

“University of Texas Southwestern Medical Center”

What Does The Kidney Have To Do With It? Renal Perspectives on Non-Renal Solid Organ Transplantation

This is to acknowledge that Mythili Ghanta, M.D. does not have any financial interests or other relationships with commercial concerns related directly or indirectly to this program. Dr. Ghanta will not be discussing off-label use in her presentation.

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Educational Objectives

- At the conclusion of this lecture the listener should be able to understand the “Devastating impact of renal dysfunction on mortality and graft loss in heart, lung and liver transplant recipients”
- At the conclusion of this lecture the listener should be able to understand the “pretransplant clinical parameters that will determine the need for kidney transplant along with heart, lung and liver transplantation and limitations of current methods of GFR assessment in pre transplant candidates”
- At the conclusion of this lecture the listener should be able to understand the “Disadvantages to the kidney alone transplant candidates from rising combined organ transplant volumes in US”
- At the conclusion of this lecture the listener should be able to understand the “Post-transplant risk factors for renal disease in heart, lung and liver transplant recipients and management”

Purpose and Overview

Renal dysfunction is an important independent predictor of mortality and graft loss in patients undergoing heart, lung and liver transplantation. Several unique pre-transplant, perioperative and post - transplant risk factors for renal disease exist in this patient population. Pretransplant renal dysfunction will need careful evaluation in potential heart, lung and liver transplant candidates and determination of need for concurrent kidney transplant remains complex. Simultaneous liver kidney and heart kidney

transplant volumes continue to rise in US which may disadvantage the kidney alone transplant recipients in the current allocation. The purpose of this presentation is to describe the prevalence, pathogenesis, risk factors and the clinical management of renal disease pertinent to heart, lung and liver transplant recipients. Evaluation of pretransplant renal dysfunction will be discussed to determine who receives a kidney transplant along with heart, lung and liver transplantation. Impact of rising combined organ transplant volumes on kidney alone transplant list will be discussed. Clinical interventions to lower the burden of renal disease after heart, lung and liver transplant recipients will be outlined.

Introduction

Increasing number of non-renal solid organ transplants are being performed in the US. Advancements in immunosuppressive protocols and post-transplant management led to improvement in long term survival of these recipients. As many more non renal solid organ transplant recipients survive well into their second and sometimes third decade of life after transplantation, their life time risk and prevalence of renal disease continues to rise. Several pre-transplant, perioperative and post - transplant risk factors for renal disease exist in this patient population. ¹Renal dysfunction remains a complex, multifaceted and critical issue as it effects a wide range of outcomes including increased cost of care, inferior graft and patient survival.

Burden of renal disease in Heart, Lung and Liver transplant recipients

Pretransplant renal dysfunction is an independent predictor of inferior patient and graft survival post heart, lung and liver transplantations. Especially when pretransplant glomerular filtration rate (GFR) drops to < 40 ml/min/m² it is associated with increased mortality after transplantation. ²Analysis of trends of acute kidney injury (AKI) in prevalent liver and heart transplant recipients utilizing a large inpatient US national database revealed a 3-fold increase in risk of AKI during hospitalizations over the past decade. Approximately 25 to 33% of hospitalizations in heart and liver transplant recipients are complicated by AKI during more recent years. This rise reflects the advancing age and comorbidity profile of the recipients receiving these transplants and remains 10 fold higher when compared to general population. ³ As we transplant older and high-risk recipients there is a need to develop transplant specific inpatient protocols to reduce the risk of AKI after heart, lung and liver transplantations. Furthermore, post-transplant immunosuppression especially calcineurin inhibitors (Tacrolimus, Cyclosporine) add to nephrotoxicity. It is a well-established fact that recurrent episodes of AKI lead to progressive chronic kidney disease (CKD) and subsequent end stage renal disease (ESRD). Specific risk factors pertinent to each phase of transplantation are included in Table 1.

Advanced chronic kidney disease (CKD) or end stage renal disease (ESRD) is the most dreaded complication in patients receiving heart, lung and liver transplantation. The most comprehensive and largest US database analysis of 70,000 non renal solid organ transplant recipients revealed that the adjusted risk of stage 4, 5 CKD and ESRD is approximately 6 to 25% at 5 years post transplantation. ⁴A third of these recipients with CKD stage 4 and 5 eventually require renal replacement therapy. Table 2 summarizes the 5-year cumulative incidence of CKD stage 4,5 and ESRD by organ type. In this study, interestingly liver transplant recipients had increased incidence of CKD compared to thoracic organ recipients despite traditionally requiring lower calcineurin inhibitor (CNI) troughs for maintenance immunosuppression, highlighting the role of variable causes of renal dysfunction independent of CNIs in these patients.

