



The High Risk Recipient

O-9

Cardiac Evaluation Prior to Kidney Transplantation in National Practice: Are We Screening Too Often or Not Enough?

Krista L. Lentine, Mark A. Schnitzler, Daniel C. Brennan, Jon Snyder, Kevin C. Abbott, Paul Hauptman, David Axelrod, Paolo R. Salvalaggio and Bertram Kasiske.

Saint Louis University Center for Outcomes Research, St. Louis, MO

Aims: Formal evaluation for ischemic heart disease with non-invasive stress testing and/or coronary angiography is a common but un-standardized practice prior to kidney transplant. We performed a retrospective study of a large national sample of renal allograft recipients with aims to: 1) quantify the frequency of pretransplant cardiac evaluation (CE) in relation to patient characteristics; 2) quantify the yield of pretransplant CE in terms of subsequent revascularization procedures; 3) describe the risk of post-transplant myocardial infarction among patients transplanted without CE.

Methods: Data describing Medicare beneficiaries who received a kidney transplant in 1991-2004 were drawn from the United States Renal Data System. We limited the sample to 27,786 patients who also received dialysis prior to transplantation and were insured by Medicare parts A and B from dialysis initiation through transplantation. We stratified the expected risk of ischemic heart disease (IHD) based on clinical practice guidelines of the American Society of Transplantation, wherein "high risk" (N=16,029) was defined by diabetes, prior IHD, or ≥2 risk factors. 11,757 patients without these traits were classified as "lower" risk. Pretransplant CE were identified by billing claims for non-invasive stress testing and angiography submitted from dialysis initiation until transplant. We quantified the revascularization yield of CE as the number of individuals with billing claims for percutaneous coronary angioplasty or coronary artery bypass grafting between the date of CE and transplantation. Post-transplant acute myocardial infarction (AMI) events were abstracted from billing claims and death records

Results: Overall, 46.3% of patients received some form of CE, which comprised noninvasive stress tests in 40.8% and angiography in 19.4% of the sample; 13.9% of patients received both modalities. The frequency of any CE was 65.4% among the high risk and 20.4% among the lower risk groups.

According to multivariable logistic regression adjusted for an array of clinical factors, the decision to transplant without CE increased sharply with younger patient age and shorter pretransplant dialysis duration. The adjusted odds ratio for transplant without CE (aOR for no CE) was modestly increased among women compared to men (aOR 1.12), black vs. white race persons (aOR 1.39), and underweight vs. patients of other weight groups (aOR 1.36). The likelihood of forgoing CE was markedly reduced (i.e., cardiac testing was more likely) among patients with ischemic heart disease (aOR 0.21 for no CE); testing was also more likely in association with diabetes (aOR 0.48) and hypertension (aOR 0.74) as causes of renal failure, and with any single IHD risk factor. Significant regional variations in practice emerged after adjustment for patient characteristics, such that the likelihood of forgoing CE was approximately 40% higher in regions 3 and 5 compared to regions 4, 6-8, and 11. Similar patterns

were observed within sub-samples defined by clinical IHD risk group. Regardless of risk group, CE was more likely to be deferred among women, black patients, and patients in regions 3 and 5.

Overall, CE was followed by pretransplant revascularization in 9.5% of patients, but there was substantial variation in yield according to clinical risk group (Table). Whereas 11.6% of CE were followed by coronary interventions in high risk patients, revascularization was performed among <1% of evaluated low risk patients. On

Most recent CE by Test Type & Risk Group	Revascularization Procedures Following Cardiac Evaluation			Number of CE per Revascularization
	Angioplasty and/or Stent	Coronary Artery Bypass Grafting	Any Revascularization	
	Number (%)	Number (%)	Number (%)	
CE of any form				
Full cohort (N=12,876)	705 (5.5)	557 (4.3)	1,228 (9.5)	10.5
High risk (N=10,482)	701 (6.7)	554 (5.3)	1221 (11.6)	8.6
Lower risk (N=2,394)	4 (0.2)	3 (0.1)	7 (0.3)	342.0
Noninvasive Stress Test				
Full cohort (N=11,341)	254 (2.2)	174 (1.5)	411 (3.6)	27.6
High risk (N=9,120)	251 (2.7)	173 (1.9)	407 (4.5)	22.4
Lower risk (N=2,221)	3 (0.1)	1 (0.1)	4 (0.2)	555.3
Coronary angiography				
Full cohort (N=5,385)	667 (12.4)	531 (9.9)	1172 (21.8)	4.6
High risk (N=4,957)	664 (13.4)	529 (10.7)	1167 (23.5)	4.2
Lower risk (N=428)	3 (0.7)	2 (0.5)	5 (1.2)	85.6



