CRITICAL CARE

Outcomes and prognostic factors in patients with haematological malignancy admitted to a specialist cancer intensive care unit: a 5 yr study

G. T. Bird¹, P. Farquhar-Smith¹, T. Wigmore¹, M. Potter² and P. C. Gruber^{1*}

¹ Department of Anaesthesia and Intensive Care, The Royal Marsden NHS Foundation Trust, Fulham Road, London SW3 6JJ, UK
² Department of Haematology and Bone Marrow Transplantation, The Royal Marsden NHS Foundation Trust, Downs Road, Sutton SM2 5PT, UK

* Corresponding author. E-mail: pascale.gruber@rmh.nhs.uk

Editor's key points

- Patients with haematological malignancy requiring intensive care unit (ICU) care are often assumed to have a poor prognosis.
- Analysis of 199 patients in a specialist centre had a lower ICU mortality (33%) than earlier studies.
- Failure of ≥2 organ systems and mechanical ventilation were independently associated with in-hospital mortality.
- The prognosis for haematological malignancy patients admitted to the ICU appears to be improving.

Background. Long-held assumptions of poor prognoses for patients with haematological malignancies (HM) have meant that clinicians have been reluctant to admit them to the intensive care unit (ICU). We aimed to evaluate ICU, in-hospital, and 6 month mortality and to identify predictors for in-hospital mortality.

Methods. A cohort study in a specialist cancer ICU of adult HM patients admitted over 5 yr. Data acquired included: patient characteristics, haematological diagnosis, haematopoietic stem cell transplant (HSCT), reason for ICU admission, and APACHE II scores. Laboratory values, organ failures, and level of organ support were recorded on ICU admission. Predictors for in-hospital mortality were evaluated using uni- and multivariate analysis.

Results. Of 199 patients, median age was 58 yr [inter-quartile range (IQR) 46–66], 51.7% were emergency admissions, 42.2% post-HSCT, 51.9% required mechanical ventilation, median APACHE II was 21 (IQR 16–25), and median organ failure numbered 2 (IQR 1–4). ICU, in-hospital, and 6 month mortalities were 33.7%, 45.7%, and 59.3%, respectively. Univariate analysis revealed bilirubin $>32 \mu$ mol litre⁻¹, mechanical ventilation, ≥ 2 organ failures, renal replacement therapy, vasopressor support (all P<0.001), graft-vs-host disease (P=0.007), APACHE II score (P=0.02), platelets $\le 20 \times 10^9$ litre⁻¹ (P=0.03), and proven invasive fungal infection (P=0.04) were associated with in-hospital mortality. Multivariate analysis revealed that ≥ 2 organ failures [odds ratio (OR) 5.62; 95% confidence interval (95% CI), 2.30–13.70] and mechanical ventilation (OR 3.03; 95% CI, 1.33–6.90) were independently associated with in-hospital mortality.

Conclusions. Mortality was <u>lower</u> than in <u>previous</u> studies. <u>Mechanical ventilation</u> and ≥ 2 organ failures were <u>independently</u> associated with in-hospital mortality. 'Traditional' variables such as neutropenia, transplantation status, and <u>APACHE II score no longer</u> appear to be <u>predictive</u>.

Keywords: haematologic neoplasms; intensive care unit; prognosis

Accepted for publication: 6 October 2011

In 2008, there were 237 390 new cases of haematological malignancy diagnosed in Europe.¹ Of those admitted to hospital in the UK, 7% become critically ill requiring intensive care unit (ICU) admission.² Traditionally, the perception has been that patients with haematological malignancy have a poor prognosis and therefore clinicians have been reluctant to admit these patients to the ICU.³⁻⁶ However, recent advances in chemotherapy and conditioning regimes, haematopoietic stem cell transplantation (HSCT), and general ICU care have led to better outcomes for these patients.⁷⁻¹¹

Unfortunately, there are still some groups of patients, such as those requiring <u>invasive mechanical ventilation</u> or those with <u>multi-organ</u> failure after allogeneic HSCT, for whom the <u>prognosis</u> remains particularly <u>poor.¹²⁻¹⁴</u>

Previous studies have identified several indicators of poor prognosis, including older age,¹¹ disease progression,¹⁵ high APACHE II scores,^{3 8 11 16 17} high Simplified Acute Physiology Score (SAPS) II,^{2 4 16 18 19} multi-organ failure,^{2 5 14 17 20} invasive mechanical ventilation,^{3 8 17-19 21} renal replacement therapy,^{17 19} neutropenia,^{3 5 6 16} allogeneic HSCT,^{18 20} hepatic dysfunction,² ¹⁷ graft-vs-host disease (GvHD),²² sepsis,⁴ ¹⁸ ²¹ and invasive fungal infection.²⁰ However, published studies have yielded <u>conflicting</u> results and the prognostic significance of some variables has changed in the last few years, an example being HSCT which is no longer associated with increased mortality.³ ¹¹ ²⁰ ²³ The ability to identify key prognostic variables of outcome within the first few days may help clinicians recognize those patients who are most likely to benefit from ICU therapy and may allow development of treatment decision models of ICU care for these patients.

