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Clinical Comparison of MASCC and CISNE Scores in Neutropenic Febrile Patients in the Emergency Department

Acil Serviste Nötropenik Ateşli Hastalarda MASCC ve CISNE Skorlarının Klinik Karşılaştırılması

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ABSTRACT

Objective: *Febrile neutropenia is an important condition that needs to be well managed in the emergency department. Home treatment and hospitalization requirements of the patients are made according to some risk classifications. The most commonly used MASCC score may involve risks in terms of early discharge. Our aim in this study is to show that these risks can be reduced if the MASCC score is supported by the CISNE score. In addition, it is to determine the contribution of procalcitonin values to these classifications.*

Material and Method: *Neutropenic febrile patients over the age of 18 who came to the emergency department between 2019 and 2020 were included in the study. MASCC and CISNE scores of the patients were calculated. The relationship between scores and mortality was examined. Mortality estimation was made by using MASCC and CISNE scores together. In addition, patients were divided into 4 groups according to their proclacytonin values. The relationship between MASCC, CISNE and mortality between the groups was examined.*

Results: *Of the 103 patients included in the study, 70.9% were male. The most common reason for admission was found to be acute gastroenteritis with 22.3%. 40.8% of the patients died. According to the MASCC score, 35.9% of the patients were found to be at high risk. Despite this, 85.4% of them were hospitalized and treated. There was an inverse, moderate statistically significant correlation with MASCC (r=-0.542, p=0.000), and a weak statistically significant correlation with CISNE (r=0.385, p=0.000). There was a moderately significant correlation between procalcitonin, one of the acute phase indicators, and mortality (r=-0.555, p=0.000).*

Conclusion: *Evaluating neutropenic febrile patients with MASCC score for high-risk patients and CISNE score for low-risk patients in the emergency department gives more accurate results in determining poor prognosis. If these two scores are evaluated together with procalcitonin, the out-of-hospital mortality rate can be further reduced. For this, prospective studies in which risk scores are modified with a marker such as procalcitonin are needed.*

ÖZET

Amaç: *Febril nötropeni acil serviste iyi yönetilmesi gereken önemli bir durumdur. Hastaların ev tedavisi ve hastane yatış gerekliliği bazı risk sınıflamalarına göre yapılmaktadır. En sık kullanılan MASCC skoru erken taburculuk yönünden riskler içerebilmektedir. Bu çalışmadaki amacımız MASCC skorunun CISNE skoru ile desteklenmesi durumunda bu risklerin azaltılabileceğini göstermektir. Ayrıca prokalsitonin değerlerinin bu sınıflamalara katkısını belirlemektir.*

Gereç ve Yöntem: *2019-2020 yılları arasında acil servise gelen 18 yaş üstü nötropenik ateşli hastalar çalışmaya dahil edildi. Hastaların MASCC ve CISNE skorları hesaplandı. Skorlar ile mortalite ilişkisi incelendi. MASCC ve CISNE skorunun birlikte kullanılarak mortalite tahmini yapıldı. Ayrıca proklasitonin değerlerine göre hastalar 4 gruba ayrıldı. Gruplar arası MASCC, CISNE ve mortalite ilişkisi incelendi.*

Bulgular: *Çalışmaya dahil edilen 103 hastanın %70,9'u erkekti. En sık başvuru nedeni %22,3 ile akut gastroenterit olarak bulundu. Hastaların %40,8'i öldü. MASCC skoruna göre %35,9 oranında hasta yüksek riskli bulundu. Buna rağmen %85,4'ü hastaneye yatırılarak tedavi altına alındı. MASCC ile ters yönlü, orta dereceli istatistiksel olarak önemli korelasyon vardı (r=-0.542, p=0.000), CISNE ile zayıf istatistiksel olarak önemli korelasyon vardı (r=0.385, p=0.000). Akut faz göstergelerinden prokalsitonin ile mortalite arasında orta derece anlamlı bir korelasyon vardı (r=-0.555, p=0.000).*

Sonuç: *Nötropenik ateşli hastaları acil serviste yüksek riskli olanları MASCC skoru ile düşük riskli hastaları ise CISNE skoru ile değerlendirmek kötü prognozu belirlemede daha doğru sonuçlar veriyor. Bu iki skor eğer prokalsitonin ile birlikte değerlendirilirse hastane dışı mortalite oranı daha da azaltılabilir. Bunun için risk skorlarının prokalsitonin gibi bir belirteçle modifiye edildiği prospektif çalışmalara ihtiyaç var.*

Keywords:
CISNE score
Febrile neutropenia
MASCC score
Mortality
Procalcitonin

Anahtar Kelimeler:
CISNE skoru
Febril nötropeni
MASCC skoru
Mortalite
Prokalsitonin

