complexity mortality risk model is able to predict CI-AKI in patients undergoing PCI after ST elevation myocardial infarction (STEMI).

METHODS: We have included patients with STEMI submitted to primary PCI in a tertiary hospital. The definition of CI-AKI was a raise of 0.3mg/dl or 50% in post procedure (24-72h) serum creatinine compared to baseline. Age, Glomerular filtration and Ejection Fraction were used to calculate ACEF-MDRD score.

RESULTS: We have included 347 patients with mean age of 60 years. In univariate analysis, age, diabetes, previous ASA use, Killip 3 or 4 at admission, ACEF-MDRD and Mehran scores were predictors of CI-AKI. After multivariate adjustment, only ACEF-MDRD score and diabetes remained CI-AKI predictors. Areas under the ROC curve of ACEF-MDRD and Mehran scores were 0.733 (0.68-0.78) and 0.649 (0.59-0.70), respectively. When we compared both scores with DeLong test ACEF-MDRDs AUC was greater than Mehran`s (p=0.03). An ACEF-MDRD score of 2.33 or lower has a negative predictive value of 92.6% for development of CI-AKI.

CONCLUSION: ACEF-MDRD score is a user-friendly tool that has an excellent CI-AKI predictive accuracy in patients undergoing primary percutaneous coronary intervention. Moreover, a low ACEF-MDRD score has a very good negative predictive value for CI-AKI, which makes this complication unlikely in patients with an ACEF-MDRD score of < 2.33.

INTRODUCTION

Contrast-induced acute kidney injury (CI-AKI) is a common event after percutaneous coronary intervention (PCI), and it is associated with increased morbidity, mortality, hospital length-of-stay and healthcare costs [1]. Yet, it is still unclear whether CI-AKI is a direct cause of major events or it is just a marker of high risk patients. The strength of association between CI-AKI and mortality varies among different studies, and a recent meta-analysis suggests that the relationship between CI-AKI and subsequent clinical outcomes are substantially confounded by baseline clinical characteristics that simultaneously predispose to both kidney injury and mortality [2].

Presently, the main strategy to avoid CI-AKI lies in its prevention, since pharmacologic prophylaxis remains controversial [3]**.** In order to identify high risk patients, several CI-AKI prediction models have been created. Mehran et al [4] have developed probably the most widely used risk model, which performs well in patients undergoing PCI [5-7].

Age, creatinine and ejection fraction (ACEF) score [8] is a simple risk model developed to predict mortality in patients undergoing elective coronary artery bypass graft (CABG), with a similar or better predictive accuracy compared to more complex scores. This model was later validated in patients submitted to PCI in both stable and unstable coronary artery disease to stratify risk of mortality and myocardial infarction [9, 10]. Using glomerular filtration rate as a semi-continuous variable (ACEF-MDRD) instead of serum creatinine improves the predictive accuracy of ACEF score in patients undergoing PCI [11].

Our aim is to determine whether a simple user-friendly mortality risk model is able to predict CI-AKI in patients undergoing primary PCI and outperforms a validated and well known model developed exclusively to predict CI-AKI, using a consensus CI-AKI definition [12].

METHODS

This was a registry that included patients with ST elevation myocardial infarction (STEMI) submitted to primary PCI in a tertiary university hospital in Southern Brazil between April, 2011 and December, 2015. Exclusion criteria were dialytic chronic kidney disease, missing creatinine (at baseline and 48-72g after procedure), absence of echocardiogram during admission and lack of follow-up. STEMI was defined as typical chest pain associated with ST-segment elevation of at least 1 mm in two contiguous leads in the frontal plane or 2 mm in the horizontal plane, or typical pain in patients with a presumably new left bundle-branch block. Exclusion criteria were absence of admission laboratory testing or echocardiogram and lack of 30-day follow-up. This study was approved by the Institutional Research and Ethics Committee and informed consent was obtained from all individual participants included in the study.

Study protocol

Blood samples were collected before PCI as part of routine patient care. All patients were pre-treated with a loading dose of acetylsalicylic acid (300mg) and clopidogrel (600mg), and unfractioned heparin was used during procedure (70-100 IU/Kg). Use of IIb/IIIa glycoprotein, aspirative thrombectomy and PCI technical strategies (i.e. pre-dilation, direct stent placement, post-dilation) were performed according to the operator`s choice. Coronary flow before and after the procedure was assessed and described according to the Thrombolysis in Myocardial Infarction

(TIMI) criteria [13]. Creatinine was measured at baseline and 48-72 hours post-procedure. LVEF was determined early after STEMI diagnosis using transthoracic echocardiography. After hospital discharge, clinical follow-up was performed with either outpatient visit or telephone contact.

Clinical definitions

Creatinine clearance was estimated according to the Modification of Diet in Renal Disease (MDRD) equation [14]. The definition of CI-AKI was a raise of 0.3 mg/dL or 50% in post procedure (24-72 hours) creatinine compared to baseline, proposed by the Acute Kidney Injury Network (AKIN) as a standardized definition of acute kidney injury [12, 15]. Hypotension was defined as systolic blood pressure <80 mmHg for at least 1 hour requiring inotropic support with medications or intra-aortic balloon pump (IABP) within 24 hours periprocedurally. Anemia was defined according to World Health Organization criteria: baseline hematocrit value < 39% for men and < 36% for women [16]. Previous chronic kidney disease (CKD) was defined as creatinine at baseline > 1.5 mg/dL or being on dialysis program.

MACCE were defined as death from any cause, new myocardial infarction (MI), stroke, Canadian Cardiovascular Society class III/IV angina or re-hospitalization for congestive heart failure 30 days after primary PCI. New MI was defined as recurrent chest pain with ST-segment elevation or new Q waves and raise of serum biomarkers after their initial decrease. Stroke was defined as a new, sudden-onset focal neurological deficit, of presumably cerebrovascular cause, irreversible (or resulting in death) and not caused by other readily identifiable causes.

