Risk Identification Index for Ventricular Dysfunction Resulting from Antineoplastic Treatment: Development and Content Validation

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Índice de Identificação do Risco de Disfunção Ventricular Decorrente do Tratamento Antineoplásico: Elaboração e Validação de Conteúdo

Índice de Identificación del Riesgo de Disfunción Ventricular Derivada del Tratamiento Antineoplásico: Elaboración y Validación de Contenido

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ABSTRACT

Introduction: The risk of cardiotoxicity associated with antineoplastic treatments, particularly ventricular dysfunction, highlights the need for effective and multidisciplinary tools for the prevention, detection, and management of these complications. **Objective:** Develop and validate the content of the Risk Identification Index for Ventricular Dysfunction Resulting from Antineoplastic Treatment. **Method:** Methodological study focused on the development and content validation of an index conducted in two phases. In the first phase, a literature review was carried out, from which the index was developed. In the second phase, the initial version was prepared by the authors and submitted for evaluation by 33 experts. Six consensus meetings were held between August and October 2022. **Results:** The review stage identified the risk factors for ventricular dysfunction related to the current systemic antineoplastic treatment, to the current radiotherapy, to previous antineoplastic treatment, patient-related and to lifestyle. The current version of the instrument serves as a guide for anamnesis/screening of individuals with cancer until its predictive capacity is confirmed. **Conclusion:** Following the validation process, the final version of the index included an instructional text for completion, consisting of 21 items grouped according to the nature of the risk factors and their respective response options, without statistically defined item weights.

Key words: Antineoplastic Agents/adverse effects; Radiotherapy/adverse effects; Cardiotoxicity/prevention & control; Ventricular Dysfunction/prevention & control; Risk Assessment.

RESUMO

Introdução: O risco de cardiotoxicidade associada aos tratamentos antineoplásicos, especialmente a disfunção ventricular, evidencia a necessidade de instrumentos eficazes e multiprofissionais para prevenção, detecção e manejo dessas complicações. **Objetivo:** Elaborar e validar o conteúdo do Índice de Risco de Disfunção Ventricular Decorrente do Tratamento Antineoplásico. **Método:** Estudo metodológico de elaboração e validação de conteúdo de um índice, dividido em duas fases. Na primeira fase, realizou-se uma revisão da literatura, a partir da qual o índice foi desenvolvido. Na segunda fase, a versão inicial foi elaborada pelos autores e submetida à apreciação de 33 especialistas. Seis reuniões de consenso foram realizadas entre agosto e outubro de 2022. **Resultados:** Na etapa de revisão, foram identificados os fatores de risco para disfunção ventricular relacionados ao tratamento sistêmico antineoplásico atual, à radioterapia atual, ao tratamento antineoplásico prévio, ao paciente e ao estilo de vida. A versão atual do instrumento serve como guia para anamnese/triagem de pessoas com câncer, até que sua capacidade preditiva seja confirmada. **Conclusão:** Após o processo de validação, a versão final do índice passou a contar com um texto instrucional para seu preenchimento, composto por 21 itens agrupados conforme a natureza dos fatores de risco e as respectivas alternativas de resposta, sem pesos estatísticos dos itens claramente definidos.

Palavras-chave: Agentes Antineoplásicos/efeitos adversos; Radioterapia/efeitos adversos; Cardiotoxicidade/prevenção & controle; Disfunção Ventricular/prevenção & controle; Medição de Risco.

RESUMEN

Introducción: El riesgo de cardiotoxicidad asociado a los tratamientos antineoplásicos, en particular la disfunción ventricular, pone de manifiesto la necesidad de instrumentos eficaces y multidisciplinarios para la prevención, detección y manejo de estas complicaciones. **Objetivo:** Elaborar y validar el contenido del Índice de Identificación del Riesgo de Disfunción Ventricular Derivada del Tratamiento Antineoplásico. **Método:** Estudio metodológico de elaboración y validación de contenido de un índice, dividido en dos fases. En la primera fase se realizó una revisión de la literatura, a partir de la cual se desarrolló el índice. En la segunda fase, la versión inicial fue elaborada por los autores y sometida a la evaluación de 33 especialistas. Entre agosto y octubre de 2022 se llevaron a cabo seis reuniones de consenso. **Resultados:** En la etapa de revisión se identificaron los factores de riesgo para disfunción ventricular relacionados con el tratamiento sistémico antineoplásico actual; con la radioterapia actual; con el tratamiento antineoplásico previo; con el paciente; y con el estilo de vida. La versión actual del instrumento funciona como guía para la anamnesis y el tamizaje de personas con cáncer, hasta que su capacidad predictiva sea confirmada. **Conclusión:** Tras el proceso de validación, la versión final del índice pasó a contar con un texto instructivo para poderlo completar, compuesto por 21 ítems agrupados según la naturaleza de los factores de riesgo y sus respectivas opciones de respuesta, sin ponderaciones estadísticas claramente definidas para los ítems.

