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Outcome of cancer patients considered for intensive care unit admission in two university hospitals in the Netherlands: the danger of delayed ICU admissions and off-hour triage decisions

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Abstract

Background: Very few studies assessed the association between Intensive Care Unit (ICU) triage decisions and mortality. The aim of this study was to assess whether an association could be found between 30-day mortality, and ICU admission consultation conditions and triage decisions.

Methods: We conducted a retrospective cohort study in two large referral university hospitals in the Netherlands. We identified all adult cancer patients for whom ICU admission was requested from 2016 to 2019. Via a multivariable logistic regression analysis, we assessed the association between 30-day mortality, and ICU admission consultation conditions and triage decisions.

Results: Of the 780 cancer patients for whom ICU admission was requested, 332 patients (42.6%) were considered 'too well to benefit' from ICU admission, 382 (49%) patients were immediately admitted to the ICU and 66 patients (8.4%) were considered 'too sick to benefit' according to the consulting intensivist(s). The 30-day mortality in these subgroups was 30.1%, 36.9% and 81.8%, respectively. In the patient group considered 'too well to benefit', 258 patients were never admitted to the ICU and 74 patients (9.5% of the overall study population, 22.3% of the patients 'too well to benefit') were admitted to the ICU after a second ICU admission request (delayed ICU admission). Thirty-day mortality in these groups was 25.6% and 45.9%. After adjustment for confounders, ICU consultations during off-hours (OR 1.61, 95% CI 1.09–2.38, p-value 0.02) and delayed ICU admission (OR 1.83, 95% CI 1.00–3.33, p-value 0.048 compared to "ICU admission") were independently associated with 30-day mortality.

Conclusion: The ICU denial rate in our study was high (51%). Sixty percent of the ICU triage decisions in cancer patients were made during off-hours, and 22.3% of the patients initially considered "too well to benefit" from ICU admission were subsequently admitted to the ICU. Both decisions during off-hours and a delayed ICU admission were associated with an increased risk of death at 30 days. Our study suggests that in cancer patients, ICU triage decisions

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should be discussed during on-hours, and ICU admission policy should be broadened, with a lower admission threshold for critically ill cancer patients.

Keywords: Intensive Care Unit, Critical care, Triage, Admission decisions, Malignancy, Cancer, Mortality

Introduction

Overall mortality of cancer patients has decreased over the past decades, due to improvement in early detection and innovative cancer treatments [1, 2]. At the same time, the probability of life-threatening events requiring Intensive Care Unit (ICU) treatment related to these novel therapies has increased [3]. Therefore, intensivists are increasingly confronted with cancer patients for whom ICU admission is requested [4, 5].

Several studies assessed the influence of early versus late ICU admission on outcome in cancer patients [6–12]. However, the majority of these studies focussed on specific subgroups of critically ill cancer patients (e.g., acute respiratory failure or leukemia) [6–9]. To the best of our knowledge, only Thiery et al. compared outcome between cancer patients immediately admitted to the ICU and cancer patients who initially remained in the ward, but were subsequently admitted to the ICU during the same hospitalization [10]. Thus, the effect of triage decisions on outcome in acutely ill cancer patients remains mostly unknown.

In addition, the association between ICU admission consultation conditions, such as ICU consultation during on-hours versus off-hours or the number of physicians involved, and the outcome of patients was not evaluated in these studies. Although it is a common belief that patients admitted to the ICU during off-hours have a higher risk of death [13], this remains a controversial issue [13, 14].

The aim of our study was to evaluate whether ICU admission consultation conditions and ICU triage decisions were associated with 30-day mortality after adjusting for baseline confounders. Furthermore, to explore whether associations found in this analysis persisted over time (at 90 days, 180 days and 1 year).

Methods

Participating hospitals

We conducted a retrospective cohort study in two large referral university hospitals in the Netherlands (Erasmus Medical Center, Rotterdam and University Medical Center Utrecht, Utrecht). Both hospitals had a mixed, closed ICU with 56 and 36 beds, respectively. In one of the hospitals, a medium care was present, which could be a suitable alternative for ICU care, for example for administering a low dose of vasopressors. The

Netherlands has a healthcare insurance program covering all residents without ICU admission restrictions or restrictions in indicated ICU treatments.

In general, ICU admission was considered when ICU treatment was requested by the referring specialist, either by a junior or senior physician. No ICU triage protocol with predefined ICU admission criteria existed in both hospitals during the study period. The national guideline for ICU triage of critically ill patients in general is outdated (2005) and currently under revision [15]. During our study period, ‘at risk’ patients on the ward were not routinely discussed by oncologists or hematologists and ICU physicians. Referring physicians used the Modified Early Warning Score (MEWS) and clinical assessment for ICU referral decisions. During on-hours, the patient was evaluated by an intensivist, whom subsequently decided whether to admit or reject admission. During off-hours, the patient was evaluated by a fellow (intensivist in training), who subsequently consulted the senior ICU attending. The final decision was made together (fellow and attending). In both hospitals, treatment recommendations for patients denied ICU admission were provided by the intensivist or fellow.

In general, decisions to admit were based on severity of illness and patient-related factors such as age, cancer status, comorbidities and performance status. ICU physicians used these factors to estimate whether an ICU admission would be inappropriate, either because the patient is very likely to recover without intensive care treatment (patients ‘too well to benefit’) or because an ICU admission is very unlikely to prevent death (patients ‘too sick to benefit’).

Ethics

The institutional review board of the Erasmus Medical Center approved the study. Local approval was obtained for the University Medical Center Utrecht. No additional patient consent was required due to the non-invasive retrospective nature of the study.