Risk models

Mehran score [4] included 8 clinical and procedural variables and its weighted integers: hypotension (5 points), intra-aortic balloon pump (IABP) (5 points), congestive heart failure (5 points), estimated glomerular filtration rate (eGFR) (2 points for an eGFR between 60 and 40 mL/min/1.73m^2, 4 points for an eGFR between 40 and 20 mL/min/1.73m^2, and 4 points for an eGFR < 20 mL/min/1.73m^2), age > 75 years (4 points), diabetes (3 points), anemia (3 points), and volume of contrast (1 point for each 100 cc^3).

ACEF-MDRD score [11] was calculated as follows: (age / left ventricle ejection fraction) + 1 point was added for every 10 mL/min/1.73m^2 reduction in eGFR < 60 mL/min/1.73m^2 (up to a maximum of 6 points). Therefore, an eGFR of between 50 and 59 mL/min/1.73m^2, 40 to 49 mL/min/1.73m^2 and 30 to 39 mL/min/1.73m^2 would receive 1, 2, and 3 points, respectively.

Statistical Analysis

Continuous variables were expressed as mean (± standard deviation) or median (interquartile range). Categorical variables were represented by relative and absolute frequencies. ROC curves were used to evaluate the discriminatory power of the different scores. Comparison of ROC curves was performed by DeLong test using the software MedCalc (version 12.5.0.0, bvba Belgium). Youden index analysis was performed to determine the best cutoff value of ACEF-MDRD score (considering sensibility and specificity) to predict CI-AKI. Patient groups were compared using Student t test (for normally distributed variable) or the Wilcoxon rank-sum test (for other variables) for continuous variables and $\chi 2$ test or Fisher exact tests for categorical variables. Multivariate analysis was performed by logistic regression. P value was considered significant at < 0.05 level. Data were analyzed using SPSS (version 18.0.0; IBM Company).

RESULTS

During the study period, 406 patients were submitted to primary PCI for STEMI at our hospital, and 59 of them were excluded from the analysis due to missing data (Figure 1). Mean age was 60 years, and 65% were male. At presentation, 12.4% of the patients had hypotension, and 8.9% developed cardiac arrest before or during hospitalization. Contrast-induced nephropathy occurred in 13.3% of the patients. In-hospital death occurred in 7.7 % of cases, and 23.9% of the patients developed 30-day MACE. Clinical characteristics of patients according to the presence of CI-AKI are present in Table 1.

CI-AKI occurred more frequently in patients with diabetes, ejection fraction < 50%, previous ASA use, previous coronary intervention (surgical or percutaneous) and Killip 3 or 4 at admission. In univariate analysis, age, diabetes, previous ASA use, Killip 3 or 4 at admission, ACEF-MDRD and Mehran scores were predictors of CI-AKI. After multivariate adjustment, only ACEF-MDRD score and diabetes remained CI-AKI predictors (Table 2).

ROC curves are presented in Figure 2. Areas under the ROC curve (95% CI) of ACEF-MDRD and Mehran scores were 0.733 (0.68-0.78) and 0.649 (0.59-0.70), respectively. Comparing both scores with DeLong test, ACEF-MDRDs AUC was greater than Mehran`s ($p = 0.03$). An ACEF-MDRD score cutoff point of 2.33 yielded a sensitivity of 54.3% and specificity of 87.4% (Figure 3). CI-AKI was developed by 7.4% of the patients with ACEF-MDRD score below 2.33, and by 39% of them when ACEF-MDRD score was above cutoff. Low risk score had an excellent negative predictive value of 92.6% (88.9% – 95.3%), while a high risk score had a positive predictive value of 39.1% (27.1% - 52.1%) (Table 3).

Contrast induced nephropathy was a significant predictor of 30-day MACCE in our registry. Age, male sex, hypotension and Killip 3 or 4 at admission, ACEF-MDRD and Mehran

scores, TIMI flow 0 or 1 after angioplasty and CI-AKI had statistical significance in this matter. However, only CI-AKI and TIMI flow 0 or 1 after procedure were independent predictors of events (Table 4).

DISCUSSION

In our cohort of STEMI patients undergoing primary PCI, we found that the ACEF-MDRD score, initially developed to predict clinical outcomes, is also an excellent tool to identify patients at high risk for developing CI-AKI. Besides being low-complexity score, it is a better predictor of CI-AKI than a widely used score created specifically for this matter [4].

CI-AKI is a common complication in invasive cardiology, and even more common in patients with STEMI. In order to identify high-risk patients, multiple prediction models for the development of CI-AKI have been created using discrepant outcome definitions [4, 17-20]. Given the different clinical characteristics of each population, it is not possible for a risk model alone to predict events equally in different scenarios. Brown et al [17], for example, validated a model after a National Veterans Health Administration cohort, with all its features and peculiarities. Further, we have compared two different risk models in a population from northwest USA undergoing elective or urgent PCI [7].

Most of these risk models were created in stable patients, and few of them were evaluated specifically in STEMI. At this clinical presentation, Mehran score seems to add little to the discrimination of patients, especially in high-risk individuals [21]. Liu et al [22] have found that GRACE score is an independent predictor of CI-AKI in patients undergoing primary PCI, with a similar AUC compared to ACEF-MDRD score in our study (0.723 and 0.733, respectively). However, GRACE score is a more complex model containing eight variables, compared to three

variables of ACEF-MDRD score. SYNTAX score have also been tested for CI-AKI prediction and performed well [23], but it also has the disadvantage of being even more complex and time-consuming.

ACEF score, from where ACEF-MDRD was derived, was shown to be an independent predictor of CI-AKI defined as rise in serum creatinine ≥ 0.5 mg/dl [24]. A broader definition of CI-AKI (rise in serum creatinine ≥ 0.5 mg/dl and/or ≥ 25% increase in baseline serum creatinine) was also tested in this study, where ACEF did not perform so well. We believe that a contemporary and standard CI-AKI definition should be used broadly in this setting, and the Acute Kidney Injury Network (AKIN) have proposed such standardization [12]. Centola et al found that AKIN definition of CI-AKI provided a better accuracy in predicting long-term mortality than a rise in serum creatinine ≥ 0.5 mg/dl and/or ≥25% within 72 hours after PCI [25]. Liu and cols [26] found a low predictive value of several prediction models (including AGEG and ACEF) using both definitions of CI-AKI. Because a broader definition includes patients who often have no post-procedural relevant deterioration in renal function, they are at a lower risk of adverse events at follow-up and therefore the prediction models do not perform well.

