# Improved outcomes for stem cell transplant recipients requiring pediatric intensive care

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***Objectives:*** **Survival for hematopoietic stem cell transplant patients requiring pediatric intensive care unit admission may be improving. This study was conducted to review outcomes for patients undergoing hematopoietic stem cell transplantation requiring admission to our pediatric intensive care unit and to identify variables impacting survival.**

***Design:*** **Retrospective database review.**

***Setting:*** **Pediatric intensive care unit and bone marrow transplant service of a children's hospital.**

***Patients:*** **Patients undergoing hematopoietic stem cell transplantation at our center from July 2004 through June 2010 requiring pediatric intensive care unit admission during the same period.**

***Measurements and Main Results:*** **Thirty-five percent of patients (155 of 448) undergoing hematopoietic stem cell transplantation required 319 admissions over this period. Of these 155 patients, 63% (97 of 155) were discharged alive following their most recent admission with a 100-day survival of 51% (79 of 155). Forty-five percent (69 of 155) of patients were still alive on long-term follow-up. Intubation and mechanical ventilation were required for 57% (88 of 155) of patients, with 39% (34 of 88) of patients surviving their last pediatric intensive care unit admission. Renal support was utilized for 25% (38 of 155) of patients with 34% (13 of 38) survival to pediatric intensive care unit discharge. Admissions surviving to pediatric intensive care unit discharge had significantly lower Pediatric Risk of Mortality II scores, shorter pediatric intensive care unit length of stay, lower utilization of intubation and mechanical ventilation with fewer ventilator days, and lower use of renal support when compared to nonsurvivors. Of note, each prior pediatric intensive care unit admission significantly reduced the odds of pediatric intensive care unit survival.**

***Conclusions:*** **We report a 63% survival to pediatric intensive care unit discharge, with 45% surviving at a median follow-up of over 2 yrs for all hematopoietic stem cell transplantation patients admitted to our pediatric intensive care unit over a 6-yr period. Our data suggest improved survival outcomes for this high risk patient population. (Pediatr Crit Care Med 2012; 13:e336–e342)**

**Key Words: bone marrow transplant; mechanical ventilation; outcomes, pediatric intensive care unit; stem cell transplant; survival**

Hematopoietic stem cell transplantation (HSCT) is a life-saving therapeutic option for children with multiple hematologic, oncologic, and immunologic disorders. A proportion of children undergoing HSCT develop complications that necessitate admission to the pediatric intensive care unit (PICU). The proportion of children requiring PICU admission following HSCT is variable, with up to 44% of children undergoing HSCT requiring PICU admission in some series (1, 2). Historically, outcomes for this cohort of patients have been poor. A recent meta-analysis suggested a wide range of overall PICU mortality, ranging between 25% and 91% (1). Despite improvement in single-center outcomes, overall severity-adjusted outcomes for children requiring PICU admission have changed little over time, especially for children that develop organ failure (3). However, the literature describing overall PICU outcomes for children in this cohort is not representative of current outcomes, as all published studies utilize data prior to 2004 (1). Hence, it is important to ascertain PICU outcomes in this cohort utilizing contemporary data from children requiring intensive care following HSCT.

Our institution is amongst the largest centers performing HSCT in children. Children undergoing HSCT at our center represent a high-risk group, as most grafts come from unrelated donors, many with significant human leukocyte antigen mismatch. We performed a retrospective review to determine outcomes for children who had undergone HSCT requiring admission to our PICU. Furthermore, we sought to identify clinical variables at PICU admission that were associated with poor prognosis. We hypothesized that overall survival to PICU discharge has improved when compared to published data for children having undergone HSCT.

## MATERIALS AND METHODS

We performed a retrospective review and analysis of outcomes for all patients admitted to the PICU following HSCT from July 1, 2004, through June 30, 2010, at our institution, with approval from our Institutional Review Board. Due to the retrospective nature of our study, the need for informed consent was waived. Patients were identified using our PICU and HSCT databases. We reviewed all patients who underwent HSCT at our institution during this time frame and who subsequently required admission to the PICU during this same period. Patients were excluded if they underwent HSCT and/or PICU admission prior to July 2004 or after June 2010, underwent HSCT at another institution, or were admitted to the

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The authors have not disclosed any potential conflicts of interest.

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**DOI: 10.1097/PCC.0b013e318253c945**

PICU for performance of a procedure. For this review we included HSCT patients admitted to the intensive care unit (ICU) following surgical procedures for postoperative care.