CKD in heart, lung and liver transplant recipients commonly presents with a large loss in glomerular filtration rate (GFR) in the first 6 months' post-transplant, often 30 to 50%. There after the GFR usually stabilizes or decreases more slowly.

Consequences of renal dysfunction on outcomes of Heart, Lung and Liver transplant recipients

Renal dysfunction is obviously a serious and common complication in these patients. The impact of AKI requiring renal replacement therapy involves 1-year recipient survival rate of 25-40% when compared to 1-year survival of 92% in recipients without AKI requiring renal replacement therapy. ⁵Furthermore, CKD leads to serious medical complications listed below and increases the use of health care resources.

- 4-fold increased risk of mortality
- Increased frequency of hospitalization and infections
- Challenges with drug dosing
- Increased risk of non-renal allograft dysfunction
- Uncontrolled HTN

Evaluation of pretransplant renal dysfunction

Severe renal insufficiency, GFR < 40 ml/min/m² affects 20-30% of recipients undergoing evaluation for heart, lung and liver transplantation. Fortunately, most of the renal dysfunction is functional and related to primary organ dysfunction (example hepato-renal syndrome, cardio-renal syndrome) and is reversible with heart, lung and liver transplantation alone. However, a small subset of these pretransplant candidates do have irreversible renal disease with advanced structural changes in the renal parenchyma and are at risk for progression to ESRD or advanced CKD if transplanted with heart, lung or liver transplantation alone. The renal disease when irreversible has major implications on primary organ transplant candidacy which often times may need to be deferred unless a concurrent kidney transplantation is offered. The distinction between reversible and irreversible forms of pretransplant renal disease is extremely

complex, as the current available tools to assess renal disease are not well validated and perform poorly in these pretransplant candidates. ⁶Furthermore, the ethical implications of making an incorrect distinction between reversible and irreversible forms of renal injury often times involves the risk of wasting deceased donor kidneys if potential for renal recovery is under estimated. On the other hand, if irreversible renal injury remains unrecognized it can lead to ESRD with in first year of primary organ transplantation and futility of primary organ transplant as well. In one of the largest series the cumulative incidence of renal non-recovery (meaning progression to ESRD) within first 6 months after liver transplantation was 8.9%. Diabetes, duration of renal replacement therapy pre transplant and older age are risk factors for renal non recovery. ⁷

Determination of combined organ transplant candidacy

1. Severity of pre-transplant renal dysfunction
2. Etiology of renal dysfunction
3. Duration of pre-transplant renal dysfunction

Renal function Assessment

Severity of renal dysfunction is measured by assessment of GFR. The more severe the pretransplant renal dysfunction less likely chances of renal recovery with primary organ transplantation. GFR is widely accepted as the best index of kidney function and accurate values are needed to make clinical decision. Estimated GFR based on serum creatinine is widely accepted in most clinical circumstances and is sufficient for decision making. However, in pretransplant candidates for liver, heart and lung transplantation, GFR estimates may be inaccurate due to decreased creatinine generation from the muscle. ⁸Many of these patients have decreased muscle mass, malnutrition and catabolic state leading to decreased creatinine generation. If GFR estimates are inadequate to make decision regarding primary organ transplant +/- concurrent kidney transplant, measured GFR can be helpful. Endogenous creatinine clearance measured by 24-hour urine collection is the most commonly used method, however pitfalls of this tool related to inaccuracy of timed urine collections, variable tubular secretion of creatinine needs to be considered while interpreting the results. Methods for GFR measurement utilizing urinary or plasma clearance of an exogenous filtration marker remains a gold standard tool. Plasma clearance of nonradioactive markers such as iohexol is being widely used and has been implemented for use here at UT Southwestern starting December 2017. The advantage of iohexol is the lack of radiation exposure. In general, measurement of GFR with clearance of an exogenous marker is time consuming, expensive and may not be practical to perform on all pre-transplant recipients. Furthermore, many of pre-transplant candidates are not in steady state which makes interpretation of these results difficult. In patients with ascites, effusions, edema the volume of distribution of the exogenous markers can be altered leading to inaccurate results. No single available method of assessing GFR in the pretransplant

situation is ideal. A combination of above approaches keeping in mind their inaccuracies in this clinical context will help make the best assessment.