The High Risk Recipient

average, one revascularization resulted for every 8.6 CE among high risk patients, but 342 CE were performed per revascularization in the lower risk group.

Among patients transplanted without CE, the 3-yr incidence of post-transplant AMI ranged from 3% to 10% on average within groups clinically-defined as low and high risk, respectively. Incidence also varied with individual clinical characteristics (dominantly age and cardiac disease history) within these sub-cohorts.

Conclusions: In national practice, 1) CE is more common among transplant candidates classified as “high” compared to “lower” IHD risk by traditional factors, but is not universal in the high risk group. 2) The decision to transplant without CE appears dominantly related to younger age, shorter dialysis duration and the absence of traditional risk factors. However, transplant is also more likely to proceed without CE for women, black persons, and patients in certain geographic regions. 3) Based on risk of post-transplant AMI, certain subgroups not receiving CE may also warrant additional attention and care prior to transplant. 4) Relatively low proportions of screened patients receive prophylactic coronary revascularization in recent practice. Knowledge of pretransplant CE practices may provide a framework for investigations of clinical and cost effectiveness.



The High Risk Recipient

O-10

Are Patients with Portal Vein Thrombosis High-Risk Liver Transplant Candidates?

Michael J. Englesbe, Wajeehullah Muhammad, David Ranney, Shaza Al-Holou, James Kubus, Christopher J. Sonnenday, Theodore Welling, Jeffrey D. Punch and Shawn J. Pelletier.

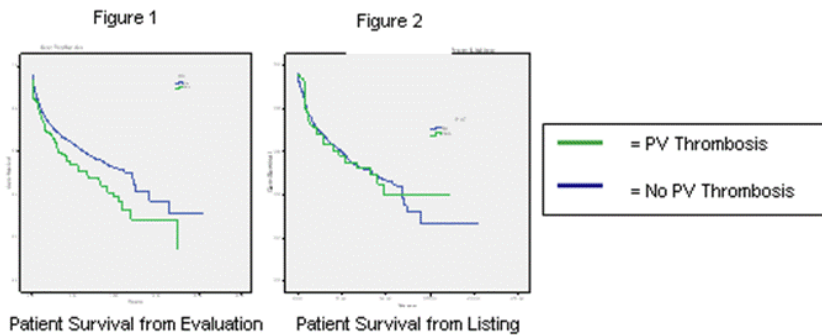
Transplant Surgery, University of Michigan, Ann Arbor, MI

Introduction: Even though patients with portal vein thrombosis are frequently given MELD exception points toward transplantation, little is known about either the pre-transplant or post transplant outcomes of patients with portal vein thrombosis.

Methods: We evaluated all chronic liver disease patients who presented for liver transplant evaluation at the University of Michigan between January 1, 1995 and March 30, 2007. For the analysis, the outcome variable was survival and the exposure variable was occlusive (not partial) portal vein thrombosis (time-dependent). Differences between patients with and without portal vein thrombosis were initially assessed using uni-variate analysis. Both Kaplan-Meier survival analysis and Cox multi-variable regression modeling were used to assess differences in survival among patients with and without portal vein thrombosis for the following time intervals: time from transplant evaluation to death, time from liver transplant listing to death, and time from liver transplant operation to death. Multivariable logistic regression was used to assess independent risk factors for mortality within one year following liver transplantation.