Palabras clave: Agentes antineoplásicos/efectos adversos; Radioterapia/efectos adversos; Cardiotoxicidad/prevención & control; Disfunción Ventricular/prevención & control; Medición de Riesgo.

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INTRODUCTION

Cancer is a known public health issue worldwide. In Brazil, according to estimations, for each year of the 2023-2025 triennium, the National Cancer Institute (INCA) expects there will be 704 thousand new cancer cases[1]. In the USA, 1,958,310 new cases and 609,820 deaths from cancer are projected[2]. These numbers show the magnitude of the neoplastic disease.

After diagnosis, patients are usually submitted to antineoplastic treatments, which can include surgery, radiotherapy, and systemic therapy (classic chemotherapy, hormone therapy, target therapy, and immunotherapy), either in isolation or combination[3,4]. However, both radiotherapy and systemic therapy can cause clinical manifestations known as toxicities, since they not only affect tumoral cells, but also healthy tissues, including the cardiovascular system[4,5].

The possible cardiovascular manifestations associated with cardiotoxicity include systemic hypertension, pulmonary hypertension, thromboembolic accidents, carotid artery diseases, heart failure, myocarditis, stroke and pericardial tamponade, ischemia, and myocardial infarction, in addition to ventricular dysfunction[6]. The latter is considered a severe complication, associated with high rates of morbimortality, which can happen during or after finishing treatment[7].

Both the *Diretriz Brasileira de Cardio-Oncologia*[7], elaborated by the Brazilian Society of Cardiology in partnership with the Brazilian Society of Clinical Oncology, and publications by the American Society of Clinical Oncology[8], recommend that possible adverse effects of oncological treatment are discussed from the beginning of the therapeutic planning, with continuous follow-up after ending the treatment. The European Society for Medical Oncology[9], in turn, stresses the importance of prevention, detection, screening, and treatment of cardiovascular toxicities, highlighting the central role of clinical assessment.

However, it must be noted that the term cardio-oncology is still predominantly used in the medical scope, when its application should stretch to other health professionals, specifically when it comes to the assessment of cardiac toxicities like ventricular dysfunction. Moreover, there is a delay in the identification of risk factors and in beginning appropriate clinical conduct, even between doctors.

Literature research identified three instruments targeted at toxicity assessment related to cancer treatment. Two of them are aimed at chemotherapy in elderly: the Hurria Toxicity Score[10,11], already translated into Brazilian Portuguese[12], and the CRASH Score[13], which has not yet been formally translated. These instruments are used for general toxicity assessment. The third one, CHEMO-RADIAT Score[14], was developed to prevent cardiovascular effects in women with breast cancer; however, it presents methodological limitations and applicability restrictions in the Western context.

With all that in consideration, this study aims to develop and validate the content of the Risk Identification Index for Ventricular Dysfunction Resulting from Antineoplastic Treatment to provide a specific instrument for this cardiac toxicity, without restricting it to the type of neoplasm, and thus, qualifying the clinical assessment of health professionals in oncology care. The developed index will thus promote integration between specialties (oncology and cardiology), enabling the early detection of cardiac complications, contributing to patient safety and reduction of eventual costs with cardiovascular health, elements that influence the rational use of resources by the Brazilian National Health System (SUS).

METHOD

Methodological study conducted according to the guidelines from the COnsensus-based Standards for the selection of health Measurement INstruments (COSMIN)[15]. The research was structured in two steps: the first consisted of a literature review to identify risk factors associated with the development of ventricular dysfunction in patients submitted to systemic antineoplastic treatment and radiotherapy. In the second step, based on the review, an instrument was elaborated, submitted to evaluation by specialists for content validation and presentation. Due to its nature, the study was not grounded on the Enhancing the Quality and Transparency of health Research (EQUATOR) network guidelines for the main investigations in the health field.

