

Paediatric oncology and intensive care treatments: changing trends

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Abstract

Objectives—To review the outcome of patients with childhood malignancy requiring intensive care treatment and to assess whether there is any secular trend for improved outcome.

Design—Retrospective chart reviews of 74 consecutive admissions to a paediatric intensive care unit from a regional paediatric oncology centre between 1990 and 1997. During the same period there were 6419 admissions to the oncology unit, 814 of whom were new cases.

Results—The overall survival at discharge from the intensive care unit was 49 of 74. Patients with either systemic or respiratory infection requiring ventilation had the poorest survival (13 of 31) whereas postoperative patients had the best survival (15 of 15). However, patients with respiratory or systemic infection who required inotropic support with more than three agents all died compared with about one quarter of those needing no inotrope. All patients with systemic or respiratory infective illness were neutropenic and positive microbiological identification was possible in 13 of 21 and five of 18, respectively. Non-survivors had a higher mean acute physiology and chronic health evaluation system (APACHE-II) score than survivors (24.2 v 15.94, respectively) but no patient with a score of > 27 survived.

Conclusion—Compared with previous series, there has been a great improvement in survival of oncology patients admitted to the intensive care unit especially those with either systemic or respiratory infection needing ventilation. Full intensive care treatment should be provided for these patients.

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Keywords: intensive care; oncology; haematology; infection; ventilation; inotropes; survival

Recent developments using intensive chemotherapeutic treatment regimens have led to an increase in survival of children with both haematological and solid malignancies.¹⁻⁴ However, after such treatment, patients have a greatly increased susceptibility to infection, especially septicaemia, and may require admission to the paediatric intensive care unit (PICU) for supportive treatment. Other indications for admission to the PICU include the direct effect of the malignant disease on organ

function, drug toxicity, metabolic complications such as tumour lysis syndrome,⁵ and life threatening haemorrhage associated with severe thrombocytopenia. Such events are usually potentially reversible, and with the improved long term prognosis for these patients, admission to an intensive care unit with all the necessary support infrastructure is usually considered essential for good outcome. Mortality among paediatric oncology patients with acute illness remains high especially in those with systemic or respiratory infection. Butt *et al* in 1988 reported a mortality of more than 84% in children with either respiratory failure requiring ventilation, or those who had circulatory failure needing inotropic support.⁶ They suggested that either treatment should be improved significantly or the intensive care doctors should be realistic and advise parents and physicians accordingly of the high risk involved. Heney *et al* in 1992 reported a mortality of 100% in children with systemic infection requiring ventilation and advised against ventilation for such patients.⁷

The aim of our study is to report on the recent survival trends of patients with childhood malignancies who were admitted to a regional PICU.

Patients and methods

This is a retrospective review of all paediatric oncology patients who were admitted to the PICU at the Royal Manchester Children's Hospital between August 1990 and August 1997. This hospital offers both a regional oncology and intensive care service to the north west of England and some adjacent districts. The oncology unit is the third largest in the UK with about 120 new referred cases each year (10% of the UK total).⁸ During our study period there were 6419 admissions to the oncology unit 814 of which were new cases. Patients were admitted to the PICU for cardiovascular and/or respiratory support but occasionally for invasive monitoring. The diagnosis of systemic infection was made if fever, peripheral circulatory collapse, and signs of focal infection with or without bacteriological confirmation were present. The diagnosis of circulatory collapse was based on hypotension (mean arterial blood pressure < 2 SD below the mean for age), poor perfusion (cold, pale extremities, with capillary refill time of > 3 seconds), hypoxaemia (P_{aO_2} < 60 mm Hg in 40% O_2), and persistent metabolic acidosis (pH < 7.3 with a base deficit of > 6). The oncologists ensured uniformity in the treatment provided by having standard policies

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Table 1 Survival after admission to paediatric intensive care unit in relation to underlying diagnosis

