

Research Article

Prevalence of Cachexia in Cancer Patients

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Introduction. Cachexia is a syndrome characterized by the loss of musculoskeletal mass, with or without adipose mass, which cannot be reversed by nutritional support. In Chile, there are no data on cachexia in cancer patients that allows for decision making on better interdisciplinary management. In this study, the prevalence of cachexia in inpatient and outpatient cancer patients was investigated. **Methods.** An observational, descriptive, and cross-sectional study was carried out. Eighty-six inpatients and outpatients were evaluated. Cachexia was evaluated by applying the miniCASCO tool, its weight by bioimpedance, and inflammation by blood parameters. Comparisons and correlations were made considering $p < 0.05$ as the threshold for statistical significance. **Results.** Forty patients met the inclusion criteria, 35% were men and 65% were women. In all, 27.5% of patients had cachexia secondary to cancer. Of the total number of patients with the syndrome, approximately 45.4% had mild cachexia, 36.3% had severe cachexia, and 18.1% had moderate cachexia. In addition, there was a significant positive correlation ($p = 0.0150$) and moderately strong ($r = 0.7209$) match between the final scores and the stage of cancer. **Conclusion.** The prevalence of cachectic patients is reported for the first time through the application of the miniCASCO tool. A moderate positive match was detected between the final miniCASCO score and the stages of cancer patients. Finally, an early discovery of cachexia would allow therapeutic interventions aimed at improving the prognosis of cancer patients.

1. Introduction

Cancer is the leading cause of death worldwide, with 12 million deaths from cancer projected for 2028 [1]. In Chile, cancer occupies the second place in mortality rates after cardiovascular diseases, with a rate of 139 per 100,000 inhabitants [2].

Systemic inflammation, typical of cancer, is a factor that causes a multifactorial syndrome called cachexia, which consists of an involuntary loss of musculoskeletal mass with or without loss of adipose mass and that cannot be

completely reversed with nutritional support [3–5]. Cachexia is related to involuntary weight loss, causing metabolic and energetic alterations that often lead to a poor prognosis [3, 6].

In the United States, reports suggest that 80% of cancer patients develop cachexia, and 20% of cancer deaths are due to cachexia syndrome [7–9]. Cancer is prevalent in 0.5% of the European population, and of patients diagnosed with cancer, 90% are at risk of developing cachexia, while for patients at risk, 30% develop the cachectic syndrome, which is equivalent to one million people, leading to a mortality

rate of 20%–60% in 1 year [10]. In addition to this, studies have observed that male patients experience greater weight loss, muscle wasting, reduction of grip strength, and loss of functionality compared with female cancer patients, providing evidence for developmental gender differences in cancer cachexia [11–13].

Given the aforementioned, a cachexia classification system would be beneficial not only for measuring the severity of the syndrome but also for choosing the best course of treatment [14]. The Cachexia Score (CASCO), which classified cachexia quantitatively according to the severity of the syndrome, was proposed in 2011 by Argilés et al. [14]. Subsequently, an abbreviated version, called miniCASCO, was proposed, which contains the five dimensions of the original CASCO tool, with a high correlation ($r=0.964$) between both instruments, and facilitates the classification of the cachectic syndrome stage in cancer patients [14, 15].

Among the treatments for cachexia, one can find diet, pharmacological treatment, and exercise [16]. Regarding exercise, there is no difference between cancer patients with and without cachexia, nor is there a difference between the different stages of cachexia, since there are few tools to correctly diagnose the problem [17].

Taking into account the mortality rates of cachexia, it is necessary to determine its prevalence and severity in cancer patients, characterize its presence, and be able to guide early treatments that positively impact patients' prognosis and quality of life.

2. Materials and Methods

This research was reviewed and approved by the Scientific Ethics Committee of the Catholic University of Maule and the Maule Health Service (folio AE N°007), with the informed consent of all participants.

A cross-sectional, descriptive, observational study was conducted. Eighty-six patients of both sexes aged 18 to 60, inpatients and outpatients, from the cancer service of the Regional Hospital of Talca, took part between November 2019 and January 2020. However, the sample size was not probabilistic for patients admitted to the cancer care unit. The flow of the recruitment process is detailed in Figure 1.

