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Prognostic impact of mechanical ventilation after liver transplantation: A national database study

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Abstract

Background—The impact of mechanical ventilator support (MCVS) on mortality and graft loss after liver transplantation (LT) is not well-described.

Methods—Multivariate analysis of a novel database linking national transplant registry and Medicare claims data was used to assess the impact of early MCVS on mortality and graft survival following LTs performed between 2002–2008.

Results—Among 10,517 LT recipients, 6.9% (n=726) required post-operative MCVS, 25.6% of who required < 96 hrs, 24.2% ≥ 96 hrs, and 50.1% an unspecified duration. Significant predictors of prolonged MCVS included older age, female gender, pre-transplant dialysis requirement and ascites. After multivariate adjustment, MCVS ≥ 96hrs was associated with nearly 3-times the adjusted hazard ratio (aHR) of mortality (2.95, P=<0.001), while MCVS <96 hrs was not significantly associated with mortality (aHR 0.88, P=0.55).

Conclusions—Recognition of LT patients at-risk for prolonged MCVS may help to reduce the incidence and consequences of this complication.

Keywords

Graft failure; Liver transplantation; Mechanical ventilation; Medicare; Mortality

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INTRODUCTION

Even in the current environment of public disclosure of procedural outcomes, transplant centers are uniquely subject to regulatory scrutiny. Transplant centers find themselves at the difficult nexus of pressure to increase transplant rates and organ acceptance practices to care for listed patients, while, at the same time, limiting the risk of poor post-transplant outcomes to ensure the program's survival (1). Transplant programs evaluate potential recipients to assess their candidacy for transplantation and, potentially, to identify factors that can be modified to reduce the incidence of post-operative complications. Patients deemed to have an excessive risk of poor outcomes are excluded from transplant given the need to maximize the benefit of the limited organ supply (2).

In the surgical literature, post-operative respiratory failure is associated with increased in-hospital morbidity, mortality and costs, as well as late mortality (3). In study of 180,359 veterans undergoing vascular and general surgical procedures in 2001–2004, factors that predicated the need for prolonged post-operative mechanical ventilatory support (defined as >48 hours or unanticipated re-intubation) included older age, male gender, history of smoking, emergency operations, elevated creatinine, albumin less than 3.5 mg/dl, presence of ascites and abdominal cases considered “complex” (4). The 30-day mortality was markedly higher (26.5% vs. 1.4%, $P<0.0001$) among those requiring prolonged mechanical ventilation compared to those without mechanical ventilatory support. Liver transplant patients share similar characteristics with this risk population including ascites, hypoalbuminemia, and large abdominal incisions; however, they also possess unique concerns, including pre-operative pleural effusions, and ventilation instability pre-operatively with impaired gas exchange and concern for hyperventilation secondary to unknown mechanisms associated with liver disease (5–7). The frequency, correlates and consequences of respiratory failure after liver transplant surgery have not been well described in a large population.

To advance understanding of the prognostic implications of requirements for mechanical ventilation early after liver transplant surgery in a nationally representative cohort, we examined a novel database that integrates the national transplant registry with Medicare claims data. Specifically, we sought to quantify the incidence of mechanical ventilatory support early after transplant among patients who were not receiving mechanical ventilation before transplant, define the clinical correlates, and quantify associated post-transplant patient and graft survival.

MATERIALS AND METHODS

Data Sources and Study Sample

Study data were assembled by linking Organ Procurement and Transplantation Network/United Network for Organ Sharing records for United States deceased donor liver transplant recipients (2002–2008) with administrative billing data from Medicare. The Organ Procurement and Transplantation Network maintains records for all solid organ transplant candidates and recipients in the United States including recipient and donor demographic data and specific clinical outcomes. Medicare billing claims include diagnostic and

procedure codes for patients with Medicare fee-for-service primary or secondary insurance. After approval by the Health Resources and Services Administration and the Saint Louis University Institutional Review Board, beneficiary identifier numbers from Medicare's electronic databases were linked using Social Security Number, gender, and birthdates to unique Organ Procurement and Transplantation Network identifiers. Because of the large sample size, the anonymity of the patients studied, and the non-intrusive nature of the research, a waiver of informed consent was granted per the Department of Health and Human Services Code of Federal Regulations (Title 45, Part 46, Paragraph 46.116). Analyses were performed using Health Information Portability and Accountability Act-compliant, limited datasets with all direct identifiers removed. This study was approved by the Saint Louis University Institutional Review Board.

