Original Article
A simple score for predicting renal artery stenosis in patients with ischemic heart disease

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Abstract: Background: Previous risk score is not simple for predicting existence of atherosclerotic renal artery stenosis (ARAS). Our study aims to develop a simple score to predict ARAS in eastern people with ischemic heart disease. Methods: There were two data sources involved in this study. From the data source of patients with acute myocardial infarction, we developed a clinical score for predicting existence of ARAS. After this, we validated this clinical score in data source of patients with ischemic heart failure. Results: By multivariable logistic regression analysis, only age, hypertension, stroke or intermittent claudication, serum creatinine were involved in this model. Receiver operating characteristic curve was plotted. In the first data source, area under curve is 0.808 to predict ARAS, and 0.762 for bilateral ARAS. In the second data source, area under curve is 0.721 to predict ARAS, and 0.827 for ARAS. Cutoff value of 35.0 yields a sensitivity of 82.4% and a specificity of 51.0% for ARAS, a sensitivity of 78.9% and a specificity of 47.1% for bilateral ARAS. In the second data source, this cutoff value yields a sensitivity of 85.0% and a specificity of 30.5% for ARAS, a sensitivity of 85.7% and a specificity of 17.5% for bilateral ARAS. Conclusions: We have developed a simple score for eastern people to predicting existence of ARAS with acceptable sensitivity and specificity in patients with ischemic heart disease. This score is still needed to be validated in general population or patients with no coronary heart disease.

Keywords: Renal artery obstruction, heart failure, systolic, coronary artery disease, myocardial infarction

Introduction
Atherosclerotic renal artery stenosis (ARAS) is defined as atherosclerotic narrowing of the renal artery lumen, which usually involves the ostium and proximal third of the main renal artery and the perirenal aorta [1]. Atherosclerosis accounts for approximately 90% of renal artery stenosis cases [2]. As for patients with ARAS, experts are concerned about the risk for deterioration of kidney function as well as for worsening cardiovascular morbidity and mortality [1, 2]. Reported prevalence of renal artery stenosis is different in different study populations [3]. In patients with clinical characteristics suggestive of renovascular hypertension, pooled renal artery stenosis prevalence is about 14.1% [3]. In patients with end-stage renal failure, pooled renal artery stenosis prevalence is about 40.8% [3]. In patients with confirmed coronary heart disease, renal artery stenosis prevalence is about 10.9%-14.8% [4, 5].

Although randomized trials such as ASTRAL and CORAL did not demonstrate benefits of angioplasty for ARAS, angioplasty for ARAS was believed to be beneficial in some population with ARAS [6-8]. In addition, ARAS was believed to be associated with deterioration of renal function in patients taking ACEI/ARB [9]. ACEI/ARB is indicated in patients with myocardial infarction or heart failure [10-12].

Although screening for ARAS can be accomplished by noninvasive or invasive methods, such as duplex ultrasound, computed tomography angiography, magnetic resonance angiography, and invasive angiography, it is still necessary to develop a score to perform preliminary assessment of possible existence of ARAS. Previous established predicting algorithms has
enrolled so many predictors or included invasive procedure [13-15]. So, we think it is necessary to develop a more simple approach. In this study, we developed a score to predict the existence of ARAS in patients with myocardial infarction, and testified its efficacy in patients with ischemic heart failure.

Methods

Data source

There were two data sources involved in this study. The first data source is acute myocardial infarction patients with renal arteriography, which has been published elsewhere [16]. From this data source, we developed a score for predicting existence of ARAS. After this, we validated this system in the second data source, i.e. RASHEF database. RASHEF database was founded to investigate Renal Artery Stenosis in HEart Failure (RASHEF), including heart failure patients screened for renal artery stenosis. This study was approved by Anzhen Hospital ethics committee.

The first data source has been reported previously [16]. Briefly, Data of patients with acute myocardial infarction was retrieved from the database of hospitalization in Beijing Anzhen Hospital, Capital Medical University. From 2006 to 2010, 9384 patients were admitted as acute myocardial infarction. In the 9384 patients, 257 patients with coronary artery angiography and renal artery angiography performed during hospital stay were included in this study. Patients receiving renal arteriography had the following characteristics: (a) multi-vessel coronary artery disease; (b) refractory angina; (c) history of accelerated hypertension; (d) resistant hypertension; (e) unexplained renal dysfunction. Written informed consent was obtained before angiography or invasive procedures [16].

