Nutrición Hospitalaria

Trabajo Original

Otros

Nutritional status in patients with COVID-19 and cancer: the experience of the National Cancer Institute in Mexico

Estado nutricional en pacientes con COVID-19 y cáncer: la experiencia del Instituto Nacional de Cancerología de México

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Abstract

Background: nutritional status might vary according to different underlying illnesses such as cancer or infectious diseases, including COVID-19. In this context, data from developing countries remain scarce.

Objectives: the objective of this study was to assess the nutritional status and outcomes of Mexican cancer patients diagnosed with COVID-19 at a tertiary care center.

Methods: this was a retrospective study including 121 consecutive cancer patients diagnosed with COVID-19 at the National Cancer Institute, Mexico City, during four months.

Results: the most frequent oncological diagnoses were gynecological (19 %) and hematological (17 %). Most patients were overweight (35 %). In the univariate analysis, ≥ 65 years, intubation, hypoalbuminemia, high creatinine, lymphopenia, nutrition-impact symptoms, and ECOG 2-4 were statistically associated with lower survival. The median survival of the cohort was 41 days.

Conclusions: to our best knowledge, this is the first study of its kind performed in Mexico, and as other studies from other regions, our results might aid in identifying cancer patients most at risk for severe COVID-19, and could be potentially useful to enhance public health messaging on self-isolation and social distancing among Mexican cancer patients.

Keywords:

Body mass index. Cancer. COVID-19. Mortality. Nutrition.

Resumen

Antecedentes: el estado nutricional puede variar según las diferentes enfermedades subyacentes, como el cáncer o las enfermedades infecciosas, por ejemplo, la COVID-19. En este contexto, los datos de los países en desarrollo siguen siendo escasos.

Objetivos: el objetivo de este estudio fue evaluar el estado nutricional y los resultados de pacientes mexicanos con cáncer diagnosticados de COVID-19 en un centro de atención terciaria.

Métodos: se trata de un estudio retrospectivo que incluyó a 121 pacientes consecutivos con cáncer diagnosticados de COVID-19 en el Instituto Nacional del Cáncer de la Ciudad de México durante cuatro meses.

Resultados: los diagnósticos oncológicos más frecuentes fueron los ginecológicos (19 %) y hematológicos (17 %). La mayoría de los pacientes tenían sobrepeso (35 %) y obesidad (31 %). En el análisis univariado, ≥ 65 años, intubación, hipoalbuminemia, creatinina alta, linfopenia, síntomas de impacto nutricional y ECOG 2-4 se asociaron estadísticamente con una menor supervivencia. La mediana de supervivencia de la cohorte fue de 41 días.

Conclusiones: hasta donde sabemos, este es el primer estudio de este tipo realizado en México y, al igual que otros estudios de otras regiones, nuestros resultados podrían ayudar a identificar a los pacientes con cáncer y mayor riesgo de COVID-19 grave; también podrían ser potencialmente útiles para mejorar los mensajes de salud sobre el autoaislamiento y el distanciamiento social entre los pacientes mexicanos con cáncer.

Palabras clave:

Estado nutricional. Cáncer. COVID-19. Mortalidad. Nutrición.