Etiology of Pretransplant renal dysfunction

Majority of pre-transplant renal dysfunction is mediated by the hemodynamic effects on the kidney from the primary organ dysfunction (cardio-renal syndrome and hepato-renal syndrome). Classically this form of renal damage is characterized by functional renal injury which should be reversible with a new environment created by primary transplant alone (heart or liver) as there will be no major structural changes in the renal parenchyma. However, a small fraction of patients do have intrinsic renal disease such as diabetic nephropathy, HCV related glomerulonephritis unrelated to the primary organ failure, this will not be irreversible with primary organ transplantation and will need a concurrent kidney transplant.

Distinction between functional renal disease and structural renal disease in pre-transplant candidates definitively requires a kidney biopsy. Kidney biopsy however is associated with increased bleeding risks (5-10 % reported incidence) in pre-transplant candidates due to coagulopathies. Furthermore, if pre-transplant patients are critically ill it may be challenging to perform kidney biopsy. Compared to percutaneous kidney biopsy trans-jugular approach appears to be safer in-terms of bleeding risk. Clinical history and noninvasive tools such as urinalysis with microscopy are helpful but may not suggest the definitive etiology of renal dysfunction. It is recommended to quantify proteinuria while evaluating pretransplant renal dysfunction. In general, presence of > 500 mg/day proteinuria is suggestive of intrinsic renal disease.

Pichler et al reported their experience with for cause pretransplant kidney biopsies in potential liver transplant candidates with kidney dysfunction. The results of this study reveal that the clinical history often times fails to predict the etiology of actual underlying kidney disease. The most common renal pathologies identified in this study were membrano-proliferative glomerulonephritis, Ig A nephropathy and acute tubular necrosis.⁹

Duration of renal dysfunction

Renal biopsy also helps to assess the chronicity of renal disease and provides prognostic information regarding the need for concurrent kidney transplantation. Labban et al reported lack of correlation between clinical assessment and degree of chronicity on the renal biopsy in patients undergoing heart transplant evaluation with renal dysfunction. The degree of glomerulosclerosis > 30% and interstitial fibrosis > 40% predicts renal non-recovery post-transplant. Although these biopsy criteria are not listed with in current United nations organ sharing network (UNOS) guidelines for combined organ listing, they are commonly utilized in clinical practice as cut offs to determine combined organ candidacy.¹⁰

Based on a large cohort of liver transplant candidates Sharma et al designed renal risk index which predicts the chances of renal non-recovery in pre-liver transplant candidates taking into account 14 recipient variables. It offers a promising tool for pretransplant evaluation in addition to the above described assessment.¹¹

Criteria for combined liver kidney transplant listing

Table 3 shows the current combined liver kidney listing criteria mandated by UNOS, implemented as of August 2017. This is a huge accomplishment with in the past decade to standardize the practice of liver kidney transplant candidate eligibility in US. More outcomes based prospective studies utilizing the current UNOS liver kidney criteria are needed to assess post implementation utility.

Criteria for combined heart kidney transplant listing

At present, there are no nationally accepted UNOS mandated heart kidney listing criteria. This leaves the centers to form their own locally accepted criteria with in the transplant center. Described below are the UTSW combined heart kidney listing criteria.

- GFR <40 ml/min/1.73 m² more than three months in a compensated CHF state
- Nephrotic syndrome proteinuria >3.5 grams/day
- Acute kidney injury GFR<25 ml/min or requiring intermittent hemodialysis/continuous renal replacement therapy for > 6 weeks duration
- If renal biopsy is performed, minimum of two of the following criteria must be met:
 - Tubular atrophy/Interstitial fibrosis > 40%
 - Glomerulosclerosis > 40%
 - Severe arteriosclerosis
 - Diffuse glomerular pathology > 50% of the glomeruli

Lack of guidelines brings issues of heterogeneity to practice.

Combined Lung kidney transplantation

When compared to heart kidney and liver kidney transplants, very few lung kidney transplants are performed in US, likely due to the severity of illness. UNOS database analysis of 31 lung kidney transplants performed shows similar survival rates compared to lung transplant alone in carefully selected candidates and hence it is a feasible therapeutic option for select group of lung transplant candidates with significant renal dysfunction.¹² It is important however to realize that this cohort comprises of predominantly young recipients (mean age 45).