Early Post-Transplant Mechanical Ventilation

Early post-transplant MCVS was defined by identification of Medicare claims with corresponding diagnosis (International Classification of Diseases Code 9th Edition Clinical Modification Procedure codes (96.70, 96.71, 96.72, 96.04) within 30 days after transplantation. Code 96.71 defines ventilation duration as <96 consecutive hours, whereas as 96.72 defines duration as ≥ 96 consecutive hours. Patients with claims for mechanical ventilation within 30 days prior to liver transplantation were excluded.

Recipient and Graft Characteristics

Information on center-reported recipient clinical traits, demographic characteristics and donor factors were drawn from Organ Procurement and Transplantation Network Liver Transplant Candidate Registration and Transplant Recipient Registration files (Table 1). Recipient illness severity at transplant was categorized by the Model for End Stage Liver Disease (MELD) score, as previously described (9). For patients who were transplanted with “tumor or exception” points, the “biologic” MELD was used for all calculations. Creatinine values greater than 4.0 mg/dl were set equal to 4.0 mg/dl. The MELD score was then capped at a lower limit of 6 and an upper limit of 40. Allograft quality was classified by Donor Risk Index (DRI) according to the formula by Feng et al. which incorporates donor race, height, cause of death, donation after cardiac death, split/partial grafts, organ location and ischemic time (10). We considered DRI levels as approximate quartiles, and considered DRI ≥ 1.8 as defining a high risk donor, as previously reported (11).

Survival and Length of Stay

Length of transplant stay, dates of death, and dates of graft failure were defined by Organ Procurement and Transplantation Network reports. Observation time was censored at the date of each individual's last expected follow-up report submission based on the requiring reporting intervals (12), end of study data (December 20008), or one year post-transplant.

Statistical Analyses

Data management and analyses were performed with SAS for Windows software, version 9.3 (SAS Institute Inc., Cary, NC). Continuous data were summarized as means and standard deviations, and categorical data were summarized as proportions, with stratification

according to early mechanical ventilatory support requirements. Bivariate associations of baseline factors with mechanical ventilation were examined with the Chi-square test, while independent correlates of mechanical ventilation requirements were identified by multivariate logistic regression with stepwise selection (adjusted odds ratios, aOR), using a retention threshold of $P < 0.05$. Variation in one-year patient and graft survival according to the requirement for early mechanical ventilation was compared by the Kaplan-Meier method, and the Log-Rank test was used to assess the statistical significance of differences in unadjusted survival. Multivariate Cox regression was used to examine associations of the requirement for early post-transplant mechanical ventilation with the relative risks of death and graft failure (adjusted hazards ratios, aHR) including adjustment for baseline recipient, donor and transplant factors listed in Table 1. Several sensitivity analyses were performed to assess the robustness of the primary outcomes models, including exclusion of patients with mechanical ventilatory support of unspecified duration, exclusion of liver-kidney transplant recipients, and analyses limited to liver-kidney transplant recipients. Finally, length of the transplant hospitalization was compared according to mechanical ventilatory support requirements using the non-parametric Wilcoxon Rank Sum. Analyses were stratified according to donor quality (DRI < 1.8 and DRI ≥ 1.8).

RESULTS

Frequency and Clinical Correlates of early Post-Transplant Mechanical Ventilation

Overall, among 10,517 eligible patients in the integrated database, 7% required mechanical ventilatory support within 30 days of liver transplantation. Of these cases, 26% required mechanical ventilation < 96 hrs, 24 % ≥ 96 hrs, while the duration was unspecified in 50%. In unadjusted analyses, as compared to those who did not require mechanical ventilation, patients who received mechanical ventilatory support ≥ 96 hrs were more commonly women, black race, and older. In addition, they also more commonly had Hepatitis C and other causes of end-stage liver disease, pre-transplant ascites, required pre-transplant dialysis, and received combined liver-kidney transplants (Table 1).