INTRODUCTION

Chemotherapy not only affects rapidly proliferating mucosal cells, but also leads to a decrease in the number of neutrophils. The patient who has both lost the mucosal barrier and has neutropenia becomes open to infections (1). Infections are an important cause of mortality in cancer patients (2). While the risk of developing respiratory, heart and kidney failure is 25-30%, death can reach up to

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11%. If the condition progresses to sepsis, especially in-hospital mortality approaches 50%. For this reason, early initiation of antibiotic therapy and/or antifungal therapy is recommended for these patients, and hospitalization is recommended according to the risk classification (3). Orally home treatment amoxicillin clavunate or quinolone is recommended. In the hospital, intravenous (iv) antibiotics such as broad-spectrum piperacillin-tazobactam are recommended (4). The Multinational Association of Support Care in Cancer (MASCC) score is commonly used to determine risk. A score above 21 is defined as low risk. Significant complications were observed in 11% of patients with low risk. For this, it is recommended to use the Clinical Index of Stable Febrile Neutropenia (CISNE) scoring. In addition to these scores, the socioeconomic opportunities of the patient are effective in the decision of hospitalization (3). An important reason for some problems in determining the risk is that solid masses show an occlusive feature in the area where they are located. Therefore, the risk of aspiration pneumonia, cholangitis or serious urinary infections may make it difficult to determine the risk (5). There are studies in which the mortality rate is 80% in hematological cancer patients admitted to the intensive care unit. This suggests that a MASCC score below 21 is not an indicator of high risk alone. Additional diseases of the patient, the presence of a catheter, leukemia or myeloproliferative dysplasia are among the other high-risk causes that are not included in the MASCC score (6).

Emergency departments are a difficult part of hospitals where intensive, rapid and critical decisions are made. Febrile neutropenia (FN) is a condition that requires quick decisions about where and how to treat. The number of studies comparing MASCC and CISNE scores is scarce in the literature. Our aim in this study is to see the effect of the two scores on the clinical decision making process in the emergency department. We aimed to show the contribution of acute phase indicators, especially procalcitonin value, to risk scores and mortality by examining the relationship. Thus, it is to determine the most appropriate approach in terms of use in the emergency department.

MATERIAL AND METHOD

Study design

This study was planned as a single-center and retrospective study in the emergency department of a training and research hospital. Patients admitted to the emergency department due to FN between 01/January/2019-31/December/2020 were determined. The information was obtained from the hospital data processing system. The study was carried out according to the Declaration of Helsinki. After obtaining the approval of the ethics committee, the data were performed as an archive scan over the computer system.

Study protocol and selection of patients

Data of 230 patients with febrile neutropenia were scanned. 30 patients were neutropenic without FN and due to missing data, 97 patients were excluded due to different reasons such as bleeding from the gingiva, epistaxis and gastrointestinal tract, trauma, cerebrovascular disease, myocardial infarction and acute abdomen. 103 patients were included in the study. Patients over the age of 18 who met the FN criteria were included in the study. Neutropenic patients under the age of 18, with missing data and who did not meet the FN criteria were excluded

Table 1: MASCC and CISNE scores

MASCC Variables	Point		CISNE Variables	Point	
Disease symptom	Asymptomatic/mild	+5	ECOG** Performance Status	<2	0
	Moderate	+3		≥2	+2
	Severe	0			
Hypotension	No	+5	Baseline blood glucose ≥121 mg/dL or ≥250 mg/dL in diabetics or taking steroids	No	0
	Yes	0		Yes	+2
COPD*	No	+4	COPD*	No	0
	Yes	0		Yes	+1
Type of cancer	Solid	+4	Cardiovascular disease	No	0
	Hematogenous + no fungal infection	+4		Yes	+1
	Hematogenous + There is fungal infection	0			
Dehydration	No	+3	Monocyte	≥200/µL	0
	Yes	0		<200/µL	+1
Age	<60	+2	Mucositis grade ≥2 Painful erythema, edema or ulcer, but eating/swallowing possible	No	0
	≥ 60	0		Yes	+1
Fever	Outpatient	+3	0 points low risk, 1-2 points medium risk, ≥3 points high risk		
	Inpatient	0			
Total point ≥ 21 low risk, <21 high risk			0,1,2 outpatient, ≥3 inpatient		

**COPD: Chronic obstructive pulmonary disease, **ECOG: Eastern Cooperative Oncology Group*

from the study. A form was prepared for the study. Age, gender, comorbidities, neutrophil counts, leukocyte counts (WBC), C-reactive protein (CRP), procalcitonin (PCT), MASCC/CISNE scores, foci of infection, culture results, patient's treatment impression (home therapy/ hospitalization) and mortality were recorded. Neutrophil, leukocyte, CRP and PCT values were correlated with mortality. The superiority of MASCC and CISNE scores (low risk/high risk) over mortality was examined. The relationship between using the scores separately and using them together was determined. In addition, patients were divided into 4 different subgroups according to their PCT values. PCT value below 0.5 ng/mL was determined as group 1, 0.5-2 ng/mL group 2, over 2 ng/mL group 3, and over 10 ng/mL group 4. The relationship of these four groups with MASCC, CISNE and mortality was examined.

