OUTCOMES OF CANCER PATIENTS AFTER UNPLANNED ADMISSION TO GENERAL INTENSIVE CARE UNITS

CHAPTER 3

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Abstract

Background: Acute admission to an intensive care unit (ICU) of cancer patients is considered with increasing frequency due to a better life expectancy and more aggressive therapies. The aim of this study was to determine the characteristics and outcomes of cancer patients with unplanned admissions to general ICUs, and to compare these with outcomes of critically ill patients without cancer.
Materials and Methods: All unplanned ICU admissions in the Netherlands collected in the National Intensive Care Evaluation registry between January 2007 and January 2011 were analyzed.
Results and Conclusion: Of the 140,154 patients with unplanned ICU admission 10.9 % had a malignancy. Medical cancer patients were more severely ill on ICU admission in comparison with medical non-cancer patients, as reflected by higher needs for mechanical ventilation (50.8% vs 46.4%, $p<0.001$) and vasopressors within 24 hours after admission (41.5% vs 33.0%, $p<0.001$), higher Acute Physiology and Chronic Health Evaluation (APACHE) IV scores (88.1 vs 67.5, $p<0.001$) and a longer ICU stay (5.1 vs 4.6 days, $p<0.001$). In contrast, surgical cancer patients only displayed a modestly higher APACHE IV score on admission when compared with non-cancer surgical patients, whereas the other afore mentioned parameters were lower in the surgical cancer patients group. In-hospital mortality was almost twice as high in medical cancer patients (40.6%) as in medical patients without cancer (23.7%). In-hospital mortality of surgical cancer patients (17.4%) was slightly higher than in patients without cancer (14.6%). These data indicate that unplanned ICU admission is associated with a high mortality in patients with cancer when admitted for medical reasons.

Introduction

Survival of cancer patients has increased over the last three decades due to a greater awareness of early signs and better treatment possibilities [1]. These treatments are more intense and may cause significant toxicity and side effects due to chemotherapy, radiation therapy and/or extensive radical surgery. The more aggressive care has led to an increase in the need for vital life support and life-sustaining treatments. Consequently, referral to an intensive care unit (ICU) is increasingly considered in cancer patients [2].

Decisions for ICU admissions in patients with advanced cancer are complex, and the knowledge of survival rates and prognostic factors is essential to these decisions. Ten years ago, in guidelines for ICU admission, a taskforce of the American College of Critical Care Medicine concluded that patients with hematological or metastasized solid malignancies are poor candidates for ICU admission considering their high risk of mortality [3]. In accordance, cancer patients are more likely to be denied ICU admission [4]. More recent data suggest that the prognosis of critically ill cancer patients admitted to an ICU has improved considerably [5, 6]. However, these encouraging data are almost exclusively derived from single-center studies conducted in specialized hemato-oncologic ICUs, which may not reflect outcome of cancer patients on general ICUs.

Two relatively large multicenter studies examined the impact of cancer on the outcome of patients admitted to general ICUs [7, 8]. These studies did not distinguish between planned and unplanned cancer patients. Many ICU admissions in cancer patients are planned, especially in the context of postoperative care. The dilemma whether or not to admit a patient with a malignancy to the ICU in particular applies to unplanned emergency situations. Therefore, the objective for the present study was to analyze the characteristics and outcome of cancer patients with unplanned admissions to general ICUs, and to compare these with outcomes of critically ill patients without cancer. For this we analyzed all ICU admissions in the Netherlands collected in the National Intensive Care Evaluation (NICE) registry from January 2007 through January 2011 [9].

Materials and Methods

Patient data

The database of the Dutch National Intensive Care Evaluation (NICE) registry was used in this observational study [9]. In 1996 the NICE foundation started collecting data on patients admitted to Dutch ICUs. The participating ICUs provide information on all ICU admissions with the aim to assess and compare the performance of the ICUs and to improve the quality of care. For each ICU admission variables are collected that describe patient characteristics, severity of illness during the first 24 hours of ICU admission, and the ICU and in-hospital mortality and length of stay. The data are encrypted such that all patient-identifying information, including name and patient identification number, are untraceable. The recorded variables were used to calculate probabilities of death for each patient using the Acute Physiology and Chronic Health Evaluation (APACHE) IV prognostic model [10]. Data for the current study were collected from all consecutive admissions to 80 ICUs between January 2007 and January 2011. The study was strictly observational and every clinical decision was at the discretion of the responsible physician.

