Brief Communication

Safety of COVID-19 Vaccines among Individuals with Cardiopathies

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Introduction

The first cases of COVID-19 were reported in December of 2019. The SARS-CoV-2 virus has infected over 664 million people and caused over 6,7 million deaths worldwide.[1] Brazil was one of the most affected countries, with over 36 million confirmed cases and nearly 700 thousand reported obits.[1]

Although most cases were characterized as oligosymptomatic and self-limited, people older than 60 years and with comorbidities were at higher risk of presenting with severe forms, including acute respiratory distress syndrome (ARDS), myocarditis, thromboembolic events, sepsis, and shock.[2]

The rapid development of effective and safe vaccines was set as a priority by governments and pharmaceutical organizations worldwide, and the first vaccine was approved for emergency use in December 2020.[3] In Brazil, four vaccines were initially approved: inactivated whole-virion SARS-CoV-2 vaccine (CoronaVac), BNT162b2 mRNA (Pfizer), ChAdOx1 nCoV-19 (AstraZeneca) and Ad26.COV2.S (Janssen).[4] The accelerated development of immunizers raised concerns about the safety of the vaccines, especially among people with morbidities such as cardiopathies, who would benefit the most from effective immunization.[1]

As for adverse effects of the vaccines, mild symptoms such as fever, fatigue, local pain, and myalgia were common, and severe AEs were rarely reported in pivotal trials. In studies carried out with mostly healthy individuals, AEs were found to occur up to 6 weeks after vaccination.[5] Conversely, the safety of COVID-19 vaccines among patients with cardiopathies and other comorbidities was not properly investigated.

The present study aimed to assess the safety of the immunizers against Sars-Cov-2 available in Brazil in a population of patients with cardiopathies followed up in a reference cardiology outpatient facility.

Keywords

COVID-19; Vaccines; Drug-Related Side Effects and Adverse Reactions; Heart Diseases

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Manuscript received December 14, 2023, revised manuscript February 17, 2024, accepted March 06, 2024

DOI: https://doi.org/10.36660/abchf.20230094

Methods

The study was an observational unicentric retrospective cohort. A convenience sample was drawn from cardiac patients followed up at a cardiology reference service of an outpatient facility in Salvador, Bahia, Brazil. Patients aged over 18 years, previously diagnosed with cardiopathies, and who received at least one dose of any COVID-19 vaccine were included. Information regarding sociodemographic data, clinical history, vaccination coverage, and AEs associated with COVID-19 immunization were collected. Data collection was only started after approval by the local ethics committee.

AE were defined as any undesirable medical occurrences after vaccination and were categorized as severe adverse events (SAEs) or non-severe adverse events (NSAEs). AE was considered severe when they required hospitalization, leading to significant organic dysfunction, permanent disability, and/or risk of death. NSAE was defined as any self-limited symptoms that did not meet the criteria for SAE, such as local soreness, fever, adynamia, myalgia, headache, or others (dizziness, nausea, sore throat, palpitations, abdominal pain, and diarrhea) with a duration of less than 3 days.

