UNIVERSIDADE FEDERAL DO RIO GRANDE DO SUL

FACULDADE DE MEDICINA

PROGRAMA DE PÓS-GRADUAÇÃO EM CIÊNCIAS DA SAÚDE: CARDIOLOGIA E CIÊNCIAS CARDIOVASCULARES

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ESTUDOS DE CUSTOS NO MANEJO CLÍNICO DE PACIENTES COM INSUFICIÊNCIA CARDÍACA AVANÇADA

Porto Alegre

2024

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Tese apresentada ao Programa de Pós-Graduação em Ciências da Saúde: Cardiologia e Ciências Cardiovasculares da Faculdade de Medicina da Universidade Federal do Rio Grande do Sul como requisito parcial para a obtenção do título de Doutora em Cardiologia.

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Co-orientadora: Ana Paula Beck da Silva Etges

Porto Alegre

2024

CIP - Catalogação na Publicação

Goldraich, Livia Adams
ESTUDOS DE CUSTOS NO MANEJO CLÍNICO DE PACIENTES COM INSUFICIÊNCIA CARDÍACA AVANÇADA / Livia Adams Goldraich. -- 2024.
87 f.
Orientador: Nadine Clausell.

Tese (Doutorado) -- Universidade Federal do Rio Grande do Sul, Faculdade de Medicina, Programa de Pós-Graduação em Ciências da Saúde: Cardiologia e Ciências Cardiovasculares, Porto Alegre, BR-RS, 2024.

1. Custos do tratamento clinico da insuficiência cardíaca avançada. I. Clausell, Nadine, orient. II. Título.

Elaborada pelo Sistema de Geração Automática de Ficha Catalográfica da UFRGS com os dados fornecidos pelo(a) autor(a).

AGRADECIMENTOS

A realização desta tese não seria possível sem o apoio de diversas pessoas e instituições, às quais expresso minha mais profunda gratidão.

À Professora Nadine, pelos mais de 20 anos de trabalho em conjunto, sempre buscando trilhar um caminho diferenciado para profissionais e pacientes no âmbito da insuficiência cardíaca. Agradeço também pelo auxílio para direcionar o foco necessário para a conclusão desta tese, superando as dificuldades da etapa profissional na qual eu me encontro.

À Professora Ana Paula Beck Da Silva Etges, pelos incríveis ensinamentos e grande envolvimento com o nosso trabalho e a nossa especialidade, sempre com um entusiasmo genuíno que contagia a todos no grupo de pesquisa. Agradeço pela visão contemporânea que nos oportunizou vivenciar e valorizar a integração de disciplinas para a avaliação das diferentes dimensões e implicações dos custos de tratamentos em saúde, nos incentivando a querer contribuir para as discussões no cenário nacional.

À equipe de pesquisa, com quem tive inúmeros aprendizados e sem a qual o desenvolvimento desta tese e dos artigos originais não seria possível: Carisi Anne Polanczyk, Daniela Meirelles do Nascimento, Dayanna Machado Lemos, Miriam Marcolino Zago, Laura Caroline Tavares Hastenteufel e Lucas Porto Santos. Meu agradecimento pelo grande envolvimento que tiveram com os projetos, pelos ensinamentos multidisciplinares e pelo incentivo para seguir adiante, além do auxílio com o manejo de diferentes plataformas, softwares e formatações.

Aos Professores Andreas Zukerman e Mandeep Mehra, pela perspectiva internacional e pelas contribuições que qualificaram o estudo de microcusteio.

Ao Instituto de Avaliação de Tecnologia em Saúde pelo apoio logístico e pelas oportunidades para a participação em estudos que possam contribuir para a incorporação de tratamentos e tecnologias de maneira equânime e fundamentada.

À coordenação financeira do Hospital de Clínicas de Porto Alegre, pela disponibilização de dados financeiros, que foram fundamentais para a condução do estudo de microcusteio, de maneira extremamente ágil.

À Coordenação de Aperfeiçoamento de Pessoal de Nível Superior – Brasil (CAPES) pelo apoio estrutural através do Programa de Pós-Graduação em Ciências da Saúde: Cardiologia e Ciências Cardiovasculares da Faculdade de Medicina da Universidade Federal do Rio Grande do Sul.

À equipe do Programa de Transplante Cardíaco e Suporte Circulatório Mecânico do Hospital de Clínicas de Porto Alegre, que tem possibilitado ampliarmos o atendimento de pacientes com insuficiência cardíaca avançada com excelência no sul do país e que nos estimula a procurarmos viabilizar exames e tratamentos contemporâneos para qualificarmos ainda mais o nosso trabalho.