Ethics

The NICE initiative is officially registered according to the Dutch Personal Data Protection Act. The need for ethical committee approval is waived by the Central Committee on Research Involving Human Subjects, because the study was purely retrospective and because only anonymous patient data were used.

Selection of patients with a malignancy

Patients were identified as being admitted with a malignancy when their APACHE IV reason for admission contained the term cancer, neoplasm, leukemia, lymphoma, malignancy and/or tumor or if one of the APACHE II fields *metastasized neoplasm* or *hematological malignancy* was chosen as co-morbid condition within the six months prior to ICU admission.

Statistical analysis

Categorical variables are presented as percentages and continuous variables are presented as mean and standard deviation (SD), or in case of non-normally distributed variables as median and interquartile range (IQR). We used χ^2 tests for comparisons of categorical variables, independent *t* test to assess differences for normally distributed continuous variables, and the Mann-Whitney U-test to assess differences for non-normally distributed continuous variables. Standardized mortality ratios (SMRs) were calculated by dividing the actual in-hospital mortality by the expected mortality as calculated by the APACHE IV prognostic model. Multivariate logistic regression analyses were performed to assess the associations between the type of malignancy and in-hospital mortality. To adjust for severity of illness, the APACHE III severity of illness score (consisted of the APACHE III/IV acute physiology score (APS), age, and comorbidities) was included in the model as covariate [10, 11]. We applied the APACHE IV inclusion criteria to select patient data for the multivariate logistic regression analyses and the calculation of SMRs [10]. Results were considered statistically significant if p-values were below 0.05. All statistical analyses were performed using PASW statistics 18 (SPSS, Chicago).

Results

Patients

251,748 patients were admitted to the participating ICUs during the study period (Figure 1). Of these, 34,067 (13.5%) had a diagnosis of malignancy on admission to the ICU; 217,681 patients (86.5%) did not have such a diagnosis. In this overall cohort, most ICU admissions in patients with a malignancy were planned (54.2% versus 45.8% unplanned); for patients without cancer most ICU admissions were unplanned (68.0% versus 32.0% planned). This difference was mainly caused by a large proportion of planned surgical procedures in cancer patients who most commonly had a very brief and uncomplicated stay on the ICU (data not shown). Since our primary objective was to examine the impact of cancer on the outcome of non-elective ICU admissions, our analysis focused on this subgroup. For this analysis 15,211 unplanned patients with a malignancy and 124,943 unplanned patients without a malignancy were available (Figure 1 and Table 1). Most unplanned ICU admissions amongst patients with cancer were for a surgical indication (59.3%), whereas most unplanned ICU admissions in non-cancer patients were for a medical reason (67.0%). Of the 15,211 unplanned patients with a malignancy, 14,087 satisfied the APACHE IV inclusion criteria and were included in the multivariate logistic regression analyses and for the calculation of SMRs.

Figure 1: Overview and selection of patients admitted to the participating ICUs from January 2007 until January 2011