The searches were conducted on the Latin American and Caribbean Center on Health Sciences Information (LILACS) and PubMed databases, using the *Descritores em Ciências da Saúde* (DeCS) and Medical Subject Headings (MeSH) combined among them with the Boolean operator AND (*Antineoplásicos* AND *Cardiotoxicidade* AND *Fatores de Risco*; Drug Therapy AND Cardiotoxicity AND Risk Factors; *Cardiotoxicidade* AND *Antraciclinas*; Cardiotoxicity AND Anthracyclines; Cardiotoxicidade AND *Anticorpos Monoclonais*; Cardiotoxicity AND Antibodies, Monoclonal; *Cardiotoxicidade* AND *Alquilantes*; Cardiotoxicity AND Alkylating Agents; *Cardiotoxicidade* AND *Inibidores de Proteassoma*; Cardiotoxicity AND Proteasome Inhibitors; *Cardiotoxicidade* AND *Taxoides*; Cardiotoxicity AND Taxoids; *Cardiotoxicidade* AND *Radioterapia*; Cardiotoxicity AND Radiotherapy).

During the search performed with the standardized descriptors, non-standardized terms were identified in both databases accessed, and a new search was conducted using the following combinations: *Cardiooncologia* AND *Fatores de Risco*; Cardiooncology AND Risk Factors; *Cardiotoxicidade* AND *Agentes anti-HER2*; Cardiotoxicity AND Anti-HER2 agents; *Cardiotoxicidade* AND *Inibidores de sinalização VEGF*; Cardiotoxicity AND VEGF signaling inhibitors; *Cardiotoxicidade* AND *Inibidores BRAF e MEK*; Cardiotoxicity AND BRAF and MEK inhibitors.

For the search, no time period or language was established. A total of 11,224 studies were identified, of which 3,021 were review articles. We chose not to establish systematic selection criteria, and the selected studies were those that answered the review question: "What are the risk factors not related to the development of ventricular dysfunction derived from the antineoplastic treatment?"[16]. Reviews published in the form of guidelines by the societies of reference in the cardio-oncology theme were prioritized: American Society of Clinical Oncology; European Society for Medical Oncology; American Association for Cancer Research; Union for International Cancer Control; European Society for Radiotherapy and Oncology; Multinational Association of Supportive Care in Cancer; *Sociedade Brasileira de Oncologia Clínica*; *Sociedade Brasileira de Cardiologia*; in addition to the reviews that addressed the cardiac risk factors of the antineoplastic systemic therapy and radiotherapy.

In view of that, 25 articles were selected, as there was saturation regarding the repetition of relevant information. After the analysis, the identified risk factors were grouped in five categories: Risk Factors Related to the Current Systemic Antineoplastic Treatment; Risk Factors Related to the Current Radiotherapy; Risk Factors Related to the Previous Antineoplastic Treatment; Risk Factors Related to the Patient; and Risk Factors Related to Lifestyle.

After identifying the risk factors described in the literature, a preliminary version of the instrument was drafted. The first part has an instructional text, destined to guide the health professional or researcher regarding the objective and completion of the instrument, based on patient records and assessments. Then, the risk factors were organized into five categories. For the 22 initial items, the responses varied from 0 (absence) to 1 (presence). One item, which evaluated the simultaneous presence of thoracic irradiation and systemic antineoplastic treatment, received a 2 score (item 8). The choice was to attribute points only to the presence of factors, without attributing differentiated weights.

In the category "Risk Factors Related to Current Systemic Antineoplastic Treatment", the items were organized by pharmacological group, like "prescription of anthracyclines". A complementary document was elaborated, based on the *Diretriz Brasileira de Cardio-oncologia*[7], containing medications with recognized cardiotoxicity, annexed to the instrument.

After structuring came the step of content and face validation. According to the COSMIN[15] group, content validation assesses how much the items reflect the construct of interest, while face validation verifies if the items converge to assess this construct. The assessed construct was the risk of ventricular dysfunction associated with oncological therapy, defined as structural changes that compromise pre-load, post-load, and cardiac contractility, resulting in a drop in left ventricular ejection fraction (LVEF)[17]. In oncology, a reduction of ≥10% of LVEF, with a final value of ≤50%, is considered a ventricular dysfunction[7].

