Investigation Route of the Coronary Patient in the Public Health System in Curitiba, São Paulo and in Incor – IMPACT Study

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Abstract

Background: The investigation of stable coronary artery disease (CAD) and its treatment depend on risk stratification for decision-making on the need for cardiac catheterization and revascularization.

Objective: To analyze the procedures used in the diagnosis and invasive treatment of patients with CAD, at the Brazilian Unified Health System (SUS) in the cities of Curitiba, São Paulo and at InCor-FMUSP.

Methods: Retrospective, descriptive, observational study of the diagnostic and therapeutic itineraries of the Brazilian public health care system patient, between groups submitted or not to prior noninvasive tests to invasive cardiac catheterization. Stress testing, stress echocardiography, perfusion scintigraphy, catheterization and percutaneous or surgical revascularization treatment procedures were quantified and the economic impact of the used strategies.

Results: There are significant differences in the assessment of patients with suspected or known CAD in the metropolitan region in the three scenarios. Although functional testing procedures are most often used the direct costs of these procedures differ significantly (6.1% in Curitiba, 20% in São Paulo and 27% in InCor-FMUSP). Costs related to the procedures and invasive treatments represent 59.7% of the direct costs of SUS in São Paulo and 87.2% in Curitiba. In InCor-FMUSP, only 24.3% of patients with stable CAD submitted to CABG underwent a noninvasive test before the procedure.

Conclusion: Although noninvasive functional tests are the ones most often requested for the assessment of patients with suspected or known CAD most of the costs are related to invasive procedures/treatments. In most revascularized patients, the documentation of ischemic burden was not performed by SUS. (Arq Bras Cardiol. 2014; [online].ahead print, PP.0-0)

Keywords: Coronary Artery Disease / therapy; Coronary Artery Disease / surgery; Investigative Techniques; Unified Health System.

Introduction

In the last decade, major clinical studies have reassessed the issue of stable coronary artery disease (CAD) investigation and its treatment1,2. Currently, the assessment of patients with suspected or established stable obstructive CAD depends on the risk stratification for proper decision-making on the need for cardiac catheterization (CC) and clinical benefits of revascularization1-2.

Interventional cardiac procedures have high cost and technological adjustments are necessary to operate these services at high levels of resolution and efficiency. Thus, non-invasive stress tests are recommended as screening tests in patients at risk for CAD, being important to select higher-risk patients who may benefit from invasive, higher-cost treatments. These tests also provide relevant prognostic information3 with treatment implications, by defining the need for revascularization in patients with significant ischemia4.

To evaluate the sequence of diagnostic investigation and currently used treatment in patients with suspected or established CAD in two major metropolitan areas, São Paulo and Curitiba, as well as a referral cardiology institution, is an important step towards understanding how the resources of the Brazilian Unified Health System (SUS) are being used and identify whether there are opportunities for improvement.

Methods

This was a retrospective, descriptive, observational study of the diagnostic and therapeutic routes of patients with suspected or known CAD, treated by SUS in the cities of Curitiba and Sao Paulo, between the groups submitted or not to noninvasive tests prior to invasive cardiac catheterization. The respective economic impact of the strategies observed from the perspective of SUS was also evaluated. Similarly, patients treated at Instituto do Coração
of Hospital das Clínicas da Faculdade de Medicina of Universidade de São Paulo (Incor-FMUSP), were evaluated, due to having the largest population of patients with CAD and Latin America, as well as a structured database that allows this type of survey, including the report of procedures in a computerized system.

A survey was carried out in DATASUS regarding the number of procedures performed by SUS during the investigation of CAD in Curitiba and São Paulo, data that were corrected and cross-analyzed with a review of the High Complexity Outpatient Procedure Authorization (HCOPA) forms.

Outpatient treatment reports (OTRs), High Complexity Outpatient Procedures Authorization forms (HCOPAs) and hospital admission authorization forms (HAAs) in the period 2008-2010, of patients undergoing stress test, scintigraphy, stress echocardiography, angioplasty and coronary artery bypass grafting by SUS in the cities of Curitiba and São Paulo were assessed. Starting with the name of the patients, it was possible to determine which and how many procedures each patient was longitudinally submitted to during the study period. According to directions from the Municipal Health Secretariat of Curitiba, this survey was accompanied by auditors from the secretariat itself, and cross-checked with the costs of examinations.

