

# Characteristics and Outcome of Cancer Patients Admitted to the ICU in England, Wales, and Northern Ireland and National Trends Between 1997 and 2013

Marlies Ostermann, MD, PhD<sup>1</sup>; Paloma Ferrando-Vivas, BSc<sup>2</sup>; Carmen Gore, MD<sup>3</sup>; Sarah Power, MSc<sup>2</sup>; David Harrison, PhD<sup>2</sup>

**Objective:** To describe trends in outcomes of cancer patients with an unplanned admission to the ICU between 1997 and 2013 and to identify risk factors for mortality of those admitted between 2009 and 2013.

**Design:** Retrospective analysis.

**Setting:** Intensive Care National Audit & Research Centre Case Mix Programme Database including data of ICUs in England, Wales, and Northern Ireland.

**Patients:** Patients (99,590) with a solid tumor and 13,538 patients with a hematological malignancy with an unplanned ICU admission between 1997 and 2013; 39,734 solid tumor patients and 6,652 patients with a hematological malignancy who were admitted between 2009 and 2013 were analyzed in depth.

**Interventions:** None.

**Measurements and Main Results:** In solid tumor patients admitted between 2009 and 2013, hospital mortality was 26.4%. Independent risk factors for hospital mortality were metastatic disease (odds ratio, 1.99), cardiopulmonary resuscitation before ICU admission (odds ratio, 1.63), Intensive Care National Audit & Research Centre Physiology score (odds ratio, 1.14), admission for gastrointestinal (odds ratio, 1.12), respiratory (odds ratio,

1.48) or neurological (odds ratio, 1.65) reasons, and previous ICU admission (odds ratio, 1.18). In patients with a hematological malignancy admitted between 2009 and 2013, hospital mortality was 53.6%. Independent risk factors for hospital mortality were age (odds ratio, 1.02), cardiopulmonary resuscitation before ICU admission (odds ratio, 1.90), Intensive Care National Audit & Research Centre Physiology Score (odds ratio, 1.12), admission for hematological (odds ratio, 1.48) or respiratory (odds ratio, 1.56) reasons, bone marrow transplant (odds ratio, 1.53), previous ICU admission (odds ratio, 1.43), and mechanical ventilation within 24 hours of admission (odds ratio, 1.33). Trend analysis showed a significant decrease in ICU and hospital mortality and length of stay between 1997 and 2013 despite little change in severity of illness during this time.

**Conclusions:** Between 1997 and 2013, the outcome of cancer patients with an unplanned admission to ICU improved significantly. Among those admitted between 2009 and 2013, independent risk factors for hospital mortality were age, severity of illness, previous cardiopulmonary resuscitation, previous ICU admission, metastatic disease, and admission for respiratory reasons. (*Crit Care Med* 2017; XX:00–00)

**Key Words:** cancer; critical care; hematological malignancy; outcome; risk factors; solid tumor

<sup>1</sup>Department of Critical Care, King's College London, Guy's & St Thomas' Hospital, London, United Kingdom.

<sup>2</sup>Intensive Care National Audit & Research Centre, London, United Kingdom.

<sup>3</sup>Department of Intensive Care, University College Hospital, London, United Kingdom.

Supplemental digital content is available for this article. Direct URL citations appear in the printed text and are provided in the HTML and PDF versions of this article on the journal's website (<http://journals.lww.com/ccmjjournal>).

The authors have disclosed that they do not have any potential conflicts of interest.

For information regarding this article, E-mail: Marlies.Ostermann@gstt.nhs.uk

Copyright © 2017 by the Society of Critical Care Medicine and Wolters Kluwer Health, Inc. All Rights Reserved.

DOI: 10.1097/CCM.0000000000002589

The number of patients with cancer has steadily increased due to an aging population, better diagnostic tools, and advances in therapies. As a result, more patients require admission to the ICU. The main reasons are complications of the underlying malignancy, side effects of treatment, and medical problems not directly related to cancer (1). Data from a large international observational study showed that one in seven patients admitted to general ICUs in Europe had cancer (2). Analysis of registry data from Scotland confirmed that between 2000 and 2009, one in 20 patients with a non-hematological malignancy required ICU admission within 2 years of

cancer diagnosis (3). ICU mortality was highest among those admitted as an emergency for medical reasons (41.7%) and lowest following elective surgery, especially if organ support was not necessary (0.6%).

Historically, the presence of cancer has been a common reason for refusal of admission to ICU (4). However, assessing the severity of illness and predicting the outcome of acutely unwell cancer patients can be challenging especially since traditional physiological scores do not perform well in this patient cohort (5–10). Thiéry et al (11) showed that 20% of patients who were referred to ICU but not admitted because they were considered to be “too well for ICU” died in hospital. Importantly, of the patients considered to be “too sick” to benefit from ICU care, 26% were still alive 30 days later.

In order to offer life-sustaining therapies to cancer patients with an acceptable prognosis and to avoid unnecessary suffering in those who are approaching the end of their life, it is essential to understand the epidemiology better and to identify prognostic factors specific to this patient population. A systematic literature review of adult patients with a solid cancer admitted to ICU between 2000 and 2014 revealed that hospital mortality rates ranged from 4.6% to 76.8% (12). In an analysis of the Intensive Care National Audit & Research Centre (ICNARC) Case Mix Programme Database (CMPD), we previously showed that hospital mortality of adult patients with a hematological malignancy admitted to an ICU in the United Kingdom between 1995 and 2007 was 59% (13).

