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Trabajo Original

Obesidad y síndrome metabólico

Incidence of high body mass index in critically ill cancer patients

Incidencia de índice de masa corporal elevado en pacientes con cáncer críticamente enfermos

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Abstract

Objective: The aims of this study were to describe the incidence of obesity and overweight in critically ill cancer patients, and to evaluate the clinical characteristics and Intensive Care Unit (ICU) outcomes of critically ill cancer patients with obesity and overweight.

Methods: An observational cohort study. There were no interventions.

Results: During the study period, 483 critically ill cancer patients were admitted to ICU, and 59.2% of them (258 patients) had high body mass index (BMI). Comparing the groups of patients with BMI < 25 kg/m^2 and ≥ 25 kg/m^2, we observed that those with BMI ≥ 25 kg/m^2 were older at the time of admission to the ICU. The global mortality in ICU was of 22.4%. ICU mortality was similar between patients with BMI < 25 kg/m^2 and ≥ 25 kg/m^2 (21.3% *versus* 23.0%, p = 0.649). Univariate analysis indicated that the following five factors were associated with ICU death in patients with BMI ≥ 25 kg/m^2 as the outcome variable of interest: age, sepsis, invasive mechanical ventilation, type 2 diabetes, ≥ two organ failures. Multivariate analysis identified ≥ two organ failures as independent prognostic factor of ICU death.

Conclusion: Critically ill cancer patients have a high incidence of high BMI; approximately six of every ten patients admitted to the ICU with a serious condition are overweight or show several degrees of obesity. The ICU mortality of the patients with a body mass index < 25 kg/m^2 and ≥ 25 kg/m^2 was similar. The independent prognostic factor of ICU death in critically ill patients with a BMI ≥ 25 kg/m^2 was the number of organ dysfunctions, especially when two or more organs were affected.

Key words:

Incidence. High body mass index. Critically ill cancer patients. Intensive Care Unit. Obesity. Outcomes.

Resumen

Objetivo: Describir la incidencia de obesidad y sobrepeso en pacientes graves con cáncer y evaluar las características clínicas y el pronóstico de los pacientes oncológicos gravemente enfermos con sobrepeso y obesidad.

Métodos: Estudio observacional y descriptivo. No se realizó ninguna intervención.

Resultados: Durante el periodo de estudio, 483 pacientes graves con cáncer fueron ingresados a la unidad de cuidados intensivos (UCI); el 59.2% (258 pacientes) tuvo índice de masa corporal (IMC) elevado. Al comparar los pacientes con IMC < 25 kg/m^2 y con IMC ≥ 25 kg/m^2, se observó que los pacientes con IMC ≥ 25 kg/m^2 eran de mayor edad al momento de ingresar en la UCI. La mortalidad en la UCI fue del 22.4%. La mortalidad fue similar en los grupos con IMC < 25 kg/m^2 y ≥ 25 kg/m^2 (21.3% *versus* 23.0%, p = 0.649). El análisis multivariado determinó que las siguientes variables fueron asociadas con muerte en la UCI en el grupo de pacientes con IMC ≥ 25 kg/m^2: edad, sepsis, ventilación mecánica invasiva, diabetes mellitus tipo 2 y cursar con dos o más fallas orgánicas. El análisis multivariado identificó como factor pronóstico independiente para muerte en la UCI cursar con dos o más fallas orgánicas.

Conclusión: los pacientes graves con cáncer tienen una alta incidencia de IMC elevado; aproximadamente seis de cada diez pacientes ingresados en la UCI con una condición que pone en peligro la vida tienen sobrepeso o son obesos. La mortalidad fue similar en los grupos con IMC < 25 kg/m^2 y ≥ 25 kg/m^2. En el grupo de pacientes con IMC ≥ 25 kg/m^2 se identificó como factor pronóstico independiente para muerte en UCI el número de fallas orgánicas especialmente cuando dos o más órganos están afectados.

