ORIGINAL ARTICLE

Use of MASCC score in the inpatient management of febrile neutropenia: a single-center retrospective study

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Abstract

Purpose The Multinational Association for Supportive Care in Cancer (MASCC) score is used to risk stratify outpatients with febrile neutropenia (FN). However, it is rarely used in hospital settings. We aimed to describe management, use of MASCC score, and outcomes among hospitalized patients with FN.

Methods We conducted a retrospective cohort study of patients with cancer and FN. We collected patient demographics, cancer characteristics, microbiological profile, MASCC score, utilization of critical care therapies, documentation of goals of care (GOC), and inpatient deaths. Outcomes associated with low- (≥ 21) versus high-risk (< 21) MASCC scores are presented as absolute differences.

Results Of 193 patients, few (2%, $n = 3$) had MASCC scores documented, but when calculated, 52% ($n = 101$) had a high-risk score (< 21). GOC were discussed in 12% ($n = 24$) of patients. Twenty one percent ($n = 40$) required intermediate/ICU level of care, and 12% ($n = 23$) died in the hospital. Those with a low-risk score were 33% less likely to require intermediate/ICU care (95% CI 23 to 44%) and 19% less likely to die in the hospital (95% CI 10% to 27%) compared to those with high-risk score.

Conclusions MASCC score was rarely used for hospitalized patients with FN, but high-risk score was associated with worse outcomes. Education efforts to incorporate MASCC score into the workflow may help identify patients at high risk for complications and help clinicians admit these patients to a higher level of care (e.g., intermediate/ICU care) or guide them to initiate earlier GOC discussions.

Keywords Febrile neutropenia · Cancer · Goals of care · Multinational Association for Supportive Care Score · Neutropenic fever

Introduction

Febrile neutropenia (FN) is a common complication in patients with cancer, occurring in 5–10% of patients with solid tumors [1], 85–95% of patients with acute leukemia, and 20–25% of patients with other hematologic malignancies [2]. Neutropenia is defined as an absolute neutrophil count (ANC) of < 500 neutrophils/mcL or the combination of

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ANC of < 1000 neutrophils/mcL and a predicted decline of ≤ 500 neutrophils/mcL over the next 48 h. FN exists once there is a temperature ≥ 38.3 °C orally or ≥ 38 °C for a duration longer than 1 h with associated neutropenia [3]. FN accounts for about 40–50% of the total cost of hospitalizations in cancer care, with mortality rates ranging between 3 and 10% [4].

Prior literature reports that 20–30% of patients with FN have an identifiable site of infection and 10–25% of patients have positive blood cultures [5–8]. Experts recommend the early introduction of empiric antibiotic therapy in all patients with FN because of the high risk for progression to sepsis and death [7, 9, 10]. Historically, *Pseudomonas aeruginosa* was the most prevalent causative organism, but the changing microbiological profile of FN now reveals that gram-positive bacteria are more common [11, 12].

As patients at low risk for complications could be successfully treated in the outpatient setting, several organizations including the American Society of Clinical Oncology (ASCO), National Comprehensive Cancer Network (NCCN), Infectious Disease Society of America (IDSA), and European Society of Medical Oncology (ESMO) recommend using the Multinational Association for Supportive Care in Cancer (MASCC) score to risk stratify patients [7, 13, 14]. Developed in 2000, the score incorporates patient and cancer characteristics to quantify the risk of FN-related complications. Higher scores indicate lower risk, with a maximum of 26 points. A cutoff value of ≥ 21 points is used to discriminate patients with low risk from those with high risk (< 21 points) for serious FN-related complications [15]. Patients identified as low risk may be managed in the outpatient setting safely with oral antibiotics. Several studies have validated this score for both hematological and solid tumors in the inpatient setting and recommend early discharge of patients with low-risk FN on oral antibiotics [16–19]. Despite evidence supporting its use in the inpatient setting, MASCC score is rarely used during hospitalization [20, 21].

FN admissions are commonly managed by hospitalists or internists rather than oncologists in the community; a tool like the MASCC score could be used to guide them around risk for clinical deterioration or death [22]. Patients with FN and lower MASCC score might be placed in a higher level of care or, alternatively, be prioritized for earlier discussion around goals of care. Therefore, we aimed to describe the management of FN among hospitalized patients with cancer, current use of MASCC score, and the association of MASCC score on presentation with poor outcomes.