In multivariate logistic regression including adjustment for other factors, independent correlates of the requirement for any early mechanical ventilatory support included older age (age 36–60: aOR 1.68, 95% CI 1.00 to 2.78, age > 50 : aOR 2.43, 95% CI 1.48 to 3.98, versus age ≤ 35), female sex (aOR 1.36, 95% CI 1.17 to 1.58), pretransplant diabetes (aOR 1.24, 95% CI 1.06 to 1.46), pretransplant dialysis requirement (aOR 1.58, 95% CI 1.22 to 2.06), and ascites (aOR 1.56, 95% CI 1.23 to 1.97). While mechanical ventilation was more common among recipients of combined liver-kidney transplantation when considered alone, after covariate adjustment including dialysis treatment, combined liver-kidney transplant was independently associated with reduced likelihood of mechanical ventilation (aOR 0.58, 95% CI 0.42 to 0.82). Intensive care prior to transplant (aOR 0.59, 95% CI 0.39 to 0.89) was associated with decreased odds of mechanical ventilation, likely impacted by restriction of the study sample to patients who were not receiving mechanical ventilation before transplantation. Independent correlates of increased likelihood of prolonged mechanical ventilation ≥ 96 hrs included age > 50 (aOR 1.54, 95% CI 1.10 to 2.14), female gender (aOR 1.45, 95% CI 1.08 to 1.93), pretransplant dialysis requirement (aOR 1.90, 95% CI 1.34 to

2.85) and ascites (aOR 1.91, 95% CI 1.12 to 3.25). Hepatitis C as cause of liver failure was more common among patients requiring prolonged mechanical ventilation when considered as a single factor, but was associated with reduced likelihood of mechanical ventilation ≥96 hrs compared with other diagnoses (aOR 0.57, 95% CI 0.34 to 0.96) after covariate adjustment. Only age >50 (aOR 1.64, 95% CI 1.18 to 2.28) and pretransplant diabetes (aOR 1.42, 95% CI 1.06 to 1.90) were associated with mechanical ventilation <96 hrs by multivariate regression. There were no independent associations of recorded donor or transplant factors with MCVS requirements in multivariate models.

Patient and Graft Survival According to Early Post-Transplant Mechanical Ventilation Status

Among recipients of allografts with DRI <1.8, first-year patient survival was markedly low among those who required mechanical ventilatory support ≥96 hr at 70%, compared to 72% with mechanical ventilation of unspecified duration, 89% with mechanical ventilation <96 hrs, and 88% in those who did not require mechanical ventilation ($P<0.0001$, Figure 1). Relative one-year patient survival patterns were similar among recipients of high risk allografts (DRI ≥1.8): 55% with mechanical ventilation ≥96 hrs, 75% with mechanical ventilation of unspecified duration, 84% with mechanical ventilation <96 hrs, and 85% in those without mechanical ventilation ($P<0.0001$).

For recipients of liver transplants with DRI <1.8, those who required ≥96 hrs of mechanical ventilatory support had 68% one-year graft survival compared to 71% with unspecified MCVS, 86% with mechanical ventilation <96 hrs, and 86% without mechanical ventilation ($P<0.0001$, Figure 1). First-year graft survival among recipients of high DRI transplants also varied by mechanical ventilatory support requirements: 50% with mechanical ventilation ≥96 hrs, 71% with mechanical ventilation of unspecified duration, 78% with mechanical ventilation <96 hrs, and 81% in those without mechanical ventilatory support ($P<0.0001$).

Associations of Early Post-Transplant Mechanical Ventilation with Death and Graft Loss

