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MINIREVIEWS

Intensive care outcomes in adult hematopoietic stem cell transplantation patients

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Abstract

Although outcomes of intensive care for patients undergoing hematopoietic stem cell transplantation (HSCT) have improved in the last two decades, the short-term mortality still remains above 50% among allogeneic HSCT patients. Better selection of HSCT patients for intensive care, and consequently reduction of non-beneficial care, may reduce financial costs and alleviate patient suffering. We reviewed the studies on intensive care outcomes of patients undergoing HSCT published since 2000. The risk factors for intensive care unit (ICU) admission identified in this report were primarily patient and transplant related: HSCT type (autologous *vs* allogeneic), conditioning intensity, HLA mismatch, and graft-versus-host disease (GVHD). At the same time, most of the factors associated with ICU outcomes reported were related to the patients' functional status upon development of critical illness and interventions in ICU. Among the many possible interventions, the initiation of mechanical ventilation was the most consistently reported factor affecting ICU survival. As a consequence, our current ability to assess the benefit or futility of intensive care is limited. Until better ICU or hospital mortality prediction models are available, based on the available evidence, we recommend practitioners to base their ICU admission decisions on: Patient pre-transplant comorbidities, underlying disease status, GVHD diagnosis/grade, and patients' functional status at the time of critical illness.

Key words: Stem cell transplantation; Intensive care; Mechanical ventilation; Comorbidity; Outcome prediction

Core tip: The outcome of hematopoietic stem cell transplantation (HSCT) patients admitted to intensive care remains poor but not "futile". While risk factors for intensive care unit (ICU) admission are mostly patient and transplant related, prognostic factors for HSCT patients admitted to ICU are primarily related to patients' functional status and interventions in ICU. Based on the available evidence, we recommend patient

selection for ICU to be based on patient pre-transplant comorbidities, underlying disease status, graft-versus-host disease diagnosis/grade, and patients' functional status at the time of critical illness.

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INTRODUCTION

The role of hematopoietic stem cell transplantation (HSCT) has been established in the treatment of various high-risk malignancies and non-malignant conditions. Due to the intense conditioning prior to HSCT and slow post-transplant immune recovery, patients undergoing HSCT are prone to develop infectious and other complications that may lead to death. In fact, transplant related mortality (TRM) is a significant cause of HSCT failure and TRM rates as high as 50% have been reported in high-risk transplants/patients[1]. The factors related to the patient (performance status, comorbidities) and the transplant (conditioning regimen intensity, donor and graft type) determine post-transplant immune recovery and organ damage extent, hence influence the risk and severity of the treatment complications[2-7]. While the pace of post-transplant immune recovery is variable; its pattern is more predictable and may be divided into 3 phases: Pre-engraftment, early post-engraftment, and late post-engraftment. The primary immune defects leading to infections are innate immunity in the pre-engraftment phase; cell-mediated immunity in the early post-engraftment phase; cell-mediated and humoral immunity in the late post-engraftment phase.

Post-transplant complications may be life-threatening and require intensive care due to respiratory failure, shock, organ failure, and others. Even though intensive care unit (ICU) outcomes have improved over the last few decades, ICU admission after allogeneic HSCT (AlloSCT) is still associated with poor prognosis. Consequently, the benefit of intensive care has been challenged in this patient population. In this manuscript, we review the outcomes of intensive care in adult patients undergoing HSCT with emphasis on the factors leading to intensive care and outcome prediction. As practices of intensive care and HSCT have evolved over years, we will focus on seventeen reports published since 2000 summarized in Table 1.

FACTORS ASSOCIATED WITH ICU ADMISSION RATES

In cohorts including only AlloSCT patients, ICU admission rates have been consistently reported to range between 9%-20%[8-12] with only two outliers[13,14]. Naeem *et al*[14] reported an ICU admission rate of 57% among patients who received umbilical cord blood grafts. However, the advent of double-cord blood transplants has improved the immune recovery since that study was published; the ICU admission rate after cord blood transplants is very likely lower now. The small variation in ICU admission rates among the rest of the studies may be explained by different patient selection criteria and varying patient/disease characteristics of the study cohorts.

The ICU admission rate reported in the only study including exclusively autologous HSCT (AutoSCT) patients was 3.3%[15]. Similarly, the reported ICU admissions rates in cohorts including both Allo and AutoSCT[12,16] are lower than those reported in exclusively AlloSCT cohorts[8,10,11,17,18]. The lower admission rates after AutoSCT are likely due to less frequent pulmonary post-transplant complications compared to AlloSCT[19].