Intricacies of combined organ allocation and impact on kidney alone transplant list

Trends of combined organ transplants

With introduction of model for end stage liver disease (MELD) score into deceased donor liver allocation the number of liver kidney transplants performed in US has increased from 135 in 2000 to 730 in 2016. This has raised several concerns about utilization and practice patterns. MELD based liver donor allocation policy was introduced in Feb 2002 to achieve the goal of transplant to sickest person first. In examining MELD equation, serum creatinine has the greatest impact on the overall score, reflecting the influence of renal dysfunction on wait list mortality in liver transplant

candidates. An unintended consequence of MELD based allocation, is the rise of liver kidney transplant volumes. Similar to liver kidney transplants, between 2000-2015 the rate of combined heart kidney transplantation has increased 5 fold.¹³ This is related to expanding recipient eligibility criteria and acceptance of candidates with advancing age and higher comorbidity profile for heart kidney transplantation.

Impact of rising combined organ transplant volumes on kidney transplant alone candidate wait list

The biggest challenge facing transplant community is organ shortage. It is important to realize that with limited number of deceased donor kidneys available, rising trends of heart and liver transplants with concurrent kidney transplants means compromise in the donor pool available for ESRD patients waiting for kidney alone transplant. At the current rates of combined organ transplants performed in the US, 6 to 8% of the deceased donor kidneys will be allocated for combined organ recipients, bypassing the kidney alone candidate pool.¹⁴

In the current deceased donor kidney allocation when a patient is listed for combined organ transplant and the primary transplant organ, heart or the liver is available the kidney automatically follows the primary organ in allocation, bypassing and depriving kidney alone transplant candidates. This is justified based on the fact that the mortality rate of patients listed for combined organ transplants is much higher than the candidates waiting for kidney alone.

When wait times for combined organ candidates are compared to kidney alone transplant candidates, there is a disproportionate discrepancy in the waiting times for a kidney transplant. Typical wait time for a liver kidney or heart kidney transplant is a few weeks to months, where-as on average candidates waiting for a kidney alone transplant wait 5-10 years to receive an offer. In addition, the quality of the deceased donor kidneys allocated to combined organ transplant recipients are superior compared to kidneys allocated to kidney alone wait list (average KDPI 35 % vs 45% for combined organ vs kidney alone wait list respectively).¹⁵ All these facts raise concerns regarding equity and utility of current kidney donor allocation process. Despite receiving higher quality kidney transplants with a much shorter wait time compared to kidney alone recipients, the one-year graft survival of kidney allograft of a subgroup of high risk combined organ transplant recipients remains inferior compared to kidney alone recipients.¹⁶ Concerns regarding utilization of deceased donor kidney to their full potential are raised. The proper use of deceased donor kidneys becomes more and more important with growing kidney alone transplant wait list to > 94,000 candidates. More studies analyzing the impact of current kidney allocation practice on the outcomes of combined organ and kidney alone candidates may help answer these concerns. Identifying high risk recipient characteristics that would predict futility of combined organ transplants, would be helpful to make the maximum use of this limited resource.

Predictors of poor survival with combined organ transplantation

Based on UNOS data Russo et al have identified pretransplant predictors of poor outcomes following combined heart kidney transplantation. ¹⁷These include

1. Peripheral vascular disease
2. Recipient age > 65
3. Non ischemic etiology of heart failure
4. Dialysis dependence at the time of transplant
5. Use of left ventricular assist device as a bridge to transplant.

In heart kidney candidates with above risk factors, judicious use of transplants is warranted.

Similarly, reported equivalent kidney allograft outcomes for liver kidney and kidney transplant alone at a low MELD center justify current approach. However long-term survival of kidney allografts in liver kidney recipients significantly decreases at MELD > 23 in comparison to recipients with ESRD undergoing KT alone. ¹⁶A failed kidney allograft after combined organ transplant represents an actuarial loss of 7.2 years of life if the kidney was allocated to a patient on the kidney transplant wait list. Thus all efforts should be made to avoid performing combined organ transplant in cases where renal allograft failure is likely.