Aos pacientes com insuficiência cardíaca avançada que realizam acompanhamento no Programa de Transplante Cardíaco e Suporte Circulatório Mecânico do Hospital de Clínicas de Porto Alegre, pelas histórias de superação e ensinamentos, que diariamente nos estimulam a querer contribuir para melhorar o acesso e a qualidade dos tratamentos para a doença no nosso meio.

SUMÁRIO

RESUMO

A progressão da insuficiência cardíaca (IC) para fases avançadas, o que pode ocorrer em 5-10% da população com este diagnóstico, é caracterizada por hospitalizações repetidas, utilização de recursos em saúde e indicação de terapias avançadas, que podem aumentar a sobrevida com qualidade de vida em pacientes selecionados. No entanto, apenas uma pequena proporção de pacientes com IC avançada, tanto por características clínicas como por limitada acessibilidade, recebe tratamento com transplante cardíaco ou implante de dispositivos de assistência ventricular esquerda (DAVE), enquanto que a maioria é tratada conservadoramente com manejo clínico. As terapias avançadas para IC possuem custos elevados; no entanto, os custos do tratamento clínico, única alternativa disponível no Sistema Único de Saúde (SUS) brasileiro, são pouco conhecidos. A trajetória da IC avançada, os desfechos e o impacto da utilização de recursos e custos no sistema público de saúde de pacientes tratados com manejo clínico precisam ser melhor estudados para que se possa avaliar os potenciais benefícios da incorporação de tecnologias como os DAVE no país.

Nesta tese, abordamos o tema do custo envolvido no tratamento clínico de pacientes com IC avançada de duas formas: 1) revisão de escopo sobre o tema a fim de mapear o conhecimento e lacunas do conhecimento quanto ao custo envolvido no cuidado destes pacientes, identificar os maiores componentes envolvidos no custo total mapeado, e, por fim, conhecer o custo total envolvido em diferentes regiões no mundo; 2) estudo avaliando retrospectivamente uma coorte de pacientes referenciados ao Programa de Transplante Cardíaco do Hospital de Clínicas de Porto Alegre que apresentaram contra-indicações ao transplante

cardíaco, mas que teriam sido elegíveis ao tratamento com DAVE com foco na estimativa de custos e utilização de recursos do sistema de saúde.

Na revisão de escopo, selecionamos 16 artigos que apresentaram heterogeneidade metodológica nos registros do custo do tratamento clínico de pacientes com IC avançada, independente da perspectiva da fonte pagadora, se pública ou privada, e do ambiente, se ambulatorial, hospitalar ou instituições de longa permanência. Nestes 16 estudos, a maioria oriunda dos Estados Unidos, mas também envolvendo países da Europa e da Ásia, os custos foram elevados, tendo as hospitalizações como principal componente do custo total. Estes achados são relevantes e reforçam a importância de políticas de custeio em saúde que sustentem o cuidado que estes pacientes necessitam.

No artigo retrospectivo, foram incluídos 20 pacientes (90% masculinos, idade média 50 $\pm$ 15 anos, 65% etiologia isquêmica) com IC avançada e potenciais candidatos a DAVE, que foram seguidos por 15 meses, com sobrevida de 40% no período. Custos diretos do tratamento foram obtidos através da metodologia de microcusteio. O custo médio por paciente foi Int$ 120.457 $\pm$ 78.029, sendo que as hospitalizações foram o principal determinante do custo (72% do custo total), e pacientes mais graves (classificação de INTERMACS $\leq$ 3) custaram cerca de 70% mais que os pacientes em INTERMACS > 3 no momento da indicação do dispositivo.

Com base nos resultados dos dois estudos, é possível concluir que:

1. apesar da heterogeneidade metodológica existente entre os estudos abordando custos da IC avançada, dados apontam para gastos elevados em diferentes países;
2. pacientes com IC avançada candidatos a DAVE de longa duração, mas

sem acesso à terapia, representaram elevado custo para o sistema de saúde brasileiro, mesmo sendo considerado apenas custos diretos.

O conjunto desses achados sugere que os custos envolvidos no tratamento clínico de pacientes com IC avançada não é trivial e merece atenção de políticas de saúde. Futuros estudos de custo-efetividade com a utilização de terapias avançadas para este subgrupo de pacientes podem eventualmente estimular discussões acerca de projetos públicos que busquem ampliar o acesso a estes tratamentos, assim como qualificar e otimizar recursos para o manejo conservador da IC avançada.

Palavras-chave: insuficiência cardíaca avançada, custo, tratamento clínico.