The reported risk factors for ICU admission among AlloSCT patients are myeloablative conditioning, acute graft-versus-host disease (GVHD), and HLA mismatch between donor and recipient[9,13,14]; all of which are transplant-related and not surprisingly also increase TRM[6,20,21]. In the only recent study that methodologically assessed the ICU admission risk factors, Benz *et al*[9] did not find patient age, gender, disease type or stem cell source to affect ICU admission risk. While the association between patient pre-transplant comorbidities and ICU admission risk has never been evaluated, comorbidities have been shown to significantly increase patient's risk for critical illness as they influence both TRM[7] and ICU outcomes[8].

The most common reasons for ICU admission after HSCT are respiratory failure and septic shock; pulmonary infections can cause both simultaneously. Nevertheless, non-infectious pulmonary diseases, *i.e.*, diffuse alveolar hemorrhage and acute respiratory distress syndrome, may also lead to respiratory failure after HSCT. Other reported reasons for ICU admission include cardiac dysfunction, neurological disorders, and gastrointestinal bleeding. These may arise due to treatment itself, *i.e.,* busulfan induced seizures and alkylator induced congestive heart failure; development of GVHD; and patients' comorbidities.

PROGNOSTIC FACTORS AND ICU OUTCOMES

Despite the improvement in general ICU outcomes, prognosis for HSCT patients admitted to ICU is still poor with reported hospital mortality ranging from 46% to 84% in series published between 2000 and 2015 (Table 1). The wide range is likely due to inclusion of AutoSCT patients in some of the cohorts and different patient selection criteria between centers. In cohorts including only AlloSCT patients, hospital mortality and overall

Table 1 Summaries of the studies of adult hematopoietic stem cell transplantation patients admitted to intensive care unit published between 2000-2015

Ref. (study period)	No. of patients admitted to ICU [total N of HSCTs (%)], ICU admission risk factors	Reasons for ICU admission (%)	Interventions (%)	Outcomes	Factors evaluated for outcome prediction	Predictors of outcome on mutlivariate analysis	Notes
Boyaci *et al*[31] (2007-2010)	48 patients (7 Auto and 41 AlloSCT)	Respiratory failure 86%, sepsis/septic shock 75%, renal failure, liver failure, AMS	MV 75%	Mortality: 79% in hospital	Age, gender, underlying disease, remission status, HSCT type, HLA match, conditioning intensity, cause of ICU admission, GVHD, SOS, APACHE Ⅱ, GCS, SOFA, # of organ failures, various vitals and lab values, VA, MV	APACHE Ⅱ score and VA in ICU a/w higher mortality	
Bayraktar *et al*[8] (2001-2010)	389 AlloSCT patients a/to ICU within 100 d of HSCT [Of 3039 patients (13%)]	Respiratory failure 61%, septic shock 12%, AMS 9%, arrhythmia 5%, non-GI, non-CNS bleeding 4%	N/R	Mortality: 64% in hospital	Age > 55, underlying disease, year of HSCT was, HSCT period at ICU admission, graft source, HLA match status, donor relation, conditioning intensity, aGVHD at ICU admission, HCT-CI score	HCT-CI ≥ 2, ablative conditioning, aGVHD at ICU admission a/w higher mortality. ICU admission during conditioning regimen a/w lower mortality	HCT-CI score, a measure of pre-transplant comorbidities, can be calculated even prior to HSCT
van Vliet *et al*[17] (2004-2009)	49 AlloSCT [Of 319 (15%)]	Infectious complications 86%, respiratory failure 67% Ablative conditioning and unrelated donor grafting a/w increased risk for ICU admission	N/R	1-yr OS: 15% Mortality: 33% in ICU, 53% in hospital		NR	Univariate analyses demonstrated improved 100-d survival between 2004-2005 to 2008-2009
Agarwal *et al*[30] (1998-2008)	123 HSCT patients (73% AlloSCT)			Mortality: 41% in ICU, 62% in hospital. OS @ 1yr: 24%	Age, underlying disease, type of HSCT, GVHD, neutropenia, hospital admission-ICU interval, organ failures, sepsis type, APS, APACHE Ⅱ, MV	Fungal infection and number of organ failures a/w higher ICU mortality	Hard to explain why GVHD was a/w lower ICU mortality
Depuydt *et al*[33] (2000-2007)	44 AlloSCT	Bacterial infections 32%, non-bacterial infections 30%, non-infectious causes 39%. Overall, pulmonary related causes 39%	MV (73%), RRT (27%)	Mortality: 61% in ICU, 75% in hospital, 80% @ 6 m	Age, gender, bacterial infection, GVHD grade, HSCT-ICU interval, SOFA	Bacterial infection as the cause of ICU admission a/w lower hospital mortality	Improvement in SOFA score by 5th d of ICU was sig better in patients with bacterial infections
Benz *et al*[9] (1998-2007)	33 AlloSCT [Of 250 (13%)] ICU admission risk factors: aGVHD grade Ⅱ-Ⅳ and HLA mismatch	Pulmonary complications 33%, sepsis 24%, neurological disorders 18%, cardiovascular problems 6%,	MV 64%, VA 42%, RRT 27%	OS @ 1yr: 28%		NR	SAPS Ⅱ and SOFA scores did not reliably predict survival
Townsend *et al*[13] (1996-2007)	164 AlloSCT (majority TCD) [Of 552 (30%)]. ICU admission risk factors: Ablative conditioning	Sepsis 67%, respiratory failure 55%	MV 50%	Survival: 32% in ICU OS @ 1yr: 19% overall, 61% in patients who survived ICU	Donor type, conditioning intensity, reason for ICU admission, NIV, MV, VA, RRT, various labs, APACHE Ⅱ, duration of ICU stay, duration of MV	MV, raised BUN at admission and ablative conditioning a/w worse ICU survival	
Trinkaus *et al*[15] (2001-2006)	34 AutoSCT patients admitted within 100 d of SCT [Of 1013 (3.3%)]	Sepsis 32%, respiratory failure 29%, cardiovascular failure 26%		ICU mortality: 38%		NR	