Our institution is a free-standing children's hospital and serves as a referral center for patients requiring HSCT. Patients undergoing HSCT are cared for in a specialized unit by physicians from the bone marrow transplant service. Admission to our PICU is not based upon specific criteria or a clinical scoring system. Rather, the merit of each admission is determined by review of each patient's case and clinical need, and the decision for admission is made jointly by the bone marrow transplant service and critical care team. Of note, HSCT patients requiring any inotrope/vasopressor support, ventilatory support (including noninvasive ventilation), or initiation of renal support (continuous or intermittent) are admitted to the PICU. While in the PICU, these patients are cared for by a multidisciplinary team consisting of intensivists and bone marrow transplant physicians, as well as clinical pharmacists, social workers, nursing staff, respiratory therapy staff, and nutrition specialists.

We abstracted data directly from the medical records and PICU/HSCT databases and entered the data directly into password-protected Microsoft Excel spreadsheets. Data abstracted included demographic parameters such as date of birth, sex, race, and ethnicity as well as clinical data pertaining to each patient's HSCT and PICU course. Specific HSCT data included date of transplant, age at transplant, transplant number, primary disease requiring transplant, transplant type, stem cell source, and type of graft versus host disease prophylaxis. PICU data included age at PICU admission, admission number, reason for ICU admission (medical vs. surgical), Pediatric Risk of Mortality (PRISM) II score, PRISM calculated risk of mortality, and ICU length of stay as well as the need for invasive mechanical ventilation, renal support (intermittent or continuous), and inotrope/vasopressor usage. Admissions requiring invasive mechanical ventilation were categorized as having primary or secondary respiratory failure. Primary respiratory failure included admissions needing invasive mechanical ventilation for airway obstruction, lung disease, fluid overload, and abdominal distension, whereas secondary respiratory failure included admissions needing invasive mechanical ventilation for shock including cardiac arrest, seizures, encephalopathy, and operative procedures. We compared PICU admission and intervention characteristics between those who survived to PICU discharge and those who did not survive to PICU discharge.

*Statistical Analysis.* Categorical and continuous data were compared utilizing chi-square or Mann–Whitney rank-sum tests, respectively. For model building, mechanical ventilation (invasive), inotrope/vasopressor usage, and renal support (intermittent or continuous) were utilized as surrogates for organ failure, whereas PICU length of stay and number of prior PICU admissions were used as surrogates of morbidity. Using these variables, we estimated the likelihood of survival to PICU discharge as well as survival to 100 days following the last PICU admission. Since HSCT patients could have had multiple PICU admissions resulting in multiple survival outcomes that are correlated among themselves, we used a generalized linear mixed effects model with an auto regressive order of 1 in order to account for multiple visits that may belong to one patient as well as the intercorrelation of survival outcomes. We assessed the odds of survival to PICU discharge utilizing a simple and multiple generalized linear mixed effects model regression analysis to assess the effect of each variable separately and all variables concurrently. The odds of surviving to 100 days following the last PICU admission for all patients were assessed using a logistic regression model for survival probability. Since multiple patients in our cohort had greater than one PICU admission and varying duration of follow-up after their last PICU discharge, we normalized risk factors accumulated during multiple PICU admissions for the length of follow-up time. Lastly, we also documented those patients who were currently alive (defined as of January 1, 2011). Thess data represent a period of 6 months from the last patient included in our cohort. In all analyses, a $p$ value <.05 was considered significant. Statistical analysis was performed using SAS software (Cary, NC) version 9.2.

**Table 1.** Demographics and survival of hematopoietic stem cell transplantation patients admitted to the pediatric intensive care unit

| Demographic | Total n = 155 (%) | Pediatric Intensive Care Unit Survival[a] n = 97 (%) |
|---|---|---|
| Male | 93 (60) | |
| Female | 62 (40) | |
| Diagnosis | | |
| Nonmalignant | 99 (64) | 55 (56) |
| • Bone marrow failure | 29 (19) | 17 (59) |
| • Genetic/metabolic disorder | 6 (4) | 4 (67) |
| • Immune disorders | 64 (41) | 34 (53) |
| Malignant | 56 (36) | 42 (75)[b] |
| Stem cell source | | |
| Allogeneic | 134 (86) | 79 (59) |
| • Unrelated adult donor | 96 (62) | 56 (58) |
| • Unrelated cord blood | 18 (12) | 10 (56) |
| • Matched sibling donor | 18 (12) | 12 (67) |
| • Mismatched sibling donor | 1 (0.6) | 0 (0) |
| • Haploidentical parent | 1 (0.6) | 1 (100) |
| Autologous | 21 (14) | 18 (86)[c] |
| Conditioning regimen | | |
| • Myeloablative | 98 (63) | 64 (65) |
| • Nonmyeloablative[d] | 57 (37) | 33 (58) |