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INTRODUCTION

Nutritional status is a key element within the health of an individual. Thus, nutrition is considered an important component of treatment for most diseases (1,2). In fact, according to the World Health Organization (WHO), the body mass index (BMI) is a widely accepted measure for indicating nutritional status in adults. Furthermore, the presence of malnutrition, an imbalanced intake of energy or protein for long periods, is relatively high among hospitalized patients (3). On the other hand, the coronavirus disease 2019 (COVID-19), caused by the severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), has represented a burden for healthcare systems worldwide by increasing the number of patients during a short interval of time (4). It has been demonstrated that COVID-19 mortality associates with older age, hypoalbuminemia, and comorbidities such as diabetes *mellitus* type 2 (DM2), hypertension, and obesity (5,6). Further, nutritional status has appeared as a relevant factor influencing the outcomes of COVID-19 patients, but studies remain scarce (1). Also, some studies have indicated that COVID-19 patients experience a series of symptoms that influence their nutritional status (7,8). Moreover, nutritional status has been widely associated with survival in cancer patients (9,10); in fact, its assessment and support are usually considered a valuable measure within the overall oncology strategy. In the context of COVID-19 and cancer, a patient with malnutrition might have a longer or more difficult recovery due to suboptimal immunity. Additionally, despite limited evidence, it has been accepted that patients with cancer receiving systemic treatments are at higher risk from the disease than their counterparts (11). Overall, the prevalence of the coexistence of COVID-19 and cancer remains reasonably low and most studies are small and restricted to few single centers (11). More importantly, in this scenario there is a paucity of data from developing countries. Therefore, the objective of this study was to assess the nutritional status and outcomes of cancer patients diagnosed with COVID-19 at a tertiary care center in Mexico City.

PATIENTS AND METHODS

PATIENTS AND DATA

This retrospective study included consecutive cancer patients diagnosed with COVID-19 at the National Cancer Institute in Mexico City, from April 8 to August 19, 2020. Hospitalized staff with COVID-19 and patients with mild COVID-19 (positive test without symptoms) who were followed ambulatorily were excluded. Data were obtained from electronic medical records (INCanet). The project was approved by the Institutional Review Board (number 2020/0087) but informed consent was waived due to its retrospective nature.

ENDPOINTS AND DEFINITIONS

The diagnosis of COVID-19 was achieved using the real-time polymerase chain reaction (RT-PCR) test by the qualitative detection of nucleic acid from SARS-CoV-2 in upper respiratory specimens (nasopharyngeal swab). Nutritional status was assessed with the body mass index (BMI) according to the standard classification. Patients under active treatment referred to those under chemotherapy. The following nutrition-impact symptoms were evaluated: constipation, diarrhea, dysphagia, nausea, and vomit. Overall survival was calculated as the time in days between admission and death or discharge.

STATISTICAL ANALYSIS

Continuous variables were described by the median and interquartile range using the frequency analysis. Categorical variables were described by frequencies and percentiles. Categorical variables were compared with the chi-square or Fisher's exact test. Cox regression multivariate analysis was used to examine variables affecting the survival time of patients. Kaplan-Meier curves were used to analyze survival. Differences in scores were analyzed by the log-rank test. The SPSS v.21 (IBM, Chicago, IL) program was used. A two-sided p-value of ≤ 0.05 was considered significant.

RESULTS

PATIENT DEMOGRAPHICS AND CLINICAL CHARACTERISTICS

One hundred and twenty-one cancer patients with the diagnosis of moderate and severe COVID-19 were included. Most were female (n = 68, 56 %). The median age was 56 years (range, 18-84). The most frequent oncological diagnoses were gynecological (19 %), hematological (17 %), breast (16 %), and urological (15 %); 62 patients (51 %) had advanced stages. Fifty-two patients (43 %) were under active chemotherapy treatment. Sixty-one patients presented 90 comorbidities, with hypertension being the most common comorbidity (37 %); from the patients with comorbidities (51 %), 29 % only presented one, 19 % presented 2 comorbidities, and 3 % presented 3. Most patients had ECOG 1 (44 %). Overall demographic and clinical characteristics are shown in table I.

NUTRITIONAL STATUS

The median height and weight among the patients were 1.59 meters (range, 1.39-1.80) and 68 kilograms (range, 42.7-152), respectively. Most patients were overweight (35 %). Median serum albumin was 3.5 g/dL (range, 1.5-4.9); median fasting glucose was 107 mg/dL (range, 53-778); median serum creatinine was 0.75 mg/dL (range, 0.4-8.8); and median absolute lymphocyte count was 0.90×10^9/L (range, 0.1-4.1). Table II shows the nutrition-impact symptoms and nutritional interventions during the inpatient period. Sixty-eight patients presented 102 nutrition-impact symptoms; the most common was dysphagia (30 %). From these

