Cardiovascular Complications in ESRD and Transplant: Special Patients with Special Hearts

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OHSU Kidney Transplant
Medical Director, Portland VA Kidney Transplant

Overview

- Risk factors for coronary and peripheral vascular disease
- Special Considerations in the dialysis population
- Cardiovascular Evaluation of transplant recipients
- Transplant risk factors

Traditional cardiac risk factors

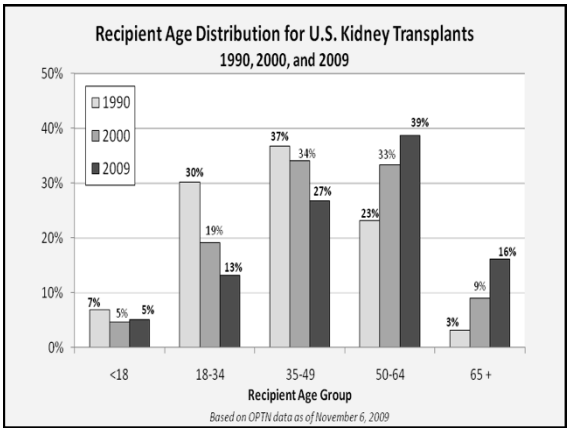
- Modifiable
  - Dyslipidemia (elevated LDL, decreased HDL)
  - Tobacco smoking
  - Hypertension and Volume status
  - Diabetes Mellitus/metabolic syndrome
  - Lack of physical activity
- Nonmodifiable
  - Advanced age
  - Male sex
  - Heredity (>44 y/o in men, >54 y/o in women)

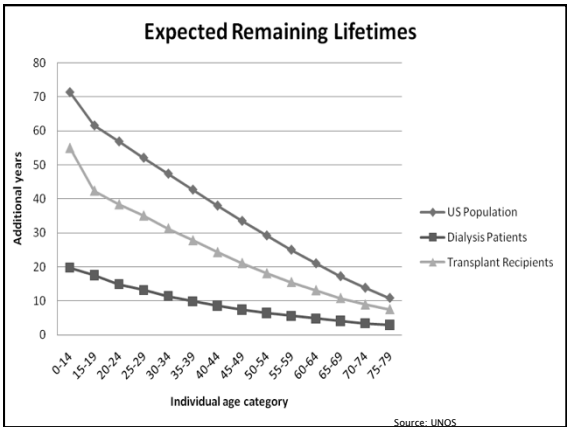
KIDNEY DISEASE?

3

AGE

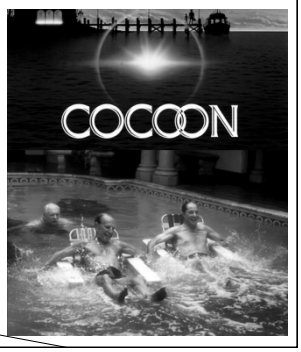
4


Recipient Age Distribution for U.S. Kidney Transplants
1990, 2000, and 2009
1990
2000
2009
50%
40%
30%
20%
10%
0%
7%
5%
5%
30%
19%
13%
37%
34%
27%
23%
33%
39%
3%
9%
16%
<18
18-34
35-49
50-64
65 +
Recipient Age Group
Based on OPTN data as of November 6, 2009

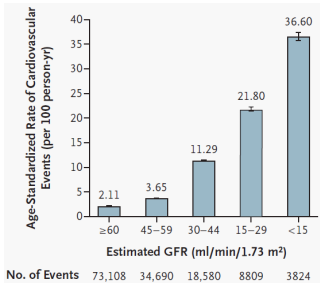

Expected Remaining Lifetimes
Additional years
80
70
60
50
40
30
20
10
0
0-14
15-19
20-24
25-29
30-34
35-39
40-44
45-49
50-54
55-59
60-64
65-69
70-74
75-79
Individual age category
US Population
Dialysis Patients
Transplant Recipients
Source: UNOS

Kidney transplant in advanced age

- No true age cut off
- Consider comorbidities and functional status
  - Morphologic age vs. chronologic age
  - Frailty
  - Neuropsychosocial status relative to ability to administer adequate self-care



Chronic Kidney Disease as a Risk Factor



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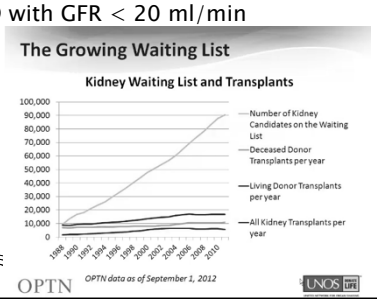
NEJM 2004;351:1296-305.