[a]Pediatric intensive care unit survival for last pediatric intensive care unit admission during the study period; [b]$p$ = .004 when compared to patients with nonmalignant disorders; [c]$p$ = .04 when compared to patients undergoing allogeneic transplant; [d]nonmyeloablative conditioning includes reduced intensity conditioning and no conditioning of which there was only one patient.

## RESULTS

Between July 1, 2004, and June 30, 2010, 448 patients received HSCT at our institution. Of these, 155 patients (35%) required PICU care, accounting for 319 total PICU admissions over this 6-yr period. The most frequent reasons for HSCT were immune disorders (41%) and malignancy (36%) (Table 1). The median age at the time of HSCT was 6 yrs (interquartile range [IQR] 1.8, 14.3), and 60% of patients were male (Table 1). Nearly 85% of the cohort received stem cells from another person (allogeneic transplants), and the majority of the grafts were from an unrelated donor (Table 1). Conditioning regimens were myeloablative in 63% of patients; of these, nearly 50% received total body irradiation (Table 1).

Over 6 yrs we observed an increase in stem cell transplant activity at our center; this was associated with a marked increase in PICU admissions for patients having undergone HSCT at our institution (Fig. 1*A*). The majority of patients required one to two admissions to the PICU (mean admissions/patient 2 ± 1.5, mode 1); however, 45 patients (29%) required more than two admissions. Of the 319 admissions, only 9% (29) were for postoperative management. The median time to admission following transplant was 38 days (IQR 8.3, 145) with a median age of 6.6 yrs (IQR 2.5, 16.4). The median PRISM II score for this cohort at PICU admission was 8 (IQR 4, 14) with a median length of stay in the PICU of 4 days (IQR 2, 11), both being