ABSTRACT

The progression of heart failure (HF) to advanced stages, which can occur in 5-10% of the population with this diagnosis, is characterized by repeated hospitalizations, use of health resources and indication of advanced therapies, which can increase survival with quality of life in selected patients. However, only a small proportion of patients with advanced HF, both due to clinical characteristics and limited accessibility, receive treatment with heart transplantation or implantation of left ventricular assist devices (LVAD), while the majority are treated conservatively with medical management. Advanced therapies for HF have high costs; however, the costs of clinical treatment, the only alternative available in the Brazilian Unified Health System (SUS), are poorly known. The trajectory of advanced HF, the outcomes and the impact of the use of resources and costs to the public health system of patients who are medically managed need to be better studied so that potential benefits of incorporating technologies such as LVAD in the country can be assessed.

In this thesis, we approached the topic of costs involved in the clinical treatment of patients with advanced HF in two ways: 1) we conducted a scoping review on the topic in order to map knowledge and assess gaps regarding the cost involved in the care of these patients, determine the largest components involved in the total mapped cost, and, finally, identify the total costs in different regions of the world; 2) we performed a retrospectively study evaluating a cohort of patients referred to the Heart Transplant Program at Hospital de Clínicas de Porto Alegre who presented contraindications to heart transplantation, but who would have been eligible for LVAD treatment, with a focus on estimating costs and use of health

system resources.

In the scoping review, we selected 16 articles and identified methodological heterogeneity in recording the cost of clinical treatment of patients with advanced HF, regardless of the perspective of the paying source, whether public or private, and the clinical settings, whether outpatient, hospital or long-term care facilities. In these 16 studies, most from the United States, but also involving countries in Europe and Asia, costs were high, and hospitalizations were the main component of the total cost. These findings are relevant and reinforce the importance of health financing policies that support the care that these patients need.

In the retrospective article, 20 patients (90% male, mean age 50 ± 15 years, 65% ischemic etiology) with advanced HF and potential candidates for LVAD were included and followed for 15 months, with a survival rate of 40% during the period. Direct treatment costs were obtained through the microcosting methodology. The average cost per patient was Int$ 120,457 ± 78,029, with hospitalizations being the main determinant of the cost (72% of the total cost), and more severe patients (INTERMACS status < 3) costing around 70% more than patients in INTERMACS status > 3 at the time of device indication.

Based on the results of the two studies, it is possible to conclude that:

1) despite the methodological heterogeneity existing among studies addressing the costs of advanced HF, the findings point to high expenses in different countries;
2) patients with advanced HF who were candidates for long-term LVAD, but without access to therapy, represented a high cost for the Brazilian healthcare system, even when only direct costs were considered.

All of these findings suggest that the costs involved in the medical treatment

of patients with advanced HF are not trivial and deserve health policy attention. Future cost-effectiveness studies using advanced therapies for this subgroup of patients may eventually stimulate discussions about public projects that seek to expand access to those treatments, as well as qualify and optimize resources for the conservative management of advanced HF.

Keywords: advanced heart failure, cost, medical management.

INTRODUÇÃO

A insuficiência cardíaca (IC) avançada, um estágio da doença caracterizado pela refratariedade às terapias farmacológicas e não-farmacológicas tradicionais, está associada a morbidade, mortalidade, uso de recursos de saúde e custos de cuidados de saúde significativos para os indivíduos e a sociedade (1) . À medida que as populações envelhecem e que as terapias para doenças cardiovasculares avançam, a prevalência de IC avançada aumenta com incrementos substanciais nos custos e na perda de produtividade (2).

O contingente de pacientes com insuficiência cardíaca avançada pode chegar a 5-10% da população com diagnóstico de insuficiência cardíaca (3). Com a progressão da doença, esta fase é caracterizada por hospitalizações repetidas, utilização de múltiplos recursos de sistemas de saúde e indicação de terapias avançadas - transplante cardíaco e implante de dispositivos de assistência ventricular esquerda (DAVE) - que podem aumentar a sobrevida com qualidade de vida em pacientes selecionados (3,4). Apenas uma pequena proporção de pacientes com IC avançada, tanto por características clínicas como pela limitada acessibilidade, recebe tratamento com terapias avançadas, enquanto que a maioria é tratada conservadoramente com manejo clínico (5). As terapias avançadas possuem custos elevados (5,6); no entanto, os custos do tratamento clínico são pouco conhecidos.

A utilização de recursos de saúde e o custo dos cuidados em pacientes com IC avançada tratados exclusivamente sem a oportunidade de receberem um DAVE ou um transplante cardíaco podem representar um encargo financeiro que não é

facilmente percebido por indivíduos, financiadores e governos e, em circunstâncias selecionadas, a utilização do DAVE pode ser sustentável em um sistema de saúde.

