ORIGINAL ARTICLE ARTIGO ORIGINAL

Resource utilization and costs related to the management of obstructive hypertrophic cardiomyopathy under the Brazilian supplementary healthcare system's perspective: results from a modified Delphi panel

Utilização de recursos e custos relacionados ao manejo da cardiomiopatia hipertrófica obstrutiva sob a perspectiva do sistema de saúde suplementar brasileiro: resultados de um painel Delphi modificado

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DOI: 10.21115/JBES.v15.n3.p190-199

Keywords:

hypertrophic cardiomyopathy, supplementary health, costs and cost analysis, Delphi technique

ABSTRACT

Objective: To generate data on the costs associated with the diagnosis and treatment of obstructive hypertrophic cardiomyopathy (HCM) from the perspective of the private health system in Brazil. Methods: A modified Delphi panel including seven different specialists (three clinical cardiologists with experience in obstructive HCM, two hemodynamicists with experience in septal ablation and two cardiac surgeons with expertise in myectomy), from two Brazilian states (São Paulo and Pernambuco), was conducted between August and November 2022. Two rounds of questions about the use of healthcare resources according to the functional class (NYHA I-IV) and a panel in a virtual platform were conducted to obtain the final consensus. Micro-costing defined costs and unit values were determined based on official price lists. Results: The total diagnosis cost per patient was estimated at BRL 11,486.81. The obstructive HCM management costs analysis showed average annual costs per patient of BRL 17,026.74, BRL 19,401.46, BRL 73,310.07, and BRL 94,885.75 for the functional classes NYHA I, NYHA II, NYHA III, and NYHA IV, respectively. The average costs per patient related to procedures in a year were BRL 12,698.53, BRL 13,462.30, BRL 58,841.67, and BRL 75,595.90 for the functional classes NYHA I, II, III, and IV, respectively. Conclusions: The annual costs of HCM management increased according to the functional class, highlighting the need for safe and effective strategies to improve patient's NYHA functional class while promoting a decrease in the need for invasive therapies.

Received on: 08/03/2024. Approved for publication on: 01/04/2024.

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Conflict of interests: This study was funded by Bristol Myers Squibb, Brazil.

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Palavras-chave:

cardiomiopatia hipertrófica, saúde suplementar, custos e análise de custo, técnica Delfos

RESUMO

Objetivo: Gerar dados acerca dos custos associados ao diagnóstico e tratamento da cardiomiopatia hipertrófica (CMH) obstrutiva, sob a perspectiva do sistema de saúde privado no Brasil. Métodos: Um painel Delphi modificado incluindo sete especialistas (três cardiologistas clínicos com experiência em CMH obstrutiva, dois hemodinamicistas com experiência em ablação de septo e dois cirurgiões cardíacos com experiência em miectomia) de dois estados brasileiros (São Paulo e Pernambuco) foi conduzido entre agosto e novembro de 2022. Foram realizadas duas rodadas de perguntas acerca da utilização de recursos de acordo com a classe funcional (NYHA I-IV) e uma reunião virtual para obtenção do consenso final. Os custos foram definidos por meio de microcusteio, e os valores unitários foram definidos com base em listas de preço oficiais. Resultados: O custo total do diagnóstico por paciente foi estimado em R\$ 11.486,81. A análise de custos de manejo da CMH obstrutiva mostrou custos médios anuais por paciente de R\$ 17.026,74, R\$ 19.401,46, R\$ 73.310,07 e R\$ 94.885,75 para as classes funcionais NYHA I, NYHA II, NYHA III e NYHA IV, respectivamente. Os custos médios por paciente relacionados a procedimentos em um ano foram de R\$ 12.698,53, R\$ 13.462,30, R\$ 58.841,67 e R\$ 75.595,90 para as classes NYHA I, II, III e IV, respectivamente. Conclusões: Os custos anuais com o manejo da CMH aumentam de acordo com a classe funcional, destacando a necessidade de estratégias seguras e eficazes capazes de melhorar a classe funcional NYHA do paciente, ao mesmo tempo que promove diminuição da necessidade de terapias invasivas.

Introduction

Cardiomyopathies represent a heterogeneous group of diseases that affect the myocardium. They can be classified as primary, involving only the heart, or secondary, resulting from a systemic disorder (Tanenbaum, 2003; Zamorano *et al.*, 2014). Among the primary conditions, hypertrophic cardiomyopathy (HCM) is characterized by increased left ventricular wall thickness not derived from abnormal load conditions (Zamorano *et al.*, 2014).

Clinically, HCM is defined by ≥15 mm thickness in the ventricular walls at the diastole end without any other cause. The thickness can be lower in patients with a family history of HCM. Typically, this diagnosis is based on echocardiography, cardiac magnetic resonance imaging, or both (Ommen et al., 2020). Hypertrophic cardiomyopathy can be subdivided into obstructive and non-obstructive according to the hemodynamic classification (Albanesi, 1996). Obstructive HCM is characterized by left ventricular hypercontractility, hypertrophy, reduced compliance, and left ventricular outflow tract (LVOT) obstruction, resulting in symptoms such as exertional dyspnea, fatigue, chest pain, and limited exercise capacity (Heitner et al., 2019) and is associated with an increased risk of long-term cardiac complications such as heart failure, atrial fibrillation and stroke (Maron et al., 2003; Rowin et al., 2017; MacIntyre & Lakdawala, 2016; Maron et al., 2002).