Our aim was to produce up-to-date data reflecting the current clinical practice. Using the CMPD, the objectives were 1) to describe the characteristics and outcome of cancer patients with an unplanned admission to ICU between 2009 and 2013; 2) to identify risk factors present at admission to ICU that were independently associated with hospital mortality, and 3) to analyze the trends in patient characteristics and epidemiology between 1997 and 2013.

## MATERIALS AND METHODS

### Clinical Database

The Case Mix Programme (CMP) is the national comparative audit of adult, general critical care units in England, Wales, and Northern Ireland, coordinated by ICNARC. The CMPD contains pooled case mix and outcome data on consecutive admissions to ICUs participating in the CMP. Participation in the CMPD has increased over time. There are currently 216 adult, general critical care units contributing to the CMPD, equating to coverage of 100% of all such units in England, Wales, and Northern Ireland. Some units are ICUs providing level 3 care only, and others are combined intensive care and high-dependency units caring for level 2 and level 3 patients. Data quality is ensured by the use of precise rules and definitions, and both local and central validation checks. The CMPD was independently assessed and scored highly by the Directory of Clinical Databases against their 10 domains.

### Patient Population

Using the CMPD, we extracted data on consecutive admissions of adult cancer patients between January 1997 and

December 2013. We included adult patients who had a cancer diagnosis reported as reason for unplanned ICU admission or an unplanned admission which was for nononcological reasons but related to having cancer. “Unplanned admission” relates to patients who underwent surgery and for whom a bed in the ICU had not been booked before the start of surgery but admission to ICU later became necessary due to unforeseen complications. We differentiated between patients with hematological malignancies and solid tumors. Patients transferred from another ICU were excluded to avoid double analysis. In patients with multiple ICU admissions, we only analyzed the last admission.

### Data Collection

To describe the current practice, we extracted the following data of patients with an unplanned admission to an ICU between 2009 and 2013: demographics, type of cancer, source of ICU admission, location prior to ICU admission, surgical status and urgency (non-surgery, emergency surgery, or elective surgery), reason for admission to ICU, and need for cardiopulmonary resuscitation (CPR) prior to admission. Hematological and biochemical parameters at admission to ICU were extracted to calculate the ICNARC Physiology Score (14) and the Acute Physiology and Chronic Health Evaluation (APACHE) II score (15) based on the most abnormal physiological variables within the first 24 hours in ICU. Sepsis was defined based on the previous consensus criteria (16). We collected data on pre-existing “severe respiratory disease,” “end-stage renal failure,” “severe cardiovascular disease,” and “severe liver disease” as defined by the APACHE II criteria (15). (Supplementary Table 1, Supplemental Digital Content 1, <http://links.lww.com/CCM/C713>).

We also recorded the type of organ support required during stay in ICU, i.e., mechanical ventilation, inotropic/vasopressor support, and renal replacement therapy (RRT) as defined in the Department of Health Critical Care Minimum Dataset (Supplementary Table 1, Supplemental Digital Content 1, <http://links.lww.com/CCM/C713>). The primary outcome was hospital mortality. Other outcomes of interest were ICU mortality, length of stay in ICU and hospital, and proportion of patients who were discharged to a hospice. For the longitudinal trend analysis, we included patients with an unplanned ICU admission between 1997 and 2013 and extracted patient demographics, ICNARC Physiology Score and APACHE II score, length of stay, and ICU and hospital outcome.

### Statistical Analysis

To determine independent predictors of hospital mortality, variables selected in the univariable analysis ( $p < 0.25$ ) and those previously identified in the published literature were included in a multivariable logistic regression analysis adjusting for age, severity of illness, CPR status, and reason for ICU admission. We incorporated spline terms for age (four knots restricted cubic splines) when departures from linearity were significant. The following potential determinants were considered: presence of metastases, neutropenia (neutrophils

$< 0.5 \times 10^9/L$ ), previous ICU admission during the same hospital stay, severe sepsis, mechanically ventilated in first 24 hours, and admission type (unplanned medical admission/unplanned admission following elective surgery/unplanned admission following emergency surgery). Separate models were developed for patients with solid tumors and hematological malignancies. The predictive performance of the model was estimated by the area under the receiver operating characteristic curve (AUC), adjusted for optimism using **bootstrapping**, and **Brier's score**. **Calibration** was assessed graphically using calibration plots **with 20 equal-sized risk groups**.

To evaluate changes in characteristics and outcomes between 1997 and 2013, we used logistic regression for categorical variables and linear regression for continuous variables, using the year of admission as the predictor variable. For non-normally distributed data, the Jonckheere-Terpstra trend test was performed.

### Ethics

Support for the collection and use of patient identifiable data without consent was obtained under Section 251 of the National Health Service Act 2006 (approval number PIAG 2–10(f)/2005) from the Confidentiality Advisory Group of the Health Research Authority.