Methods

Design, setting, and population We conducted a retrospective cohort study at a tertiary care academic medical center. The Institutional Review Board (IRB) at Baystate Medical Center approved this study. We identified patients hospitalized with a principal diagnosis of FN and cancer admitted to Baystate Medical Center between October 1, 2015, and April 1, 2019. Patients were included in the study if they were 18 years of age or older, were admitted to the inpatient service or intensive care unit (ICU), and carried both a diagnosis of cancer and FN. FN was identified using ICD-10 diagnosis codes (D70 and R50) in an administrative billing database. We also included patients with cancer who were admitted for an alternative diagnosis if they developed FN during their hospitalization. If patients developed multiple episodes of FN, we randomly selected a single admission for this study. We excluded patients who did not meet diagnostic criteria for FN (defined below) and those transferred out of our facility to another acute care hospital. FN related to causes other than cancer (e.g., primary immunodeficiency or liver disease) was also excluded from the study.

Data collection Two physicians (PB and ME) reviewed the electronic health record (EHR), first examining approximately 10 of the same patients' records. Any differences were resolved via discussion to standardize chart extraction and reduce inter-observer variability. Four other physicians (FA, JC, AS, and RW) who conducted chart extraction were subsequently trained by PB and ME to ensure uniformity in data collection. After collection of data, PB and ME randomly selected 75 charts for quality control purposes and confirmed uniformity of extraction methods.

Variables extracted from the EHR included patient demographics; Eastern Cooperative Oncology Group (ECOG) performance status; use of granulocyte colony-stimulating factor (GCSF) 14 days prior to or during hospitalization; documentation of MASCC score; clinical characteristics of cancer including type, stage, and cycle of chemotherapy received; microbiological profile including the presence of positive blood cultures, source of infection, initial empiric antibiotics, use of antimicrobial prophylaxis, duration of antibiotics, and documentation of goals of care discussion; and utilization of different consult services including oncology, infectious diseases, and palliative care. Clinical course including ICU level of care, septic shock requiring vasopressor use, acute respiratory failure requiring non-invasive or mechanical ventilation, documented delirium, acute kidney injury requiring hemodialysis, and inpatient death was also obtained. Admission to the ICU and the need for critical care therapies were obtained from a review of medical records. In-hospital mortality was identified by documentation of discharge status as "expired" in our billing database. All data were manually entered into the REDCap database [23].

Definition of febrile neutropenia We defined FN based on criteria from the IDSA as an ANC of < 500 neutrophils/mcL or an ANC of < 1000 neutrophils/mcL and a predicted decline

of ≤ 500 neutrophils/mcL over the next 48 h as well as a temperature of ≥ 38.3 or ≥ 38 °C for longer than 1 h either prior to admission or during hospitalization when admitted for an alternative diagnosis [7].

ECOG performance status ECOG performance status describes a patient's level of functioning in terms of their ability to care for themselves, daily activity, and physical ability [24]. It ranges from 0 to 5 with 0 indicating a fully active person who is able to carry on all pre-disease performance without restriction and 5 indicating death. This score was obtained as documented on the last oncology outpatient note prior to hospitalization or oncology consult note during hospitalization.

MASCC scoring system MASCC scores were calculated by study investigators for all patients irrespective of documentation status. We calculated the weighted MASCC risk index using the following variables: burden of illness, blood pressure, presence or absence of chronic obstructive pulmonary disease, solid tumor or hematological malignancy with or without a history of previous fungal infection, dehydration, inpatient or outpatient status at the time of onset of neutropenic fever, and age. Table 1 provides details about the calculation of the score and weighting of characteristics.

Statistical analyses

We used descriptive statistics (means, standard deviations, range, and percent as appropriate to the scale of measurement) to describe the patient sample and characteristics of those with low- versus high-risk MASCC scores. Low- versus high-risk MASCC scores were used to predict hospital outcomes such as the presence of positive blood cultures, goals of care discussions, requirement of intermediate/ICU care, and death. For each association, we estimated the area under the curve (AUC) and calculated the absolute risk difference and 95% confidence interval (CI). The analysis was conducted using Stata v16.0, StataCorp, LP, College Station, TX.