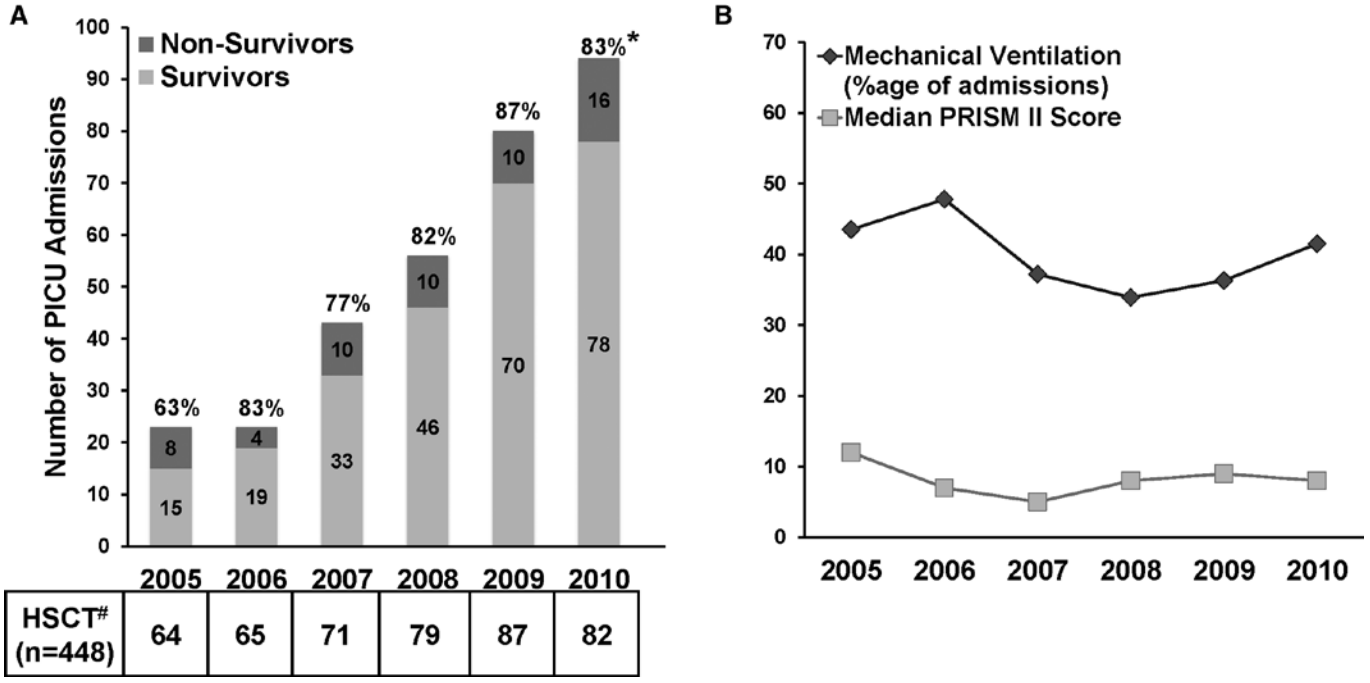


Figure 1. *A*, Hematopoietic stem cell transplantation (*HSCT*) admissions to the pediatric intensive care unit (*PICU*) and number of patients undergoing HSCT by fiscal year. Each bar depicts the numbers of HSCT admissions that survived and did not survive to PICU discharge for that fiscal year. *Percentage of HSCT admissions surviving to PICU discharge; #number of patients undergoing HSCT. *B*, Line graph demonstrating trend of median Pediatric Risk of Mortality (*PRISM*) II score and mechanical ventilation use (% age) for HSCT admissions to the PICU by fiscal year over the study period.

significantly higher ($p < .001$) when compared to non-HSCT admissions over the same period (median PRISM II score 4 [IQR 1, 7] and median length of stay 2 days [IQR 2,4]). To ascertain if this trend of increased admissions was not a consequence of a lower severity of illness, we assessed the yearly utilization of invasive mechanical ventilation over this period as an index of severity of illness. As expected, there was variation in the yearly need for mechanical ventilation; however, yearly admission mortality did appear to be associated with the percentage of admissions needing mechanical ventilation (Fig. 1). Furthermore, there was minimal variation in PRISM II score over this period (Fig. 1*B*). Taken together these data suggest that the improved survival to PICU discharge is not a consequence of admissions having a lower severity of illness.

We specifically assessed mechanical ventilation, inotrope use, and renal support for HSCT admissions during this period. Mechanical ventilation was needed for 57% (88 of 155) of patients and 39% (124 of 319) of admissions, as some patients were admitted more than once. Nearly 60% (73 of 124) of admissions needed mechanical ventilation for primary respiratory failure, while 40% (50 of 124) were intubated and ventilated for secondary respiratory failure. For the admissions requiring mechanical ventilation, the median ventilator days were 6.5 days (IQR 2, 15). Renal support was required for 25% (38 of 155) of patients. This resulted in 55 episodes of renal support in the PICU out of 319 admissions. The modalities utilized during these 55 episodes were intermittent hemodialysis (n = 24), continuous renal replacement therapy (n = 11), or both (n = 20). Inotropes and vasopressors were utilized in 61% (95 of 155) of patients. Overall 37% (119 of 319) of admissions required the use of an inotrope or vasopressor agent. The utilization of PICU interventions (mechanical ventilation, inotrope use, and renal support) amongst HSCT recipients was not impacted by underlying primary disease (malignant vs. nonmalignant) and transplant characteristic (allogeneic vs. autologous transplant, myeloablative vs. nonmyeloablative conditioning) (Table 2). However, there was a trend toward lower utilization of PICU interventions in patients who underwent autologous transplant when compared to allogeneic transplants.

We compared PICU admission and intervention characteristics amongst admissions surviving to those not surviving to PICU discharge. When compared to nonsurvivors, admissions surviving to PICU discharge had significantly lower PRISM II score (7 vs. 13.5, $p < .001$) and spent significantly fewer days (3 vs. 12.5, $p < .001$) in the PICU (Table 3). Additionally, HSCT admissions surviving their PICU stay had significantly lower utilization of mechanical ventilation (28% vs. 90%, $p < .001$) and fewer ventilator days (5 vs. 10.5, $p < .001$) when compared to nonsurvivors (Table 3). Importantly, 58% (72 of 124) of admissions requiring ventilation survived to PICU discharge. This translated to 39% (34 of 88) of patients who required ventilation during any admission surviving through their last PICU discharge, with 34% (30 of 88) surviving at least 100 days after their last PICU discharge. Furthermore, we observed an 80% (12 of 15) survival for patients who received mechanical ventilation, but did not require inotrope support or renal support; we noted a 32% (11 of 34) survival for those patients who were ventilated and required renal support as well. Survivors to PICU discharge had significantly lower use of renal support (12% vs. 41%, $p < .001$) and inotropes/vasopressors (28% vs. 79%, $p < .001$) when compared to nonsurvivors (Table 3). Of the 38 patients who required renal support, 34% (13 of 38) survived all their PICU admissions, with 29% (11 of 38) surviving at least 100 days after their last

