Comparison of two risk models in predicting contrast-induced nephropathy after coronary computed tomography angiography and percutaneous coronary intervention

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ABSTRACT - Background: Contrast-induced nephropathy is one of the main causes of hospital-acquired acute renal failure. The Mehran risk score and the contrast medium volume used/creatinine clearance ratio could help identifying patients at higher risk of developing contrast-induced nephropathy. This study aimed to compare these two scores. Methods: A retrospective, single-center observational study including hospitalized patients with baseline creatinine >1.3mg/dL, under observation for at least 48 hours after coronary computed tomography angiography and/or percutaneous coronary intervention. Mehran risk score and contrast medium volume used/creatinine clearance ratio were calculated for all patients, and the incidence of contrast-induced nephropathy was analyzed according to different cutoff points of both scores. Receiver Operating Characteristic curves were plotted to determine the accuracy of the methods in predicting contrast-induced nephropathy. The effectiveness of both methods was analyzed using Pearson’s correlation test. Results: We included 102 patients and the incidence of contrast-induced nephropathy was 27.4%. The outcome occurred in 24.7% of patients when Mehran risk score ≥6, in 32.7% when Mehran risk score ≥10, and in 57.8% when Mehran risk score ≥15, in 28.7% of patients with contrast medium volume used/creatinine clearance ratio ≥2, 29.8% with contrast medium volume used/creatinine clearance ratio ≥3, and 34.3% with contrast medium volume used/creatinine clearance ratio ≥5. Receiver Operating Characteristic curves demonstrated area under the curve with moderate predictive capacity for Mehran risk score (0.7), and reduced/borderline for contrast medium volume used/creatinine clearance ratio (0.6). The correlation between the two scores was moderate. Conclusion: Mehran risk score demonstrated greater accuracy in predicting contrast-induced nephropathy when compared to contrast medium volume used/creatinine clearance ratio, however both presented similar values. The cutoff points with the closest incidence between the two scores were ≥10 for Mehran risk score (32.7%) and ≥5 for volume used/creatinine clearance ratio (34.3%).

Keywords: Acute renal injury; Contrast media/adverse effects; Kidney diseases/chemically induced; Cardiac catheterization; Percutaneous coronary intervention; Risk assessment

RESUMO - Introdução: A nefropatia induzida por contraste é uma das principais causas de insuficiência renal aguda adquirida em ambiente hospitalar. O escore de risco de Mehran e a relação entre volume de meio de contraste utilizado e clearance de creatinina podem ajudar a identificar pacientes com maior risco de desenvolver nefropatia induzida por contraste. Este estudo teve como objetivo comparar esses dois escores. Métodos: Estudo observacional retrospectivo unicêntrico que incluiu pacientes hospitalizados com creatinina basal >1,3mg/dL, sob observação por pelo menos 48 horas após angiotomografia coronariana e/ou intervenção coronária percutânea. O escore de risco de Mehran e a relação entre volume de meio de contraste utilizado e clearance de creatinina foram calculados para todos os pacientes, e a incidência de nefropatia induzida por contraste foi analisada de acordo com diferentes pontos de corte de ambos os escores. As curvas Característica de Operação
INTRODUCTION

Contrast-induced nephropathy (CIN) is defined as an increase in serum creatinine levels by, at least, 0.3mg/dL or greater than 50% from baseline, in the first 48 hours after a contrast-enhanced procedure. The incidence of this complication ranges from 3 to 14% in patients undergoing percutaneous coronary intervention (PCI). Currently, the occurrence of CIN may become more prevalent due to the increasing number of diagnostic and interventional cardiac procedures that require iodinated contrast.

Given that the treatment of CIN is limited, medical actions are essentially aimed to prevent its occurrence, identify the most susceptible individuals, and initiate prophylactic measures when indicated. The Mehran risk score (MRS), created in 2004, is able to identify the individual risk of patients of developing CIN after PCI. However, MRS is old and not routinely recommended. Its use may fail in some situations or populations.