EVALUATION OF THE KIDNEY TRANSPLANT RECIPIENT

9

Indications for Renal Transplant

- ESRD on dialysis
- CKD with GFR < 20 ml/min



Transplant Complications

- Surgical
  - Vascular compromise
  - Urinary leak/obstruction
  - Wound defect/infection
- Rejection
  - Hyperacute rejection
  - Acute cellular rejection
  - Antibody mediated
  - Chronic rejection
- Recurrent and de novo kidney disease
- Infections
  - UTI/Pneumonia
  - Wound infection
  - Donor derived
  - Opportunstic infections
    - CMV, BK, PCP, fungal, etc
- Malignancy
  - PTLD, skin cancer, et al.
- Drug toxicity
- Cardiovascular disease

Contraindications to transplant

- Active ischemia or severe cardiomyopathy
- Active infection
- Active malignancy
- High probability of peri-operative mortality
- Low life expectancy
- Anatomy that makes transplantation technically impossible
- Active drug use, alcoholism, or psychosis
- High potential for medical noncompliance

Conditions that Increase the Risks of Transplantation

- Significant cardiac disease
- Significant pulmonary disease
- Significant gastrointestinal disease
- Severe vascular disease
- Advanced Age
- Obesity
- Significant potential for recurrent disease
- Psychosocial / Financial limitation leading to inadequate follow up care

Physician History

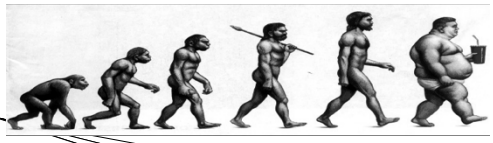
- Cause of kidney disease
  - Biopsy
- ESRD management (dialysis prescription)
- Medical Comorbidities
- Prior abdominal or urologic surgeries
- Urine output
- Renal infections/UTIs
- Family Hx
  - Diabetes, kidney disease, h/o CVA if PCKD
- Sensitizing events (blood transfusion, pregnancy, prior transplant)
- History of viral infections (HSV, Chickenpox, zoster)
- Functional status

Physical Exam

- Transplant specific focus
  - Cardiovascular
    - Carotid and abdominal bruits
    - Aortic disease
    - Femoral and pedal pulses
  - Diabetes: ulcers
  - Kidney size (PCKD)
  - GU exam
  - Functional status

Obesity in Renal Transplant

- Obesity with increased risk for:
  - Graft loss
  - Delayed graft function
  - DVT
  - Wound dehiscence
  - Wound infection



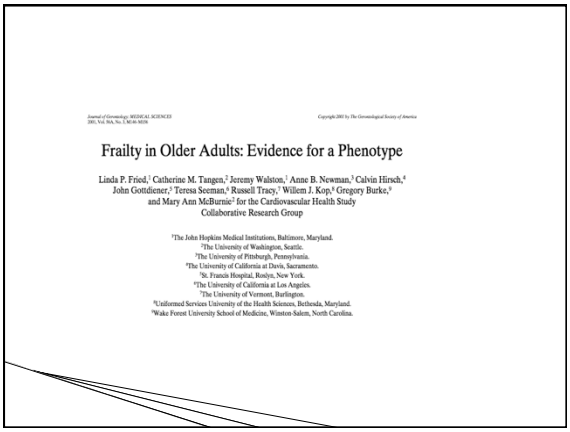
Transplant Selection Conference

Transplant Selection Conference

- Members of transplant team present
  - Transplant Surgeons
  - Transplant Nephrologists
  - Nurse coordinators
  - Social worker
  - **Renal Transplant nutrition specialist**

Transplant Nutrition Specialist

- Assess current nutrition needs as the relate to ESRD and diabetes
- Educate patients on major macro, micro nutrients and recommended nutrient goals pre transplant.
- Educate patients on herbal supplements and relation to immunosuppression.
- Assessment of Frailty