**Table 2.** Characteristics and use of pediatric intensive care unit interventions for hematopoietic stem cell transplantation patients

| Hematopoietic Stem Cell Transplantation Characteristic | Mechanical Ventilation Use (%) | Inotrope Vasopressor Use (%) | Renal Support (%) |
|---|---|---|---|
| Malignant disorder (n = 56)[a] | 29 (52) | 33 (59) | 11 (19) |
| Nonmalignant disorder (n = 99)[a] | 59 (60) | 62 (63) | 27 (27) |
| Allogeneic transplant (n = 134)[a] | 80 (60) | 85 (63) | 35 (26) |
| Autologous transplant (n = 21)[a] | 8 (38) | 10 (48) | 3 (14) |
| Myeloablative conditioning (n = 98)[a] | 57 (58) | 65 (66) | 24 (24) |
| Nonmyeloablative conditioning (n = 57)[a] | 31 (54) | 30 (53) | 14 (25) |

[a]Number of patients.

**Table 3.** Hematopoietic stem cell transplantation admissions—characteristics and interventions of pediatric intensive care unit nonsurvivors and survivors

| | Nonsurvivors n = 58 | Survivors n = 261 | $p$[a] |
|---|---|---|---|
| Age at pediatric intensive care unit Admission (yrs) | 8.8 (2.9–17.7)[b] | 6.5 (2.4–16.3)[b] | .3 |
| Pediatric Risk of Mortality II score | 13.5 (9–21)[b] | 7 (3–12.3)[b] | <.001 |
| Pediatric intensive care unit length of stay (days) | 12.5 (5–23)[b] | 3 (2–7)[b] | <.001 |
| Mechanical ventilation use (%) | 52 (90) | 72 (28) | <.001 |
| Ventilator days | 10.5 (3–20)[b] | 5 (2–11)[b] | .012 |
| Inotrope/vasopressor use (%) | 46 (79) | 73 (28) | <.001 |
| Renal support (%) | 24 (41) | 31 (12) | <.001 |
| • Intermittent hemodialysis | 3 | 21 | |
| • Continuous renal replacement therapy | 9 | 2 | |
| • Both | 12 | 8 | |

[a]$p$ value reflects the difference between admissions that survived and did not survive to pediatric intensive care unit discharge by Mann–Whitney rank-sum test for continuous data and chi-square test for categorical data; [b]median value with interquartile range (25–75 percentile).

admission. This corresponded to a 56% survival (31 of 55) to PICU discharge for all admissions requiring renal support. For those admissions that required the use of an inotrope or vasopressor agent, we observed a 61% (73 of 119) survival to PICU discharge.

Overall survival for HSCT patients following last PICU discharge was 63% (97 of 155) (Fig. 2). This translated to 82% (261 of 319) of HSCT admissions surviving to PICU discharge; in comparison, survival to PICU discharge for non-HSCT admissions over the same period was significantly higher at 97.5% ($p < .001$). On further follow-up, 51% (79 of 155) of HSCT patients were alive at 100 days, and nearly 45% (69 of 155) of patients were alive at a median follow-up of 2.5 yrs after their last PICU discharge (IQR, 1, 3.5; range, 6 months to 6 yrs) (Fig. 2). In contrast, 98% of HSCT patients not admitted to the PICU over the same period were alive at 100 days following transplant. On further follow-up, 88% were alive at 1 yr. PICU survival was significantly higher for patients who underwent HSCT for a diagnosis of malignancy compared to those with nonmalignant disorders (75% vs. 56%, $p = .004$) (Table 1); this higher mortality for nonmalignant disorders may reflect inclusion of a large proportion of patients undergoing HSCT for immune disorders, most commonly hemophagocytic lymphohistiocytosis. Additionally, patients who received autologous transplants had significantly higher PICU survival when compared to those receiving an allogeneic transplant (86% vs. 59%, $p = .04$) (Table 1). In contrast, PICU survival was not affected by the type of conditioning regimen (Table 1).

