Sepsis epidemiology and prognosis in cancer patients: a multicenter prospective observational study

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Introduction

Sepsis in cancer patients

- poor prognosis
- long hospitalization
- high mortality
- re-admission to the hospital

Mirouse A, Vigneron C, Llitjos JF, Chiche JD, Mira JP, Mokart D, Azoulay E, Pène F. Sepsis and Cancer: An Interplay of Friends and Foes. Am J Respir Crit Care Med. 2020 Dec 15;202(12):1625-1635.

Torres LK, Pickkers P, van der Poll T. Sepsis-Induced Immunosuppression. Annu Rev Physiol. 2022 Feb 10;84:157-181.

Objective

To assess

- risk factors for sepsis
- sources of the sepsis
- causative microorganisms
- prognosis in cancer patients

Method

✓Multicenter (11 center)

✓Prospective

✓Observationally

- Patients diagnosed with cancer and hospitalized for any reason, followed for at least 72 hours, were included and observed up until discharge

Method

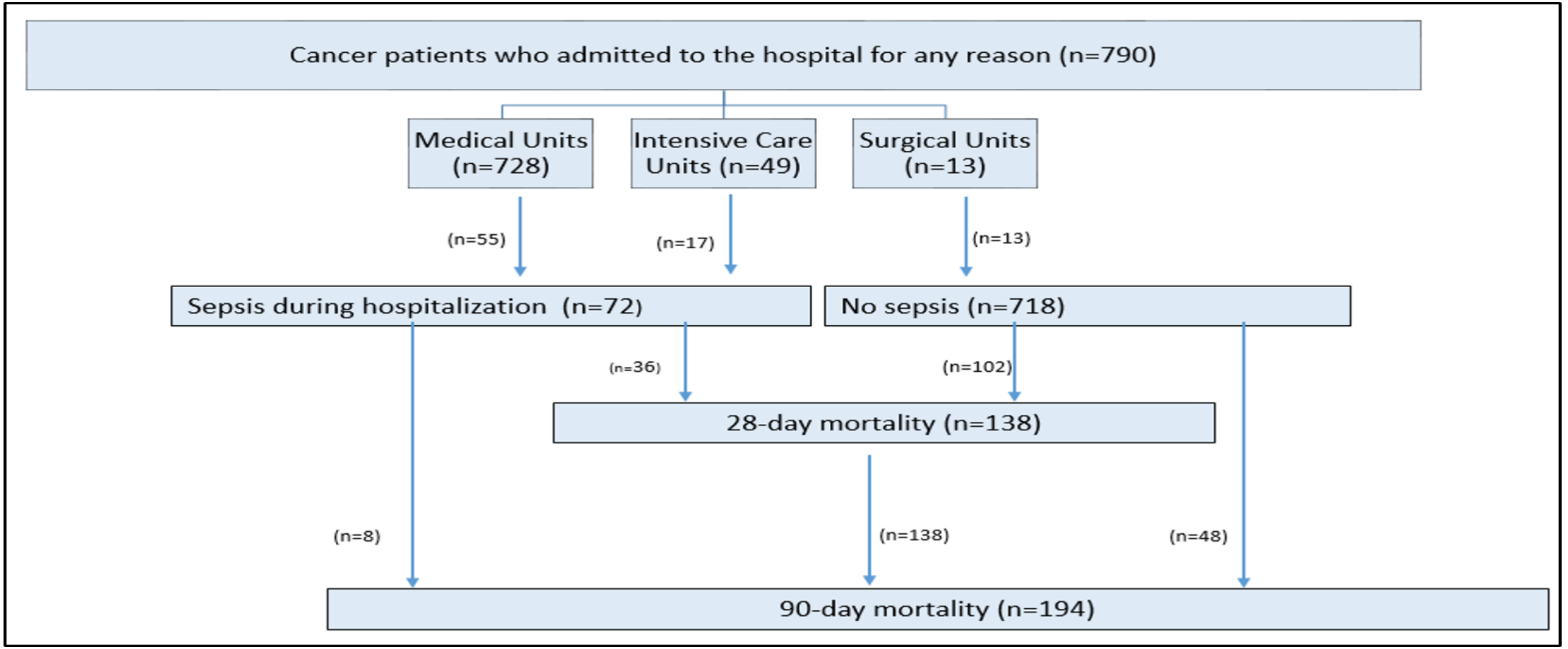
- ✓Demographic data,
- ✓Type of cancer
- ✓Co-morbidities
- ✓Presence of invasive devices before sepsis
- ✓Chemotherapy and antimicrobial treatment usage before sepsis were recorded