The same survey was carried out in Incor-FMUSP, in patients treated by SUS, only. When evaluating HCOPA, HAA and OTR forms, we analyzed the National Registry of Health Care Institutions (CNES) to verify whether there was no overlapping with data from Incor-USP and other centers in the city of São Paulo. Empirical data observed in the realities of the health departments of Curitiba and São Paulo, as well as the Incor-USP were compared. Considering the currently prevailing conditions at Incor-USP in each year of the study, we analyzed the assessment and monitoring of approximately four thousand patients undergoing cardiac catheterization.

The distribution of absolute and relative frequencies of the study procedures allows estimating the probabilities of use of these diagnostic and therapeutic resources, according to the observed diagnostic and comorbidity strata, age and gender of the patients. The final outcome (death) in each identified investigation stratum has been reported in the Mortality Information System (MIS) up to the date of 12/31/2012, and the annual mortality rate was calculated.

Administrative data were received from municipal health secretariats and data mining techniques were used, which, regardless of the activity met, are divided into seven steps: cleaning, integration, selection, data processing and mining, evaluation of standards and representation of knowledge.

In parallel with these development activities, we also evaluated data from electronic medical records of patients from Incor-FMUSP. It is a known fact that Incor receives patients from many other cities and states and this study included all patients treated by SUS, regardless of city of origin. In both databases, the evaluation of diagnostic and therapeutic standards was performed based on the quantities and qualities of assistance resources used to in both groups of patients: those undergoing prior noninvasive tests and those referred directly to invasive cardiac catheterization.

The model of the decision tree was used to allow the observation and quantification of examinations and health resources required by each group of patients. The procedure costs were calculated in each group of patients according to Datosus surveys and the empirical reality observed in Incor-FMUSP.

Statistical analyses were performed using Microsoft Excel 2007 (Microsoft, USA) and STATA version 11.0 (Stata Corp, College Station, United States), with a level of significance < 0.05. The descriptive analysis was performed by calculating the percentage of patients who underwent stress test, scintigraphy or CC as the initial diagnostic test. The frequency of the following tests, the overall incidence of revascularization and incidence of revascularization after CC in each strategy group was also calculated. The chi-square test was used to test differences between groups.

Results

SUS in the metropolitan region of Curitiba

It is estimated that the metropolitan region of Curitiba has 3,168,980 inhabitants. Among the 66,987 procedures for cardiac evaluation and treatment of CAD in the period of January 2008 to December 2010, the exercise test was the most frequent examination, followed by the percutaneous and surgical revascularization procedures. These same procedures accounted for 1.5% and 87.2% of total direct costs involved in the diagnosis and invasive treatment of patients with CAD in the metropolitan region of Curitiba.

It is noteworthy that, while there were 10,809 percutaneous and surgical revascularization procedures, only 6,517 catheterizations were performed in the same period.

After excluding transthoracic and transesophageal echocardiography procedures, which can be used in other indications in addition to CAD, the number of procedures has a final direct cost of nearly 60 million reais, taking into account the estimated population of about 3.1 million inhabitants, with an average cost per capita of R$ 18.90 (Table 1). Figure 1 shows the number of procedures and their respective costs.

Among the HAAs and HCOPA, which data were provided by the Municipal Health Secretariat, of 6,076 catheterization procedures, only 14.5% of cases were assessed with functional imaging exams prior to catheterization. It was not possible to assess how many of these patients underwent a stress test, as there was no record of the name of the patients submitted to the examination in the reports of the health departments (municipal or state and even the Ministry of Health registry, which included only the identification number of the health care provider and the total value spent on stress test during the period).

Regarding the HAAs of 6,489 revascularization procedures analyzed, only 13.5% had been previously assessed with functional imaging exams.

In the group of patients subsequently submitted to percutaneous revascularization, the annual mortality rate was 4.8%, whereas for patients undergoing CABG it was 5.6%. In patients undergoing catheterization, but not
Table 1 – Absolute and relative frequency distribution of diagnostic and therapeutic procedures and respective costs related to CAD in the metropolitan region of Curitiba, Paraná, Brazil

