Original Article

Availability of Natriuretic Peptide Testing in Primary Public Health Care in Brazil

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Abstract

Background: Early detection of heart failure makes it possible to intervene in risk factors, and treatment is capable of modifying the natural history of the disease. For diagnostic confirmation, natriuretic peptide (NP) testing or transthoracic echocardiography can be performed; the former is preferable when considering cost and accessibility. Although this test was incorporated into the Brazilian Unified Health System (SUS) in 2018, requests for this test were registered in only 4.63% of municipalities in the SUS Outpatient Information System (SIA/SUS) in 2022. This leads to difficulties in both heart failure diagnosis and access to specific treatments, given that the use of sacubitril valsartan sodium depends on the performance of this test.

Objective: To evaluate the availability of NP testing in the SUS.

Methods: Cross-sectional study carried out by means of telephone contact with a probabilistic sample of 255 Brazilian municipal health departments.

Results: NP testing was reported as available in 20.78% (53/255) of contacts, either within the municipality (16.86% [43/255]) or in the reference municipality (3.92% [10/255]), while 78.04% (199/255) of interviewees reported that the test was not available through the SUS.

Conclusion: Although NP testing has been incorporated into the SUS since 2018, we observed that the test was available in 12.23% of municipalities, in addition to those that actually registered a request in the SIA/SUS during the year studied (2022). This suggests that, in addition to the fact that the test is not offered in a uniform manner throughout the country, there are still municipalities where the test is available, but its use has not been registered.

Keywords: Heart Failure; Brain Natriuretic Peptide; Unified Health System; Health Equity; Effective Access to Health Services.

Introduction

Heart failure (HF) is considered the fourth most common cause of cardiovascular death,[1] with an estimated incidence of 5.7 to 7.9 per 1000 person-years in those over 45 years of age, reaching 21.1 per 1000 person-years in those over 65 years of age.[1–3] It is estimated that 49 million people were living with HF worldwide in 2019,[4] with nearly 1.7 million in Brazil alone.[5]

The identification of patients with HF in primary care is the key to early detection and initiation of appropriate treatment.[6] HF diagnosis remains a challenge; it is based on clinical assessment and can be made incorrectly in up to 70% of cases.[7] To assist diagnosis of patients with clinical suspicion of HF and low or moderate likelihood according to the Boston criteria, the public system provides transthoracic echocardiogram or measurement of serum levels of brain natriuretic peptides (NP), which can be either natriuretic peptide type B (BNP) or N-terminal pro-hormone B-type natriuretic peptide (NTproBNP).[8] For patients with a high likelihood of HF, no additional tests are necessary to diagnose the disease.[9]

In the context of the Brazilian Unified Health System (SUS), NP testing is preferable for diagnosing HF, as the test is considered easy to implement and interpret,[10] with lower potential cost. This can reduce inequity in HF diagnosis, as it is possible to rule out HF diagnosis in patients with BNP values below 35 pg/dl and NTproBNP values below 125 pg/dl, and only those with BNP or NTproBNP values equal to or greater than these reference values would be referred for echocardiography, making it possible to focus echocardiography on more complex diagnoses and patient follow-up.[9] When implementing HF diagnosis with tests

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performed in series, it is estimated that, for every 2.93 NP tests, an echocardiogram is spared.[8]

NP testing is considered an important element for diagnosis, and it is useful in ruling out diagnosis of HF in the screening of patients with low or moderate likelihood of HF due to its high negative predictive value.[7,11] Furthermore, this test is necessary to guarantee access to some specific pharmacological treatments for HF with reduced ejection fraction in the SUS, such as sacubitril valsartan sodium.[12]

On the other hand, although NP testing was incorporated into the SUS in November 2018,[8] between May 2020 (the month the code was included in SIGTAP)[13] and May 2021, only 3,761 tests were carried out in just 2.8% of Brazilian municipalities, reaching 4.63% of municipalities by August 2022, according to registrations in the SUS Outpatient Information System (SIA/SUS).[14]

Therefore, considering the importance of NP testing in the context of HF in the SUS, the objective of this study was to evaluate the effective availability of the test in primary care in municipalities in different regions of Brazil.

Methods

A cross-sectional study was developed, in which interviews were carried out via telephone with Brazilian municipal health departments, with the aim of evaluating the availability of NP testing through the SUS.