The estimated adult prevalence of obstructive HCM is 16 per 100,000 inhabitants (Butzner *et al.*, 2022a). For 2023, estimated prevalence is 160,384,382 adults in Brazil, according to the Brazilian Institute of Geography and Statistics (*Instituto Brasileiro de Geografia e Estatística* – IBGE) estimates (IBGE, 2022). Therefore, it is anticipated that 25,661 Brazilians would be diagnosed with or live with obstructive HCM in 2023.

The New York Heart Association (NYHA) functional classification is one of the most useful tools for assessing the symptoms' severity and functional limitations as a classification instrument with widely established validity. Such classification is used in several heart failure studies as an inclusion criterion for patient selection. In addition, it helps to develop clinical conduct in numerous national and international guidelines (Yap *et al.*, 2015).

The NYHA classification evaluates the symptomatic effect of heart disease and cardiomyopathies, making it possible to stratify the degree of limitation on daily activities. It reflects symptom severity in patients with structural heart disease (Bennett *et al.*, 2002).

Although many patients are asymptomatic or have mild symptoms, the condition is associated with systolic heart failure progression, sudden death, and atrial fibrillation (Bazan *et al.*, 2020; Veselka *et al.*, 2017). In this way, the disease is associated with an important impact on individuals diagnosed with obstructive HCM and society. In a case-control study, Jain *et al.* (2021) reported that obstructive HCM patients have a higher hospitalization frequency due to any cause, longer length of stay, and greater need for outpatient visits than controls with other clinical conditions (Jain *et al.*, 2021).

HCM management may involve different strategies such as beta-blockers, calcium channel blockers and disopyramide, whose definition is related to severity. For patients who do not tolerate or remain symptomatic despite optimized pharmacological therapy, interventional therapy is indicated: septal reduction therapy (septal alcoholization or myectomy) (Ommen *et al.*, 2020; Authors/Task Force members *et al.*, 2014). European guidelines were updated in August 2023 and advocated a new approach to treating HCM, including cardiac myosin ATPase inhibitors (a therapy that target the disease's fundamental pathophysiologic mechanism) (Arbelo *et al.*, 2023).

Some studies have been conducted in countries like the United States, the United Kingdom and Sweden to analyze the resource utilization and costs linked to obstructive HCM management. These studies have highlighted the significant economic impact of the disease (Jain *et al.*, 2021; Hurst *et al.*, 2022; Owens *et al.*, 2022; Butzner *et al.*, 2022c; Yandrapalli *et al.*, 2022; Javidgonbadi *et al.*, 2021). Unfortunately, there is a lack of Brazilian data regarding this matter. Therefore, this study aimed to generate data about costs related to obstructive HCM diagnosis and treatment from the perspective of the private health system in Brazil, through a modified Delphi Panel and micro-costing analyses.

Methods

Modified Delphi methodology

The modified Delphi methodology was selected to establish a consensus among specialists in Brazil on the resource utilization related to adult obstructive HCM management in the Supplementary Health System context. Although the Delphi methodology is a validated method for eliciting consensus from a group of experts, the modification within this context is related to capturing quantitative estimates and the relative variation in these estimates within the group. This approach uses various surveys to verify consensus on statements related to a domain (Dalkey & Helmer, 1963; Hsu & Sandford, 2007; Diamond *et al.*, 2014; Hasson *et al.*, 2000; Powell, 2003).

The project was conducted between August and November 2022, consisting of the steps outlined in Figure 1. An outside expert validated the questionnaire before sending it to respondents.

Selection of experts

Physicians currently treating obstructive HCM patients and working in Brazilian reference institutions were identified for the group selection. Various medical specialties were considered to address the different stages and clinical scenarios of managing obstructive HCM. Clinical cardiologists with obstructive HCM management experience, experts on hemodynamics with septal ablation experience, and cardiac surgeons with myectomy experience made up the inclusion criteria. Fourteen physicians were identified and invited to participate in the study. Seven physicians were available and agreed to participate.

Individual questionnaire – Round 1

The first questionnaire was developed after a literature review conducted with the aim to understand the resource utilization pattern. We searched the literature on patient

diagnosis and management for obstructive HCM in the Medline database through PubMed, Lilacs, and Cochrane. We also performed an open search for national publications to identify guidelines and local recommendations. Articles published until July 2022 that met the inclusion criteria for the study were considered. The resource utilization pattern was defined based on the information in the literature review. It used laboratory and imaging tests and hospital resources, including visits, emergency care, hospitalizations (clinical, surgical, and intensive care unit), medications, and procedures. In addition, the percentage of each resource's use and frequency of service were also collected. The questionnaire was segmented according to the patient's functional class (NYHA functional classes I, II, III, and IV), procedures (septal reduction therapy by alcoholization and myectomy), and resources for disease diagnosis.