<table>
<thead>
<tr>
<th>Procedure</th>
<th>n</th>
<th>(%)</th>
<th>Direct cost</th>
<th>(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stress testing</td>
<td>41,206</td>
<td>61.5%</td>
<td>R$ 894,360,00</td>
<td>1.5%</td>
</tr>
<tr>
<td>Stress echocardiography</td>
<td>1,592</td>
<td>2.4%</td>
<td>R$ 248,259,00</td>
<td>0.4%</td>
</tr>
<tr>
<td>Myocardial scintigraphy</td>
<td>6,862</td>
<td>10.2%</td>
<td>R$ 2,539,585,45</td>
<td>4.2%</td>
</tr>
<tr>
<td>Synchronized scintigraphy of cardiac chambers</td>
<td>1</td>
<td>0.0%</td>
<td>R$ 146,30</td>
<td>0.0%</td>
</tr>
<tr>
<td>Cardiac catheterization</td>
<td>6,517</td>
<td>9.7%</td>
<td>R$ 4,006,130,24</td>
<td>6.7%</td>
</tr>
<tr>
<td>Revascularization</td>
<td>10,809</td>
<td>16.1%</td>
<td>R$ 52,213,651,95</td>
<td>87.2%</td>
</tr>
<tr>
<td>Total</td>
<td>66,987</td>
<td></td>
<td>R$ 59,902,132,94</td>
<td></td>
</tr>
</tbody>
</table>

Mean cost per inhabitant                      | R$ 18.90

![Figure 1](image-url) - Frequency ratio of diagnostic and therapeutic procedures and their respective costs related to CAD in the metropolitan region of Curitiba, Paraná, Brazil.

Municipal Health Secretariat of São Paulo

It is estimated that the population of the metropolitan area of São Paulo is of 20,309,647 inhabitants. In the period from 2008 to 2010, 457,436 procedures for cardiologic assessment and treatment of CAD were performed, according to DATASUS. Among them, the stress test was the most frequently used test, followed by myocardial scintigraphy; revascularization was performed in 7.6% of cases. These same procedures accounted for 2.9%, 16.5% and 59.7% of total costs spent, respectively, in the diagnosis and invasive treatment of patients with CAD in the metropolitan region of São Paulo.

Excluding transthoracic and transesophageal echocardiography procedures, which can be used in other indications, in addition to CAD, the number of procedures showed a final direct cost of almost 240 million reais, taking into account the estimated population of approximately 20 million inhabitants with a mean cost per capita of R$ 11.69 (Table 2). The ratio of the number of procedures and costs is shown in Figure 2.

It was possible to evaluate, in patients from the metropolitan region, mortality rates in the stratum of patients undergoing catheterization and subsequent revascularization. In patients undergoing percutaneous revascularization, the annual mortality rate was 5.5%, whereas for patients undergoing CABG it was 6.3%. In patients undergoing catheterization, but not revascularization, mortality was significantly lower, 1.2%. It was not possible to assess mortality in patients undergoing functional tests, considering that patients undergoing exercise testing are not nominally reported to the Municipal Health Secretariat.

Results from InCor-FMUSP

Considering that InCor-FMUSP is a referral center for highly complex cardiovascular procedures accredited by SUS, it is estimated that it should cover a service area of

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Table 2 – Absolute and relative frequency distribution of diagnostic and therapeutic procedures and respective costs related to CAD in the metropolitan region of São Paulo, São Paulo, Brazil

<table>
<thead>
<tr>
<th>Procedure</th>
<th>n</th>
<th>(%)</th>
<th>Direct cost (R$)</th>
<th>(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stress testing</td>
<td>230,900</td>
<td>50.5%</td>
<td>6,927,000,00</td>
<td>2.9%</td>
</tr>
<tr>
<td>Stress echocardiography</td>
<td>6,301</td>
<td>1.4%</td>
<td>982,344,00</td>
<td>0.4%</td>
</tr>
<tr>
<td>Myocardial scintigraphy</td>
<td>104,239</td>
<td>22.8%</td>
<td>39,261,431,37</td>
<td>16.5%</td>
</tr>
<tr>
<td>Synchronized scintigraphy of cardiac chambers</td>
<td>2,948</td>
<td>0.6%</td>
<td>462,412,06</td>
<td>0.2%</td>
</tr>
<tr>
<td>Cardiac catheterization</td>
<td>78,250</td>
<td>17.1%</td>
<td>48,101,840,00</td>
<td>20.3%</td>
</tr>
<tr>
<td>Revascularization</td>
<td>34,798</td>
<td>7.6%</td>
<td>141,585,187,21</td>
<td>59.7%</td>
</tr>
<tr>
<td>Total</td>
<td>457,436</td>
<td></td>
<td>237,320,214,64</td>
<td></td>
</tr>
</tbody>
</table>

Cost per inhabitant: R$ 11.69

Figure 2 – Frequency ratio of diagnostic and therapeutic procedures and their respective costs related to CAD in the metropolitan region of São Paulo, São Paulo, Brazil.
approximately five million inhabitants. In the period 2008-2010, 78,792 patients were evaluated in the institution with suspected or established CAD. Of these, 18,994 were excluded because they were admitted to an emergency unit, transferred from another institution or due to a diagnosis of acute myocardial infarction or high-risk unstable angina. The final cohort consisted of 59,798 patients with suspected or stable CAD.