Results: There were 3295 patients who are evaluated for liver transplant and fulfilled inclusion criteria. There were 148 (4.5%) diagnosed with portal vein thrombosis. Patients with and without portal vein thrombosis were similar with respect to gender, race, cause of liver disease, age at evaluation, and age at transplant. Patients with portal vein thrombosis were significantly more likely to be dead at the conclusion of follow-up (54.7% vs. 37.2%, $p < 0.0001$). Patients with portal vein thrombosis had significantly worse survival from the time of evaluation (figure 1), but upon controlling for MELD, hepatitis C, age, and race, portal vein thrombosis was not independently associated with higher mortality. Patients with and without portal vein thrombosis had similar survival from time of listing (figure 2) and following transplant, and this remained true when controlling for MELD, hepatitis C, age, and race.

Conclusion: Patients with complete portal vein thrombosis are not at unusually high risk for death either while waiting for liver transplant, after listing for transplant, or post-transplant. Therefore, organ allocation policies should neither favor the ability for these patients to receive a transplant (MELD exception points), nor disfavor the opportunity for transplant.



Sunday, 1.27.08



The High Risk Recipient

O-11

Expanded Criteria Donors and Elderly Patients: Allocation and Outcomes

Dorry L. Segev, Lauren M. Kucirka and Robert A. Montgomery.

Transplant Surgery, Johns Hopkins Medical Institutions, Baltimore, MD

In the last five years, deceased donation has increased by about 20%, and most of this is attributable to increased utilization of expanded criteria donors (ECD). However, evidence suggests that many transplantable ECD kidneys are still discarded, likely because of the fear that ECD kidneys are associated with significantly increased risk of graft loss and death when compared with standard criteria donor (SCD) kidneys. However, the ECD criteria were determined by population-based studies, and we hypothesized that the adverse effects of ECD kidneys might be attenuated in elderly patients. The goal of this study was to determine the relative risk of receiving an ECD kidney versus receiving an SCD kidney, by age group. Furthermore, we investigated current patterns of listing older patients for ECD kidneys as well as the effects of such decisions on overall survival. Methods: We analyzed 44,641 adult recipients of deceased donor kidneys since 2000, of whom 6,417 were over 65. We also analyzed 21,852 patients over 65 who registered for the deceased donor list since 2000, and 8,745 patients over 65 who were still waiting for a kidney transplant on April 27, 2007. Patients who registered for the deceased donor list but subsequently received a live donor transplant were excluded from analysis. Multivariate models were adjusted for age, BMI, angina, CVD, diabetes, COPD, peptic ulcer disease, peripheral vascular disease, hypertension, diabetes, time on dialysis, type of dialysis, ethnicity, PRA, insurance coverage, hospitalization, cause of renal failure, prior transplant, and year of listing. Post-transplant survival models were also adjusted for cold ischemic time, HLA mismatch, type of storage, and donor factors as specified. Willingness to accept an ECD kidney (ECD-willing) was analyzed by multivariate logistic regression. The effect of being ECD-willing was analyzed by intention-to-treat survival analysis from the day of registration for the waiting list. Survival data were analyzed by multivariate Cox proportional hazards models. The center-level proportion of ECD-willing patients was analyzed as an interaction term in both the post-transplant and post-listing survival models.

Results: For patients aged 18-45, as expected, receiving an ECD kidney was independently associated with 58% higher risk of death when compared with receiving an SCD kidney. The risk was lower in patients aged 45-65 (adjusted hazard ratio [AHR] 1.45). For patients over 65, the risk of an ECD was modest (AHR 1.26, $p < 0.001$), and being ECD-willing offered a significant reduction in death from the time of listing (AHR 0.84, $p = 0.02$). However, only 61% of patients over 65 were ECD-willing. Center-specific listing practices were widely varied (with proportions ranging from 0% at some centers to 100% at others) but not associated with any variation in post-transplant or post-listing survival.

Conclusions: Relative to SCD kidneys, ECD kidneys do not carry the same magnitude of risk when transplanted in patients over 65 as they do in younger patients. Furthermore, older patients willing to accept an ECD kidney have significantly improved survival from the time they register for the waiting list. Further research is required to understand the wide variation in center-specific ECD listing practices for older patients.