Journal of Gerontology: MEDICAL SCIENCES
2001, Vol. 56A, No. 3, M146-M156

Frailty in Older Adults: Evidence for a Phenotype

Linda P. Fried,[1] Catherine M. Tangen,[2] Jeremy Walston,[1] Anne B. Newman,[3] Calvin Hirsch,[4] John Gottdiener,[5] Teresa Seeman,[6] Russell Tracy,[7] Willem J. Kop,[8] Gregory Burke,[9] and Mary Ann McBurnie[2] for the Cardiovascular Health Study Collaborative Research Group

[1]The John Hopkins Medical Institutions, Baltimore, Maryland.
[2]The University of Washington, Seattle.
[3]The University of Pittsburgh, Pennsylvania.
[4]The University of California at Davis, Sacramento.
[5]St. Francis Hospital, Roslyn, New York.
[6]The University of California at Los Angeles.
[7]The University of Vermont, Burlington.
[8]Uniformed Services University of the Health Sciences, Bethesda, Maryland.
[9]Wake Forest University School of Medicine, Winston-Salem, North Carolina.

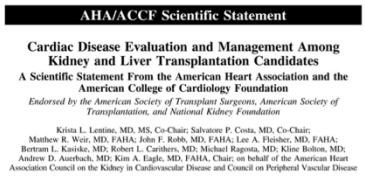
Frailty Assessment

- Shrinking.
- Hand Grip Strength using hand dynamometer.
- Physical Activity.
- Walking Speed based on Sex.
- Exhaustion.

Transplant Selection Conference

- Review H+P, chart, reports, labs, radiology results, all evaluations
- Identify risk factors for transplant
- Determine candidacy for transplant
  - Acceptable and able to list on kidney transplant list
  - Further work up required
  - Not acceptable for transplant

Cardiovascular Disease



AHA/ACCF Scientific Statement

Cardiac Disease Evaluation and Management Among Kidney and Liver Transplantation Candidates

A Scientific Statement From the American Heart Association and the American College of Cardiology Foundation

Endorsed by the American Society of Transplant Surgeons, American Society of Transplantation, and National Kidney Foundation

Krista L. Lentine, MD, MS, Co-Chair; Salvatore P. Costa, MD, Co-Chair; Matthew R. Weir, MD, FAHA; John F. Robb, MD, FAHA; Lee A. Fleisher, MD, FAHA; Bertram L. Kasiske, MD; Robert L. Carithers, MD; Michael Ragosta, MD; Kline Bolton, MD; Andrew D. Auerbach, MD; Kim A. Eagle, MD, FAHA, Chair; on behalf of the American Heart Association Council on the Kidney in Cardiovascular Disease and Council on Peripheral Vascular Disease

Circulation 2012;126:617-63

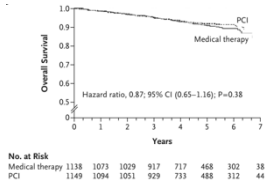
Cardiovascular Risk Stratification

- Points to consider:
  - ESRD from Diabetic Nephropathy = **Coronary Risk Equivalent**
  - Cardiovascular events are **THE** major cause of morbidity and mortality in ESRD and after transplant

Goals of Risk Stratification

- Reduce Cardiovascular Morbidity / Mortality
  - Benefit > harm
  - Actionable outcome of + test
- Exclude patients at exceptionally high risk

Courage Trial – K-M Survival Curve



N Engl J Med 2007;356:1503-16.

BARI 2D – K-M Survival Curve

COURAGE (2007) and BARI 2D (2009) made a strong case against routine revascularization via PCI for stable coronary disease

N Engl J Med 2009;360:2503-15.