A first evaluator reviewed the clinical record to obtain data on the type of cancer, tumour stage, and blood parameters. A second evaluator asked the questions from the miniCASCO scale. The same evaluator obtained the height with a stadiometer and the weight, BMI, and percentage of lean and fat mass using a bioimpedance meter (Omron BHF-514). A third blinded rater recorded and subsequently analysed the data.

The inclusion criteria were as follows: patients between 18 and 60 with a diagnosis of solid cancer and available clinical history. The exclusion criteria included pathologies associated with cachexia, diagnosis of nutritional disorders, immobilisation syndrome, pain in the lower extremities, and difficulty standing.

The CASCO tool was validated by Argilés et al., in Cagliari, Italy, between 2011 and 2014 [15]. The tool consists of five items to determine the presence and degree of

cachexia in cancer patients. The first component measures the loss of body weight and lean mass through the difference between the initial weight obtained from the clinical record and a measurement made during the evaluation. The second measures the presence of inflammation, metabolic alterations, and immunosuppression through the review of laboratory tests. The third assesses physical performance through a physical performance questionnaire. The fourth assesses anorexia through the Simplified Nutrition Assessment Questionnaire and, finally, the fifth item is related to quality of life, which is measured with 25 questions from EORTC QLQ-C30 [18].

A simplified version of the CASCO, the miniCASCO (MCASCO), was designed to avoid an excessive number of clinical measurements, which may be unavailable in some medical centres [15]. The MCASCO consisted of the same five components as mentioned above, but divided into three sections: (1) body weight change (BWC) and lean body mass loss; (2) inflammation/metabolic disturbances/immunosuppression (IMD) (measurement of CRP, plasma albumin levels, and absolute lymphocyte number); and (3) questionnaires: two questions regarding physical performance, two questions regarding anorexia, and 11 questions about the quality of life [15] (for more details on the miniCASCO tool, see <https://www.ub.edu/cancerresearchgroup/>). For the weight and lean mass assessment item, an Omron BHF-514 bioimpedance meter, BMI, was used, while a stadiometer was used to measure the patient's height.

2.1. Statistical Analysis. The information on each patient was anonymously input into a database of GraphPad Prism 8.0.2 software for Windows 10. Normality tests were run for the data using the Shapiro–Wilk test. Student's *t*-test was used for parametric statistics, and the Mann–Whitney and Wilcoxon signed-rank tests were used for nonparametric data, showing the median and interquartile ranges (first and third quartiles). Statistical significance was considered at $p < 0.05$. Pearson's correlation was used considering a significant difference of $p < 0.05$. The point prevalence of the population with cachexia secondary to cancer was used to determine the prevalence in inpatients, which was the number of existing or prevalent inpatient cases at a given time [19].

3. Results and Discussion

Of a total of 86 patients evaluated, 25 had some of the exclusion criteria and 21 did not have the data requested by the miniCASCO tool. The study included 14 men (mean age 49 ± 14.6 years) and 26 women (mean age 50 ± 7.7 years). The weights recorded for men and women were 74.45 ± 16.08 and 70.97 ± 10.45 kilos, respectively, without significant differences between the two. However, the women had a statistically significant increase in BMI compared to men (28.8 ± 6.2 kg/m² and 23.8 ± 3.5 kg/m²; $p < 0.05$, respectively). Although weight did not decrease significantly in men, patients should be reviewed individually because when reviewing the score of the other