Patient data

Using our Electronic Health Records (EHR), we identified all adult cancer patients for whom ICU treatment was requested from 2016 to 2019. Patients with a planned ICU admission, an emergency surgery or intervention, after cardiopulmonary resuscitation or transferred from

another ICU were excluded, as these patients are generally admitted to the ICU without previous discussions between referring physicians and ICU physicians.

Reasons for ICU admission consultation noted in the EHR by the referring specialism were collected (i.e., shock, respiratory insufficiency, altered consciousness, sepsis, acute kidney injury (AKI), high MEWS, hemodynamic instability or other).

Patients who were transferred to another ICU due to bed unavailability were included in the ICU admission group. Patients who were initially denied admission, but admitted after a second request during the same hospitalization were defined as 'delayed ICU admission'. We collected reasons for ICU denial and acceptance, together with context parameters: (1) time (on-hours or off-hours), (2) place (emergency room, ward or other, such as post-anesthesia care unit), and (3) number of physicians involved in the decision.

Baseline characteristics

Clinically relevant baseline characteristic such as age, comorbidities and underlying malignancy were collected. A metastatic solid tumor was defined as the presence of cancer cells present in distant organs, determined from the medical charts. We defined controlled cancer as 'cancer in remission or stable', while we considered recently diagnosed malignancies and progressive malignancies as "uncontrolled cancer". We used the Eastern Cooperative Oncology Group Performance Status (ECOG PS) to evaluate performance status 1 month to 14 days before hospital admission and the Charlson Comorbidity Index (CCI) for comorbidities [16]. To evaluate severity of critical illness before the ICU consultation, the MEWS was used, as this score is used in both hospitals by physicians and nurses [17, 18]. Cancer patients were not automatically considered as 'immunocompromised'. Patients were only considered immunocompromised when they met one of the five National Intensive Care Evaluation criteria: (1) long-term immunosuppressive therapy; (2) corticosteroid use (either short-term high dose or long-term low dose); (3) chemotherapy or radiotherapy in the past year; (4) chemotherapy or radiotherapy for Hodgkin or non-Hodgkin lymphoma at any time before ICU admission; (5) documented humoral or cellular deficiencies.

Primary and secondary endpoints

The primary objective of this study was to evaluate the association between 30-day mortality, and ICU admission consultation conditions and triage decisions in critically ill cancer patients.

The secondary objectives were the association between 90-day, 180-day and 1-year mortality, and ICU admission consultation conditions and triage decisions.

Statistical analysis

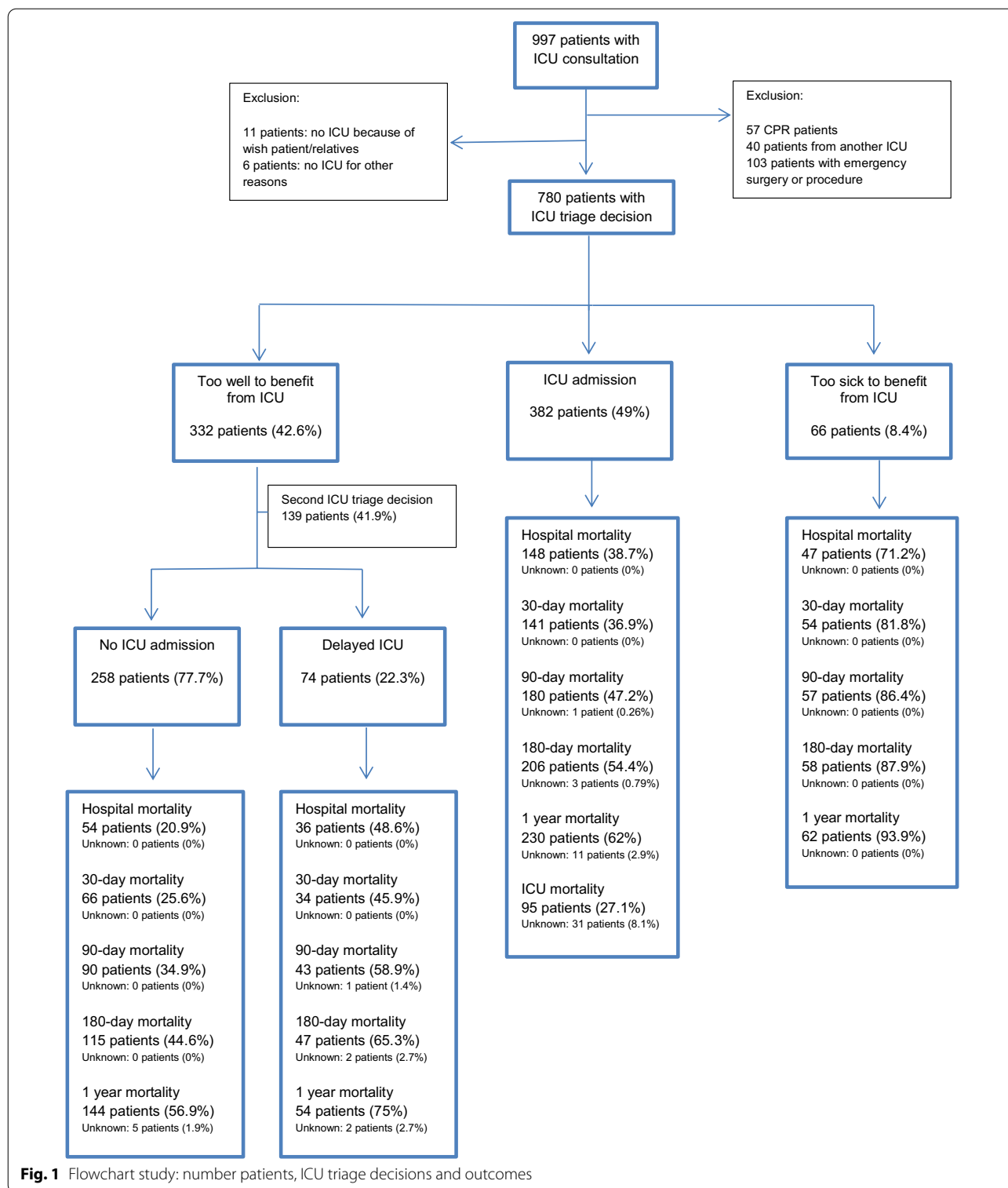
We categorized the patient population into four groups according to the triage decision: (1) patients considered too well to benefit from ICU treatment, never admitted to the ICU; (2) patients with a delayed ICU admission (initially considered too well to benefit, however, admitted to the ICU after a second ICU request); (3) patients immediately admitted to the ICU and (4) patients considered too sick to benefit from ICU treatment. Descriptive statistics were used to describe patient characteristics. We reported categorical variables as numbers with percentage, and continuous variables as median with 25th–75th interquartile range (IQR). To assess differences between the groups, we used Pearson's Chi-square tests for categorical variables and the Kruskal–Wallis test for continuous variables. A statistical test with a two-tailed p value ≤ 0.05 was considered as significant.