Neumann *et al*[18] (1999-2006)	64 AlloSCT [Of 319 (20%)]	Pulmonary complications 53%, Sepsis 22%, renal failure 9%, bleeding 3%, status epilepticus 3%		ICU mortality: 66%	Age, gender, underlying disease, remission status, conditioning intensity, HLA match status, GVHD, ICU admission indication, HSCT-ICU interval, SOFA, various labs, SOS	SOFA ⩾ 12 and BUN > 60 a/w higher ICU mortality	
Gilli *et al*[10] (1995-2005)	91 AlloSCT (29% < 18 yrs old) [Of 661 (14%)]	Respiratory failure 41%, septic shock 31%, neurological events 12%	MV 48%, RRT 5%, VA 58%	Mortality: 58% in ICU, 70% @1m	Conditioning intensity, reason for ICU transfer APACHE II, SOFA, VA, RRT, IMV	SOFA score a/w 30 d mortality	APACHE Ⅱ underestimated mortality
Naeem *et al*[14] (1998-2003)	25 UCBT [Of 44 (57%)] ICU admission risk factors: Ablative conditioning	Pneumonia 52%, GI bleeding (12%), Sepsis 8%, renal failure 8%	MV 48%	ICU mortality: 72%		NR	
Pène *et al*[11] (1997-2003)	209 AlloSCT [Of 1025 patients (20%)]	Repiratory 67%, hemodynamic 23%, neurologic 18%, renal 17%, other 5%	MV (58%), RRT (28%), VA (47%)	Survival: 48% in ICU, 32% in hospital, 27% @ 6 m, 21% @ 1 yr MV patients: 18% in ICU, 16% in hospital	Age, gender, underlying disease, remission status, conditioning intensity, graft source, HSCT-ICU interval ⩽ 30 d, corticosteroid Rx, serum bilirubin level, MV, VA, RRT	Corticosteroid Rx, serum bilirubin level at ICU admission, MV	None of the 35 patients with admission LOD score > 10 survived the hospital stay
Scale *et al*[41] (1992-2002)	504 patients (264 AlloSCT) who were admitted to ICU following the BMT hospitalization [Of 2653 (19%)]		MV 51%, RRT 7%	1-yr mortality: 67%		NR	
Kim *et al*[42] (1999-2001)	18 AlloSCT [Of 210 (9%)]	Respiratory failure 50%, renal failure 39%, septic shock 11%		ICU mortality: 94%			
Soubani *et al*[16] (1998-2001)	85 HSCT patients (45 AlloSCT) [Of 745 (11%)]	Respiratory 48%, Sepsis 23%, cardiac 19%, neurologic 6%, bleeding 2%	MV in 60%	Mortality: 39% in ICU, 59% in hospital, 72% @ 6 m CU mortality 63% among patients with MV	Age, gender, smoking history, race, underlying disease, HSCT type, HLA match, HSCT-ICU interval, GVHD, various labs	High lactate level, MV, > 2 MOFs during ICU stay a/w higher ICU mortality	
Kew *et al*[12] (1992-2001)	37 HSCT patients (28 AlloSCT) [Of 440 (9%)]	Respiratory failure 65%, hemodynamic instability 57%,	MV in 68%	29 patients died within 1 yr	Pre-ICU patient characteristics, MV, VA	VA a/w shorter OS	
Afessa *et al*[32] (1996-2000)	111 patients (62 Auto, 50 AlloSCT)	Respiratory failure 40%, cardiac reasons 26%, sepsis 14%, CNS dysfunction 5%, GI bleeding 5%	MV 55%	Mortality: 33% in ICU, 46% in hospital 30-d mortality was 78% among AlloSCT patients	Type of HSCT, graft source, post-transplant days @ ICU admission, GVHD, APACHE III, APACHE II, ARDS, MOF, sepsis, MV, VA	Higher APACHE III score @ ICU admission, AlloSCT, MV, ARDS, MOF, sepsis, VA a/w higher 30-d mortality	AUC of receiver operating characteristic curve for APACHE III and hospital mortality was 0.704