Likewise, the contrast medium volume/creatinine clearance (V/CrCl) ratio may help predicting risk in patients exposed to iodinated contrast, as well as evaluating prognosis one year after PCI. This tool is simple, useful, and easy to apply, but it lacks further evidence. Given the importance of identifying and preventing the occurrence of CIN, and the lack of an ideal risk stratification tool, this study aimed to analyze and compare the MRS and V/CrCl ratio in predicting CIN after cardiac catheterization.

METHODS

Study design and population

A single-center retrospective observational study, based on data collected from medical records of patients admitted at a tertiary-care teaching hospital, a regional reference in cardiovascular diseases at the Unified Health System (SUS, acronym from Portuguese).

The sample consisted of patients who underwent coronary computed tomography angiography and/or PCI from January 2019 to March 2021. Patients admitted with serum creatinine ≥1.3mg/dL before the procedure and who remained hospitalized for at least 48 hours after the procedure were included. Patients on dialysis at the time of the procedure and patients with no renal function control within 48 hours before, and 72 hours after the procedure were excluded.

Analyzed variables

The analyzed variables were sex; age; history of high blood pressure; diabetes mellitus; dyslipidemia; smoking (current or not); peripheral arterial occlusive disease; heart failure; prior coronary artery disease; previous PCI; previous myocardial revascularization surgery; hematocrit; previous serum creatinine (within 48 hours before the procedure) and after contrast exposure (24 to 72 hours after the procedure); pre- and post-procedure creatinine clearance using the Cockcroft-Gault formula; and volume of contrast used. Mehran risk score and V/CrCl scores were calculated for all patients included.

Outcomes

The occurrence of CIN from 24 to 72 hours after the procedure was considered the primary outcome of the study. Contrast-induced nephropathy was defined as an increase by at least 0.3mg/dL or 50% in serum creatinine levels after the procedure, compared to baseline values.

Statistical analysis

The incidence of CIN in the sample was analyzed using the two risk scores as a reference. If the MRS proved to be superior in terms of predicting the outcome, the best cut-off point for the V/CrCl would be identified in relation to the MRS, according to similarity in incidence of CIN between both in the analyzed cut-off points. Scores 6, 10 and 15 were used for the MRS and cut-off points 2, 3 and 5 for the V/CrCl. Receiver Operating Characteristic (ROC) curves were plotted to determine the accuracy of both tools in predicting CIN. Sensitivity and specificity were calculated for each cut-off point of both scores.

Statistical Package for the Social Sciences (SPSS) version 23.0 software was used for statistical analysis. Categorical variables were described as absolute frequency and
percentage. Continuous variables were described as mean and standard deviation, or median and interquartile range, in case of an abnormal distribution. ROC curves were used to compare the predictive capacity of MRS and V/CrCl. For predictive capacity analysis, area under the curve >0.7 was considered high, 0.5 to 0.69 moderate, and <0.5 low. Pearson’s correlation test was performed for direct comparison of the predictive capacity of both evaluated tools.

Ethical aspects
The study followed the recommendations of Resolution 466 of 2012 of the Conselho Nacional de Saúde (CNS) and was approved by the Ethics Committee in Research with Human Beings of the organization, under protocol 3.669.280.

RESULTS
A total of 708 patients underwent coronary computed tomography angiography and/or PCI in the period, and 166 met the study inclusion criteria. Of these, 64 patients were excluded for not having renal function tests in the 48 hours before and 72 hours after the procedure. Therefore, the final study sample consisted of 102 patients. The mean serum creatinine before the procedure was 2.0mg/dL, and the median was 1.6mg/dL. After the procedure, the mean serum creatinine was 2.2mg/dL and the median was 1.6mg/dL. The median MRS in the sample was 11 and the V/CrCl was 3.4. Mean creatinine clearance pre-procedure was 38±14.1 mL/minute and post-procedure was 41±19.5 mL/minute. The clinical characteristics of the included patients are shown in table 1.