In order to determine the risk factors that impacted survival to PICU discharge, we used need for interventions such as mechanical ventilation, hemodynamic support, and renal support as surrogates for organ failure. Furthermore, we used PICU length of stay and number of prior PICU admissions as surrogates of morbidity. The odds of survival to PICU discharge were significantly higher for patients not requiring mechanical ventilation or renal support (Table 4). Similarly, each prior PICU admission following HSCT decreased the odds of PICU survival significantly (odds ratio 0.8, $p = .014$) (Table 4). However, PICU length of stay did not appear to have a significant effect on the odds of PICU survival once adjusted for the effects of the other risk factors (Table 4). These results suggest that the odds of PICU mortality for HSCT patients are likely dependent on organ failure and maybe independent of PICU length of stay. For patients who survived their last PICU admission during this period, we determined risk factors that impacted 100-day survival following their last PICU discharge. Since patients in our cohort had multiple admissions and varying duration of follow-up following their last PICU discharge, we normalized risk factors accumulated during multiple PICU admissions for the length of follow-up time. After normalizing for risk factors and follow-up time, the 100-day odds of survival were significantly lower for patients requiring mechanical ventilation, renal support, or a combination of mechanical ventilation and renal support during their last PICU admission (Table 5). Notably, the use of inotropes/vasopressors did not impact 100-day survival following last PICU discharge.

## DISCUSSION

Our study describes outcomes for a large contemporary cohort of stem cell transplant patients from a single center requiring PICU admission over a 6-yr period. We observed an increasing number of admissions for patients undergoing HSCT at our institution over this period, in parallel with increased transplant activity in our program. For this patient cohort, we report a 63% survival to PICU discharge with an overall survival of 45% at a median follow-up of over 2 yrs. We believe these data are encouraging and show better outcomes than previous reports. These data indicate that aggressive PICU support can be beneficial for HSCT patients, and that patients can survive even prolonged PICU stays.

The primary impetus for our analysis was a paucity of recent data describing outcomes for patients requiring admission to a PICU following HSCT. The frequency of PICU admission after HSCT is variable in literature reports. A recent meta-regression analysis that analyzed data from 23 retrospective studies spanning a 15-yr period in children demonstrated an admission rate between 5% and 44% (1). In addition, a recent single center analysis observed an PICU admission rate of 35% for children undergoing stem cell transplantation for primary immunodeficiency over a 5-yr period (4). Hence, our data seem to be in keeping