The aims of this study were to re-evaluate the ICU, in-hospital, and 6 month mortality of patients admitted with haematological malignancy to a specialist cancer ICU over a 5 yr period. Secondary aims were to identify key variables prognostic of in-hospital mortality.

Methods

The Royal Marsden NHS Foundation Trust is a tertiary referral cancer centre treating over 40 000 patients a year. The ICU is a 12-bed dedicated cancer unit. ICU management consists of standard supportive care, with invasive and non-invasive mechanical ventilation using lung protective strategies, renal replacement therapy, vasopressors, and the Surviving Sepsis Campaign guidelines for the management of sepsis.²⁴ Haemodynamic monitoring includes the use of central venous monitoring, arterial pressure monitoring, and LIDCOTM for cardiac output measurement. The hospital does not have an emergency department, but there is a 24 h Clinical Assessment Unit where patients known to the hospital are reviewed and admitted if necessary.

After local approval from the Committee of Clinical Research to undertake the project, data were collected on all patients admitted to the ICU with haematological malignancy as a primary diagnosis or a concurrent co-morbidity over a 5 yr period (October 1, 2004-September 30, 2009). The hospital information system, medical notes, and ICU charts were reviewed. Variables recorded were: patient characteristics, type of haematological malignancy, reason for ICU admission (Table 1), HSCT (type, date, conditioning regime; Table 2), presence of GvHD, use of steroids, APACHE II score, number of organ failures as defined by Knaus and colleagues,²⁵ and type of organ support during the first 24 h of ICU admission, that is, invasive mechanical ventilation, renal replacement therapy, vasopressors, and inotropes. Laboratory data, including haemoglobin, neutropenia (defined as a neutrophil count of $<1.0\times10^9$ litre⁻¹), platelet count, C-reactive protein, urea, creatinine, albumin, and liver function tests, were collected in the first 24 h of admission. Evidence of invasive fungal infection, defined as a positive blood culture or histological specimen, was recorded. ICU, hospital length of stay, and time in-hospital before ICU admission were noted. Patients were followed-up for 6 months from the day of ICU admission. Patients who were admitted to ICU for <8 h were excluded from the study.

Patient characteristic data ($n=199$)	
Age (yr) [median (IQR)]	58 (46-66)
Male [n (%)]	112 (56.3)
Haematopoietic stem cell transplantation [n (%)]	84 (42.2)
Neutropenia [n (%)]	89 (44.7)
Graft-vs-host disease [n (%)]	22 (11.1)
Haematological malignancy [n (%)]	
Acute leukaemia	67 (33.7)
Chronic leukaemia	24 (12.1)
Myeloma	27 (13.6)
Lymphoma	80 (40.2)
Other	1 (0.5)
Primary reason for ICU admission [n (%)]	
Respiratory	67 (33.7)
Cardiac	14 (7.0)
Renal	16 (8.0)
Gastrointestinal	6 (3.0)
Neurology	5 (2.5)
Postoperative	40 (20.1)
Sepsis	42 (21.1)
Other	3 (1.5)
Unknown	6 (3.0)
ICU admission data	
APACHE II score [median (IQR)]	21 (16–25)
Number of organ failures [median (IQR)]	2 (1-4)
Number of emergency admissions [n (%)]	103 (51.7)
Organ support on ICU [n (%)]	
Invasive mechanical ventilation	95 (51.9)
Renal replacement therapy	79 (40.9)
Vasopressors	87 (51.5)
Inotropes	13 (8.1)

The primary outcome was ICU mortality, defined as the number of patients with haematological malignancy who died in ICU divided by the total number of patients admitted to ICU with haematological malignancy during the study period. Secondary outcomes were in-hospital and 6 month mortality defined by similar means. The plan for statistical analysis was agreed a priori, and variables in which \geq 20% of data were missing were excluded from multivariate analysis. The data were analysed using Microsoft Excel and SPSS for Windows software[™]. All data were treated as non-parametric. Key prognostic variables in determining in-hospital mortality were assessed using univariate (χ^2 for categorical and the Mann-Whitney U for continuous data) and multivariate analysis by binary logistic regression model using a forward stepwise method. A P-value of <0.05 was considered statistically significant.