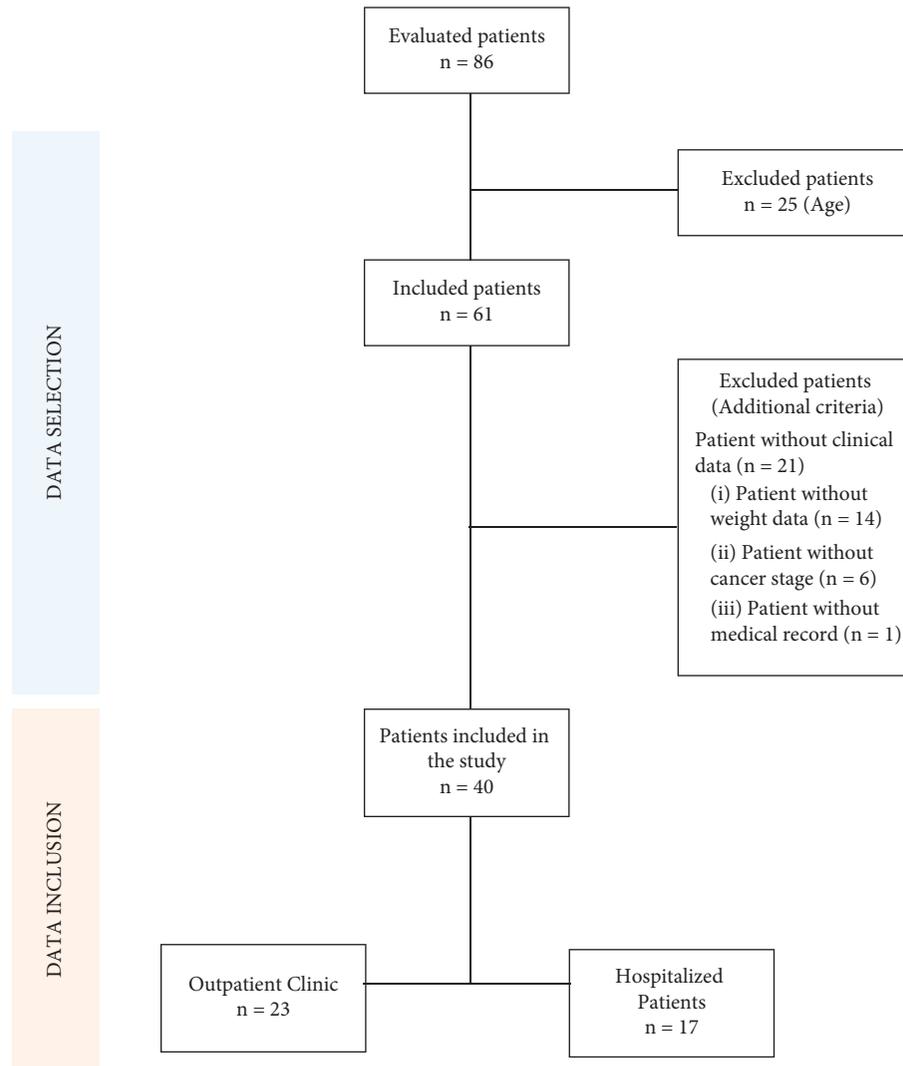


FIGURE 1: Study patient selection flowchart—the study began with the assessment of 86 cancer patients, and the selection process allowed the inclusion of 40 patients in the study.

miniCASCO components, some men could still have cachexia.

The types of cancer that patients had are described in Table 1.

When analysing the cancer stage of the evaluated patients, 45% are in stage III. The cancer stages by gender are shown in Table 2.

In this study, there were no statistically significant differences in weight loss ($p = 0.2881$), inflammation ($p = 0.3683$) (Table 3), physical performance ($p = 0.0808$), anorexia ($p = 0.1708$), and quality of life ($p = 0.2470$) when comparing scores across the 4 stages of cancer (Table 4) (statistical analysis performed using the Kruskal-Wallis test).

According to the scores obtained using the miniCASCO tool, 27.5% of the patients who entered the study presented cachexia. Within the group that presented the syndrome, mild cachexia was the most prevalent (45.45%), followed by severe cachexia (36.36%), and finally moderate cachexia (18.18%). When analysing the results, it was found that the

final miniCASCO score correlated significantly with the cancer stage ($r = 0.6847$; $p = 0.0201$) (Figure 2). According to the miniCASCO categorisation, cachexia occurred in 21.43% and 30.77% of men and women diagnosed with cancer, respectively. However, no statistically significant differences were found in the miniCASCO scores between the two genders ($p = 0.2752$). As a way of reconciling the miniCASCO scores with the patients' weight loss, the participants were divided into two groups: patients with stages I and II cancer and patients with stages III and IV cancer. For patients with stages I-II cancer, the correlation between the miniCASCO score and weight loss was $r = 0.2248$ ($p = 0.7162$), and for stages III-IV patients, it was $r = 0.7755$ ($p = 0.06$).