Recent studies have questioned the true impact of CI-AKI in hard outcomes, suggesting that it is just a marker of high risk patients that will develop clinical events despite of CI-AKI [2, 27, 28]. The fact that Mehran score is a MACCE predictor in univariate analysis in our sample and an independent predictor in other studies [29, 30] could be another indirect evidence that when we are predicting CI-AKI we are actually predicting MACCE. Yet, it is of great importance to anticipate CI-AKI while this doubt remains unsolved. Nevertheless, in our study, CI-AKI was an independent predictor of MACCE.

Unlike Mehran score, diabetes and ACEF-MDRD were independent predictors of CI-AKI at the present analysis. This information in a relatively small sample of patients suggests a strong association between variables, and including diabetes in future CI-AKI prediction models should be considered. Ando et al [31] have studied 507 patients submitted to primary PCI and found four independent CI-AKI predictors, including ejection fraction, glomerular filtration rate, age and TIMI 0-2 after procedure. They have also found an excellent AUC of ACEF-MDRD score for CI-AKI prediction. Different from our study, they have not performed any statistical analysis to determine differences in AUC`s of ACEF-MDRD and Mehran scores, and they have not followed-up patients after discharge. Moreover, they have used a different CI-AKI definition, which we believe is not the most appropriate as commented above.

According to recent guidelines on myocardial revascularization [32], management of patients at high estimated risk for CI-AKI consists in saline hydration and avoiding excessive use of contrast-media. In our study, we found a negative predictive value of 92.6%, which means that an operator could acquire more projections to secure a good angiographic result in patients with low ACEF-MDRD score, for example. In another scenario, patients at risk for pulmonary congestion with a low ACEF-MDRD score could avoid excessive hydration. Because of our limited number of patients, larger samples are needed determine a more accurate cutoff point to identify high risk patients.

There are some limitations in our study. First, the retrospective design may have influenced the quality and consistency of the data collected. Second, the absence of a routine echocardiography acquisition after STEMI diagnosis (either before or right after PCI) could make uncertain the utility of ACEF-MDRD score as a prediction tool. Meantime, point of care echocardiography is a reality in developed countries, and thus LVEF can be readily acquired

without delaying PCI. Third, Mehran score was developed and validated in both stable and unstable acute coronary syndromes, and we have compared it with ACEF-MDRD score in a limited clinical setting of patients with STEMI submitted to primary PCI; however, it may also be a strength, by proving ACEF-MDRD`s utility in such patients. Fourth, the fact that the study was conducted at a single center may also be considered a limitation. Because of different baseline characteristics, every population should ideally have their risk prediction tool. Fifth, because this study was derived from a third world country registry, medications and devices used during procedure may have changed outcomes, and event prediction may consequently differ.

In conclusion, ACEF-MDRD score is a simple user-friendly tool that is independently predictive of CI-AKI in patients undergoing primary PCI. Moreover, a low ACEF-MDRD score has an excellent negative predictive value for CI-AKI, and this might be of clinical relevance. It was developed to predict major cardiovascular outcomes but predicts CI-AKI better than a validated and well known scores developed for this matter, although not in patients with STEMI. Because pharmacologic prophylaxis remains controversial, the main strategy to avoid CI-AKI lies in its prevention, and identification of high risk patients is essential.

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CONFLICTS OF INTEREST

The authors declare that they have no conflicts of interest.

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Table 1. Baseline characteristics: Overall, patients with contrast induced acute kidney injury (CI-AKI) and patients without CI-AKI. Values are expressed as mean ± standard deviation, median (interquartile range) or number (%). ASA: Acetylsalicylic acid; AMI: Acute myocardial infarction; LVEF: Left ventricle ejection fraction; CKD: Chronic kidney disease; DES: Drug-eluting stents; IABP: Intra-aortic balloon pump.

Characteristics	All (n=347)	CI-AKI (n=46)	No CI-AKI (n=301)	P
Demographic				
Age	60.0 (±12)	64.7 (±11)	59.4 (±12)	0.660
Male gender (%)	227 (65.4)	32 (69.6)	195 (64.8)	0.525
White (%)	192 (55.3)	29 (63)	163 (57.5)	0.392
Hypertension (%)	215 (62.1)	34 (73.9)	181 (60.3)	0.102
Diabetes (%)	83 (23.9)	19 (39.1)	64 (21.6)	0.015
Current smoking (%)	183 (52.9)	23 (50.0)	160 (53.3)	0.568
Previous ASA use (%)	80 (23.1)	17 (37.0)	63 (21.0)	0.023
Previous AMI (%)	20 (5.8)	7 (15.2)	13 (8.0)	0.159
Previous coronary intervention (%)	38 (11.0)	9 (19.6)	29 (9.7)	0.046
Previous stroke (%)	20 (5.8)	3 (6.5)	17 (5.7)	0.738
LVEF	51 (±13)	46 (±12)	52 (±13)	0.103
LVEF < 50% (%)	170 (49.0)	30 (65.2)	140 (46.5)	0.013
Baseline creatinine	1.06 (±0.93)	1.21 (±1.88)	1.04 (±0.78)	0.069
Previous CKD (%)	32 (9.2)	9 (15.2)	23 (8.3)	0.166
Baseline hemoglobin	13.1 (±1.6)	12.8 (±2.08)	13.1 (±1.53)	0.226
Anemia (%)	124 (35.7)	18 (39.1)	106 (35.2)	0.359
Pain-to-door time	4.0 (2.5, 6.0)	4.3 (3.0, 7.1)	4.0 (2.5, 6.0)	0.126
Anterior AMI (%)	154 (44.4)	25 (54.3)	129 (42.9)	0.327
Killip 3 or 4 at presentation (%)	41 (11.7)	11 (23.9)	30 (9.8)	0.011
Hypotension (%)	43 (12.4)	9 (19.6)	34 (11.3)	0.146
Cardiac arrest (%)	31 (8.9)	4 (8.6)	27 (8.9)	0.774
Procedure				
Femoral access (%)	144 (41.5)	22 (47.8)	122 (40.5)	0.422
Thrombus aspiration (%)	122 (35.1)	9 (18.6)	113 (37.6)	0.016
DES (%)	13 (3.7)	6 (13.3)	7 (4.0)	0.020