Of the 59,798 patients, 34,626 (57.9%) were first evaluated by stress test (Group 1), 16,221 (27.1%) were initially submitted to scintigraphy (Group 2), whereas 8,951 (14.9%) were initially submitted to CC (Group 3).

Patients initially assessed by stress test (ST)

Of the total cohort, 34,626 (57.9%) patients were initially evaluated by ST. The annual mortality rate in this group was 0.5%. These patients were divided into three subgroups:

1. CC: in 797 patients (2.3%) CC was performed after ST. Of these, 410/797 (51.4%) did not undergo CABG. While 387/797 patients (48.6%) underwent CABG, 256 underwent elective PCI, 98 patients underwent CABG and 33 underwent PCI and CABG.

2. Scintigraphy: It was the next test in 1,865 patients (5.4%). Of these, 1,748/1,865 (93.7%) did not undergo CC. Of 117/1,865 (6.3%) patients submitted to CC, 69/117 (59.0%) underwent CABG, 46 patients underwent PCI, 20 underwent CABG and three CABG and PCI.

3. The remaining 31,964 patients (92.3%) were followed clinically without subsequent CC or scintigraphy.

The incidence of overall coronary artery bypass grafting was 1.3% (456/34,626), whereas the incidence of revascularization after CC was 49.9% (456/914) in this diagnostic strategy group.

Patients initially evaluated by myocardial perfusion scintigraphy

Of the 16,221 patients initially evaluated by myocardial perfusion scintigraphy, 1,959 (12.1%) were subsequently submitted to CC with an overall revascularization incidence of 6.0% (971/16,221). The annual mortality rate in this group was 2.7%.

The incidence of myocardial revascularization after CC was 49.6% (971/1,959) in myocardial perfusion scintigraphy group, with 760 patients undergoing PCI, 179 CABG and 32 CABG and PCI.

Patients initially evaluated by cardiac catheterization

Cardiac catheterization was the initial diagnostic test in 8,951 patients, with a revascularization incidence of 28.9% (2,583/8,951) in this group, of which 1,624 (62.9%) patients underwent PCI, 857 (33.2%) underwent CABG and 102 (3.9%) both. The annual mortality rate in this group was 3.8%.

Proportion of CC, prior noninvasive testing and subsequent revascularization rates

Of the 12,132 patients undergoing catheterization, in 8951 (73.8%), no prior functional test was performed to document ischemia; 914/12,132 in patients (7.5%), ST was the first examination performed, and in 1,959/12,132 patients (16.1%), myocardial perfusion scintigraphy was performed initially. Thus, only 2,873/12,132 (23.7%) of the patients submitted to elective CC underwent a stress test in the 180 days before the procedure.

The incidence of CC that did not result in revascularization was not significantly different between the groups initially submitted the ST and myocardial perfusion scintigraphy (50.1% versus 50.4%, respectively, p = 0.74), but this incidence was significantly higher in the group initially assessed by CC (71.1%, p < 0.001) - Figure 3. Finally, a third of the 4,010 patients who underwent revascularization – 1.427/4,010 (35.6%) – underwent a noninvasive stress test before the procedure.

Direct costs related to the investigation procedures and invasive treatment in patients with known or suspected CAD in InCor-FMUSP are shown in Table 3 and Figure 4.

Discussion

Coronary angioplasty and coronary artery bypass grafting are treatment options for patients with stable CAD, with established benefits in high-risk populations. Guidelines for elective coronary intervention published jointly by the American College of Cardiology, American Heart Association and the Society of Cardiovascular Angiography and Intervention indicate that for patients with stable angina, the revascularization intervention is indicated when stenosis is “associated with moderate or high-degree ischemia at noninvasive testing”12. Previous studies have shown that patients undergoing elective angioplasty in accordance with these guidelines have better therapeutic outcomes11.

