

BMJ Open Short-term and medium-term survival of critically ill patients with solid tumours admitted to the intensive care unit: a retrospective analysis

Richard Fisher,^{1,2} Carole Dangoisse,^{1,3} Siobhan Crichton,⁴ Craig Whiteley,¹ Luigi Camporota,¹ Richard Beale,¹ Marlies Ostermann¹

To cite: Fisher R, Dangoisse C, Crichton S, *et al*. Short-term and medium-term survival of critically ill patients with solid tumours admitted to the intensive care unit: a retrospective analysis. *BMJ Open* 2016;**6**:e011363. doi:10.1136/bmjopen-2016-011363

► Prepublication history for this paper is available online. To view these files please visit the journal online (<http://dx.doi.org/10.1136/bmjopen-2016-011363>).

Received 31 January 2016
Revised 17 June 2016
Accepted 27 June 2016



CrossMark

For numbered affiliations see end of article.

Correspondence to

Dr Marlies Ostermann;
Marlies.Ostermann@gstt.nhs.uk

ABSTRACT

Objectives: Patients with cancer frequently require unplanned admission to the intensive care unit (ICU). Our objectives were to assess hospital and 180-day mortality in patients with a non-haematological malignancy and unplanned ICU admission and to identify which factors present on admission were the best predictors of mortality.

Design: Retrospective review of all patients with a diagnosis of solid tumours following unplanned admission to the ICU between 1 August 2008 and 31 July 2012.

Setting: Single centre tertiary care hospital in London (UK).

Participants: 300 adult patients with non-haematological solid tumours requiring unplanned admission to the ICU.

Interventions: None.

Primary and secondary outcomes: Hospital and 180-day survival.

Results: 300 patients were admitted to the ICU (median age 66.5 years; 61.7% men). Survival to hospital discharge and 180 days were 69% and 47.8%, respectively. Greater number of failed organ systems on admission was associated with significantly worse hospital survival ($p<0.001$) but not with 180-day survival ($p=0.24$). In multivariate analysis, predictors of hospital mortality were the presence of metastases (OR 1.97, 95% CI 1.08 to 3.59), Acute Physiology and Chronic Health Evaluation II (APACHE II) Score (OR 1.07, 95% CI 1.01 to 1.13) and a Glasgow Coma Scale Score <7 on admission to ICU (OR 5.21, 95% CI 1.65 to 16.43). Predictors of worse 180-day survival were the presence of metastases (OR 2.82, 95% CI 1.57 to 5.06), APACHE II Score (OR 1.07, 95% CI 1.01 to 1.13) and sepsis (OR 1.92, 95% CI 1.09 to 3.38).

Conclusions: Short-term and medium-term survival in patients with solid tumours admitted to ICU is better than previously reported, suggesting that the presence of cancer alone should not be a barrier to ICU admission.

INTRODUCTION

Advances in the field of oncology have led to a substantial improvement in survival rates in

Strengths and limitations of this study

- With 300 individual patients with solid tumours following unplanned admission to the intensive care unit (ICU), our study is one of the largest available.
- Survival rates up to 180 days following ICU admission were reported in 98% of our cohort (with only 2% of patients lost to follow-up).
- The analysis focussed on relevant risk factors which were present on admission to ICU in order to aid future decision-making.
- Only routinely available data were retrospectively collected.
- Information related to performance status preadmission to ICU and quality of life after discharge from ICU were not available.
- All patients were admitted to the ICU in a hospital with a tertiary cancer service, thereby potentially limiting the generalisability of our findings.

patients with cancer but also an increase in the number of patients requiring admission to the intensive care unit (ICU). A recent study showed that around one in seven patients admitted to general ICUs in Europe had a malignancy, the majority being solid tumours.¹ The most common reasons for ICU admission include postoperative routine care, complications of the underlying disease, side effects of cancer treatment and medical or surgical problems not directly related to malignancy.² Cancer registry data from West Scotland confirmed that between 2000 and 2009, 1 in 20 patients with a non-haematological cancer experienced a critical illness requiring ICU admission within 2 years of cancer diagnosis.³ ICU mortality was greatest among unplanned medical admissions (41.7%). In contrast, ICU mortality was lowest (0.6%) in patients who were elective surgical admissions that did not require organ support.

Historically, the presence of malignant disease has been a common reason for refusal of admission to ICU, even in the absence of a decision to limit life-sustaining therapies.⁴ Predicting outcome is difficult in clinical practice, especially since traditional physiological scores do not perform well in this patient group.^{5–8} In a prospective study that evaluated the outcome of critically ill patients with cancer considered for ICU admission, 20% of patients who were not admitted because they were considered to be ‘too well for ICU’ died in hospital and of the patients considered to be ‘too sick’ to benefit from ICU admission, 26% were alive on day 30 and 17% on day 180.⁹

A systematic review including 48 papers published between 2000 and 2014 showed that ICU mortality of patients with solid tumours was between 4.5% and 85%, while hospital mortality was reported in less studies and ranged from 4.6% to 76.8%.¹⁰ The studies varied in patient populations, primary malignancies, type of critical care setting (specialised oncological ICU vs general ICU) and duration of follow-up. Some studies only included unplanned admissions, whereas others comprised both patients admitted as medical emergencies and after elective surgery. The difference in outcome among these groups has been clearly demonstrated.¹¹ The majority of studies (35/48) included ICU mortality rates. Hospital mortality was reported in 31/48 studies but outcome beyond 3 months after discharge from hospital was assessed in only 8 studies. This is particularly relevant since not all patients with cancer who leave hospital alive actually return home. Sharma *et al*¹² highlighted that 43% of patients with lung cancer discharged alive from hospital were transferred to another institution, including nursing home. To offer life-sustaining therapies to patients with cancer who have an acceptable prognosis and to avoid unnecessary suffering in those who are approaching the end of their life, more long-term outcome data beyond discharge from hospital and better understanding of prognostic factors in this patient population are needed.¹³

The main objective of this study was to determine the outcome of patients with solid tumours with unplanned admission to a general ICU of a large teaching hospital with particular focus on hospital and 180-day outcome. We also aimed to identify factors present on admission to ICU and routinely available to the treating clinicians which were predictors of survival up to 180 days.