Diagnosis	Cases	Survivors (%)
ALL	26	16 (62)
AML	12	5 (42)
NHL	6	3 (50)
HD	1	1 (100)
Histiocytosis	1	0 (0)
Solid tumours	28	24 (86)
Total	74	49 (66)

ALL, acute lymphoblastic leukaemia; AML, acute myeloid leukaemia; NHL, non-Hodgkin's lymphoma; HD, Hodgkin's disease.

for the management of all oncological malignancies and their complications. The list of oncology patients admitted to the PICU was obtained from the PICU admissions book. Data were collected from the hospital records, which detailed each patient's personal details, diagnosis, previous treatment, reason for admission to the PICU, treatment received in the PICU, and outcome. One researcher (FS) collected all the data to minimise recorder bias. The worst physiological variables recorded during the first 24 hours of admission to the PICU were used to determine the acute physiology and chronic health evaluation system (APACHE-II) scores.⁹ Patients were categorised as non-survivors and survivors depending on the outcome at the time of leaving the intensive care unit. The Student's *t* test was used to compare the mean APACHE-II scores between survivors and non-survivors. A result was considered as significant when $p < 0.05$.

Results

There were 74 oncology admissions to the PICU during our study period, comprising 42 boys and 32 girls, with a mean age of 5.4 years (range, 1 month to 16 years). These PICU admissions accounted for 1.2% of the total admissions, or 11% of new referrals, to the oncology unit over the same period.

Table 1 shows the underlying oncological diagnoses and survival rate and table 2 shows survival in relation to reason for admission. The overall survival at discharge from the PICU was 49 of 74. All patients admitted with infective illness (systemic or respiratory) were neutropenic. Positive identification of the causative organisms was possible in 13 of the 21 patients with systemic infection compared with five of the 18 patients with respiratory infection.

Twenty one patients had systemic infection, 13 of whom survived, whereas only eight of the 18 patients admitted with respiratory infection

Table 2 Survival in relation to reason for admission

Reason for admission	Patients	Ventilated		Not ventilated	
		Total	Survived (%)	Total	Survived (%)
Systemic infection	21	15	7 (47)	6	6 (100)
Respiratory infection	18	16	6 (38)	2	2 (100)
Neurological	11	9	6 (67)	2	1 (50)
Postoperative	15	8	8 (100)	7	7 (100)
Tumour mass effect	4	4	4 (100)		
After cardiac arrest	3	3	1 (33)		
Metabolic effects	1	1	0 (0)		
Cardiac tamponade	1	1	1 (100)		
Total	74	57	33 (58)	17	16 (94)

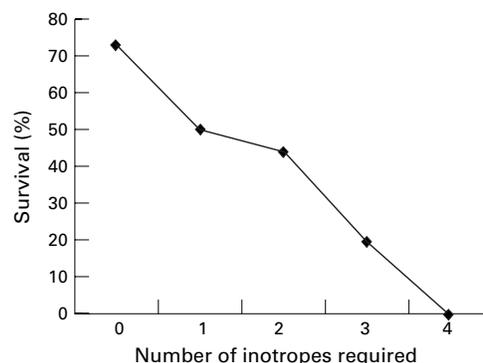


Figure 1 The association between survival and inotropic requirement. A steady decline in survival is seen as the number of inotropes required increases.

survived. Patients with infective illness requiring ventilation had the poorest survival rate (13 of 31) whereas postoperative patients had the best survival (15 of 15).

Inotropic support was required in 21 of the 34 patients with infective illness. None of the patients who required more than three inotropic agents survived in contrast to approximately one quarter of those in whom no inotrope was needed (fig 1).

Eleven patients had neurological disease (six intracranial tumours and five acute lymphoblastic leukaemia (ALL) associated with central nervous system involvement). Four out of the six survivors had subsequent neurological deficits related to either the primary disease or the immediate cause of admission to the PICU.