Table I. Demographics and clinical characteristics (n = 121)

Characteristic	n (%)
Gender	
Female	68 (56)
Male	53 (44)
Median age in years (range)	56 (18-84)
Type of cancer	
Breast	19 (16)
Gastrointestinal	15 (12)
Gynecological	24 (19)
Head and neck	12 (10)
Hematological	20 (17)
Neurological	1 (1)
Lung	5 (4)
Skin and soft tissue	6 (5)
Urological	18 (15)
Other	1 (1)
Stage	
Early	59 (49)
Advanced	62 (51)
Active chemotherapy treatment	
Yes	52 (43)
No	69 (57)
Comorbidities	
Yes	61 (51)
No	60 (49)
Number of comorbidities	
None	60 (49)
One	35 (29)
Two	23 (19)
Three	3 (3)
Type of comorbidity	
Diabetes *mellitus* type 2	27 (22)
Hypertension	45 (37)
Smoking	20 (17)
Median weight in kilograms (range)	68 (42.7-152)
Median in height in meters (range)	1.59 (1.39-1.80)
Body mass index	
Normal	41 (34)
Overweight	42 (35)
Obese	38 (31)
Median albumin, gr/dL (range)	3.5 (1.5-4.9)
Median glucose, mg/dL (range)	107 (53-778)
Median creatinine, mg/dL (range)	0.75 (0.4-8.8)
Median lymphocytes x 10^9/L (range)	0.90 (0.1-4.1)
ECOG	
0	15 (12)
1	53 (44)
2	35 (29)
3	11 (9)
4	7 (6)

Table II. In-patient clinical characteristics (n = 121)

Characteristic	n (%)
Median days of hospitalization (range)	7 (0-92)
Nutrition-impact symptoms	
Yes	68 (56)
No	53 (44)
Number of nutrition-impact symptoms	
None	53 (44)
One	41 (34)
Two	20 (16)
≥ 3	7 (6)
Type of nutrition-impact symptom	
Constipation	10 (8)
Diarrhea	28 (23)
Dysphagia	36 (30)
Nausea	20 (16)
Vomit	13 (11)
Intubation	
Yes	20 (16)
No	101 (84)
Nutritional support	
None	102 (84)
Enteral	11 (9)
Enteral + oral	5 (4)
Parenteral	1 (1)
Parenteral + oral	2 (2)

symptomatic patients (56 %), 34 % presented one symptom, 16 % presented 2 symptoms, and 6 % presented 3 or more symptoms. Twenty patients (16 %) required intubation, and nutritional support was given to 19 patients (16 %).

CHARACTERISTICS ASSOCIATED WITH SURVIVAL

Table III shows the univariate and multivariate analyses of the characteristics associated with lower survival among cancer patients with COVID-19. The statistically significant variables in the univariate analysis were: ≥ 65 years (HR: 2.3, 95 % CI (1.0-5.7); p = 0.02), intubation (HR: 5.2, 95 % CI (1.9-14.5); p = 0.001), hypoalbuminemia (HR: 2.7, 95 % CI (1.1-6.7); p = 0.04), high creatinine (HR: 3.4, 95 % CI (0.9-12.8); p = 0.04), lymphopenia (HR: 3.3, 95 % CI (1.3-8.3); p = 0.007), nutrition-impact symptoms (HR: 4.2, 95 % CI (1.5-11.4); p = 0.02), and ECOG 2-4 (HR: 6.6, 95 % CI (2.5-17.3); p < 0.0001). None of the variables were significant in the multivariate analysis.

Also, as shown in figure 1, survival estimates were obtained by dichotomizing the variables that were included in themultivariate analysis to further compare these results with the hazard ratios mentioned above.