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JUSTIFICATIVA

As terapias avançadas para IC (transplante cardíaco e DAVE) possuem acessibilidade restrita, tanto por limitações inerentes à doação e captação de órgãos como por custos elevados, ou ambos. Portanto, conhecer os custos envolvidos no manejo de pacientes com IC avançada que não recebem nenhum destes tratamentos, os quais representam a grande maioria, é relevante para que se possa auxiliar os gestores a desenhar estratégias de custeio destes pacientes e também fomentar estudos de custo-efetividade na perspectiva de potencial implementação de terapias hoje indisponíveis pelo SUS, como os DAVE para esta população específica.

OBJETIVOS

Objetivo geral

O objetivo do presente estudo foi revisar retrospectivamente a trajetória de pacientes com IC avançada referenciados ao Programa de Transplante Cardíaco do Hospital de Clínicas de Porto Alegre que apresentaram contra-indicações ao transplante cardíaco, mas que teriam sido elegíveis ao tratamento com DAVE, com foco na utilização de recursos do sistema de saúde e estimativa de custos.

Objetivos específicos

1. estimar o custo de pacientes com IC avançada elegíveis para DAVE no Brasil;
2. avaliar a composição de custos de pacientes com IC avançada elegíveis para DAVE no Brasil.

Objetivo secundário

1. mapear, através de uma revisão de escopo, os custos envolvidos no tratamento clínico de pacientes com IC avançada internacionalmente, conhecendo os maiores componentes do custo total envolvido.

CONSIDERAÇÕES FINAIS E IMPLICAÇÕES FUTURAS DA TESE

Nos dois estudos que compõem esta tese, buscamos contribuir para o conhecimento dos custos do manejo clínico de pacientes com IC avançada. Através de uma revisão de escopo, descrevemos o estado atual do conhecimento sobre os custos envolvidos no cuidado de pacientes com IC avançada envolvendo 16 estudos oriundos de vários países. No estudo retrospectivo, avaliamos 20 pacientes em tratamento medicamentoso considerados elegíveis para terapia avançada com DAVE e analisamos, através de metodologia de microcusteio, os custos envolvidos no cuidado destes pacientes.

Com base nos resultados dos dois estudos, é possível concluir que:

1. apesar da heterogeneidade metodológica existente entre os estudos abordando custos da IC avançada, dados apontam para gastos elevados em diferentes países;
2. pacientes com IC avançada candidatos a DAVE de longa duração, mas sem acesso à terapia, representam elevado custo para o sistema de saúde brasileiro, mesmo sendo considerado apenas custos diretos.

Considerando os nossos achados de que o custo do tratamento clínico de pacientes com IC avançada não é trivial tanto no Brasil quanto em outros países,

seria desejável que estratégias que possam prover acessibilidade a DAVE, e, mesmo ampliar o acesso ao transplante cardíaco, fossem implementadas. Para tanto, estudos de custo-efetividade são necessários para fundamentar políticas de incorporação destas tecnologias de maneira racional e com qualidade. Com o avanço do conhecimento na área de tecnologias em saúde e de custo-economia, é importante que tais práticas contemporâneas sejam desenvolvidas para a implementação de tratamentos em saúde, e que se tornem disponíveis para a sociedade.

MATERIAL SUPLEMENTAR

Artigo 3: Protocolo da revisão de escopo submetido na revista Systematic Reviews em 12-07-2024.

Open Science Framework (OSF) Register Identifier: DOI 10.17605/OSF.IO/54GQN

Costs of medical treatment of advanced heart failure: a scoping review protocol

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Abstract

Background: A portion of patients with heart failure (HF) progress to advanced stages, representing an estimated 5-10% of the whole HF population. In this phase, specific therapies are knowingly expensive, in particular heart transplant and left ventricular assist devices (LVAD), both of which increase survival and quality of life of patients. However, there is a large proportion of patients with advanced HF who are ineligible to either of those therapies and/or have no access to them. Nonetheless, the cost of medical treatment of these patients is largely unknown, especially in the Latin American context where this type of information can be crucial to implement healthcare policies to improve both survival and quality of life of selected patients with advanced HF. The objective of this scoping review is to summarize the evidence on costs of advanced HF patients who were not eligible or did not have access to advanced therapies, such as heart transplant or LVAD implantation.