Method

Septic patients;

- ✓Interventions
- ✓Sepsis scores
- ✓Source of sepsis
- ✓Causative microorganisms
- ✓Antimicrobial susceptibility
- ✓Mortality were recorded

Results


Cancer patients who admitted to the hospital for any reason (n=790)
Medical Units (n=728)
Intensive Care Units (n=49)
Surgical Units (n=13)
(n=55)
(n=17)
(n=13)
Sepsis during hospitalization (n=72)
No sepsis (n=718)
(n=36)
(n=102)
28-day mortality (n=138)
(n=8)
(n=138)
(n=48)
90-day mortality (n=194)

Results

Comparison of Demographic Data, Cancer Type, Co-morbidities in Patients with and without Sepsis

	With Sepsis n = 72 (%)	Without sepsis n = 718 (%)	Total n=790 (%)	p	Multivariate Analyze OR (95% CI), p
Age	62.1±16.2	56.7±16.1	57.2±16.1	0.007	
Age>63	40 (55.6)	272 (37.9)	312 (39.5)	0.005	**1.81 (1.03-3.19), 0.037**
Male	50 (69.4)	419 (58.4)	469 (59.4)	0.078	
Reason for hospitalization					
Chemotherapy	25 (34.7)	314 (43.7)	339 (42.9)		
Infection	23 (31.9)	124 (17.3)	147 (18.6)		
Supportive Therapy	14 (19.4)	136 (18.9)	150 (19)		
Chemotherapy complication	2 (2.8)	14 (1.9)	16 (2)	0.189	
Disease complication	4 (5.6)	55 (7.7)	59 (7.5)		
Transplant preparation	2 (2.8)	38 (5.2)	40 (5.06)		
Other	1 (1.4)	17 (2.4)	18 (2.3)		
Followed Clinic					
Medical	55(76.4)	673 (93.7)	728 (92.2)	**<0.001**	
Surgical	0	13 (100)	13 (1.6)		
Intensive care unit	17 (34.7)	32(4.5)	49 (6.2)		
Hematological Malignancies	33 (45.8)	419 (58.4)	452 (57.2)	0.028	1.73 (0.86-3.47), 0.119
AML	15 (45.5)	150 (35.5)	165 (36.3)		
ALL	6 (18.2)	61 (14.5)	67 (14.7)		
MM	2 (6.1)	62 (14.7)	64 (14.1)		
HL	4 (12.1)	19 (4.5)	23 (5.1)		
NHL	4(12.1)	92 (21.8)	96 (21.1)	0.33	
CML	0	3 (0.7)	3 (0.7)		
MDS	0	11 (2.6)	11 (2.4)		
CLL	1 (3.0)	7 (1.7)	8 (1.8)		
Other	1 (3.0)	17 (4.0)	18 (4.0)		

Results

Comparison of Demographic Data, Cancer Type, Co-morbidities in Patients with and without Sepsis