METHODS

Setting

Guy’s & St Thomas’ NHS Foundation Trust is a tertiary referral centre for oncology, serving the populations of South-East London and South-East England—UK. Oncology inpatient and outpatient services are based at the Guy’s Hospital site where critical care support is provided in a 13-bed multidisciplinary ICU by consultant-led multidisciplinary ICU team. The Guy’s

Hospital site does not have an Emergency Department, and referrals to the ICU are made predominantly by inpatient teams caring for patients on the medical and surgical wards, as well as from the chemotherapy day-unit or from other hospitals within the region. All admissions to the ICU are discussed and approved by the ICU consultant in charge. The ICU operates a ‘closed’ model where decisions regarding care are made by the ICU consultant in close collaboration with the consultant-led oncology team who are available on a 24-hour basis. The ICU has a fully computerised electronic patient record system where all medical entries, physiological observations and laboratory data are recorded at time of generation. Data entries related to the presence of sepsis are mandatory fields. Full multiorgan support including haemodynamic, renal and advanced respiratory support can be provided at all times.

Study design and data collection

We retrospectively screened the records of all admissions to the ICU between 1 August 2008 and 31 July 2012 and identified adult patients (18 years or older) with a diagnosis of non-haematological malignancy admitted as an emergency. Planned admissions following elective surgery were not included.

Following review of the literature and identification of the most common risk factors in patients with cancer, we screened the patients’ computerised electronic medical notes and laboratory records and collected the following data: demographics, site of primary tumour, presence of metastases, reason for admission to ICU, number of previous ICU admissions, presence of sepsis (≥ 2 criteria for Systemic Inflammatory Response Syndrome and proven or suspected infection¹⁴), neutropenia (white cell count $< 1.0 \times 10^9/L$),¹⁵ thrombocytopenia (platelet count $< 20 \times 10^9/L$), Acute Physiology and Chronic Health Evaluation (APACHE) II¹⁶ and Sequential Organ Failure Assessment (SOFA) Score¹⁷ on admission to ICU (with greater scores representing a greater degree of physiological derangement and more severe illness), presence of a ‘Do Not Attempt Cardio Pulmonary Resuscitation’ (DNACPR) order and presence of significant comorbidities (excluding those directly relating to cancer). Organ failure on admission to ICU was defined as follows: neurological failure was defined by a Glasgow Coma Score (GCS) $< 7/15$;¹⁵ respiratory failure was defined as the need for mechanical ventilatory support with differentiation between non-invasive ventilation (NIV) via a face-mask versus mechanical ventilation via an endotracheal tube; circulatory failure was defined as the need for a continuous infusion of any vasopressor or inotropic drug; renal failure was defined as the need for renal replacement therapy (RRT) and haematological failure was defined as neutropenia (white cell count $< 1.0 \times 10^9/L$),¹⁵ thrombocytopenia (platelet count $< 20 \times 10^9/L$) or anaemia (haematocrit < 0.2). Decisions to

initiate organ support were made by the ICU team on a patient by patient basis and were not protocolised.

The main outcomes were survival to hospital discharge and to 180 days following ICU admission. Every effort was made to determine 180-day outcome. When patients were no longer being followed up by the oncology team at our hospital and a date of death was not recorded in the electronic patient record, the patient's general practitioner was contacted for further details. If the general practitioner had not been in contact with the patient and was unable to confirm whether they were still alive, we elected not to contact the patient or next of kin directly to avoid any unnecessary distress. These patients were not included in the 180-day outcome analysis. Where patients had >1 admission to the ICU, data were collected for each admission but only exposures and potential confounder variables from the first admission to analyse hospital and 180-day outcomes.

Statistical analysis

Categorical data were summarised as frequency (percentage), and continuous variables were summarised as median (IQR). Survival rates at hospital discharge and 180 days were compared across groups of patients using a χ^2 or Fisher's exact test, as appropriate. Comparisons between survivors and non-survivors were made using a Mann-Whitney test when the characteristics were summarised using a continuous scale.

Logistic regression models were used to identify factors known at the time of admission which were independently associated with hospital and with 180-day survival. All variables included in the univariable analysis were considered for inclusion with the exception of SOFA Score to avoid collinearity resulting from the inclusion of other variables which are components of the SOFA Score. Variables which were independently associated with survival were added to the multivariable model using a forward stepwise selection procedure. Alongside the estimated ORs for factors which were identified as being significantly associated with mortality, the estimated ORs for the excluded variables were estimated by adding each variable in turn to the multivariable model. The goodness of fit of the logistic models was assessed using the Hosmer-Lemeshow test, and the area under the receiver operating curve (AUC) for both models was calculated.