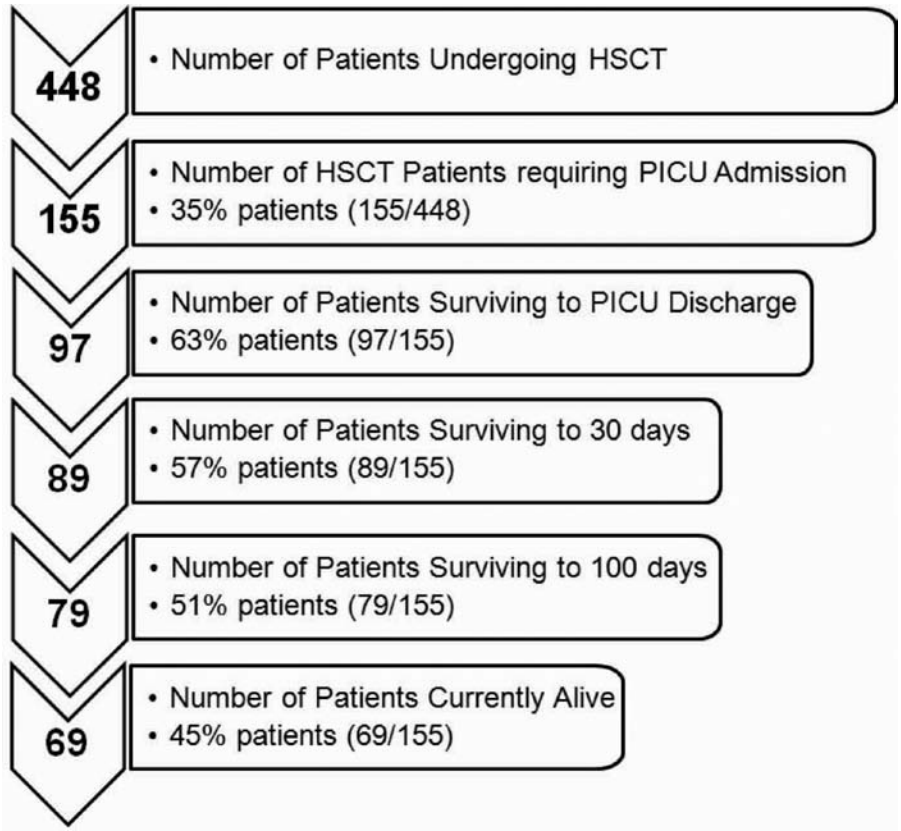


**Figure 2.** Survival for hematopoietic stem cell transplantation (*HSCT*) patients requiring pediatric intensive care unit (*PICU*) admission. Flowchart depicts survival for 155 HSCT patients requiring PICU admission during the study period. Survival depicted at PICU discharge, 30 days, 100 days, and to date following last PICU discharge during the study period.

**Table 4.** Factors affecting pediatric intensive care unit survival

| Risk Factor | Odds Ratio (95% Confidence Interval)[a] | $p^b$ |
|---|---|---|
| Simple generalized linear mixed effects model regression analysis | | |
| Ventilator use (no vs. yes) | 22.8 (9.3–55.7) | <.001 |
| Renal support (no vs. yes) | 5.2 (2.6–10.2) | <.001 |
| Inotrope/vasopressor use (no vs. yes) | 9.8 (4.85–19.9) | <.001 |
| PICU length of stay[c] | 0.81 (0.7–0.94)[c] | .002 |
| Mechanical ventilation duration[c] | 0.61 (0.37–1.03)[c] | <.001 |
| Prior PICU admission[d] | 0.82 (0.71–0.94)[d] | .01 |
| Multiple generalized linear mixed effects model regression analysis | | |
| Ventilator use (no vs. yes) | 19.1 (7.3–49.9) | <.001 |
| Renal support (no vs. yes) | 2.8 (1.3–5.8) | .013 |
| Ventilator + renal support (no/no vs. yes/yes) | 53.1 (18.8–150.4) | |
| PICU length of stay[c] | 0.98 (0.89–1.07)[c] | .63 |
| Prior PICU admission[d] | 0.77 (0.64–0.92)[d] | .014 |

PICU, pediatric intensive care unit.

[a]Odds ratio (OR) for PICU survival with 95% confidence intervals; [b]*p* value represents statistical significance for each variable independent of the others (simple generalized linear mixed effects model regression) or adjusted for the effects of the others (multiple generalized linear mixed effects model regression); [c]OR represents change in odds of survival by the reported factor for each additional week of PICU stay or mechanical ventilation: e.g., the odds of survival differ by $OR^x$ for x additional weeks; [d]OR represents change in odds of survival by the reported factor for each prior admission: e.g., the odds of survival differ by $OR^x$ for x additional prior admissions.

with recent published data wherein a third of patients undergoing HSCT required PICU admission at some time following their transplant. In our report, the vast majority of patients had only one or two admissions, with postoperative admissions accounting for <10% of admissions. Mechanical ventilation was needed in 57% of patients admitted to the ICU, which is comparable to published studies (2, 5, 6). Renal support was utilized for 25% of patients, resulting in 55 episodes of renal support during the study. The use of mechanical ventilation, inotropes, and renal support were similar amongst patients undergoing transplant for malignant vs. nonmalignant disorders and myeloablative vs. nonmyeloablative conditioning. Similar use was also seen in patients receiving allogeneic or autologous transplant; however, this lack of difference is possibly confounded by the relatively few patients in our cohort receiving autologous transplants.

Overall, we observed an 82% survival to PICU discharge for these 319 admissions. This translated to 63% (97 of 155) of HSCT patients surviving their last PICU admission, with 51% (79 of 155) being alive at 100 days. On longer follow-up, 45% were still alive. This suggests that in our cohort the majority of deaths occur in the PICU or within 100 days of discharge. All similar studies published over the last decade have had far fewer patients, and with a lower survival to PICU discharge. The range of survival to PICU discharge for patients in these studies varies between 30% and 47% (2, 5–10). Only a single small study that evaluated data over a 4-yr period for 33 patients demonstrates a similar survival rate (2). In our study, 81% (79 of 97) of patients that survived to PICU discharge were still alive 100 days later. This is an important improvement in survival compared to 54% observed by Kache et al (2) in their 2000–2004 cohort. However, the lack of specific admission criteria for our cohort leaves open the possibility that admissions of patients with a lower severity of illness may have affected our outcomes. Unlike prior studies, we followed patients in our cohort longer, with a median follow-up of nearly 2.5 yrs. Hence, our data demonstrate an improvement in survival for patients requiring PICU admission following HSCT, and that the improved outcome leads to long-term survival.