In multivariate Cox regression including adjustment for baseline factors, liver transplant recipients who required mechanical ventilatory support ≥96 hrs had nearly 3-times the relative risk of death within the first year post-transplant as those who did not require mechanical ventilation (aHR 2.95, 95% CI 2.27 to 3.85). This strong association was similar among sub-groups stratified by allograft quality, with approximately 2.5-fold relative risk for transplants with DRI <1.8 (aHR 2.53, CI 1.75 to 3.66) and more than 3-times relative risk for transplants with DRI ≥1.8 (aHR 3.40, CI 2.32 to 4.97) (Figure 2). Mechanical ventilation of unspecified duration was also associated with increased first-year mortality of similar magnitude as prolonged mechanical ventilation (DRI <1.8: aHR 2.51, 95% CI 1.92 to 3.27; DRI ≥1.8: aHR 1.80, 95% CI 1.26 to 2.57), while mechanical ventilation <96hr was not significantly associated with death in the first year. Other significant correlates of first-year mortality in the full sample included recipient age >50 yrs (aHR 1.79, CI 1.3 to 2.46), MELD scores 30–39 (aHR 1.70 CI 1.39 to 2.07) and 20–29 (aHR 1.44, CI 1.26 to 1.65) compared to MELD <20, cold ischemic time ≥12 hrs compared with <12 hrs (aHR 1.49 CI 1.22 to 1.80), previous abdominal surgery (aHR 1.47, 95% CI 1.31 to 1.65), dialysis requirement prior to transplant (aHR 1.77, 95% CI 1.49 to 2.11), intensive care prior to

transplant (aHR 1.29, 95% CI 1.06 to 1.58), portal vein thrombosis (aHR 1.47, CI 1.21 to 1.77), portal bleed in the 48 hrs prior to transplant (aHR 1.83, 95% CI 1.40 to 2.40) and DRI 1.8 (aHR 1.56, 95% 1.18 to 2.06).

With regard to graft failure, liver transplant recipients with early mechanical ventilatory support ≥ 96 hrs had 2.7-times the relative risk as those without post-operative mechanical ventilation (aHR 2.69, 95% CI 2.10 to 3.44). This association of prolonged mechanical ventilation with graft failure was similar among subgroups stratified by allograft quality, with 2.3-fold relative risk for transplants with DRI <1.8 (aHR 2.30, 95% CI 1.62 to 3.26) and more than 3-times relative risk for transplants with DRI ≥ 1.8 (aHR 3.11, 95% CI 2.19 to 4.41) (Figure 2). Mechanical ventilatory support of unspecified duration was also associated with increased first-year graft loss of similar magnitude as prolonged mechanical ventilation (DRI <1.8 : aHR 2.02, 95% CI 1.55 to 2.61; DRI ≥ 1.8 : aHR 1.49, 95% CI 1.07 to 2.10), while mechanical ventilation <96 hrs was not significantly with first year graft loss. Other independent correlates of first-year graft loss included: MELD score 30–39 (aHR 1.49 95% CI 1.24 to 1.79) and MELD 20–29 (aHR 1.29, 95% CI 1.15 to 1.46), unknown cause of liver failure (aHR 1.23, 95% CI 1.05 to 1.44) compared to hepatitis C, and cold ischemic time ≥ 12 hrs (aHR 1.61, 95% CI 1.34 to 1.94) compared with <12 hrs, previous abdominal surgery (aHR 1.36, 95% CI 1.23 to 1.50), dialysis requirement prior to transplant (aHR 1.58, 95% CI 1.34 to 1.86), intensive care prior to transplant (aHR 1.29, 95% CI 1.07 to 1.54), portal vein thrombosis (aHR 1.33, CI 1.11 to 1.58), portal bleed in the 48 hrs prior to transplant (aHR 1.68, 95% CI 1.30 to 2.16) and DRI ≥ 1.8 (aHR 1.66, 95% 1.29 to 2.13).

Sensitivity analyses yielded results similar to the primary analyses. Specifically, after exclusion of patients with mechanical ventilatory support of unspecified duration from the analytic sample, mechanical ventilation ≥ 96 hrs was associated with nearly 3-times the relative risk of first-year death (aHR 2.98, 95% CI 2.28 to 3.87) and 2.7-times the risk of graft loss (aHR 2.70, 95% CI 2.11 to 3.46), but there were no significant associations of MCVS <96 hrs with patient or graft survival ($P=0.57$ and $P=0.95$, respectively). Results were also similar after additional exclusion of liver-kidney transplant recipients ($N=936$): mechanical ventilation >96 hrs – aHR for death 2.93 (95% CI 2.20 to 3.90) and aHR for graft loss 2.67 (95% CI 2.05 to 3.48); MCVS <96 hrs – no significant associations with these outcomes. Finally, patterns were similar among the liver-kidney transplant recipients analyzed alone: mechanical ventilation ≥ 96 hrs – aHR for death 3.58 (95% CI 1.81 to 7.07) and aHR for graft loss 3.05 (95% CI 1.55 to 6.00); mechanical ventilation <96 hrs – no significant outcomes associations.