Statistical analysis

In order to define the sampling plan, we first considered the municipalities that could request the test, namely, those with a primary health care unit with full municipal or state level of medium complexity.[8,15] There were 2,849 municipalities with these characteristics available in Brazil in 2022. Accordingly, to estimate the percentage of test requests that are statistically representative of these locations, a point estimate of 2% was considered (according to the number of tests carried out between May 2020 and May 2021, according to data from SIA/SUS),[14] with a margin of error of 5% and a 95% confidence interval. Therefore, it would be necessary to contact at least 255 municipalities to establish the data.

Thus, the sample was defined based on a random drawing stratified by Brazilian regions, weighted by their respective populations. The municipalities were randomly drawn using a script developed in R software.[16]

The following characteristics were extracted from the selected municipalities: average life expectancy (2010), average population of the municipality (2021), average per capita gross domestic product (GDP) (2019), average Municipal Human Development Index (MHDI) (2010),[17] and the average distance from the municipality's centroid to the state capital, with geodesic correction, based on the coordinates available through the Brazilian Institute of Geography and Statistics (IBGE).[18]

Variables were tested for normality using the Kolmogorov-Smirnov test. Those considered normal were described using mean and standard deviation; otherwise, median and interquartile range (IQR) were used. To compare the characteristics of the municipalities that reported that the test was available and those that reported that the test was unavailable, the Mann-Whitney test was used.

Multivariate analyses were planned for the presence of significant differences in 2 or more characteristics of the municipalities that reported that the test was available or unavailable, which was not observed.

Materials, procedures, and techniques

Telephone interviews were carried out with employees of the municipal health department of the selected municipalities, during the month of July 2022, respecting the order of the random drawing.

Contact data were obtained by searching a browser for the website of the health department or city hall. After 3 unsuccessful attempts, the next municipality drawn in the same region was contacted, until reaching the minimum number of municipalities planned for contact.

The interview was carried out following a pre-established script and the informed consent form was read in full. After verbal agreement with the informed consent form, the interview began with the collection and recording of the following data in a form developed in Microsoft Excel®:[19]

- Agreement with the informed consent form;
- Name of the municipality, state, and region;
- Data of the professional who agreed to the informed consent form and responded to the interview;
- Availability of NP testing (BNP/NTproBNP) within the municipality or in the reference municipality through the SUS, which was always confirmed by the SIGTAP code: 02.02.01.079-1;[13]

The data collected during the interview were analyzed using the following software: R (version 4.0)[16] and jamovi (version 1.6).[20]

The following variables were considered: availability of the test in the municipality or reference municipality through the SUS, average life expectancy (2010), average population of the municipality (2021), average per capita GDP (2019), average MHDI (2010),[17] and the average distance from the municipality's centroid to the state capital, with geodesic correction, based on the coordinates available through the IBGE.[18]

This study was approved by the Research Ethics Committee of the Brazilian National Institute of Cardiology (CAAE 58125722.6.0000.5272).

Results

In order to meet the minimum quantitative criteria for sampling, 647 municipalities were contacted (68 in the North Region, 353 in the Northeast, 130 in the Southeast, 84 in the South, and 12 in the Central-West), and 255 municipalities were successfully interviewed (16 in the North Region, 81 in the Northeast, 81 in the Southeast, 68 in the South, and 9 in the Central-West).

As shown in Figure 1, the availability of the test through the SUS, during the study period, was reported in 20.78%

(53/255) of interviews; in 16.86% (43/255) it was possible to perform the test within the municipality, and in 3.92% (10/255) it was only possible in the reference municipality. The test was not available through the SUS in 78.03% (199/255) of municipalities. Of the total, only 1.18% (3/255) of those contacted were unable to inform whether the test was available.

The regions where the test was most frequently available were the Southeast with 28.40% (23/81), followed by the North with 25% (4/16), and the South with 22.06% (15/68). The test was reported as unavailable in 100% (9/9) in the Central-West and in 85.19% (69/81) in the Northeast (Figure 2).

The municipalities that reported that the test was available through the SUS were more frequently closer to the capital than the municipalities where the test was unavailable (188 km [IQR: 91.4 to 336] versus 240 km [IQR: 143 to 366]). MHDI (0.704 [IQR: 0.634 to 0.740] versus 0.665 [IQR: 0.612 to 0.721]) and life expectancy (74.9 [IQR: 72.3 to 76.1] versus 73.4 [IQR: 71.5 to 75.0] years) were higher where it was reported that the test was offered through the SUS, when compared to those that reported that it was unavailable, as shown in Table 1.