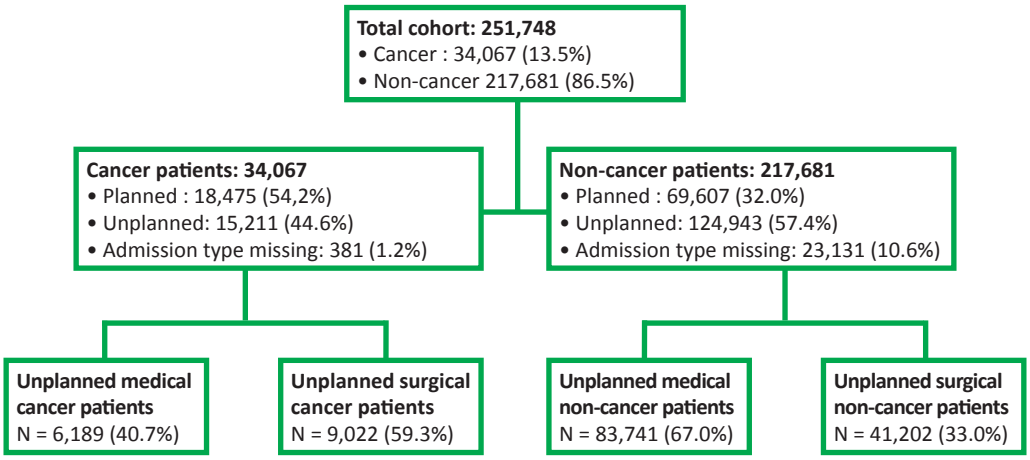


Table 1 shows patient characteristics, comorbidities and severity of illness scores of all patients with unplanned ICU admissions, stratified according to the presence or absence of cancer and the indication for admission (medical versus surgical). Medical cancer patients had a higher incidence of confirmed infection, pneumonia and sepsis when compared with medical patients without cancer. Infections (including pneumonia and sepsis) were less common in surgical patients in general and differences (albeit statistically significant) between cancer and non-cancer patients were modest at best. As expected, immunodeficiency was far more common amongst the medical cancer patients. In addition, the proportion of medical cancer patients with acute renal failure and need for vasopressors and mechanical ventilation was higher than in medical patients without a malignancy. With regard to chronic comorbidity differences between cancer and non-cancer patients were modest, with the former group harboring fewer patients with heart failure. In accordance with the observed differences in acute comorbidity, cancer patients had much higher APACHE IV scores than patients without cancer, especially those with a medical indication for ICU admission. Medical, but not surgical, cancer patients had a longer length of stay on the ICU than the corresponding patients without cancer.

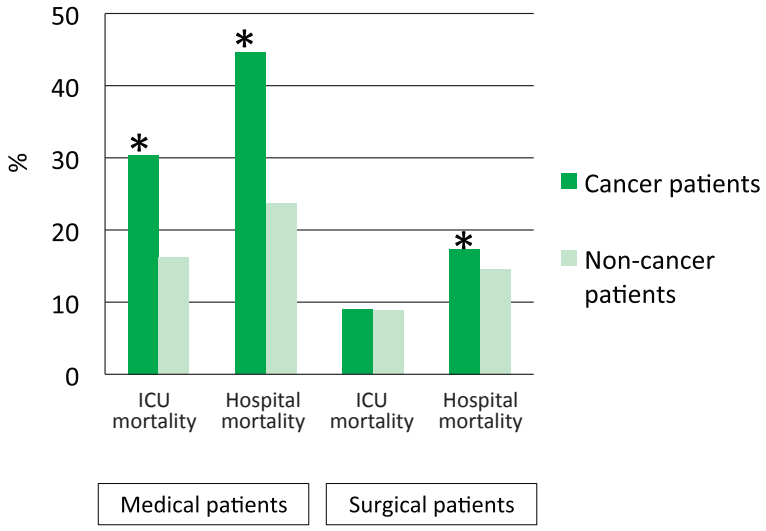
Mortality

Figure 2 shows mortality rates stratified according to distinct patient subgroups. ICU and in-hospital mortality were almost twice as high in unplanned medical cancer patients as in medical patients without cancer (ICU mortality 30.4% vs. 16.2% respectively; in-hospital mortality 44.6% vs. 23.7% respectively; both $p < 0.001$). In contrast, ICU mortality in unplanned surgical cancer patients and unplanned surgical non-cancer patients was similar (9.0% vs. 8.9% respectively; $p = 0.8$); in-hospital mortality was higher in surgical cancer patients than in surgical non-cancer patients (17.4% vs. 14.6% respectively; $p < 0.001$).