Palabras clave:

Incidencia. Índice de masa corporal elevado. Paciente grave con cáncer. Unidad de Cuidados Intensivos. Obesidad. Pronóstico.

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INTRODUCTION

Overweight is defined as a body mass index (BMI) from 25 to 29.9 kg/m^2 and obesity, as a BMI higher than 30 mg/m^2 (1,2). Worldwide, obesity has doubled since 1980, and in 2014 more than 1.9 billions of adults over 18 years were overweight, more than 600 million of whom are obese (1,2). In 2012, the national health survey reported that 73% of women and 69.4% of men in Mexico have some degree of obesity or overweight (3). Currently, high BMI is considered as a major health problem that is associated directly with high mortality and serves as a trigger to develop cardiovascular, metabolic, musculoskeletal and oncologic diseases (4,5). According to data from the Institute for Health Metrics and Evaluation (IMHE) for 2010, 70% of the adult population over 20 years had some degree of obesity or overweight (6). Obesity and overweight are considered as chronic inflammatory processes with consequent changes in immune response of acute events, such as sepsis (7-12). It has been reported that obesity is associated with 20% in women and 14% in men of all causes of death of oncologic patients (13), and obesity is considered to be a factor related to the development of multiple neoplasia (10). However, in the context of critically ill oncologic patients with high BMI, the impact on mortality is unknown. Different reports have described that in patients with sepsis and septic shock, obesity is a protective factor against death (14-18).

The purpose of this study was to describe the incidence of obesity and overweight in critically ill cancer patients, and to evaluate the clinical characteristics and Intensive Care Unit (ICU) outcomes of critically ill cancer patients with obesity and overweight.

METHODS

This prospective, observational cohort study was performed at the Instituto Nacional de Cancerología (INCan) located in Mexico City. We included all consecutive critically ill cancer patients admitted to the ICU during the period between January 2013 and April 2015. Critically ill cancer patients over 18 years of age with more than 12 hours of stay in the ICU were included. We registered the demographic, clinical and laboratory data of the patients during their stay in the ICU, including age, gender, weight at admission to ICU, size, oncologic disease, comorbidities, organic support requirement, days of ICU stay, days of invasive mechanical ventilation, sepsis and mortality in the ICU. Sepsis was defined according to the Third International Consensus Definitions for Sepsis and Septic Shock (19). We calculated the Acute Physiology and Chronic Health Evaluation (APACHE) II score (20) during the first 24 hours of ICU stay; Sequential Organ Failure Assessment (SOFA) (21,22) and the Mexican sequential organ failure assessment (MEXSOFA) scores (23) for the evaluation of organic failures were also calculated. The APACHE II, SOFA and MEXSOFA scores were calculated with the worst clinical and laboratory values during the first 24 hours of ICU stay. We calculated the BMI with the weight and size recorded at the time of the acute event for which the patient admitted to the ICU, and data were stratified according to the criteria of the World Health Organization and the Mexican Official Standard (*Norma Oficial Mexicana,* NOM-008-SSA3-2010) for the treatment of overweight and obesity. BMI was categorized as < 25 kg/m^2 and ≥ 25 kg/m^2. Performance status was measured using the Eastern Cooperative Oncology Group performance status scale (24):

- 0: fully active, able to carry on all pre-disease performance without restriction.
- 1: restricted in physically strenuous activity but ambulatory and able to carry out.
- 2: ambulatory and capable of all self-care but unable to carry out any work activities; up and about more than 50% of waking hours work of a light or sedentary nature (e.g., light house work, office work).
- 3: capable of only limited self-care, confined to bed or chair more than 50% of waking hours.
- 4: completely disabled; cannot carry on any self-care; totally confined to bed or chair.

The Bioethics Committee of INCan approved this study, and the need for informed consent was waived.