Furthermore, per capita GDP was higher in municipalities where the test was available, when compared to those where the test was unavailable (R$ 21,991.00 [12,600.00 to 29,151.00] versus R$ 18,352.00 [11,277.00 to 30,178.00]) (Figure 3).

Among the variables studied, life expectancy in the municipalities was the only variable with a statistically significant difference regarding whether or not the test was available through the SUS, as shown in Table 2.

Discussion

This study identified that the test was available through the SUS in 20.78% of the municipalities during the study period. It was more accessible in the North and Southeast and less accessible in the Central-West and Northeast Regions.

Contact with municipalities in the North and Northeast was more complex, because, in some of these municipalities, the telephone number provided on the website of the health department or city hall was unavailable or incorrect, or the call was not answered. It was necessary to contact 68 municipalities in the North Region to carry out 16 successful interviews and 353 municipalities in the Northeast Region for 81 successful interviews. In the Central-West and South Regions, it was necessary to contact 12 and 84 municipalities to obtain 9 and 68 successful interviews, respectively.

The test was available in 12.23% of municipalities, in addition to those that registered the test by August 2022, according to data from SIA/SUS (16.86% (43/255) versus 4.63% [132/2849]),[14] indicating that, even 4 years after the technology was incorporated into the SUS,[8] the test is not offered in a uniform manner in all Brazilian municipalities, and there are still municipalities where, even though it is offered, the test is not requested, which may suggest the attending physicians' lack of knowledge about its availability in the health care network or about the diagnostic flow of patients with HF in primary care. This fact is not limited to diagnostic technologies; it has also been observed for several medications incorporated into the SUS, in which it was possible to show that the time between the final recommendation for incorporation by the National Commission for the Incorporation of Technologies (CONITEC) and the effective dispensing may vary greatly, such as 115 days for sofosbuvir in the treatment of hepatitis C,[21] or up to 23 months for memantine, which was incorporated

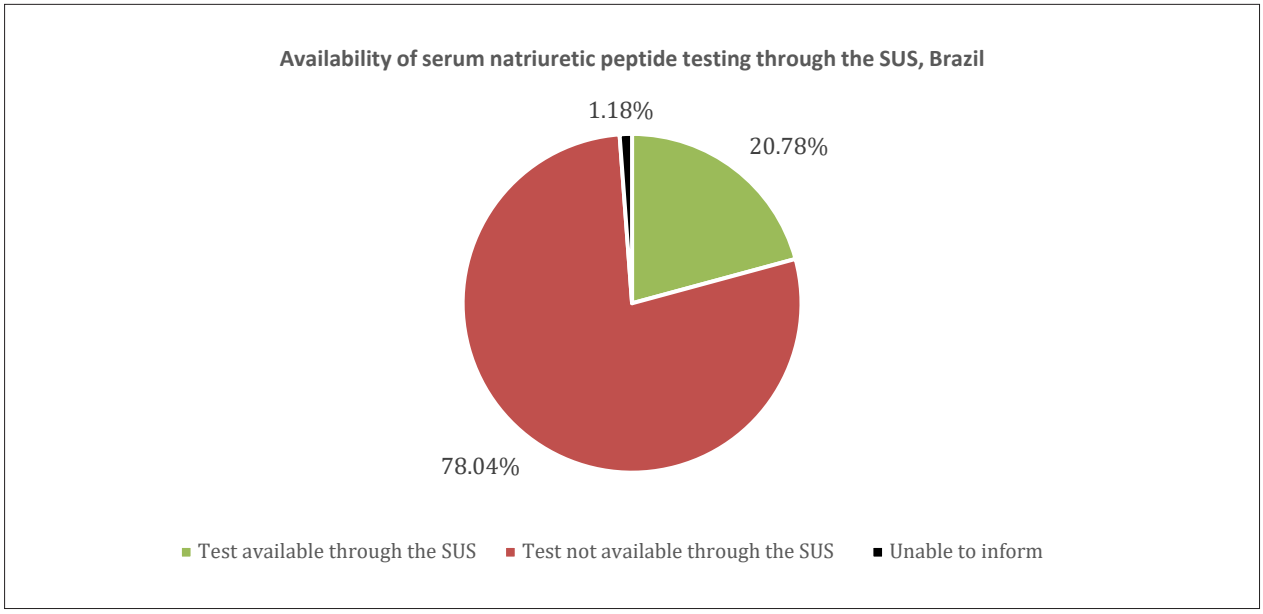

Figure 1 – *Availability of serum natriuretic peptide testing in Brazil. Unable to inform: The interviewee was unable to inform whether natriuretic peptide testing was available through the SUS. Test available through the SUS: Natriuretic peptide testing was available through the SUS within the municipality or in the reference municipality. Test not available through the SUS: Natriuretic peptide testing was not available through the SUS. Source: the authors.*

in November 2017, with the first registration of dispensation through the SUS in October 2019.[22]