Specialist judges on the theme and instrument validation methodology were selected for validation.

As inclusion criteria, it was established that expert judges on the topic should be nurses or pharmacists with experience in caring for people with cancer, or doctors working in oncology, mastology, hematology, radiotherapy, or cardiology. No experience criterion was used, as it is understood that, when working in the care of people with cancer, professionals understand that the treatment reverberates on other systems of the human body; therefore, everyone could contribute to the content validation process. The method-specialists were researchers with experience in the construction and validation of health instruments. It is worth highlighting that all judges had a social connection with the research authors, a fact that facilitated adjusting each judge to a theme and method of investigation.

The selection of judges was done by snowball sampling[18]. The invitations, sent by email or messaging app, informed the study objectives and dates for online meetings. Six meetings were held between August and October 2022, with reminders sent 48 hours earlier. The meetings followed the consensus technique, adapted from focus groups[19], recognized by COSMIN[15]. Up to 10 people participated per meeting, with moderation from experienced researchers in qualitative data collection and validation of instruments.

Sixty professionals were invited, of whom 33 accepted. A total of 24 theme specialists (13 nurses, 6 pharmacists, and 5 doctors) and 8 method specialists (7 professors/researchers and 1 statistician) participated. The experience ranged from less than 2 years to over 5 years. Of the total, 14 worked in healthcare, 13 in teaching/research, and 4 in both. Seventeen had a *stricto sensu* post-graduation degree (5 masters and 14 doctors).

The meetings took place via videoconference, with the link being sent in advance. After presentation of the objective and submission of the Free and Informed Consent Form via Google Forms®, the researchers explained the construct and application of the instrument, targeted to oncological patients before the start of therapy. This is recommended for professionals like nurses, doctors, and pharmacists. Three criteria guided the assessment: relevancy, scope, and understandability of the items[20].

The data collection instrument was inserted in the Google Forms® and shared with the participants during the consensus meetings. The instrument was divided into eight forms with distinct links: (1) sociodemographic data of the participants; (2) assessment of the instructional text; (3 to 7) assessment of categories I to V; (8) score assessment. This division was needed to collect the judges' assessments in each step.

The theme specialist judges analyzed the topics and answered three questions: "1. Is this item relevant to assessing the risk of ventricular dysfunction in the target population? 2. Is this item clearly defined and understandable? 3. Do the presented items encompass all the risk factors related to the current systemic antineoplastic treatment and associated with ventricular dysfunction?". The answer options were: Yes, No, and Maybe.

The method-specialist judges assessed only the clarity of the items, answering the question: "Is this category clearly defined and comprehensible?", with an ordinal scale of four points: (1) Incomprehensible; (2) Requires significant review; (3) Requires slight review; (4) Comprehensible. All the judges also assessed the instructional text and the instrument score through the following questions: "Do you agree with the instruction text?" and "Do you agree with the proposed score?", using the same three answer options: Yes, No, and Maybe.

During the meetings, the form links were made available in the videoconference chat, and a researcher followed the summary of the answers. When 90% or more of the judges marked "Yes", it was considered that a consensus was reached on the evaluated item. In case this percentage was not reached, the judges who answered "No" or "Maybe" were invited to justify their answers. Only after reaching a 90% agreement on an item did the validation move to assess the next item. This process was applied to all the forms during the meetings.

The method specialist judges focused only on clarity since they did not master the specific content of the instrument (antineoplastic treatment and ventricular dysfunction). However, they participated in the discussion about attributing values to the presence or absence of risk factors.

During the meeting, the authors made alterations to the instrument and, always in the following meeting, each consensus group was presented with an updated version so they could manifest their agreement or disagreement with the instrument. The instrument was altered six times in total. The sixth version was sent to a mastologist with a doctorate in the field and over five years of experience in clinics and in research with oncological patients. The Free and Informed Consent Form (FICF) and the survey forms were sent by email in the first week of November, with a one-week deadline. Their answers and suggestions were analyzed and incorporated by the team, consolidating the final version of the instrument.

A consensus was considered when 90% of the theme specialists answered "Yes" and 90% of the method specialists checked "Comprehensible", which is equivalent to a Kappa Content Validity Index of 0.90, a value considered excellent by the COSMIN[21] group.