The incidence of CIN in the sample was 27.4%. According to risk assessed by MRS, the outcome occurred in 24.7% (24/97) of patients when MRS ≥6, in 32.7% (20/61) when MRS ≥10, and in 57.8% (11/19) when MRS ≥15. Analyzing the incidence at the cut-off points defined for V/CrCl, the outcome occurred in 28.7% (23/80) of patients with V/CrCl ≥2, 29.8% (17/57) with V/CrCl ≥3, and 34.3% (11/32) with V/CrCl ≥5. The sensitivity and specificity of these cutoff points are described in table 2.

The incidence of the outcome numerically close between the two variables, when comparing the cutoff points defined for each score, was MRS ≥10 and V/CrCl ≥5, in which the incidence of CIN was, respectively, 32.7% and 34.3%. In the analysis of the ROC curves, MRS presented a larger area under the curve compared to V/CrCl (Figure 1). However, both showed mild to moderate predictive capacity, with an area under the curve of 0.7 for MRS and 0.6 for V/CrCl. Pearson’s correlation test was 0.55 between the tools, determining a moderate correlation between them in predicting the event.

Table 1. Clinical characteristics of the sample

<table>
<thead>
<tr>
<th>Clinical characteristics</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mehran risk score</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤5</td>
<td>5/102 (0.5)</td>
<td>36/102 (35.2)</td>
</tr>
<tr>
<td>≥6 and &lt;10</td>
<td>32/102 (31.4)</td>
<td></td>
</tr>
<tr>
<td>≥10 and &lt;15</td>
<td>22/102 (21.6)</td>
<td></td>
</tr>
<tr>
<td>≥15</td>
<td>23/102 (22.5)</td>
<td></td>
</tr>
<tr>
<td>≥2 and &lt;3</td>
<td>22/102 (21.6)</td>
<td></td>
</tr>
<tr>
<td>≥3 and &lt;5</td>
<td>23/102 (22.5)</td>
<td></td>
</tr>
<tr>
<td>≥5</td>
<td>25/102 (24.5)</td>
<td></td>
</tr>
</tbody>
</table>

Results expressed as %.

Table 2. Sensitivity and specificity according to the Mehran risk score and contrast medium volume/creatinine clearance ratio

<table>
<thead>
<tr>
<th>Clinical characteristics</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mehran risk score</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥6 and &lt;10</td>
<td>85.7</td>
<td>1.4</td>
</tr>
<tr>
<td>≥10 and &lt;15</td>
<td>71.6</td>
<td>44.6</td>
</tr>
<tr>
<td>≥15</td>
<td>39.2</td>
<td>89.2</td>
</tr>
<tr>
<td>Contrast medium volume/creatinine clearance ratio</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥2 and &lt;3</td>
<td>82.1</td>
<td>22.9</td>
</tr>
<tr>
<td>≥3 and &lt;5</td>
<td>60.7</td>
<td>45.9</td>
</tr>
<tr>
<td>≥5</td>
<td>39.3</td>
<td>71.6</td>
</tr>
</tbody>
</table>

Results expressed as %.
DISCUSSION

Contrast-induced nephropathy occurred in approximately one-quarter of patients at greater risk after a contrast-enhanced coronary procedure, which is comparable to data from previous studies.\(^5\)\(^-\)\(^7\) However, when compared to contrast-enhanced radiological procedures in general, our study had a higher incidence of CIN.\(^8\) This fact can be attributed to the complex profile of patients at the organization, and mainly to the clinical status (hospitalized patients), determining more patients with risk factors involved. In addition, intra-arterial administration of contrast medium contributes to a higher incidence of CIN.\(^9\)