Accuracy of non-invasive testing in ESRD Patients

Table 5. Accuracy of Noninvasive Testing for Detection of Coronary Artery Stenosis in End-Stage Renal Disease Patients

Authors, Year	Study Population	n	Stress Test	Endpoint	Endpoint Prevalence	Sensitivity	Specificity	PPV	NPV
Marwick et al[61]	100% KT candidates Mean age 49±11 y 56% had diabetic nephropathy	45	Dipyridamole thallium SPECT	CAS >50% CAS >70%	0.42 0.31	0.37 0.29	0.73 0.68	0.50 0.29	0.61 0.68
Boudreau et al[64]	100% KT candidates 100% had diabetes mellitus	80	Dipyridamole thallium	QCAS >70%	0.53	0.86	0.79	0.82	0.83
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		35	Exercise thallium	CAS >50% CAS >75%	0.46 0.40	0.44 0.50	0.63 0.67	0.50 0.50	0.57 0.67
Dahan et al[66]	HD for 6 mo, no overt CAD Mean age 54±11 y 23% had diabetes mellitus	60	Dipyridamole/exercise thallium SPECT	CAS >70%	0.22	0.92	0.89	0.71	0.98
Herzog et al[67]	100% KT candidates Mean age 51±11 y 79% had diabetic nephropathy	50	DSE	QCAS >50% QCAS >70% CAS >75%	0.54 0.24 0.32	0.52 0.75 0.75	0.74 0.71 0.76	0.70 0.45 0.60	0.57 0.90 0.87
Wortsley et al[68]	100% KT candidates Mean age 50±9 y 70% had diabetes mellitus	40	Exercise/pacing tetrofosmin nuclide imaging	CAS >70%	0.38	0.87	0.88	0.81	0.92
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Sharma et al[70]	100% KT candidates Mean age 52±12 y 39% had diabetes mellitus 55% were on dialysis	125	DSE	CAS >70%	0.29	0.89	0.94	0.86	0.95
Ferreira et al[71]	100% KT candidates Mean age 52±9 y 27% had diabetic nephropathy	148	Dobutamine/atropine echocardiography	CAS >50% CAS >70%		0.53 0.71	0.87 0.85		

Circulation 2012;126:617-63

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Circulation 2012;126:617-63

Cardiovascular Risk Stratification

- Consider non-invasive testing in candidates with no active cardiac disease on the basis of risk factors (≥3) regardless of functional status
  - DM, prior CV disease, dialysis > 1 year, LVH, age > 60, smoking, HTN, dyslipidemia

Circulation 2012;126:617-63

OHSU Transplant Program Approach

- Non invasive stress testing for patients with:
  - Prior cardiovascular disease
  - Peripheral vascular disease/cerebrovascular disease
  - Diabetes
  - Age > 45 (men) or > 50 yo (women)
  - Symptoms consistent with cardiovascular disease
- Cardiology evaluation for patients with positive stress test

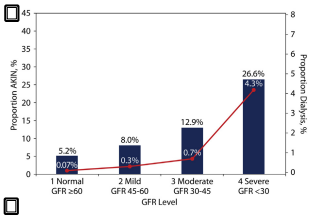
What to do with a positive stress test?

- Coronary Angiography recommended
- Consider risk factors and functional status
  - Poor pre-transplant functional status associated with decreased post transplant survival

Complications from diagnostic angiography

- Overall risk of a major complication is less than 2%
  - Death 0.11%
  - Myocardial infarction 0.05%
  - Stroke 0.07%
  - Vascular complication 0.43%
  - Contrast reaction 0.37%
  - Hemodynamic complication 0.26%

Incidence of AKI or dialysis stratified by severity of chronic kidney disease



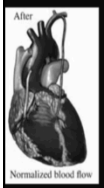
J Am Coll Cardiol Intv 2014;7:1–9.