This study has been approved by the Research Ethics Committee, report number 5,096,879 (CAAE (submission for ethical review): 52745021.4.0000.5564), in compliance with Resolution 466/12[22] of the National Health Council. The participation was voluntary and authorized by the digital FICF.

RESULTS

From this literature review, the following groups of medications with potential cardiotoxic effects associated with ventricular dysfunction were identified: anthracyclines[7,8,23-25], anti-HER2 (Human Epidermal Growth Factor Receptor 2) agents[7,26-28], alkylating agents[7,29,30], VEGF (Vascular Endothelial Growth Factor) signaling inhibitors [7,29-32], Proteasome Inhibitors[7,30,32-34], BRAF and MEK inhibitors (related to the cellular multiplication in melanomas)[7,30,32,35,36], and taxanes[7,24,30,32]. The previous use of anthracyclines is known as an additional risk factor for cardiotoxicity[7,9,25,37-40], magnifying the risks of current treatments.

Systemic antineoplastic treatments combined with mediastinal or left chest radiotherapy also presented cardiotoxic risk[7-9,25,38,39,41,42], just like isolated radiotherapy in these regions. Radiation can cause fibrosis, thickening, and calcification of cardiac valves, resulting in ventricular dysfunction. Patients with a previous history of radiotherapy in these areas may already present cardiac lesions, aggravated by new treatments[7,37-42].

Regarding risk factors related to the patient, we highlight a previous history of cardiovascular disease[7-9,24,25,40,43], family history for these diseases, and the possibility of asymptomatic cardiovascular disease[7-9,24,25,40,43]. Age is another relevant risk factor, with increased risk for patients

aged ≥60 years that underwent systemic antineoplastic therapy[7,8,23,25,43] and <50 years exposed to radiotherapy[38,41].

Chronic non-communicable diseases, like systemic arterial hypertension and diabetes mellitus, also increase the risk of ventricular dysfunction when associated with oncological treatments[7-9,24,25,40,43]. Obesity assessed by the Body Mass Index (BMI), according to the World Health Organization (WHO)[44] and the Brazilian Association for the Study of Obesity and Metabolic Syndrome (Abeso)[45], was also recognized as a risk factor, as well as dyslipidemia[7-9,24,25,40,43].

Other factors related to lifestyle include smoking, drinking, and a sedentary lifestyle[7-9,24,25,40,43]. Alcohol consumption will be assessed according to the WHO[46] criteria and sedentary lifestyle as sedentary behavior, following the same organization's criteria[47]. Smoking, on the other hand, will be initially assessed on a yes/no basis, with the possibility of adjusting this later.

At the first consensus meeting, the judges suggested adjustments to the instruction text, considered long and confusing. Modifications were made only if 90% of evaluators disagreed, and they only moved on to the next topic when reaching 90% agreement on the current topic. There was also a suggestion to change the title of the first category from "Risk Factors Related to Current Chemotherapy" to "Risk Factors Related to Current Systemic Antineoplastic Treatment".

In the second category, item 8 was rephrased from "Mediastinal or left chest irradiation associated with chemotherapy" to "Mediastinal or left chest irradiation associated with systemic antineoplastic treatment", adjusting the terminology to the clinical practice. This alteration was also applied to the general title of the instrument and to item 14, which now indicates "≥60 years for systemic antineoplastic treatment".

In the third category, "Risk Factors Related to Previous Treatments", no alterations were suggested. Whereas in the fourth category, "Risk Factors Related to the Patient", item 13 was rephrased from a question to an affirmation: "Presence of cardiovascular disease in the family".

The fifth category, "Risk Factors Related to Lifestyle", kept its question-based structure, with guidance for the interviewer to assess alcohol intake, smoking, and sedentary behavior. There was debate between the judges on the relevance and form of assessment of these factors, but it was decided to keep the initially proposed structure, with the possibility of reviewing further steps of the study.

In the instrument score evaluation step, the judges recommended not attributing different weights to risk factors at this point. A footnote was added to the instrument, guiding interviewers to consult the complementary document in case of doubts regarding category I.