The NYHA strategy was considered to determine the patients' functional class, allocating individuals into four categories based on physical limitations during physical activity: NYHA I (no limits to performing the physical activity; daily physical activity does not cause fatigue, palpitations, and dyspnea); NYHA II (minor limitations to performing the physical activity; comfortable at rest; daily physical activity causes fatigue, palpitations and dyspnea); NYHA II (marked limitations to performing the physical activity; comfortable at rest; slight daily physical activities cause fatigue, palpitations, and dyspnea); NYHA IV (unable to perform any physical activity without discomfort; symptoms of heart failure at rest; if any physical activity is performed, discomfort is increased) (American Heart Association, 2021).

The instrument was sent to respondents and returned within two weeks. The answers were synthesized and analyzed to allow the elaboration of the second questionnaire.

Individual questionnaire – Round 2

A second questionnaire was developed using the analysis and responses from the first instrument. The answers obtained in the first round were aggregated, using quantitative and qualitative strategies, and resource utilization patterns were defined. Specialists were asked to indicate their agreement or disagreement with the statements provided in the questionnaire. The questionnaires were emailed, and the specialists were given two weeks to respond.



Figure 1. Study stages.

J Bras Econ Saúde 2023;15(X):190-9

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Panel discussion

To reach a final consensus, a virtual panel discussion with the group of experts was scheduled. The answers obtained in the second round were aggregated, using quantitative and qualitative strategies, and used to support the panel discussion. A four-hour meeting was used to define the consensus to be considered in the final analysis.

External validation

Both questionnaires were validated by an independent and external expert in HCM in Brazil. The expert evaluated whether the survey contained questions that covered all aspects of the diagnosis and treatment of obstructive HCM patients, specifically whether the duration and language were appropriate to increase the quality of the instrument.

Micro-costing

Micro-costing was done using a bottom-up approach to determine obstructive HCM diagnosis, treatment, and management costs. This methodology values cost components from the bottom up through fees, taxes, complementary exams, medications, or supplies unit prices per patient (Brasil, 2019). Only direct costs were considered from the perspective of the Brazilian Supplementary Health System as a paying source.

Unit costs were defined based on official price lists. Fees, complementary exams, and procedures derived from the Hierarchical Brazilian Classification of Medical Procedures (Classificação Brasileira Hierarquizada de Procedimentos Médicos - CBHPM) published in 2018 with 2021 values (AMB, 2018). Drug costs were obtained from the official list of the Chamber of Regulation of the Market of Medicines (Câmara de Regulação do Mercado de Medicamentos - CMED), using the factory price with an 18% increase of the Tax Movement of Goods and Services (Imposto sobre Circulação de Mercadorias e Serviços – ICMS) (Brasil, 2020) consulted in December 2022. For some hospital packages, the reference values publication of the Health Assistance System for State Public Servants of Bahia (Sistema de Assistência à Saúde dos Servidores Públicos Estaduais da Bahia – Planserv) was used as a source (Governo do Estado da Bahia, 2022).

Costs were divided into resources related to diagnosis and treatment. The analysis was performed according to the different functional classes (NYHA I-IV). For each functional class, follow-up (visits and rehabilitation), laboratory tests, cardiological exams, medications, procedures, emergency care, and hospitalization were considered. We evaluated the percentage of patients who used each cost item and the average amount used during the study period. The final result was the average cost per patient/year, expressed in Brazilian Real (BRL) for 2022.

Statistical analysis

Quantitative data was analyzed using descriptive statistics (frequency, mean, maximum, and minimum) and calculated

do sistema de saúde suplementar brasileiro: resultados de um painel Delphi modificado for each study round within Microsoft[®] Excel. Due to the sample size, additional statistical analyses were not performed.

The results obtained after the second questionnaire round were graphically represented to support efficient communication and discussion in the subsequent stage. In the last round, qualitative comments provided were discussed in groups.

All reported results were pooled and anonymized.

Results

Experts and reaching a consensus

A group of experts was assembled to cover the various stages of obstructive HCM management. This group included three clinical cardiologists with experience in obstructive HCM, two hemodynamicists with experience in septum ablation, and two cardiac surgeons with experience in myectomy. All specialists were involved in every phase of the study. After two rounds of questionnaires, discussions were held to address discrepancies, and a consensus was reached during a four-hour virtual expert panel.

Frequency and percentage of resource usage

After two rounds of questionnaires and a virtual meeting, the experts defined a resource utilization pattern. The supplementary material shows data on the proportion of patients and the amount of resources used per individual, categorized by NYHA functional class, within a one-year timeframe defined in a consensus by the experts. This data is presented from the perspective of the Supplementary Health System in Brazil and supports calculating disease costs.

Costs of disease diagnosis

The obstructive HCM diagnosis costs were considered on a one-off basis, only when obstructive HCM is diagnosed, and not considered a recurring cost. For cost driver analysis, three categories were created: visits, complementary exams (which include electrocardiogram, Holter, transthoracic echocardiogram, physical stress echocardiogram and cardiac MRI), genetic testing, and family counseling.

As shown in Figure 2, the total diagnosis cost per patient was estimated at BRL 11,486.81. The main cost driver was the group represented by genetic tests and family counseling, which corresponded to 52.17% of the total.