Results

Patient characteristics

Of the 322 unique patients identified as having FN between October 1, 2015, and April 1, 2019, we excluded 129 patients; l00 patients did not meet the criteria for FN, 23 patients did not have a diagnosis of cancer, 5 patients did not meet criteria for FN or have a diagnosis of cancer, and 1 patient was transferred out of our facility. Of the 193 eligible patients, the mean age was 60 years, and more than half (107/193, 55.4%) were women. Most

patients were white (162/193, 83.9%). ECOG performance status was documented for 63.7% (123/193) patients. Of these, 74.0% (91/123) had an ECOG of 0 or 1, and 7.3% (9/123) had an ECOG of 3 or 4 (Table 2).

Nearly half the patients (102/193, 52.5%) had hematological malignancies, with most of these being acute myeloid leukemia (33/102, 32.4%), and non-Hodgkin lymphoma (28/102, 27.5%). Among solid tumors, breast (31/91, 34.1%), thoracic (21/91, 23.1%), and gastrointestinal (14/91, 15.4%) were the most common cancers. Over two-thirds of patients with solid tumors (64/91, 70.3%) were clinical stage III or IV.

Most patients were receiving chemotherapy (172/193, 89.1%) at the time of diagnosis of FN. The median cycle of chemotherapy patients received was one (range, 1–4) (Table 2). More than a third of the patients (66/193, 34.2%) had used GCSF 14 days prior to hospitalization or were given GCSF during hospitalization.

A MASCC score was documented in 1.6% (3/193) of all patients by the admitting provider. A MASCC score was calculated for all patients by the study investigators based on information available from admission and emergency department visit note (Table 1). More than half of the patients (101/193, 52.3%) were high risk based on MASCC score of < 21, and the remainder (92/193, 47.7%) were low risk. Of the patients with hematological malignancies, 57.8% (59/102) were considered high risk, and 42.2% (43/102) were considered low risk. Of the patients with solid tumors, 46.2% (42/91) were considered high risk, and 53.8% (49/91) were considered low risk.

Microbiological profile (Table 2)

A definitive source of infection was identified in 59.1% (114/193) of patients. A quarter of the patients (53/193, 27.5%) had positive blood cultures, with a slight preponderance of gram-negative rods (26/53, 49.1%) when compared to gram-positive cocci (23/53, 43.4%). Forty percent (41/101) of patients with high-risk MASSC score had positive cultures, while 13.0% (12/92) of patients with low-risk MASSC score had positive cultures.

Resistant organisms such as methicillin-resistant *Staphylococcus aureus* (MRSA) or pseudomonas were relatively rare, occurring in only 5.6% (3/53) and 7.5% (4/53) of patients, respectively. Forty-two percent (81/193) received empiric antibiotics for MRSA coverage, and 96.4% (189/193) received empiric antibiotics for pseudomonas coverage (Table 3).

A viral infection was identified in 15.5% (30/193) of patients. Approximately 11.9% (12/101) of patients with high-risk MASCC score and 19.6% (18/92) of patients with low-risk MASCC score had a viral infection.

Table 1 Multinational Association for Supportive Care in Cancer scoring system [37]

Calculated MASCC score	Total N = 193	< 21 (high risk) N = 101	≥ 21 (low risk) N = 92
Mean (SD)	18.51 (4.99)	14.86 (4.15)	22.52 (1.61)
Median (Q1, Q3)	20.0 (16.0, 22.0)	16.0 (11.0, 19.0)	22.5 (21.0, 23.5)
Min, Max	4.0, 26.0	4.0, 20.0	21.0, 26.0
MASCC components			
Burden of illness			
Severe (0)	37 (19.2%)	37 (36.6%)	0 (0.0%)
Moderate (+3)	88 (45.6%)	56 (55.4%)	32 (34.8%)
None or mild (+5)	68 (35.2%)	8 (7.9%)	60 (65.2%)
Hypotension (SBP < 90)			
Yes (0)	33 (17.1%)	33 (32.7%)	0 (0.0%)
No (+5)	160 (82.9%)	68 (67.3%)	92 (100.0%)
Active COPD			
Yes (0)	15 (7.8%)	15 (14.9%)	0 (0.0%)
No (+4)	178 (92.2%)	86 (85.1%)	92 (100.0%)
Cancer type			
Hematological malignancy with prior fungal infection (0)	22 (11.4%)	21 (20.8%)	1 (1.1%)
Solid tumor or hematological malignancy with no prior fungal infection (+4)	171 (88.6%)	80 (79.2%)	91 (98.9%)
Dehydration requiring IV fluids			
Yes (0)	142 (73.6%)	89 (88.1%)	53 (57.6%)
No (+3)	51 (26.4%)	12 (11.9%)	39 (42.4%)
Status at onset of fever			
Inpatient (0)	41 (21.2%)	32 (31.7%)	9 (9.8%)
Outpatient (+3)	152 (78.8%)	69 (68.3%)	83 (90.2%)
Age at onset			
≥ 60 (0)	111 (57.5%)	78 (77.2%)	33 (35.9%)
< 60 (+2)	82 (42.5%)	23 (22.8%)	59 (64.1%)