Methods: This scoping review will be reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analysis extension for Scoping Reviews (PRISMA-ScR). This review will consider articles evaluating direct costs of advanced HF patients not treated with advanced therapies - heart transplant or LVADs - due to clinical profile/contraindications or access to treatments. PubMed/MEDLINE, EMBASE, SCOPUS, and BVS will be used as data sources for searching. Two independent reviewers will assess titles and abstracts, screen full-texts studies, and extract data from the included studies, verified by consensus.Studies will be extracted and data items such as methodological categorization, such as micro or macrocosting, study perspectives and cost information reported, including the cost per patient and the main cost driver will be registered. The results will be described in a narrative summary.

Discussion: This review will summarize the evidence available on the direct costs of medical treatment of advanced HF and identify gaps in the literature which can serve as directions for future research in the area.

Registration: Open Science Framework (July 4, 2024)

Keywords: Heart failure, Costs, Medical therapy, Outcomes

Background

Heart failure (HF) prevalence is increasing worldwide contributing to improvements on emerging technologies for different stages of the disease (1). Clinical presentation of HF is broad, but in general its progression is inevitable. Different healthcare systems face the challenges of caring for patients with HF, which now reaches 6.7 million patients in the US only in 2023, 15 million in Europe and 2.8 million people in Brazil (2–4).

Given the variety of settings and complexity of HF presentation, obtaining accurate data of the financial burden of the disease is challenging. In the US it is estimated that 39.2 billion USD are spent every year (2) and up to almost GBP 1 billion in the UK only (5). In Brazil, in 2015, the expenditure with HF reached USD 6.8 billion,involving both hospitalization and societal loss, without discriminating between different stages of the disease(4).

Although scarce, data from outpatients with HF in Brazil are emerging. Ghisleni et al. have shown that costs of these patients increase as the disease progresses, according to an assessment based on 198 patients, by means of the Time-driven Activity-based Costing (TDABC) microcosting analysis. Compared to New YorkHeart Association class I patients, those in class III/IV had over 100% increment in costs, from U$ 215 to U$ 667 respectively. Laboratory exams represented 30% of the costs in NYHA I and 74% in Class III/IV (6). At a day hospital facility, data from 20 Brazilian patients with HF and signs of congestion who required diuretic infusion sessions in 2020 were analyzed. The median cost *per* service was Int$54 (min Int$37 max Int$63). Most of this cost was attributed to the work of professionals (58%), followed by exams (23%) (7).

A portion of patients with heart failure progress to advanced stages, representing an estimated 5-10% of the whole HF population (8). In this phase, specific therapies are knowingly expensive, in particular heart transplant and left ventricular assist devices (LVAD), both of which increase survival and quality of life of patients. However, only a minority of patients with advanced HF receive either of these advanced therapies. Heart transplant is limited by organ shortage and although it has increased in numbers globally, only a limited number of patients that may benefit from the procedure, are transplanted (9). Implant of LVAD is still scarcely available from both public or private healthcare systems in different countries, mainly due to high costs (10). Thus, there is a large proportion of patients with advanced HF who are not eligible to either of those therapies and/or have no access to them. Nonetheless, the cost of medical treatment of these patients is largely unknown, especially in the Latin American context. At the same time that the financial information is scarce, the low- and middle-income characteristics of most Latin American countries makes the availability of accurate cost information more valuable for the establishment of effective and sustainable health policies. By using accurate data, the chances of introducing fair models that allow increased access to advanced therapies is amplified, resulting in positive implications for survival rates and quality of life for HFpatients.

The objective of this scoping review is to summarize the evidence on costs of advanced HF patients who were not eligible or did not have access to advanced therapies, such as heart transplant or LVAD implantation. This scoping review also aims to identify potential gaps in the literature related to costs in advanced HF and provide insights into future research in this field.

Methods

The present protocol has been registered within the Open Science Framework. The proposed scoping review will be reported in accordance with the reporting guidance provided in the Preferred Reporting Items forSystematic Reviews and Meta-analyses (PRISMA) extension for Scoping Reviews (PRISMA-ScR) (11) (**Additional file 1**). The scoping review methodology will be conducted in accordance with the Joanna Briggs Institute (JBI) methodological framework for scoping studies (12).

Questions to be answered by this scoping review:

1. What are the known costs of advanced HF of patients not eligible for advanced therapies?
2. In which type of setting costs of advanced HF were studied?
3. What are the main drivers of health costs in advanced HF?

Eligibility criteria

The review will include papers focused on advanced HF patients not treated with advanced therapies - heart transplant or LVADs - due to clinical profile/contraindications or access to treatments. Patients with advanced HF both at the inpatient, outpatient or in long term care facilities (hospice) level will be included as well in end-of-life stages.