Disease management costs overview

The obstructive HCM management costs analysis showed average annual costs per patient of BRL 17,026.74, BRL 19,401.46, BRL 73,310.07, and BRL 94,885.75 for functional classes NYHA I, NYHA II, NYHA III, and NYHA IV, respectively. For analytical purposes, costs were divided into seven categories: clinical follow-up, laboratory tests, cardiological exams, medicines, procedures, emergency care, and hospitalizations. Costs segmented by NYHA category and functional class are shown in Table 1 and Figure 3. Oliveira APCD, Caluz N, Ribeiro-Pereira ACP, Fernandes RA, Fernandes F, Simões MV, Correia EB, Dias RR, Ribeiro HB, Medeiros Filho HM, Barros e Silva PG, Ribeiro GCA, Decimoni T

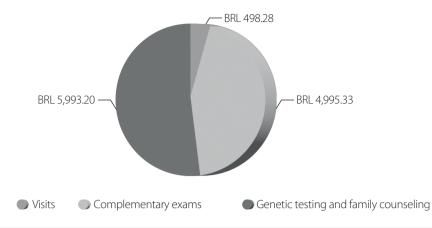




Table 1.Average costs of obstructive HCM disease management per patient by NYHA functional class in one year, from the perspective
of the Supplementary Health System in Brazil

	NYHA I (BRL)	NYHA II (BRL)	NYHA III (BRL)	NYHA IV (BRL)	
Clinical follow-up	521.44	521.44	1,673.82	996.56	
Laboratory tests	517.58	517.58	577.54	637.50	
Cardiac tests	2,142.44	3,753.38	7,757.80	6,122.98	
Drugs	1,146.76	1,146.76	1,311.67	1,311.67	
Procedures	12,698.53	13,462.30	58,841.67	75,595.90	
Emergency care	0.00	0.00	1,119.71	1,919.50	
Hospitalizations	0.00	0.00	2,027.86	8,301.65	



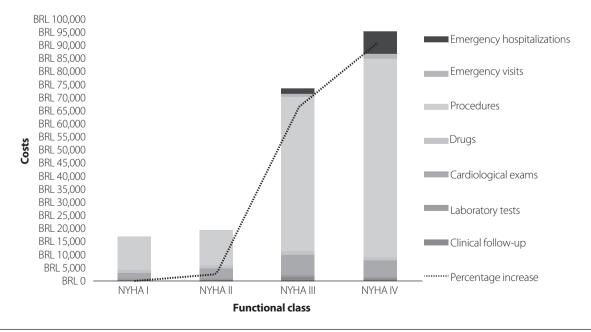


Figure 3. Distribution of average annual costs of obstructive HCM management per patient by NYHA functional class and cost category from the perspective of the Supplementary Health System in Brazil.

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Data analysis showed that the total cost of managing obstructive HCM increases with disease progression. When considering the total burden of disease management costs, the uplift comparing patients with a NYHA class I classification with those with a NYHA IV classification is greater than 450%. The largest uplift in total disease management burden was between NYHA class II and III, with an increase of approximately 280%.

Procedures (*e.g.*, implantable cardioverter-defibrillator for NYHA I and alcohol septal ablation and septal myectomy for the other groups, as discussed further in a latter section) represented the main cost driver for all functional classes: 74.58% of values for NYHA I, 69.39% for NYHA II, 80.26% for NYHA III, and 79.67% for NYHA IV. It is important to highlight that despite procedures being included in total costs, those are not recurrent resources, and patients may use them only once.

Procedure cost analysis

A detailed category analysis was performed since the procedures are the greatest cost drivers in obstructive HCM patient management in all functional classes. The procedures' do sistema de saúde suplementar brasileiro: resultados de um painel Delphi modificado average costs per patient in a year were BRL 12,698.53, BRL 13,462.30, BRL 58,841.67, and 75,595.90 for NYHA functional classes I, II, III, and IV, respectively. Between NYHA class I and IV, this equated to a ~500% uplift, with the biggest class change again observed between NYHA class II and III (+340%). Despite results being shown in an annual time horizon, procedures are not used as recurrent resources, and patients may only use them once.

Procedures within scope included alcohol septal ablation, myectomy, Mitraclip® implantation, mitral valve replacement, implantable cardioverter-defibrillator placement, and electrical cardioversion. The cost distribution is shown in Table 2 and Figure 4.

For patients in NYHA functional classes I and II, implantable cardioverter-defibrillator placement represented the main source of procedural costs (90.56%). For those in NYHA functional classes III and IV, myectomy was the main cost driver (46.48% and 45.23%, respectively), followed by alcohol ablation (22.71% and 22.73%, respectively).