The second data source is RASHEF data. Data source of RASHEF patients was retrieved from DHC-PACS/RIS system in Beijing Anzhen Hospital, Capital Medical University. In this DHC-PACS/RIS system from January 2010 to June 2012, renal duplex sonography was performed in 2075 hospitalized patients, including 1925 patients with echocardiography performed during hospital stay. In this 1925 patients, there were 169 patients diagnosed as heart failure. Definition of heart failure in this study was: stage II, III or IV (according to the New York Heart Association classification) heart failure and left ventricular ejection fraction < 0.50 by echocardiography. Renal duplex sonography in 2 of the 169 patients was technically inadequate for interpretation. In the remaining 167 patients, 98 patients were diagnosed as ischemic heart failure. Definition of ischemic heart failure in this study was: stage II, III or IV (according to the New York Heart Association classification) heart failure due to coronary artery disease and left ventricular ejection fraction < 0.50 by echocardiography.

Renal angiography

Procedure has been described previously [16, 17]. In this present study, atherosclerotic artery lesion with ≥ 60% (not ≥ 70%) diameter stenosis was termed as ARAS. All the lesions in this data source were diagnosed as atherosclerotic. The reason that we define ARAS as ≥ 60% whereas not ≥ 70% diameter stenosis is to develop a score in accordance with renal duplex sonography. Renal duplex sonography can discriminate ≥ 60% ARAS from < 60% ARAS accurately [18].

Renal duplex sonography

Renal duplex sonography was performed with Philips iU22G4 ultrasound system or GE Logiq E9 ultrasound system. All the lesions of significant renal artery stenosis in patients with ischemic heart failure were assumed to be atherosclerotic. Patients were classified as with or without significant renal artery stenosis according to the following criteria: 1, a renal-aortic ratio < 3.5 and peak systolic velocity of < 200 cm/s identified patients with < 60% ARAS; 2, a renal-aortic ratio ≥ 3.5 or a peak systolic velocity ≥ 200 cm/s (or both) identified patients with ≥ 60% ARAS; 3, occlusion of renal artery was diagnosed by absence of a flow signal in the renal artery and by a low-amplitude parenchymal signal. This criteria can discriminate ≥ 60% ARAS from < 60% renal artery stenosis accurately [18].

Development of score for ARAS

In this study, we aimed to develop a simple score that can help to identify ARAS in patients with ischemic heart disease. In the first data source, we first performed multivariable logistic regression analysis to identify significant predictors for ARAS. Then, significant variables selected from logistic regression analysis were
assigned integer score which was proportional to their adjusted odds ratio for ARAS. Score was calculated by sum of weighted variables present. Gold standard of ARAS was defined as narrowing of vessel diameter ≥ 60% by renal artery angiography. Cutoff value for ARAS was set by sensitivity of 80%.

Validation of this score was assessed in the second data source, i.e. RASHEF patients. Sensitivity and specificity were calculated. Receiver operating characteristic curve was also plotted to present the area under curve.

**Statistical analysis**

Continuous variables are presented as means and standard deviations. Categorical variables are presented as numerals and percentages. Group comparisons were performed with t test or Kruskal-Wallis test for continuous variables, chi-square test or Fisher’s exact test for categorical variables. Multivariable logistic regression analysis was performed to identify predictors for existence of ARAS. Hosmer-Lemeshow goodness-of-fit test was used to evaluate the goodness of fit of the regression model. A value of $P < 0.05$ was considered to be statistically significant. Data were processed by SPSS v 13.0 (SPSS Inc., USA).

**Results**

**Patient characteristics**

Baseline characteristics of patients with myocardial infarction were summarized in Table 1. In this study, criteria for ARAS were defined as ≥ 60% (not ≥ 70%) diameter stenosis. Data are presented as patients with or without ARAS. There were 257 patients involved for score development. By definition of ≥ 70% ARAS, there were 51 (19.8%) patients diagnosed as ARAS, including 34 (13.2%) unilateral ARAS (16 left ARAS, 18 right ARAS) and 17 (6.6%) bilateral ARAS. By definition of ≥ 60% ARAS, there were 51 (19.8%) patients diagnosed as ARAS, including 32 (12.5%) unilateral ARAS (16 left ARAS, 16 right ARAS) and 19 (7.4%) bilateral ARAS. All these stenotic lesions were designated as atherosclerotic.