In fact, in patients from InCor-FMUSP with suspected or diagnosed CAD, those with the highest mortality rates are the ones submitted to tests of higher complexity: patients initially evaluated by ST have an annual mortality of 0.5%, whereas patients initially evaluated by scintigraphy, the mortality rate was 2.7% and in patients initially evaluated by cardiac catheterization, 3.8%. This is important because interventional cardiology laboratories have high operational costs and must be operated at the highest levels of efficiency and resolution.

Thus, when there is high probability of revascularization need, it is cost-effective to directly initiate the diagnostic evaluation with cardiac catheterization and, if possible, percutaneous revascularization intervention in the same procedure. However, in lower risk patients, the noninvasive evaluation test prior to CC is associated with lower overall cost of diagnosis, shorter hospital stays and lower rates of revascularization, without increase in adverse events, such as cardiac death or myocardial infarction14,15.

To assess whether invasive tests, such as CC, are being performed in appropriately selected patients is critical to providing high quality medical care. In this sense, our results suggest that current diagnostic strategies can be substantially improved in SUS, as even in InCor-FMUSP, a high-level educational institution, only 23.7% of patients with confirmed or suspected stable CAD submitted to
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Figure 3 – Ratio of revascularized and nonrevascularized patients after cardiac catheterization in patients whose first examination was the stress testing, scintigraphy or catheterization itself at InCor-FMUSP.

Table 3 – Absolute and relative frequency distribution of diagnostic and therapeutic procedures and respective costs related to CAD in InCor-FMUSP

<table>
<thead>
<tr>
<th>Procedure</th>
<th>n</th>
<th>(%)</th>
<th>Direct cost</th>
<th>(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stress testing</td>
<td>46,217</td>
<td>42.1%</td>
<td>R$ 1,386,510,00</td>
<td>2.5%</td>
</tr>
<tr>
<td>Stress echocardiography</td>
<td>2,481</td>
<td>2.3%</td>
<td>R$ 386,795,03</td>
<td>0.7%</td>
</tr>
<tr>
<td>Myocardial scintigraphy</td>
<td>34,775</td>
<td>31.6%</td>
<td>R$ 13,098,237,68</td>
<td>23.2%</td>
</tr>
<tr>
<td>Synchronized scintigraphy of cardiac chambers</td>
<td>1,258</td>
<td>1.1%</td>
<td>R$ 197,325,09</td>
<td>0.3%</td>
</tr>
<tr>
<td>Cardiac catheterization</td>
<td>19,468</td>
<td>17.7%</td>
<td>R$ 11,967,368,96</td>
<td>21.2%</td>
</tr>
<tr>
<td>Revascularization</td>
<td>6,956</td>
<td>6.3%</td>
<td>R$ 29,606,786,03</td>
<td>52.5%</td>
</tr>
<tr>
<td>Total</td>
<td>109,898</td>
<td></td>
<td>R$ 56,643,022,79</td>
<td></td>
</tr>
<tr>
<td>Cost per inhabitant</td>
<td></td>
<td></td>
<td>R$ 11.33</td>
<td></td>
</tr>
</tbody>
</table>

catheterization underwent noninvasive testing before the procedure provided by SUS, unlike what one would expect in a developing country, where the most cost-effective strategies should be encouraged. In comparison, in the United States, Topol et al15 and Lin et al16 described better results with higher rates of functional stress testing prior to elective CC in Medicare patients (44.5% and 29%, respectively).

Another measure of efficiency is the revascularization rate per strategy group, assuming that the perfect approach would be to select only those patients requiring percutaneous or surgical revascularization to undergo more invasive and costly procedures. An ideal strategy would prevent the greater number of catheterizations with outcomes without significant stenosis, or "normal" studies, when possible. At InCor-FMUSP, the incidence of CC that did not result in revascularization occurred in approximately half of patients initially evaluated with noninvasive tests, while in the group in which cardiac catheterization was performed as the initial diagnostic test, it resulted in revascularization in only 28.9% of patients. In the other SUS patients in São Paulo, of the patients submitted to catheterization, only 27% underwent revascularization.

Moreover, in patients from InCor-FMUSP, only 35.6% of patients had documented ischemic burden in SUS through noninvasive stress testing before the elective CABG procedure. In Curitiba, only 13.5% of revascularized patients were
Procedures and their costs also varied significantly between the two metropolitan areas and InCor-FMUSP. Although functional testing procedures are more often used to assess patients with CAD in the three scenarios, the direct costs of these procedures differ significantly, representing only 6.1% in Curitiba, 20% in São Paulo and 27% at InCor-FMUSP.