	NYHA I (BRL)	NYHA II (BRL)	NYHA III (BRL)	NYHA IV (BRL)
Alcohol septal ablation	0.00	763.77	13,366.06	17,184.93
Septal myectomy	0.00	0.00	27,352.54	34,190.67
Mitraclip®	0.00	0.00	2,047.66	1,023.83
Mitral valve replacement	0.00	0.00	426.21	213.11
Implantable cardioverter-defibrillator	11,499.64	11,499.64	13,142.45	19,713.67
Electrical cardioversion	1,198.88	1,198.88	2,506.76	3,269.69
Total	12,698.53	13,462.30	58,841.67	75,595.90

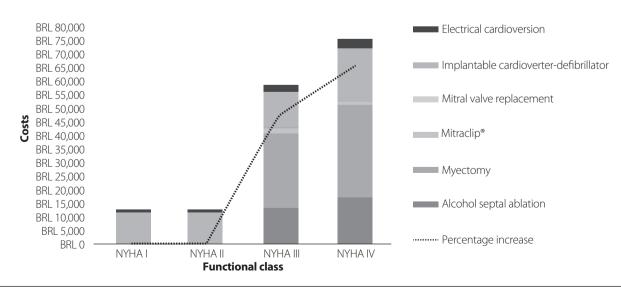


Figure 4 Distribution of average procedures costs in a year per obstructive HCM patient, segmented by NYHA functional class, from the perspective of the Supplementary Health System in Brazil.

Discussion

This study aimed to gather information on the expenses involved in diagnosing and treating obstructive HCM within the private healthcare system in Brazil. There is a lack of national data regarding the resource utilization and costs associated with this disease. Conducting this research can enhance comprehension and planning for managing such patients with obstructive HCM.

The modified Delphi Panel and the micro-costing technique were used for this purpose. The Delphi method is used to obtain a consensus among specialists on a given topic and to define questions related to the diagnosis of HCM (Dalkey & Helmer, 1963; Hsu & Sandford, 2007; Diamond et al., 2014; Hasson et al., 2000; Powell, 2003; Mammen et al., 2014; Smid et al., 2014). The modified technique still allows for consensus. However, this may not be achieved due to the limitation of two rounds of review rather than unlimited in the original method (Broder et al., 2022). In our analysis, experts defined a consensus during a virtual meeting, reducing the bias inherent to the method. Regarding estimating resource utilization and costs, the Delphi method has been used in other cardiology publications to determine a consensus after elaborating on micro-costing (Giorgi et al., 2015; Aras et al., 2016; Çavuşoğlu et al., 2022).

The disease management average annual cost per patient was estimated according to functional class and ranged from BRL 17,026.74 to BRL 94,885.75 in NYHA I and NYHA IV individuals, respectively. Jain *et al.* (2021) described an average annual cost of USD 10,467.00 per asymptomatic patient and USD 43,586.00 per symptomatic patient (Jain *et al.*, 2021). Similarly, Hurst *et al.* (2022) reported that a positive association between increasing NYHA class and economic burden was observed among patients from the UK (Hurst *et al.*, 2022). The burden of the disease is even greater as indirect costs were not included in our analysis.

It should also be underlined that despite an increase in the cost of managing obstructive HCM due to worsening in NYHA class, a decrease in costs attributable to clinical follow-up from NYHA III to NYHA IV was also verified. Such differences might be explained by the absence of costs related to cardiac rehabilitation. Physical rehabilitation has been proven to improve functional capacity among patients with HCM; however, available studies do not include individuals in NYHA IV, reinforcing the expert opinion provided in this analysis (Wasserstrum *et al.*, 2019; Klempfner *et al.*, 2015).

The main cost drivers analysis by Jain *et al.* (2021) highlights hospitalization, while procedures represent most of the estimated value in the present study (Jain *et al.*, 2021). Similarly, Owens *et al.* (2022) reported that patients undergoing procedures demand greater resource utilization and costs (Owens *et al.*, 2022). In our analysis, costs related to emergency visits and hospitalization increase among NYHA III and IV patients, especially hospitalizations in the later group. This finding is corroborated by previous analysis and is expected once worsening in the NYHA class is associated with a higher risk of several outcomes, including hospitalization (Hurst *et al.*, 2022; Wang *et al.*, 2023).

Considering the context that the procedures represented the major driver of costs, a detailed analysis of this category was carried out. Initially, the costs of the procedures were stratified between the different functional classes, and an increasing gradient was observed according to the worsening of the disease severity. This finding is consistent with the disease characteristics, but the authors are unaware of other studies that corroborate or refute this finding.

It is important to note that procedure costs are impacted by the fact that invasive SRT may expose patients to the inherent risks of cardiac surgery or coronary instrumentation and is associated with peri-procedural and potentially severe post-surgery complications. There may be a possibility of pacemaker implantation and re-intervention and, following surgery, there may also be an increased risk of developing left ventricular systolic dysfunction (Ho *et al.*, 2018; Marstrand *et al.*, 2020).

In functional classes III and IV individuals diagnosed with obstructive HCM, myectomy was the main cost driver for procedures. These findings are consistent with previous analyses that reported a significantly higher cost with myectomy procedures when compared to alcohol septal ablation (Yandrapalli *et al.*, 2022; Butzner *et al.*, 2022b).

Despite the relevant findings, this analysis' results reflect the context experienced by the participants in their clinical practice; there is also the possibility of a false consensus since the specialists can sometimes only follow the opinion of one of the members. Additionally, the methodology used is susceptible to recall biases since specialists may find it easier to remember more severe cases than patients with fewer complications. Costs were calculated on an annual basis. However, procedures are not recurrent and are taken into account only once. Thus, a significant difference may be observed between the first and subsequent years. In addition, another aspect that can impact obstructive HCM costs is the procedures' success rate and the occurrence of complications, not assessed in the present analysis due to variabilities observed across the country (access to procedures, quality of care). Finally, the NYHA class was the method chosen to classify disease severity, and despite its being widely used, it has various limitations in terms of its accuracy in precisely determining heart failure symptoms.