Results

During the study period, 199 patients with haematological malignancies (HM) were admitted to the ICU, representing 5.3% of all ICU admissions (Tables 1 and 2). The median

 Table 2
 HSCT characteristics. *BEAM, carmustine, etoposide, cytarabine-arabinoside, melphalan; FMC, fludarabine, melphalan, campath; FBC, fludarabine, bulsulphan, campath; C, campath; TBI, total body irradiation; Cy, cyclophosphamide

logous 33 (39.3%)
splant
4 11
-dose 22
ohalan
heral 77 (91.7%)
e 5 (6.0%)
ow
2 (2.4%)

time in-hospital before ICU admission was 6 days [interquartile range (IQR) 1–15] and the median duration of ICU and hospital stay were 5 (IQR 2–17) and 27 days (IQR 12–47), respectively.

ICU, in-hospital, and 6 month mortalities were 67/199 (33.7%), 91/199 (45.7%), and 118/199 (59.3%), respectively. Further analysis excluding all patients with haematological malignancy who had undergone elective surgery showed an ICU and in-hospital mortalities of 38.2% and 51.4%, respectively. Mortality figures from the first year (commencing October 2004) were compared with those of the last year (ending September 2009) and showed reductions of 10.9% in ICU mortality, 11% for in-hospital mortality, and 11.2% for 6 month mortality. However, these reductions did not reach statistical significance.

As with previous studies,⁸ the most common reason for ICU admission was respiratory failure (33.7%) due to bacterial pneumonia. Other causes of respiratory failure included viral pneumonia (cytomegalovirus, parainfluenza, and respiratory syncytial virus), fungal pneumonias (*Aspergillus* spp.), *Pneumocystis jirovecii* pneumonia, upper airway obstruction due to tumour, diffuse alveolar haemorrhage, and bronchiolitis obliterans. Ninety-five patients (51.9%) required invasive mechanical ventilation. Cardiac causes for admission were cardiac arrest, arrhythmias, cardiac failure, myocardial infarction, and myocarditis. Vasopressor drugs including norepinephrine, epinephrine, and/or vasopressin were initiated on 87 patients (51.5%). Dobutamine was commenced on 13 patients (8.1%). Steroids were given to 78 patients (39.2%) for a variety of indications,

including chemotherapy, sepsis, pneumocystis jiroveci pneumonia, and vasculitis.

Six (3.0%) patients were admitted with gastrointestinal complications mainly due to upper gastrointestinal bleeding and five (2.5%) patients were admitted with neurological complications including posterior reversible encephalopathy syndrome, central nervous system infection, and intracranial bleeding.

Univariate analysis revealed that the following were significantly associated with in-hospital mortality: invasive mechanical ventilation, renal replacement therapy, vasopressor use, ≥ 2 organ failures, a bilirubin $>32 \ \mu$ mol litre⁻¹ (all P<0.001), GvHD (P=0.007), inotrope use (P=0.01), APACHE II score (P=0.02), duration in-hospital before ICU admission of >6 days (P=0.02), platelet count $\leq 20 \times 10^9$ litre⁻¹ (P=0.03), and invasive fungal infection (P=0.04) (Table 3). Variables that were not predictive of in-hospital mortality were: HSCT (P=0.19), neutropenia (P=0.06), duration of ICU stay >5 days (P=0.25), type of haematological malignancy (P=0.41), and age (P=0.51) (Table 3).

Multivariate analysis showed that failure of ≥ 2 organ systems, odds ratio (OR) 5.62 [95% confidence interval (95% CI), 2.30–13.70), and invasive mechanical ventilation, OR 3.03 (95% CI, 1.33–6.90), were independent predictors of in-hospital mortality (Table 4).

Discussion

This study is one of the <u>largest</u> single-centre studies in the literature of ICU patients with haematological malignancy and includes a significant proportion of HSCT patients. It is unique, in that it includes contemporaneous data from a dedicated cancer ICU. Our ICU, in-hospital, and 6 month mortalities were <u>33.7%</u>, 45.7% and <u>59.3%</u>, respectively. A recent multi-centre study from the UK reported <u>ICU</u> and <u>in-hospital</u> mortalities of <u>43.1%</u> and <u>59.2%</u>, respectively, for patients admitted to ICU with <u>haematological malignancy</u> as a primary or secondary diagnosis¹¹ (Table 5).