Points attributed to the variable "burden of illness" are not cumulative. The maximum theoretical score is therefore 26

Table adapted from Klastersky et al.

Consults (Table 2)

Half of the patients were seen by an infectious disease specialist (98/193, 50.8%), 82.4% (159/193) were seen by a hematologist/oncologist, and 6.7% (13/193) were seen by a palliative care specialist.

Goals of care discussions (Table 2)

Goals of care discussion were initiated in 24/193 (12.4%) of patients; the primary team/hospitalists were responsible for the majority (19/24, 79.2%). The oncology team initiated this conversation for 4/24 (16.7%) patients; all of them had a high-risk MASCC score.

Outcomes (Table 3)

Inpatient death occurred in 11.9% (23/193) and 20.7% (40/193) required ICU level of care. About 9.8% (19/193) of our sample required vasopressor support for septic

shock, 9.3% (18/193) developed respiratory failure during their hospitalization requiring either non-invasive or mechanical ventilation, 6.2% (12/193) had documented delirium, and 1.0% (2/193) had acute kidney injury requiring dialysis. Of the patients who died, 69.6% (16/23) patients required intermediate/ICU hospitalization. Of these 16 patients, 12 of them had documented goals of care discussion. Mean MASCC score was lower among patients who died vs. those who survived (14.0 vs. 19.1) and those with positive vs. negative blood cultures (16.0 vs. 19.4).

We observed that MASCC score was predictive of poor outcomes (AUC's ranging from 0.67 to 0.76). In particular, those with a low-risk MASCC score were 33% less likely to require intermediate/ICU care (95% CI = 23 to 44%) compared to those with a high-risk MASCC score. In addition, those with a low-risk MASCC score were 28% less likely to have a positive blood culture (95% CI = 16 to 39%) and nearly 19% less likely to die in the hospital (95% CI = 10 to 27%) compared to those with a high-risk MASCC score.