Multivascular coronary disease (%)	75 (21.6)	9 (19.4)	66 (21.8)	0.683
Left main disease (%)	12 (3.4)	3 (6.5)	9 (3.0)	0.683
SYNTAX score	16 (8.2)	19.9 (8.7)	15.4 (8.0)	0.987
Pacemaker (%)	29 (8.4)	5 (11.1)	24 (8.0)	0.562
IABP (%)	12 (3.4)	3 (6.5)	9 (3.0)	0.164
Procedural complications (%)	53 (15.2)	6 (13.3)	47 (15.7)	0.826
Fluoroscopy time	15 (10.5, 21.4)	15.7 (11.1, 23.8)	14.4 (10.1, 21.1)	0.743
Contrast volume	199 (±92)	210 (±81)	197 (±94)	0.913
Post-procedure TIMI 2 or 3 (%)	334 (96.3)	45 (97.8)	289 (96.0)	1.000
Outcomes				
In-hospital death (%)	27 (7.7)	8 (17.3)	19 (6.3)	0.022
30 day MACCE (%)	83 (23.9)	20 (43.4)	63 (20.9)	0.004

Table 2: Predictors of contrast induced acute kidney injury (CI-AKI) in univariate and multivariate analysis. Values are expressed in odds ratio (OR) and confidence interval (CI) of 95%. ASA: Acetylsalicylic acid.

CI-AKI predictors in univariate analysis

Characteristic	**OR**	**95% CI**	**P**
Age	1.04	1.01-1.06	0.006
Diabetes	2.33	1.20-4.45	0.011
Previous ASA use	2.20	1.12-4.23	0.019
Killip 3 or 4	2.90	1.29-6.20	0.007
Mehran	1.11	1.03-1.18	0.004
ACEF-MDRD score	1.72	1.424-2.10	< 0.001

CI-AKI predictors in multivariate analysis

Characteristic	**OR**	**95% CI**	**P**
Age	1.02	0.99-1.05	0.232
Diabetes	2.32	1.01-5.38	0.049
Previous ASA use	1.52	0.70-3.29	0.286
Killip 3 or 4	1.63	0.59-4.49	0.345
Mehran	0.91	0.81-1.01	0.100
ACEF-MDRD score	1.76	1.35-2.28	< 0.001

Table 3: 2 x 2 table showing frequencies (N) and percentages (%) of contrast-induced acute kidney injury (CI-AKI) in patients with AGEF score below and above 2.33. NPV: Negative predictive value; PPV: Positive predictive value.

		No CI-AKI	CI-AKI	Total	
ACEF-MDRD < 2.33	N	262	21	283	NPV:
	%	92.6	7.4	100	92.6% (88.9 – 95.4%)
ACEF-MDRD > 2.33	N	39	25	64	PPV:
	%	60.9	39.1	100	39.1% (27.1 – 52.1%)
	Total	301	46	347	

Table 4: Predictors of major cardiovascular and cerebrovascular events (MACCE) in univariate and multivariate analysis. Values are expressed in odds ratio (OR) and confidence interval (CI) of 95%.

MACCE predictors in univariate analysis

Characteristic	**OR**	**95% IC**	**P**
Age	1.04	1.01-1.06	0.006
Male sex	1.73	1.03-2.88	0.036
Killip 3 or 4	2.71	1.33-5.45	0.005
Hypotension	2.20	1.09-4.32	0.023
TIMI flow 0 or 1	4.62	1.56-14.44	0.001
CI-AKI	2.74	1.41-5.27	0.002
Mehran	1.11	1.03-1.18	0.004
ACEF-MDRD	1.72	1.42-2.10	< 0.001

MACCE predictors in multivariate analysis

Characteristic	**OR**	**95% IC**	**P**
Age	1.01	0.98-1.03	0.771
Male sex	1.65	0.944-2.90	0.078
Killip 3 or 4	1.60	0.63-4.08	0.321
Hypotension	1.31	0.43-3.99	0.626
TIMI flow 0 or 1	6.51	2.09-20.21	0.002
CI-AKI	2.33	1.12-4.87	0.024
Mehran	1.01	0.90-1.11	0.997
ACEF-MDRD	1.18	0.932-1.493	0.168

Figure 1: Inclusion of patients flowchart.