Ethics

The study had institutional approval. As per Governance Arrangements for Research Ethics Committees published by the UK Health Departments, formal review by a Research Ethics Committee and need for individual informed consent were not required since the research was limited to secondary use of information previously collected in the course of normal care and the patients were not identifiable to the research team carrying out the research.¹⁸

RESULTS

During the 4-year study period (August 2008 to July 2012), there were 3577 admissions to the ICU of which 356 (10.0%) were unplanned admissions of 300 patients with a solid tumour. Forty-one patients had >1 admission. The median age of patients was 66.5 years, and 61.7% were men (table 1). The median SOFA and APACHE II Scores were 4 (IQR 2–6) and 18 (IQR 14–21), respectively. The most frequently present tumours were lung (43%), head and neck (17.3%), renal (6.7%) and bladder (6.3%). One-third of patients was known to have distant metastases. The main reasons for ICU admission were respiratory failure, sepsis, acute kidney injury and bleeding.

Only 13 patients (4.3%) had a non-malignancy related significant comorbidity: cirrhosis (1.7%), severe respiratory disease (1%), chronic RRT (1%), 'very severe' (New York Heart Association grade IV) cardiovascular disease (0.3%) and HIV infection (0.3%). Nine patients (3%) had a DNACPR order prior to ICU admission of whom 6 survived to ICU discharge and 1 survived to hospital discharge, but no patient survived beyond 180 days after admission to ICU.

A total of 153 patients were admitted to ICU with respiratory failure of whom 93 patients were treated with NIV or mechanical ventilation on admission. The remaining 60 patients were treated with high-flow oxygen therapy. Thirty-three patients survived to ICU discharge without needing any respiratory support, 26 deteriorated and required respiratory support at a later stage and 1 patient died in ICU without treatment with NIV or mechanical ventilation.

The median survival of the total cohort following ICU admission was 156 days. ICU survival was 79.3%, and hospital survival following first ICU admission was 69.0%. Furthermore, 180-day outcome data were available for 293 patients (97.7%) and showed a survival rate of 47.8%. All 7 patients with missing 180-day outcome data had a primary lung cancer. The median ICU length of stay was 4 days (IQR 2–8 days) for all patients.

Risk factors

Univariable analysis

Non-survivors had significantly higher SOFA and APACHE II Scores on admission to ICU compared to survivors, but there was no difference in age and gender (table 2). Patients admitted with non-neutropenic sepsis or following in-hospital cardiac arrest had significantly lower than average hospital survival (69/114 and 1/6, respectively).

The type of the cancer primary was not associated with hospital and 180-day survival ($p=0.68$ and $p=0.15$, respectively), but patients with metastatic disease had significantly lower hospital and 180-day survival rates (57/100 and 31/100, respectively, p values 0.001 and <0.001 , respectively) (table 2).

As the number of failed organ systems on admission to ICU increased, the likelihood of survival to hospital

Table 1 Demographics and baseline data

Parameter	Patients with solid tumours (n=300)
Age, median (IQR)	66.5 (58–73.5)
Male gender, n (%)	185 (61.7)
Type of malignancy	
Lung cancer, n (%)	128 (42.7)
Head and neck cancer, n (%)	52 (17.3)
Renal cancer, n (%)	20 (6.7)
Bladder cancer, n (%)	19 (6.3)
Oesophageal cancer, n (%)	18 (6.0)
Colorectal cancer, n (%)	14 (4.7)
Prostate cancer, n (%)	9 (3.0)
Breast cancer, n (%)	8 (2.7)
Other, n (%)	32 (10.6)
Metastatic disease, n (%)	100 (33.3)
Main reasons for first admission to ICU*	
Respiratory failure, n (%)	153 (51)
Non-neutropenic sepsis, n (%)	114 (38)
Neutropenic sepsis, n (%)	12 (4)
Acute kidney injury, n (%)	27 (9)
Bleeding, n (%)	22 (7.3)
Postcardiac arrest, n (%)	16 (5.3)
Cardiac emergency, n (%)	6 (2)
Other, n (%)	36 (11.9)
>1 ICU admission, n (%)	41 (13.7)
Severity of illness on admission to ICU	
SOFA Score, median (IQR)	4 (2–6)
APACHE II Score, median (IQR)	18 (14–21)
Confirmed or suspected sepsis, n (%)	201 (67)
Neutropenia, n (%)	17 (5.7)
Thrombocytopenia, n (%)	7 (2.3)
GCS <7, n (%)	23 (7.7)
Number of failed organ systems on admission to ICU	
0 OF, n (%)	112 (37.3)
1 OF, n (%)	125 (41.7)
2 OF, n (%)	36 (12)
3 OF, n (%)	22 (7.3)
>3 OF, n (%)	5 (1.7)
Need for organ support on admission to ICU	
Treatment with vasopressors/inotropes, n (%)	59 (19.7)
RRT	24 (8)
Respiratory support with non-invasive ventilation, n (%)	79 (26.3)
Respiratory support with mechanical ventilation, n (%)	54 (18)
Outcome	
Hospital survival following first ICU admission (%)	69
180-day survival following first ICU admission (%)†	47.8
Days in ICU, median (IQR)	4 (2–8)

*A proportion of patients had more than one reason for admission to ICU.

†Data not available for seven patients.