In the following meetings, changes were minimal. In the second meeting, the term "left" was removed from items 8 and 9 for not being frequently recorded information in medical charts, in addition to acknowledging that right chest irradiations may also present a risk. Items 19 and 20 were reorganized in tables, improving clarity of instructions on the assessment of smoking and drinking.

In the third meeting, the judges requested adjustments to the scoring explanatory text, including the way scoring is done and the absence of factors. The new wording is: "The instrument is composed of five categories. Score zero (0) in the absence and one (1) in the presence of the risk factor; except for item 8, which should be scored either (0) or (2). The sum of points can vary from 0 to 22, in which the greater the score, the greater the risk of ventricular dysfunction."

In addition, the title of the third category was adjusted to "Risk Factors Related to the Previous Antineoplastic Treatment". A side column informing the source of data for each item (medical record or interview) was included to guide the interviewer during completion.

In the fourth meeting, doubts persisted regarding the fifth category items (19, 20, and 21), especially regarding the clarity of questions and their influence on the outcome studied. With no consensus, it was decided to keep the items, leaving possible alterations for future validations.

In the fifth meeting, the group asked to read the complementary document and proposed replacing the term "drugs" with "medications", adding "daunorubicin" to the anthracyclines group, and organizing the drug names alphabetically.

In the sixth and last meeting, with the method specialists, there were clarifications on the risk factors. The group suggested that, in a future phase, the instrument was assessed with all the items scoring equally (except item 8) and that statistical tests were applied to verify its predictive capacity.

The sixth version was sent to a specialist in the field, who reinforced previous discussions on the fifth category and the scoring of items. He suggested attributing distinct weights, but the team chose to keep the sixth version format. The complete final version of the instrument and the complementary document are in the Supplementary Material of this article. Chart 1 presents the items that remained after the judges' evaluation.

DISCUSSION

For the development, content validation, and presentation of the proposed instrument, the research team chose to follow the COSMIN[15] group referential, broadly used in psychometric studies. This choice

Chart 1. Categories and items of the final version of the instrument according with content validation

I. Risk factors related to current systemic antineoplastic treatment
1. Prescription of anthracyclines
2. Prescription of anti-HER2 (Human Epidermal Growth Factor Receptor 2) agents
3. Prescription of alkylating agents
4. Prescription of VEGF (Vascular Endothelial Growth Factor) signaling inhibitors
5. Prescription of proteasome inhibitors
6. Prescription of BRAF and MEK (genes related to neoplastic cell multiplication in melanomas) inhibitors
7. Prescription of taxanes
Partial scoring
II. Risk factors related to current radiotherapy
8. Mediastinal or chest irradiation concomitant to systemic antineoplastic treatment
9. Isolated mediastinal or chest irradiation
Partial scoring
III. Risk factors related to previous systemic antineoplastic treatment
10. Previous use of anthracyclines
11. Previous mediastinal or chest radiotherapy
Partial scoring
IV. Risk factors related to the patient
12. Previous cardiovascular disease
13. Presence of cardiovascular disease in the family
14. Age: ≥60 years for systemic antineoplastic treatment; or <50 years for radiotherapy
15. Systemic arterial hypertension
16. Diabetes *mellitus*
17. Dyslipidemia
18. Obesity (BMI ≥30 kg/m^2)
Partial Scoring
V. Risk factors related to lifestyle
19. Were you a smoker before the diagnosis?/Are you currently a smoker? Guidance to the evaluator: Score (1) if the answer is positive for at least one of the questions
20. Do you consume alcoholic drinks? If yes, on how many days a week? If the alcohol intake is <2 days a week, ask: How many doses of alcoholic drinks do you usually consume? Guidance to the evaluator: Standard dose: 1 can of beer; 1 dose of spirit; 1 glass of wine; 1 small glass of liqueur or similar If the intake is over 2 days a week, score (1); or if the standard dose intake is over 2 doses a day, score (1)
21. Consider that a sedentary person spends most of their day lying down, seated, and does not do any regular physical activity. Thinking of your weekly routine before the diagnosis, would you consider yourself a sedentary person?

was based on the familiarity of the researchers with methodologies aimed at creation and validation of Patient-Reported Outcome Measures (PROM). However, during the validation step with judges, some impasses came up regarding the attribution of points to the items, which led to the search for similar studies. We found, for instance, the development and content validation study of the "Assessment scale of risk for surgical positioning injuries"[48], whose methodology is similar to the current proposal, although its scoring was based on the literature review and expertise of authors, and later validated by the judges – an approach that could not be replicated here due to the absence of consensus among the evaluators on the weight of each item in the risk of ventricular dysfunction.