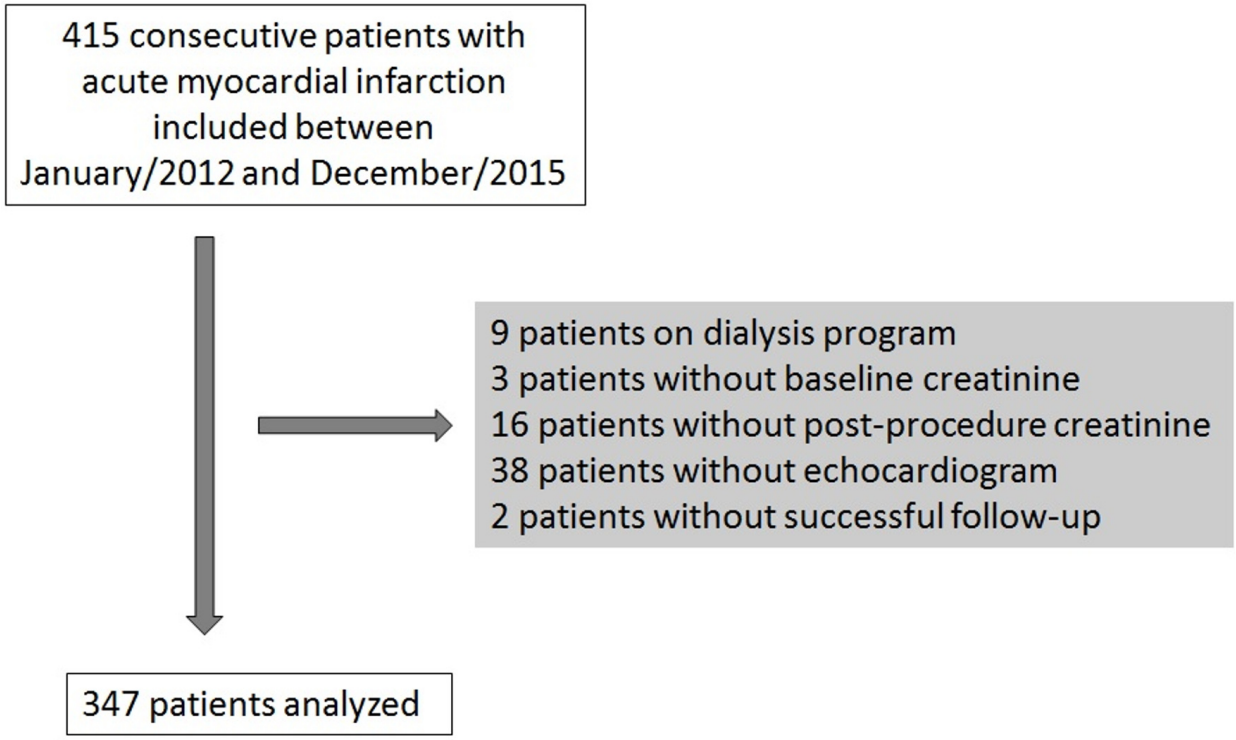


Figure 2: Receiver operator characteristic (ROC) showing areas under the curve (AUC) of ACEF-MDRD and Mehran scores for contrast induced nephropathy.

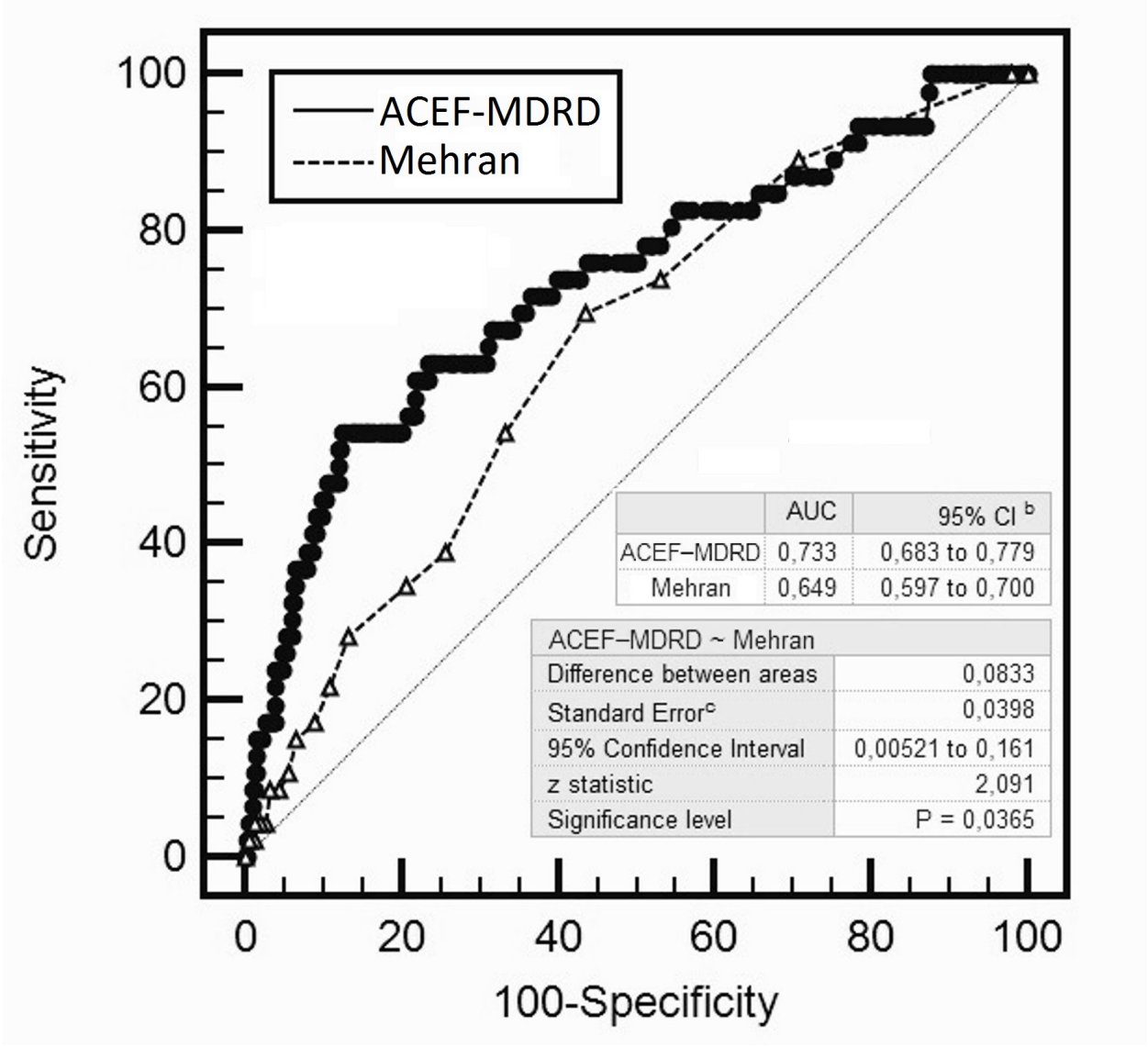
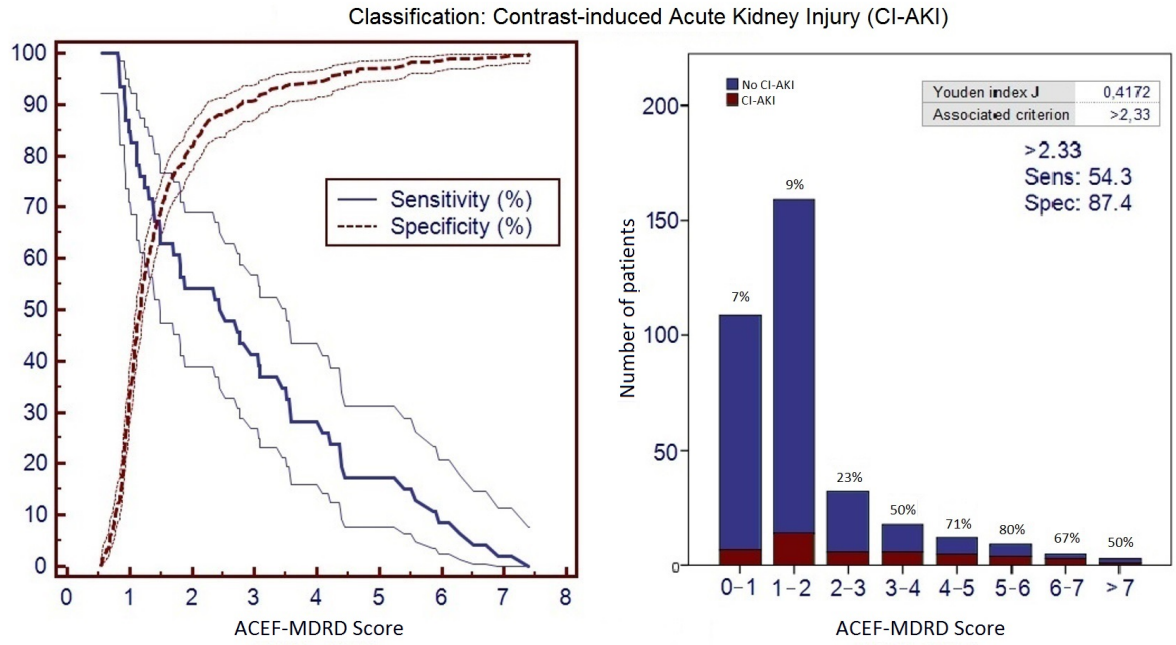