According to Brazilian Recommendation Report Number 386 of the Technical-Scientific Opinion on Type B Natriuretic Peptides (BNP and NTproBNP) for the Diagnosis of Heart Failure,[8] NP testing is easy to implement, and it has fewer logistical restrictions than referring a patient to a specialist or echocardiogram, as both have a waiting list. In the city of Rio de Janeiro alone, for example, around 3,528 patients were waiting for an appointment with a cardiologist, and 10,257 users were waiting to undergo an echocardiogram, according to data from the Regulation System (SisREG) in 2021.[23]

The wait for echocardiography is related to more complex logistics for the SUS, when compared to carrying out NP testing, as the former requires equipment and an echocardiography specialist.[8] Between 110,000 and 150,000 outpatient echocardiography exams were performed per month in the SUS (data from 2021 and 2022), and echocardiography devices are concentrated in the Southeast Region, which is responsible for performing almost 50% of the country's echocardiography exams.[14] These data may suggest a potential undersupply of exams for HF diagnosis in the North and Northeast Regions, in addition to highlighting unequal distribution, which underscores the importance of universally offering NP testing, as this test can be carried out in small municipalities that lack the infrastructure to carry out more complex exams, thus helping to reduce health inequities and facilitate access to specialized treatments.[8]

The differences between the municipalities that offer NP testing in Brazil mirror health inequities, which occur when some subgroups present avoidable differences in health due to lack of access.[24] Socially disadvantaged groups are exposed to higher risk living and working conditions, and they may present accelerated aging and a higher prevalence of chronic