We assessed the association between ICU admission consultation conditions and triage decisions, and the 30-day mortality via logistic regression analysis. We performed a univariable logistic regression analysis, in which we included patient characteristics (e.g., age, gender, cancer type, performance status, etc.), ICU triage decision (i.e., the four groups as described above) and ICU admission consultation characteristics. All variables with a p value of < 0.2 in this regression analysis were included in the multivariable model. We tested for an interaction between ICU triage decisions and on-hours consultation, between ICU triage decisions and cancer type, and between metastatic disease and cancer type, all three interaction terms were statistically not significant (p -value 0.21, 0.44 and 0.57, respectively).

Finally, we assessed the association between 90-day, 180-day and 1-year mortality, and ICU admission consultation conditions and ICU triage decisions in a similar way. In a post hoc analysis, we assessed the severity of illness, time of ICU consultation (on-hours vs. off-hours) and consult reasons of the second ICU triage decision in patients with delayed ICU admission. Data were analyzed using IBM®SPSS® Statistics 24.0 (IBM, Chicago, IL, USA).

Results

We included 780 cancer patients with an ICU admission request. Of these patients, 332 (42.6%) were considered 'too well to benefit from ICU', 382 (49%) were admitted to the ICU and 66 (8.4%) were considered 'too sick to benefit from ICU' (Fig. 1). For 139 patients (41.9%)



of the ‘too well to benefit’ group, ICU admission was requested a second time during the same hospitalization. Of the 332 patients initially considered ‘too well to benefit’, 258 patients (77.7%) were never admitted to the

ICU, 74 patients (22.3%) were admitted to the ICU after the second request (delayed ICU admission, Fig. 1). The median time between first and second admission request was 1 day [0–2.5].

Table 1 Baseline characteristics by ICU triage decision

	Total study population N = 780	Too well to benefit— No ICU N = 258	Too well to benefit— Delayed ICU N = 74	ICU N = 382	Too sick to benefit N = 66	p-value
Age	64 [56–70]	63 [54–69]	66 [59–70]	65 [58–72]	63 [56–70]	0.04*
Male	499 (64%)	166 (64.3%)	44 (59.5%)	248 (64.9%)	41 (62.1%)	0.82
Solid malignancy	503 (64.7%)	163 (63.2%)	41 (55.4%)	244 (63.9%)	55 (83.3%)	0.005*
Hematological malignancy	274 (35.3%)	94 (36.4%)	33 (44.6%)	136 (35.6%)	11 (16.7%)	
Both	3 (0.4%)	1 (0.4%)		2 (0.5%)		
Metastatic solid malignancy	245 (31.4%)	75 (29.1%)	20 (27%)	108 (28.3%)	42 (63.6%)	< 0.001*
Cancer recurrence	71 (9.1%)	33 (12.8%)	5 (6.8%)	27 (7.1%)	6 (9.1%)	0.09
Uncontrolled cancer	408 (52.4%)	145 (56.2%)	33 (44.6%)	173 (45.4%)	57 (86.4%)	< 0.001*
CCI	4 [2–6]	4 [2–6]	3 [2–6]	4 [2–6]	6 [4–7]	< 0.001*
ECOG PS before hospital	1 [1–2]	1 [1–2]	1 [1–1]	1 [0–2]	2 [1–3]	< 0.001*
0	181 (23.2%)	54 (20.9%)	17 (23%)	108 (28.3%)	2 (3%)	
1	298 (38.2%)	93 (36%)	39 (52.7%)	148 (38.7%)	18 (27.3%)	
2	191 (24.5%)	74 (28.7%)	15 (20.3%)	81 (21.2%)	21 (31.8%)	
3	90 (11.5%)	31 (12%)	3 (4.1%)	36 (9.4%)	20 (30.3%)	
4	15 (1.9%)	5 (1.9%)	0 (0%)	6 (1.6%)	4 (6.1%)	
Unknown	5 (0.6%)	1 (0.4%)	0 (0%)	3 (0.8%)	1 (1.5%)	
MEWS	5 [3–6]	4 [2–6]	5 [4–7]	5 [4–7]	5 [3–6]	< 0.001*
Unknown	80 (10.3%)	14 (5.4%)	4 (5.4%)	54 (14.1%)	8 (12.1%)	
Cancer treatment before ICU	684 (88%)	223 (86.8%)	65 (87.8%)	343 (90.3%)	53 (80.3%)	0.12
Unknown	3 (0.4%)					
Immunocompromised	560 (71.8%)	199 (77.1%)	49 (66.2%)	265 (69.4%)	47 (71.2%)	0.13
Year ICU consult						0.20
2016	214 (27.4%)	67 (26%)	22 (29.7%)	114 (29.8%)	11 (16.7%)	
2017	204 (26.2%)	62 (24%)	18 (24.3%)	108 (28.3%)	16 (24.2%)	
2018	222 (28.5%)	78 (30.2%)	18 (24.3%)	99 (25.9%)	27 (40.9%)	
2019	140 (17.9%)	51 (19.8%)	16 (21.6%)	61 (16%)	12 (18.2%)	
Earlier ICU admission before consult	77 (9.9%)	24 (9.3%)	8 (10.8%)	45 (11.8%)	0 (0%)	0.03*
One ICU physician	318 (40.8%)	109 (42.2%)	35 (47.3%)	158 (41.4%)	16 (24.2%)	0.007*
Two ICU physicians	385 (49.4%)	130 (50.4%)	37 (50%)	176 (46.1%)	42 (63.6%)	
More than two ICU physicians	77 (9.9%)	19 (7.4%)	2 (2.7%)	48 (12.6%)	8 (12.1%)	
One referring physician (ref)	164 (21.2%)	59 (23%)	19 (26%)	80 (21.2%)	6 (9.1%)	< 0.001*
Two referring physicians	496 (64.2%)	175 (68.1%)	41 (56.2%)	240 (63.7%)	40 (60.6%)	
More than two referring physicians	113 (14.6%)	23 (8.9%)	13 (17.8%)	57 (15.1%)	20 (30.3%)	
Location consult						< 0.001*
Emergency room (ref)	137 (17.6%)	30 (11.6%)	4 (5.4%)	81 (21.2%)	22 (33.3%)	
Ward	483 (61.9%)	197 (76.4%)	55 (74.3%)	190 (49.7%)	41 (62.1%)	
Other	160 (20.5%)	31 (12%)	15 (20.3%)	111 (29.1%)	3 (4.5%)	
On-hours (ref)	315 (40.4%)	95 (36.8%)	27 (36.5%)	163 (42.7%)	30 (45.5%)	0.34
Off-hours	465 (59.6%)	163 (63.2%)	47 (63.5%)	219 (57.3%)	36 (54.5%)	