Figure 3: Specificity and sensibility curves for ACEF-MDRD score values (left). Percentage of contrast-induced acute kidney injury development among stratum of ACEF-MDRD score (right).



CONCLUSÕES E CONSIDERAÇÕES FINAIS

Nefropatia induzida por contraste (NIC) é um evento comum após a intervenção coronariana percutânea (ICP), com uma incidência média de até 14% nestes pacientes. O real significado deste problema com relação às suas consequências, no entanto, segue duvidoso. Pelo fato de grande parte da evidência ser baseada em estudos observacionais, e pelo fato de a NIC compartilhar os mesmos fatores de risco que o desfecho mortalidade (diabetes, disfunção ventricular, doença renal crônica prévia), estudos recentes vêm questionando se há realmente uma relação causal entre NIC e mortalidade ou se a primeira é somente um marcador de alto risco para a segunda (21, 25). Esta dúvida somente poderá ser esclarecida com grandes ensaios clínicos randomizados, e enquanto esta dúvida permanece, é importante que se tente antecipar a NIC identificando os pacientes de mais alto risco para esta complicação.

Nesta tese de doutorado, publicamos dois artigos. No primeiro, em uma população norte-americana com mais de cinco mil pacientes submetidos a cateterismo cardíaco (eletivo e de urgência/emergência), comparamos dois escores desenvolvidos exclusivamente para predizer nefropatia induzida pelo contraste, e amplamente utilizados para este fim. O escore de Mehran mostrou maior poder discriminatório em relação ao escore WBH, justificando o fato de ser o escore de predição de NIC mais frequentemente utilizado na cardiologia intervencionista.

No segundo artigo da tese, utilizamos um registro local de pacientes com infarto agudo do miocárdio submetidos à intervenção coronariana percutânea primária. Pacientes com infarto do miocárdio têm maior incidência de NIC e maior mortalidade. Por este motivo, nos questionamos se um escore desenvolvido para predição de mortalidade (ACEF-MDRD) também não seria acurado para predizer NIC. Além disso, o fato de este

escore ter poucas variáveis (e de fácil obtenção) faz com que ele tenha mais fácil aplicação. Assim como esperado, o escore ACEF-MDRD não só foi acurado para predizer NIC, com alto valor preditivo negativo, como foi melhor que um escore desenvolvido exclusivamente para este fim. Como aplicabilidade prática, é possível que, em pacientes com escore ACEF-MDRD baixo, o cardiologista intervencionista possa tratar lesões não culpadas na mesma intervenção conforme orientação das diretrizes mais recentes, sabendo que o risco de desenvolver NIC é baixo. Em outro cenário, é possível evitar hidratação excessiva pré e pós procedimento em pacientes com risco de congestão pulmonar e escore ACEF-MDRD baixo. Estudos maiores, de preferência ensaios clínicos randomizados, são necessários para comprovar estas hipóteses.

Como plano futuro, além da possibilidade de testar as hipóteses acima comentadas, pretendemos desenvolver um escore ainda mais simples e disponível no momento da chegada do paciente com IAMCSST na emergência. Das variáveis do ACEF-MDRD, a fração de ejeção necessita de um ecocardiograma à beira do leito, nem sempre disponível, e o resultado da creatinina sérica não está pronto desde o momento da chegada. Será um desafio desenvolver este escore, mas com o banco de IAMCSST cada vez mais numeroso é uma tarefa possível de se realizar.

ANEXOS

TERMO DE CONSENTIMENTO LIVRE E ESCLARECIDO

Nº do projeto GPPG: 15-0557

Título do Projeto: Coorte de Pacientes com Infarto Agudo do Miocárdio Atendidos no Hospital de Clínicas de Porto Alegre

Você está sendo convidado(a) a participar de uma pesquisa cujo objetivo é obter maior conhecimento a respeito das características dos pacientes com diagnóstico de infarto agudo do miocárdio e submetidos à angioplastia coronariana e das características deste procedimento realizado no hospital. Esta pesquisa está sendo realizada pelo Serviço de Hemodinâmica do Hospital de Clínicas de Porto Alegre (HCPA). Dessa forma, estamos realizando este convite porque você realizou o procedimento de angioplastia coronariana no HCPA.