A/to: Admitted to; a/w: Associated with; AlloSCT: Allogeneic HSCT; AutoSCT: Autologous HSCT; AMS: Altered mental status; APACHE: Acute Physiology and Chronic Health Evaluation; APS: Acute physiological score; ARDS: Adult Respiratory Distress Syndrome; BUN: Blood urea nitrogen; CNS: Central nervous system; GCS: Glasgow Coma Score; GI: Gastrointestinal; GVHD: Graft-versus-host disease; HCT-CI: Hematopoietic cell transplantation-specific comorbidity index; HSCT: Hematopoietic stem cell transplantation; LOD: Logistic Organ Dysfunction score; m: Months; MOF: Multiorgan failure; MV: Invasive mechanical ventilation; NIV: Non-invasive ventilation; NR: Not reported; OS: Overall survival; pts: Patients; RRT: Renal replacement therapy; Rx: Treatment; SAPS: Simplified Acute Physiology Score; SOFA: Sequential Organ Failure Assessment; SOS: Sinusoidal obstruction syndrome; UCBT: Umbilical cord blood transplantation; VA: Vasoactive drug treatment.

survival (OS) at one year range from 53% to 75% and from 15% to 28%, respectively.

The ICU outcomes in HSCT patients were even more dismal prior to 2000. In reports published prior to 2000,

Table 2 Possible reasons for improved outcomes in patients who are admitted to intensive care unit after hematopoietic stem cell transplantation

Improvements in HSCT
Reduced intensity conditioning
Better antimicrobial prophylaxis
Pre-emptive therapy of cytomegalovirus infections
Improved antifungal therapy
Improvements in intensive care
Early use of non-invasive ventilation
Early goal-directed therapy for septic shock
Better patient selection
Improved recognition of clinical deterioration and earlier ICU admission
Use of palliative care for patients with a slim chance of recovery

HSCT: Hematopoietic stem cell transplantation; ICU: Intensive care unit.

Table 3 Factors that were found to be associated with outcomes of intensive care among hematopoietic stem cell transplantation patients

Patient/disease related factors
Pre-transplant comorbidities
Transplant related factors
Type of HSCT (allogeneic *vs* autologous)
Conditioning regimen intensity
Graft-*vs*-host disease
Patient functional status at ICU admission
Serum bilirubin level
Serum lactate level
Blood urea nitrogen level
APACHE Ⅱ / Ⅲ scores
SOFA
Type of infection (bacterial *vs* fungal)
Post-ICU admission factors
Mechanical ventilation
Vasopressor support

APACHE: Acute Physiology and Chronic Health Evaluation; SOFA: Sequential Organ Failure Assessment; HSCT: Hematopoietic stem cell transplantation; ICU: Intensive care unit.

hospital mortality ranged from 77% to 98% and long-term survival ranged from 3% to 10%[22-29]. Similarly, Agarwal *et al*[30] reported higher ICU mortality rates between 1988-1998 compared to 1998-2008 in a single center. The improvement in ICU outcomes over the last few decades may have been due to improvements in intensive care, HSCT, and patient selection (Table 2).