APACHE, Acute Physiology and Chronic Health Evaluation; ICU, intensive care unit; OF, failed organ systems; RRT, renal replacement therapy; SOFA, sequential organ failure assessment.

discharge decreased significantly (table 2). Hospital survival among patients with no organ failure at admission was 76.8%, falling to 72.8%, 52.8% and 50% with 1, 2 and 3 failed organ systems, respectively. No patient with >3 failed organ systems at admission survived to hospital discharge. This difference was no longer significant by 180 days. Likewise, the need for any type of organ support (vasopressors/inotropes, RRT or ventilatory support) on admission to ICU was associated with worse outcomes in hospital, but only RRT was still a significant risk factor of death at 180 days (table 2).

Multivariable analysis

Multivariate analysis showed that the presence of metastases, a GCS <7 and a higher APACHE II Score on admission to ICU were independent risk factors for hospital mortality (table 3). The AUC was 0.72. Age, male gender, presence of neutropenia and thrombocytopenia and need for organ support on admission to ICU (RRT, inotropes, respiratory support) were not independently associated with higher hospital mortality.

Metastatic disease, a higher APACHE II Score and the presence of sepsis were independent risk factors for 180-day mortality (table 3). The AUC was 0.67. There was no evidence of a lack of goodness of fit for the models for hospital survival ($p=0.157$) or 180-day survival ($p=0.252$).

DISCUSSION

This retrospective analysis showed that patients with cancer with unplanned admission to the ICU had a hospital survival of 69% and a 180-day survival rate of 48%. Presence of metastases and a higher APACHE II Score on admission to ICU were independent risk factors for reduced chances of survival. Need for organ support on admission to ICU was not predictive of long-term mortality.

There are not many studies in the literature to compare our 180-day outcome data with since most studies only report ICU and/or hospital outcome. However, the survival rates in our cohort compare favourably with other published series. Soares *et al*¹⁹ analysed the data of 772 critically ill patients with cancer of whom 83% had a solid tumour. Their 6-month survival was comparable to ours at 46%. Studies focussing on patients with lung cancer admitted to ICU found 6-month mortality rates of 13–51.8%.^{20–23} Using data from a large lung cancer registry (49 373 patients admitted to an ICU in the USA between 1992 and 2007), Slatore *et al*²⁴ reported 6-month survival rates of 34.6%. For comparison, 180-day survival in patients with lung cancer in our cohort was 48.8%.

When caring for patients with cancer, the challenge for ICU clinicians and oncologists is to identify those who are likely to benefit from admission to ICU and to

Table 2 Comparison between survivors and non-survivors (univariable analysis)

Factors on admission to ICU	Hospital survivors (n=207)	Hospital non-survivors (n=93)	p Value	180-day survivors*† (n=140)	180-day non-survivors*† (n=153)	p Value
Age, median (IQR)	66 (58–73)	68 (58–75)	0.62	66.5 (59–73.5)	66 (58–74)	0.60
Male gender, n (%)	129 (62)	56 (60)	0.87	88 (62.9)	97 (63.4)	0.90
SOFA Score, median (IQR)	4 (2–5)	4 (3–8)	<0.001	4 (2–5)	4 (3–6)	0.048
APACHE II Score, median (IQR)	16 (13–20)	19 (16–25)	<0.001	16 (12–20)	19 (15–23)	0.001
Metastatic disease, n (%)	57 (27.5)	43 (46)	0.001	31 (22)	69 (45)	<0.001
Confirmed or clinically suspected sepsis, n (%)	133 (64)	68 (73)	0.13	87 (62)	114 (74.5)	0.03
Neutropenia, n (%)	8 (3.9)	9 (9.7)	0.04	6 (4.3)	11 (7.2)	0.29
GCS <7, n (%)	8 (3.9)	15 (16.1)	<0.001	8 (5.7)	15 (9.8)	0.19
Number of failed organ systems						
0 OF, n (%)	86 (41.5)	26 (28)	<0.001	58 (41.4)	54 (35.3)	0.24
1 OF, n (%)	91 (44)	34 (36.6)		58 (41.4)	64 (41.8)	
2 OF, n (%)	19 (9.2)	17 (18.3)		18 (12.9)	18 (11.8)	
3 OF, n (%)	11 (5.3)	11 (11.8)		9 (6.4)	12 (7.8)	
>3 OF, n (%)	0	5 (5.4)		0	5 (3.3)	
Need for organ support						
Vasopressor/inotrope Rx, n (%)	32 (15.5)	27 (29)	0.006	26 (18.6)	31 (20.3)	0.83
RRT, n (%)	11 (5.3)	13 (14)	0.01	5 (3.6)	18 (11.8)	0.009
No ventilatory support, n (%)	125 (60.4)	42 (45.2)	0.043	84 (60)	82 (53.6)	0.347
Non-invasive ventilation, n (%)	50 (24.2)	29 (31.2)		30 (21.4)	44 (28.8)	
Mechanical ventilation, n (%)	32 (15.5)	22 (23.7)		26 (18.6)	27 (17.6)	

*Data unavailable for seven patients.

†Including patients who died in hospital.