Table 1: Patient characteristics, comorbidities and severity of illness scores of all patients with unplanned ICU admissions, stratified according to indication for admission (medical versus surgical) and the presence or absence of cancer

	Unplanned Cancer patients n = 15,211			Unplanned Patients without cancer n = 124,943			Medical cancer versus medical non-cancer	Surgical cancer versus surgical non-cancer
	Medical n = 6,189	Surgical n = 9,022	*p*	Medical n = 83,741	Surgical n = 41,202	*p*	*p*	*p*
male (%)	59.5	56.8	*0.001*	56.3	55.4	*<0.001*	*<0.001*	*0.016*
age (median (IQR))	66 (58-74)	71 (61-77)	*<0.001*	64 (50-75)	67 (53-77)	*<0.001*	*<0.001*	*<0.001*
acute comorbid diseases (%)								
- confirmed infection	29.9	15.6	*<0.001*	19.9	16.5	*<0.001*	*<0.001*	*0.023*
- pneumonia	18.9	1.5	*<0.001*	16.3	0.9	*<0.001*	*<0.001*	*<0.001*
- sepsis	21.2	6.8	*<0.001*	13.2	7.4	*<0.001*	*<0.001*	*0.034*
- immunodeficiency	32.5	8.3	*<0.001*	5.7	3.5	*<0.001*	*<0.001*	*<0.001*
- cardiac dysrhythmia	10.9	5.6	*<0.001*	11.1	6.1	*<0.001*	*0.556*	*0.100*
- acute renal failure	17.5	5.6	*<0.001*	11.0	6.7	*<0.001*	*<0.001*	*<0.001*
- mechanical ventilation	50.8	40.4	*<0.001*	46.4	50.2	*<0.001*	*<0.001*	*<0.001*
- vasopressors	41.5	31.8	*<0.001*	33.0	34.7	*<0.001*	*<0.001*	*<0.001*
chronic comorbid disease (%)								
- COPD	10.9	10.1	*0.069*	15.0	9.3	*<0.001*	*<0.001*	*0.010*
- chronic renal insufficiency	6.9	3.4	*<0.001*	6.9	4.5	*<0.001*	*0.918*	*<0.001*
- heart failure	3.5	3.4	*0.788*	5.4	5.9	*0.230*	*<0.001*	*0.001*
- diabetes	12.7	11.6	*0.023*	4.5	11.9	*<0.001*	*<0.001*	*0.463*
ICU severity of illness								
- APACHE IV score (mean (SD))	88.1 (36.3)	58.4 (28.3)	*<0.001*	67.5 (36.7)	54.9 (30.4)	*<0.001*	*<0.001*	*<0.001*
- ICU length of stay (days) (median (IQR))	2.0 (0.81-5.4)	1.0 (0.79-2.9)	*<0.001*	1.8 (0.74-4.6)	1.1 (0.72-3.7)	*<0.001*	*<0.001*	*<0.001*

Figure 2: ICU and hospital mortality rates in unplanned cancer versus non-cancer population for medical and surgical patient groups



** P < 0.001 versus non-cancer patients*

Severity of illness and outcome in cancer patients

The NICE registry collects information about the primary cancer diagnosis only when cancer is one of the main reason for admission to the ICU; in other cases malignancy is scored as hematological malignancy or neoplasm/metastasized carcinoma without further specification. Table 2 shows diagnoses of cancer patients with unplanned ICU admissions. For the majority of medical cancer patients malignancy was not the main reason for ICU admission (71.8%). In medical patients for whom cancer was the primary reason for admission, the most common diagnoses included respiratory tract carcinoma (7.5%) and hematological malignancy (leukemia 5.6%; lymphoma 4.9%); in this subgroup of medical cancer patients confirmed infection was frequently present in especially patients with hematological malignancy and lower gastrointestinal carcinoma (32.4 – 40.5%)(Table 3). Mortality was high across all diagnoses, especially so in patients with hematological malignancy and respiratory tract carcinoma (hospital mortality 48.5 – 53.2%). In general, the APACHE IV model adequately predicted mortality in medical cancer patients with cancer as main reason for ICU admission, as reflected by SMRs approaching 1.00. In contrast to medical cancer patients, the majority of surgical cancer patients had cancer as main indication for ICU admission (75.8%), the most common being lower gastrointestinal carcinoma (32.2%)(Table 3). Patients with lower gastrointestinal carcinoma displayed ICU and in-hospital mortalities of 7.6% and 16.2% respectively; ICU and in-hospital mortalities amongst surgical patients with upper gastrointestinal carcinoma were also relatively high (8.2% and 15.7% respectively)(Table 4). Mortality rates amongst surgical patients with other cancer diagnoses were much lower. Notably, mortality was lower than predicted by the APACHE IV model in most subgroups of surgical cancer patients.