Descriptive statistics were used for the data presentation. The Kolmogorov-Smirnov test was performed to determine the distribution of the data. Numerical variables are expressed as the mean and standard deviation, or as median values with their respective interquartile range for the variables with normal distribution. The categorical or nominal variables are expressed as a percentage. To compare the continuous variables, we used Student's t test or Mann-Whitney U test according to the sample distribution. For the analysis of the categorical variables, the χ^2 test was used. Survival curves were constructed using the Kaplan-Meier method, and compared with the log-rank method. Univariate and multivariate logistic regressions were used to identify factors associated with hospital mortality. Variables with a $p < 0.2$ in the univariate analysis were entered into the model using a forward stepwise procedure. The results were summarized as odds ratios (ORs) and respective 95% confidence intervals (CI). The area under the receiver operating characteristic curve was used to evaluate the ability of the model to discriminate between patients who lived and those who died (discrimination). Goodness-of-fit (Hosmer-Lemeshow) was calculated to assess the relevance of the logistic regression model. In all cases, a p value of < 0.005 was considered as statistically significant. SPSS 22.0 was used.

RESULTS

During the study period, 483 critically ill cancer patients were admitted to the ICU; 59.2% (258 patients) had high BMI. The mean age was 48.4 ± 16.6 years, and 53.2% of the patients were women. One hundred and twenty-one ICU admissions (25.1%) were due to septic shock. The second most common cause for ICU admission was acute respiratory failure, with 82 (17.2%) ICU admissions, and all of those patients required mechanical ventilation. Table I shows the clinical characteristics of the patients on admission to the ICU.

Table I. Clinical characteristics of patients on ICU admission

Characteristics	Results
Age, years (mean ± SD)	48.4 ± 16.6
Gender (female), n (%)	257 (53.2)
Body mass index (BMI), (median with IQR)	26.1 (22.7-29.1)
≥ 25 kg/m^2, n (%)	286 (59.2)
< 25 kg/m^2, n (%)	197 (40.8)
Low weight (BMI ≤ 18.5 kg/m^2), n (%)	16 (3.3)
Normal weight (18.5-24.99 kg/m^2), n (%)	181 (37.5)
Overweight (25-29.99 kg/m^2), n (%)	192 (39.8)
Obesity (30-39.99 kg/m^2), n (%)	82 (17.1)
Morbid obesity (≥ 40), n (%)	12 (2.5)
Admission source	
Operating room, n (%)	235 (48.7)
Medical wards, n (%)	222 (46)
Emergency department, n (%)	26 (5.4)
Scoring systems	
APACHE (median with IQR)	16 (12-21)
MEXSOFA (median with IQR)	7 (4-10)
SOFA (median with IQR)	6 (3-9)
Type of oncologic disease	
Solid tumors, n (%)	354 (73.3)
Hematologic malignancy, n (%)	129 (26.7)
Comorbidities	
Systemic arterial hypertension, n (%)	88 (18.8)
Type 2 diabetes mellitus, n (%)	84 (17.4)
Stroke, n (%)	18 (3.7)
Pulmonary thromboembolism, n (%)	15 (3.1)
Sepsis, n (%)	157 (32.5)
ICU treatment	
Mechanical ventilation requirement, n (%)	316 (65.4)
Hemodialysis requirement, n (%)	7 (1.4)
Vasopressor requirement, n (%)	280 (58)
Organ failures	
Number of organ failures at admission	
≤ 2, n (%)	383 (79.3)
> 2, n (%)	100 (20.7)
Hemodynamic failure, n (%)	280 (58)
Respiratory failure, n (%)	273 (56.5)
Hematologic failure, n (%)	90 (18.6)
Renal failure, n (%)	79 (16.4)
Hepatic failure, n (%)	15 (3.1)
Performance status	
0-2, n (%)	403 (83.4)
3-4, n (%)	80 (16.6)
Days of ICU stay, (median, IQR)	3 (1-3)
Days on mechanical ventilation, (median, IQR)	4 (1-7)
ICU mortality, n (%)	108 (22.4)
Hospital mortality, n (%)	158 (32.7)

