Brazilian Cardiology Interventional Registry during COVID-19 pandemic (RBCI-COVID19)

Registro Brasileiro da Cardiologia Intervencionista durante a pandemia da COVID-19 (RBCI-COVID19)

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ABSTRACT – Background: The outbreak of coronavirus disease 2019 (COVID-19), a disease caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), was characterized as a pandemic by the World Health Organization, with high fatality rate. The number of registered cases has skyrocketed, as well as the number of deaths. Half of the patients with COVID-19 have chronic conditions, especially cardiovascular and cerebrovascular diseases, followed by diabetes mellitus, increasing their morbidity and mortality. Several studies have demonstrated this correlation, however a concomitant SARS-CoV-2 infection may trigger new clinical manifestations, such as myocarditis, arrhythmias, left ventricular dysfunction, systemic embolism and myocardial infarction, and this need to be understood within the context of each country’s reality. Delays in diagnosis and treatment of these patients could result in a poorer prognosis. Methods: This will be a prospective, multicenter registry including approximately 2,000 patients in 40 cath labs in Brazil. We will include male and female patients, aged over 18 years, admitted to interventional cardiology labs to perform a cardiovascular procedure during the COVID-19 pandemic. The primary outcomes will be death from any cause, acute myocardial infarction and stroke, and need for reintervention. As secondary outcomes, we will observe delays in completing the procedures due to the COVID-19 pandemic, and symptom-to-door, door-to-balloon, and door-to-table times. The availability and proper use of standard personal protective equipment will also be analyzed. Conclusion: The analysis of the outcomes of this multicenter registry will allow for a better understanding of the scenario of cardiovascular diseases during the COVID-19 pandemic in interventional clinical practice in Brazil.

Keywords: Coronavirus infections; COVID-19; Pandemics; Interventional cardiology; Medical registries; Brazil

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Myocardial injury occurs in 8% to 12% of cases of COVID-19. Direct myocardial injury, systemic inflammation effects, myocardial oxygen demand-supply mismatch, acute coronary event, a state of hypercoagulability and endothelial dysfunction appear to be the most common mechanisms responsible for cardiac injury and have been associated with increased levels of biomarkers, such as troponin I, B-type natriuretic peptide (BNP), and D-dimer. When treating patients with COVID-19, cardiologists should be aware of new clinical manifestations, such as myocarditis, arrhythmias, left ventricular dysfunction and systemic embolism, which may be associated with the condition, as well as the occurrence of a myocardial infarction triggered by the concomitant SARS-CoV-2 infection.

The COVID-19 pandemic could also affect delivery of care to patients with acute CVD, such as acute myocardial infarction (MI). The definition of acute MI management in patients with COVID-19 must take into account the resources locally available, such as: effective cath labs, coronary care unit and/or intensive care unit (ICU) beds, and adequate safety and protection measures against COVID-19. The Sociedade Brasileira de Hemodinâmica e Cardiologia Intervencionista (SBHCI) recommends postponing the performance of elective procedures in infected or suspected patients; limit the performance of cath lab procedures to situations of cardiovascular emergency (in cases with no instability criteria, postpone them until a non-infective phase); in services with more than one cath lab, it is recommended that one of them is reserved for procedures in infected patients.

In cases of ST-segment elevation myocardial infarction (STEMI) with hemodynamic stability, fibrinolysis may be an alternative in COVID-19 positive patients during respiratory epidemics, which renders it necessary to categorize these patients in risk levels. Length of hospital stay while waiting for additional procedures for complete revascularization is an important concern. Decisions must be individualized, considering the risk of exposure to COVID-19 versus the risk of delay in diagnosis or therapy. In addition, it is important to distinguish MI caused by unstable plaque rupture from type 2 MI or myocarditis on the differential diagnosis of AMI.