Appropriate Use Criteria, Diabetes

Appropriate Use Score (1–9)		Asymptomatic				Ischemic Symptoms			
		Not on AA Therapy or With AA Therapy		Not on AA Therapy		On 1 AA Drug (BB Preferred)		On ≥2 AA Drugs	
Indicat		PCI	CABG	PCI	CABG	PCI	CABG	PCI	CABG
Patients Undergoing Renal Transplantation, Diabetes Present									
48.	■ One- or two-vessel CAD, no proximal LAD involvement, with low-risk noninvasive findings	M (5)	A (9)	M (4)	A (9)	M (5)	M (6)	A (7)	M (6)
49.	■ One- or two-vessel CAD, no proximal LAD involvement, with intermediate- or high-risk noninvasive findings	M (5)	M (4)	M (5)	M (4)	M (6)	M (6)	A (7)	A (7)
50.	■ One- or two-vessel CAD, including proximal LAD, with low-risk noninvasive findings	M (5)	M (5)	M (5)	M (6)	M (5)	A (7)	A (7)	A (7)
51.	■ One- or two-vessel CAD, including proximal LAD, with intermediate- or high-risk noninvasive findings	M (6)	M (6)	M (6)	A (7)	M (6)	A (7)	A (7)	A (8)
52.	■ Left main and/or three-vessel disease, with intermediate- or high-risk noninvasive findings (e.g., SYNTAX >22)	M (6)	A (8)	M (6)	A (8)	M (6)	A (8)	A (7)	A (9)
53.	■ Left main and/or three-vessel disease, with intermediate- or high-risk noninvasive findings (e.g., SYNTAX >22)	M (5)	A (8)	M (5)	A (8)	M (5)	A (9)	M (5)	A (9)

JACC 2017;69(17):2212–41.

AHA/ACC Recommendations for Revascularization Prior to Renal Transplant

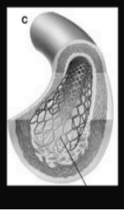


Recommendations

Coronary revascularization before transplantation surgery should be considered in patients who meet the criteria outlined in the "2011 ACCF/AHA Guidelines for Coronary Artery Bypass Graft Surgery" (*Class I; Level of Evidence B*). It is

tation candidates, the risk of coronary revascularization may outweigh the risk of transplantation and these risks must be weighed by the multidisciplinary transplantation team on a case-by-case basis until further studies are performed in this population.

2. CABG is probably recommended in preference to PCI to improve survival in patients with multivessel CAD and diabetes mellitus (*Class IIa; Level of Evidence B*).
3. CABG to improve survival and/or to relieve angina despite optimal medical therapy may be reasonable for patients with ESRD with significant (>50%) left main stenosis or significant (≥70%) stenoses in 3 major vessels or in the proximal left anterior descending artery plus 1 other major vessel, regardless of left ventricular systolic function (*Class IIb; Level of Evidence B*).
4. It is not recommended that routine prophylactic coronary revascularization be performed in patients with stable CAD, absent symptomatic or survival indications, before transplantation surgery (*Class III; Level of Evidence B*).



TRIVIA!

37


Northwest
What Important event took place in 1959?
Fidel Castro comes to power in Cuba after Revolution with the first communist state in the west
Hawaii becomes the 50th US State
First Kidney Transplant at OHSU
Barbie Doll is launched
All of the above
Start the presentation to see live content. Still no live content? Install the app or get help at PollEv.com/app


OHSU
Celebrating 60 Years of Kidney Transplantation at OHSU
Saturday, September 28, 2019
Robertson Life Sciences Building
Portland, Oregon

How would you rate the quality (sensitivity) of non-invasive cardiac testing in ESRD patients?

Good

Fair

Lousy

Start the presentation to see live content. Still no live content? Install the app or get help at PollEv.com/app

Over the past 30 years, which age group has witnessed the highest rate of increase in kidney transplantation?

18-34

35-49

50-64

65+

Start the presentation to see live content. Still no live content? Install the app or get help at PollEv.com/app

Aortic Valve Disease

Recommendation

1. It may be reasonable to consider ESRD patients with moderate aortic stenosis to be equivalent to demonstrated "rapid progressors" who warrant a yearly echocardiogram and monitoring for early symptoms (*Class IIb; Level of Evidence C*).

Valvular Heart Disease

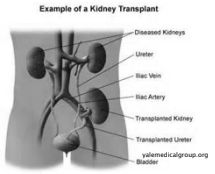
Rate of aortic stenosis progression:

- Non-dialysis: 0.05-0.1 cm^2/yr
- Dialysis: 0.23 cm^2/yr

Am J Kidney Dis 2005; 45 (Suppl 3):S1-153

Peripheral Vascular Disease

- Evaluate pelvic vessels in patients with history of claudication or diminished pulses
  - Pelvic plain film -> non contrast CT scan
  - Identify targets for renal anastamosis