Table III. Univariate and multivariate analysis
of characteristics associated with survival

| Univariate			Multivariate (adjusted) Cox regression		
Variable	HR (95 % CI)	p	Variable	HR (95 % CI)	p

Age
  ≥ 65 years
	2.3 (1.0-5.7)	0.04*	*Age*
			  ≥ 65 years
				1.3 (0.6-3.0)	0.5

Gender
  Female
	1.0 (0.5-2.6)	0.9	*Gender*
			  Female
				-	-

Body mass index < 25	1.2 (0.5-2.7)	0.7	*Body mass index* < 25	-	-

Any comorbidity
  Yes
	1.4 (0.6-3.3)	0.4	*Any comorbidity*
			  Yes
				-	-

Number of comorbidities
  > 1
	2.3 (0.9-5.9)	0.07	*Number of comorbidities*
			  > 1
				-	-

Hypertension
  Yes
	1.6 (0.7-3.9)	0.2	*Hypertension*
			  Yes
				-	-

Diabetes type 2
  Yes
	2.1 (0.8-5.4)	0.09	*Diabetes type 2*
			  Yes
				-	-

Smoking
  Yes
	1.4 (0.5-3.9)	0.6	*Smoking*
			  Yes
				-	-

Type of cancer
  Lung
	4.9 (0.8-31.1)	0.06	*Type of cancer*
			  Lung
				-	-

Stage of disease
  Advanced
	1.9 (0.8-4.5)	0.1	*Stage of disease*
			  Advanced
				-	-

Active chemotherapy
  Yes
	1.2 (0.5-2.7)	0.6	*Active chemotherapy*
			  Yes
				-	-

Intubation
  Yes
	5.2 (1.9-14.5)	0.001*	*Intubation*
			  Yes
				1.1 (0.5-2.4)	0.8

Glucose
  > 99 mg/dL
	1.4 (0.6-3.4)	0.4	*Glucose*
			  > 99 mg/dL
				-	-

Albumin < 3.5 g/dL	2.7 (1.1-6.7)	0.02*	*Albumin* < 3.5 g/dL	1.1 (0.5-2.6)	0.7

Creatinine
  > 1.21 mg/dL
	3.4 (0.9-12.8)	0.05*	*Creatinine*
			  > 1.21 mg/dL
				2.4 (0.8-7.3)	0.1

Absolute lymphocytes < 1.0×10^3	3.3 (1.3-8.3)	0.007*	*Absolute lymphocytes* < 1.0×10^3	2.1 (0.8-5.2)	0.1
Hospitalization days < 1 week	2.0 (0.9-4.8)	0.08	*Hospitalization days* < 1 week	-	-

Nutrition-impact symptoms
  Yes
	4.2 (1.5-11.4)	0.02*	*Nutrition-impact symptoms*
			  Yes
				1.0 (0.4-2.7)	0.9

Number of symptoms
  > 1
	2.1 (0.8-5.4)	0.09	*Number of symptoms*
			  > 1
				-	-