Baseline characteristics of RASHEF patients were summarized in Table 2. Data are presented as patients with or without ARAS. There were 98 patients involved for validation of this score. Twenty patients were diagnosed as ARAS, including 13 (13.3%) unilateral ARAS (4 left ARAS, 9 right ARAS) and 7 (7.1%) bilateral ARAS. All these stenotic lesions were assumed as atherosclerotic.

Different from Tables 1 and 2 indicates that age, hypertension, serum creatinine are not significantly different between patients with ARAS and those without ARAS. This might be attributed to limited sample size in the second data source. In a larger sample, we think that the efficacy of this scoring system might be improved.

**Development of score**

**Multivariate analysis of predictors for ARAS:** As shown in Table 1, difference of age, hyperten-
Efficacy of developed score in patients with myocardial infarction (the 1st data source): Receiver operating characteristic curve was plotted to give a cutoff value for diagnosis of possible existence of ARAS (Figure 1A). The area under curve is 0.808. We choose cutoff value for ARAS set by the value when the sensitivity is ≈80%. Cutoff value of 35.0 yields a sensitivity of 82.4% and a specificity of 51.0%. Cutoff values for different sensitivity are listed in Table 5.

As for bilateral ARAS, Cutoff value of 35.0 yields a sensitivity of 78.9% and a specificity of 47.1%. After receiver operating characteristic curve was plotted, area under curve is 0.762 (Figure 1B).

Validation of developed score in patients with ischemic heart failure (the 2nd data source): According to cutoff value of 35.0, sensitivity of this score for diagnosis of ARAS is 85.0%, speci-
Table 4. Score for existence of ARAS

<table>
<thead>
<tr>
<th>Predictors</th>
<th>Score</th>
<th>Predictors</th>
<th>Score</th>
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</thead>
<tbody>
<tr>
<td>Age (years) &lt; 50</td>
<td>0</td>
<td>Hypertension</td>
<td>4</td>
</tr>
<tr>
<td>50-59</td>
<td>3</td>
<td>Stroke or intermittent claudication</td>
<td>3</td>
</tr>
<tr>
<td>60-69</td>
<td>6</td>
<td>Serum creatinine (mg/dL)</td>
<td></td>
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<tr>
<td>Ser (μmol/L)/88.4 × 30</td>
<td></td>
<td></td>
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<tr>
<td>70-79</td>
<td>9</td>
<td></td>
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<tr>
<td>≥ 80</td>
<td>12</td>
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</table>

Figure 1. Receiver operating characteristic curve was plotted. In the first data source, area under curve is 0.808 for our score to predict ARAS (A), and 0.762 to predict bilateral ARAS (B). In the second data source, area under curve is 0.721 to predict ARAS (C), and 0.827 to predict bilateral ARAS (D).
As for bilateral ARAS, cutoff value of 35.0 yields a sensitivity of 85.7% and a specificity of 17.5%. After receiver operating characteristic curve was plotted, area under curve is 0.827 (Figure 1D).

Discussion

The major findings of this study were: (1) we developed a score for predicting existence of ARAS in patients with myocardial infarction; (2) this score showed acceptable sensitivity and specificity in its validation in patients with ischemic heart failure.

Why to develop a score

Risk score can help to screen out possible ARAS. Score must be simple. Angiotensin-converting enzyme inhibitor or angiotensin receptor blocker is recommended in the scenario of acute myocardial infarction and heart failure [10-12]. Although there exists different reports about the safety of ACEI/ARB in patients with ARAS, the prevalence of ARAS still remind us of the possible deterioration of renal dysfunction after initiation of angiotensin-converting enzyme inhibitor/angiotensin receptor blocker [9 19]. Inhibition of the renin-angiotensin system leads to a decrease in renal perfusion pressure and efferent arteriolar dilation, which can decrease glomerular filtration rate in patients with renal artery stenosis. Neglecting existence of ARAS may lead to serious sequel, and miss the opportunity for delaying the deterioration of renal insufficiency. Our score takes into medical history and serum creatinine, comes to conclusion very easily. As for invasive procedure indication to screen ARAS, which is still controversial, our score can help to select proper patient to perform renal arteriography [8].