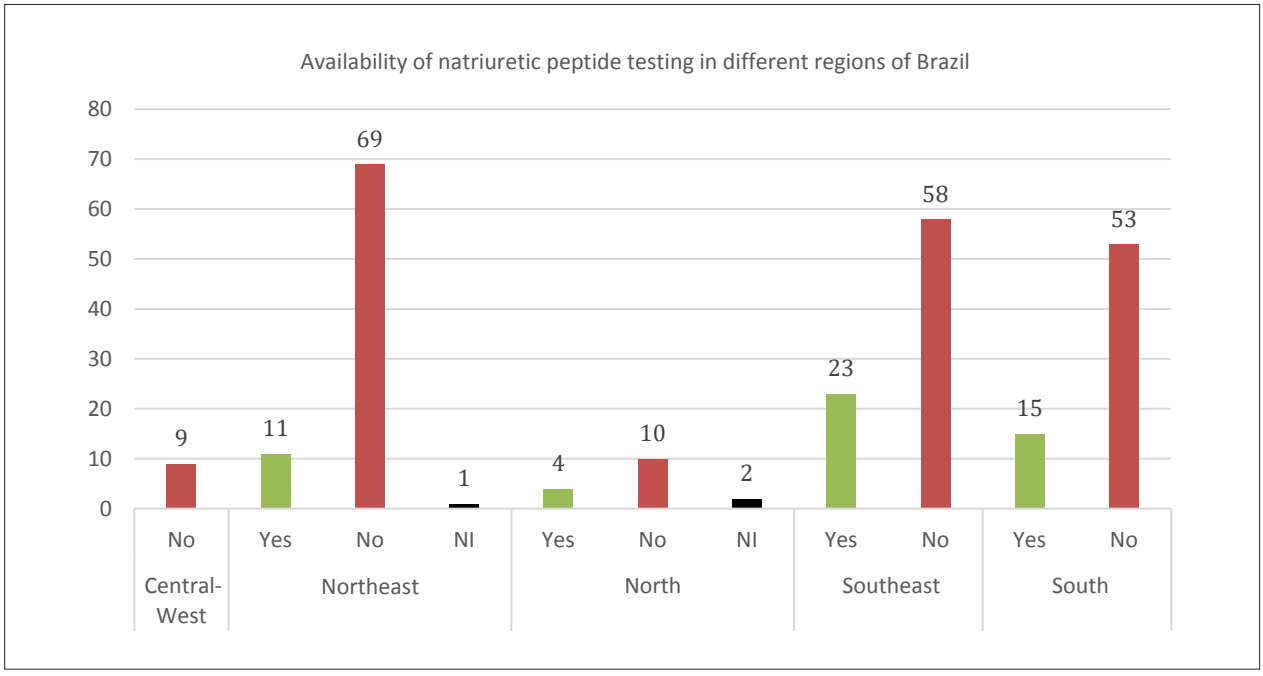

Figure 2 – *Availability of natriuretic peptide testing in different regions of Brazil. NI (not informed): The interviewee was unable to inform whether natriuretic peptide testing was available; Yes: Natriuretic peptide testing was available through the SUS within the municipality or in the reference municipality. No: Natriuretic peptide testing was not available through the SUS. Source: the authors.*

Table 1 – Test availability and characteristics of municipalities (median and interquartile range)

Availability of NP	Population	Distance (km)	GDP per capita (R$)	Life expectancy (years)	MHDI
Yes	20,228 (7,588-65,788)	188 (91.4-336)	21,991 (12,600-29,151)	74.9 (72.3-76.1)	0.704 (0.634-0.740)
No	14,497 (7,073-34,408)	240 (143-366)	18,352 (11,277-30,178)	73,4 (71.5-75.0)	0.665 (0.612-0.721)

Availability of NP: Availability of natriuretic peptide (NP) testing; No: Natriuretic peptide testing was not available in the municipality or reference municipality through the SUS; Yes: NP testing was available through the SUS. GDP (gross domestic product) per capita in Brazilian reals (R$), 2019.[17] Life expectancy in years, 2010.[17] MHDI (Municipal Human Development Index), – 2010.17 Distance (km) is the distance in kilometers from the municipality's centroid to the state capital, with geodesic correction.[18] Reference year: population, 2021. Source: the authors.[16,20]

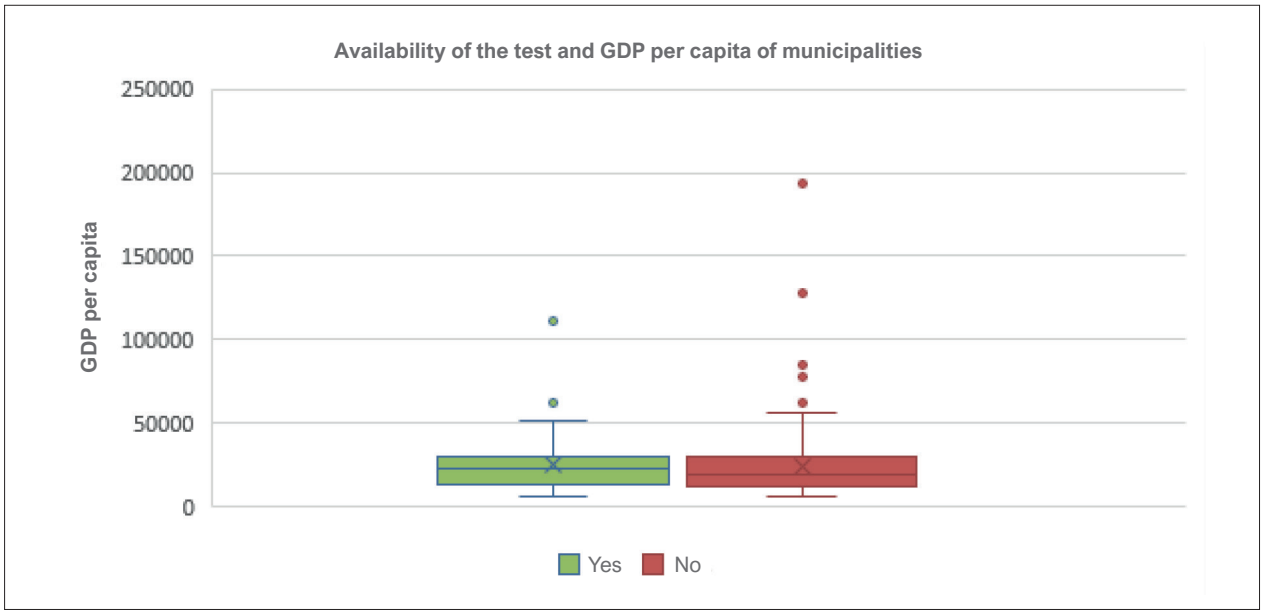

Figure 3 – *Availability of the test and GDP per capita of the municipalities. Yes: Natriuretic peptide testing was available through the SUS within the municipality or in the reference municipality. No: Natriuretic peptide testing was not available through the SUS.[18] Per capita GDP (gross domestic product) of the municipality interviewed for the year 2019. Source: the authors.[16,20]*

diseases with an impact on health outcomes, including quality of life and well-being.[24,25] Data on the availability of NP testing represent difficulty not only in access to the test, but also to specialized treatments for individuals assisted in poorer municipalities, with lower life expectancy and lower per capita income.