In this research, it was possible to estimate a point prevalence of 27.5% of cancer cachexia, a result consistent with that presented in the study by Peterson et al. [20], who mentioned a range between 15% and 60%. However, in other studies, the presence of sarcopenia has also been reported in 15% to 50% of older patients (mean 63.7 years), while

TABLE 1: Distribution of the type of cancer by gender.

Type of cancer	Men	Women	Total
Breast cancer	0	12	12 (30%)
Testicular cancer	4	0	4 (10%)
Colon cancer	1	2	3 (7.5%)
Rectal cancer	3	0	3 (7.5%)
Uterine sarcoma	0	1	1 (2.5%)
Gastric cancer	3	0	3 (7.5%)
Ovarian cancer	0	2	2 (5%)
Anal cancer	1	0	1 (2.5%)
Pancreatic cancer	0	1	1 (2.5%)
Adrenal carcinoma	0	1	1 (2.5%)
Endometrial cancer	0	1	1 (2.5%)
Cervical cancer	0	1	1 (2.5%)
Maxillary sinus cancer	1	1	2 (5%)
Gastrointestinal stroma	0	1	1 (2.5%)
Under study	1	3	4 (10%)
	14 (35%)	26 (65%)	40 (100%)

Absolute values are cancer, and the relative percentage with respect to total number of patients is given in parentheses. In bold the total sum is shown in absolute value and in parentheses the relative value, with respect to the total number of patients in the study.

TABLE 2: The absolute values for men and women are presented by the stage of cancer.

	Men	Women	Total
Stage I	2 (5%)	1 (2.5%)	3 (7.5%)
Stage II	4 (10%)	8 (20%)	12 (30%)
Stage III	5 (12.5%)	13 (32.5%)	18 (45%)
Stage IV	3 (7.5%)	3 (7.5%)	6 (15%)
Unclassified	0 (0%)	1 (2.5%)	1 (2.5%)
Total	14 (35%)	26 (65%)	40 (100%)

The relative percentage with respect to total number of patients is given in parentheses.

TABLE 3: The weights recorded in the clinical record and the weight at the time of evaluation (average + SD) are presented. (IMD) The number of men and women who were classified with CRP, inflammation, and metabolic disturbances by miniCASCO is also presented.

Body weight change (BWC)			
	Men	Women	
Initial weight	70.97 ± 10.45	74.45 ± 16.08	
Final weight	70.56 ± 9.9	70.84 ± 15.08	
<i>Inflammation/Metabolic Disturbances/Immunosuppression (IMD)</i>			
	Interval	Men (n)	Women (n)
C-reactive protein (CRP)	5 mg/L < CRP < 10 mg/L	9	18
	10 mg/L < CRP < 20 mg/L	5	8
	CRP > 20 mg/L	—	—
	Not tested or CRP < 5 mg/L	—	—
Metabolic disturbances	Plasma albumin < 3.2 g/dL	11	11
	Anaemia: Hb < 12 g/dL	3	12
	Both	—	3
Absolute lymphocyte number (ALN)	Normal	11	19
	ALN < 1200/μL	3	7

cachexia syndrome is present in 25% to 80% of patients of the same age [20–22]. Sarcopenia is defined as a loss of muscle mass and function associated with aging, generally present in patients older than 60 years [23]. On the other hand, cachexia is defined as weight loss due to an underlying disease such as cancer [23]. Sarcopenia and cachexia are

different muscle wasting disorders, and they can be easily confused. Sarcopenia and cachexia are physiopathologically different syndromes, but they could coexist in the same individual, generating similar physical consequences. It is important that researchers consider these variables, which can lead to confusion and bias the results. This shows the

TABLE 4: Results obtained in miniCASCO questionnaires.