## RESULTS

Between 2009 and 2013, 48,640 unplanned ICU admissions related to cancer were registered. Following exclusion of 603 patients with incomplete data and 1,656 repeated admissions, we analyzed the data of 46,381 patients. Patients (39,734; 85.7%) had a solid tumor and 6,652 (14.3%) had a hematological malignancy, including 292 patients with a bone marrow transplant. The median age of solid tumor patients was 68 years (interquartile range [IQR], 59–77) compared with 63 (IQR, 52–70) in patients with a hematological malignancy (**Table 1**). At admission to ICU, the median APACHE II and ICNARC Physiology Scores were 15 (IQR, 10–22) and 22 (IQR, 16–29), respectively.

### Patients With Solid Tumors

In solid tumor patients, the **most common malignancies** were **bowel** cancer (33.8%), followed by genitourinary cancer (7.5%) and lung cancer (5.9%) (**Table 1**). In 18.6% of patients, the primary cancer was not known. Patients (22.1%) were known to have metastases. In the majority of cases (45.3%), the reason for admission to ICU was recorded as an emergency directly related to the primary tumor; pneumonia was the second most commonly reported reason (12.1%) for admission to ICU (**Supplementary Table 2**, Supplemental Digital Content 2, <http://links.lww.com/CCM/C714>).

During their stay in ICU, **43%** of patients required **mechanical ventilation**, **22%** needed inotropic/vasopressor support, and **9%** received **RRT** (**Supplementary Table 3**, Supplemental Digital Content 3, <http://links.lww.com/CCM/C715>). Patients (60.1%) needed two types of organ support, and 11.8% had three types. **Hospital mortality was 26.4%**.

The following factors were independently associated with hospital mortality: presence of metastases (odds ratio [OR], 1.99), CPR prior to ICU admission (OR, 1.63), higher ICNARC Physiology Score (OR, 1.14 per point), admission for gastrointestinal reasons (OR, 1.12), respiratory (OR, 1.48) or neurological (OR, 1.65) reasons compared with cardiovascular causes, and previous ICU admission (OR, 1.18) (**Table 2**).

Having rejected the hypothesis of linearity, age was modeled by restricted cubic splines with four knots (39, 63, 73, and 85) at percentiles 20%, 40%, 60%, and 80% in the logistic regression model. Due to the difficulty in interpreting the regression coefficient of the expanded terms, we tabulated the OR associated to this nonlinear relationship for several values of the original age to facilitate the presentation, interpretation and comparison (**Table 3**). Age less than 60 years, admission after elective (OR, 0.27) or emergency (OR, 0.55) surgery compared with nonsurgical admissions, and admission for genitourinary reasons (OR, 0.70) or endocrine/metabolic reasons (OR, 0.72) were independently associated with reduced hospital mortality. The model showed good performance in 200 repeated validation samples (AUC, 0.84; Brier's score, 0.133), and internally, calibration of the model was excellent.

### Patients With Hematological Malignancies

Among patients with a hematological malignancy, **lymphoma**, and **leukemia** were the **most common types** of cancer (**Table 1**). **Pneumonia** was the **most commonly** reported reason for admission to ICU (30.3%), followed by an emergency related to the primary hematological malignancy (Supplementary Table 2, Supplemental Digital Content 2, <http://links.lww.com/CCM/C714>).

Patients (**46%**) required **mechanical ventilation**, **32%** needed inotropic/vasopressor support, and **22%** received **RRT** while in the ICU (Supplementary Table 3, Supplemental Digital Content 3, <http://links.lww.com/CCM/C715>). Patients (60.6%) had two types of organ support, and 21.8% needed three types. **Hospital mortality was 53.6%**.

The following factors were independently associated with hospital mortality: age (OR, 1.02 per year), CPR prior to ICU admission (OR, 1.90), higher ICNARC Physiology Score (OR, 1.12 per point), admission for hematological reasons (OR, 1.48), or respiratory reasons (OR, 1.56) compared with cardiovascular reasons, need for mechanical ventilation within 24 hours of ICU admission (OR, 1.33), previous admission to ICU (OR, 1.43), and previous bone marrow transplant (OR, 1.53) (**Table 3**). No departures from linearity were found for age. Admission after elective (OR, 0.31) or emergency surgery (OR, 0.35) and **neutropenia** at admission to ICU (OR, 0.55) were **independently associated with reduced hospital mortality**. The model had an AUC and Brier's score of 0.77 and 0.191, respectively, and good calibration.

### Trend Analysis

Between 1997 and 2013, 99,590 patients with a solid tumor and 13,538 patients with a hematological malignancy had an unplanned admission to ICU. There was a significant improvement in ICU and hospital mortality in both cohorts during this