Table 1 (continued)

	Total study population N = 780	Too well to benefit— No ICU N = 258	Too well to benefit— Delayed ICU N = 74	ICU N = 382	Too sick to benefit N = 66	p-value
Weekend	244 (31.3%)	77 (29.8%)	25 (33.8%)	118 (30.9%)	24 (36.4%)	0.73
Consult reason						
Shock	150 (19.2%)	30 (11.6%)	5 (6.8%)	103 (27%)	12 (18.2%)	< 0.001*
Respiratory insufficiency	483 (61.9%)	147 (57%)	50 (67.6%)	242 (63.4%)	44 (66.7%)	0.20
Altered consciousness	139 (17.8%)	36 (14.0%)	7 (9.5%)	80 (20.9%)	16 (24.2%)	0.01*
Sepsis	214 (27.4%)	47 (18.2%)	22 (29.7%)	135 (35.3%)	10 (15.2%)	< 0.001*
Acute kidney injury	94 (12.1%)	18 (7%)	10 (13.5%)	60 (15.7%)	6 (9.1%)	0.008*
High MEWS	23 (2.9%)	16 (6.2%)	3 (4.1%)	2 (0.5%)	2 (3%)	0.001*
Hemodynamic instability	280 (35.9%)	86 (33.3%)	21 (28.4%)	152 (39.8%)	21 (31.8%)	0.14
Other	99 (12.7%)	42 (16.3%)	9 (12.2%)	36 (9.4%)	12 (18.2%)	0.05

Table shows data of first ICU consultation of the hospital admission

A p-value of < 0.05 is considered significant (marked by an *)

CCI Charlson Comorbidity Index, ECOG PS Eastern Cooperative Oncology Group Performance Status, MEWS Modified Early Warning Score, On-hours during dayshift

Patient characteristics, severity of illness scores and admission consultation characteristics of the total study population and the 4 groups are shown in Table 1. The different types of cancer are reported in Additional file 1: Table S1. The 'too sick to benefit' group had more patients with solid malignancy, metastatic disease and uncontrolled cancer when compared to the other groups. In addition, the CCI and ECOG performance status were higher in patients 'too sick to benefit' than in the other groups. The MEWS was the lowest in patients 'too well to benefit', and comparable in the other 3 groups.

Patients 'too sick to benefit' were more often seen in the emergency room, and more physicians, both referring and ICU physicians, were involved in the decision-making. Reasons for ICU admission consultation differed between groups (Table 1).

In Additional file 2: Table S2, data of patients (e.g., APACHE IV score and length of ICU stay) are shown.

Mortality rates of the 4 groups are shown in Fig. 1. The crude 30-day mortality of patients 'too well to benefit' was 30.1%, in patients admitted to the ICU 36.9%, and in patients 'too sick to benefit' 81.8% (Fig. 1). The 30-day mortality was 25.6% in patients 'too well to benefit, never admitted to the ICU', and 45.9% in patients with a delayed ICU admission.

Primary and secondary outcome

The results of the univariable and multivariable logistic regression analysis with 30-day mortality as endpoint are provided in Table 2. The following factors of the

multivariable analysis were associated with 30-day mortality: age, a hematological type of cancer, uncontrolled cancer, ECOG PS of 2, 3 and 4, MEWS, ICU triage decisions 'delayed ICU admission' and 'too sick to benefit', ICU consultations during off-hours, 'altered consciousness' as reason for ICU admission request and 'AKI' as reason for ICU admission request.

We presented in Tables 3 and 4 a comparison between patients immediately admitted to the ICU and patients with a delayed ICU admission, and a comparison between patients with a consultation during on-hours and patients with a consultation during off-hours.