Table 2 Baseline characteristics of patients

Patient characteristics		MASCC score	
	Total N = 193 (100%)	< 21 (high risk) N = 101 (52.3%)	≥ 21 (low risk) N = 92 (47.7%)
Age, mean (SD)	60.3 (15.0)	64.9 (14.3)	55.3 (14.1)
Female, n (%)	107 (55.4)	50 (49.5)	57 (62.0)
Race and ethnicity, n (%)			
White	162 (83.9)	90 (89.1)	72 (78.3)
Hispanic	18 (9.3)	7 (6.9)	11 (12.0)
African American	10 (5.2)	3 (3.0)	7 (7.6)
Asian/unknown	3 (1.5)	1 (1.0)	2 (2.2)
Insurance type, n (%)			
Medicare/Medicaid	116 (61.1)	68 (68.7)	48 (52.8)
Private	74 (38.9)	31 (31.3)	43 (47.3)
Documented ECOG PS, n (%)$^\alpha$	123 (63.7)	58 (57.4)	65 (70.7)
0	43 (35.0)	14 (24.1)	29 (44.6)
1	48 (39.0)	26 (44.8)	22 (33.8)
2	23 (18.7)	11 (19.0)	12 (18.5)
3	8 (6.5)	6 (10.3)	2 (3.1)
4	1 (0.8)	1 (1.7)	0 (0.0)
Documentation of MASCC score, n (%)	3 (1.6)	2 (2.0)	1 (1.1)
Cancer characteristics			
Hematological malignancy, n (%)	102 (100.0)	59 (57.3)	43 (42.7)
AML	33 (32.4)	22 (37.3)	11 (25.6)
Other hematologic malignancy$^\eta$	16 (15.7)	9 (15.3)	7 (16.3)
Non-Hodgkin lymphoma	28 (27.5)	16 (27.1)	12 (27.9)
ALL	8 (7.8)	3 (5.1)	5 (11.6)
CLL	5 (4.9)	2 (3.4)	3 (7.0)
Hodgkin lymphoma	6 (5.9)	3 (5.1)	3 (7.0)
Multiple myeloma	4 (3.9)	2 (3.4)	2 (4.7)
CML	2 (2.0)	1 (1.7)	1 (2.3)
Solid tumors, n (%)	91 (100.0)	42 (46.2)	49 (53.8)
Breast	31 (34.1)	6 (14.3)	25 (51.0)
Thoracic$^\epsilon$	21 (23.1)	16 (38.1)	5 (10.2)
Gastrointestinal$^\infty$	14 (15.4)	7 (16.7)	7 (14.3)
Genitourinary$^\pounds$	8 (8.8)	2 (4.8)	6 (12.2)
Head and neck	5 (5.5)	4 (9.5)	1 (2.0)
Gynecologic$^\yen$	7 (7.7)	3 (7.1)	4 (8.2)
Soft tissue (non-lymphomas)	4 (4.4)	3 (7.1)	1 (2.0)
CNS tumors (brain, spinal cord-non-myeloma)	1 (1.1)	1 (2.4)	0 (0.0)
Stage of cancer (solid tumors only; N = 91)			
I	9 (9.9)	1 (2.4)	8 (16.3)
II	20 (22.0)	8 (19.0)	12 (24.5)
III	20 (22.0)	8 (19.0)	12 (24.5)
IV	42 (46.2)	24 (57.1)	18 (36.7)
Patient receiving chemotherapy, Yes, n (%)	172 (89.1)	89 (88.2)	83 (90.2)
Cycle of chemotherapy (n = 172), median (IQR)	1.00 (1.00; 4.00)	1.00 (1.00; 3.00)	1.00 (1.00; 4.00)
Use of GCSF prior/during hospitalization, n (%)	66 (34.2)	38 (37.6)	28 (30.4)
Use of prophylactic antimicrobials, Yes, n (%)	43 (22.3)	26 (25.7)	17 (18.5)
Microbiological profile			
Viral infection at time of admission	30 (15.5)	12 (11.9)	18 (19.6)
Positive blood cultures, n (%)	53 (27.5)	41 (40.6)	12 (13.0)
Gram-positive cocci	23 (43.4)	17 (41.5)	6 (50.0)
MRSA	3 (5.6)	3 (7.3)	0 (0.0)
Gram-negative rods	26 (49.1)	21 (51.2)	5 (41.7)
Pseudomonas	4 (7.5)	4 (9.7)	0 (0.0)
Fungi$^\beta$	4 (7.5)	3 (7.3)	1 (8.3)

Table 2 (continued)

Patient characteristics		MASCC score	
	Total $N = 193$ (100%)	< 21 (high risk) $N = 101$ (52.3%)	≥ 21 (low risk) $N = 92$ (47.7%)
Fungi identified as source of infection, *n* (%)	4 (7.5)	3 (7.3)	1 (8.3)
Duration of antibiotics (in days), median (IQR)	8 (6; 14)	8 (6; 15)	8 (5;14)
Source of infection identified, *n* (%)	114 (59.1)	67 (66.3)	47 (51.1)
Pulmonary[*]	43 (37.7)	27 (40.3)	16 (34.0)
Line/port infection	20 (17.5)	15 (22.4)	5 (10.6)
Other[Ω]	19 (16.7)	5 (7.5)	14 (29.8)
GI[†]	16 (14.0)	11 (16.4)	5 (10.6)
GU[‡]	13 (11.4)	7 (10.4)	6 (12.8)
Osteomyelitis	2 (1.8)	1 (1.5)	1 (2.1)
CNS[π]	1 (0.9)	1 (1.5)	0 (0.0)
Consults, *n* (%)			
Hematology/oncology	159 (82.4)	86 (85.1)	73 (79.3)
Infectious diseases	98 (50.8)	60 (59.4)	38 (41.3)
Palliative care	13 (6.7)	12 (11.9)	1 (1.1)
Documented goals of care discussion, *n* (%)	24 (12.4)	21 (20.8)	3 (3.3)
Primary team	19 (79.2)	16 (76.2)	3 (100.0)
Hematology/oncology team	4 (16.7)	4 (19.0)	0 (0.0)
Primary care physician	1 (4.2)	1 (4.8)	0 (0.0)