	With Sepsis n = 72 (%)	Without sepsis n = 718 (%)	Total n=790 (%)	p	Multivariate Analyze OR (95% CI), p
Diseases Stage					
Newly diagnosis	24 (33.8)	245 (35.2)	269 (35.1)		
Remission	18 (25.4)	190 (27.3)	208 (27.1)	0.85	
Refractory-Relapse	29 (40.8)	261(35.7)	290 (37.8)		
HSCT	5 (7.9)	58 (8.5)	63 (8.4)	0.440	
Autologous	2 (40)	36 (63)	38 (61)		
Allogeneic	3 (60)	21 (36.8)	24 (38.7)	0.308	
Co-morbidities					
Hypertension	29 (59)	188 (54)	217 (54.7)	0.479	
Diabetes	17 (34.7)	148 (42.5)	165 (41.6)	0.279	
Coronary artery disease	18 (36.7)	103 (29.6)	121 (30.5)	0.310	
Chronic pulmonary disease	7 (14.3)	61 (17.5)	68 (17.1)	0.370	
Chronic renal failure	8 (16.3)	37 (10.7)	45 (11.4)	0.242	
Heart failure	7 (14.3)	27 (7.8)	34 (8.6)	0.295	
Cerebrovascular disease	4 (8.2)	18 (5.2)	22(5.5)	0.392	
Hospitalization due to any infection	23 (31.9)	124 (17.3)	147 (18.6)	0.002	**2.26 (1.13-4.50), 0.020**
Pneumoniae	9 (12.5)	54 (7.5)	63 (7.9)	0.001	0.69 (0.26-1.85), 0.467
Urinary tract infection	7 (9.7)	18 (2.5)	25 (3.1)		
Febrile neutropenia	2 (2.7)	27 (2.7)	29 (3.6)		
Skin and Soft tissue infection	2 (2.7)	10 (1.3)	12 (1.5)		
Intraabdominal infection	1 (1.3)	9 (1.2)	10 (1.2)		
Catheter associated bloodstream infection	2 (2.7)	1 (0.8)	3 (0.3)		
CMV viremia in the last three months	2 (2.8)	71 (9.9)	73 (9.2)	0.052	
GVHD in the last three months	3 (4.2)	7 (1)	10 (1.3)	0.055	**6.54 (1.36-31.28), 0.019**
Prolonged neutropenia	19 (24)	139 (19.4)	158 (20)	0.178	**2.17 (1.05-4.56), 0.035**
Invasive procedures before the occurrence of sepsis	52 (72)	439 (61)	491 (62)	0.065	1.07(0.55-2.10), 0.83
Urethral Catheter	29 (40.3)	91 (12.7)	120 (15.2)	<0.001	**4.76 (2.46-9.23), 0.001**

Results

Comparison of Demographic Data, Cancer Type, Co-morbidities in Patients with and without Sepsis

	With Sepsis n = 72 (%)	Without sepsis n = 718 (%)	Total n=790 (%)	p	Multivariate Analyze OR (95% CI), p
Previous hospitalization in last three months (n=496)	42(58.3)	472 (65.7)	514 (65.1)	0.243	0.56 (0.31-1.01), 0.55
Previous ICU hospitalization in last three months	10 (13.9)	40 (5.6)	50 (6.3)	0.006	1.74 (0.75-4.02), 0.193
Previous bacterial infection in the last three months	39 (54.2)	284 (39.6)	323 (40.9)	0.016	**1.78 (1.03-3.08), 0.038**
Antimicrobial prophylaxis in the last three months	25 (36.2)	268 (38.4)	293 (38.2)	0.796	
Previous IFI in the last three months	5 (6.9)	58 (8.1)	63 (8.0)	0.730	
Rectal VRE colonization in the last one year (n=433)	4 (9)	32 (8.2)	36 (8.3)	0.519	
Rectal CRE colonization in the last one year (n=472)	1 (2.3)	39 (5.9)	40 (8.4)	0.316	
Previous COVID-19 infection in the last three months (n=663)	13 (20)	116 (19.3)	129 (19.4)	0.303	
Previous chemotherapy in the last three months	50 (69.4)	563 (80.0)	613 (79.0)	0.037	0.79 (0.40-1.53), 0.489
Number of Chemotherapy Cures	3.0 (1.0-37)	3.0 (1.0-28.0)	3.0 (1.0-37)	0.519	
GCSF	25 (45.5)	246 (40.5)	271 (40.9)	0.477	
Radiotherapy	11 (20.0)	94 (15.5)	105 (15.8)	0.377	
Corticosteroid	18 (32.7)	205 (33.6)	223 (33.5)	0.901	
Methylprednisolone (total mg)	800 (80-2400)	360 (8.0-5000.0)	400 (8.0-5000.0)	0.110	
Dexamethasone (total mg)	80 (28.0-400.0)	100 (4.0-1200.0)	100 (4.0-1200.0)	0.820	
Mortality (28 days)	36 (50.0)	102 (14.1)	138 (17.5)	<0.001	
Mortality (90 days)	44 (59.7)	150 (20.9)	194 (24.4)	<0.001	

