



+

When Does Cardiovascular Disease Preclude Consideration of Renal Transplantation?



Kul Aggarwal, MD, MRCP (UK), FACC
Professor of Clinical Medicine
Division of Cardiology
University of Missouri
&
Chief, Cardiology Section
Harry S Truman Veterans Hospital
Columbia, Missouri



+ Background

- Cardiovascular (CV) disease is the major cause of mortality and morbidity in CKD patients
- 50% of patients with CKD5 have some form of CVD
- CV mortality 5 x times higher in dialysis patients
- Survival from MI is lower in Dialysis patients
- There appears to be a significant reduction in CV mortality in transplant patients more recently (more risk with higher Age, DM, impaired graft function)

Foley RN et al. *Am J Kidney Dis* 1998;32:S112-119
Herzog CA et al. *N Eng J Med* 1998. 339:799-805
Pilmore H et al. *Transplantation*. 2010;89(7):851-857. doi: 10.1097/TP.0b013e3181caee

+ High Risk Features Are Prevalent in Dialysis Patients

■ Age >60 yrs	■ 1 in 5
■ ESRD 2ndary to DM	■ 1 in 4
■ Diabetes Mellitus	■ 1 in 2
■ Hypertension	■ 1 in 12
■ Known CAD	■ 1 in 5
■ Duration of dialysis > 2 years	■ 1 in 2

Lentine KL et al; *J Am Soc Nephrol* 2005; 16: 496-506

+ Some considerations

- Trend towards older patients getting renal transplant
- Diabetes mellitus
- Coronary calcification increases with dialysis vintage, thereby increasing atherosclerotic burden and making it more difficult to perform coronary revascularization
- Renal transplantation offers better quality of life and survival

**+ CV Assessment Factors:
What are we worried about?**

- Coronary Artery Disease
- LV function
- Pulmonary Hypertension
- Valvular Heart Disease
 - Aortic stenosis
 - Mitral regurgitation
- Arrhythmias
 - Atrial fibrillation
 - Ventricular Arrhythmias

+ Atrial Fibrillation

- Medicare patients retrospectively reviewed
- 6.4% (3794) patients had AF
- Mean 4.9 years of follow-up
- All cause death 40.6% Vs 24.9%
- All cause death, ischemic stroke much higher in AF group

Am J Transplant. 2013 Jun;13(6):1566-75. doi: 10.1111/ajt.12197.
Outcomes after kidney transplantation of patients previously diagnosed with atrial fibrillation.
Lenihan CR¹

+ Risk stratification: Clinical

- Low Risk
 - Young age
 - Non-diabetic
 - No known CV disease
 - Exercise capacity > 4 METs
- High risk
 - Presence of multiple risk factors
- Very High Risk
 - Known CAD, especially multi-vessel with symptoms
 - Severe aortic stenosis

+ Overview of Data Needed

- History
 - Symptoms
 - Exercise capacity
- Echocardiogram
 - Left ventricular function
 - Regional wall motion abnormality
 - Valvular heart disease
 - PA pressure
 - Pericardial effusion
- Stress test
 - CAD

+ Various Guidelines

Source	Recommendations
2012 American College of Cardiology/American Heart Association (ACC/AHA) Scientific statement	Non-invasive testing in high risk subjects
2007 ACC/AHA	>4METs no testing <4 METs non-invasive testing
2007 Lisbon Conference	Non-invasive testing in high-risk patients
2005 NKF/KDOQI Guidelines	Annual non-invasive testing DM, CAD, prior PCI or CABG Every 2 years in other high-risk
2001 AST Guidelines Circulation 2012;126:617-63 Semin Dial . 2010 ; 23(3): 324-329. doi:10.1111/j.1525-139X.2010.00725.x.	Non-invasive for high risk Invasive and Revascularization for abnormal stress test

+ Cardiac Disease Evaluation and Management in Kidney and Liver Transplant Candidates: ACC/AHA Guidelines

Circulation 2012;126:617-63

+ ACC/AHA Guidelines

- Thorough history and physical
- Non-invasive testing in individuals with no active cardiac disease but 3 or more of the following risk factors:
 - Diabetes Mellitus
 - Prior CV disease
 - Dialysis > 1 yr
 - LVH
 - Age > 60
 - Smoking
 - HTN
 - Dyslipidemia

Circulation 2012;126:617-63

+ Prohibitive Risk

- Unstable angina or recent myocardial infarction
- Multivessel coronary artery disease, not revascularized
- Severe valvular aortic stenosis
- Congestive heart failure
- Severe LV systolic dysfunction: Low LVEF <35%

+ Very High or Prohibitive Risk

Patients with:

- recent myocardial infarction (MI) or unstable angina
- decompensated heart failure (HF)
- high-grade arrhythmias, or
- hemodynamically important valvular heart disease (aortic stenosis in particular)

are at very high risk for perioperative MI, HF, ventricular fibrillation or primary cardiac arrest, complete heart block, and cardiac death. All such patients should be optimally treated, with possible referral to a cardiologist for further evaluation and management

■ Tashiro T Eur Heart J 2014;35(35):2372

+ Echocardiography

- Reasonable to perform an echocardiogram pre-op
 - LVEF
 - Systolic and diastolic dysfunction
 - Regional wall motion abnormality
 - Valvular Heart Disease
 - PA pressure
- No evidence for or against repeated testing

+ Uremic Cardiomyopathy

- Unless explained by large MI as seen on ECG, Imaging such as nuclear scan or MRI: consider differential diagnosis of
 - Uremic cardiomyopathy as differential diagnosis along with
 - non-ischemic cardiomyopathy or
 - tachycardia induced cardiomyopathy
- Some evidence to demonstrate that LVEF may improve with more intense or more frequent dialysis
- Unless severely depressed, LVEF may significantly improve after transplantation

[Alhaj E et al. Congestive Heart Failure Volume 19, Issue 4, E40-42, 2013. DOI: 10.1111/CHF.12030](#)

+ Heart Failure and Cardiomyopathy

- Systolic and Diastolic dysfunction
- Hypertension
- AV fistula and anemia with high cardiac output state
- Volume status
- Management
 - Blunted response to medical therapy
- Implantable devices and device infections
 - Vascular access and infection challenges
 - Subcutaneous ICDs

+ Aortic stenosis

- Dialysis patients are generally "Rapid progressors"
- Mild to moderate AS should undergo yearly echocardiograms
- Non-dialysis progression rate of 0.05-0.1 cm²/year
- Dialysis patients 0.23 cm²/year
- If they do need surgical replacement of the aortic valve, KDOQI says either bioprosthetic or mechanical valve OK

KDOQI: http://www2.kidney.org/professionals/kdofi/guidelines_cvd/guide5.htm
Nephron Clin Pract. 2003;94(2):c40-5

+ Severe Aortic Stenosis

- For those that are at high risk for surgical replacement of the Aortic valve, Transcatheter Aortic Valve Implantation (TAVI or TAVR) could be considered
- Experience in Dialysis patients is limited. Higher mortality but comparable to Surgical AVR
- Experience for TAVR in Renal Transplant patients even more limited but encouraging

Catheter Cardiovasc Interv. 2016 Jun;87(7):1314-21.
doi: 10.1002/ccd.26347. Epub 2016 Mar 4.

J Renal Inj Prev. 2016; 5(1): 1-7.
Published online 2016 Jan 18. doi: [10.15171/jrip.2016.01](https://doi.org/10.15171/jrip.2016.01)
Transcatheter Aortic Valve Replacement: a Kidney's Perspective
[W Cheungpasitporn et al](#)

+ Pulmonary Hypertension

- Common in dialysis patients (more in HD, lower in PD)
- PH Mean pulmonary arterial pressure ≥ 25 mmHg
- PAH: Mean pulmonary arterial pressure ≥ 25 mmHg; PCWP < 15 mm Hg; PVR > 3 Wood Units
- Look for causes
- Left heart disease, sleep apnea, AV fistula, anemia
- Consider Right heart catheterization
- Treat cause: Sleep apnea, heart failure; ?? Vasodilator trial

PH Review: Hoepfer MM et al. J Am Coll Cardiol 2013;62:D42-50
 PH in Dialysis: Am J Kidney Dis. 2013;61(4):612-622.

+ WHO Classification of PH

Class	Definition	Conditions
I	Idiopathic, familial, and associated PAH	Connective tissue diseases, HIV, congenital heart disease, portal HTN and pulmonary veno-occlusive disease, drugs and toxins
II	PH associated with left-sided heart disease	Left-sided heart systolic dysfunction, left-sided heart diastolic dysfunction, left-sided valvular disease (mitral and/or aortic)
III	PH associated with lung diseases and/or hypoxia	COPD, interstitial lung disease, sleep apnea
IV	Chronic thromboembolic PH	Obstruction of pulmonary arterial vessels (proximal or distal)
V	PH with unclear or multifactorial causes	Dialysis-dependent CKD; several hematologic, systemic, and metabolic disorders; miscellaneous

J Am Coll Cardiol. 2013;62(25_S):. doi:10.1016/j.jacc.2013.10.029

+ Coronary Artery Disease (CAD): Challenges in Dialysis Patients

- Symptoms
 - Atypical
 - Shortness of breath
 - Dizziness
- Signs
- ECG
 - LVH with repolarization abnormality
 - Hyperkalemia, acidosis
- Cardiac Enzymes
 - Mild increase in Troponins not unusual