**TABLE 1. Demographics, Baseline Data, and Outcomes**

| Characteristics                       | Patients With Hematological Malignancy (n = 6,652)  | Patients With Solid Tumors (n = 39,734)  |
|---------------------------------------|---|--|
| Age (yr), median (IQR)                | 63 (52–70)  | 68 (59–77)   |
| Male gender (%)                       | 61.4  | 55.8   |
| Ethnicity (%)                         |   |  |
| White                                 | 88.3  | 93.1   |
| Asian                                 | 4.4   | 2.1  |
| Black                                 | 3.2   | 1.6  |
| Mixed                                 | 0.3   | 0.3  |
| Other                                 | 1.4   | 0.7  |
| Missing data                          | 1.9   | 2.2  |
| Type of cancer (%)                    | Lymphoma: 44.3<br>Leukemia: 43.5<br>Myeloma: 10.4<br>Combinations: 0.6<br>Not reported <sup>a</sup> : 1.2 | Bowel: 33.8<br>Genitourinary: 7.5<br>Lung: 5.9<br>Head + neck: 5.5<br>Gynecological: 5.4<br>Brain: 5.2<br>Hepatobiliary: 2.9<br>Esophageal: 2.9<br>Stomach: 2.2<br>Pancreas: 2.2<br>Prostate: 2.1<br>Breast: 1.9<br>Other: 3.8<br>Not reported <sup>a</sup> : 18.6 |
| Bone marrow transplant (%)            | 4.0   | –  |
| Presence of metastases (%)            | –   | 22.1   |
| Past medical history <sup>b</sup> (%) |   |  |
| Severe respiratory disease            | 1.3   | 1.9  |
| End-stage renal failure               | 1.5   | 0.8  |
| Severe cardiovascular disease         | 0.6   | 1.0  |
| Severe liver disease                  | 0.6   | 1.1  |
| Location prior to ICU admission (%)   |   |  |
| Outside hospital                      | 64.3  | 18.6   |
| Ward                                  | 33.5  | 78.4   |
| High-dependency unit                  | 2.1   | 2.9  |
| Type of unplanned admission, n (%)    |   |  |
| Medical                               | 6,240 (93.8)  | 18,464 (46.5)  |
| After elective surgery                | 80 (1.2)  | 8,722 (21.5)   |
| After emergency surgery               | 332 (5.0)   | 12,548 (32.0)  |

(Continued)

**TABLE 1. (Continued). Demographics, Baseline Data, and Outcomes**

| Characteristics  | Patients With Hematological Malignancy (n = 6,652) | Patients With Solid Tumors (n = 39,734) |
|--|--|---|
| Review by outreach team prior to ICU (%)                                       | 36.8   | 16.8                                    |
| Severity of illness at admission to ICU  |  |   |
| Intensive Care National Audit & Research Centre Physiology Score, median (IQR) | 22 (16–29)   | 15 (10–22)                              |
| Acute Physiology and Chronic Health Evaluation II score, median (IQR)          | 24 (20–28)   | 17 (13–22)                              |
| Parameters at admission to ICU   |  |   |
| Severe sepsis (%)  | 54.7   | 22.8                                    |
| Hemoglobin (g/dL), mean (SD)   | 8 (1.8)  | 10 (1.9)                                |
| Maximum lactate (mmol/L), mean (SD)  | 4 (3.7)  | 3 (2.7)                                 |
| Platelet count ( $\times 10^9/L$ ), mean (SD)                                  | 105 (121)  | 234 (131)                               |
| WBC ( $\times 10^9/L$ ), mean (SD)   | 14 (42.8)  | 11 (8.1)                                |
| Level 3 care received in first 24 hr in ICU (%)                                | 47.2   | 45.2                                    |
| Outcome  |  |   |
| Length of stay in ICU in days, mean (SD)                                       | 6 (8.3)  | 4 (7.1)                                 |
| ICU mortality (%)  | 41.3   | 17.1                                    |
| Hospital mortality (%)   | 53.6   | 26.4                                    |
| Transfer to hospice, n   | 40   | 358                                     |

IQR = interquartile range.

<sup>a</sup>For patients with hematological malignancy, ICU admission due to malignancy related emergency but specific type of hematological disease was not reported; for patients with solid tumors, ICU admission related to a cancer related emergency but type of underlying solid tumor was not reported

<sup>b</sup>As defined by Acute Physiology and Chronic Health Evaluation II classification (13) and outlined in Supplementary Table 1, Supplemental Digital Content 1, <http://links.lww.com/CCM/C713>.

period despite little change in severity of illness scores (Figs. 1 and 2; **Supplementary Table 4**, Supplemental Digital Content 4, <http://links.lww.com/CCM/C716>; and **Supplementary Table 5**, Supplemental Digital Content 5, <http://links.lww.com/CCM/C717>). Among patients with solid tumors, median length of stay in ICU increased from 1.9 (IQR, 0.8–3.6) to 2.2 (IQR, 1.0–4.7) days ( $p < 0.001$ ) (**Supplementary Fig. 1**, Supplemental Digital Content 6, <http://links.lww.com/CCM/C718>—**legend**, Supplemental Digital Content 8, <http://links.lww.com/CCM/C720>). In patients with hematological malignancies, median ICU length of stay increased from 2.2 days (IQR, 0.8–5.6 d) to 3.2 days (IQR, 1.5–6.9 d) ( $p < 0.001$ ) (**Supplementary Fig. 2**, Supplemental Digital Content 7, <http://links.lww.com/CCM/C719>—**legend**, Supplemental Digital Content 8, <http://links.lww.com/CCM/C720>). However, length of stay in hospital fell significantly in both cohorts during this period (Supplementary Table 4, Supplemental Digital Content 4, <http://links.lww.com/CCM/C716>; Supplementary Table 5, Supplemental Digital Content 5, <http://links.lww.com/CCM/C717>).