APACHE, Acute Physiology and Chronic Health Evaluation; GCS, Glasgow Coma Score; ICU, intensive care unit; OF, organ failure; RRT, renal replacement therapy; Rx, treatment; SOFA, sequential organ failure assessment.

avoid prolonged suffering with futile treatments and unrealistic expectations in those who are approaching the end of their life and have low probabilities of a meaningful survival. Favourable outcomes are commonly observed among patients with cancer admitted to the ICU for postoperative care, administration of chemotherapy or immunomodulatory agents and management of tumour lysis syndrome.^{11 25} Our data show that the probability of leaving hospital alive was also greater in patients without established organ failure on admission to ICU, which may be a consequence of early recognition and treatment of complications before the onset of multiorgan dysfunction. In fact, 37.3% of patients included in our analysis had no established organ failure at the time of ICU admission. Interestingly, 60 patients were admitted to ICU with respiratory failure as the main reason for admission but did not receive NIV or mechanical ventilation (MV) at the time of admission. Their ICU survival was 83%. They were all treated with high-flow oxygen therapy, but 26 patients subsequently deteriorated and required respiratory support at a later stage. Although it is not possible to make any firm recommendations related to optimal timing of ICU admission, current data suggest that patients with multiorgan failure related to delayed admission to ICU have an increased risk of dying.²⁶ Early admission offers an opportunity for organ support before progression to multiorgan failure but also provides opportunities for

high-risk diagnostic investigations which may not be safely undertaken on the general ward.

Most studies have demonstrated an association between short-term mortality and severity of acute illness,^{27–30} greater number of failed organ systems^{31–37} and increased requirement for organ support including mechanical ventilation,^{23 30 38–40} vasopressors^{36 38 39 41} and RRT.^{29 42} Our analysis showed that APACHE II Score on admission to ICU was independently associated with worse hospital and 180-day mortality. Although a greater number of failed organ systems and the need for organ support at ICU admission were associated with worse hospital mortality in univariate analysis, only the need for RRT remained an independent risk factor for 180-day mortality. This suggests that while these factors will affect an individual's probability of surviving the acute illness, there is no lasting impact on risk of death beyond this episode if the cause determining admission to ICU is reversible. Two-thirds of patients in this study had suspected or confirmed sepsis on admission to ICU (even if this was not their stated reason for admission). Interestingly, they were not significantly more likely to die in hospital compared to patients without sepsis but had an increased risk of dying within 180 days (OR 1.92, 95% CI 1.09 to 3.38).

The association between stage of malignant disease and prognosis in ICU is not fully established. In our study, a third of patients were known to have metastatic disease at

Table 3 Multivariable analysis of factors associated with hospital and 180-day mortality

Factor	Hospital mortality			180-day mortality*†		
	OR	95% CI	p Value	OR	95% CI	p Value
Variables included in the multivariable model						
Presence of metastases	1.97	1.08 to 3.59	0.03	2.82	1.57 to 5.06	0.001
APACHE II Score	1.07	1.01 to 1.13	0.03	1.07	1.01 to 1.13	0.02
GCS <7	5.21	1.65 to 16.43	0.005			
Confirmed or suspected sepsis				1.92	1.09 to 3.38	0.02
Variables excluded from the multivariable model						
GCS <7				2.13	0.69 to 6.55	0.19
Confirmed or suspected sepsis	1.60	0.84 to 3.03	0.15			
Age	1.0	0.97 to 1.02	0.79	0.99	0.97 to 1.01	0.47
Male gender	1.37	0.77 to 2.44	0.28	1.47	0.86 to 2.51	0.16
Thrombocytopenia	0.87	0.09 to 8.13	0.91	4.39	0.38 to 50.59	0.24
Neutropenia	1.28	0.32 to 5.05	0.72	0.60	0.16 to 2.28	0.45
Need for vasopressor/inotropic support	0.86	0.37 to 1.99	0.72	0.55	0.24 to 1.25	0.15
Need for RRT	1.93	0.72 to 5.15	0.19	2.62	0.84 to 8.18	0.097
No ventilation	1			1		
Need for NIV	1.51	0.79 to 2.86	0.21	1.48	0.80 to 2.75	0.21
Need for MV	1.15	0.47 to 2.84	0.76	1.24	0.53 to 2.87	0.62

Variables included in the final multivariable model were selected using a forward selection procedure. ORs for variables that were not included were estimated by adding each of the variables to the multivariable model in turn.

*Data unavailable for seven patients.

†Including patients who died in hospital.

APACHE, Acute Physiology and Chronic Health Evaluation; GCS, Glasgow Coma Score; ICU, intensive care unit; MV, mechanical ventilation; NIV, non-invasive ventilation; RRT, renal replacement therapy; SOFA, sequential organ failure assessment.

the time of ICU admission. This was associated with an almost doubling of the risk of in hospital mortality and approaching threefold risk of death by 180 days (OR 1.97, 95% CI 1.08 to 3.59, and OR 2.82, 95% CI 1.57 to 5.06, respectively). Toffart *et al*⁴³ evaluated the outcomes of patients with lung cancer admitted to ICU and also found that 90-day mortality was significantly higher in patients with metastatic disease (OR 1.9, 95% CI 1.08 to 3.33). It is certainly possible that the intensity of treatment in the ICU is influenced by the stage of the underlying cancer. Interestingly, others reported no association between lung cancer stage and hospital survival.^{21–23 44} Similarly, Azoulay *et al*⁴⁵ analysed the data of 120 consecutive patients with cancer and also found that 30-day mortality was not correlated with disease stage and tumour progression.