The differences in mortality observed between studies, including ours, may in part be explained by variations in case mix, admission and discharge criteria, treatment decisions, and the implementation of end-of-life decisions and the authors fully acknowledge the limitations of comparing crude mortality figures between studies. However, the lower mortality in our study may be attributable to prompt on-site access to senior haematological expertise and chemotherapy on ICU, effective triaging of patients to identify those most likely to benefit from ICU care, early admission of patients identified as being at risk of multi-organ dysfunction, to developments in radiotherapy and drug therapies, and to the high case volume seen in our ICU. There is emerging evidence that patients with HM may benefit from being managed in ICUs with higher caseloads²⁶ and at our institution patients with haematological malignancy account for 5.3% of all ICU admissions and 21.2% of medical ICU admissions (vs most general ICUs where patients with haematological malignancy account for only

Table 3	Variables	predictive	of in-hospital	mortality on	univariate (analysis

Variable	All patients [n (%)]	Survivors [n (%)]	Non-survivors [n (%)]	P-value
Male gender	112/199 (56.3)	58 (51.8)	54 (48.2)	0.43
In-hospital time before ICU admission >6 days	92/199 (46.2)	42 (45.7)	50 (54.3)	0.02
Duration of ICU $>$ 5 days	94/199 (47.2)	47 (49.5)	47 (50.0)	0.25
HSCT	84/199 (42.2)	41 (48.8)	43 (51.2)	0.19
Neutropenia	89/198 (44.9)	42 (47.2)	47 (52.8)	0.06
Renal replacement therapy	79/193 (40.9)	30 (38.0)	49 (62.0)	< 0.001
Invasive mechanical ventilation	95/183 (51.9)	34 (35.8)	61 (64.2)	< 0.001
Vasopressors	87/169 (51.5)	34 (39.1)	53 (60.9)	< 0.001
Inotropes	13/160 (8.1)	3 (23.1)	10 (76.9)	0.01
Invasive fungal infection	9/197 (4.6)	2 (22.2)	7 (78.8)	0.04
Graft-vs-host disease	22/199 (11.1)	6 (27.3)	16 (72.7)	0.007
Organ failures ≥ 2	121/197 (61.4)	45 (37.2)	76 (62.8)	< 0.001
Platelets $\leq 20 \times 10^9$ litre ⁻¹	24/197 (12.2)	8 (33.3)	16 (66.7)	0.03
Bilirubin $>$ 32 μ mol litre ⁻¹	44/197 (22.3)	13 (29.5)	31 (70.5)	< 0.001
Underlying haematological malignancy				
Acute leukaemia	67/199 (33.7)	35 (52.2)	32 (48.8)	0.41
Chronic leukaemia	24/199 (12.1)	11 (45.8)	13 (54.2)	
Lymphoma	80/199 (40.2)	49 (61.3)	31 (38.7)	
Myeloma	27/199 (13.5)	13 (48.1)	14 (51.9)	
Others	1/199 (0.5)	0 (0)	1 (100)	

 Table 4
 Variables predictive of in-hospital mortality on multivariate analysis

Variable	Odds ratio	95% confidence interval
Invasive mechanical ventilation	3.03	1.33-6.90
Failure of \geq 2 organ systems	5.62	2.30-13.70

1.5% of admissions) 11 and this may account for some of the difference.

It is already a standard practice to focus the care of certain conditions (such as poly-trauma and head injuries) in specialist centres, and our work adds to the body of evidence that poses a similar question for critically ill patients with haematological malignancy. The recent UK National Confidential Inquiry in Patient Outcome and Deaths (NCEPOD) report highlighted the need for clear clinical cancer pathways, local policies for the management of neutropenic sepsis, appropriately trained staff, and specialist oncological advice to be readily available.²⁷ It noted that nearly half of emergency admissions after chemotherapy were cared for by general medical teams rather than oncologists and questioned whether this was appropriate.²⁷ The ICU management of these patients is intimately dependent upon integrated multi-professional teams of specialists working to deliver individualized care based on consensus guidelines.⁵ The ability to access highly specialized integrated multi-disciplinary teams, experimental drugs, novel

chemotherapeutic agents, microbiology expertise, specific diagnostic, and therapeutic therapies, including bone marrow aspiration, HSCT, and <u>plasmapheresis</u> in comprehensive cancer centres, are likely to have significant impact on patients' outcomes. Post-ICU rehabilitation, pastoral and psychological support, outpatient follow-up, and palliative care services specifically tailored to the needs of patients with HM and their families are an important consideration. Such resources are a persuasive argument for the early transfer of critically ill patients with haematological malignancy to specialized units. However, it may not be possible to refer all such patients on grounds that they may be too sick to be transferred or that the resources to admit them to specialist centres may not be present without substantial investments in infrastructure and staffing.