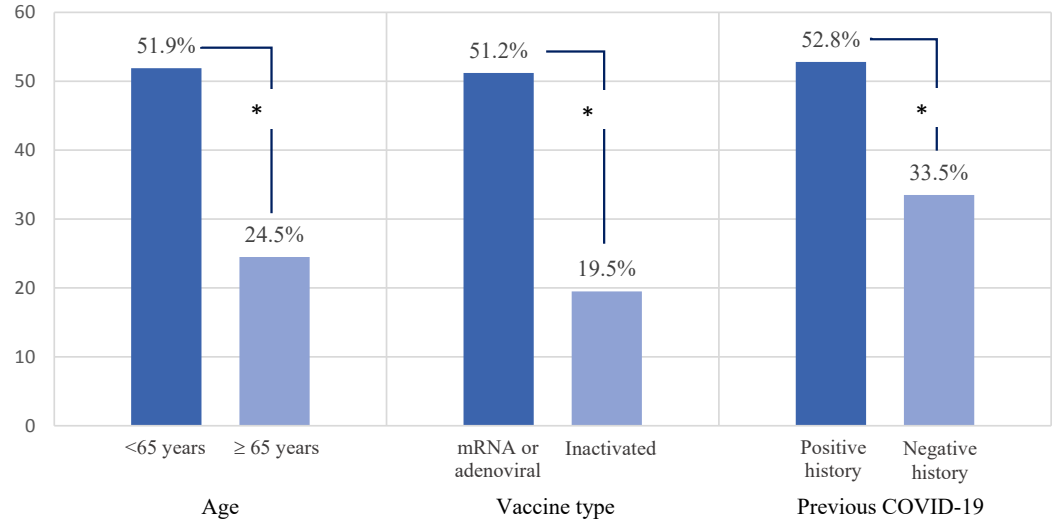
Statistical analyses were performed with R, version 4.1.2. Categorical variables were described as proportions and quantitative variables were described as average (standard deviation) and medians (interquartile interval). The normality of the distribution of variables was assessed by the Shapiro-Wilk test and by characteristics of the distribution. Inferential analyses were exploratory. Concerning the vaccine used, CoronaVac was considered as a reference category. Student's t-test and Fisher's exact test were used to compare categorical variables or means, respectively. Multivariate logistic regression models were used for adjusted analysis between selected characteristics and the presence of post-vaccination AEs, estimating the prevalence ratio as a measure of association. The significance level adopted was 5%.

Results

Between November 2021 and July 2022, 329 patients were included. The mean age was 62 (± 15.5) years. Women corresponded 64.5% (211) of the sample and 84.4% (265) were black/ brown. Sociodemographic and clinical data are presented in Table 1. The most common comorbidities were hypertension, dyslipidemia, diabetes mellitus, and chronic kidney disease.

278 (84.5%) received a full vaccination course, which was considered at the time as a single dose of Janssen or 2 doses of other immunizers. Of those, 122 (43.9%) received CoronaVac,

Central Illustration: Safety of COVID-19 Vaccines among Individuals with Cardiopathies



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*Incidence of post-vaccination adverse events according to age, vaccine type, and previous COVID-19 infection. Incidence was described as a percentage (%). *All differences between proportions had p-values < 0.05.*

109 (39.2%) received AstraZeneca, 42 (15.1%) Pfizer, and 5 (1.8%) Janssen. By the end of the study, 129 (42.6%) patients had received a third dose of vaccine, of which 124 (96.1%) were given Pfizer and 3 (2.3%) received CoronaVac.

Of the total vaccinated, 110 (33.4%) reported AEs, all non-serious. Of those who reported AEs, 46 (41.8%) reported local soreness, 44 (40%) reported fever, 32 (29.1%) reported adynamia, 31 (28.2%) referred myalgia, 21 (19.1%) had headaches and 9 (0.8%) reported other NSAE. The bivariate analysis demonstrated that AEs were more frequently reported after immunization with Pfizer, AstraZeneca, and Janssen vaccines compared to CoronaVac (51.2% vs. 19.5%; $p < 0.01$), as well as among patients under 65 years in comparison with older individuals (51.9% vs. 24.5%; $p<0.01$). Besides that, patients with a history of COVID-19 infection also reported a higher rate of AEs (52.8% vs 33.5%; $p=0.03$) when compared to non-infected individuals (Central Illustration).

In an exploratory multivariate analysis including age, type of vaccine (considering the Corona Vac vaccine as reference), and previous COVID-19, type of vaccine and age remained significantly associated with the occurrence of post-vaccination AEs, although age had a very borderline association (Table 2).

Discussion

Although frequent, AEs were mostly mild and self-limited. These findings agree with those reported by systematic reviews and meta-analysis, which included both data from vaccine clinical trials and post-marketing AEs reporting databases.[6-8]

Patients with previous Sars-Cov-2 infection were more likely to report AEs, as well as younger patients (< 65 years). The latter was also systematically reported in the literature.[6,7] In agreement with previous studies, AEs were more frequently reported after immunization with mRNA (Pfizer) or adenoviral carrier (AstraZeneca and Janssen) vaccines than with inactivated vaccines (CoronaVac).[7,8] This finding is of particular interest considering that the CoronaVac vaccine was largely distributed in Brazil, especially among populational groups considered at higher risk for COVID-19 infection complications, which include patients with cardiopathies. AEs were also more frequent in non-elderly individuals, which could have been due to greater use of immunization with mRNA or adenoviral carrier vaccines in that group. However, this finding remained statistically significant after adjustment for vaccine type, even though the adjusted association was borderline.