Sunday, 1.27.08



The High Risk Recipient

O-12

Liver Transplantation in the Recipient with Extreme BMI

Andre A. S. Dick, James D. Perkins, Austin Spitzer, Catherine F. Seifert, Oren Fix and Jorge D. Reyes.

Division of Transplantation, University of Washington, Seattle, WA

Hypothesis: Patients undergoing liver transplantation at the extremes of body mass index (BMI) have increased morbidity and mortality.

Study Design: A retrospective review of the United Network for Organ Sharing (UNOS) Star Files from 1987 until 2007 revealed 73,538 adult liver transplants. 71,446 patients had follow up and accurate BMI information. Patients were stratified into the following 6 BMI categories established by the World Health Organization (WHO): underweight < 18.5 kg/m², normal 18.5-24.9 kg/m², overweight 25-25.9 kg/m², obese 30-34.9 kg/m², severely obese 35-39.9 kg/m², and very severely obese ≥ 40 kg/m². Survival rates were compared among these 6 categories using Kaplan-Meier survival curves with log-rank test.

Results: The underweight and severely obese groups had significantly lower survival than all the other groups. (Figure 1.) The survival differences were significant in all time periods of liver transplantation. There were 1,872 patients in the underweight group, 1,447 patients in the severely obese group and 68,172 patients in all the 4 other groups, which became our control group. The groups with extreme BMI (<18.5 and ≥40) were compared to our control group to assess statistically significant differences among the groups. When compared to the control group the underweight group was younger (45 years ± 13.6 vs 50.2 years ± 10.8), had a higher proportion of females (56.9% vs 36.6%), required more retransplants (21.1% vs 10.5%), had more cholestatic disease (27.8% vs 14%), had an increased rate of dialysis prior to transplantation (10.4% vs 7.3%) and showed more marked muscle wasting (45.7 vs 24.1%). The underweight group also had increased length of stay (32.5 ± 42 days vs 23 ± 35 days), increased rejection episodes in the first 6 months (43% vs 29%), and for those with failing grafts, more failed for vascular thrombosis (39.5% vs 17.2%). The severely obese group when compared to the control group had more patients with the potential of metabolic syndrome (diabetes: 27.2% vs 12.6 %) (hypertension: 22.1% vs 11.6%), had a higher incidence of encephalopathy (72% vs 59.9%) and had more ascites (87.1% vs 80.5%). At the time of discharge the severely obese group had a higher serum creatinine (1.8 ± 1.2 vs 1.4 ± 1.1) and total bilirubin level (4.5 ± 7.5 vs 3.8 ± 6.5). They also had a higher number of infection events (26.1% vs 21.5%)

Conclusion: Liver transplantation holds increased risk for patients at the extremes of BMI. Identifying these patients and instituting an aggressive nutritional regimen to optimize their nutritional status prior to liver transplantation may improve outcomes.

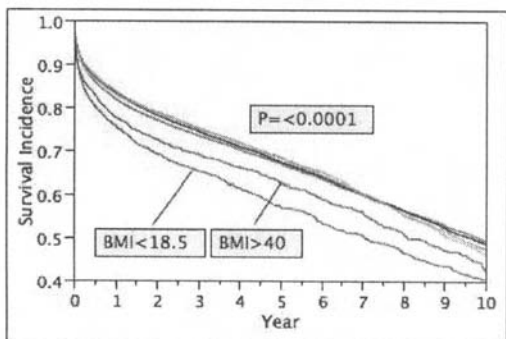


Figure 1. Patient survival



The High Risk Recipient

O-13

Combined Heart-Lung Transplantation: A Fifteen-Year, Single Center Experience

Joshua M. Rosenblum, Gosta Pettersson, Nicholas Smedira and G.V. Gonzalez-Stawinski.

Cardiothoracic Surgery, The Cleveland Clinic, Cleveland, OH

Background: Traditionally, the high-risk transplant recipient is the patient with multiple co-morbid illnesses, often related to their primary organ failure. However, patients with multiple organ failure, such as those awaiting combined heart-lung transplant, are among the riskiest in thoracic transplantation. This retrospective review details the outcomes of patients at our institution undergoing combined heart-lung transplant as a result of both heart and lung end-organ failure.