Se você aceitar participar da pesquisa, os procedimentos envolvidos em sua participação são os seguintes:

A equipe de pesquisa realizará o preenchimento de uma ficha de registro baseada nos dados de seu prontuário do hospital contendo informações sobre seu estado de saúde atual, resultados de exames e descrição de procedimentos. Por isso, solicitamos a sua autorização para este acesso.

Após 30 dias da alta hospitalar desta internação, será realizado contato telefônico pela equipe de pesquisa para verificar se você teve alguma nova intercorrência neste período como, por exemplo, problemas de saúde, visita à emergência, nova internação hospitalar.

Este estudo será apenas de revisão de registros em prontuários e acompanhamento, não havendo nenhuma interferência no tratamento clínico ou cirúrgico indicado pela equipe assistencial, que será o mesmo independentemente de você aceitar ou não a participação na pesquisa.

Não são conhecidos riscos pela participação na pesquisa em si, exceto a possibilidade de ocorrer quebra de confidencialidade dos dados. Entretanto os pesquisadores tomarão o cuidado para que isto não ocorra, utilizando sempre um número único para identificação dos participantes, sem a utilização do seu nome.

Não é esperado nenhum benefício direto ao participante, pois não será realizado nenhum tratamento adicional. Contudo, esperamos um benefício para os pacientes com infarto agudo do miocárdio, pois com a conclusão deste trabalho poderemos avaliar melhor o perfil dos pacientes e possíveis complicações dos procedimentos envolvidos. As informações obtidas podem servir para aprimorar o atendimento futuro de pacientes que procuram o serviço de emergência por dor torácica.

Sua participação na pesquisa é totalmente voluntária, ou seja, não é obrigatória. Caso você decida não participar, ou ainda, desistir de participar e retirar seu consentimento, não haverá nenhum prejuízo ao atendimento que você recebe ou possa vir a receber na instituição.

Não está previsto nenhum tipo de pagamento pela sua participação na pesquisa e você não terá nenhum custo com respeito aos procedimentos envolvidos.

Os dados coletados durante a pesquisa serão sempre tratados confidencialmente. Os resultados serão apresentados de forma conjunta, sem a identificação dos participantes, ou seja, o seu nome não aparecerá na publicação dos resultados.

Caso você tenha dúvidas, poderá entrar em contato com o pesquisador responsável

Marco Vugman Wainstein, pelo telefone 51 33598342, com o pesquisador Felipe Homem Valle, pelo telefone 51 33598342 ou com o Comitê de Ética em Pesquisa do Hospital de Clínicas de Porto Alegre (HCPA), pelo telefone (51) 33597640, ou no 2º andar do HCPA, sala 2227, de segunda à sexta, das 8h às 17h.

Esse Termo é assinado em duas vias, sendo uma para o participante e outra para os pesquisadores.

_____
Nome do participante da pesquisa

_____
Assinatura

_____
Nome do pesquisador que aplicou o Termo

_____
Assinatura

Local e Data: _____

FICHA DE COLETA

REGRISTRO IAM ACTP PRIMARIA

1.Paciente:_____

2.Data do Procedimento: ____/____/_____

3.Data Alta ____/____/____

4.Sexo: (M) (F)

5.Idade: _____

6.Cor:_____

7. Telefones: ( )_____

8. Prontuário:_____

9. Número do Exame:_____

10. Procedência:_____

11. Entrada via: (1) E-HCPA (2)SAMU (3)Intra-Hosp (4) Transferência

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Quadro Clínico

Primária Território (1) Anterior (2) Inferior (3) Lateral
Tempo dor-porta: _____H_____min Tempo porta-balão:_____min
Tempo lido-balão: _____min Tempo cronômetro-balao: _____min
Tempo de Transferência:_____H_____min
Horário: (1) 08-20 horas (2) 20-24h (3)24-08h
Dia Semana: (1) Segunda a Sexta (2)Sábado ou domingo

Exame Físico

Killip I (1) Killip II (2) Killip III (3) Kilip IV (4)
BAVT (0) Não (1) Sim PCR (0) Não (1) Sim
Necessidade de MP (0) Não (1) Sim BIA (0) Não (1) Sim
PA admissão:_____/_____mmHg **- Hipotensão Sistólica <80mmHg** (0) Não (1) Sim
FC admissão:_____**bpm**

Características Clínicas

HAS (0) Não (1) Sim
DM (0) Não (1) Sim
Insulina (0) Não (1) Sim
Tabaco (0) Não (1) Sim (2) Ex-Tabagista
Antiplaquetários Uso prévio: AAS: (0) Não (1) Sim Clopidogrel: (0) Não (1) Sim
IAM Prévio (0) Não (1) Sim
AVC Prévio (0) Não (1) Sim **DPOC:** (0) Não (1) Sim
ICC conhecido (0) Não (1) Sim
IRC conhecida (DCE< 60) (0) Não (1) Sim **Dialítica** (0) Não (1) Sim
DVP (0)Não (1) Sim

TIMI SCORE

- Idade > 75 (3)
- Idade 65-74 (2)

- DM/HAS OU Angina (1)
- ✓ PAS < 100mmHg (3)
- ✓ FC>100 bpm (2)
- ✓ Killip II, III ou IV (2)
- ✓ Peso < 67kg (1)
- ❖ Delta T até reperfusão >4horas (1)
- ❖ Supra de ST na parede Anterior ou BRE de 3º Grau (1)