In Additional file 3: Table S3, multivariable analyses of 90-day mortality, 180-day mortality and 1-year mortality are shown. Delayed ICU admission remained associated with mortality, while the effect of on-hours compared to off-hours disappeared.

In Additional file 4: Table S4, MEWS, number of consultations during on-hours and consult reasons of the second ICU admission consultation for patients with a delayed ICU admission are shown. The MEWS of patients during the second consultation was comparable to the MEWS of the first consultation, a second consultation was more often performed during on-hours.

Last, in Additional file 5: Table S5 and Additional file 6: Table S6, crude mortality rates by ICU triage decision for patients with solid cancer and patients with a hematological malignancy separately are shown.

Table 2 Univariable and multivariable analysis: factors associated with 30-day mortality

	30-day Mortality	Univariable analysis			Multivariable analysis		
		Odds ratio	95% CI	p-value	Odds ratio	95% CI	p-value
Age	–	1.02	1.01–1.03	0.001*	1.04	1.02–1.05	<0.001*
Male	192 (38.5%)	1.08	0.80–1.46	0.61			
Solid malignancy (ref)	176 (35%)						
Hematological malignancy	117 (42.7%)	1.39	1.02–1.87	0.03*	1.63	1.02–2.60	0.04*
Metastatic disease	101 (41.2%)	1.23	0.91–1.68	0.19	1.05	0.56–1.96	0.89
Cancer recurrence	32 (45.1%)	1.39	0.85–2.27	0.19	1.39	0.74–2.60	0.31
Controlled cancer (ref)	98 (26.4%)						
Uncontrolled cancer	197 (48.3%)	2.60	1.92–3.52	<0.001*	2.30	1.54–3.41	<0.001*
CCI	–	1.08	1.01–1.15	0.02*	1.02	0.89–1.15	0.82
ECOG PS before hospital admission							
0 (ref)	47 (26%)						
1	107 (35.9%)	1.60	1.06–2.40	0.02*	1.33	0.81–2.18	0.27
2	82 (42.9%)	2.15	1.38–3.33	0.001*	1.84	1.07–3.19	0.03*
3	44 (48.9%)	2.73	1.61–4.64	<0.001*	2.40	1.21–4.77	0.01*
4	13 (86.7%)	18.53	4.03–85.19	<0.001*	12.42	2.34–65.93	0.003*
MEWS		1.13	1.05–1.20	<0.001*	1.13	1.04–1.23	0.006*
Cancer treatment	252 (36.8%)	0.77	0.50–1.20	0.25			
Immunocompromised	214 (38.2%)	1.09	0.79–1.51	0.61			
ICU triage decision							
ICU admission (ref)	141 (36.9%)						
Too well to benefit—no ICU admission	66 (25.6%)	0.59	0.42–0.83	0.003*	0.66	0.42–1.04	0.08
Too well to benefit—delayed ICU	34 (45.9%)	1.45	0.88–2.40	0.15	1.83	1.00–3.33	0.048*
Too sick to benefit	54 (81.8%)	7.69	3.98–14.87	<0.001*	7.78	3.38–17.89	<0.001*
Year ICU consult							
2016 (ref)	78 (36.4%)	–	–	–			
2017	77 (37.7%)	1.06	0.71–1.57	0.78			
2018	87 (39.2%)	1.12	0.76–1.66	0.56			
2019	53 (37.9%)	1.06	0.68–1.65	0.79			
Earlier ICU admission before consult	18 (23.4%)	0.47	0.27–0.81	0.007*	0.82	0.41–1.64	0.57
One ICU physician (ref)	109 (34.3%)						
Two ICU physicians	155 (40.3%)	1.29	0.95–1.76	0.10	0.97	0.64–1.46	0.87
More than two ICU physicians	31 (40.3%)	1.29	0.78–2.15	0.33	0.95	0.48–1.87	0.88
One referring physician (ref)	53 (32.3%)						
Two referring physicians	195 (39.3%)	1.36	0.93–1.97	0.11	1.27	0.80–2.03	0.31
More than two referring physicians	45 (39.8%)	1.39	0.84–2.28	0.20	1.24	0.64–2.38	0.53
Location consult							
Emergency room (ref)	57 (41.6%)	–	–	–			
Ward	188 (38.9%)	0.89	0.61–1.32	0.57	1.42	0.86–2.35	0.18
Other	50 (31.3%)	0.64	0.40–1.03	0.07	1.70	0.90–3.20	0.10
On-hours (ref)	103 (32.7%)						
Off-hours	192 (41.3%)	1.45	1.07–1.95	0.02*	1.61	1.09–2.38	0.02*
Weekend	95 (38.9%)	1.07	0.79–1.46	0.67			
Consult reason							
Shock	68 (45.3%)	2.49	1.48–4.19	0.001*	1.78	0.97–3.26	0.06
Respiratory insufficiency	188 (38.9%)	1.48	1.02–2.17	0.04*	1.18	0.77–1.83	0.45
Altered consciousness	68 (48.9%)	2.12	1.35–3.34	0.001*	1.73	1.06–2.83	0.03*
Sepsis	87 (40.7%)	1.28	0.84–1.97	0.25			
Acute kidney injury	50 (53.2%)	2.70	1.65–4.41	<0.001*	2.47	1.41–4.34	0.002*
High MEWS	10 (43.5%)	1.93	0.80–4.64	0.14	2.00	0.70–5.72	0.20
Hemodynamic instability	102 (36.4%)	0.69	0.42–1.14	0.15	0.70	0.42–1.18	0.18
Other	34 (35.4%)	1.14	0.70–1.87	0.59			

Table 2 (continued)

Table shows data of first ICU triage decision of the hospital admission

A *p*-value of <0.05 is considered significant (marked by an *)

CCI Charlson Comorbidity Index, ECOG PS Eastern Cooperative Oncology Group Performance Status, MEWS Modified Early Warning Score, On-hours during dayshift

Discussion

Our study evaluated the association between 30-day mortality, and ICU admission consultation characteristics and triage decisions in cancer patients. After adjustment for confounders, we found a statistically significant relationship between 30-day mortality, and triage decisions and ICU consultation during off-hours. The association between triage decisions and mortality might even persist over time.