ECOG PS Eastern Cooperative Oncology Group Performance Status, *MASCC* Multinational Association for Supportive Care in Cancer, *GCSF* granulocyte colony-stimulating factor, *AML* acute myeloid leukemia, *ALL* acute lymphoblastic leukemia, *CML* chronic myeloid leukemia, *CLL* chronic lymphocytic leukemia, *CNS* central nervous system, *MRSA* methicillin-resistant *Staphylococcus aureus*, *IQR* interquartile range

[α] As documented in the last oncology note either inpatient or outpatient

[η] Other hematological malignancies identified were Myelodysplastic Syndrome, Primary Myelofibrosis, and Waldenström macroglobulinemia

[ϵ] Includes lung, thymus, mediastinum, trachea, and esophagus

[∞] Includes pancreas, liver, biliary tract, and gastrointestinal tract (stomach, small intestine, colon, rectum, anal)

[£] Includes bladder, prostate, kidney, testicular, and penile cancer

[¥] Includes ovarian, uterine, vaginal, vulvar, and pelvic masses

[β] Fungi found include candida species and Aspergillus species

[*] Includes pneumonia

[Ω] Includes all infections that do not fall into any of the other categories. Further information on the type of infection was not collected

[†] Includes colitis and bacterial translocation in the gut

[‡] Includes UTI, cystitis, and pyelonephritis

[π] Includes meningitis and spinal epidural abscess

Discussion

In this single-center retrospective cohort of patients with FN and cancer (in which more than half of the patients had a hematologic malignancy), nearly 60% of inpatients had an identifiable source of infection with a substantial number of these testing positive for a virus. MASCC score, although rarely used, was predictive of poor outcomes. Goals of care discussions were rarely initiated, even in patients considered high risk. Our findings suggest a need for hospitalist-focused education efforts and quality improvement initiatives to incorporate MASCC score into oncologic hospitalists' workflow.

The proportion of patients with an identifiable source of infection was higher than prior studies have reported [7, 25].

Most published studies examined patients with fever and neutropenia prior to widespread use of rapid viral testing (e.g., for influenza and RSV). Notably, our study was conducted before the onset of the COVID-19 pandemic, so there were no COVID-positive patients in this sample [26]. The incidence of MRSA and Pseudomonas was low compared to other studies across the USA [7], but most patients received empiric antibiotic therapy appropriately per current guidelines because of the high risk for progression to fatal sepsis and mortality associated with these organisms [7, 9, 10].

Use of MASCC score among inpatients in our study was predictive of poor outcomes including the need for intermediate/ICU level care, respiratory failure necessitating ventilation, septic shock requiring vasopressor use, and

Table 3 Outcomes

	Total events N (%)	MASCC score		AUC	Absolute risk Difference (95% CI)
		< 21 high risk 101 (52.3%) N (%)	≥ 21 low risk 92 (47.7%) N (%)		
Inpatient death	23 (11.9)	21 (20.8)	2 (2.2)	0.721	− 18.6% (− 27.1 to − 10.2)
Required intermediate or ICU level of care[€]	40 (20.7)	37 (36.6)	3 (3.3)	0.753	− 33.4% (− 43.5 to − 23.3)
Goals of care discussion	24 (12.4)	21 (20.8)	3 (3.3)	0.701	− 17.5% (− 26.2 to − 8.8)
Respiratory failure[‡]	18 (9.3)	16 (15.8)	2 (2.2)	0.702	− 13.7% (− 21.4 to − 6.0)
Documented delirium	12 (6.2)	11 (10.9)	1 (1.1)	0.710	− 9.8% (− 16.2 to − 3.4)
AKI requiring new dialysis[†]	2 (1.0)	2 (2.0)	0 (0.0)	0.741	− 2.0 (− 4.7 to 0.7)
Septic shock requiring pressors	19 (9.8)	19 (18.8)	0 (0.0)	0.764	− 18.8 (− 26.4 to − 11.2)
Positive blood cultures	53 (27.5)	41 (40.6)	12 (13.0)	0.673	− 27.6% (− 39.3 to − 15.8)