SD: Standard deviation; IQR: Interquartile range; SOFA: Sequential Organ Failure Assessment; APACHE: Acute Physiology and Chronic Health Evaluation; MEXSOFA: Mexican Sequential Organ failure Assessment; ICU: Intensive Care Unit. Performance status was measured using the Eastern Cooperative Oncology Group performance status scale as follows: 0: fully active, able to carry on all pre-disease performance without restriction; 1: restricted in physically strenuous activity but ambulatory and able to carry out; 2: ambulatory and capable of all self-care but unable to carry out any work activities; up and about more than 50% of waking hours work of a light or sedentary nature (e.g., light house work, office work); 3: capable of only limited self-care, confined to bed or chair more than 50% of waking hours; 4: completely disabled; cannot carry on any self-care; totally confined to bed or chair (24).

Comparing the groups of patients with BMI < 25 kg/m^2 and ≥ 25 kg/m^2, we observed that those with BMI ≥ 25 kg/m^2 were older at the time of admission to the ICU (Table II). Patients with BMI ≥ 25 kg/m^2 had a tendency to require longer invasive mechanical ventilation. The global mortality in ICU was of 22.4%. ICU mortality was similar between patients with BMI < 25 kg/m^2 and ≥ 25 kg/m^2 (21.3% *versus* 23.0%, p = 0.649) (Table II). Figure 1 shows the survival curves during the hospital stay of patients with BMI < 25 kg/m^2 and ≥ 25 kg/m^2.

When comparing patients with ≤ 2 and ≥ 3 organ failures, in the group of BMI ≥ 25 kg/m^2, we observed a higher mortality in patients with ≥ 3 organ failures at the time of ICU admission (15.5% [36/231] *versus* 54.5% [30/55], p < 0.001).

Univariate analysis indicated that the following five factors were associated with ICU death in patients with BMI ≥ 25 kg/m^2 as the outcome variable of interest: age, sepsis, invasive mechanical ventilation, type 2 diabetes, ≥ two organ failures (Table III). Multivariate analysis identified ≥ 2 organ failures as independent prognostic factor of ICU death (Table III).

DISCUSSION

The main findings of the present study were as follow:

1. The incidence of high BMI was 59.2%.
2. The group of patients with BMI ≥ 25 kg/m^2 were older, and required long-term mechanical ventilation.
3. The ICU mortality of patients with BMI < 25 kg/m^2 and ≥ 25 kg/m^2 was similar. The ICU mortality in critically ill patients with a BMI ≥25 kg/m^2 depends primarily on the number of organ failures, especially when two or more organs are affected.

The incidence of high BMI in patients enrolled in the present study was higher than those described by other authors, who have report-

Table II. Comparison of clinical features of critically ill cancer patients according to body mass index

Characteristics	BMI < 25 kg/m^2 n = 197	IMC ≥ 25 kg/m^2 n = 286	p
Age (mean ± SD)	45.5 ± 17.5	50.5 ± 15.7	0.001
Gender			
Female, n (%)	101 (51.2%)	156 (54.5%)	0.478
Performance status			
0-2, n (%)	161 (81.7%)	242 (84.6%)	0.401
3-4, n (%)	36 (18.2%)	44 (15.3%)	
Scoring systems			
APACHE (median, IQR)	16 (12-22)	16 (11-21)	0.323
MEXSOFA (median, IQR)	7 (4-10)	7 (4-10)	0.586
SOFA (median, IQR)	6 (3-9)	6.5 (3-9)	0.810
Length of stay in ICU (median, IQR)	3 (1-6)	3 (1-7)	0.900
Days on mechanical ventilation (median, IQR)	3 (1-6)	4 (1-8)	0.122
Number of organ failures:			
≤ 2, n (%)	152 (77.1)	231 (80.7)	0.336
> 2, n (%)	45 (22.8)	55 (19.2)	
Hemodynamic failure, n (%)	123 (62.4)	157 (54.8)	0.099
Respiratory failure, n (%)	108 (54.8)	165 (157.6)	0.532
Hematologic failure, n (%)	40 (20.3)	50 (17.4)	0.434
Renal failure, n (%)	33 (16.7)	46 (16)	0.845
Hepatic failure, n (%)	5 (2.5)	10 (3.4)	0.551
Sepsis, n (%)	64 (32.4)	93 (32.5)	0.994
Mechanical ventilation requirement	127 (64.4)	189 (66)	0.713
ICU mortality, n (%)	42 (21.3)	66 (23)	0.649
Hospital mortality, n (%)	69 (35)	89 (31)	0.387