In our study, 60% of the ICU triage decisions in cancer patients were made during off-hours, half of the patients for whom ICU admission was requested were immediately admitted to the ICU. Triage decisions were made by two or more ICU and referring physicians in nearly 50% of the patients 'too well to benefit' from ICU, and in 80% of the patients 'too sick to benefit'. Only one patient initially considered 'too sick to benefit' was admitted to the ICU after a second ICU triage decision. These results suggest that in our hospitals, patients were often discussed by multiple physicians, before considering them 'too sick to benefit' from ICU. However, 22% of the patients initially considered "too well to benefit" from ICU admission (9.5% of the overall population) were subsequently admitted to the ICU after a median of 1 day. Severity of illness, measured by the MEWS, was comparable between the first and second consultation by intensivists in this group, suggesting no overt rapid deterioration in the clinical status of these patients. Worrisome is that both off-hours consultation, and admission to the ICU after initially being considered "too well to benefit" from ICU admission (i.e., delayed ICU admission), were associated with an increased 30-day mortality, even after adjusting for confounders present at the moment of consultation and patient-related confounders. Moreover, the detrimental effect of delayed ICU admission might persist till 1 year after the initial triage decision.

Studies that describe the association between mortality and ICU admission during off-hours in critically ill patients show contradictory results [13, 19, 20]. Where Brunot et al. [13] found that time of admission, especially off-hour admissions, did not influence the prognosis of ICU patients, two other studies [19, 20] found an association between off-hours ICU admissions and hospital mortality. Our results suggest that in cancer patients, the oncologists or hematologists should draw attention of the on-hour intensivist for any situation that could deteriorate rapidly. In addition, although off-hours assessment of patients' condition seemed not detrimental in the

long-term, ICU physicians should be aware of the vulnerability of cancer patients for whom ICU admission during off-hours is requested, and need to consider ICU admission carefully. Daily rounds by a multidisciplinary team are associated with lower mortality among ICU patients [21]. Although not described in studies before, we assume that the outcome of critically ill cancer patients will improve when an ICU physician and a hematologist or oncologist discusses the need of an ICU admission for patients 'at risk' during rounds.

In line with previous literature [3, 22–27], age, cancer type (solid or hematological), cancer status, performance status, and severity of critical illness were associated with 30-day mortality in our study and should therefore be taken into consideration during triage decisions. In earlier studies, the association between ICU admission reasons and short-term mortality has been reported [28–30]. Our study adds to these results that altered consciousness, AKI and shock as reason for consultation need special consideration, as these are associated with either short-term (Table 2) or long-term mortality (Additional file 3: Table S3).

ICU denial rate in our study was higher than in studies including general patients [31–35], patients with advanced disease [36] or hematological patients [37]. In our study, short-term mortality of patients with immediate ICU admission (i.e., ICU mortality, hospital mortality or 30-day mortality) was variable when compared to other studies reporting similar [29, 38–40] or lower mortality [26, 30, 41]. It would be expected that with a high denial rate, the mortality would be lower. However, when compared to the median-predicted hospital mortality (using the APACHE IV score), the actual hospital mortality was similar (predicted 40.8%, actual hospital mortality 38.7%). The higher mortality when compared to other studies could be explained by differences in case mix (e.g., planned surgical patients were included in those studies as well) and severity of illness.

The 30-day mortality of patients 'too well to benefit, never admitted to the ICU' was high (25.6%), especially when compared to the study of Thiery et al. [10] (6% 30-day mortality). However, the study of Thiery et al. [10] had a small sample size and did not show data regarding severity of illness, complicating a direct comparison. In our study, patients were more frequent considered 'too well to benefit' (42.6% versus 22.8%), which might explain the difference in mortality. However, mortality of patients with a delayed ICU admission was lower in our study