The challenges imposed during the pandemic are great, not only in the management of patients with CVD who need to continue their treatment and may or may not be affected by COVID-19, but also in the treatment of the complex cardiovascular manifestations of SARS-CoV-2, such as myocarditis, Takotsubo cardiomyopathy, and myocardial injury, which can mimic STEMI. Adding to this equation are a delayed care seeking due to fear of contamination, an increased incidence of MI with and without obstructive lesion, and a poorer prognosis in cases of myocardial infarction associated with COVID-19.

A study reporting the experience of Campania, Italy, during 60 days, starting in January 2020, showed that there...
was a reduction in the incidence of percutaneous coronary interventions (PCI) for MI, from 178 to 120 PCI/100 thousand inhabitants, during a 4-week period before and after the COVID-19 outbreak (incidence rate=0.68), with a reduction in both ST-segment elevation MI and non-ST-segment elevation MI (from 80 to 54, and from 98 to 66 PCI/100 thousand inhabitants per year, respectively). The decrease was more evident in female and elderly patients. The greatest difference found was in the interval between the onset of symptoms and the first medical contact.

Data from Chinese patients during COVID-19 demonstrated numerically greater median times in all components when compared to historical data from the previous year (time from onset of symptoms to the first medical contact, door-to-device time, cath lab arrival time). The greatest difference found was in the interval between the onset of symptoms and the first medical contact. The decrease was more evident in female and elderly patients.

New prospective studies need to be conducted to assess the care delivered to patients with heart disease during the COVID-19 pandemic. The objective of the Brazilian Interventional Cardiology Registry during the COVID-19 pandemic (RBCI-COVID19) will be to report the care of patients with heart disease during the COVID-19 pandemic who will need assistance in the Interventional Cardiology laboratories of the participant hospitals, during a 4-month period, or while the COVID-19 pandemic lasts (Figure 1). We also intend to record clinical, laboratory, and imaging variables, the outcomes upon admission and the outcomes resulting from procedures performed in interventional cardiology laboratories. We will also observe whether the differences reported between sexes and age groups will be replicated in the cases reported in Brazil.

METHODS

Selection of patients and inclusion and exclusion criteria

This is a prospective, multicenter registry, including approximately 2,000 patients in 40 cath labs in Brazil. Male and female patients, aged over 18 years, admitted to interventional cardiology laboratories for cardiovascular procedures will be included. Patients who refuse to sign the Informed Consent Form or those whose legal guardians refuse consent (https://www.mulheresemacao.online/rbci-covid19) will be excluded from the study, as well as peripheral, neurological and vascular intervention procedures and placement of devices for artificial cardiac stimulation.

Participating centers

The participating centers were included by spontaneous registration and by invitation sent through social media, telephone and WhatsApp to cath labs in all regions of Brazil. The included centers and their managers are listed in Table 1.