Results

Empirical Treatment (n=72)	
Carbapenem	45 (62)
Glycopeptide	35 (49)
Beta lactam-Beta lactamase	22 (30.5)
Floroquinolone	5 (7)
Aminoglycoside	4 (5.5)
Colistin	4 (5.5)
Liposomal Amp-B	7 (9.7)
Echinocandine	2 (2.7)

Empirical treatment was continued in 31 patients

Prolonged Febrile Neutropenia on day 5	n=20
Carbapenem	14
Aminoglicoside	4
Glycopeptide	2
Colistin	8
Voriconazole	2
Liposomal Amp-B	3

Modification After Laboratory/Radiology results	n= 21
Carbapenem	10
Aminoglicoside	3
Glycopeptide	5
Colistin	5
Voriconazole	4
Beta lacatm-Beta lactamase	3
Floroquinolone	1

De-escalation	n=10
Beta lacatm-Beta lactamase	2
Cephalocporine	2
Carbapenem	4
Glycopeptide	2
Colistin	1
Voriconazole	1

Results

Comparison of risk factors for 28-day mortality in septic patients

	Survivor n=36 (%)	Non-survivor n=36 (%)	p	Multivariate Regression Analysis OR (95% CI), p
Previous bacterial infection in the last three months	22 (61.1)	19 (52.8)	0.634	
Time from admission to hospital to development of sepsis	13.6±12.8	16.91±13.19	0.434	
SIRS score	3.2±0.9	3.3±0.6	0.641	
qSOFA score	2.0±0.8	2.3±0.7	0.074	
SOFA>7	16 (44.4)	20 (74.1)	0.023	0.66 (0.10-6.62), 0.416
APACHE II score	18.8±5.1	21.8±8.5	0.068	0.89 (0.88-1.11), 0.881
Septic shock	14 (38.9)	23 (63.9)	0.054	0.81 (0.48-10.69), 0.810
Crystalloid use	24 (66.7)	30 (83.3)	0.102	
Crystalloid onset time (h)	2.0± 1.5	1.6±1.3	0.247	
Charlson Co-morbidity index	5.5±3.7	5.4±3.0	0.918	
The source of the sepsis			0.010	1.20 (0.83-1.73), 0.320
Lung	9 (25.0)	20 (55.6)	0.008	
Central venous catheter	4 (11.1)	5 (13.9)		
Urinary system	5 (13.9)	3 (8.3)		
Intra-abdominal	10 (27.8)	1 (2.8)		
Primary blood stream	2 (5.6)	4 (11.1)		
Other	6 (15.7)	3(8.3)		
Antibiotic initiation time	3.0±3.9	2.2±2.9	0.418	
Microorganism isolation rate				
Gram Negative	13 (36.1)	22 (61.1)	0.738	
Gram Positive	2 (5.6)	3 (8.3)		
Carbapenem resistant bacteria	5 (13.9)	13 (36.1)	0.029	**15.47 (1.45-64.17), 0.023**
COVID-19 positivity	2 (5.6)	1 (2.8)	0.091	
Appropriateness of empirical treatment	27 (79.4)	14 (48.3)	0.010	**5.02 (0.17-7.61), 0.025**
Duration of the treatment	14.8±8.3	7.0±6.1	<0.001	
Source control requirement	14 (38.9)	8 (24.2)	0.209	
Source control	11 (78.6)	5 (62.5)	0.624	0.91 (0.98-5.49), 0.763
Microbiological response on 5th day	11 (30.6)	3 (8.6)	0.061	1.43 (0.65-5.65), 0.231
Clinical response on 5th day	30 (83.3)	4 (11.1)	<0.001	**10.58 (0.39-28.25), 0.021**

Results

Comparison of risk factors in patients who developed and did not develop 90-day mortality