Table 3 Differences immediate ICU admission vs. delayed ICU admission

	ICU admission N = 382	Too well to benefit—delayed ICU N = 74	p-value
Age	65 [58–72]	66 [59–70]	0.98
Male	248 (64.9%)	44 (59.5%)	0.37
Solid malignancy	244 (63.9%)	41 (55.4%)	0.15
Hematological malignancy	136 (35.6%)	33 (44.6%)	
Metastatic solid malignancy	108 (28.3%)	20 (27%)	0.83
Cancer recurrence	27 (7.1%)	5 (6.8%)	0.92
Uncontrolled cancer	173 (45.4%)	33 (44.6%)	0.90
CCI	4 [2–6]	3 [2–6]	0.64
ECOG PS before hospital	1 [0–2]	1 [1–1]	0.54
0	108 (28.3%)	17 (23%)	
1	148 (38.7%)	39 (52.7%)	
2	81 (21.2%)	15 (20.3%)	
3	36 (9.4%)	3 (4.1%)	
4	6 (1.6%)	0 (0%)	
Unknown	3 (0.8%)	0 (0%)	
MEWS	5 [4–7]	5 [4–7]	0.13
Unknown	54 (14.1%)	4 (5.4%)	
Cancer treatment before ICU	343 (90.3%)	65 (87.8%)	0.53
Unknown			
Immunocompromised	265 (69.4%)	49 (66.2%)	0.55
Year ICU consult			0.66
2016	114 (29.8%)	22 (29.7%)	
2017	108 (28.3%)	18 (24.3%)	
2018	99 (25.9%)	18 (24.3%)	
2019	61 (16%)	16 (21.6%)	
Earlier ICU admission before consult	45 (11.8%)	8 (10.8%)	0.82
One ICU physician	158 (41.4%)	35 (47.3%)	0.045*
Two ICU physicians	176 (46.1%)	37 (50%)	
More than two ICU physicians	48 (12.6%)	2 (2.7%)	
One referring physicians	80 (21.2%)	19 (26%)	0.48
Two referring physicians	240 (63.7%)	41 (56.2%)	
More than two referring physicians	57 (15.1%)	13 (17.8%)	
Location consult			< 0.001*
Emergency room	81 (21.2%)	4 (5.4%)	
Ward	190 (49.7%)	55 (74.3%)	
Other	111 (29.1%)	15 (20.3%)	
On-hours	163 (42.7%)	27 (36.5%)	0.32
Off-hours	219 (57.3%)	47 (63.5%)	0.62
Weekend	118 (30.9%)	25 (33.8%)	
Consult reason			
Shock	103 (27%)	5 (6.8%)	< 0.001*
Respiratory insufficiency	242 (63.4%)	50 (67.6%)	0.49
Altered consciousness	80 (20.9%)	7 (9.5%)	0.02*
Sepsis	135 (35.3%)	22 (29.7%)	0.35
Acute kidney injury	60 (15.7%)	10 (13.5%)	0.63
High MEWS	2 (0.5%)	3 (4.1%)	0.008*
Hemodynamic instability	152 (39.8%)	21 (28.4%)	0.06
Other	36 (9.4%)	9 (12.2%)	0.42
Hospital mortality	148 (38.7%)	36 (48.6%)	0.11

Table 3 (continued)

	ICU admission N = 382	Too well to benefit—delayed ICU N = 74	p-value
30-day mortality	141 (36.9%)	34 (45.9%)	0.14
90-day mortality	180 (47.2%)	43 (58.9%)	0.07
180-day mortality	206 (54.4%)	47 (65.3%)	0.09
1 year mortality	230 (62%)	54 (75%)	0.04*

Table shows data of first ICU consultation of the hospital admission

A p-value of < 0.05 is considered significant (marked by an *)

CCI Charlson Comorbidity Index, ECOG PS Eastern Cooperative Oncology Group Performance Status, MEWS Modified Early Warning Score, On-hours during dayshift

(45.9% versus 61.5%). In addition, approximately 20% of the patients considered ‘too sick to benefit’ was still alive on day 30. Therefore, we assume that decisions to refuse ICU treatment were partly based on ‘long-term’ prognostic factors, where cancer control might be limited, but the patient is not necessarily going to die immediately. Both the high mortality of patients ‘too well to benefit’ from ICU as the lower mortality than expected of patients ‘too sick’ suggest that, despite clinical experience of physicians and current scoring systems, whether or not ICU treatment should be given remains difficult. Errors in judgement of ICU physicians whether ICU admission would be inappropriate care may lead to higher mortality of acutely ill cancer patients. If possible, a MEWS specified to cancer patients should be developed to more adequately address a timely admission and benefit from an ICU admission. In addition, more frequent intra- and interdisciplinary discussions might improve clinical assessment.

The current findings suggest room for a broader admission policy with a lower threshold for critically ill cancer patients in the hospitals that participated in this study. However, bed shortage is associated with ICU refusal [31, 42] and unfortunately, we were not able to collect data on bed availability. We are aware that, unless ICU capacity increases, admitting more cancer patients to the ICU may limit the possibility of ICU admissions for other critically ill patients. A way to deal with these problems is the use of a time-limited ICU trial [43–46]. Previous literature describes that for patients with a solid tumor, an ICU admission of 5 days is sufficient to determine whether a patient will survive the ICU admission [43, 45], and for patients with a hematological malignancy, a maximum of 14 days is sufficient [44]. In order to successfully conduct an ICU trial, clear agreements must be made with oncologists, hematologists, patients and relatives before ICU admission.

Limitations

First, ICU admission triage varies across hospitals, and in particular high-volume hospitals may have different admission policies. However, we think that our study still shows an important message to many hospitals. Physicians should critically evaluate their own ICU triage policy, and a close collaboration between referring physicians and ICU physicians should be pursued.

Second, where we tried to reduce the heterogeneity by adjusting for patient characteristics such as type of cancer (solid or hematological) and cancer status, this still limits the interpretation of the results.

Third, given the observational design of the study, we cannot rule out residual confounding. We tried to reduce this issue by adjusting for the maximum number of factors which was available at the moment of the consultation. Moreover, limitations with regard to retrospective studies should be acknowledged.

Fourth, we found a significant relationship between ICU triage decisions and 1-year mortality via logistic regression analysis. However, this result might be biased by short-term mortality and residual confounding. Thus, we should interpret this result with caution.

Last, it must be emphasized that by categorizing our cohort according to the triage decisions, we assumed that readmission to the ICU can be predicted with a 100% accuracy by consulting physicians. Although this practice is common in medical research, it does not reflect the real-life situation. Future studies should assess the impact of delayed ICU admission via causal inference techniques, where the longitudinal probability of transitions in care can be taken into account [47].