ECOG
  > 1
	6.6 (2.5-17.3)	< 0.0001*	*ECOG*
			  > 1
				1.7 (0.7-4.2)	0.2
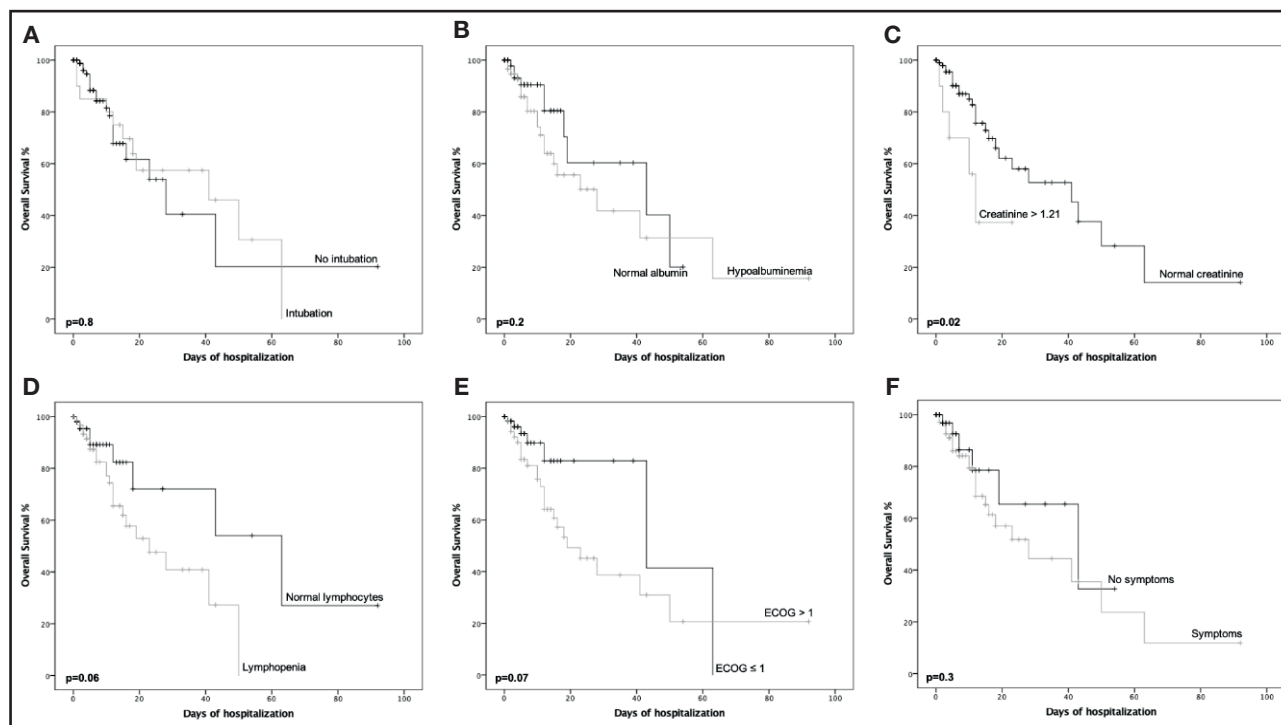
Figure 1.

Survival estimations according to: intubation (A), serum albumin (B), creatinine (C), lymphocytes (D), ECOG (E), and nutrition-impact symptoms (F).

Median survival was as follows: 41 days versus 28 days for intubation and no intubation, respectively (p = 0.8); 28 days versus 43 days for serum albumin < 3.5 g/dL and ≥ 3.5 g/dL, respectively (p = 0.2); 12 days versus 41 days for creatinine > 1.21 mg/dL and ≤ 1.21 mg/dL, respectively (p = 0.02); 23 days versus 63 days for lymphocytes < 1.0×10^3 and ≥ 1.0×10^3, respectively (p = 0.06); 19 days versus 43 days for ECOG 0-1 and 2-4, respectively (p = 0.07); and 28 days versus 43 days for nutrition-impact symptoms and no symptoms, respectively (p = 0.3).

OVERALL SURVIVAL

At the last follow-up, 30 patients were dead (25 %). The median survival of all the cohort was 41 days (Fig. 2). The median survival by nutritional status was 28 days versus 23 days versus 50 days (p = 0.7) for normal BMI, overweight, and obesity, respectively.

DISCUSSION

The coronavirus outbreak has rapidly spread worldwide and represents a threat to human health. The leading cause of death among the infected population is basically an acute respiratory distress syndrome characterized by generalized inflammation (12).

Current knowledge about the SARS-CoV-2 is rapidly evolving, and data from different countries have arisen. Nonetheless, there
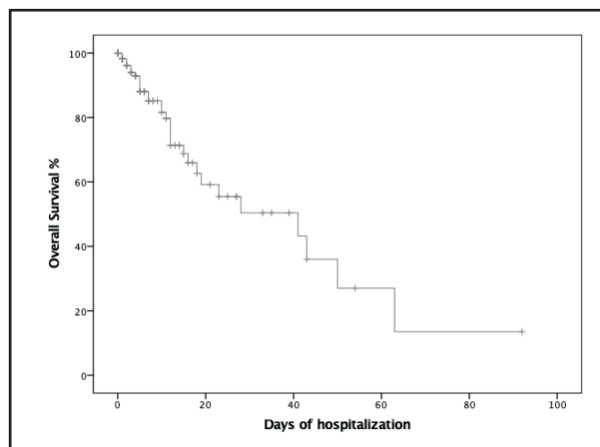

Figure 2.