Table 1. Study participating centers and principal investigator

<table>
<thead>
<tr>
<th>Principal investigator</th>
<th>Organization</th>
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<tbody>
<tr>
<td>Alysson Moça Fadiga/Marcos Hertz</td>
<td>Clínica Angiopar, São José dos Pinhais (PR)</td>
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<tr>
<td>Ana Tereza Azeredo Bastos</td>
<td>Hospital das Clínicas da Universidade Federal de Goiás, Goiânia (GO)</td>
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<td>André Francisco de Paula Antongelio</td>
<td>Hospital Universitário Onofre Lopes, Natal (RN)</td>
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<td>Antonio Augusto Farias</td>
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<td>Cesar de Oliveira Lopes Dušek</td>
<td>Hospital do Rocio, Campo Largo (PR)</td>
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<td>Cristiano Guedes/Thais C. V. Tamaanato</td>
<td>Hospital Ana Nery, Salvador (BA)</td>
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<td>Cyro Rodrigues</td>
<td>Hospital de Caridade São Vicente de Paulo, Jundiaí (SP)</td>
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<td>Danilo Maksud</td>
<td>Hospital das Clínicas Luiza de Pinho Melo, Mogi das Cruzes (SP)</td>
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<td>Eder Voloholini</td>
<td>Hospital Nossa Senhora Aparecida, Umuarama (PR)</td>
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<td>Énio Eduardo Guitiers</td>
<td>Hospital Pilar/Hospital de Clínicas da Universidade Federal do Paraná, Curitiba (PR)</td>
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<td>Emersalci Ferreira</td>
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<td>Felipe Bortot César</td>
<td>Hospital Santa Rita de Cassia, Vitória (ES)</td>
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<td>Fernanda Marinho Mangione/José Armando Mangione</td>
<td>A Beneficência Portuguesa de São Paulo, São Paulo (SP)</td>
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<td>Flávio Azeredo/Rodrigo Cantarelli</td>
<td>Hospital Metropolitano Sul Don Hilder Câmara, Cabo de Santo Agostinho (PE)</td>
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<td>Frederico Toledo Campo D’Orto</td>
<td>Hospital do Coração de Poços de Caldas, Poços de Caldas (MG)</td>
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<td>Gabriella de Araújo Cunha Lima</td>
<td>Hospital Alberto Uecka Wanderley, João Pessoa (PB)</td>
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<td>Giordana Zeferino Mariano</td>
<td>Hospital São João Batista, Criciúma (SC)</td>
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<td>Gustavo Ishamar Souto Maior</td>
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<td>Luiz Fernando Alves Campos</td>
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<td>Luiz Kohn</td>
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<td>Marcel Rogers Ravanelli</td>
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<td>Marcelo Harada</td>
<td>SOS Cardin, Florianópolis (SC)</td>
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<td>Marco José da Costa Montenegro</td>
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<td>Maria Cristina Meira Ferreira</td>
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<td>Mayara Viana</td>
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<td>Ricardo Barbosa</td>
<td>Fundação Santa Casa de Mucireicódia de Franca, Franca (SP)</td>
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<tr>
<td>Ricardo Monteiro Lourenço</td>
<td>Hospital Angélica Caren/Hospital Pilar, Campina Grande do Sul/Curitiba (PR)</td>
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<td>Rodrigo Costa Guerreiro</td>
<td>EMCOR (Hospital do Coração de Nova Iguaçu), Rio de Janeiro (RJ)</td>
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<tr>
<td>Stefan Costa Silveira</td>
<td>Hospital das Nações, Curitiba (RJ)</td>
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<td>Wangles Jotão Geraldo</td>
<td>Hospital Promater, Natal (RN)</td>
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<tr>
<td>Wellington Guimarães</td>
<td>Hospital Antônio Prudente, Natal (RN)</td>
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Figure 1. Logo of the Brazilian Interventional Cardiology Registry during the COVID-19 pandemic.
Operational procedures and outcomes

The procedures to be analyzed during the study are shown in figure 2. The primary outcomes will be the occurrence of death from any cause, MI and stroke, and the need for reinterventions. As secondary outcomes, we will observe delays in completing the procedures due to the COVID-19 pandemic, and symptom-to-door, door-to-balloon, and door-to-table times, as shown in figure 3. The availability and proper use of standard personal protective equipment (PPE) will also be analyzed.28

ICF: Informed Consent Form; MI: myocardial infarction.

**Figure 2.** Procedures to be performed in the cath lab and 30 days after the intervention.

Data collection

Information about the study will be presented to potential research participants (or their legally authorized representative) and/or impartial witness, and questions will be asked to determine possible eligibility. The screening procedures will start only after the Informed Consent Form is presented, discussed and signed. The study will have a telephone number for direct contact with one of the study coordinators, as well as messages via WhatsApp, which will be answered immediately, about patients’ eligibility and data collection, as well as their insertion in the database.