Methods: A retrospective chart review was conducted on all heart-lung transplant recipients transplanted from 1992 to 2006. Short- and long-term outcomes were collected and reported herein.

Results: Between 1992 and 2006, 12 patients underwent combined heart-lung transplant at our institution. There were 5 (41.7%) males and 7 (58.3%) females, with a mean age of 31.8 years (range, 2-53 years). The most common cause of combined organ failure was congenital heart disease (8 patients, 66.7%). All patients underwent en-bloc heart-lung transplant with the aid of cardio-pulmonary bypass. Peri-operative complications occurred in 7 (58.3%) patients with the most common being inadequate hemostasis and bleeding. Four (33.3%) patients required intra-operative extracorporeal membrane oxygenation, and one patient (8.3%) died intra-operatively due to uncontrolled hemorrhage. Post-op complications occurred in 7 (58.3%) patients with exploration for bleeding being the most common cause for re-operation. Thirty-day mortality was 25% and overall survival at last follow-up, all-cause deaths, was 50%.

Conclusion: Combined transplantation carries greater intra-operative and post-operative morbidity than most single-organ thoracic transplants, and while the patient population requiring combined heart-lung transplantation is diminishingly small, these recipients represent an important group of patients with significant illness who still benefit greatly from combined transplantation.

Sunday, 1.27.08



The High Risk Recipient

O-14

Sustained Clearance of Serum HCV RNA Predicts Long-Term Survival in Liver Transplant Patients with Recurrent Hepatitis C

Arno Kornberg, Erik Bärthel, Katharina Thrum, Olaf Habrecht, Bernadett Küpper, Jens Wilberg and Utz Settmacher.

General, Visceral and Vascular Surgery, Friedrich-Schiller-University of Jena, Jena, Germany

Background: Long-term survival after liver transplantation (LT) in hepatitis C virus (HCV) positive patients is significantly inferior compared to other indications. The establishment of an effective antiviral therapy for these high-risk recipients is therefore one of the most urging problems of transplantation in these days. The aim of this study was to determine the influence of an antiviral long-term therapy with interferon alfa 2b plus ribavirin on long-term survival in liver transplant recipients with recurrent hepatitis C.

Patients and methods: A total of 30 liver recipients with morphologically confirmed disease recurrence were included in this trial. All of them received a combined antiviral therapy consisting of interferon and ribavirin for a minimum of 12 months, followed by maintenance therapy, as long as tolerable. Allograft function and viral loads were continuously determined. Protocol allograft biopsies were performed once yearly to analyze development of necroinflammation (grading) and fibrosis (staging), according to Ishak and Knodell. The impact of several clinical (age, antiviral therapy, cold/warm ischemia, immunosuppression, BMI, allograft function) and virological (viral loads, CMV infection) factors on development of allograft fibrosis and long-term survival were analyzed using Cox regression model.

Results: Overall follow-up currently ranges between 3 and 160 months post-LT (mean: 86 mo). Sustained clearance of serum HCV RNA could be achieved in 18 patients (60%). Protocol allograft biopsies demonstrated fibrosis progression in 7 virological non-responders (66,6%), and none of recipients with loss of viremia (0%; $P < 0,001$).

Patients under persistent antiviral therapy demonstrated trend of fibrosis regression, while it increased after therapy cessation ($P = 0,003$).

Univaritely, low pretransplant viral loads, the lack of CMV infection, as well as biochemical and virological response to antiviral therapy revealed a beneficial impact on outcome ($P < 0,05$). Only antiviral treatment related sustained clearance of viremia, however, was identified as independent predictor of long-term survival ($P = 0,02$). Five-year survival in patients with sustained loss of HCV RNA was 100%, compared to 43% in recipients with persistent viremia (log rank $< 0,001$).

Conclusion: Our data clearly suggest, that an aggressive posttransplant antiviral combination therapy aiming at clearing serum of HCV RNA seems to be justified after recurrent hepatitis C, since it predicts long-term survival in this special cohort of high risk liver recipients.