Data of interest will include costs (direct or indirect), primary or secondary, prospective or retrospective, involving patients with advanced HF under medical treatment. Pre- prints, conference abstracts; editorials or comments; narrative, scoping or systematic reviews will be excluded. Articles evaluating only indirect costs focused on cost- effectiveness metrics/analysis; secondary cost sources (i.e., costs

extracted from other studies); cost projections (no actual measurement of resource metrics, i.e., days of hospitalization, tests and treatments) will also be excluded. No language restrictions will be applied.

Information sources

Original full manuscripts, peer-reviewed, published. To account for contemporary studies, a literature search was conducted till April 2024, across PubMed/MEDLINE, EMBASE, SCOPUS, and BVS databases. If needed, authors were contacted to obtain full manuscripts not available in usual databases.

Search strategy

The search string contains a combination of the following medical subject heading terms, “heart failure”, “transplant-ineligible”, and "costs and cost analysis". The final search results will be exported into Rayyan® (13), and duplicates removed by an experienced researcher [MMZ] and further refined through team discussion. The final search strategy for MEDLINE can be found in **Additional file 2**.

Study selection

Following the search, all identified citations will be collated after duplicates had been previously removed. Next,titles will be screened by two independent pairs of reviewers for assessment against inclusion criteria for the review. We will exclude studies that did not measure direct costs, were not original papers, reported only specific therapies other than medical management or did not study advanced HF patients. Reasons for exclusion of sources of evidence at full text that do not meet inclusion criteria will be recorded and reported.Any disagreement that occurred

between the reviewers will be solved through discussion, or with additional reviewers. The searching and screening results will be reported in full in the final scoping review according to the PRISMA-ScR and illustrated in a PRISMA-ScR flow diagram (**Figure 1**).