Defination

The criterion for the diagnosis of FN is fever equal to or higher than 38°C for at least 1 hour or 38.3°C once orally. The criterion for neutropenia is neutrophil count less than 500 µL or decrease from 1000 µL to less than 500 µL within 48 hours. MASCC and CISNE scores are summarized in table 1 (3).

PCT below 0.5 ng/mL is mild risk of progression to severe infection (sepsis-septic shock), intermediate risk between 0.5-2 ng/mL, high risk above 2ng/ml and high probability of sepsis above 10 ng/ml. It can be defined as septic shock (7).

Outcome

Our main outcome is that the mortality rate increases with decreasing MASCC score. Our other outcomes were an increase in the CISNE score, an increase in acute phase reactants, and an increase in the mortality rate.

Statistical analysis

Study data were analyzed with SPSS for Windows v.17 and MedCalc trial version 23. Data are presented as frequency (n), percentage (%), median, and interquartile range. The distribution of continuous data was evaluated using the Kolmogorov-Smirnov test. They were found to not normally disperse. Therefore, Mann-Whitney U test, which is one of the non-parametric tests, was used. $p<0.05$ was considered statistically significant.

RESULTS

Considering the gender distribution of the patients, 70.9% (n=73) were seen in men. The patients were found to be at high risk with the MASCC score of 35.9% and the CISNE score of 44.6%. The high risk was found to be 46.6% when the two scores were used together. The most common reason for admission was acute gastroenteritis with 22.3% (n=23). 85.4% (n=88) of our patients were hospitalized and treated for intravenous (iv.) antibiotic therapy. Our rate of patients with solid malignancy was 67%. Considering the culture results of our patients, there was a growth rate of 43.7%. The most frequent growth occurred in blood cultures with 32 patients. 40.8% of our patients died. These data of the patients are summarized in Table 2.

There was a weak, statistically significant inverse correlation between mortality and WBC (r=-0.322, p=0.001). There was a weak but statistically significant correlation between mortality and CRP (r=0.278, p=0.005). A moderate correlation between mortality and PCT and there was a statistically significant correlation (r=-0.555, p=0.000). The data are summarized in table 3.

There was a moderate statistically significant correlation between subgroups of PCT value and mortality (r=0.579, p=0.000). There was an inverse, moderate statistically significant correlation between MASCC score and mortality (r=-0.542, p=0.000). Weak statistical correlation between CISNE and mortality. There was a significant correlation (r=0.385, p=0.000). The data are summarized in table 4.

Table 2: The distribution of neutropenic fever patients by gender, score, focus of infection, culture results and mortality status

Variable		n	%
Gender	Male	73	70.9
	Female	30	29.1
Groups to the value of procalcitonin	Group 1	49	47.6
	Group 2	13	12.6
	Group 3	19	18.4
	Group 4	22	21.4
MASCC* score	< 21	37	35.9
	≥ 21	66	64.1
CISNE** score	High risk	46	44.6
	Low risk	57	55.4
MASCC+CISNE	İnpatient	48	46.6
	Outpatient	55	53.4
Source of infection	None	29	28.2
	Pneumonia	15	14,6
	Mucositis	11	10.7
	Urinary tract infection	16	15.5
	Acute gastroenteritis	23	22.3
	Esophagitis	1	1
	Bacteremia	6	5.8
	Dental abscess	1	1
	Perianal abscess	1	1
Type of malignancy	Solid	71	69
	Hematogenous	32	31
Antibiotic	Intravenous	88	85.4
	Oral	15	14.6
Hospitalization	Inpatient	88	85.4
	Outpatient	15	14.6
Mortality	Alive	61	59.2
	Death	42	40.8
Culture	Negative	40	38.9
	Positive	45	43.7
	None	18	17.5
Culture type	No reproduction	57	55.3
	Blood	32	31.1
	Urine	10	9.7
	Trachea	2	1.9
	Sputum	2	1.9

**MASCC: Multinational Association of Support Care in Cancer, **CISNE: Clinical Index of Stable Febrile Neutropenia*

Table 3: Distribution of patients' age and acute phase indicators according to mortality

Variable	Alive	Death	p
Age	65 (15)	66 (13)	0.06
WBC*	0.80 (0:70)	0.50 (0.44)	0.001
CRP** (mg/L)	88.40 (131.8)	140.50 (157)	0.005
PCT*** (ng/mL)	3.31 (1.62)	4.65 (21.85)	0.000