Definition of cutoff value

To find out all the possible ARAS with an acceptable specificity is the goal of this clinical score. We define the cut off value for ARAS by a sensitivity of 80%, and get a sensitivity of 82.4% and a specificity of 51.0%. We have select cutoff value by Yoden index. The most Yoden index corresponded to a sensitivity of 50% and a specificity of 90%. This is not compatible with the aim of this study. Neglecting of ARAS is not acceptable.

According to cutoff value 35.0, sensitivity for ARAS is 85.0% and specificity is 30.5% in RASHEF patients. Because it is important to identify ARAS in heart failure, this sensitivity and specificity is acceptable. After receiver operating characteristic curve was plotted, area under curve is 0.721. Decreased glomerular filtration rate in patients with heart failure might explain the decreased specificity. Pre-renal azotemia in heart failure might have increased the false positive value.

Innovation of this clinical score

Previous studies had proposed sophisticated risk scores to estimate possible existence of ARAS. Krijnen et al had proposed a prediction rule for renal artery stenosis that can be used to select patients for renal angiography [13]. Age, sex, atherosclerotic vascular disease, recent onset of hypertension, smoking history, body mass index, presence of an abdominal

<table>
<thead>
<tr>
<th>Table 5. Sensitivity and specificity by different cutoff value in development of our score</th>
<th>Table 6. Sensitivity and specificity by different cutoff value in validation of our score</th>
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<tbody>
<tr>
<td>Cutoff value</td>
<td>Sensitivity (%)</td>
</tr>
<tr>
<td>63</td>
<td>10</td>
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<tr>
<td>55</td>
<td>20</td>
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Simple score for renal artery stenosis

bruit, serum creatinine concentration, and serum cholesterol level were selected as predictors. This prediction rule was reliable (goodness-of-fit test, \( P > 0.2 \)), discriminated well between patients with stenosis and those with essential hypertension (area under the receiver-operating characteristic curve, 0.84), and had a sensitivity of 72% and a specificity of 90%. They further validate this prediction rule in a cohort of patients with consecutive patients with drug-resistant hypertension [14]. This prediction rule discriminated reasonably between patients with and without stenosis in the validation sample with an area under the receiver operating characteristic curve of 0.71 [14]. Against its efficacy, so many predictors were involved that this predict rule was not simple for practice.

Cohen et al aimed to identify simple predictors of significant RAS among patients undergoing coronary angiography [15]. Stenosis of more than 75% were considered significant. Independent predictors were older age, higher serum creatinine levels, peripheral vascular disease, number of cardiovascular drugs, hypertension, female sex, and 3-vessel coronary artery disease or previous coronary artery bypass graft. The concordance index of the model was 0.802. Cutoff value of 11 yielded a sensitivity of 76% and a specificity of 71%. This score yielded no better sensitivity and specificity than previous score, but included invasive coronary angiography in risk analysis. Again, this score is not simple.

In our score, if cutoff value was set by sensitivity of 70%, specificity would be 70% in development and 56% in validation (Tables 5, 6), which is similar to Cohen et al’s score. In the second data source, area under curve is 0.721 to predict ARAS, and 0.827 to predict bilateral ARAS, which is similar to Krijnen’s or Cohen’s study. Further, our score system is quite simple, with only four predictors included.

Limitations

This score for ARAS is sensitive, with an unsatisfactory but acceptable specificity. Secondly, this score was developed from patients with myocardial infarction, validated in patients with ischemic heart failure. In methods, selection of patients for renal arteriography had a bias towards hypertension and renal dysfunction. This bias could have affected the development of this scoring system. It is necessary to validate our score in patients with no coronary heart disease or general population.

Conclusion

We have developed a score for predicting existence of ARAS in eastern people. In patients with acute myocardial infarction or ischemic heart failure, sensitivity and specificity of this score was acceptable, which needed to be validated in general population or patients with no coronary heart disease.

Acknowledgements

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Disclosure of conflict of interest

None.

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References


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