AKI acute kidney injury, *ICU* intensive care unit, *AUC* area under the curve, *CI* confidence interval

[†] Per the kidney disease: improving global outcomes definition

[‡] Requiring use of non-invasive ventilation like continuous positive airway pressure, bi-level continuous positive airway pressure, high-flow nasal cannula; and use of mechanical ventilation with intubation

[€] Intermediate unit defined as a step-up or step-down unit between the general ward and ICU

inpatient death. However, less than 2% of patients had a MASCC score documented on admission, suggesting that hospitalists do not routinely use this score to identify patients at high risk. MASCC score does have limitations; it was developed as a tool intended to prevent admission or reduce time to discharge for low-risk patients, and it may miss up to 10% of low-risk patients who later developed complications [15, 19, 27, 28]. However, the Clinical Index of Stable Febrile Neutropenia (CISNE) scaore [29], the alternative to MASCC score, has poor sensitivity and thus has limited usefulness in high-risk patients.

While prior investigators have validated the MASCC score in low-risk patients hospitalized for FN, its use in high-risk patients has been less frequently studied [30–35]. One validation study, with a goal of identifying high-risk patients who might be candidates for hematopoietic growth factor, correctly predicted 98.3% of low-risk patients and 86.4% of high-risk patients [30]. Other studies have (a) identified patients at a high risk of complications by calculating the score at 48 and 72 h, adding a measure of organ dysfunction [31]; (b) attempted to combine MASCC score of < 21 with C-reactive protein or procalcitonin to predict poor outcomes [32–34]; and (c) examined MASCC score's calibration to identify the risk of mortality and the need for ICU level of care among patients with hematologic malignancies [35]. These studies were limited in that most were done in the ED setting, and none of them examined the use of goals of care discussions in patients with a high risk of poor outcomes.

It is not clear why goals of care were infrequently discussed with patients. We hypothesize that because neutropenic fever is a common, predictable, and manageable complication of cytotoxic therapy, there is often uncertainty regarding who should initiate these conversations. Internists may believe that goals are best discussed by the primary oncologist treating a patient's cancer. They may also fear that they lack the advanced training required to independently prognosticate various stages of cancer and navigate goals of care in those receiving active systemic therapy, especially in an era of evolving cancer therapeutics. There are also known differences in perception of cancer outcomes between physicians [36], which may have contributed to the failure to initiate conversations. Qualitative studies would help to refine these early hypotheses.

Nearly three-quarters of patients who died during hospitalization in our cohort required intermediate/ICU level of care prior to their death. This suggests that these patients experienced clinical deterioration and, either at that time or prior to it, decided to escalate care. While this may have been consistent with patient preferences, it may also have been a missed opportunity to initiate goals of care conversation between the patient, hospitalists, and oncologists in patients with high-risk FN.

There are limitations to our study. First, it is a single-center study with a small sample size, and these results may not be generalizable to larger populations. Second, this study is a retrospective analysis with a risk of misclassification bias in calculating scores. For example, the MASCC score contains subjective characteristics like "burden of illness" and "dehydration." We did go to great lengths to standardize these definitions across reviewers. However, it is possible that those with worse outcomes were more likely to be classified with a high-risk MASCC score. Validation of the score to identify

high-risk patients in a larger, multi-institutional sample of in-patients may be warranted. We also did not create multivariable models to examine the association between MASCC score and outcomes. Our goal, however, was primarily to demonstrate that groups with high and low MASCC scores are different, and increased utilization of this scoring system will allow hospitalists to clarify these differences and improve patient care.

Conclusions

In a single-center study of patients with fever and neutropenia, nearly 60% had an identifiable source of infection. Although the incidence of multidrug-resistant bacteria was low, patients mostly received empiric antibiotics appropriately to cover for these organisms to reduce the risk of sepsis and mortality per current guidelines. Patients with a high-risk MASCC score had worse outcomes, i.e., higher inpatient mortality and utilization of critical care therapies, but MASCC score was not commonly used by treating clinicians. Routine use of the MASCC score may help clinicians identify patients at high risk for complications, allowing for risk stratification at the time of admission. MASCC score could aid with triage, unit placement, and need to address and document goals of care discussions during hospitalization. Hospitalist-focused education efforts about MASCC score should be considered a way to identify patients at high risk for complications and facilitate goals of care discussions.

Declarations

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