Table 2: Cancer diagnosis in the unplanned population in the NICE registry

All unplanned cancer patients (type of cancer) n = 15,211			
	Medical n = 6,189	Surgical n = 9,022	p
Primairy cancer diagnosis [1] (%)			
• Respiratory tract cancer	7.5	11.3	<0.001
• Leukemia	5.6	0.1	<0.001
• Lymphoma	4.9	0.2	<0.001
• Upper gastrointestinal cancer	3.9	12.3	<0.001
• CNS malignancy	2.7	5.4	<0.001
• Lower gastrointestinal cancer	2.2	32.2	<0.001
• Urological tract cancer	1.0	10.2	<0.001
• Other	0.2	1.5	<0.001
• Female cancer	0.1	2.5	<0.001
Underlying malignancy [2] (%)	**71.8**	**24.2**	**<0.001**
• Hematological malignancy	29.6	4.3	<0.001
• Metastasized solid tumor	42.2	19.8	<0.001
Total (%)	100	100	

[1] Patients admitted for a primary cancer diagnosis (APACHE IV).

[2] Patients admitted for other reasons, but having an underlying malignancy

Adjusted effect estimates of type of malignancy on in-hospital mortality

We performed multivariate logistic regression analyses to assess the associations between the type of malignancy and in-hospital mortality (Table 5). In unplanned medical cancer patients admission for respiratory tract cancer (adjusted odds ratio 2.15), upper gastrointestinal cancer (1.42) and leukemia (1.35) were associated with a higher risk for mortality. Patients with hematological cancer as comorbidity had lower risk for mortality. In unplanned surgical cancer patients adjusted risk was lower for patients admitted with respiratory tract cancer, urological cancer and female cancer whereas mortality risk was higher in patients with metastasized solid tumor as comorbidity.

Discussion

We here report on the characteristics and outcome of more than 15,000 cancer patients with an unplanned emergency admission to general ICUs. Our main finding is that medical cancer patients have strongly increased hospital mortality (40.6%) when compared with medical non-cancer patients (23.7%), which is associated with a higher incidence of acute comorbidity and a greater severity of illness on admission in the former group.

The current study used data extracted from the Dutch National Intensive Care Evaluation (NICE) database, collected during a four year period, to obtain insight in the epidemiology and outcome of cancer patients on general ICUs. Our study differs from several previous investigations that reported on prognostic factors for cancer patients on ICUs in that these mainly

Table 3: Demographic characteristics and outcomes for medical cancer patients stratified according to the type of malignancy

Unplanned medical cancer patients[1]											
Type of cancer	**Respiratory tract**	**Leukemia**	**Lymphoma**	**Upper GI**	**CNS**	**Lower GI**	**Urinary tract**	**Other**	**Female**	**Underlying malignancy**	
										Hematological	**Metastasized solid tumor**
Confirmed infection (%)	20.5	40.5	34.2	21.1	10.8	32.4	28.6	13.3	20.0	35.3	28.0
Vasopressors (%)	33.5	46.3	47.8	37.6	21.7	36.7	38.1	26.7	40.0	45.5	40.8
Mechanical ventilation (%)	60.3	62.4	55.5	39.3	57.2	36.7	39.7	26.7	20.0	56.4	44.9
Length of ICU stay (days) (median (IQR))	1.81 (0.78-3.97)	2.86 (0.85-7.50)	2.99 (0.97-7.78)	1.72 (0.77-3.79)	1.08 (0.70-2.80)	1.88 (0.82-5.00)	1.89 (0.83-4.50)	1.89 (0.90-4.75)	0.89 (0.45-1.60)	2.67 (0.98-7.33)	1.75 (0.71-4.20)
ICU mortality (%)	33.5	42.8	37.2	31.8	16.9	21.6	20.6	6.7	-	31.8	28.
Hospital mortality (%)	48.6	53.2	48.5	45.0	27.7	40.3	36.5	13.3	-	46.5	42.7
APACHE IV score (mean(SD))	77.7 (31.0)	90.6 (31.7)	94.8 (38.0)	85.1 (38.3)	66.6 (30.2)	81.6 (36.0)	78.6 (30.0)	52.2 (20.3)	69.5 (13.9)	96.3 (34.8)	87.4 (35.3)
APACHE IV SMR (CI)*	0.86 (0.74-0.98)	1.07 (0.90-1.25)	0.90 (0.74-1.07)	0.94 (0.74-1.16)	0.88 (0.63-1.17)	0.86 (0.62-1.14)	1.02 (0.60-1.54)	-	-	0.87 (0.81-0.95)	0.85 (0.79-0.91)