Beside evaluation by clinicians has been deemed a poor tool for prognostication of outcome in ICU patients with cancer.⁹ In an effort to identify better those patients likely to benefit from ICU admission and those for whom prolonged ICU care would not be appropriate, some experts suggest a ‘trial period in ICU’ with clear goals and stopping criteria.^{46–48} This recommendation is certainly supported by the findings of the ICU trial, a prospective study of 188 patients with haematological malignancies or solid tumours requiring mechanical ventilation and having at least one other organ failure.⁴⁹ All patients enrolled in the study were admitted to the ICU for full treatment followed by a reappraisal of care on day 5. Patients who were bedridden or receiving palliative care as their only cancer treatment option were excluded. All patients who required

escalation of organ support after 3 days in the ICU died. The authors showed that organ failure scores were more accurate on day 6 than at admission and therefore concluded that treatment-limitation decisions should be considered only after 5–6 days of full ICU management. In case of lack of improvement after this trial period, transition to comfort or end-of-life care should be contemplated.

With 300 individual patients, our study is larger than many other single centre studies, despite limiting our inclusion criteria to only those patients with unplanned admission to the ICU. In addition, we are able to report mortality up to 180 days following ICU admission (with only 2% of patients lost to follow-up). We focused on those factors which were present on admission to ICU in order to aid future decision-making. Despite these strengths, it is important to acknowledge some limitations. First, patient identification and data collection were retrospective and relied on the accuracy of the electronic records and entries made at the time. Data collection was limited to factors which are routinely collected as part of routine critical care. As a result, we were not able to evaluate the impact of performance status preadmission to ICU. We acknowledge that several studies reported an association between worse performance status at admission and greater mortality.^{11 21–22 50–53} Likewise we do not have data on all potential comorbidities, disease stage, details related to the oncological treatment, response to chemotherapy prior to ICU admission and whether treatment was given with curative or palliative intentions. Second, we have no data on the

outcome of patients who were referred for ICU admission but declined, either on the basis of being too well or having such a poor prognosis that ICU care was deemed to be futile. Similarly, we have no outcome data for patients with cancer who became critically unwell on cancer ward but were not referred to the ICU team (In a recent study of patients with lung cancer developing new organ failure, only 35.0% were referred for ICU admission by the treating team⁵⁴). Third, the proportion of patients admitted with each cancer type reflects the range of tertiary services based at our hospital and the data may not be generalisable to general ICUs in hospitals without a tertiary cancer service. Fourth, patients admitted to our ICU were less sick with lower APACHE II and SOFA Scores on day of admission compared to other similar studies in the literature,^{28 29 43 48} which may reflect differences in admission policy and bed availability. The Guy's Hospital site has no separate high-dependency unit, and 37.3% of patients in our study did not require organ support at time of admission, rather they were admitted for enhanced monitoring. This difference in severity of illness is likely to at least in part explain the differences in observed mortality between our study and previous reports. Fifth, we analysed the data of patients with solid tumours but did not make comparisons with other patient cohorts or all-comers. Sixth, while we had 180-day survival data for 98% of patients, we were not able to collect data on functional status or quality of life postdischarge in survivors. Similarly, we do not have data on the type of anticancer therapies survivors received after ICU discharge. We were also unable to determine how many patients were discharged from ICU and hospital on a purely palliative pathway. Finally, we did not collect the causes of death and do not know how many patients died after a clinical decision to withdraw life-sustaining therapies.

Our analysis adds to a growing number of studies that report improved outcomes in patients with cancer admitted to ICU. The majority of patients admitted to our ICU were discharged from hospital alive after a relatively short intensive care admission, and nearly half of patients were still alive 180 days after admission. Patients with organ failure requiring vasopressor or ventilatory support on admission had similar long-term outcomes to patients without organ failure.

In conclusion, short-term and medium-term survival in patients with solid tumours admitted to ICU is better than previously reported. Predictors of hospital mortality were the presence of metastases, a higher APACHE II Score and a GCS <7 on admission to ICU and risk factors for 180-day mortality were the presence of metastases, a higher APACHE II Score and sepsis on admission to ICU. The presence of cancer per se should not be a reason for refusal of ICU admission. Instead, the decision to admit critically ill patients with cancer to the ICU should be based on the probability of surviving the acute illness. More research and guidance is necessary to decide which patients with cancer to admit to the ICU for intensive life-sustaining therapies and when to

shift focus of care towards palliation and symptom control.

Author affiliations

¹Department of Critical Care, King's College London, Guy's & St Thomas' Hospital NHS Foundation Trust, London, UK

²Department of Critical Care, Royal Brompton and Harefield NHS Foundation Trust, London, UK

³Department of Critical Care, King's College Hospital NHS Foundation Trust, London, UK

⁴Division of Health and Social Care Research, King's College London, London, UK

Acknowledgements The authors are grateful to Dr Lorna Starsmore, Dr Thubeena Manickavasagar and Dr Sofia Slanova for assisting with the data collection. Some of the data were presented at the State of the Art meeting of the Intensive Care Society UK in December 2014 and the International Symposium of Intensive Care & Emergency Medicine in Brussels in March 2015.

Collaborators Lorna Starsmore; Thubeena Manickavasagar; Sofia Slanova.

Contributors MO and RF designed the protocol and led the project. RF, CD and CW collected the necessary data. SC performed the statistical analysis. RF wrote the first draft. LC, RB and CD assisted with the interpretation of the data. All authors contributed to the final manuscript. All authors approved the final manuscript.

Funding This research received no specific grant from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Ethics approval Governance Department at Guy's & St Thomas Hospital.

Provenance and peer review Not commissioned; externally peer reviewed.

Data sharing statement Extra data can be accessed via the Dryad data repository at <http://datadryad.org/> with the doi:10.5061/dryad.t383q.