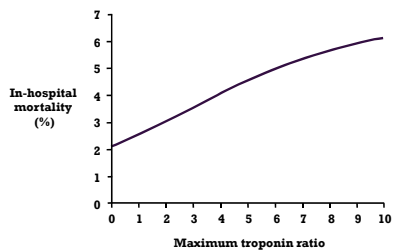
+ Cardiac Stress Testing

- Treadmill based exercise testing not feasible in many dialysis patients due to inability to exercise or marked baseline ECG abnormalities
- Cardiac MRI with stress testing has high image quality and accuracy but Gadolinium issues with fibrosis makes it not so desirable in CKD patients
- Nuclear stress testing or dobutamine stress echocardiography are generally the preferred modalities of stress testing in the dialysis population

+ Cardiac CT Coronary Angiography

- Non-invasive assessment of coronary arteries
- Requires contrast administration
- Faster scanners making it much better
- However, calcification makes it harder to evaluate the lumen of the coronary artery
- Unfortunately, most dialysis patients have significant calcification of the coronary arteries, making this promising technique not so useful in this group of patients

+ In-hospital mortality higher with any degree of troponin elevation in NSTEMI patients CRUSADE: N = 23,298



Reference limit: maximum troponin ratio 0-1x upper limit of normal
Roe MT et al. Arch Intern Med. 2005;165:1870-6.

+ Indications for Coronary Revascularization

- Symptoms/Presentation
 - STEMI
 - NSTEMI
 - Unstable Angina
 - Stable Angina
- Ischemia
- High-risk features
 - LV dysfunction
 - Diabetes mellitus
 - Large area of ischemia or multiple areas of ischemia
 - Left main or proximal LAD coronary disease

+ PCI for Stable Coronary Artery Disease: Temporal trends & Impact of DES

- Retrospective analysis of 8912 patients undergoing elective PCI between 1979 and 2006

	PTCA	Early Stents	BMS	DES	P value
Procedural success	81%	92%	96%	97%	<0.001
In-hospital mortality	1.0%	0.8%	0.1%	0.1%	<0.001
1 yr TLR	29%	26%	13%	8%	<0.001

TLR=Target lesion revascularization JACC Intv 2010;3:172-179

+ PCI or CABG in dialysis patients

- USRDS database (n= 546,160 eligible dialysis patients, 2004-2009), retrospective study identified dialysis patients who were hospitalized for their 1st coronary revascularization procedure after initiation of dialysis (n= 23,033). 6178 CABG patients, 5011 BMS patients, and 11,844 DES patients

	In-hospital Mortality (%)	1 yr all-cause survival	2 yrs	5 yrs
CABG	8.2	70	57	28
PCI DES	2.7	71	53	24

- Independent predictors of mortality were similar in both cohorts: age >65 years, white race, dialysis duration, peritoneal dialysis, and congestive heart failure, but not diabetes. Survival was significantly higher for CABG patients who received internal mammary grafts (IMG) (HR 0.83, P<0.0001)
- Conclusions: In-hospital mortality was higher after CABG but long-term survival was superior with IMGs. In-hospital mortality was lower for DES patients, but probability of repeat revascularization was higher. Revascularization decisions for dialysis patients should be individualized.

Shroff GR et al. 2013. DOI: 10.1161/CIRCULATIONAHA.112.001264

+ Pre-emptive Coronary Revascularization in Dialysis Patients

- 687 high-risk patients over 3 years
- Coronary angiography
- 184 subjects (28%) had CAD
- 16 declined revascularization
- 168 underwent revascularization
- 63.6% PCI others CABG
- 1 and 3 year survival:
 - 75% and 37% in non-revascularized
 - 98% and 88.4% post transplant in revascularized
 - Revasc and awaiting transplant 94% and 90%

Kumar N et al. Clin J Am Soc Nephrol 2011.6;1912-19

+ Coronary Revascularization

- Percutaneous Coronary Intervention (PCI) challenges
 - Calcification of coronary arteries
 - Diffuse disease
- CABG
 - Complete revascularization
 - Durability
- PCI Versus CABG
 - No mortality difference
 - Increased likelihood of repeat revascularization in PCI patients compared to CABG

+ Medical therapy

- Mostly follows along the same lines as non-dialysis population
- Weigh risk of bleeding
- Dose adjustment of medications
- Statins: continue if already on them
 - Useful in the transplant population

+ CONCLUSIONS

- Cardiovascular disease is very prevalent in the Dialysis patient
- Work-up is not straightforward.
- Choice of risk stratification of any single patient should be individualized
- Unstable angina, MI, Moderate to severe Aortic stenosis and severe LV dysfunction are high risk features
- Consider an echocardiogram in all patients being considered for renal transplant
- Stress testing is the most common form of further stratification (DSE)
- If stress test is moderately or highly abnormal, coronary angiography should be recommended
- Percutaneous coronary interventions becoming safer and more effective and trend likely to continue
- Special challenges remain in the Dialysis population

+ Thank You