Physical performance (PHP) questions	0: not at all		1: a little		2: quite a bit		3: very much			
	Men (n)	Women (n)	Men (n)	Women (n)	Men (n)	Women (n)	Men (n)	Women (n)		
Did you have to put more effort into climbing stairs? Have you felt tired after walking approximately half a kilometer?	5	6	7	11	—	2	1	3		
	5	6	4	9	—	4	1	3		
<i>Quality of Life (QoL) Questions</i>										
	0: not at all		1: a little		2: quite a bit		3: very much			
	Men (n)	Women (n)	Men (n)	Women (n)	Men (n)	Women (n)	Men (n)	Women (n)		
Do you need to stay in bed or on a chair during the day?	7		2	7	3	3	2	4		
Were you limited in doing either your work or other daily activities?	5	2	4	5	3	3	2	4		
Were you limited in pursuing your hobbies or other leisure time activities?	9	3	2	4	2	2	1	5		
Have you had pain?	8	4	4	1	2	2	2	7		
Did you need to rest?	5	4	5	3	2	2	1	5		
Did you feel weak?	6	5	3	4	4	1	4	2		
Did pain interfere with your daily activities?	7	5	6	5	1	2	2	4		
Have you had difficulty concentrating on things, like reading a newspaper or watching television?	4	4	6	3	2	3	2	4		
Has your physical condition or medical treatment interfered with your family life?	8	5	6	4	6	4	1	1		
	Excellent		Fine		Poor		Very poor			
How would you rate your overall health during the past week?			10	7	4	4		2		
How do you rate your overall quality of life during the past week?			11	3	3	4		2		
<i>Anorexia (ANO) Questions</i>										
	0: very poor		1: poor		2: average		3: good		4: very good	
	Men (n)	Women (n)	Men (n)	Women (n)	Men (n)	Women (n)	Men (n)	Women (n)	Men (n)	Women (n)
My appetite is										
When I eat	6	6	2	10	2	3	9	5	1	8
I feel full after eating only a few mouthfuls			2	10		3				
I feel full after eating about a third of a meal										
I feel full after eating over half a meal										
I feel full after eating most of the meal										
I hardly ever feel full										
Men (n)	6	6	2	10	2	3	9	5	1	8
Women (n)	6	6	2	10	2	3	9	5	1	8
Men (n)	6	6	2	10	2	3	9	5	1	8
Women (n)	6	6	2	10	2	3	9	5	1	8

PHP-QoL-ANO tables: they indicate the number of responses by patients and by gender. Each response receives a certain score that, when added together, indicates the degree of cachexia of the patient. (For more details, contact the CASCO/miniCASCO/CASC-IN developer at <https://www.ub.edu/cancerresearchgroup/>).

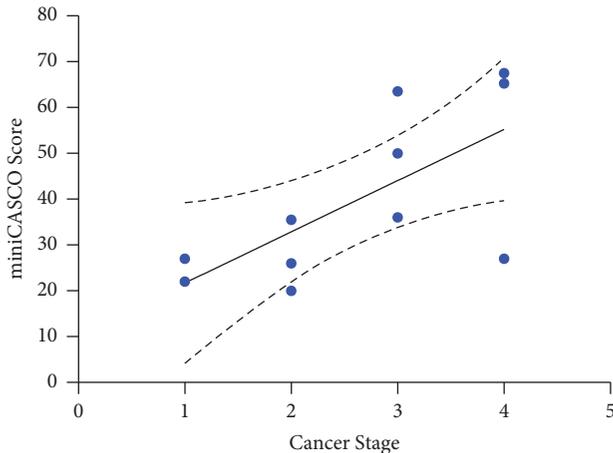


FIGURE 2: The final score of the miniCASCO tool according to the stage of cancer. A positive moderate-high correlation is presented between both variables (Pearson's correlation $r = 0.6847$; $p = 0.0201$).