## DISCUSSION

This is one of the **largest studies** in the literature confirming a **significant improvement in ICU and hospital mortality and**

length of stay between 1997 and 2013 in cancer patients with an unplanned admission to ICU. More detailed analysis of more than 46,000 patients admitted to ICU between 2009 and 2013 demonstrated that **hospital mortality** of patients with **solid tumors was 26%**, which is **lower** than that of other patient cohorts with **nonmalignant diseases** who are routinely admitted to the ICU. **Hospital mortality** of patients with **hematological malignancies** was **56%**, which was **slightly better** than that observed in **1995–2007** (13). The main risk factors for hospital mortality were age, admission for respiratory reasons, higher severity of illness, need for CPR prior to ICU admission, previous ICU admission, and metastatic disease (for patients with solid tumors).

Clinicians caring for cancer patients face the challenge to identify those who are likely to benefit from escalation of therapy, including admission to ICU, and to avoid futile treatments and unrealistic expectations in patients who are approaching the end of their life. Among cancer patients admitted to the ICU, **favorable outcomes** are commonly observed in those admitted for **postoperative care**, administration of **chemotherapy**, or management of **tumor lysis syndrome** (17). Previous studies have also demonstrated better outcomes in patients with lower severity of acute illness (18, 19), lower number of failed organ systems (20–26), and lower need for organ support, including

**TABLE 2. Adjusted Model of Hospital Mortality for Solid Tumor Patients Admitted to ICU**

| Parameter  | OR   | 95% CI    | p       |
|--|------|-----------|---------|
| Age (yr) (restricted cubic splines 39, 63, 73, 85)*              |      |           | < 0.001 |
| 20   | 0.80 | 0.65–0.97 |         |
| 40   | 0.87 | 0.80–0.95 |         |
| 70   | 1.20 | 1.14–1.26 |         |
| 80   | 1.73 | 1.62–1.86 |         |
| 90   | 2.81 | 2.51–3.13 |         |
| Presence of metastases   | 1.99 | 1.87–2.12 | < 0.001 |
| Cardiopulmonary resuscitation prior to admission                 | 1.63 | 1.40–1.89 | < 0.001 |
| Intensive Care National Audit & Research Centre Physiology Score | 1.14 | 1.14–1.15 | < 0.001 |
| Admission following elective surgery <sup>a</sup>                | 0.27 | 0.24–0.30 | < 0.001 |
| Admission following emergency surgery <sup>b</sup>               | 0.55 | 0.51–0.59 | < 0.001 |
| Reason for admission <sup>c</sup>                                |      |           |         |
| Genitourinary  | 0.70 | 0.61–0.79 | < 0.001 |
| Endocrine/metabolic  | 0.72 | 0.58–0.89 | 0.02    |
| Dermatological   | 0.98 | 0.70–1.38 | 0.92    |
| Gastrointestinal   | 1.12 | 1.01–1.24 | 0.04    |
| Hematological  | 1.13 | 0.89–1.42 | 0.32    |
| Musculoskeletal  | 1.16 | 0.89–1.51 | 0.27    |
| Respiratory  | 1.48 | 1.34–1.64 | < 0.001 |
| Neurological   | 1.65 | 1.45–1.89 | < 0.001 |
| Severe sepsis  | 1.01 | 0.94–1.07 | 0.86    |
| Need for mechanical ventilation within 24 hr of ICU admission    | 0.96 | 0.90–1.03 | 0.24    |
| Neutropenia at admission to ICU                                  | 0.97 | 0.79–1.17 | 0.75    |
| Previous ICU admission   | 1.18 | 1.03–1.36 | 0.02    |

OR = odds ratio.

\*Restricted cubic splines (knot positions in parentheses). The significance of spline functions was tested with a joint test of all spline coefficients being simultaneously equal to 0; the coefficients for age and the spline terms were 0.00837, 0.00659, and 0.07444, respectively; odds ratios are reported for several values of age compared with a reference value of 60 years.

<sup>b</sup>Reference group: medical admission.

<sup>c</sup>Reference group: admission for cardiovascular reasons.

mechanical ventilation (27–30), vasopressors (25, 28, 30, 31), and RRT (32). Our data show that the probability of dying in hospital was greater in older cancer patients, those who had been in ICU before or had CPR prior to admission to ICU, and those who were sicker at admission to ICU. Interestingly, neutropenia at admission to ICU was independently associated with reduced hospital mortality. The exact reasons are not clear from our analysis but may be related to the fact that neutropenia is often a temporary adverse event of chemotherapy and also often amenable to treatment with granulocyte-stimulating factor. Earlier recognition of high-risk patients with neutropenia and earlier escalation of care may have also played a role.