Open Access This is an Open Access article distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>

REFERENCES

1. Taccone FS, Artigas AA, Sprung CL, *et al.* Characteristics and outcomes of cancer patients in European ICUs. *Crit Care* 2009;13:R15.
2. Bos MM, Verburg IW, Dumajl I, *et al.* Intensive care admission of cancer patients: a comparative analysis. *Cancer Med* 2015;4:966–76.
3. Puxty K, McLoone P, Quasim T, *et al.* Risk of critical illness among patients with solid cancers. A population-based observational study. *JAMA Oncol* 2015;1:1078–85.
4. Garrouste-Orgeas M, Montuclard L, Timsit JF, *et al.* Predictors of intensive care unit refusal in French intensive care units: a multiple-center study. *Crit Care Med* 2005;33:750–5.
5. Sculier JP, Paesmans M, Markiewicz E, *et al.* Scoring systems in cancer patients admitted for an acute complication in a medical intensive care unit. *Crit Care Med* 2000;28:2786–92.
6. Soares M, Fontes F, Dantas J, *et al.* Performance of six severity-of-illness scores in cancer patients requiring admission to the intensive care unit: a prospective observational study. *Crit Care* 2004;8:R194–203.
7. Soares M, Silva UVA, Teles JMM, *et al.* Validation of four prognostic scores in patients with cancer admitted to Brazilian intensive care units: results from prospective multicentre study. *Intensive Care Med* 2010;36:1188–95.
8. Salluh JIF, Soares M. ICU severity of illness scores: APACHE, SAPS and MPM. *Curr Opin Crit Care* 2014;20:557–65.
9. Thiéry G, Azoulay E, Darmon M, *et al.* Outcome of cancer patients considered for intensive care unit admission: a hospital-wide prospective study. *J Clin Oncol* 2005;23:4406–13.