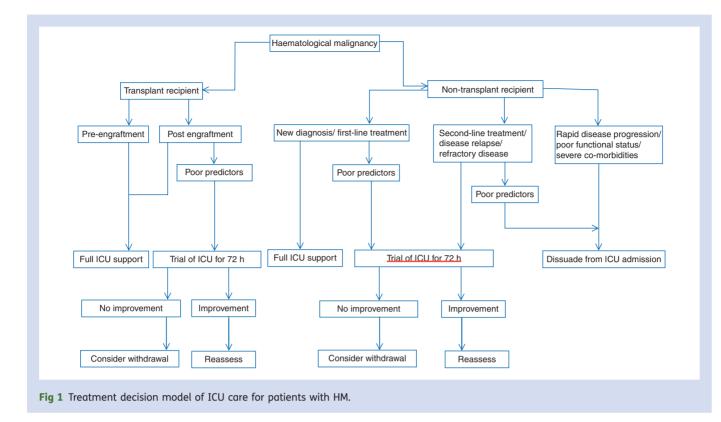
Our ICU, in-hospital, and 6 month mortalities have decreased by 11% within 5 yr. Although not statistically significant, the improvements in outcome seen over time in this study and those published in the literature may be attributed to multiple factors, including the use of targeted therapies associated with less organ toxicity,²⁸ reduced intensity regimes and/or supportive agents in patients with multiple co-morbidities,²⁹ watch and wait policies in patients with stable disease,³⁰ development of enhanced diagnostic and therapeutic strategies, anti-fungal prophylaxis,³¹ and the use of non-invasive ventilation.³² General improvements in ICU care, including protective lung strategies for invasive mechanical ventilation,³³ goal-directed therapy,³⁴ the Surviving Sepsis Campaign,²⁴ and the expansion of critical care outreach services, have undoubtedly contributed to a reduction in mortality. Early discussion and consensus agreement Table 5Previously published studies of outcomes and prognostic factors for patients with haematological malignancy.APACHE II score, AcutePhysiology and Chronic Health Evaluation II score; SOFA score, Sequential Organ Failure Assessment score; SAPS II, Simplified Acute PhysiologyII score; ODIN score; Organ Dysfunction and/or Infection score; LODS, Logistic Organ Dysfunction System

		No. of Mortality (%)			Prognostic indicators	
		patients	patients ICU In-hospi		6 months	
Lloyd-Thomas and colleagues ³	1988	60	63	78	N/A	APACHE II score, failure of malignancy to respond to chemotherapy, number of organ failures, leucopenia
Brunet and colleagues ⁴	1990	260	43	57	81	SAPS II score, >1 organ failure, intractable sepsis
Yau and colleagues ¹⁵	1991	92	N/A	77	N/A	Disease progression
Staudinger and colleagues ²¹	2000	414	53	N/A	N/A	Respiratory insufficiency, mechanical ventilation, septic shock
Massion and colleagues ²⁰	2002	84	38	61	75	Respiratory failure, fungal infection, number of organ failure, transplant status
Kroschinsky and colleagues ¹⁹	2002	104	44	N/A	67	SAPS II score, mechanical ventilation, C-reactive protein
Benoit and colleagues ⁶	2003	124	42	54	66	Leucopenia, vasopressor use, urea >0.75
Owczuk and colleagues ¹⁶	2005	40	65	N/A	N/A	SAPS II score, SOFA score, APACHE II score, neutropenia, thrombocyte count, mean arterial pressure, and necessity of catecholamine administration
Lamia and colleagues ¹⁸	2006	92	N/A	58	N/A	SAPS II, LODS, ODIN, SOFA scores
Lim and colleagues ²³	2007	55	69	N/A	N/A	Bilirubin, inotropic support, multiple organ failure
Cuthbertson and colleagues ⁸	2008	714	39	55	N/A	Cardiopulmonary resuscitation within 24 h, mechanical ventilation, inotropic support, APACHE II score
Hampshire and colleagues ¹¹	2009	7689	43	59	N/A	Age, length of hospital stay before ICU admission, severe sepsis Hodgkin's lymphoma, transplant, tachypnoea, low Glasgow Coma scale, systolic hypotension, sedation, Pa ₀₂ ;F ₁₀₂ ratio, acidaemia, oliguria, hyponatraemia, hypernatraemia, haematocrit, uraemia, alkalaemia

between concerned parties (clinicians, patients, and their families) about the merits of ICU admission and the level of organ support that should be provided is vitally important in patients with multiple variables predictive of poor outcome. The value of a proactive, rather than reactive, approach to such decisions cannot be overemphasized. 'The ICU trial' recommended that patients should receive at least 3 days of full ICU support before appraising outcomes and making end-of-life decisions.³⁵ At our institution, we have proposed a treatment decision paradiam for deciding on both ICU admission and the duration of ICU therapy for haematological malignancy patients (Fig. 1). We try to dissuade ICU admission in patients with poor functional status, serious co-morbidities, and progressive disease with a life expectancy of only a few weeks. Patients with relapsed or failed treatment, disease unresponsive to therapy, and/or successive failure of ≥ 2 organ systems, while not precluding ICU admission, require serious evaluation as to whether ICU admission can be justified. Such patients may be eligible for a 'short trial of ICU therapy', and this may include chemotherapy if appropriate.³⁵ Undoubtedly, the decision as to whether to treat these patients on ICU remains difficult and needs Downloaded from http://bja.oxfordjournals.org/ by John Vogel on March 5, 2012