[1] *All patients satisfying the APACHE IV inclusion criteria.*

** Confidence Interval*

Table 4: Demographic characteristics and outcomes for surgical cancer patients stratified according to the type of malignancy

Unplanned surgical cancer patients[1]											
Type of cancer	**Respiratory tract**	**Leukemia**	**Lymphoma**	**Upper GI**	**CNS**	**Lower GI**	**Urinary tract**	**Other**	**Female**	**Underlying malignancy**	
										Hematological	**Metastasized solid tumor**
Confirmed infection (%)	4.9	20.0	40.0	11.5	2.1	13.1	6.0	5.9	6.2	28.1	35.7
Vasopressors (%)	15.3	40.0	55.0	30.8	11.1	33.8	25.9	27.9	28.6	44.5	44.9
Mechanical ventilation (%)	25.4	60.0	70.0	36.6	36.3	36.3	28.4	27.2	33.5	65.5	61.4
Length of ICU stay (days) (median (IQR))	0.91 (0.79-1.08)	0.89 (0.78-1.66)	1.83 (0.90-12.34)	1.00 (0.84-2.71)	0.85 (0.75-0.94)	0.94 (0.80-1.91)	0.90 (0.79-1.09)	0.91 (0.79-1.05)	0.88 (0.75-1.15)	1.07 (0.81-3.58)	1.12 (0.79-3.25)
ICU mortality (%)	3.2	-	25.0	8.2	4.7	7.6	3.3	2.9	3.1	17.1	18.4
Hospital mortality (%)	6.5	-	35.0	15.7	7.6	16.2	8.1	6.6	4.4	34.0	33.0
APACHE IV score (mean(SD))	43.0 (16.1)	63.0 (25.7)	83.0 (26.1)	53.5 (25.2)	37.5 (23.8)	58.7 (24.8)	50.8 (22.0)	46.8 (21.7)	51.6 (21.2)	78.1 (30.4)	74.1 (29.0)
APACHE IV SMR (CI)*	0.64 (046-0.86)	-	1.15 (0.41-2.25)	0.82 (0.68-0.96)	0.87 (0.59-1.22)	0.73 (0.66-0.81)	1.30 (0.99-1.65)	0.63 (0.25-1.18)	0.44 (0.17-0.83)	0.99 (0.80-1.20)	0.90 (0.81-0.99)

[1] *All patients satisfying the APACHE IV inclusion criteria.*

** Confidence Interval*

Table 5: Adjusted effect estimates of type of malignancy on in-hospital mortality for unplanned medical and surgical cancer patients

Adjusted Odds ratio for unplanned cancer patients (95% Confidence Interval) [1]		
	Medical (n=5,430) [2]	Surgical (n=8,657) [2]
Primary cancer diagnosis[3]		
• Respiratory tract cancer	2.15 (1.75-2.64)	0.61 (0.45-0.82)
• Leukemia	1.35 (1.06-1.71)	0.41 (0.05-3.6)
• Lymphoma	0.89 (0.68-1.18)	1.29 (0.41-4.05)
• Upper gastrointestinal cancer	1.42 (1.05-1.92)	1.05 (0.854-1.30)
• CNS malignancy	0.78 (0.54-1.12)	0.70 (0.46-1.06)
• Lower gastrointestinal cancer	0.84 (0.60-1.19)	0.97 (0.85-1.12)
• Urological tract cancer	0.83 (0.49-1.42)	0.50 (0.37-0.67)
• Female cancer	-	0.28 (0.14-0.56)
• Other	0.88 (0.18-4.34)	0.42 (0.18-0.95)
Underlying malignancy[4]		
• Hematological malignancy	0.78 (0.68-0.90)	1.30 (0.98-1.72)
• Metastasized solid tumor	0.91 (0.80-1.03)	1.77 (1.51-2.06)

[1] Adjusted for APACHE III severity of illness score.