Although not reported in our study, SAEs to the COVID-19 immunizers were of particular concern for patients with cardiopathies, as most of the SAEs reported in clinical trials and real-world surveillance were related to cardiovascular events.[9] In 2020, the Brighton Collaboration and the World Health Organization (WHO) endorsed a priority list of AEs of special interest (AESIs), which included pulmonary embolism, acute myocardial infarction, and disseminated intravascular coagulation. The risk of these AESIs could be potentiated among patients with cardiopathies and comorbidities.[9,10]

Our study has limitations. First, the study is observational and retrospective. Second, convenience sampling and small sample size reduce the power of the study and limit inferential

statistical analysis, which compromises the internal validity of data and limits the drawing of definitive conclusions. In addition, the lack of a control group, such as healthy patients, limits definitive conclusions about vaccine safety against Covid-19 in heart disease patients. Finally, as some of the data was collected through electronic medical records, there may be uncertainty regarding the validity of the information encountered.

In conclusion, the findings presented suggest that the COVID-19 vaccines available in Brazil at the time of the study were safe for application in patients with cardiopathies and comorbidities. To our knowledge, this is the first study evaluating the safety of vaccines in this subgroup of the population, as most studies exclude patients with previous cardiovascular conditions. Our study sheds light on the issue of the harm/benefit ratio of immunizers against Sars-Cov-2 infection for these patients, yet further analysis is required to validate these results, as well as the evaluation of new vaccines available for the disease.

Author Contributions

Conception and design of the research: Nunes BA, Costa FF, Latado AL; Acquisition of data: Chiaretti ALS, Nunes BA, Costa FF; Analysis and interpretation of the data: Chiaretti ALS, Oliveira LB, Costa FF, Latado AL; Statistical analysis: Oliveira LB, Latado AL; Writing of the manuscript: Chiaretti ALS, Costa FF, Latado AL; Critical revision of the manuscript for content: Nunes BA, Oliveira LB, Costa FF, Latado AL.

Potential conflict of interest

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

Sources of funding

There were no external funding sources for this study.

Study association

This study is not associated with any thesis or dissertation work.

Ethics approval and consent to participate

This study was approved by the Ethics Committee of the Universidade Federal da Bahia - Hospital Universitário Professor Edgard Santos under the protocol number CAAE: 52313021.4.0000.0049 parecer 5.060.213. All the procedures in this study were in accordance with the 1975 Helsinki Declaration, updated in 2013. Informed consent was obtained from all participants included in the study.

Table 1 – Sociodemographic, clinical data, and vaccination coverage of the sample

Sociodemographic data	
Age (years)	62±15
Female gender	211 (64.5%)
Black or Brown race	265 (84.4%)
Smoking	14 (4.3%)
Clinical data	
Dyslipidemia	261 (79.6%)
Diabetes Mellitus	147 (45%)
Systemic Arterial Hypertension	268 (81.7%)
Chronic Kidney Disease	78 (23.9%)
Previous Acute Coronary Syndrome	96 (29.2%)
Valvopathy	72 (22%)
Heart Failure	119 (36.2%)
Atrial Fibrillation	49 (15%)
Vaccination coverage	
Full vaccination course	278 (84.5%)
CoronaVac	122 (43.9%)
AstraZeneca	109 (39.2%)
Pfizer	42 (15.1%)
Janssen	5 (1.8%)

Data are presented as numbers (percentages) and mean ± standard deviation as appropriate.

Table 2 – Multivariate analysis* for post-vaccination adverse events

	PRa	95% CI	p Value
Age (in years)	1,003	1,000 – 1,006	0.048
Vaccine type**	1,136	1,032 – 1,251	0.010
Previous COVID-19 infection	1,077	0,963 – 1,208	0.196

**Binomial logistic regression. PRa: adjusted prevalence ratio; CI: confidence interval. ** The Corona Vac vaccine was considered as a reference category and was compared to the other vaccines studied (BNT162b2 mRNA-Pfizer, ChAdOx1 nCoV-19-Astrazeneca, and Ad26. COV2.S-Janssen).*

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