Conclusion

The ICU denial rate in our study was high (51%). Sixty percent of the ICU triage decisions in cancer patients were made during off-hours, and 22.3% of the patients initially considered “too well to benefit” from ICU admission were subsequently admitted to the ICU. Both decisions during off-hours and a delayed ICU admission were

Table 4 Differences on-hours versus off-hours

	On-hours N=315	Off-hours N=465	p-value
Age	65 [57–71]	63 [56–70]	0.12
Male	208 (66%)	291 (62.6%)	0.33
Solid malignancy	207 (66.1%)	296 (63.8%)	0.50
Hematological malignancy	106 (33.9%)	168 (36.2%)	
Metastatic solid malignancy	99 (31.4%)	146 (31.4%)	0.99
Cancer recurrence	29 (9.2%)	42 (9.1%)	0.94
Uncontrolled cancer	158 (50.2%)	250 (53.9%)	0.31
CCI	4 [2–6]	4 [2–6]	0.78
ECOG PS before hospital	1 [0–2]	1 [1, 2]	0.07
0	82 (26%)	99 (21.3%)	
1	122 (38.7%)	176 (37.8%)	
2	70 (22.2%)	121 (26%)	
3	37 (11.7%)	53 (11.4%)	
4	3 (1.0%)	12 (2.6%)	
Unknown	1 (0.3%)	4 (0.9%)	
MEWS	5 [3–6]	5 [4–7]	0.99
Unknown	37 (11.7%)	43 (9.2%)	
Cancer treatment before ICU	284 (90.4%)	400 (86.4%)	0.09
Unknown			
Immunocompromised	231 (73.3%)	329 (71.1%)	0.49
Year ICU consult			0.25
2016	96 (30.5%)	118 (25.4%)	
2017	76 (24.1%)	128 (27.5%)	
2018	93 (29.5%)	129 (27.7%)	
2019	50 (15.9%)	90 (19.4%)	
Earlier ICU admission before consult	35 (11.1%)	42 (9%)	0.34
One ICU physician	184 (58.4%)	134 (28.8%)	<0.001*
Two ICU physicians	102 (34.2%)	283 (60.9%)	
More than two ICU physicians	29 (9.2%)	48 (10.3%)	
One referring physicians	77 (24.5%)	87 (19%)	0.08
Two referring physicians	187 (59.6%)	309 (67.3%)	
More than two referring physicians	50 (15.9%)	163 (35.7%)	
Location consult			0.32
Emergency room	49 (15.6%)	88 (18.9%)	
Ward	195 (61.9%)	288 (61.9%)	
Other	71 (22.5%)	89 (19.1%)	
Weekend	73 (23.2%)	171 (36.8%)	<0.001*
Consult reason			
Shock	70 (22.2%)	80 (17.2%)	0.08
Respiratory insufficiency	189 (60%)	294 (63.2%)	0.36
Altered consciousness	61 (19.4%)	78 (16.8%)	0.35
Sepsis	86 (27.3%)	128 (27.5%)	0.95
Acute kidney injury	41 (13%)	53 (11.4%)	0.50
High MEWS	9 (2.9%)	14 (3%)	0.90
Hemodynamic instability	124 (39.4%)	156 (33.5%)	0.10
Other	32 (10.2%)	64 (13.8%)	0.13
Hospital mortality	106 (33.7%)	179 (38.5%)	0.17
30-day mortality	103 (32.7%)	192 (41.3%)	0.02*
90-day mortality	143 (45.4%)	227 (49%)	0.32

Table 4 (continued)

	On-hours N=315	Off-hours N=465	p-value
180-day mortality	162 (51.6%)	264 (57.3%)	0.12
1 year mortality	188 (61.2%)	302 (66.4%)	0.15

Table shows data of first ICU consultation of the hospital admission

A p-value of <0.05 is considered significant (marked by an *)

CCI/Charlson Comorbidity Index, ECOG PS Eastern Cooperative Oncology Group Performance Status, MEWS Modified Early Warning Score, On-hours during dayshift

associated with an increased risk of death at 30 days. Our study suggests that in cancer patients, ICU triage decisions should be discussed during on-hours, and ICU admission policy should be broadened, with a lower admission threshold for critically ill cancer patients.

Abbreviations

ICU: Intensive Care Unit; OR: Odds ratio; 95% CI: 95% Confidence interval; AKI: Acute kidney injury; MEWS: Modified Early Warning Score; EHR: Electronic Health Records; ECOG PS: Eastern Cooperative Oncology Group Performance Status; CCI: Charlson Comorbidity Index; IQR: Interquartile range.

Supplementary Information

The online version contains supplementary material available at <https://doi.org/10.1186/s13613-021-00898-2>.

Additional file 1. Supplementary material Table 1; cancer types of patients at ICU admission consultation.

Additional file 2. Supplementary material Table 2; ICU data of patients immediately admitted to the ICU.

Additional file 3. Supplementary material Table 3; Multivariable analyses; factors associated with 90-day, 180-day and 1 year mortality.

Additional file 4. Supplementary material Table 4; characteristics of patients with a delayed ICU triage decision.

Additional file 5. Supplementary material Table 5; crude mortality rates of solid cancer patients by ICU triage decision.

Additional file 6. Supplementary material Table 6; crude mortality rates of hematological cancer patients by ICU triage decision.

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Authors' contributions

EZ: conceptualization, design, acquisition, analysis and interpretation of data, writing—original draft and writing—review and editing. DB: design, analysis and interpretation of data, writing—original draft and writing—review and editing. MH: data acquisition, analysis and interpretation of data, writing original draft, JB: analysis and interpretation of data, writing—review and editing. EK: analysis and interpretation of data, writing—review and editing. NK: conceptualization, design, acquisition, interpretation of data, and writing—review and editing. JE: conceptualization, design, acquisition, interpretation of data, and writing—review and editing. All authors read and approved the final manuscript.

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Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations**Ethics approval and consent to participate**

The local Medical Ethical Committee (Erasmus MC, MEC-2019-0128) approved this study. Local approval was obtained for the University Medical Center Utrecht. No additional patient consent was required due to the non-invasive retrospective nature of the study.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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