Length of Transplant Stay according to Early Mechanical Ventilation Requirements

Length of the transplant hospitalization stay varied significantly by early mechanical ventilatory support requirement. Specifically, length of stay was longest at a median of 23.5 days in those who required mechanical ventilation ≥ 96 hrs ($P<0.0001$ vs no mechanical ventilation), 17 days in those with mechanical ventilation of unspecified duration ($P<0.0001$ vs no mechanical ventilation), and 11 days in those without early mechanical ventilation. While statistically different, the magnitude of transplant stay was similar in

those with mechanical ventilator support <96 hrs and no mechanical ventilation at 13 vs 11 days ($P=0.007$).

DISCUSSION

The epidemiology of post-operative mechanical ventilatory support has been extensively examined in the general surgical literature (3, 4), but limited information has been reported on the frequency and outcomes of mechanical ventilation early after liver transplantation. We constructed a novel linkage of national transplant registry data and Medicare billing claims to examine early mechanical ventilator support requirements in large sample of liver transplant recipients who were not receiving mechanical ventilation prior to transplantation, and observed several key findings: 1) Overall, 7% of recipients required mechanical ventilation within 30 days of living transplant, of whom 26% were classified as <96 hrs, 24% as ≥96 hrs, and 50% as unspecified. 2) Independent correlates of the need for prolonged mechanical ventilation after liver transplantation included older age, female gender, pre-transplant dialysis requirement and pre-transplant ascites. 3) After adjustment for an array of baseline recipient, donor and transplant factors recorded in the registry, mechanical ventilation ≥96 hrs was associated with nearly 3-times the adjusted risk of first-year death but mechanical ventilation <96 hrs was not significantly associated with mortality. LOS also showed graded associations with mechanical ventilation requirements, at 23.5 days among those with prolonged mechanical ventilation vs 11 days in those without mechanical ventilation. 4) The relative prognostic implications of mechanical ventilator support categories were similar for recipients of high and lower DRI transplants. However, in absolute terms, patients who received high DRI organs and required prolonged mechanical ventilation had markedly poor outcomes, with first-year patient and graft survival rates of only 55% and 50%, respectively.

A high incidence of pulmonary complications after liver transplantation has been described in some single center reports to date. For example, one series reported a high frequency of post-transplant pneumonia, although mechanical ventilator support was not specifically described (13). Short versus prolonged mechanical ventilation after liver transplant generally reflects distinct clinical scenarios. There are many reasons to electively ventilate liver transplant recipients short-term early in the post-operative setting, including lack of extubation in the operating room, hemodynamic instability, excessive blood loss, temperature dis-regulation, planned take-back, and severe coagulopathy (13). In a series by Levesque et al, the median time to extubation post liver transplantation was 11 hrs and no patients were extubated on the operating room table as a general practice pattern (13). Our findings of strong associations of prolonged mechanical ventilation with increased risks of death and graft failure in the current study, compared with no clinical impacts of short mechanical ventilation, supports prolonged mechanical ventilation as an important prognostic marker that should be the focus of clinical prevention, recognition and management protocols. In contrast, short-term mechanical ventilator support may be a component of routine care without adverse prognostic implications.

In the current study, we observed that while older age was associated with increased likelihood of both short and prolonged mechanical ventilation, additional risk factors for

prolonged mechanical ventilation included female gender, pretransplant dialysis requirement and pre-transplant ascites, while hepatitis C as cause of liver failure was associated with reduced likelihood compared with other diagnoses. Due to biases from use of serum creatinine as component of MELD score, recent studies have shown that a given MELD score in a female liver transplant recipients represents higher illness acuity compared with same MELD score in men, portending increased risk of post-operative complications (14). A recent article by Burra et al, examined the complex relationship of age, hormonal status, liver disease progression and post-operative complications among women liver transplant recipients, and found that women are on average older and have higher frailty measures at the time of transplantation (14). While we found that the need for pre-operative dialysis and pre-transplant ascites increase the risk of prolonged mechanical ventilation after transplant, receiving a combined liver-kidney transplant decreases the risk of mechanical ventilation when adjusted for other factors including dialysis. In patients with concomitant liver and kidney failure, survival advantages from transplanting both organs at the same setting as opposed to transplanting a liver alone have been shown (15). Renal recovery after liver transplantation is often unpredictable and influenced by resuscitation status, intra-operative course, the need for vasopressor support, and the use of nephrotoxic drugs such as calcineurin inhibitors. However, patients who undergo combined liver-kidney transplant may have less likelihood of needing post-operative dialysis and may have improved volume and electrolyte status (16) which in turn can reduce the risk of respiratory complications and need for mechanical ventilator support.