Conducting a study with primary data collection would be able to provide more robust data on resource utilization by patients diagnosed with obstructive HCM in Brazil. However, due to its continental characteristics, including different centers across the country would be necessary. Finally, another

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limitation of the analysis is related to the values considered for the cost calculation since these may vary according to the supplementary health establishment.

Conclusions

Conducting this modified Delphi panel made it possible to understand the resource utilization pattern and to estimate the obstructive HCM management costs in the Supplementary Health System in Brazil. According to the guidelines in force when this study was performed, annual costs with disease management increase according to functional class and can reach around BRL 95,000 per patient. Thus, these findings point to the need for safe and effective strategies to improve the patient's NYHA functional class while promoting a decreased need for invasive therapies.

References

- Albanesi FM. Cardiomiopatia hipertrófica: conceito e classificação. Arq Bras Cardiol. 1996;66(2):103-5.
- American Heart Association. Classes of heart failure [Internet]. 2021 [cited 2023 Feb 14]. Available from: https://www.heart.org/en/health-topics/heart-failure/what-is-heart-failure/classes-of-heart-failure
- Aras D, Aydoğdu S, Bozkurt E, Çavuşoğlu Y, Eren M, Erol Ç, et al. Cost of heart failure management in Turkey: results of a Delphi Panel. Anatol J Cardiol. 2016;16(8):554-62.
- Associação Médica Brasileira (AMB). CBHPM-2018: Classificação Brasileira Hierarquizada de Procedimentos Médicos. São Paulo: AMB; 2018.
- Arbelo E, Protonotarios A, Gimeno JR, Arbustini E, Barriales-Villa R, Basso C, et al. 2023 ESC Guidelines for the management of cardiomyopathies. Eur Heart J. 2023;44(37):3503-626.
- Authors/Task Force members; Elliott PM, Anastasakis A, Borger MA, Borggrefe M, Cecchi F, Charron P, et al. 2014 ESC Guidelines on diagnosis and management of hypertrophic cardiomyopathy. Eur Heart J. 2014;35(39):2733-79.
- Bazan SGZ, Oliveira GO de, Silveira CF da SMP da, Reis FM, Malagutte KNDS, Tinasi LSN, et al. Cardiomiopatia Hipertrófica – Revisão. Arq Bras Cardiol. 2020;115(5):927-35.
- Bennett JA, Riegel B, Bittner V, Nichols J. Validity and reliability of the NYHA classes for measuring research outcomes in patients with cardiac disease. Heart Lung. 2002;31(4):262-70.
- Brasil. Ministério da Saúde. Câmara de Regulação do Mercado de Medicamentos (CMED). Câmara de Regulação do Mercado de Medicamentos (CMED). 2020.
- Brasil. Ministério da Saúde. Diretriz metodológica: estudos de microcusteio aplicados a avaliações econômicas em saúde. Brasília: Ministério da Saúde; 2019.
- Broder MS, Gibbs SN, Yermilov I. An Adaptation of the RAND/UCLA Modified Delphi Panel Method in the Time of COVID-19. J Healthc Leadersh. 2022;14:63-70.
- Butzner M, Leslie DL, Cuffee Y, Hollenbeak CS, Sciamanna C, Abraham T. Stable Rates of Obstructive Hypertrophic Cardiomyopathy in a Contemporary Era. Front Cardiovasc Med. 2022a;8:1-5.
- Butzner M, Maron MS, Sarocco P, Teng CC, Stanek E, Tan H, et al. Costs and Healthcare Resource Utilization for Obstructive Hypertrophic Cardiomyopathy with Septal Reduction Therapy. J Invasive Cardiol. 2022b;34(12):E866-72.