**WBC: White blood cell, **CRP: C-reactive protein,*
****PCT: Procalcitonin*

Table 4: Distribution of risk scores and procalcitonin values according to mortality of patients

Variable		**Alive**	**Death**	**p**
MASCC* score	< 21	11	26	0.000
	≥ 21	50	16	
CISNE** score	High risk	15	31	0.000
	Low risk	46	11	
MASCC+CISNE	İnpatient	18	31	0.000
	Outpatient	43	11	
Groups to the value of procalcitonin	Group 1	43	6	0.000
	Group 2	6	7	
	Group 3	8	11	
	Group 4	4	18	

**MASCC: Multinational Association of Support Care in Cancer,*
***CISNE: Clinical Index of Stable Febrile Neutropenia*

DISCUSSION

Evaluation of FN patients in the emergency department has a rapid and critical importance. Risk scoring has been developed to identify high-risk patients and initiate the hospitalization process. Although the MASCC score is often used, there are other scores such as CISNE. However, the use of scoring alone may include complications that may develop later. For this reason, studies are carried out to support the MASCC score in order to select patients who can be followed up well (3,8). In our study, MASCC included determining the poor outcome in patients who were determined to be low risk in the use of CISNE scores separately and together. In addition, we showed the contribution of acute phase indicators and especially procalcitonin value to these scores. Our study was a hospital in which oncological treatment methods were applied, in which tertiary health care was given retrospectively. For this reason, most of the oncological patients in our city are provided with emergency health services. An important point in our study is that we detected a source of infection in 81.8% of our patients. On the other hand, in 43.7% of these patients, there was growth in the cultures taken. In-hospital mortality rate of the patients in whom we detected FN was 40.8%. While gastroenteritis was the most common emergency department admission, culture growth was the most common in the blood, making us think that bacterial translocation is effective in this situation. Chemotherapy causes damage to the mucous membranes of the gastrointestinal tract and accelerates this transition. Ulcers may occur on the mucosal surfaces. It facilitates opportunistic pathogens in ulcerated tissue (9). One study found severe gram-positive bacteremia in patients with a low-risk MASCC score. Gram-negative bacteremia was more intense and fatal in those with high risk, especially in those below 15 points (10).

It was observed that the majority of the patients in our study were hospitalized and treated with iv antibiotics. This shows that patients identified as low risk are also hospitalized and monitored due to the concerns of physicians. This appeared to be a limiting factor for the study. This made it difficult for us to determine the effect of home follow-up of low-risk patients on poor outcome. Despite this, the high mortality rate of our patients in the low risk group according to the MASCC score justifies the physician's concerns. CISNE identified more high-risk patients based on the MASCC score. The combined use of the two scores suggested more hospitalization at the point of hospitalization. Coyne et al., on the other hand, found that the group with a CISNE score of 0 in low-risk patients could be safely taken to early oncology outpatient control (11). While Moon et al. recommended that the MASSC score be used in the initial evaluation in their study, they suggested that the CISNE score be evaluated secondarily in the low-risk patient group (12). Although the MASCC score was originally used to identify low-risk patients, it was found to be more successful in patients with poor outcomes. In addition, the CISNE score is more prominent in identifying low-risk patients (13-14).

When the relationship between WBC, CRP and PCT values of our patients and mortality was examined, there was a statistically significant correlation. In particular, PCT gained a little more importance. In the grouping made according to PCT values, mortality rates were higher in groups 2, 3 and 4, where the value was higher than in group 1. Mortality peaked when the value increased above 10 ng/mL. PCT had a higher mortality rate among those at high risk among PCT and risk scores. This made us think that MASCC and CISNE scores could reach more accurate results with PCT values. PCT is found at very low levels in healthy individuals. In case of serious bacterial infection, significant increases in PCT value are observed. It has been determined that the value of sepsis increases above 2 ng/mL (7,14). Keskin et al. showed that PCT increases in the early phase of sepsis and provides important information in prognosis (15). In our study, it was shown that the mortality risk of FN increased as the PCT value increased above 0.5 ng/mL.

CONCLUSION

Emergency physicians in FN may prefer MASCC or CISNE score first when identifying high-risk patients. However, in patients they consider low risk, we recommend that a secondary score or an increase in acute phase indicators, especially procalcitonin value, may contribute to the decision process. Our most important recommendation is to perform larger prospective studies with acute phase reactants modified for MASCC and CISNE scores.

Conflict of interest: The authors declare that there are no conflicts of interest.
Ethics: The study was carried out with the E1-22-2321 numbered decision of Ankara City Hospital Ethics Committee.

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