With regard to outcome implications of mechanical ventilation requirements, we found that while the relative impacts of mechanical ventilation were similar across strata of allograft quality, in absolute terms, patients who received high DRI organs and required prolonged mechanical ventilation had particularly poor outcomes, with first-year patient and graft survival rates of only 55% and 50%, respectively. While the decision to use high risk organs in particular patients generally weighs post-transplant risks against anticipated survival on the waiting list, our study suggest that use of high DRI organs in recipients at risk for prolonged mechanical ventilation after liver transplantation should proceed with caution and awareness by the patient and program of the potential risk of lower than average patient and graft survival. If respiratory failure develops and mechanical ventilation is required, relative prognostic implications were also similar among recipients of liver-kidney and liver only transplants.

Uncertainties regarding the optimal assessment of cardiovascular and respiratory function in potential transplant candidates have produced a wide variation in the clinical care of this population. There is still no consensus on which assessment algorithm confers the best outcomes (17). Future research should be devoted to optimizing protocols to identify and manage respiratory complications after liver transplantation, especially among patients with increased baseline risk. Finally, while liver failure can be associated with pulmonary vascular abnormalities such as hepatopulmonary syndrome and porto-pulmonary hypertension, both of which can contribute to hypoxia before and after transplantation, neither were noted to be associated with mechanical ventilation requirements in our study. This finding may be due, in part, to the low incidence of these pulmonary abnormalities recorded in the transplant registry and the exclusion of patients ventilated prior to transplant

surgery from our analysis. In the current regulatory environment of transplantation, and in the era of public disclosure of outcomes, centers are responsible for caring for their patients while mitigating risk in potential recipients in order to steward the donor organ to the best possible outcome, and to ensure program compliance and survival (1). While risk factors for prolonged mechanical ventilation are in some ways unavoidable in transplanting patients with advanced liver disease (e.g. age, gender, ascites), the use of higher risk organs can be limited to improve overall survival post-transplant. Our finding of very low patient and graft survival among recipients of higher DRI organs who experience prolonged mechanical ventilation may impact the use of these types of organs in smaller to medium sized transplant programs where one adverse patient outcome could contribute to significantly more than expected death or graft failure events, in turn leading to a citation for outcomes from regulatory bodies.

Limitations of the current study include selection of the sample as Medicare beneficiaries, which may limit generalizability to all transplant recipients. While our findings may not generalize to beneficiaries of other insurance systems, clinical studies among Medicare-insured transplant recipients are relevant as Medicare is the largest single payer for transplant services in the United States. The retrospective design is also a limitation. It is possible that future changes in clinical practice may modify the outcomes implications of early post-transplant mechanical ventilation. Baseline information was limited to variables captured in the registry and we did not have access to other clinical factors relevant to this topic such as the cause of respiratory failure or detailed descriptions of the surgical procedure (e.g., operative times, warm ischemic times, blood loss), or intraoperative volume management. These factors warrant examination in future research. It is important to emphasize that our results demonstrate associations, and cannot prove cause and effect. It is possible that the observed associations reflect worse pre-existing disease or other early complications not captured in the registry, making early mechanical ventilation a marker of aggregate risk including factors beyond respiratory failure alone.

In conclusion, this analysis of a large national cohort of liver transplant recipients demonstrates that, overall, 7% of liver transplant recipients require mechanical ventilator support within 30 days of transplantation, among whom 24% of cases are prolonged ≥96hrs. While short-duration of mechanical ventilation after liver transplantation does not portend worsened survival, ≥96 hrs of mechanical ventilation is a marker for poor post-transplant outcomes. Absolute patient and graft survival are particularly poor when prolonged mechanical ventilation occurs among recipients of high DRI organs. Development of clinical protocols aimed at identifying modifiable risk factors in recipients, and in the organs programs accept, may prevent the additive risk of respiratory failure and its accompanying morbidity, mortality and cost.