evaluation on a patient-by-patient basis. A prospective evaluation of the outcome of cancer patients referred for ICU admission reported that 21% of patients considered 'too well' for ICU admission died before hospital discharge and that <u>26% of the patients considered 'too sick</u>' for ICU admission went on to survive.³⁶

In this study, variables that were <u>not predictive</u> of outcome, which were in keeping with other published studies, were type of malignancy,^{20 37} age,^{6 14 16} and gender.^{2 6 11 21 38} Neutropenia, APACHE II score, or transplant status were not predictive of outcome in contrast to published studies. Neutropenia was previously shown to be an independent risk factor for increased mortality in ICU patients with haematological malignancy.⁶ ¹⁶ Some studies have not supported this finding.⁸ ¹¹ ¹⁹ ²¹ Scoring systems such as APACHE II have been of variable use in predicting mortality. Some studies have found it predictive,^{8 11 16} while others have found it to underestimate mortality.^{3 14} Other scoring systems that have been evaluated include the ICNARC model,¹¹ Sequential Oraan Failure Assessment,^{16 18} and SAPS II.^{2 4 8 11 16 18 19} Unfortunately, none is specific for predicting mortality in patients with HM. Vasopressors,⁵ ⁶ ⁸ ¹⁸ ²³ renal replacement



therapy,^{17 19} hepatic dysfunction,^{2 17 23} and increasing duration in-hospital before ICU admission⁸ ¹¹ have been shown to be useful predictors of in-hospital mortality in previous studies. The latter is possibly explained by diagnostic uncertainty causing suboptimal and delayed treatment leading to deterioration and resistance to chemotherapeutic regimens. In this study, only >2 organ failures and invasive mechanical ventilation were found to be independent predictors of in-hospital mortality. This finding is supported by other studies that have shown that multi-organ failure^{3 4 8 17 18 20} ²³ and invasive mechanical ventilation^{3 5 8 17-19 21} are frequently associated with poor outcome. Mortality figures as high as 96% have been documented in patients with haematological malignancy after HSCT who were mechanically ventilated.¹² The early use of non-invasive ventilation (NIV) has been advocated as it reduces the necessity for tracheal intubation³⁹ and ventilator-associated lung injury.⁷

After <u>HSCT</u>, in-hospital mortality was <u>51.2%</u>. Other studies have reported in-hospital mortality figures between 54% and 96%.¹² ⁴⁰ Transplant status was not found to be predictive of outcome in this study and other recently published studies.^{6 7 17 23} This may reflect advances in conditioning regimes, use of reduced intensity regimes in patients with previous transplant or co-morbidities, targeted therapies with less organ toxicity, careful patient selection, advances in pre- and post-transplant procedures such as routine use of anti-microbial prophylaxis, and granulocyte colony-stimulating factor. However, for certain patients who have been in receipt of HSCT, the outcome remains poor, particularly for those who are invasively

ventilated, $^{12}\ ^{13}$ have resistant GvHD $^{13}\ ^{14}$ or have multiorgan failure. 13

There were a number of limitations for this study. First, this is a retrospective single-centre study. However, it analyses 5 vr of data from one of the largest comprehensive cancer centres in Europe. Secondly, it is difficult to compare crude mortality from different studies and benchmark ICUs because of the variations in case mix, ICU admission, and discharge criteria, intubation rates, and end-of-life decisionmaking practices before ICU admission. Thirdly, we were only able to categorize patients into those receiving invasive mechanical ventilation, supplementary oxygen, and/or NIV and therefore were unable to provide specific data on patients receiving NIV. Finally, our local treatment decision paradigm of ICU care is not applicable to all institutions and is yet to be validated, but at our institution, it helps to clarify the decision-making process with regard to these complex patients.

Future studies should focus on validation of these treatment decision paradigms of ICU care and the cost implications and effectiveness of such models of care. Ascertaining key predictors of in-hospital mortality at 48–72 h rather than on ICU admission, long-term outcomes, and post-ICU quality of life for haemato-oncology patients are also important questions that deserve further exploration.