TOTAL(0-14):_____

Avaliação Laboratorial Basal Pré Procedimento

Creatinina _____mg/Dl **MDRD (caso <60): _____CKD-EPI_____**
Creatinina **Pós Procedimento**: _____mg/Dl
NIC (0) Não (1) Sim ( )Sem Cr controle [>0,5mg/Dl ou >25%]
Troponinas admissão: _____ng/Ml Troponinas Pico_____ng/Ml Potássio _____mEq/L
Plaquetas_____ x10³/Ml VPM: _____fl
Hemoglobina _____g/Dl Hematócrito: _____% RDW:_____% Leucócitos Totais_____ x10³/Ml Neut. Segmentados: _____x10³/Ml Bastões _____ x10³/Ml Linfócitos:_____ x10³/Ml

Função Ventricular Esquerda no Ecocardiograma

Fração Ejeção Quantitativa: _____ % *(Obs. Pode ser a média do valor)* ( ) Eco Não Realizado
Peso:_____kg Altura:_____cm

Padrão Coronariano

-Extensão da doença coronária (>70% e > 50% TCE)
(1)Uniarterial (2) Biarterial (3)Triarterial (4)TCE + 1 vaso (5) TCE + 2 vasos (6) TCE+3vasos

Intervenção prévia: (0) Não (1)Sim (2) CRM
Informações Gerais sobre a Intervenção Terapêutica
Via de Acesso: (1) Radial (2)Femoral (3) Conversão **Lado do Acesso:** (1)Direito (2)Esquerdo
Introdutor (1) 05f (2)06 f (3)07f
Características angiográficas/tratamento:
Coronária/enxertos: (1) Coronária nativa (2) MAM-E (3) PVS

Vaso Culpado

(1) ACD (2) ADA (3)ACX (4) TCE (5) Diag ou intermédio (6) Marg (7)DP
(8) Ponte Safena (9) Mamaria (10) Posteriolateral
TIMI Pré (0) (1) (2) (3)
Fluxo após passagem guia 0.014 TIMI (0) (1) (2) (3)
Fluxo pós Aspiração TIMI (0) (1) (2) (3) *(9) Não se aplica*
Tipo de Lesão Tratada: (1) Artéria Nativa (2)Trombose Intrastent
Stent Direto (0) Não (1) Sim
Pós Dilatação (0) Não (1) Sim
Overlapping (se >1 stent) (0) Não (1) Sim *(9) Não se aplica*
Aspiração Trombo (0) Não (1) Sim (2) Aspiração de Resgate

Materiais

Só Balão (0) Não (1) Sim
Stent Farmacológico (0) Não (1) Sim

Stent _____
Diâmetro _____
Comprimento ____

Stent _____
Diâmetro _____mm
Comprimento
_____

Stent _____
Diâmetro _____mm
Comprimento
_____

Quantidade de Stents utilizados no procedimento _____
Grau de Estenose após Procedimento: _____%
Timi Pós (0) (1) (2) (3)
Sucesso Angiográfico Final (1)Sucesso (0)Insucesso
Medicações Administradas durante Procedimento
( )AAS
( )Clopidogrel
( )Heparina não Fracionada
( )Heparina de baixo peso molecular
( )Abciximab
( )Ticagrelor
Contraste volume: _____ml
Complicações alérgicas graves (anfilactoides ou anafiláticas (0) Não (1) Sim
Dose de Radiação_____
Tempo de Escolpa:_____

Complicações Durante o Procedimento
(0) Não (1) no reflow (2) embolização distal (3) re-oclusão (4) perfuração (5)óbito (6)
Oclusão de Ramo (7) Estenose Residual

Lesão Grave Não culpada
(6) Da (2) CD (3) CX (4) DG (5) MG (6) TCE (7) DP

TTO ad hoc (0) Não (1) Sim
(1)ACTP Vaso (1) Da (2) CD (3) CX (4) DG (5) MG (6) TCE (7) DP
Mesma internação? (0) Não (1) Sim [se *Adhoc* = (1), *mesma internação* = (1)]
(2)CRM
(3)Tratamento clínico

Número Total de Vasos Tratados: _____

Syntax Score: **(99)** CRM prévia **(999)** Filme Não Disponível
Clínical Syntax: **(99)**CRM prévia **(999)** Sem Eco

SEGUIMENTO HOSPITALAR

Complicações vasculares antes da alta hospitalar
(0) Não (1) Hematoma >5cm (2) Fístula AV (3) Pseudo Aneurimas (4) Hematoma retroperitoneal
(5) perfuração radial
Transfusão durante a internação: (0) Não (1) Sim
Complicações antes alta:
Óbito (0) Não (1) Sim

Se óbito durante ACTP (0) Não (1) Sim
Novo IAM (0) Não (1) Sim
AVC (0) Não (1) Sim
Trombose Stent (0) Não (1) Sim

Seguimento Por contato telefônico 30 dias

Realizado ( ) Sim ( ) Não
Bolsista: _____

Complicações

1.Depois da alta do HCPA, o Sr teve alguma nova internação hospitalar? Baixou hospital de novo?
( ) Sim ( ) Não
Qual Hospital?
Foi feito novo cateterismo cardíaco?
Foi colocado stent?
2.Teve alguma visita à a emergência? **( ) Sim ( ) Não ( ) NSA**
Quando? Qual Hospital?
3. Foi feito diagnóstico de novo infarto ? ( ) Sim ( ) Não ( ) NSA
4. Depois da alta do HCPA, teve algum problema sério de saúde como derrame, AVC, isquemia cerebral? ( ) Sim ( ) Não ( ) NSA
Quando? Qual Hospital?
5. Depois da alta do HCPA, vem sentido dor no peito, angina?
( ) Sim ( ) Não ( ) NSA Classe (I) (II) (III) (IV)
6. Depois da alta do HCPA, vem sentindo falta de ar ou cansaço?
( ) Sim ( ) Não ( ) NSA NYHA Casse (I) (II) (III) (IV)

IMPRESSÃO (BANCO)
Óbito (0) Não (1) Sim
Novo IAM (0) Não (1) Sim
AVC (0) Não (1) Sim
Trombose Stent (0) Não (1) Sim
Revasc Lesão ou vaso alvo (0) Não (1) Sim
Angina Classe 3 ou classe 4 (0) Não (1) Sim **Reinternação por ICC** (0) Não (1) Sim.