Tumour mass effect resulting in respiratory compromise was seen in four patients having the following diagnoses: non-Hodgkin's lymphoma, neuroblastoma, yolk sac tumour, and teratoma. Other admissions included acute myeloid leukaemia (AML) with cardiac arrest, Hodgkin's lymphoma with tumour lysis syndrome, and ALL with cardiac tamponade.

The mean (median) APACHE-II scores for survivors and non-survivors were 15.94 (16) and 24.2 (25), respectively ($p < 0.001$; 95% confidence interval (CI), 5.2 to 11.3).

Discussion

Over the past three decades the outlook for children with malignancy has improved dramatically so that 60–70% are now expected to be long term survivors.^{1–4} Such improvement has resulted from increasingly intensive and sustained chemotherapy. One of the most serious consequences of this is an increase in myelosuppression and immunosuppression, with a risk of life threatening infection. Over the past 15 years several groups have reported the outcome of patients with malignant disease admitted to intensive care units for treatment. Unfortunately, most of these studies were on adults^{10–12} and only a few reports are on children.^{6–7} All of the paediatric studies were reported six or more years ago. Our study shows the use made of the PICU services by a regional oncology unit over the past seven years and highlights the changing pattern in outcome.

The overall survival in our series is higher than the 52% and 51% reported by Butt *et al* and Heney *et al*, respectively.^{6,7} In addition, the survival rate for ventilated patients in our study was twice that of Heney *et al*, who found an overall survival for ventilated patients of only 30%.

Patients with infective illness requiring ventilation had the lowest survival rate but this was an improvement on the results of Heney *et al*, who reported no survival for a similar category of patients. He advocated treatments other than ventilation for these children because of the very poor outcome. Similarly, Butt *et al* reported a low survival (< 16%) in patients with respiratory failure requiring ventilation. Therefore, our study shows a great improvement in the survival of oncology patients with infective illness who need ventilation and their chance of survival is nearing 50%.

Several factors may be responsible for this improved survival, including the development of paediatric intensive care units and an awareness by physicians of the improved long term survival of children with cancer, and the consequent need for acute support of these patients. Early management of sepsis using an aggressive antimicrobial, fluid, and inotropic policy, coupled with the use of granulocyte colony stimulating factor, might contribute to this improvement.

For those children with acute infective illness requiring inotropic support, survival fell greatly as the number of inotropic agents needed to maintain circulation increased. Requirement of multi-inotropic treatment after sepsis implies severe haemodynamic instability and current therapeutic approaches seem to be incapable of salvaging patients needing more than three inotropes.

The use of the APACHE-II scoring system has not been validated in children but it has been used in the past in paediatric reports.⁹ Non-survivors had a significantly higher mean APACHE-II score than survivors and no patient with a score of > 27 survived. Consequently, such high risk patients need to be assessed more thoroughly and alternative strategies considered to improve patient survival. In addition, the mean APACHE-II scores in our study are similar to those in Heney *et al*'s report, implying that the patients in the two studies are comparable to a certain degree and the improved outcome is a true reflection of changing trends rather than a result of differences in patient characteristics.

Children with solid tumours had a better survival than those with haematological malignancies. This might be because most of the patients with solid tumours were admitted either postoperatively or for invasive monitoring, as a result of the effect of tumour mass.

They were also less immunosuppressed (non-neutropenic) compared with those with haematological malignancies.

Restrictions have to be placed on the use of the PICU, not just for logistical and financial reasons,¹³ but because a realistic and compassionate approach is needed to avoid causing unnecessary suffering and anguish for the patient and family when the outcome is likely to be unfavourable.¹⁴ Close cooperation between the oncology and the intensive care teams will allow care that is most appropriate for the child in close cooperation with the family.

Conclusion

There has been an improvement in the survival of oncology patients receiving intensive care treatment, especially those with acute infective illness requiring ventilation. We recommend aggressive intensive care management for such patients to maximise the outcome.

Patients needing more than three inotropes and those with high mean APACHE-II scores have a uniformly poor prognosis and informed advice and counselling should be given to their parents. Whether new experimental treatments will improve the outcome of such patients remains to be seen.

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