In conclusion, over the last decade, studies discussing the poor prognosis for haematological malignancy patients admitted to the ICU have slowly been replaced with more optimism as more data demonstrating improved outcomes have emerged. Our data would appear to support this assertion. Invasive mechanical ventilation and ≥ 2 organ failures were the only variables independently associated with in-hospital mortality. Traditional variables that were previously associated with increased in-hospital mortality such as age, neutropenia, transplantation status, and APACHE II score no longer appear to be predictive.

Acknowledgements

The authors are grateful for the statistical support provided by Kabir Mohammed, Senior Statistician, Department of Statistics, The Royal Marsden NHS Foundation Trust, Sutton, Surrey, UK.

Declaration of interest

None declared.

References

- 1 Ferlay J, Shin HR, Bray F, Forman D, Mathers C, Parkin DM. *GLOBO-CAN 2008, Cancer Incidence and Mortality Worldwide: IARC Cancer Base No. 10.* [Internet] Lyon, France: International Agency for Research on Cancer, 2010. Available from: http://globocan.iarc.fr
- 2 Gordon AC, Oakervee HE, Kaya B, *et al.* Incidence and outcome of critical illness amongst hospitalised patients with haematological malignancy: a prospective observational study of ward and intensive care unit based care. *Anaesthesia* 2005; **60**: 340–7
- 3 Lloyd-Thomas AR, Wright I, Lister TA, Hinds CJ. Prognosis of patients receiving intensive care for lifethreatening medical complications of haematological malignancy. *Br Med J* 1988; 296: 1025–9
- 4 Brunet F, Lanore JJ, Dhainaut JF, *et al.* Is intensive care justified for patients with haematological malignancies? *Intensive Care Med* 1990; **16**: 291–7
- 5 Azoulay E, Recher C, Alberti C, *et al.* Changing use of intensive care for hematological patients: the example of multiple myeloma. *Intensive Care Med* 1999; **25**: 1395–401
- 6 Benoit DD, Vandewoude KH, Decruyenaere JM, Hoste EA, Colardyn FA. Outcome and early prognostic indicators in patients with a hematologic malignancy admitted to the intensive care unit for a life-threatening complication. *Crit Care Med* 2003; **31**: 104–12
- 7 Azoulay E, Alberti C, Bornstain C, et al. Improved survival in cancer patients requiring mechanical ventilatory support: impact of noninvasive mechanical ventilatory support. Crit Care Med 2001; 29: 519–25
- 8 Cuthbertson BH, Rajalingham Y, Harrison S, McKirdy F. The outcome of haematological malignancy in Scottish intensive care units. *J Intensive Care Soc* 2008; **9**: 135–40
- 9 Rees JKH, Gray RG, Wheatley K. Dose intensification in acute myleiod leukaemia: greater effectiveness at lower cost. Principal report of the medical research council's AML9 study. Br J Haematol 1996; 94: 89–98
- 10 Azoulay E, Afessa B. The intensive care support of patients with malignancy: do everything that can be done. *Intensive Care Med* 2006; **32**: 3–5
- 11 Hampshire PA, Welch CA, McCrossan LA, Francis K, Harrison DA. 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