Median survival (41 days) among cancer patients diagnosed with COVID-19.

is a paucity of studies from certain regions of the world, for instance from low- and middle-income countries. Thus, in this study we analyzed the nutritional status and mortality among cancer patients diagnosed with COVID-19 at a National Institute of Health in Mexico.

A recent meta-analysis (12) demonstrated that some immune-inflammatory parameters, such as the number of lymphocytes (< 1.0×10^9/L), could be associated with the progression of COVID-19. In fact, our study corroborated that lymphopenia was associated with lower survival in the univariate analysis. However, this parameter

was not statistically significant in the multivariate analysis or in the survival estimate. On the other hand, based on the early estimates in China, 75 % of dead patients had pre-existing health conditions such as diabetes and cardiovascular disease (13). In this context, individuals with DM2 are usually at greater risk for infections and mortality (RR = 2.1, 95 % CI (1.40, 3.19)) (14,15). Among our cohort, 22 % had DM2; however, it was not a factor associated with higher mortality. Moreover, in our study, hypertension and smoking were not associated with lower survival, which is in contrast with the international literature for the former (RR = 1.66, 95 % CI (1.32-2.09)) (13,15). More importantly, Singh et al. reported in their meta-analysis that cancer was significantly associated with a higher risk of severe COVID-19 (RR = 2.48, 95 % CI (1.46, 4.19)) compared to patients without comorbidities (15), increasing the risk of mortality in this group (RR = 1.77, 95 % CI (1.08, 2.88)). Interestingly, among our cohort mortality was relatively low (25 %). In this context, a European multicentric study including cancer patients reported a mortality of 71 % (16). The same study confirmed age > 65 and > 2 comorbidities to predict patient mortality, whereas our study only corroborated the former in the multivariate analysis.

On the other hand, hypoalbuminemia has been a predictive factor in COVID-19 (OR = 6.4; 95 % CI (1.31-31.09) (17). Our results coincided with this finding, as hypoalbuminemia was associated with lower survival. We also found that patients with elevated creatinine had a higher mortality, potentially explained by studies reporting increased creatinine levels or a high prevalence of kidney disease in patients with COVID-19 on admission, and the development of acute kidney injury during hospitalization (18,19), which similarly to our study was associated with in-hospital mortality.

Further studies have suggested a more frequent and severe course of COVID-19 in cancer patients undergoing active oncologic treatment (20). Our analysis also associated active chemotherapy treatment with higher mortality; moreover, compared with other studies, the percentage of patients under active treatment was higher at our institution compared to international centers (43 % versus 22-41 %) (20).

In addition, obesity has been being associated with severe COVID-19 and mortality (15). However, in our cohort the univariate analysis did not show statistical significance when associating this factor with lower survival; surprisingly, among our cohort, patients with normal BMI had a slightly higher mortality when compared to those with BMI ≥ 25 (27 % versus 24 %).

Regarding in-patient nutritional support, when compared to a large study performed in China, reporting 25 % receiving nutritional support (21), in our cohort nutritional support was only given to 16 %.

Finally, we acknowledge the limitations of our analysis: a retrospective study in a small cohort at a single center without a control group; however, to the best of our knowledge, we present the first analysis of its kind in our country and one of the few that has been performed internationally.

CONCLUSION

As other studies performed in different countries, our results might aid in identifying Mexican patients most at risk of severe complications from COVID-19, and could be potentially useful to enhance public health messaging on self-isolation and social distancing among cancer patients in our country.

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