The analysis of the V/CrCl as a possible risk predictor of CIN originated from the hypothesis that the risk of renal dysfunction is directly related to the infused volume of contrast medium, and inversely related to the baseline creatinine clearance. Although there was not such a linear relation between increase in V/CrCl and incidence of CIN – as occurred with MRS –, it was demonstrated that V/CrCl ≥2 infers a greater risk of this outcome. Our study showed a higher risk of CIN when V/CrCl was ≥2, a cut-off point comparable to that of MRS ≥10. Most studies observed a V/CrCl close to 2 as a cut-off point,\(^10\)\(^-\)\(^13\) although higher cutoff points have been described.\(^14\)

The area under the ROC curve of the two tools shows that the accuracy of the two methods for predicting the outcome was similar, although both were imprecise. This result agrees with studies conducted in other populations, showing similar values for prediction of CIN.\(^11\)\(^,\)\(^12\) Yet, MRS proved to be more accurate for predicting CIN in relation to V/CrCl, with a directly proportional increase in incidence. It is noteworthy mentioning that, despite having greater accuracy and more linear behavior in risk prediction, the MRS has limitations in its applicability, especially regarding patients who had acute myocardial infarction and need for urgent PCI, who were not analyzed when developing the score.\(^11\)

It is important to emphasize that, once CIN is installed, there is no specific treatment available.\(^15\) Preventing its occurrence is the main strategy to avoid this complication. Dialysis is required in only 1% of patients who develop CIN, and its occurrence can be identified within five days after contrast exposure.\(^16\) For this reason, it was not possible to properly correlate the occurrence of renal replacement therapy with the MRS value and the V/CrCl during the 72-hour period after contrast exposure. Although this data is of undeniable clinical interest, it was not the object of this study.

One of the independent risk factors for development of CIN is age equal to or greater than 65 years. In addition, the female sex can influence the glomerular filtration rate and lead to greater risk of developing CIN.\(^17\) Both factors may have contributed to the increased incidence of CIN in our study. Besides the higher prevalence of comorbidities and greater decline in renal function in elderly patients,\(^18\)\(^-\)\(^20\) our sample consisted of patients who were hospitalized and had to undergo coronary computed tomography angiography or PCI. This fact can confer greater severity and risk, not adequately measured in this analysis, but which can negatively interfere in prognosis and increase complications, such as CIN.

Greater volume of contrast used is a risk factor for development of CIN, being recognized as an independent predictor of this outcome.\(^21\) The classic recommendation to make efforts so that the total volume used does not exceed twice the creatinine clearance value is corroborated in the present study (V/CrCl <2).\(^22\)\(^-\)\(^24\) Furthermore, V/CrCl <2 had a sensitivity of 82%, proving to be capable of predicting the non-occurrence of CIN in a similar way to the low MRS (<5). As for the prediction of the occurrence of this outcome, V/CrCl seems to be useful and applicable, but with large gaps in its interpretation in clinical practice. MRS, despite being more complex and also imperfect, showed superior performance in predicting CIN.

CONCLUSION

Mehran risk score demonstrated greater accuracy in predicting contrast-induced nephropathy when compared to the contrast medium volume used/creatinine clearance ratio, although both have limitations. The closest values between the two models in the incidence of contrast-induced nephropathy were Mehran risk score ≥10 and contrast medium volume used/creatinine clearance ratio ≥2. The contrast medium volume/creatinine clearance ratio may be a more practical and simpler model for routine use, and has good power to identify a low risk of contrast-induced nephropathy using the cut-off value <2.
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CONFLICTS OF INTEREST

The authors declare there are no conflicts of interest.

CONTRIBUTION OF AUTHORS

Conception and design of the study: LFMB and RRB; data collection: MB, IBM, SPTP and VMBR; data interpretation: VTN, RGS, OAC, LFMB and RRB; text writing: VTN, LPL, DMR, PCGCL, MB, IBM, SPTP and RRB; approval of the final version to be published: VTN, LPL, DMR, PCGCL, MB, IBM, SPTP, VMBR, RGS, OAC, LFMB and RRB.

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