10. Puxty K, McLoone P, Quasim T, *et al.* Survival in solid cancer patients following intensive care unit admission. *Intensive Care Med* 2014;40:1409–28.
11. Soares M, Caruso P, Silva E, *et al.* Characteristics and outcomes of patients with cancer requiring admission to intensive care units: a prospective multicenter study. *Crit Care Med* 2010;38:9–15.
12. Sharma G, Freeman J, Zhang D, *et al.* Trends in end-of-life ICU use among older adults with advanced lung cancer. *Chest* 2008;133:72–8.
13. Vincent F, Bouguerba A, Bornstain C. Unsolved questions in solid tumor patients and intensive care. *Intensive Care Med* 2015;41:174–5.
14. Bone RC, Balk RA, Cerra FB, *et al.* Definitions for sepsis and organ failure and guidelines for the use of innovative therapies in sepsis. The ACCP/SCCM Consensus Conference Committee. American College of Chest Physicians/Society of Critical Care Medicine. *Chest* 1992;101:1644–55.
15. Knaus WA, Draper EA, Wagner DP, *et al.* Prognosis in acute organ-system failure. *Ann Surg* 1985;202:685–93.
16. Knaus WA, Draper EA, Wagner DP, *et al.* APACHE II: a severity of disease classification system. *Crit Care Med* 1985;13:818–29.
17. Vincent JL, De Mendonca A, Cantraine F, *et al.* Use of the SOFA score to assess the incidence of organ dysfunction/failure in intensive care units: results of a multicenter, prospective study. Working group on “sepsis-related problems” of the European Society of Intensive Care Medicine. *Crit Care Med* 1998;26:1793–800.
18. <http://www.hra.nhs.uk/resources/research-legislation-and-governance/governance-arrangements-for-research-ethics-committees/> (accessed 8 Jan 2016).
19. Soares M, Salluh JI, Ferreira CG, *et al.* Impact of two different comorbidity measures on the 6-month mortality of critically ill cancer patients. *Intensive Care Med* 2005;31:408–15.
20. Kim YJ, Kim MJ, Cho YJ, *et al.* Who should be admitted to the intensive care unit? The outcome of admission in stage IIIB-IV lung cancer patients. *Med Oncol* 2014;31:847.
21. Anisoglou S, Asteriou C, Barbetakis N, *et al.* Outcome of lung cancer patients admitted to the intensive care unit with acute respiratory failure. *Hippokratia* 2013;17:60–3.
22. Roques S, Parrot A, Lavole A, *et al.* Six-month prognosis of patients with lung cancer admitted to the intensive care unit. *Intensive Care Med* 2009;35:2044–50.
23. Adam AK, Soubani AO. Outcome and prognostic factors of lung cancer patients admitted to the medical intensive care unit. *Eur Respir J* 2008;31:47–53.
24. Slatore CG, Cecere LM, Letourneau JL, *et al.* Intensive care unit outcomes among patients with lung cancer in the surveillance, epidemiology, and end results-medicare registry. *J Clin Oncol* 2012;30:1686–91.
25. Pitello N, Treon M, Jones KL, *et al.* Approaches for administering chemotherapy in the intensive care unit. *Curr Drug Saf* 2010;5:22–32.
26. Azoulay E, Soares M, Darmon M, *et al.* Intensive care of the cancer patient: recent achievements and remaining challenges. *Ann Intensive Care* 2011;1:5.
27. Souza-Dantas VC, Salluh JI, Soares M. Impact of neutropenia on the outcomes of critically ill patients with cancer: a matched case-control study. *Ann Oncol* 2011;22:2094–100.
28. Aygençal G, Turkoglu M, Turkoz Sucak G, *et al.* Prognostic factors in critically ill cancer patients admitted to the intensive care unit. *J Crit Care* 2014;29:618–26.
29. Heo SJ, Kim G, Lee CK, *et al.* Prediction of short- and long-term survival for advanced cancer patients after ICU admission. *Support Care Cancer* 2015;23:1647–55.
30. Hawari FI, Nazer LH, Addassi A, *et al.* Predictors of ICU admission in patients with cancer and the related characteristics and outcomes: a 5-year registry-based study. *Crit Care Med* 2016;44:548–53.
31. Rosolem MM, Rabello LS, Lisboa T, *et al.* Critically ill patients with cancer and sepsis: clinical course and prognostic factors. *J Crit Care* 2012;27:301–7.
32. Chou KT, Chen CS, Su KC, *et al.* Hospital outcomes for patients with stage III and IV lung cancer admitted to the intensive care unit for sepsis-related acute respiratory failure. *J Palliat Med* 2012;15:1234–9.
33. Soares M, Darmon M, Salluh JI, *et al.* Prognosis of lung cancer patients with life-threatening complications. *Chest* 2007;131:840–6.
34. Caruso P, Ferreira AC, Laurienzo CE, *et al.* Short- and long-term survival of patients with metastatic solid cancer admitted to the intensive care unit: prognostic factors. *Eur J Cancer Care* 2010;19:260–6.
35. Kopterides P, Liberopoulos P, Ilias I, *et al.* General prognostic scores in outcome prediction for cancer patients admitted to the intensive care unit. *Am J Crit Care* 2011;20:56–66.
36. Namendys-Silva SA, Texcocano-Becerra J, Herrera-Gomez A. Prognostic factors in critically ill patients with solid tumours admitted to an oncological intensive care unit. *Anaesth Intensive Care* 2010;38:317–24.
37. Mourad M, Chow-Chine L, Faucher M, *et al.* Early diastolic dysfunction is associated with intensive care unit mortality in cancer patients presenting with septic shock. *Br J Anaesth* 2014;112:102–9.
38. Andr jak C, Terzi N, Thielen S, *et al.* Admission of advanced lung cancer patients to intensive care unit: a retrospective study of 76 patients. *BMC Cancer* 2011;11:159.
39. Azoulay E, Thiery G, Chevret S, *et al.* The prognosis of acute respiratory failure in critically ill cancer patients. *Medicine (Baltimore)* 2004;83:360–70.
40. Bonomi MR, Smith CB, Mhango G, *et al.* Outcomes of elderly patients with stage IIIB-IV non-small cell lung cancer admitted to the intensive care unit. *Lung Cancer* 2012;77:600–4.
41. Mendoza V, Lee A, Marik PE. The hospital-survival and prognostic factors of patients with solid tumors admitted to an ICU. *Am J Hosp Palliat Care* 2008;25:240–3.
42. Bissell L, Khan OA, Mercer SJ, *et al.* Long term outcomes following emergency intensive care readmission after elective oesophagectomy. *Acta Chir Belg* 2013;113:14–18.
43. Toffart AC, Minet C, Raynard B, *et al.* Use of intensive care in patients with nonresectable lung cancer. *Chest* 2011;139:101–8.
44. Hwang KE, Seol CH, Hwang YR, *et al.* The prognosis of patients with lung cancer admitted to the medical intensive care unit. *Asia Pac J Clin Oncol* 2016;12:e118–24.
45. Azoulay E, Moreau D, Alberti C, *et al.* Predictors of short-term mortality in critically ill patients with solid malignancies. *Intensive Care Med* 2000;26:1817–23.
46. Benoit DD, Soares M, Azoulay E. Has survival increased in cancer patients admitted to the ICU? We are not sure. *Intensive Care Med* 2014;40:1576–9.
47. Kostakou E, Rovina N, Kyriakopoulou M, *et al.* Critically ill cancer patient in intensive care unit: issues that arise. *J Crit Care* 2014;29:817–22.
48. Xia R, Wang D. Intensive care unit prognostic factors in critically ill patients with advanced solid tumours: a 3-year retrospective study. *BMC Cancer* 2016;16:188.
49. Lecuyer L, Chevret S, Thiery G, *et al.* The ICU trial: a new admission policy for cancer patients requiring mechanical ventilation. *Crit Care Med* 2007;35:808–14.
50. Oeyen SG, Benoit DD, Annemans L, *et al.* Long-term outcomes and quality of life in critically ill patients with hematological or solid malignancies: a single center study. *Intensive Care Med* 2013;39:889–98.
51. Park SY, Lim SY, Um SW, *et al.* Outcome and predictors of mortality in patients requiring invasive mechanical ventilation due to acute respiratory failure while undergoing ambulatory chemotherapy for solid cancers. *Support Care Cancer* 2013;21:1647–53.
52. Christodoulou C, Rizos M, Galani E, *et al.* Performance status (PS): a simple predictor of short-term outcome of cancer patients with solid tumors admitted to the intensive care unit (ICU). *Anticancer Res* 2007;27:2945–8.
53. Maccariello E, Valente C, Nogueira L, *et al.* Outcomes of cancer and non-cancer patients with acute kidney injury and need of renal replacement therapy admitted to general intensive care units. *Nephrol Dial Transplant* 2011;26:537–43.
54. Troffart AC, Pizzaro CA, Schwebel C, *et al.* Selection criteria for intensive care unit referral of lung cancer patients: a pilot study. *Eur Respir J* 2015;45:491–500.