- Butzner M, Rowin E, Yakubu A, Seale J, Robertson LA, Sarocco P, et al. Clinical Characteristics and Healthcare Resource Utilization among Patients with Obstructive Hypertrophic Cardiomyopathy Treated in a Range of Settings in the United States. J Clin Med. 2022c;11(13):1-12.
- Çavuşoğlu Y, Altay H, Aras D, Çelik A, Ertaş FS, Kılıçaslan B, et al. Cost-of-disease of Heart Failure in Turkey: A Delphi Panel-based Analysis of Direct and Indirect Costs. Balkan Med J. 2022;39(4):282-9.
- Dalkey N, Helmer O. An experimental apllication of Deplhi method to use of experts. Manag Sci. 1963;9(3);458-67.
- Diamond IR, Grant RC, Feldman BM, Pencharz PB, Ling SC, Moore AM, et al. Defining consensus: A systematic review recommends methodologic criteria for reporting of Delphi studies. J Clin Epidemiol. 2014;67(4):401-9.
- Giorgi MA, Caroli C, Giglio ND, Micone P, Aiello E, Vulcano C, et al. Estimation of the cost-effectiveness of apixaban versus vitamin K antagonists in the management of atrial fibrillation in Argentina. Health Econ Rev. 2015;5(1):17.
- Governo do Estado da Bahia. Sistema de Assistência à Saúde dos Servidores Públicos Estaduais (Planserv). Valores Referenciais. 2022.
- Hasson F, Keeney S, McKenna H. Research guidelines for the Delphi survey technique. J Adv Nurs. 2000;32(4):1008-15.
- Hsu CC, Sandford BA. The Delphi technique: Making sense of consensus. Pract Assessment Res Eval. 2007;12(10):1-8.
- Heitner SB, Jacoby D, Lester SJ, Owens A, Wang A, Zhang D, et al. Mavacamten treatment for obstructive hypertrophic cardiomyopathy a clinical trial. Ann Intern Med. 2019;170(11):741-8.
- Ho CY, Day SM, Ashley EA, Michels M, Pereira AC, Jacoby D, et al. Genotype and Lifetime Burden of Disease in Hypertrophic Cardiomyopathy. Circulation. 2018;138(14):1387-98.
- Hurst M, Zema C, Krause T, Sandler B, Lemmer T, Christodoulou J, et al. EE487 Quantifying the Economic Burden of Obstructive Hypertrophic Cardiomyopathy (HCM) in the UK. Value Health. 2022;25(12):S151.
- Instituto Brasileiro de Geografia e Estatítica (IBGE). Diretoria de Pesquisas. Coordenação de População e Indicadores Sociais. Estimativas da População [Internet]. 2022 [cited 2023 Mar 2]. Available from: https:// www.ibge.gov.br/estatisticas/sociais/populacao/9103-estimativas-de--populacao.html
- Jain SS, Li SS, Xie J, Sutton MB, Fine JT, Edelberg JM, et al. Clinical and economic burden of obstructive hypertrophic cardiomyopathy in the United States. J Med Econ [Internet]. 2021;24(1):1115-23. Available from: https:// doi.org/10.1080/13696998.2021.1978242
- Javidgonbadi D, Andersson B, Abdon NJ, Östman-Smith I. Morbidity and resource usage after myectomy- or pacing-treatment in hypertrophic obstructive cardiomyopathy: A case-control study. Int J Cardiol. 2021;322:197-203.
- Klempfner R, Kamerman T, Schwammenthal E, Nahshon A, Hay I, Goldenberg I, et al. Efficacy of exercise training in symptomatic patients with hypertrophic cardiomyopathy: Results of a structured exercise training program in a cardiac rehabilitation center. Eur J Prev Cardiol. 2015;22(1):13-9.
- MacIntyre C, Lakdawala NK. Management of Atrial Fibrillation in Hypertrophic Cardiomyopathy. Circulation. 2016;133(19):1901-5.
- Mammen L, Woodard PK, Abbara S, Dorbala S, Javidan-Nejad C, Julsrud PR, et al. ACR Appropriateness Criteria® Nonischemic Myocardial Disease with Clinical Manifestations (Ischemic Cardiomyopathy Already Excluded). J Thorac Imaging. 2014;29(4):W44-7.
- Maron BJ, Olivotto I, Bellone P, Conte MR, Cecchi F, Flygenring BP, et al. Clinical profile of stroke in 900 patients with hypertrophic cardiomyopathy. J Am Coll Cardiol. 2002;39(2):301-7.
- Maron MS, Olivotto I, Betocchi S, Casey SA, Lesser JR, Losi MA, et al. Effect of Left Ventricular Outflow Tract Obstruction on Clinical Outcome in Hypertrophic Cardiomyopathy. N Engl J Med. 2003;348(4):295-303.

Oliveira APCD, Caluz N, Ribeiro-Pereira ACP, Fernandes RA, Fernandes F, Simões MV, Correia EB, Dias RR, Ribeiro HB, Medeiros Filho HM, Barros e Silva PG, Ribeiro GCA, Decimoni T

Marstrand P, Han L, Day SM, Olivotto I, Ashley EA, Michels M, et al. Hypertrophic Cardiomyopathy with Left Ventricular Systolic Dysfunction. Circulation. 2020;141(17):1371-83.

Ommen SR, Mital S, Burke MA, Day SM, Deswal A, Elliott P, et al. 2020 AHA/ ACC Guideline for the Diagnosis and Treatment of Patients with Hypertrophic Cardiomyopathy. J Am Coll Cardiol. 2020;76(25):e159-240.