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SUMMARY

The need for post-operative mechanical ventilatory support is known to correlate with poor outcomes after complex surgical procedures. This study employs a novel linkage of transplant registry and Medicare claims data to examine the impact of post-operative mechanical ventilation on mortality and allograft loss following liver transplantation. Post-operative mechanical ventilation lasting longer than 96 hours was associated with 3-times the adjusted risks of first-year mortality and graft loss. Significant predictors of prolonged mechanical ventilation included older age, female gender, pre-transplant dialysis requirement and ascites. Recognition of patients at-risk for prolonged mechanical ventilation after liver transplant may help to reduce the incidence and consequences of this complication.

Figure 1. Patient and graft survival according to the requirement for early mechanical ventilator support after liver transplantation, by duration of mechanical ventilation and donor quality.

Figure 2.

Adjusted relative risks of death and graft loss according to the requirement for early mechanical ventilation after liver transplantation, by duration of mechanical ventilation and donor quality. *Adjusted hazards ratios (aHR) >1.0 indicate increased risk compared to reference group without MCVS, while aHRs <1.0 indicate reduced risk; whiskers denote 95% confidence intervals. Models are adjusted for recipient, donor and transplant factors summarized in Table 1.

Recipient, donor and transplant factors according to the requirement for and duration of early mechanical ventilator support after liver transplantation.

Table 1

Baseline factors	MCVS <96 hrs %	MCVS 96 hrs %	MCVS, Duration %	Unspecified %	No MCVS %
Demographic & Clinical Factors					
Recipient Age	*	*	†		
19 to 35	2	2	2		5
36 to 50	19	23	20		28
51	78	75	78		68
Recipient Female Gender	37	45*	44†		35
Recipient Race			*		
White	72	68	78		70
Black	5	9	6		9
Hispanic	18	17	12		16
Other	6	5	4		5
Primary Cause of Liver Disease		*			
Hepatitis C	30	40	32		34
Hepatitis B	4	1	2		2
Hepatocellular Carcinoma	15	9	15		16
Other	37	40	41		37
Unknown	13	10	9		10
Recipient Comorbidities					
Diabetes	34*	32*	28		25
Hypertension	22*	14	20*		16
Peripheral Vascular Disease	2	1	2		1
Previous abdominal surgery	57	57	54		52
Dialysis prior to transplantation	13	20†	9		11
ICU stay prior to transplantation	3	4	3		5
Admitted to hospital prior to transplantation	14	19	12*		15
Portal vein thrombosis	6	9	7		7
Ascites pre-transplant	86	92*	90*		85
Portal bleed 48 hours prior to transplantation	3	1	1		2

Baseline factors	MCVS <96 hrs %	MCVS 96 hrs %	MCVS, Duration Unspecified %	No MCVS %
Recipient MELD Category				
0 to 19	57	50	57	56
20 to 29	28	30	21	25
30	6	12	7	7
Unknown	9	8	16	12
Cold Ischemic Time			*	
0 to 6	32	29	28	34
6 to 9	35	36	33	34
9 to 12	16	17	16	14
>12	6	6	8	6
Unknown	11	13	15	13
Partial /Split Liver	6	3	6	4
Liver /Kidney Transplant	8	13*	3†	8
Donor Risk Index (DRI)			*	
0 to <1.2	5	4	3	6
1.2 to <1.5	26	23	24	23
1.5 to <1.8	18	18	15	19
1.8	34	40	40	37
Unknown	19	15	19	16
Donor Diabetes	8	10	7	8

Percentages indicate fractions of liver transplant recipients with the given MCVS use category who have the indicated clinical trait (column percentages). Regression models also adjusted for recipient cardiovascular disease and hepatopulmonary syndrome (not displayed due to low frequencies) P-values: * p<0.05 –0.002; † p=0.001 –0.0002; ‡ p<0.0001, for differences of distributions of clinical traits among patients in a given MCVS use category compared with no MCVS.