DS: Standard deviation; IQR: Interquartile range; SOFA: Sequential Organ Failure Assessment; APACHE: Acute Physiology and Chronic Health Evaluation; MEXSOFA: Mexican Sequential Organ Failure Assessment; ICU: Intensive Care Unit. Performance status was measured using the Eastern Cooperative Oncology Group performance status scale as follows: 0: fully active, able to carry on all pre-disease performance without restriction; 1: restricted in physically strenuous activity but ambulatory and able to carry out; 2: ambulatory and capable of all self-care but unable to carry out any work activities; up and about more than 50% of waking hours work of a light or sedentary nature (e.g., light house work, office work); 3: capable of only limited self-care, confined to bed or chair more than 50% of waking hours; 4: completely disabled; cannot carry on any selfcare; totally confined to bed or chair (24).

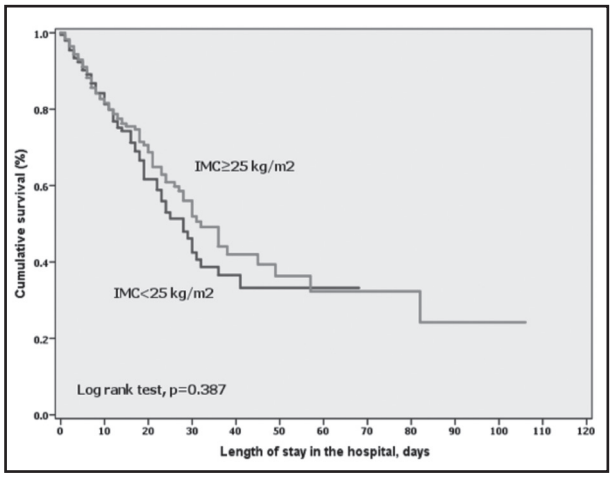

Figure 1.

Survival curves during hospital stay of critically ill patients with BMI < 25 kg/m^2 and ≥ 25 kg/m^2.

ed an incidence ranging from 5-25% (5,7,8,14,25-27), similar to the data shown in the national health survey of 2012. In the general population, an increase in the incidence of oncologic diseases was observed, which may be associated with the advent of new diagnostic techniques and treatment protocols for oncologic patients, thus allowing an improvement of the survival rate. The above is a possible explanation for the fact that oncologic patients have anthropometric characteristics similar to the general population.

Critically ill oncologic patients have the same risk to develop cardiovascular and metabolic diseases. The group of patients with overweight and obesity are at a major risk of developing chronic diseases, such as systemic arterial hypertension and diabetes mellitus; however, in our study, less than 20% of the patients had a history of those clinical entities (15,28).

The organ failure that occurred more frequently in patients with a BMI ≥ 25 kg/m^2 was respiratory failure; however, the incidence was similar in the group of BMI < 25 kg/m^2 although overweight and obese patients have decreased lung compliance, functional residual capacity and total vital capacity (29-33). In addition to the pathophysiological differences in the respiratory mechanics of both groups, the use of long-term mechanical ventilation was only observed in the group of BMI ≥ 25 kg/m^2 compared to those with BMI < 25 kg/m^2. Patients with a high BMI have an increased risk to develop acute respiratory distress syndrome, and therefore need a longer ventilatory support without influencing in their prognosis (33,34).