Post-transplant renal dysfunction

With improvement in long term survival of heart, lung and liver transplant candidates, more and more recipients now are surviving into second and third decade after transplantation. This increases cumulative lifetime exposure to calcineurin inhibitors (CNIs) which are the main key of maintenance immunosuppression and inevitable nephrotoxicity. In addition, several additional peri-transplant and post-transplant nephrotoxic factors come into play which could not be foreseen during pretransplant evaluation.

Etiology of renal disease in non-renal solid organ transplant recipients

Although CNIs are glaring culprits for CKD in these transplant recipients, their role is over estimated. Biopsy series reveal alternate histologic diagnosis in 25 to 30% of cases of heart and liver transplant recipients with ESRD such as hypertension, focal segmental glomerulosclerosis, diabetic nephropathy etc. Some cases have multiple histologic causes. ¹⁸ As the etiology of CKD in these patients remains fairly broad kidney biopsy will help establish an accurate diagnosis, this could help initiate specific therapies and avoidance of unnecessary dose reductions in immunosuppression. ¹⁹

CNI Nephrotoxicity

CNIs are essential post-transplant immunosuppressive agents with inherent nephrotoxicity that leads to acute functional and chronic irreversible nephrotoxicity. Generally, cyclosporine and tacrolimus have similar acute and chronic nephrotoxic effects. Although it seems logical to think that higher dose of CNI/higher concentration of CNI will be associated with increased risk of CKD a clear correlation between dose/

concentration has not been shown. This could largely be due to the fact that neither dose nor the troughs truly depict the CNI exposure.

Acute CNI nephrotoxicity is caused by intense vasoconstriction of the renal microcirculation, particularly afferent arteriole resulting in an acute reversible decrease in GFR. This acute hemodynamic insult is not immediately associated with damage to the renal parenchyma. CNI mediated renal vasoconstriction is mediated by an imbalance between vasoconstrictors and vasodilators: arachidonic acid metabolites (especially thromboxane) and endothelin. Local activation of sympathetic nervous system and effects on nitric oxide also play a role. More severe acute CNI toxicity may be associated with histological changes such as vacuolization of renal tubular epithelial cells.²⁰

Chronic nephrotoxicity of CNIs is related to increased synthesis of pluripotent cytokine transforming growth factor beta.²¹ Chronic toxicity is clinically characterized by lack of symptoms, bland urine sediment and gradual decline in renal function. Minimal proteinuria can be seen, but presence of nephrotic range proteinuria should trigger search for alternate causes. Histological features of chronic toxicity include striped interstitial fibrosis, nodular arteriolar hyalinosis and tubular atrophy and glomerulosclerosis and arteriosclerosis.

BK virus nephropathy in NRSOT

BK virus is a polyoma virus, remains latent in urothelium after exposure. Virus replication can accelerate with host immunosuppression following a sequence of viruria, viremia and interstitial nephritis. Viruria is not pathogenic, in renal transplant literature viremia with viral loads > 10,000 copies is associated with interstitial nephritis. The prevalence of BK virus nephropathy in heart, lung and liver transplant recipients is much lower when compared to kidney transplant recipients despite comparable levels of immunosuppression, the etiology of this remains unclear. As the prevalence remains low routine surveillance is not recommended, but in cases with unexplained renal dysfunction blood BK pcr can be checked.²² As glomeruli remain spared in this condition, urine sediment remains bland with minimal proteinuria. Treatment involves lowering immunosuppression which will need to be carefully done with informed discussions with primary transplant teams.

Management

Although CNIs cause nephrotoxicity, the critical need to maintain primary allograft function and prevent rejection without which survival is not possible makes it very prudent to make careful adjustments to the doses of these agents with the primary transplant providers to avoid precipitous and unsafe dose adjustments. Alternate etiologies of renal dysfunction need to be ruled out prior to reducing CNI doses. Appropriate and early management of risk factors for CKD such as hypertension, diabetes mellitus and hepatitis C will limit renal damage from these conditions. Calcium channel blockers improve GFR if added early as they theoretically reduce the degree of afferent arteriolar vasoconstriction caused by CNIs. Perioperative transplant specific protocols to minimize AKI risk will help reduce the risk.