[2] All patients satisfying the APACHE IV inclusion criteria.

[3] Patients admitted for a primary cancer diagnosis (APACHE IV).

[4] Patients admitted for other reasons, but having an underlying malignancy.

involved specialized oncologic ICUs, making extrapolation to general ICUs cumbersome [5, 6, 12]. Our investigation should be compared with two recent multicenter studies investigating the outcome of cancer patients in general ICUs [7, 8]. Taccone et al. used data collected during the Sepsis Occurrence in Acutely Ill Patients (SOAP) study, performed during two weeks in 198 ICUs from 24 European countries, to assess the characteristics and outcome of 473 cancer patients in general ICUs [7]. Soares et al. prospectively enrolled 717 cancer patients in a two-month observational study performed in 28 Brazilian ICUs [8]. Important differences between these studies and ours include the number of patients evaluated (140,154 of whom 15,211 with a cancer diagnosis in the current investigation) and the period during which data were collected (four years). In addition, our study focused on unplanned emergency ICU admissions, considering that this type of admission represents a common dilemma for clinicians. Whereas Taccone et al. [7] did not discriminate between planned and unplanned admissions, Soares and colleagues [8] distinguished medical patients versus scheduled and emergency surgical patients. These two previous investigations together with the present study indicate that a cancer diagnosis on admission to a general ICU is far from seldom: in our overall cohort (comprising 251,748 patients), 13.5% of patients admitted to the ICU had a diagnosis of malignancy versus 15.0% in the SOAP cohort [7] and 21.5% in the Brazilian study [8]. The current investigation further shows that amongst unplanned ICU admissions the proportion of cancer patients is lower (15,211 of 140,154 or 10.9%), which may reflect the reduced willingness of clinicians to admit cancer patients to the ICU in emergency situations.

Mortality rates especially differed between medical cancer and non-cancer patients, whereas differences between surgical cancer and non-cancer patients were either not existing (ICU mortality: 9.0 versus 8.9% respectively) or modest (hospital mortality: 17.4 versus 14.6% respectively). Medical cancer patients demonstrated almost doubled ICU and hospital mortality rates (30.4 and 40.6% respectively) when compared with non-cancer medical patients (16.2 and 23.7% respectively). In the SOAP cohort ICU and hospital mortality amongst cancer patients were 20% and 27% respectively; of note, however, in this cohort 62.4% of cancer patients were admitted postoperatively [7]. In the Brazilian investigation by Soares et al, who unlike Taccone et al [7] did discriminate between planned and unplanned surgical ICU admissions, ICU and hospital mortality for cancer patients admitted for unplanned surgery were 23 and 37% respectively; medical cancer patients did much worse with ICU and hospital mortality of 44 and 58% respectively [8]. As such, the mortality rates reported in the current survey are much lower, which may be related to differences in selection for ICU admission and/or ICU care in Brazil and the Netherlands. Although stratification based on type of malignancy yielded relatively small subgroups, absolute numbers were sufficient to establish mortality rates in different cancer categories. This analysis showed that the prognosis of medical cancer patients admitted to the ICU is grim for all types of cancer. Multivariate analyses showed that amongst medical cancer patients with unplanned ICU admission respiratory tract cancer, upper gastrointestinal cancer or leukemia were associated with a higher mortality.

In the present analysis patients with a hematological malignancy demonstrated the highest ICU and hospital mortality rates: 42.8 and 53.2% respectively for patients with leukemia as their primary diagnosis versus 37.2 and 48.5% respectively for patients with lymphoma. These mortality rates in hematological patients, although very high, are lower than reported earlier (60%-70%) [13, 14]. It appears that the prognosis of hematological patients has improved over the years. This is in agreement with a study by Azoulay et al. who found by multivariable analysis, that admission after 1996 (compared with admission between 1990 and 1996) was associated with a better outcome in medical ICU-patients with cancer, mostly leukemia, lymphoma or myeloma patients [13].