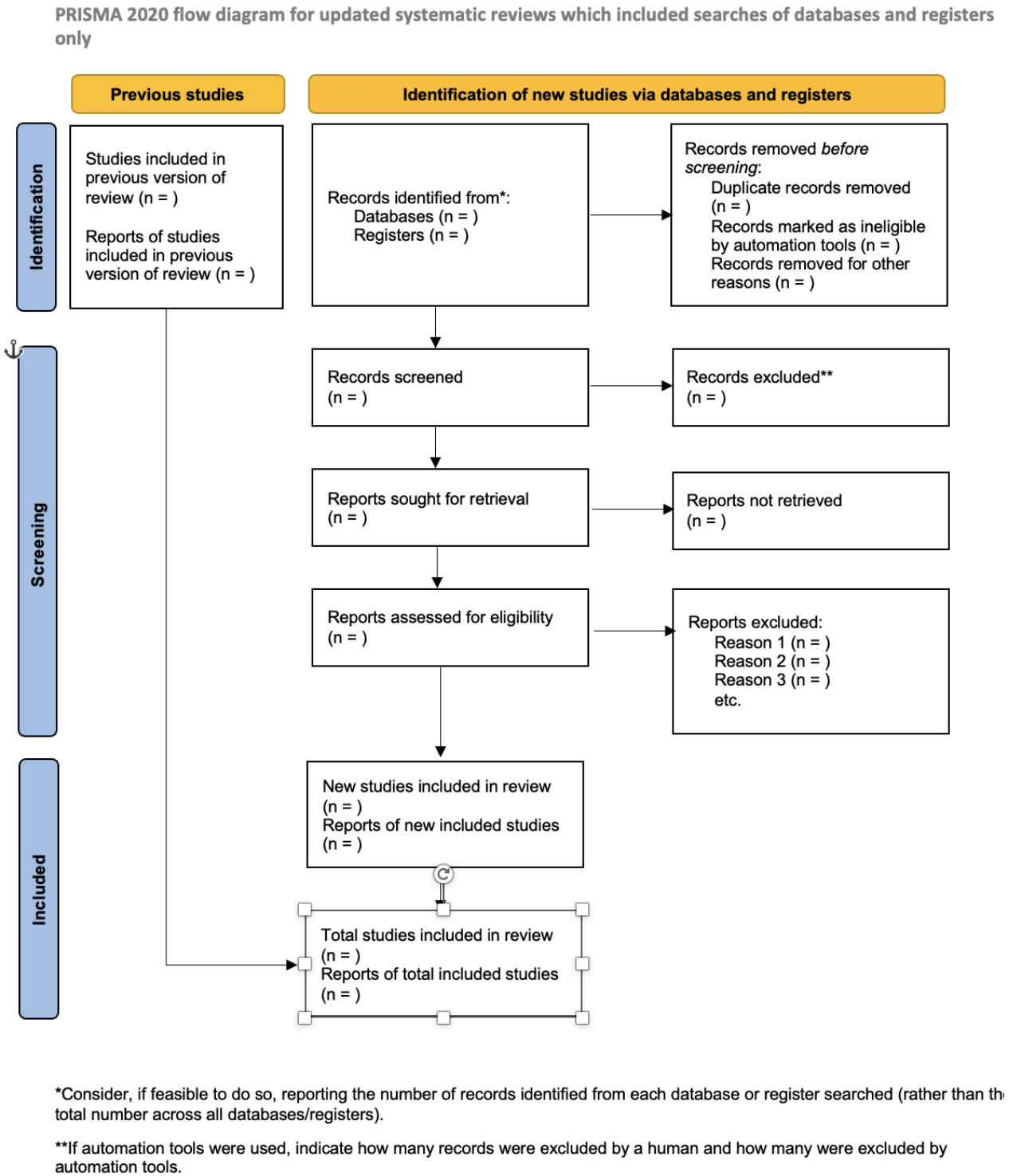

Figure 1. Study selection flow diagram recommended in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Extension for Scoping Reviews (PRISMA-ScR)

Data items

For each included study, the following variables will be extracted: title, author's names, year of publication, country, study design, study setting (outpatient, inpatient, both inpatient and outpatient, hospice), advanced HF population as stated by the authors, perspective (public, private or mixed), exclusion criteria, number of participants, age, ethnicity, ejection fraction, major comorbidities, cost methodology (microcosting, macrocosting, ratio of costs), costs by period analysis, period unit (months), cost components (emergency visits, intensive care unit (ICU) hospitalizations, no ICU hospitalizations, medications, personnel, and exams),main cost drivers (considering the components stated), currency used, and the mean total cost per patient.

Data extraction

Relevant data (see above) will be extracted from all included studies in the scoping review by two pairs of independent reviewers. A structured data recording form developed by the reviewers will be used and the information recorded on Microsoft Excel. Any disagreements arising between the reviewers will be fixed through discussion, or with the opinion of an additional reviewer/s. If appropriate, authors of papers will be contacted to request missing or additional data, where required. A data extraction form is provided with all the data items assessed (**Additional file 3**).

Data analysis and presentation

The data extraction will be structured on a descriptive Table. The results will be accompanied by a narrative summary, which will describe how the results meet the objectives and aims of this scoping review. Among the main outputs it is expected to identify the cost *per* patient measured on the applied studies worldwide, and to identify the variability in methods and financial information across the studies. We will report findings in line with the PRISMA-ScR: extension for Scoping Reviews (11)' checklist. Gap identification will detect areas where there is paucity of data on how costs are assessed in the field of advanced heart failure for those patients treated medically.

Amendments

Any amendments to this protocol when conducting the study will be outlined in Open Science Framework and reported in the final manuscript.

Discussion

Our scoping review will summarize the evidence on costs of advanced HF patients who were not eligible or did not have access to advanced therapies and identify potential gaps in the literature related to costs in this field. More specifically, we hope to dissect the nature of main cost drivers associated with this clinical scenario so that our data can provide insights to healthcare policy makers in order to provide sustainable healthcare strategies to these patients. This may be particularly relevant since only a minority of patients with advanced HFhave access to advanced therapies such as heart transplant or left ventricular assist devices.

Findings will be disseminated widely through peer reviewed publication and in various media, for example, conferences, congresses or symposia. This review will provide insights into future research in the area of medical therapy costs in advanced HF, and to guide policymakers on introducing redesigned policies for thisfield.

Abbreviations HF: Heart Failure

JBI: Joanna Briggs Institute

LVAD: Left Ventricular Assist Device

PRISMA-ScR: Systematic Reviews and Meta-Analysis extension for Scoping Reviews

Declarations

Ethics approval and consent to participate

Not applicable. **Consent to publication** Not applicable.

Availability of data and materials

All data to be analyzed and reported in this scoping review will be from published literature, which is already in the public domain.

Competing interests

The authors declare that they have no competing interests.

Funding

Study is funded by the National Institute of Science and Technology for Health Technology Assessment (IATS)-CNPq/Brazil Porto Alegre, Brazil. NC is a recipient of a research grant from the Brazilian National Research Council (CNPq).

Acknowledgements

The authors would like to thank Daniel Umpierre for providing advice during the writing of this protocol.

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Additional file 1. Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR) Checklist.