Management of CKD Complications

Anticipate and monitor complications of CKD including anemia, bone mineral disorders, electrolyte and acid base abnormalities, hypertension, volume overload and malnutrition. At present management follows guidelines for CKD in general population, however these complications could develop in much earlier stages of CKD in transplant recipients due to comorbidity profiles.¹

Renal Replacement therapy

Kidney Transplantation after Non renal solid organ transplantation

Patients progressing to ESRD after heart, lung and liver transplantation can be managed with hemodialysis or peritoneal dialysis. Sequential kidney transplantation provides survival advantage when compared to remaining dialysis dependent. It is important to realize that there is increased perioperative mortality in the first 3 months due to surgical risk followed by a sustained survival advantage. Hence careful selection of candidates who can tolerate the increased mortality risk early on to reap the survival benefit in the long run needs to be considered during evaluation for sequential kidney transplantation.²³ Non renal solid organ transplant recipients are increasingly being listed for deceased donor kidney transplant in US and contribute to the most rapidly rising subgroup on the kidney wait list.²⁴ Shown in the Table 4 is the percentage increase in the wait listing for kidney transplant in each category of non- renal solid organ transplant recipients in US. The median survival of a previous heart, lung and liver transplant recipient listed for a sequential kidney transplant is much lower when compared to kidney alone recipient on the wait list. This reinforces the need to transplant these patients sooner, which may only be feasible if a living donor is available. A safety net policy was introduced, which allows patients who received a prior liver transplant but developed either ESRD or GFR < 20 ml/min with in first 60 -365 days after liver transplant to receive expedited access to deceased donor kidney transplant prioritizing them over the kidney alone transplant candidates. This will help preserve the outcomes of liver transplant candidates who developed ESRD with in first year of transplantation.

Conclusion

Renal dysfunction is burgeoning in heart, lung and liver transplant candidates with devastating impact on patient and graft survival. Pretransplant renal dysfunction is reversible in majority of candidates with heart or liver transplant alone. Identifying the candidates who would benefit from concurrent kidney along with liver or heart transplant is challenging as current methods of GFR assessment are not perfect in these candidates. Kidney biopsy will be helpful to make a decision regarding need for concurrent kidney transplant but is associated with bleeding risk.

Combined liver-kidney and heart-kidney transplants are “consuming” increasing number of high quality kidneys with short waiting times and this places kidney alone transplant candidates at a disadvantage under current allocation. There is a certain

amount of futility when combined organ transplants are performed in high risk recipients. These kidneys could have been used for kidney only transplant candidates raising concerns about utility and equity of current kidney allocation process. De novo kidney disease may develop after non-renal solid organ transplants. Although CNIs are an important cause of post-transplant renal disease, other potentially treatable alternative causes will need to be ruled out prior to making dose reductions to CNIs which may precipitate rejection in the primary organ. Sequential kidney transplantation after a liver or heart transplant offers survival advantage if ESRD develops but there are many hurdles to overcome with long wait times and increased wait list mortality.

Table 1

Risk factors for renal disease in heart, lung and liver transplant recipients

Pre-transplant phase	Peri-operative phase	Post-transplant phase
General CKD risk factors 1. Age 2. Diabetes 3. Hypertension 4. Hepatitis C	Hemodynamic instability	Immunosuppression 1. Calcineurin inhibitors 2. Sirolimus
Risk factors related to primary organ dysfunction 1. Hepato renal syndrome 2. Cardio renal syndrome	Aortic cross clamp: heart transplant	Organ dysfunction
Infection	Primary organ dysfunction	Diabetes
Sepsis	Infection	Infections
Bleeding	Mechanical Ventilation	
Over diuresis		
Nephrotoxins : IV contrast		

Table 2

5 year CKD stage 4/5 and ESRD risk by organ type

Organ type	5 year CKD stage 4/5 and ESRD risk
Intestine	21%
Liver	18%
Lung	15%
Heart	10%
Heart –Lung	6%

Table 3

UNOS simultaneous liver kidney listing criteria

Category
CKD (GFR < 60 ml/min for 3 months) + 1. ESRD 2. GFR < 30ml/min at listing
Acute kidney injury with 1. 6 weeks of dialysis requirement 2. GFR < 25 ml/min for 6 weeks
Systemic disease related to liver and kidney 1. Primary hyperoxaluria 2. Atypical hemolytic uremic syndrome 3. Systemic familial amyloidosis 4. Methylmalonic aciduria

Table 4

Percentage increase in the wait listing for kidney transplant in heart, liver and lung transplant recipients from 1995-2008

Recipient category	% increase in wait listing for kidney transplant
Adults with prior liver transplant	330%
Adults with prior heart transplant	307%
Adults with prior lung transplant	635%

Figure 1

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