By including NP testing in the HF diagnostic algorithm, the demand for echocardiography would theoretically be reduced, because only patients who would benefit most from the imaging exam would be referred to undergo it.[8] Furthermore, given that, in some municipalities, echocardiography is only requested by a specialist, making NP testing available can minimize the costs related to the use of this resource and reduce the time for HF diagnosis.[8,9]

The main limitations of this study include the following:

- The availability of the test was informed by only one interviewee from each of the selected municipalities, and it is not possible to guarantee whether or not NP testing is actually offered by the municipality. To minimize the receipt of incorrect information, we requested that the interview be carried out with the professional with the greatest expertise in the unit contacted and that the interviewee confirm the information with the procedure code in their system.
- Contact was only made with the selected municipality via the telephone number indicated on the website of the health department or city hall; another professional with greater expertise within the municipality could be contacted using another telephone number, when solicited.
- Not all service providers affiliated with the SUS nor the reference municipality were contacted to confirm that the test was available.

Table 2 – Mann-Whitney test for characteristics of municipalities

		Statistic	p
Distance (km)	Mann-Whitney U	4589	0.147
MHDI	Mann-Whitney U	4366	0.054
Population	Mann-Whitney U	4528	0.114
GDP per capita	Mann-Whitney U	4804	0.320
Life expectancy	Mann-Whitney U	4030	0.008

Result of the non-parametric test comparing the characteristics of the municipalities that reported that serum natriuretic peptide testing was available with municipalities that reported that it was unavailable. GDP: gross domestic product; MHDI: Municipal Human Development Index. Source: the authors.[16,20]

- The physicians responsible for diagnosing and following these patients in the municipality's basic unit were not contacted to evaluate whether they were aware that the test was available.
- In this study, it is possible that there is a bias that is common to the sampling of cross-sectional studies. Failure to contact the municipalities selected by random drawing, which was more common in the North and Northeast Regions, may have led to greater uncertainty in relation to the point estimate. However, this bias was mitigated by the random replacement of uncontacted municipalities in the same region, with the purpose of reaching the planned sample size. Furthermore, although unlikely, a possible deviation in the point

estimate, if it existed, would tend to select municipalities with a greater likelihood of making the test available.

Conclusion

The reduced availability of NP testing and, consequently, the difficulty in accessing specialized treatment for HF was associated with municipalities with lower MHDI and GDP. The region with the greatest test availability is the Southeast, which is also the region that performs the most echocardiograms through the SUS in Brazil. This aspect demonstrates that areas where the availability of echocardiography is reduced also have less availability to carry out NP testing, making it necessary to refer these patients to larger centers for complementary tests or evaluation by a specialist, which can lead to delays in the diagnosis and treatment of these patients.

Finally, the viability of NP testing has the potential to represent an important alternative to expand the diagnosis of patients within the scope of primary care and, consequently, reduce inequity in HF diagnosis and allow access to adequate and timely treatment for these patients.

Author Contributions

Conception and design of the research: Braga AA, Santos MS, Tura BR; Acquisition of data: Braga AA, Barros BM, Morais QD; Analysis and interpretation of the data and Writing of the manuscript: Braga AA; Statistical analysis: Braga AA, Tura BR; Obtaining financing: Santos MS; Critical revision of the manuscript for content: Santos MS, Oliveira IG.

Potential conflict of interest

Andressa Araujo Braga - received honoraria from Novartis Biociência SA

Ione Gualandi Oliveira - Novartis employee

Sources of funding

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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 Instituto Nacional de Cardiologia under the protocol number CAAE: 58125722.6.00005272. 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.

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01/2002 que amplia as responsabilidades dos municípios na Atenção Básica; estabelece o processo de regionalização como estratégia de hierarquização dos serviços de saúde e de busca de maior eqüidade; cria mecanismos para o fortalecimento da capacidade de gestão do Sistema Único de Saúde e procede à atualização dos critérios de habilitação de estados e municípios. Brasília: Ministério da Saúde; 2022.

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