Thus, another methodology was identified in the literature: clinimetrics. Differently from psychometrics, more applied to subjective constructs, clinimetrics assesses objective clinical characteristics – such as pattern, severity, duration, disease progression, and response to treatment – with a focus on sensibility and clinical applicability[49]. Studies with this approach[10,11,50-53] follow similar steps: patient assessment through a cohort study (prospective or retrospective), selection of those who manifested the outcome of interest, statistical analysis of data (univariate, multivariate analysis, and specific tests), culminating in the construction of a predictive model. The item scoring accrues from the coefficient β, which reveals the actual contribution of each factor to the outcome.

It is noteworthy that, in these studies, the development of the instruments was not evaluated by judges, being predominantly based on statistical tests and on the research team's expertise. In the present study, although the survey of risk factors was done based on scientific literature, the team did not consider this identification enough to validate the instrument. Thus, submission to judge evaluation was considered an essential step, allowing the incorporation of clinical knowledge of professionals working in oncology care and researchers with methodological experience. This articulation enabled structural and clinical improvements to the instrument, strengthening it for future predictive validations. We highlight that, since the future clinimetric validation of the Risk Identification Index for Ventricular Dysfunction Resulting from Antineoplastic Treatment is foreseen, the item scoring may still be revised.

Studies like the validation of an instrument to assess the participation of patients in bedside handover[54] reinforce the importance of the evaluation by judges as a fundamental step for refinement, in addition to the statistical analysis. Thus, the significant contribution of these experts to the development of methodological studies is recognized, as also pointed out by other authors[48].

The development of the Risk Identification Index for Ventricular Dysfunction Resulting from Antineoplastic Treatment, guided by the COSMIN[15] group structure, resulted in a structured instrument, applicable to clinical practice and comprehensive regarding the risk factors described in the literature for ventricular dysfunction associated with antineoplastic treatments. The psychometric approach confers more methodological detailing to the initial steps, while the clinimetric approach shall be useful to the future unfolding of the instrument validation[49]. Socializing the index with the academic community with just content validation is important, since in its current format the instrument serves as a guide for health professionals to perform anamnesis and/or clinical screening of people with cancer in antineoplastic treatment, while the clinimetric properties assessment step is under development.

Finally, it is important to stress that the current structure of the instrument is limited to content validation, that is, to the literature review elaborated and the judges consensus; however, in a future investigation, other variables may influence the restructuring of the index, as long as they present statistical evidence, such as the number of radiotherapy cycles, the doses of drugs used in the antineoplastic treatment, the lifestyle of the people with cancer, as well as the instrument's score, which in statistical analysis may have its score altered to adapt to how much each item actually contributes to the occurrence of the ventricular dysfunction outcome.

CONCLUSION

The development of a clinical assessment instrument still represents a challenge, since, although there are several methodological references available, these are based on psychometrics, which possess more affinity with subjective constructs, which differ from the construct addressed in the present study. However, the development and content validation process and presentation of the Risk Identification Index for Ventricular Dysfunction Resulting from Antineoplastic Treatment carefully followed this framework, considered more structured, having rigorously consolidated its methodological approach over the years. Moreover, the guidelines for the development and content validation steps met the requirements proposed in this study, even when dealing with an objective construct. Thus, the study achieved its objective, since the Risk Identification Index for Ventricular Dysfunction Resulting from Antineoplastic Treatment was developed based on the scientific literature and the expertise of the authors and judges, the latter being fundamental for its improvement. The instrument is, therefore, ready for further validations

(which are ongoing) before being applied to clinical practice. And, in its current format, it can already function as a guide for clinical professionals who work in the care of people with cancer, and can be used for this purpose, while evaluating its predictive properties for the risk of ventricular dysfunction.

CONTRIBUTIONS

Both authors have substantially contributed to the study design, planning, acquisition, analysis, and interpretation of the data, wording, and critical review. They approved the final version for publication.

DECLARATION OF CONFLICT OF INTERESTS

There is no conflict of interest to declare.

DATA AVAILABILITY STATEMENT

All the contents associated with the article are included in the manuscript.

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