The association between stage of malignant disease and prognosis in ICU is not fully established. In our study, 22% patients with a solid tumor were known to have metastases at

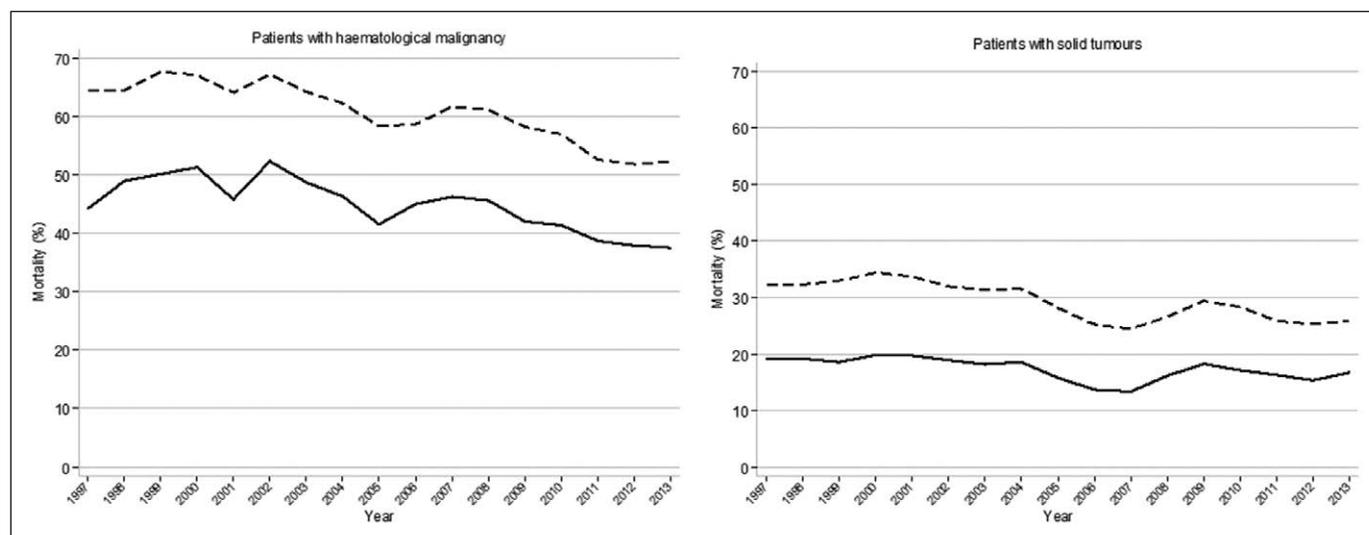
the time of ICU admission. This was associated with an almost doubling of hospital mortality. Toffart et al (33) evaluated the outcomes of lung cancer patients admitted to ICU and also showed that 90-day mortality was significantly higher in patients with metastatic disease (OR, 1.9; 95% CI, 1.08–3.33). However, others reported no association between stage of cancer and outcome (34–37).

The improvement in outcome between 1997 and 2013 is encouraging, especially because there was little change in severity of illness at admission during this time. Although others have reported similar observations (38, 39), the precise reasons are not clear but may be related to advances in critical care in general (40, 41). It is important to acknowledge that improved outcomes have not been seen for all types of cancer (42). Clearly, more study is necessary to explore this observation in more depth.

**TABLE 3. Adjusted Model of Hospital Mortality for Patients With a Hematological Malignancy Admitted to ICU**

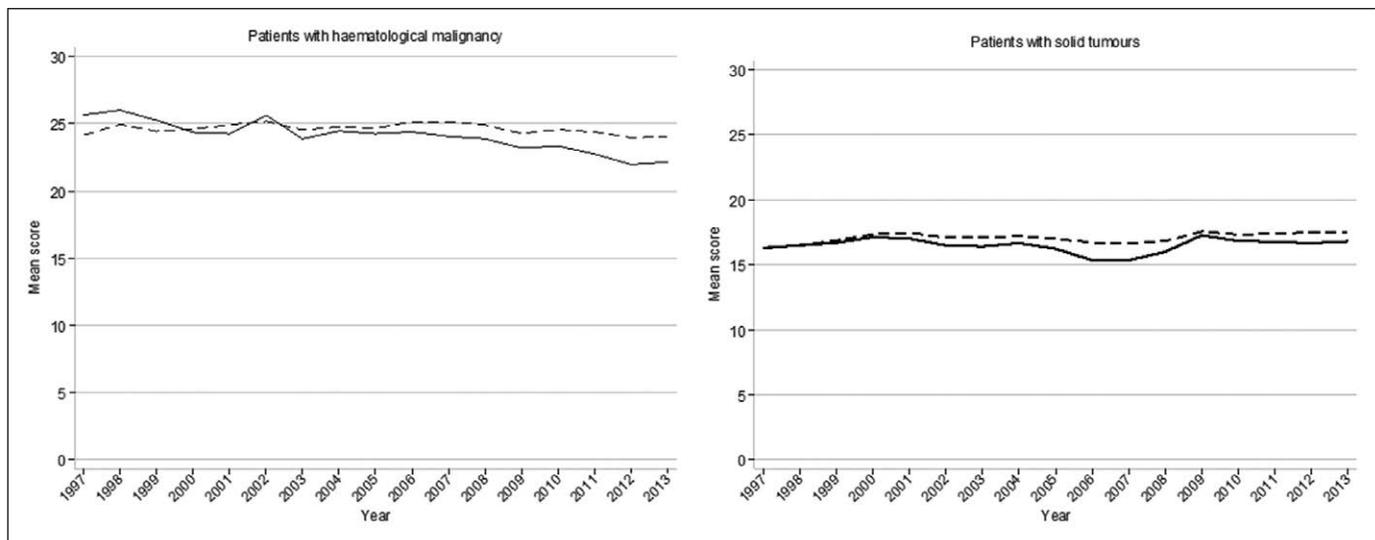
| Parameter  | OR   | 95% CI    | p       |
|--|------|-----------|---------|
| Age (yr) <sup>a</sup>  | 1.02 | 1.01–1.02 | < 0.001 |
| Cardiopulmonary resuscitation prior to admission                 | 1.90 | 1.26–2.90 | 0.003   |
| Intensive Care National Audit & Research Centre Physiology Score | 1.12 | 1.11–1.13 | < 0.001 |
| Admission following elective surgery <sup>b</sup>                | 0.31 | 0.17–0.59 | < 0.001 |
| Admission following emergency surgery <sup>b</sup>               | 0.35 | 0.25–0.48 | < 0.001 |
| Reason for admission <sup>c</sup>                                |      |           |         |
| Dermatological   | 1.14 | 0.48–2.71 | 0.77    |
| Endocrine/metabolic  | 1.17 | 0.75–1.84 | 0.49    |
| Gastrointestinal   | 1.20 | 0.90–1.61 | 0.22    |
| Genitourinary  | 1.21 | 0.85–1.47 | 0.41    |
| Neurological   | 1.32 | 0.98–1.78 | 0.07    |
| Hematological  | 1.48 | 1.23–1.78 | < 0.001 |
| Respiratory  | 1.56 | 1.31–1.86 | < 0.001 |
| Musculoskeletal  | 0.72 | 0.33–1.60 | 0.42    |
| Severe sepsis  | 1.02 | 0.90–1.16 | 0.74    |
| Need for mechanical ventilation within 24 hr of admission to ICU | 1.33 | 1.16–1.52 | < 0.001 |
| Neutropenia at admission to ICU                                  | 0.55 | 0.47–0.63 | < 0.001 |
| Previous ICU admission   | 1.43 | 1.11–1.86 | 0.007   |
| Bone marrow transplant   | 1.53 | 1.16–2.02 | 0.002   |