- Owens AT, Sutton MB, Gao W, Fine JT, Xie J, Naidu SS, et al. Treatment Changes, Healthcare Resource Utilization, and Costs Among Patients with Symptomatic Obstructive Hypertrophic Cardiomyopathy: A Claims Database Study. Cardiol Ther [Internet]. 2022;11(2):249-67. Available from: https://doi.org/10.1007/s40119-022-00257-7
- Powell C. The Delphi technique: myths and realities. J Adv Nurs. 2003;41(4):376-82.
- Rowin EJ, Maron MS, Chan RH, Hausvater A, Wang W, Rastegar H, et al. Interaction of Adverse Disease Related Pathways in Hypertrophic Cardiomyopathy. Am J Cardiol. 2017;120(12):2256-64.
- Smid BE, van der Tol L, Cecchi F, Elliott PM, Hughes DA, Linthorst GE, et al. Uncertain diagnosis of Fabry disease: Consensus recommendation on diagnosis in adults with left ventricular hypertrophy and genetic variants of unknown significance. Int J Cardiol. 2014;177(2):400-8.
- Tanenbaum HL. Hypertrophic cardiomyopathy. Trauma [Internet]. 2003;45(1):61-78. Available from: http://dx.doi.org/10.1016/j.medcle.2017.09.029

- Zamorano JL, Anastasakis A, Borger MA, Borggrefe M, Cecchi F, Charron P, et al. 2014 ESC guidelines on diagnosis and management of hypertrophic cardiomyopathy: The task force for the diagnosis and management of hypertrophic cardiomyopathy of the European Society of Cardiology (ESC). Eur Heart J. 2014;35(39):2733-79.
- Veselka J, Anavekar NS, Charron P. Hypertrophic obstructive cardiomyopathy. Lancet [Internet]. 2017;389(10075):1253-67. Available from: http://dx.doi. org/10.1016/S0140-6736(16)31321-6
- Wang Y, Gao W, Han X, Jiang J, Sandler B, Li X, et al. Cardiovascular outcomes by time-varying New York Heart Association class among patients with obstructive hypertrophic cardiomyopathy: A retrospective cohort study. J Med Econ. 2023;26(1):1495-506.
- Wasserstrum Y, Barbarova I, Lotan D, Kuperstein R, Shechter M, Freimark D, et al. Efficacy and safety of exercise rehabilitation in patients with hypertrophic cardiomyopathy. J Cardiol. 2019;74(5):466-72.
- Yandrapalli S, Harikrishnan P, Andries G, Aronow WS, Panza JA, Naidu SS. Differences in Short-Term Outcomes and Hospital-Based Resource Utilization Between Septal Reduction Strategies for Hypertrophic Obstructive Cardiomyopathy. J Invasive Cardiol. 2022;34(1):E8-13.
- Yap J, Lim FY, Gao F, Teo LL, Lam CSP, Yeo KK. Correlation of the New York Heart Association Classification and the 6-Minute Walk Distance: A Systematic Review. Clin Cardiol. 2015;38(10):621-8.

Utilização de recursos e custos relacionados ao manejo da cardiomiopatia hipertrófica obstrutiva sob a perspectiva do sistema de saúde suplementar brasileiro: resultados de um painel Delphi modificado

SUPPLEMENTARY MATERIAL

Supplementary Table 1. Proportion of patients and amount of resources used per individual, segmented by NYHA functional class, in 1 year, from the perspective of the Supplementary Health System in Brazil

	NYHA I		NYHA II		NYHA III		NYHA IV	
	%	Amount	%	Amount	%	Amount	%	Amount
Annual recurring costs								
Clinical follow-up	·							
Medical consultation with a cardiologist	100	2	100	2	100	3	100	4
Cardiac rehabilitation	1	20	1	20	40	20	-	-
Laboratory tests								
CBC	100	2	100	2	100	3	100	4
Sodium	100	2	100	2	100	3	100	4
Potassium	100	2	100	2	100	3	100	4
Urea	100	2	100	2	100	3	100	4
Creatinine	100	2	100	2	100	3	100	4
BNP/PROBNP natriuretic peptide, dosage	100	2	100	2	100	2	100	2
Creatinine	100	2	100	2	100	3	100	4
Cardiological exams								
Holter	100	1	100	1	100	1	100	1
Exercise test	100	1	100	1	100	1	-	-
Ergospirometric/cardiopulmonary test	-	-	100	1	100	1	-	-
Transthoracic echocardiogram	100	1	100	1	100	2	100	2
Physical stress echocardiogram	30	1	30	1	43	2	-	-
Transesophageal echocardiogram	0	1	5	1	17	1	26	1
Cardiac catheterization	0	1	5	1	38	1	48	1
Cardiac computed tomography angiography	5	1	5	1	20	1	30	1
Drugs								
Metoprolol succinate	90	365	90	365	90	365	90	365
Atenolol	2	365	2	365	2	365	2	365
Propranolol	4	365	4	365	4	365	4	365
Bisoprolol	4	365	4	365	4	365	4	365
Verapamil	2	365	2	365	20	365	20	365
Amiodarone	20	365	20	365	20	365	20	365
Direct anticoagulants (DOACs) – Apixaban	20	365	20	365	20	365	20	365
Disopyramide	0	365	0	365	1	365	1	365
Emergency room visits	-	-	-	-	35	2	60	2
Hospitalizations for recurrence	-	-	-	-	20	1	52	1
Non-recurring costs								
Procedures								
Cardioverter-defibrillator implant	14	1	2	1	16	1	24	1
Electrical cardioversion	11	1	14	1	23	1	30	1
Septal reduction therapy	-	-	11	1	-	-	-	-
Alcohol septal ablation	-	-	-	-	35	1	45	1
Myectomy	-	-	-	-	40	1	50	1
Mitraclip	_	-	-	-	1	1	0,5	1

CBC: complete blood count.