Lung cancer was the most frequent solid tumor in our cohort of unplanned ICU admissions. In accordance, previous studies have documented that lung cancer is the most common solid tumor to require ICU admission, accounting for 16% of all cancer-related admissions [15]. As expected, mortality was much higher in medical patients with lung cancer than in surgical patients with this type of malignancy. [16]The ICU and hospital mortality of these patients was 33.5 and 48.6% respectively, which is in the same order of magnitude as reported previously [17]. Notably, studies published over the most recent 15 years demonstrate a clear trend toward improved survival of lung cancer patients admitted to the medical ICU [16].

While mortality is high for medical cancer patients, treatment cannot be considered futile based on cancer diagnosis alone. Even for patients with leukemia, the category with highest mortality in our study, the likelihood to survive up to the hospital discharge was almost 50%. Different prognostic models have been developed to more precisely predict the outcome of critically ill patients based on diagnosis, comorbidity and severity of illness. These general prognostic models were reported to underestimate the risk of dying for cancer patients admitted to the ICU [18]. However, most investigations that addressed the usefulness of general prognostic models in cancer patients requiring ICU care are limited by relatively small sample sizes and restriction to specific patients groups and/or specialized oncologic ICUs [19, 20].

Therefore, we here reported SMRs based on the APACHE IV model in our large cohort of cancer patients admitted to general ICUs. In contrast to earlier studies [18], we found lower mortality than predicted in most patient groups

In particular medical cancer patients presented with acute comorbid diseases more frequently than medical non-cancer patients. Acute comorbidity, not the long-term prognosis of the underlying malignancy, has been implicated as an important factor in mortality after a critical illness in cancer patients [21, 22]. A high proportion of medical cancer patients had confirmed infection. In accordance, severe sepsis is a common complication in cancer patients; the incidence of severe sepsis is four times higher in cancer than in non-cancer patients [23] and approximately 15% of septic shock patients have cancer or a hematologic malignancy [24]. Previous investigations have further indicated that clinically documented infections represent a frequent cause for ICU admission in cancer patients [21, 25, 26]. In addition, acute renal failure was relatively common in medical cancer patients, confirming previous smaller studies [12, 13].

A limitation of our study is that the type of malignancy is only recorded when cancer is the main reason for admission to the ICU; otherwise malignancy is scored as hematological malignancy or neoplasm/metastasized carcinoma without further specification. In addition, our data set does not provide information of the stage of cancer or chemotherapeutic regimens used. This is caused by the fact that data collection within the NICE registry does not focus specifically on cancer patients. As such, prospective investigations on the outcome of patients suffering from specific types and/or stages of cancer and/or treated with common chemotherapeutics remain of interest. Lastly, follow up of our patients was limited to hospital discharge. We cannot exclude that some patients may have died soon after hospital discharge, e.g. after discharge to a palliative care unit or hospice outside the medical institute with the ICU facility. This may lead to a too optimistic view on survival after ICU admission in cancer patients.

We here present the largest survey to date on the epidemiology and outcome of cancer patients on general ICUs. In a cohort of 140,154 critically ill patients with an unplanned ICU admission 10.9% had a diagnosis of a malignancy on admission. ICU and hospital mortality in medical cancer patients were almost twice as high as in medical patients without cancer, whereas differences in mortality amongst surgical cancer and non-cancer patients were modest. However even in patient groups with the highest mortality risk, survival up to hospital discharge was approximately 50%. These data indicate that the decision for unplanned ICU admission of cancer patients should take the different type of admission (medical versus surgical) on mortality risk into account. In addition, prospective studies examining the impact of the type and stage of malignancy, as well as previous therapies (e.g. different chemotherapeutic regimens and radiation), on ICU outcome are warranted to assist the oncology and ICU staff in the decision whether or not to admit a cancer patient to the ICU.

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