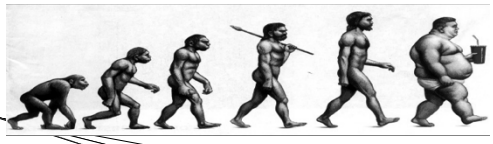


Peripheral Vascular Disease

- Carotid doppler for pts with h/o CVA/TIA or carotid bruit
- MRA brain for pts with Polycystic kidney disease to evaluate for aneurysm
  - Pts with neurologic sx
  - Pts with family history of CVA or sudden death
  - Avoid gadolinium

Obesity in Renal Transplant

- Obesity with increased risk for:
  - Graft loss
  - Delayed graft function
  - DVT
  - Wound dehiscence
  - Wound infection



Waitlist Updates

Transplant Readiness: Follow-up On-Site Evaluations

To be certain that a patient remains ready for transplant if called in, periodic on-site evaluation will be required. The frequency of these visits will be determined by age and risk factors

Patient Group / Criteria	First Cardiac Testing Update[1]	Additional Cardiac Update Testing[2]	Functional Assessment[1]	Clinic Visit[1]	Update Testing[1,3]	Social Work Consult[3]
Low Risk						
Men<45, Women<50, no history	None	None	Q 24 mo	1st visit at 24 mo. After 1st visit, Q 48 mo	Q 24 mo	Q 12 mo
Moderate Risk						
Men ≥45yo, Women≥50yo; or Abnormal EKG suggestive of ischemia	Q 24 mo	Q 24 mo	Q 12 mo	1st visit at 24 mo. After 1st visit, Q 48 mo	Q 24 mo	Q 12 mo
History of cardiovascular disease, peripheral arterial or vascular disease, or cerebrovascular disease.	Q 12 mo	Q 24 mo	Q 12 mo	Q 24 mo	Q 24 mo	Q 12 mo
Diabetics / History of diabetes	Q 12 mo	Q 12 mo	Q 12 mo	Q 24 mo	Q 24 mo	Q 12 mo
High Risk						
Age ≥70 or multiple comorbidities as defined at Committee Review	Q 12 mo	Based on above protocol	Q 12 mo	Q 12 mo	Q 24 mo	Q 12 mo

Hyperlipidemia

Dyslipidemia in the Transplant Recipient
Definitions and Prevalence

Dyslipidemia	Level (mg/dl)	Prevalence (%)
Total Cholesterol	> 200	51-97
LDL Cholesterol	> 100	72-97
Triglycerides	> 150	36
HDL Cholesterol	< 40	14-48

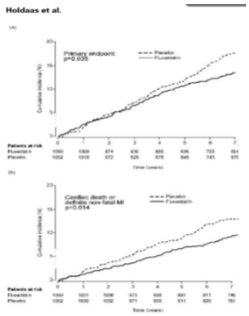
Kasiske B, et al. *Am J Transplant.* 2004
Kasiske BL, et al. *J Am Soc Nephrol.* 2000

Hyperlipidemia in Kidney Transplant

- Risk Factors:
  - Obesity, Corticosteroids, Tacrolimus, diuretics, B-blockers, DM, proteinuria
- Beneficial Effects of Statins:
  - Decrease lipid levels, reduce systemic inflammation, increase insulin sensitivity, anti-oxidant effects, enhance endothelial function, immunomodulatory?

ALERT Trial

- 74% Fluvastatin pts had reduced LDL
- Reduced risk of MACE and cardiac death and nonfatal MI
- Statin doses in existing trials are low (simva 10); benefits and harms of higher doses are unknown
- Mortality benefit has not been demonstrated to date



Pearls of Lipid MGMT

- Check at 6 mo, then every year after XP
- MYOPATHY: r/f = elderly, hi dose, low GFR, other P450 inhibitors
  - Least myopathic: Atorva, prava, fluva
- Start with low dose (convert to low at transplant) due to r/o rhabdo
- Caution with high dose Rosuva (proteinuria)
- Consider ezetimibe in treatment failure

Summary

- Diabetic Nephropathy is a coronary risk equivalent
  - Aspirin, statin, Beta blocker
- Dialysis patients, and by extension transplant patients, are at higher risk of CAD c/w general population
- Few studies to validate the proper workup for cardiovascular disease
- Nutritionist plays a major role on the care and evaluation of ESRD patients as they await transplant