Several authors have described that patients without cancer with certain degrees of obesity have better survival to clinical conditions that endanger life during the ICU stay, which has been defined as paradoxical obesity (15,26,27). In contrast, the results of the present study, which included only critically ill oncologic patients, failed to establish an association between high BMI and better prognosis in ICU; therefore, the ICU mortality of patients with BMI < 25 kg/m^2 and ≥ 25 kg/m^2 was similar. In the study by El-Solh et al. (35), morbidly obese patients in a medical ICU found the presence of organ failures to be the strongest independent predictor of mortality in these patients. Our study found that the ICU mortality in critically ill patients with a BMI ≥ 25 kg/m^2 depends primarily on the number of organ failures, especially when two or more organs are affected.

It is known that paradoxical obesity represents a good prognostic factor in the evolution of certain entities, such as in acute

Table III. Univariate and multivariate analysis of factors associated with intensive care unit death in patients with body mass index ≥ 25 kg/m^2 (n = 286)

Variable	Odds ratio	CI	p	Odds ratio	CI	p
	Univariate			Multivariate		
Age, years	0.98	0.96-0.99	0.038	0.99	0.97-1.00	0.307
Gender (women)	0.85	0.49-1.48	0.573			
Sepsis	2.25	1.28-3.97	0.005	1.58	0.83-3.01	0.160
Invasive mechanical ventilation	8.76	3.39-22.68	< 0.001			
Need for vasopressors	0.78	0.45-1.36	0.392			
Performance status (3-4)	1.49	0.73-3.05	0.270			
Systemic arterial hypertension	0.77	0.38-1.54	0.478			
Type 2 diabetes mellitus	2.47	1.06-5.76	0.035	2.24	0.88-5.69	0.088
≥ 2 organic failures	6.50	3.43-12.3	< 0.001	5.42	2.76-10.65	< 0.001

Goodness-of-fit (Hosmer-Lemeshow), $\chi^2 = 6.580$, $p = 0.582$, area under the receiver operating characteristic curve: 0.72 (95% CI, 0.65-0.80), $p < 0.001$. Performance status was measured using the Eastern Cooperative Oncology Group performance status scale as follows: 0: fully active, able to carry on all pre-disease performance without restriction; 1: restricted in physically strenuous activity but ambulatory and able to carry out; 2: ambulatory and capable of all self-care but unable to carry out any work activities; up and about more than 50% of waking hours work of a light or sedentary nature (e.g., light house work, office work); 3: capable of only limited self-care, confined to bed or chair more than 50% of waking hours; 4: completely disabled; cannot carry on any self-care; totally confined to bed or chair (24).

coronary syndromes, chronic heart failure, chronic renal disease and pneumonia (36-39). Gruber et al. described the concept of paradoxical obesity in 2002 by suggesting obesity as a good prognostic factor in patients undergoing percutaneous transluminal coronary angioplasty in short and long term (36). Recently, González et al. (37) reported that ambulatory patients with cancer and sarcopenia (low rate of fat-free mass) have a higher risk of death. The few reports that include oncologic patients suggest that obesity is a factor to consider in the response to oncologic treatment, and in the progression and resolution of oncologic disease over the medium or long term (40-42). In our institution, there are no statistics regarding the incidence of overweight and obesity in oncologic patients. According to the results of the present study, approximately six of every ten patients admitted for a serious condition to the ICU are overweight or show some degree of obesity, which could be a projection of high BMI in the oncologic population treated at our institution.

The main limitations of this work are as follows:

1. It represents the experience of a single health institution.
2. The relatively small sample size.

CONCLUSION

Critically ill cancer patients have a high incidence of high BMI; approximately six of every ten patients admitted to the ICU with a serious condition are overweight or show several degrees of obesity. The ICU mortality of the patients with a body mass index < 25 kg/m^2 and ≥ 25 kg/m^2 was similar. The independent prognostic factor of ICU death in critically ill patients with a BMI ≥ 25 kg/m^2 was the number of organ dysfunctions, especially when two or more organs are affected.

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