SECTION	ITEM	PRISMA-ScR CHECKLIST ITEM	REPORTED ON PAGE #
TITLE			
Title	1	Identify the report as a scoping review.	Click here to enter text.
ABSTRACT			
Structured summary	2	Provide a structured summary that includes (as applicable): background, objectives, eligibility criteria, sources of evidence, charting methods, results, and conclusions that relate to the review questions and objectives.	Click here to enter text.
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known. Explain why the review questions/objectives lend themselves to a scoping review approach.	Click here to enter text.
Objectives	4	Provide an explicit statement of the questions and objectives being addressed with reference to their key elements (e.g., population or participants, concepts, and context) or other relevant key elements used to conceptualize the review questions and/or objectives.	Click here to enter text.
METHODS			
Protocol and registration	5	Indicate whether a review protocol exists; state if and where it can be accessed (e.g., a Web address); and if available, provide registration information, including the registration number.	Click here to enter text.
Eligibility criteria	6	Specify characteristics of the sources of evidence used as eligibility criteria (e.g., years considered, language, and publication status), and provide a rationale.	Click here to enter text.
Information sources*	7	Describe all information sources in the search (e.g., databases with dates of coverage and contact with authors to identify additional sources), as well as the date the most recent search was executed.	Click here to enter text.

Search	8	Present the full electronic search strategy for at least 1 database, including any limits used, such that it could be repeated.	Click here to enter text.
Selection of sources of evidence†	9	State the process for selecting sources of evidence (i.e., screening and eligibility) included in the scoping review.	Click here to enter text.
Data charting process‡	10	Describe the methods of charting data from the included sources of evidence (e.g., calibrated forms or forms that have been tested by the team before their use, and whether data charting was done independently or in duplicate) and any processes for obtaining and confirming data from investigators.	Click here to enter text.
Data items	11	List and define all variables for which data were sought and any assumptions and simplifications made.	Click here to enter text.
Critical appraisal of individual sources of evidence§	12	If done, provide a rationale for conducting a critical appraisal of included sources of evidence; describe the methods used and how this information was used in any data synthesis (if appropriate).	Click here to enter text.
Synthesis of results	13	Describe the methods of handling and summarizing the data that were charted.	Click here to enter text.
RESULTS			
Selection of sources of evidence	14	Give numbers of sources of evidence screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally using a flow diagram.	Click here to enter text.
Characteristics of sources of evidence	15	For each source of evidence, present characteristics for which data were charted and provide the citations.	Click here to enter text.
Critical appraisal within sources of evidence	16	If done, present data on critical appraisal of included sources of evidence (see item 12).	Click here to enter text.
Results of individual sources of evidence	17	For each included source of evidence, present the relevant data that were charted that relate to the review questions and objectives.	Click here to enter text.
Synthesis of results	18	Summarize and/or present the charting results as they relate to the review questions and objectives.	Click here to enter text.

DISCUSSION			
Summary of evidence	19	Summarize the main results (including an overview of concepts, themes, and types of evidence available), link to the review questions and objectives, and consider the relevance to key groups.	Click here to enter text.
Limitations	20	Discuss the limitations of the scoping review process.	Click here to enter text.
Conclusions	21	Provide a general interpretation of the results with respect to the review questions and objectives, as well as potential implications and/or next steps.	Click here to enter text.
FUNDING			
Funding	22	Describe sources of funding for the included sources of evidence, as well as sources of funding for the scoping review. Describe the role of the funders of the scoping review.	Click here to enter text.

Additional file 2. Final search strategy for MEDLINE.

Index	Strategy	Hits
#1 Disease	"heart failure"[MeSH] OR "heart failure"[TIAB] OR "cardiac failure"[TIAB] OR "Myocardial Failure"[TIAB] OR "cardiac insufficiency"[TIAB]	269,565
#2 Advanced Disease	"transplant-ineligible"[TIAB] OR "transplant ineligible"[TIAB] OR "end-of-life"[TIAB] OR "end of life"[TIAB] OR "end-stage"[TIAB] OR "end stage"[TIAB] OR "terminal"[TIAB] OR "advanced"[TIAB] OR "palliative"[TIAB] OR "hospice care"[TIAB] OR "supportive care"[TIAB]	1,188,983
#3 Cost	"Costs and Cost Analysis"[Mesh] OR "Costs and Cost Analysis"[TIAB] OR "cost"[TIAB] OR "costs"[TIAB] OR "costing"[TIAB] OR "expenditure"[TIAB] OR "expenditures"[TIAB] OR "Expense"[TIAB] OR "expensive"[TIAB] OR "Affordability"[TIAB] OR "Affordable"[TIAB]	983,646
#4 Search	#1 AND #2 AND #3	1,136

Additional file 3. Data extraction form.

Study	Country	Study design	Study setting	Population (age, ethnicity)	Perspective	Exclusion criteria	N	Cost methodology	Costs period analysis	Main cost drivers	Currency and total cost