importance of considering an age limit as a criterion when investigating the presence of cachexia, given the lack of tools that allow a clinical distinction to be made between the two syndromes. On the other hand, several studies have reported a greater loss of muscle mass in men than in women [13]. Baracos et al. 2010, through computed tomography, observed greater decreases in muscle mass of 61% and 31% in men than in women, respectively. Similarly, Wallengren et al. recorded a greater decrease in muscle mass in men (59%) than in women (28%). These findings are consistent with other results obtained in patients with cachexia, where the loss of grip strength, strength in general, and muscle power in the lower extremities are more present in men than in women with cachexia secondary to cancer [11, 25]. Nevertheless, these results should be viewed with caution, since they include patients over 60, where sarcopenia associated with aging is present and is a factor that would also influence weight loss. This study did not find statistically significant differences in the miniCASCO scores between men and women ($p = 0.2752$). However, in contrast to previous studies, there was a higher prevalence of cachexia in women than in men, possibly due to the characteristics of the sample. Possibly, future studies with a larger number of patients may provide a better picture of gender differences and the presence of cachexia.

In all, 42.5% of the selected patients were hospitalised in the oncology service, a fact that is important to consider in terms of the impact of hospitalisation time and costs for patients. It is stated that in the United States, for example, the average hospitalisation for cachectic patients is 6 days, with an average expense of 10,000 dollars, compared to noncachectic cancer patients, who stayed 3 days in the hospital at an expense of 6,000 dollars [9]. Therefore, finding cachectic patients would allow an early approach and a reduction in health services [10].

When comparing weight loss between the different stages of cancer, no statistically significant differences were found. When correlating the miniCASCO score with weight

loss, for stages I-II cancer, a weak and nonsignificant correlation was obtained. However, for stages III-IV, there was a greater correlation between the miniCASCO score and weight loss ($r = 0.7755$), although given the number of patients, significance levels were not reached ($p = 0.06$). A larger sample of patients could more clearly link weight loss with the presence of cachexia in cancer stages III-IV. The types of cancer with the highest presence of cachexia are pancreatic, gastric, and oesophageal cancer, and at the moment of diagnosis, 80% of patients with upper gastrointestinal cancers have already experienced substantial weight loss ($n = 390$) [26]. In fact, 40% of people say they had unexplained weight loss when they were first diagnosed with cancer [27]. According to the literature, 80% of people with advanced cancer have weight loss and cachexia, which generally coincides with the results of this study, where there were six patients at an advanced stage, and 50% of them had cachexia according to the miniCASCO [27].

The data in this study show an upward trend in the inflammatory parameter score as the cancer stage progresses, although future studies could shed light on a possible relationship. In patients with cachexia, there is an association between average survival with albumin and CRP levels, with the survival of patients with high concentrations of CRP decreasing considerably, compared to cachectic groups with values below 10 mg/L in patients with pancreatic cancer [28, 29]. In addition, values above 15 mg/L have been found to have a 2.2-fold higher risk of mortality in advanced stage cancer patients [30]. With albumin, levels are mentioned as remaining normal in the early stages of cancer. However, hypoalbuminemia occurs in the advanced stages, determining that this biomarker becomes relevant in the prognosis of gastrointestinal, lung, breast, and ovarian cancer [29, 31].

Regarding the score in the physical performance component (two questions on the miniCASCO), although there is an upward trend in the scores, there were no significant differences between the different stages of cancer. The literature mentions that the decrease in lean mass and muscle strength is directly related to a decrease in walking performance and therefore in the functionality of the patient [32]. Similarly, weight loss is associated with respiratory muscle fatigue and inactivity, which further contributes to reduction of the patient's functional capacity [33].

Regarding the anorexia component (two questions on the miniCASCO), the highest scores were presented in stages III-IV patients, consistent with decreased appetite, decreased food intake, and the presence of nausea, vomiting, mucositis, constipation, diarrhoea, and early satiety as a secondary effect of the different treatments [34, 35].

In the quality-of-life component (11 questions on the miniCASCO), there were no significant differences between cancer stages, but there is evidence showing a feeling of discomfort and anxiety in patients with more advanced cachexia [36], which could be related to altered food intake and appetite or a consequence of treatments such as chemotherapy [37].