The data will be collected from standardized electronic files, via the internet, on e-CRF (https://covid.rbci.online), and will be inserted by the center’s teams, who will be duly trained by the coordinating center. All patients included in the study will have their clinical data and information that are relevant to the study collected by qualified personnel trained in confidentiality of information and safe storage procedures. Clinical data collected from volunteers who eventually decide to terminate their participation during the study will be collected and stored from the date of their inclusion until their participation termination date. Confidentiality of data and access to electronic platforms will be protected by the investigators at hospitals sites, who will maintain privacy and confidentiality of information, according to the requirements set by national regulatory agencies. The e-CRF must be filled in immediately after the inclusion of the patient, based on source documents. All staff members must be formally authorized by the principal investigator of the research center and properly trained in their role within the study. In the electronic data processing performed by the proposer of the study, after reviewing the e-CRFs, additional information requests may be generated, due to discrepancies. These data must be confirmed or modified by the investigator within 3 working days.

Statistical analysis

For data analysis, the Software R29 (R CORE TEAM, 2019) will be used. The tests initially employed will be the Kolmogorov-Smirnov test, the Mann-Whitney test, the Kruskal-Wallis test and the Chi-squared test. The results will be presented as frequency, mean ± standard deviation, median and interquartile range, and they will be considered significant when p<0.05.

Parametric models will also be prepared, with regressions estimated with elastic net for the choice of relevant covariates, and then re-estimated with significant and non-parametric variables, with classification and regression trees (CART), with the resulting variables of parametric models.30

Ethical aspects

The study will be carried out in accordance with the Brazilian and international standards described in the Brazilian resolution 466/12 and in the documents of the Ministry of Health Guidelines for Good Clinical Practice, Amendment 6 –
Revision 2 (http://porta.anvisa.gov.br/). The study protocol, the Informed Consent Form and other documents pertinent to this research were allocated by the Research Ethics Committee of the coordinating center, sent for evaluation by the National Research Ethics Commission (CONEP, acronym in Portuguese), and approved in protocol CAAE 30564720.0.0000.5292. All patients selected to participate in the study will sign the Informed Consent Form before any registration pertinent to the study is made. For those with severe health conditions, assent will be given by legal representatives. Survey participants or their legal representatives will be informed that their participation is voluntary and that they may withdraw their consent to participate at any time. They will be informed that, since this is a real-world observational study, the decision to participate or not in the registration will not affect the care they will receive to treat their condition.

Confidentiality
No patient identification data will be released. The data capture system will identify patients and centers by numbers. Data from printed medical records will be kept confidential by each participating center, stored in locked cabinets/drawers. The patients’ confidentiality will be preserved in all reports and in all phases of the study.

Temporality of data collection
The registry began collecting data in May 2020 and will last for 120 days, or as long as the COVID-19 pandemic lasts.

Data quality management
Various procedures will guarantee the quality of the data, including the following: all researchers will participate in a training session before the study starts, to ensure consistency of data collection; a telephone line will be available 7 days a week, 24 hours a day, for the participating centers to submit their questions and have them answered by the coordinating center; all data entered into the Data Management System will undergo several verification checks by the coordinating center; the investigator who inserts the data is notified at the time of insertion of any inconsistency; statistical techniques for identifying inconsistency and fraud will be conducted periodically (approximately every 15 days); monitoring at the centers will be carried out during the study in a remote online format; the coordinating center will review detailed reports on screening, inclusion, follow-up, consistency and data completeness on a monthly basis.

Guidelines for publication
The results will be published with the Study Steering Committee as authors, on behalf of the researchers, who will be cited at the end of the article. Up to three members (at the discretion of the principal investigator) will be considered per research team that participated in each phase of the study. Requests for inclusion of other names will be evaluated individually by the Publication Committee. The investigator may, after the first publication of the study, request the availability of data for use in publications, upon prior presentation of a research project protocol approved by the CEP and by the registry’s executive and steering committee.

Study budget
The procedures performed during the research will not be reimbursed, since this is an observational study to verify the impact of the COVID-19 pandemic on patients with heart disease who were treated in Brazilian cathlabs.

Declaration of conflicts of interest
The study coordinators have no conflicts of interest to disclose in this study.

Organization
Study Steering Committee: Viviana Guzzo Lemke, Maria Sanali Moura Paiva, Giordana Zeferino Mariano, Gláucia Maria Moraes de Oliveira and Ricardo Alves da Costa.

REFERENCES