OR = odds ratio.

<sup>a</sup>Age in linear.<sup>b</sup>Reference group: medical admission.<sup>c</sup>Reference group: admission for cardiovascular reasons.**Figure 1.** Trends in mortality of cancer patients following an unplanned ICU admission. Dotted lines represent hospital mortality and continuous lines represent ICU mortality.

Bedside evaluation by clinicians has been deemed a poor tool for prognostication of outcome in cancer patients considered for admission to ICU (11). 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, it has been suggested to consider a “trial period in ICU” with clear goals and



**Figure 2.** Trends in severity scores on first day of unplanned admission to ICU. *Dotted lines* represent Acute Physiology and Chronic Health Evaluation II score and *continuous lines* represent Intensive Care National Audit & Research Centre Physiology score.

**stopping criteria.** This recommendation is based on the findings of the French ICU trial, a prospective study of 188 cancer patients who required mechanical ventilation and had at least one other organ failure (43). All participants were admitted to an ICU in a University Hospital in France for full treatment followed by a re-appraisal on day 5. Patients who were bedridden or receiving palliative care were excluded. The key findings were that all patients who required escalation of organ support after 3 days in the ICU subsequently died, and second, organ failure scores on day 6 were more predictive than scores performed at admission.

With data of 46,381 patients admitted to 100% ICUs in the United Kingdom between 2009 and 2013, and longitudinal data covering a 17-year period, our study is one of the largest in this area. We included only unplanned admissions and analyzed risk factors that were present at admission to ICU, i.e., the time when decisions about appropriateness of escalation of care are usually made. Despite these strengths, it is important to acknowledge some limitations. First, data collection was limited to data that are routinely collected by ICNARC. Therefore, we were not able to evaluate the impact of performance status prehospitalization and acknowledge that previous studies reported an association between performance status and outcome (17, 34, 35, 44). Likewise, we do not have data on all potential comorbidities, including response to chemotherapy prior to ICU admission, and were only able to report the proportions of patients with severe chronic diseases as defined by the APACHE II classification. 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 cancer patients who were critically ill but not referred for ICU admission. We also do not have outcome data beyond hospital discharge and acknowledge that a proportion of patients may have been discharged from hospital to receive end-of-life care at home or in a hospice. Third, our study was conducted in the United Kingdom. We acknowledge that clinical practice

of accepting cancer patients to the ICU is variable, and there is no agreed official ICU admission policy in place. Therefore, our findings may not be relevant to other countries with different healthcare systems. Fourth, the data were collected before the publication of the new criteria for sepsis, and sepsis was defined according to the previous consensus classification. Finally, we were unable to collect causes of death, including death after withholding or withdrawal of care, and have no data on long-term outcome, functional status, and quality of life of survivors.

## CONCLUSIONS

The outcome of cancer patients with an unplanned admission to ICU improved significantly in the United Kingdom. Between 2009 and 2013, hospital mortality of solid tumor patients was acceptable at 26% and hospital mortality of patients with hematological malignancies was lower than 10 years earlier (13). The most important risk factors for mortality in both cohorts were metastatic disease, CPR prior to ICU admission, and admission for respiratory problems. In our opinion, the presence of cancer per se should not be a reason for refusal of ICU admission. Instead, the decision to admit critically ill cancer patients to the ICU should be based on the probability of surviving the acute illness.