The study obtained a moderate/high and statistically significant correlation ($r = 0.7209$; $p = 0.0150$) between the

miniCASCO score and the state of disease progression, values that were used as a method of concurrent validation of the research. The correlation value obtained in this study would agree with previous studies, where the cancer stage would be a factor that, together with others, would interact to positively influence the presence and progress of the cachectic syndrome [16, 38]. If the miniCASCO components are analysed individually, no statistically significant differences are found, but if considered together, they give a sample of the patient's current state of cachexia.

There is an interaction of various factors in the onset and progress of cachexia. The type of cancer is a good predictor of weight loss in patients; however, the type of cancer takes a secondary role if the patient loses a lot of weight [39]. The increase in systemic inflammation parameters is possibly the most relevant factor in the onset of cachexia. Systemic inflammation leads to an increase in the energy demand of the tissues and consequently, a high basal metabolic rate. On the other hand, there is a decrease in food intake due to a variety of symptoms typical of cancer, such as pain, nausea, vomiting, diarrhoea, or a decrease in satiety caused by the inflammation process. The increase in energy demand and the decrease in intake lead to a change in body composition with loss of muscle mass, ultimately manifesting in a decrease in the BMI and physical performance [40]. The interaction of various factors results in the progression of cachexia over time, which is demonstrated in our study, with the strong correlation that exists between the miniCASCO score and the cancer stage.

Although 72.5% of the participants were not considered cachectic according to the miniCASCO, the results must be interpreted carefully, as a significant proportion of the patients were below the score limit that would qualify them as having cachexia. Given the characteristics of the syndrome and the progress of the disease, this group of patients may be cachectic in the future. Taking into account patients who do not have cachexia according to the miniCASCO tool, 75% obtained a score close to 14 points, so regardless of whether they have weight loss or not, they could experience progression of the syndrome before weight loss occurs. This point is relevant, given that there is an increase from 27.5% classified by the tool to 75% of patients with an incipient cachectic process who have not yet been found by the miniCASCO tool. Patients who are not yet cachectic but who are advancing in the syndrome are in the precachexia stage, and early diagnosis is important for them, since they may be the target of multimodal intervention trials; hence, a clear and easy-to-use diagnostic tool is needed [41]. In response to this problem, the CASC-IN was created as a validated tool using a brief questionnaire, inflammatory parameters, and weight loss to discriminate precachectic and cachectic patients [41]. It is expected that it can be validated in the Chilean context as a complement to the miniCASCO.

The detection of cachectic syndrome in cancer patients allows an early approach through pharmacological and

nutritional strategies. However, physical treatment has been suggested to regulate muscle anabolism and improve energy metabolism and insulin sensitivity and thus prevent progression of the syndrome [42, 43]. Physical exercise in cachectic patients is suggested to preserve muscle mass, decrease inflammation, reduce depressive symptoms, and increase anabolic hormones such as IGF-1 and also helps to increase appetite in patients [6, 43, 44].

Consistent with this, using a resistance training program, significant improvements were obtained in the 6-minute walk test and the sit-stand test, and the lean mass of the lower extremities, as well as knee extensor strength, were increased, realizing that three months of training in patients with cachexia induced by pancreatic cancer led to a delay in the appearance and progression of cachexia in cancer patients, represented by an increase in lean mass compared to the control group [45]. Within the same scope, Rogers et al. demonstrated that the application of progressive resistance training to counteract the loss of fat and muscle mass was feasible and highly acceptable for cancer patients [46].

To date, no publications have been found in Chile that focuses on cachexia, so this study aims to provide a basis for future research in the area. In Chile, no public health policies have been found that mention cachexia as an important prognostic factor in cancer treatment; therefore, there is no strategy to counteract its effects, which could have repercussions on the patient's evolution.

4. Conclusions

This study reports for the first time the prevalence of cachectic patients in a hospital setting in Chile. The results obtained by miniCASCO support the clinical approach and its main cachexia identification points, through its different elements, allowing easy and rapid screening for the professional who applies it.

For this reason, it is considered essential to emphasise the evolution of these patients who remain outside the diagnosis according to miniCASCO, giving them the opportunity for early intervention that allows avoidance of syndrome progression.

Data Availability

Cachexia scoring data used to support the findings of this study are available upon request from the author; however, request is subject to Ethics Committee clearance.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

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