Poor outcomes among HSCT patients admitted to ICU is not universal. Moreover, HSCT patients surviving ICU stay do not necessarily perform worse in the long-run compared to those who never require intensive care[13]. On the other hand, non-beneficial intensive care has costs to patients, families, and the healthcare system overall. Preventing non-beneficial intensive care may provide comfort and dignity for the patient, increase bed availability for those who would benefit from intensive care, and reduce the economic burden. To identify the factors affecting outcomes in HSCT patients admitted to ICU and guide patient selection for intensive care, various small retrospective cohort studies have been performed (Table 1). These factors may be divided into four categories (Table 3).

Patient/disease related factors

Patient age, gender, and underlying disease type were not found to be associated with ICU outcomes. The only patient related factor that has been shown to affect ICU outcomes is the presence of pre-transplant comorbidities. In one of the largest cohorts reported to date, we have shown that an Hematopoietic Cell Transplantation-Specific Comorbidity Index (HCT-CI) of more than or equal to 2 was significantly and independently associated with increased hospital mortality[8]. A higher HCT-CI score, an index of pre-transplant comorbidities, was also associated with shorter OS. Available at the time of HSCT planning, HCT-CI may help providers and patients make informed decisions regarding intensive care before the need arises.

Transplant related factors

Conditioning regimen intensity and the type of HSCT (autologous *vs* allogeneic) affects a patient's risk for critical illness[13]. Whether they affect the ICU outcomes is not as clear. Of the few studies that included both allogeneic and autologous HSCT[30-32], only one demonstrated significantly worse prognosis after AutoSCT compared to AlloSCT[32]. However, these included small cohorts, and in the only recent study including exclusively AutoSCT patients[15], ICU mortality was numerically lower than that in most AlloSCT patient cohorts. Similarly, while Townsend *et al*[13] and our group have observed that ablative conditioning is associated with higher hospital mortality, other researchers have not found such association[10,11,18,31]. Additionally, Pène *et al*[11] and we observed that patients who had active GVHD or were being treated with corticosteroids at the time of ICU admission had worse prognosis than those who did not. There likely is a genuine cause-effect relationship between GVHD and ICU mortality as GVHD causes tissue damage and its treatment suppresses immune system cultivating severe infections. Finally, none of the recent studies found an association between ICU outcomes and patient age, underlying hematological diagnosis, donor type, HLA match or stem cell source.

Patient functional status at the time of ICU admission

The patient's severity of illness at the time of ICU admission is known to be predictive of general ICU survival, hence various predictive scoring systems, such as Acute Physiology and Chronic Health Evaluation (APACHE) and Sequential Organ Failure Assessment (SOFA) score, based on organ function are commonly used in clinical practice. It is evident that organ function at the time of ICU admission is also prognostic for HSCT patients. However, as results have been discrepant, there is no agreement on which measures are optimal. Elevated serum lactate[16], bilirubin[11], and blood urea nitrogen[13,18] have been inconsistently

found to be associated with worse prognosis. As for the organ function indexes, APACHE Ⅱ was not found to be predictive of ICU outcomes in HSCT population in various studies[10,13,30] except one[31]. In a cohort of 112 patients, Afessa *et al*[32] did not find APACHE Ⅱ to have prognostic value while they found APACHE Ⅲ to have a moderate discrimination and good calibration in predicting hospital mortality. Gilli *et al*[10] observed that APACHE Ⅱ underestimated mortality while higher SOFA scores were associated with higher hospital mortality. In their cohort, none of the 20 patients with a SOFA score > 11 survived. On univariate analyses, Trinkaus *et al*[15] also found SOFA to be predictive of mortality. Similarly, Neumann *et al*[18] found a SOFA score > 12 to be significantly and independently associated with higher mortality; of 45 patients with SOFA >11, only 4 survived. On the other hand, Boyaci *et al*[31] and Benz *et al*[9] did not find SOFA to be predictive of mortality in multivariate analyses. Finally, Depuydt *et al*[33] reported that patients who were admitted to ICU with bacterial infection had a better prognosis than others, likely due to the more rapid improvement of bacterial infections with antibiotic treatment. In contrast, Agarwal *et al*[30] found fungal infections to be associated with higher mortality.