## REFERENCES

1. Bos MM, Verburg IW, Dumaj I, et al: Intensive care admission of cancer patients: A comparative analysis. *Cancer Med* 2015; 4:966–976
2. Taccone FS, Artigas AA, Sprung CL, et al: Characteristics and outcomes of cancer patients in European ICUs. *Crit Care* 2009; 13:R15
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; 1:1078–1085
4. Garrouste-Orgeas M, Montuclard L, Timsit JF, et al; French ADMISIONREA Study Group: Predictors of intensive care unit refusal in French intensive care units: A multiple-center study. *Crit Care Med* 2005; 33:750–755
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; 28:2786–2792

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–R203
7. Soares M, Silva UV, Teles JM, et al: Validation of four prognostic scores in patients with cancer admitted to Brazilian intensive care units: Results from a prospective multicenter study. *Intensive Care Med* 2010; 36:1188–1195
8. Salluh JI, Soares M: ICU severity of illness scores: APACHE, SAPS and MPM. *Curr Opin Crit Care* 2014; 20:557–565
9. Shimabukuro-Vornhagen A, Böll B, Kochanek M, et al: Critical care of patients with cancer. *CA Cancer J Clin* 2016; 66:496–517
10. Cooksley T, Kitlowski E, Haji-Michael P: Effectiveness of Modified Early Warning Score in predicting outcomes in oncology patients. *QJM* 2012; 105:1083–1088
11. 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; 23:4406–4413
12. Puxty K, McLoone P, Quasim T, et al: Survival in solid cancer patients following intensive care unit admission. *Intensive Care Med* 2014; 40:1409–1428
13. Hampshire PA, Welch CA, McCrossan LA, et al: Admission factors associated with hospital mortality in patients with haematological malignancy admitted to UK adult, general critical care units: A secondary analysis of the ICNARC Case Mix Programme Database. *Crit Care* 2009; 13:R137
14. Harrison DA, Parry GJ, Carpenter JR, et al: A new risk prediction model for critical care: The Intensive Care National Audit & Research Centre (ICNARC) model. *Crit Care Med* 2007; 35:1091–1098
15. Knaus WA, Draper EA, Wagner DP, et al: APACHE II: A severity of disease classification system. *Crit Care Med* 1985; 13:818–829
16. 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; 101:1644–1655
17. Soares M, Caruso P, Silva E, et al: Brazilian Research in Intensive Care Network (BRICNet): Characteristics and outcomes of patients with cancer requiring admission to intensive care units: A prospective multicenter study. *Crit Care Med* 2010; 38:9–15
18. Kolhe NV, Stevens PE, Crowe AV, et al: Case mix, outcome and activity for patients with severe acute kidney injury during the first 24 hours after admission to an adult, general critical care unit: Application of predictive models from a secondary analysis of the ICNARC Case Mix Programme database. *Crit Care* 2008; 12 Suppl 1:S2
19. 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; 22:2094–2100
20. Rosolem MM, Rabello LS, Lisboa T, et al: Critically ill patients with cancer and sepsis: Clinical course and prognostic factors. *J Crit Care* 2012; 27:301–307
21. 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; 15:1234–1239
22. Soares M, Darmon M, Salluh JIF, et al: Prognosis of lung cancer patients with life-threatening complications. *Chest* 2007; 131:840–846
23. 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 (Engl)* 2010; 19:260–266
24. 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
25. Namendys-Silva SA, Texcocano-Becerra J, Herrera-Gómez A: Prognostic factors in critically ill patients with solid tumours admitted to an oncological intensive care unit. *Anaesth Intensive Care* 2010; 38:317–324
26. 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; 112:102–109
27. 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
28. Andréjak 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
29. Azoulay E, Thiéry G, Chevret S, et al: The prognosis of acute respiratory failure in critically ill cancer patients. *Medicine (Baltimore)* 2004; 83:360–370
30. 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; 77:600–604
31. 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; 25:240–243
32. 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
33. Toffart AC, Minet C, Raynard B, et al: Use of intensive care in patients with nonresectable lung cancer. *Chest* 2011; 139:101–108
34. 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; 17:60–63
35. 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; 35:2044–2050
36. Azoulay E, Moreau D, Alberti C, et al: Predictors of short-term mortality in critically ill patients with solid malignancies. *Intensive Care Med* 2000; 26:1817–1823
37. 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–e124
38. 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
39. van Vliet M, Verburg IW, van den Boogaard M, et al: Trends in admission prevalence, illness severity and survival of haematological patients treated in Dutch intensive care units. *Intensive Care Med* 2014; 40:1275–1284
40. Vincent JL, Singer M, Marini JJ, et al: Thirty years of critical care medicine. *Crit Care* 2010; 14:311
41. Kaukonen KM, Bailey M, Suzuki S, et al: Mortality related to severe sepsis and septic shock among critically ill patients in Australia and New Zealand, 2000-2012. *JAMA* 2014; 311:1308–1316
42. 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; 30:1686–1691
43. Lecuyer L, Chevret S, Thiéry G, et al: The ICU trial: A new admission policy for cancer patients requiring mechanical ventilation. *Crit Care Med* 2007; 35:808–814
44. 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; 39:889–898