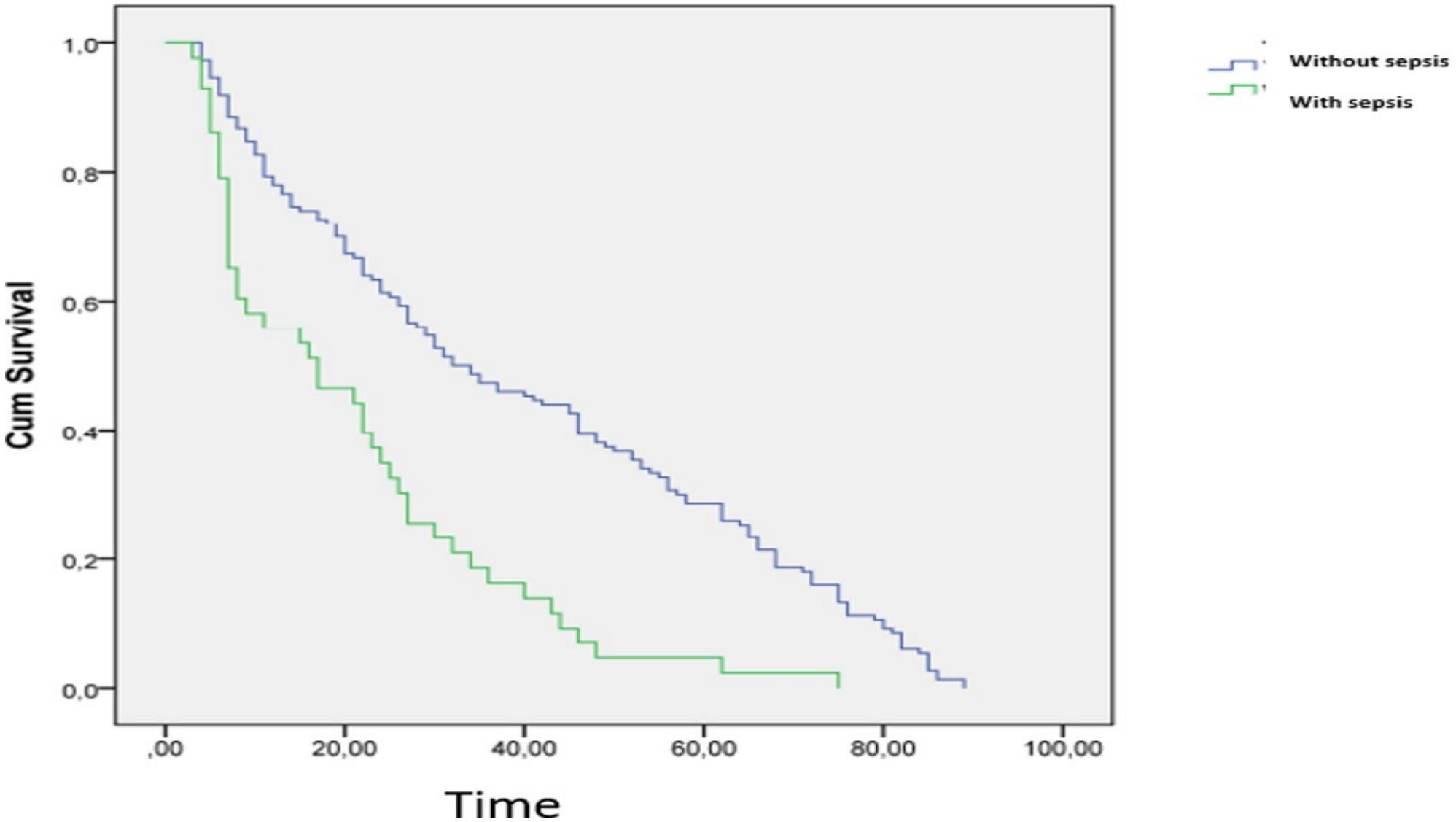
	Survivor n=596 (%)	Non-Survivor n=194 (%)	p	Multivariate Regression Analysis OR (95% CI), p
Age>60	260 (43.6)	119 (61.7)	<0.001	0.383 (0.68-2.07), 0.53
Male Gender	345 (57.7)	124 (64.2.7)	0.112	
Reason for hospitalization				
Chemotherapy	301 (50.4)	38 (19.7)		
Infection	93(15.6)	54 (28)	<0.001	1.70 (0.82-2.67), 0.191
Supportive Therapy	92 (15.4)	58 (30.1)		
Chemotherapy complication	13 (2.2)	3 (1.6)		
Disease complication	36 (6.0)	23 (11.9)		
Transplant preparation	37 (6.2)	3 (1.6)		
Other	12 (2.0)	6 (3.1)		
Hematological Malignancies	391 (65.4)	61 (31.6)	<0.001	**7.06 (1.79-6.79), 0.008**
ALL	61 (15.5)	6 (9.8)		
AML	135 (22.6)	30 (49.2)		
MM	58 (9.7)	6 (9.8)		
HL	21 (5.3)	2(3.3)		
NHL	85 (21.6)	11 (18)	0.032	
MDS	10 (2.5)	1 (1.6)		
CLL	4 (1.0)	4 (6.6)		
Other	17(4.3)	1(1.6)		
Solid Tumor	231 (38.7)	132 (68.4)	<0.001	4.07 (1.70-1.01), 0.054
Lung	37 (16.2)	33 (25.0)		
Colon	25 (4.2)	15 (11.4)		
Breast	21(9.2)	11 (8.3)		
Brain	7 (3.1)	1 (0.8)		
Prostate	17 (7.4)	10(7.6)	0.002	
Bone	11 (4.8)	0 (0)		
Stomach	15 (6.6)	18 (13.6)		
Liver	6(2.6)	7 (5.3)		
Pancreas	9(3.9)	11 (8.3)		
Bladder	11 (4.8)	4(3)		
Endometrium	6 (2.6)	4 (3)		
Other	64 (27.9)	18(13.6)		
Diseases Stage				
Newly diagnosis	215 (37.4)	54 (28)		
Remission	165(28.7)	43 (22)	0.001	2.0 (1.15-1.50), 0.157
Refractory-Relapse	195 (33.9)	95 (49.5)		