Post-ICU admission factors

Several authors demonstrated that short-term outcomes are worse in patients who required endotracheal intubation[11,13,16,32]. In fact, mechanical ventilation (MV) is the most consistently shown prognostic factor in HSCT patients admitted to ICU. Unfortunately, 48%-78% of HSCT patients require MV during their ICU stay (Table 1). Similar to MV, vasopressor support has also been found to be associated with worse short-term prognosis in a few studies[12,31]. Although significantly associated with outcomes, events that happen in ICU cannot be used for outcome prediction before a patient's ICU admission.

Overall, it can be deduced that: (1) patient/disease related factors do not play a major role in determining ICU outcomes with the exception of patient comorbidities; (2) while transplant related factors affect ICU admission risk, they do not necessarily influence ICU outcomes with the exception of transplant type and GVHD diagnosis at the time of ICU admission; (3) the major determinant of ICU outcome seems to be the patients' functional status at the time of ICU admission; (4) the value of traditional prognostic indexes has not been validated in HSCT patients but may be useful in identification of patients with a very slim chance of survival.

FUTURE OBJECTIVES AND RECOMMENDATIONS

As physicians and researchers continue improving the HSCT process and outcomes, optimization of the delivery of a comprehensive intensive care plan should become an important component of the overall patient management. This goal, requires establishment of adequate communication channels among patients, relatives, transplant physicians and intensivists. In addition, we believe that there is a need for further development of clinical algorithms to assess benefits and risks of intensive care, alternative palliative care, and appropriateness of life support and resuscitation at multiple points in time: (1) prior to HSCT; (2) when early warning signs of critical illness appear; (3) upon development of critical illness; (4) every third to fifth day of intensive care; and (5) prior to initiation of life supportive measures such as endotracheal intubation and MV.

Prior to HSCT

Transplanters should assess patients' comorbidities, calculate their HCT-CI scores, and talk to the patient about the possibility and prognosis of intensive care/intubation beforehand.

Early warning signs

Retrospective studies demonstrated HSCT patients admitted to ICU demonstrated early warning signs that could be detected by early warning score systems (EWSS) consisting of nursing observations[34] and suggested improvements in ICU outcomes among HSCT patients after such systems and early outreach teams were implemented[35]. Accordingly, we recommend implementation of EWSS and outreach teams in transplant centers.

Upon development of critical illness

In the literature, there is a lack of agreement on which factors should be used to predict ICU outcomes of HSCT patients. We believe patient pre-transplant comorbidities, underlying disease status, GVHD diagnosis/grade, and patient's functional status at the time of critical illness should be taken into account while deciding on benefits of intensive care. Although none of the previous studies showed the underlying disease or its remission status to affect short-term ICU outcomes -similar to the studies done in cancer patients[36,37]; the remission status significantly affects the long-term survival of HSCT patients[20,21], and likely would affect the long-term outcome after ICU admission. To establish a clinical algorithm for patient selection, transplanters and intensivists need a prognostic index specific for critical HSCT patients. Hence, more studies on large HSCT cohorts with multi-center validation are needed. We believe hospital mortality should be the primary outcome assessed in such future studies as long-term outcomes of HSCT patients surviving ICU is similar to those of patients who never required intensive care[13] and, in our experience, the number of patients who died on their second ICU admission but during the same hospitalization is not insignificant.

Every third to fifth day of intensive care

Although none of the recent studies showed the length of ICU stay to affect short-term ICU outcomes, in our experience the longer the patient stays in ICU, the less likely he/she is to survive. Therefore, we believe the intensivist and the transplant physician should review the benefits of intensive care every three to five days in ICU.

Prior to endotracheal intubation

Initiation of MV is a turning point in the intensive care of HSCT patients. MV is associated with shorter survival and also suffering of patient and the family[11,16,32]. The combination of hepatic and renal failure in mechanically ventilated patients is almost universally fatal[38-40]. Therefore, for HSCT patients with renal and/or hepatic failure requiring MV, a frank discussion should be made with the patients' family prior to intubation and initiation of ventilation.

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