Definitively, there is an inversion of values in terms of prevention, in which, for instance, in Curitiba, almost 90% of the total amount applied in the diagnosis and invasive treatment of patients with CAD is used in revascularization of these patients, whereas only 6.1% of the resources are used in non-invasive diagnosis. Rethinking the costs and the need for performance indicators are essential for the evaluation of how these resources are being employed. The health promotion proposals by Leavell and Clark privileged normative educational actions directed at individuals, families and groups. However, the development of Medicine in Brazil maintained the predominance of individual practice, with curative approach to health problems.

The assessed results demonstrate the different ways of approaching the patient with CAD in the metropolitan areas of Curitiba and São Paulo, as well as at InCor-FMUSP. These differences probably reflect not only differences in medical profile, but also the limitations of access to diagnostic and therapeutic procedures inherent to the system itself. The data from Curitiba are a good example, being highly unlikely that, of the nearly 11,000 patients undergoing CABG, only 6,500 have undergone prior catheterization. This finding probably reflects the fact that the catheterization was performed outside the public health system, either in private clinics or in other regions of SUS, whereas the procedure of higher cost and greater complexity must have migrated to SUS from the metropolitan region of Curitiba. Regardless of the reason, the data demonstrate the incapacity of SUS to comprehensively treat the CAD patient and reinforces the uncertainty in the cost-effective application of resources.

We are aware of the several limitations of this study. The analysis based on administrative data of SUS patients from the municipalities may not represent actual patients' clinical data. In addition, the retrospective observational analysis and its results are limited by uncertainties in patient selection and by several confounding biases that may affect the likelihood of a patient to be submitted to stress tests. The difficulties found compiling the data of this study with a very simple design (study completion was estimated at 12 months, but it took us 36 months) reflect the difficulties within SUS in building solid indicators.

There are several opportunities to improve the system as a whole, from patient access to the required tests, through quality of service, the evaluation tools for the medical management employed and its compliance with the guidelines of class societies. Currently, considering the measurable data, none of the scenarios showed apparent compliance with the guidelines for CAD research and treatment.
A simple measure such as the use of patient identification on all examinations performed and not only those of higher cost/complexity, would be more accurate indicators of health. Without precise indicators about which patients are submitted to which procedures, whether these procedures are well indicated and the mortality related to different strata of patients, it is not possible to assess whether the nearly 354 million reais were used in the most cost-effective way.

However, the start of the current situation analysis, supported by the acknowledged cross-validation strategies, such as the described sensitivity analyses, is an essential and viable first step. In the absence of more reliable databases, we believe that starting this analytical process was more important than not starting it due to the several current limitations.

**Conclusion**

There are clear differences in the management of patients with suspected or known CAD in the metropolitan regions of Curitiba and São Paulo, and InCor-FMUSP. Although noninvasive functional tests are the tests most frequently used in the evaluation of patients with CAD in the three evaluated scenarios, the percentage of resources employed to perform the functional tests is much lower in Curitiba than in the other scenarios. Most of the costs are related to invasive procedures/treatments. Significant differences were observed in InCor-FMUSP regarding rates of revascularization when comparing the initial investigation strategies by invasive and noninvasive methods. When starting with non-invasive techniques (stress test and myocardial perfusion) one attains lower rates of catheterization that do not lead to revascularization in this population.

**Author contributions**

Conception and design of the research: Cerci JJ, Trindade E, Cerci RJ, Preto D, Cesar LAM, Preto L, Stinghen L, Martinez C, Meneghetti JC; Acquisition of data: Cerci JJ, Trindade E, Cerci RJ, Preto D, Lemos PA, Cesar LAM, Preto L, Stinghen L, Martinez C, Meneghetti JC; Analysis and interpretation of the data: Cerci JJ, Trindade E, Cerci RJ, Meneghetti JC; Statistical analysis: Cerci JJ, Trindade E, Cerci RJ; Writing of the manuscript: Cerci JJ, Trindade E, Cerci RJ, Preto D, Lemos PA, Cesar LAM, Preto L, Stinghen L, Martinez C, Meneghetti JC; Critical revision of the manuscript for intellectual content: Cerci JJ, Trindade E, Cerci RJ, Preto D, Lemos PA, Cesar LAM, Preto L, Stinghen L, Martinez C, Meneghetti JC.

**Potential Conflict of Interest**

No potential conflict of interest relevant to this article was reported.

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**Study Association**

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**References**