- 12 Crawford SW, Petersen FB. Long-term survival from respiratory failure after marrow transplantation for malignancy. *Am Rev Respir Dis* 1992; **145**: 510–4
- 13 Khassawneh BY, White P Jr, Anaissie EJ, Barlogie B, Hiller FC. Outcome from mechanical ventilation after autologous peripheral blood stem cell transplantation. *Chest* 2002; **121**: 185–8
- 14 Afessa B, Tefferi A, Hoagland HC, Letendre L, Peters SG. Outcome of recipients of bone marrow transplants who required intensive care unit support. *Mayo Clin Proc* 1992; **67**: 117–22
- 15 Yau E, Rohatiner AZ, Lister TA, Hinds CJ. Long term prognosis and quality of life following intensive care for life-threatening complications of haematological malignancy. *Br J Cancer* 1991; **64**: 938–42
- 16 Owczuk R, Wujtewicz MA, Sawicka W, Wadrzyk A, Wujtewicz M. Patients with haematological malignancies requiring invasive mechanical ventilation: differences between survivors and nonsurvivors in intensive care unit. Support Care Cancer 2005; 13: 332-8
- 17 Evison J, Rickenbacher P, Ritz R, *et al.* Intensive care unit admission in patients with haematological disease: incidence, outcome and prognostic factors. *Swiss Med Wkly* 2002; **131**: 681–6
- 18 Lamia B, Hellot M, Girault C, et al. Changes in severity and organ failure scores as prognostic factors in oncohematological malignancy patients admitted to the ICU. Intensive Care Med 2006; 32: 1560–8
- 19 Kroschinsky F, Weise M, Illmer T, et al. Outcome and prognostic features of intensive care unit treatment in patients with hematological malignancies. Intensive Care Med 2002; 28: 1294-300
- 20 Massion PB, Dive AM, Doyen C, et al. Prognosis of hematologic malignancies does not predict intensive care unit mortality. Crit Care Med 2002; 30: 2260–70
- 21 Staudinger T, Stoiser B, Müllner M, *et al.* Outcome and prognostic factors in critically ill cancer patients admitted to the intensive care unit. *Crit Care Med* 2000; **28**: 1322–8
- 22 Huaringa AJ, Leyva FJ, Giralt SA, *et al.* Outcome of bone marrow transplantation patients requiring mechanical ventilation. *Crit Care Med* 2000; **28**: 1014–7
- 23 Lim ZY, Pagliuca A, Simpson S, *et al.* Outcomes of patients with haematological malignancies admitted to intensive care unit. A comparative review of allogeneic haematopoietic stem cell transplantation data. *Br J Haematol* 2007; **136**: 448–50
- 24 Dellinger RP, Carlet JM, Masur H, et al. Surviving Sepsis Campaign Management Guidelines Committee. Surviving Sepsis Campaign guidelines for management of severe sepsis and septic shock. *Crit Care Med* 2004; **32**: 858–73
- 25 Knaus WA, Draper EA, Wagner DP, Zimmerman JE. APACHE II: a severity of disease classification system. *Crit Care Med* 1985; 13: 818–29
- 26 Lecuyer L, Chevret S, Guidet B, et al. Case volume and mortality in haematological patients with acute respiratory failure. Eur Respir J 2008; 32: 748-54
- 27 National Confidential Inquiry in Patient Outcome and Deaths. For better for worse? A review of the care of patients who died within receiving 30 days of systemic anti-cancer therapy, 2008
- 28 Linker C, Damon L, Ries C, Navarro W. Intensified and shortened cyclical chemotherapy for adult lymphoblastic leukaemia. J Clin Oncol 2002; 20: 2464–71
- 29 Wossmann W, Schrappe M, Meyer U, Zimmermann M, Reiter A. Incidence of tumour lysis syndrome in children with advanced stage Burkitt's lymphoma/leukaemia before and after introduction of prophylactic use of urate oxidase. Ann Hematol 2003; 82: 160–5

- 30 Ardeshna KM, Smith P, Norton A, et al. Long-term effect of a watch and wait policy versus immediate systemic treatment for asymptomatic advanced stage non-Hodgkin lymphoma: a randomised controlled trial. Lancet 2003; 362: 516–22
- 31 Kanda Y, Yamamoto R, Chizuka A, et al. Prophylactic action of oral fluconazole against fungal infection in neutropenic patients. A met-analysis of 16 RCTs. Cancer 2000; 89: 1611–25
- 32 Hilbert G, Gruson D, Vargas F, et al. Non-invasive continuous positive airway pressure in neutropenic patients with acute respiratory failure requiring intensive care unit admission. Crit Care Med 2000; 28: 3185–90
- 33 The Acute Respiratory Distress Syndrome Network. Ventilation with lower tidal volumes as compared with traditional tidal volumes for acute lung injury and the acute respiratory distress syndrome. *N Engl J Med* 2000; **342**: 1301–8
- 34 Rivers E, Nguyen B, Havstad S, et al.; Early Goal-Directed Therapy Collaborative Group. Early goal-directed therapy in the treatment of severe sepsis and septic shock. N Engl J Med 2001; 345: 1368–77
- 35 Lecuyer L, Chevret S, Thiery G, Darmon M, Schlemmer B, Azoulay E. The ICU trial: a new admission policy for cancer

- 36 Thiery 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
- 37 Blot F, Guiguet M, Nitenberg G, Leclercq B, Gachot B, Escudier B. Prognostic factors for neutropenic patients in an intensive care unit: respective roles of underlying malignancies and acute organ failures. Eur J Cancer 1997; 33: 1031–7
- 38 Benoit DD, Depuydt PO, Vandewoude KH, et al. Outcome in severely ill patients with hematological malignancies who received intravenous chemotherapy in the intensive care unit. Intensive Care Med 2006; 32: 93–9
- 39 Hilbert G, Gruson D, Vargas F, et al. Noninvasive ventilation in immunosuppressed patients with pulmonary infiltrates, fever, and acute respiratory failure. *N Engl J Med* 2001; **344**: 481–7
- 40 Price KJ, Thall PF, Kish SK, Shannon VR, Andersson BS. Prognostic indicators for blood and marrow transplant patients admitted to an intensive care unit. *Am J Respir Crit Care Med* 1998; **158**: 876–84