Results

Comparison of risk factors in patients who developed and did not develop 90-day mortality

	Survivor n=596 (%)	Non-Survivor n=194 (%)	p	Multivariate Regression Analysis OR (95% CI), p
Diseases Stage				
Newly diagnosis	215 (37.4)	54 (28)		
Remission	165(28.7)	43 (22)	0.001	2.0 (1.15-1.50), 0.157
Refractory-Relapse	195 (33.9)	95 (49.5)		
HSCT	56 (9.8)	7 (3.8)		
Co-morbidities	279 (46.9)	118 (61.1)	0.001	
Hypertension	155 (55.6)	62 (52.2)	0.58	
Diabetes	116 (41.6)	49 (41.5)	0.54	
Coronary artery disease	74 (26.5)	47 (39.8)	0.008	2.24 (0.88-2.42), 0.134
Chronic pulmonary disease	42(15.1)	26 (22)	0.063	
Chronic renal failure	29 (10.4)	16 (13.6)	0.37	
Heart failure	23 (8.3)	11 (9.3)	0.76	
Cerebrovascular disease	14(5.0)	8 (6.8)	0.48	
Previous hospitalization in last three months	394 (66)	120 (62.2)	0.33	
Previous ICU hospitalization in last three months	30 (5.0)	20 (10.4)	0.008	
Previous bacterial infection in the last three months	239 (40)	84 (43.5)	0.391	
Previous IFI in the last three months	51 (8.5)	12 (6.3)	0.316	
Rectal VRE colonization in the last one year (n=433)	26 (4.3)	10 (6.3)	0.326	
Rectal CRE colonization in the last one year (472)	36 (6.0)	4 (2.1)	0.008	
Previous COVID-19 infection in the last three months (n=663)	107 (17.8)	23 (11.9)	0.014	
Previous chemotherapy in the last three months	483 (82.2)	130 (67.4)	<0.001	2.24 (0.33-1.13), 0.11
GCSF*	200 (38.2)	71 (51.1)	0.006	
Radiotherapy*	60 (11.5)	45 (31.9)	<0.001	
Corticosteroid*	241 (41.3)	64 (33.2)	0.137	
Antimicrobial prophylaxis in the last three months	248 (42.8)	45 (24.1)	<0.001	
Presence of Sepsis	29 (4.8)	43 (22.3)	<0.001	**13.42 (1.79-6.83), 0.001**

Results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Time
Without sepsis
With sepsis

Conclusion

- The rate of sepsis in cancer patients was **9%**
- **The invasive devices, prolonged neutropenia, GVHD, and previous bacterial infections** were related with sepsis
- The presence of carbapenem-resistant microorganisms has also been shown to be a risk factor for mortality in patients with sepsis
- Mortality was found to be **13 times higher** in patients with sepsis
- **Rational use of catheters** (if necessary, in accordance with asepsis, short-term use) is an important issue

THANK YOU…