We were particularly interested in outcomes for HSCT patients who needed mechanical ventilation and/or renal support during their PICU stay, as historically outcomes for these patients have been poor. At our center nearly 40% of the 88 patients ventilated at any time over the 6-yr study period survived through their last PICU admission, with 34% surviving at least 100 days after

**Table 5.** Multiple logistic regression analysis: Interventions affecting 100-day survival following last pediatric intensive care unit discharge adjusted for normalized risk factors accumulated over prior pediatric intensive care unit admissions[a]

| Intervention[b] | Odds Ratio (95% Confidence Interval) | *p* |
|---|---|---|
| Ventilator use (no vs. yes) | 5.3 (2.4–11.8) | <.001 |
| Renal support (no vs. yes) | 3.1 (1–9.3) | .048 |
| Ventilator + renal support (no/no vs. yes/yes) | 16.3 (4.6–57.5) | |

[a]Risk factors accrued during prior admissions over the study period were normalized for the time period over which the pediatric intensive care unit admissions occurred and were included as explanatory variables; [b]intervention must have occurred during the patients last pediatric intensive care unit admission within the study period

PICU discharge. Since multiple studies report mechanical ventilation outcomes by admissions rather than by patient numbers (some patients were admitted more than once), we observed a 58% survival to PICU discharge for HSCT admissions requiring mechanical ventilation. These numbers represent improvements over historical reports. Van Gestel et al (9) demonstrated a mean ICU survival of 29% for HSCT patients requiring mechanical ventilation in their meta-regression analysis. Our results are similar if not better than recent studies reporting a 45% and 58% survival for HSCT admissions requiring mechanical ventilation (11–13). For patients needing renal support at our center, survival to PICU discharge and 100-day survival following last PICU discharge were 34% and 29%, respectively, not dissimilar to the Continuous Renal Replacement Therapy Registry Group recently reporting a 45% patient survival to PICU discharge for HSCT patients requiring continuous renal replacement therapy (13). While this survival is improved relative to our results, the severity of illness and underlying disorder leading to these patients HSCT is not reported and, therefore, makes correlations to our cohort difficult. However, a more comparable study by Rajasekaran et al (14) demonstrated a 33% ICU survival for HSCT patients undergoing continuous renal replacement therapy. A combination of mechanical ventilation and renal support was used in 34 of our patients, with a 32% survival to ICU discharge. These data contrast with a recent study reporting that 17% of such patients survived to PICU discharge (15). Taken together, our survival data for HSCT patients needing mechanical ventilation and/or renal support reveal an improvement compared to published data. However, the need for mechanical ventilation and/or renal support significantly diminished the likelihood of PICU and 100-day survival for these patients. These findings are not surprising to healthcare providers caring for these patients, as prior studies have demonstrated worsening outcomes for HSCT patients with multiple organ failure (9, 10).

The number of prior PICU admissions for HSCT patients at our center proportionally decreased their odds of survival. However, prior studies have not studied this or have demonstrated no effect of admission number on PICU survival (4). The reason for this difference is unclear; however, repeated PICU admissions may be a marker of increased complications following transplant. Notably, the PICU length of stay did not impact PICU survival. While we describe improved outcomes for this cohort of patients, we could identify no single intervention or change in management that could account for the improved outcomes observed in our high-risk patient population. Although difficult to evaluate and quantify in a retrospective study, we believe that our multidisciplinary approach to the management of HSCT patients, with both teams present on rounds, plays an important role in our observed outcomes. Ultimately it is most likely that improved outcomes are most likely a result of the additive effect of multiple small changes in management of these patients from both the transplant and intensive care standpoint.

## CONCLUSIONS

In conclusion, our study demonstrates a 63% survival to ICU discharge with a 45% long-term survival for HSCT patients needing PICU care. Our study bolsters the belief that outcomes for this cohort of patients are improving and challenges previously held dogmas of universally poor outcomes for HSCT patients requiring admission to the PICU. We suggest that aggressive, well-coordinated, multidisciplinary care can lead to long-term survival.

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