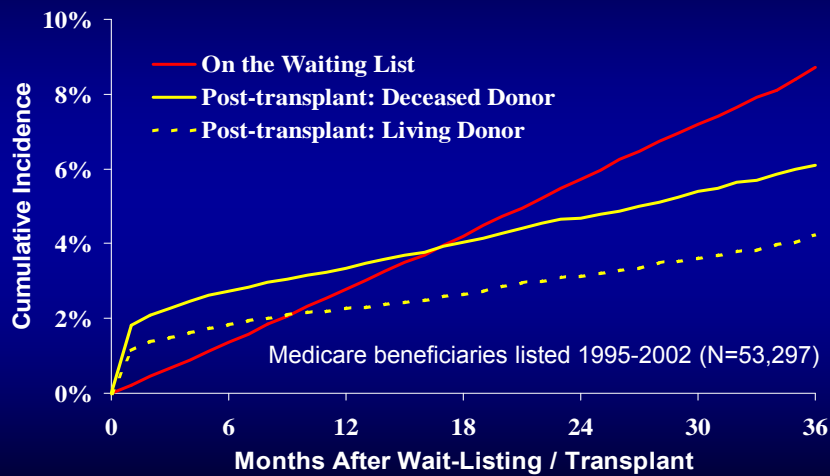


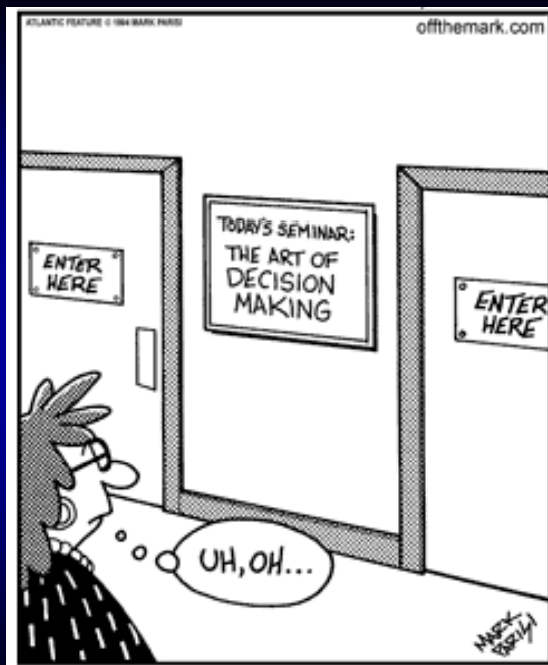
Screening and Management of Pre-Transplant CVD

AMI: Waiting List v. Transplantation

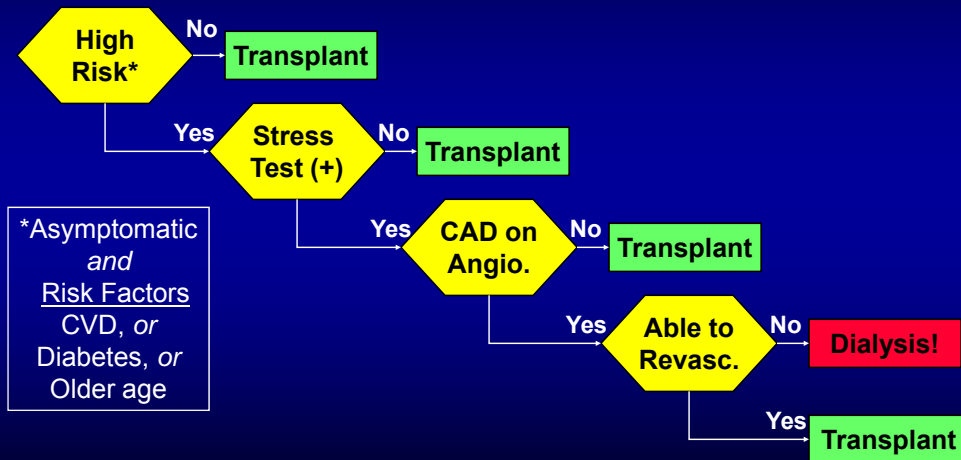


Kasiske et al, *JASN* 2006; 17:900

Should we screen patients for CAD prior to transplantation?



Standard Pre-Transplant Screening



Do noninvasive stress tests predict who has CAD lesions amenable to revascularization?

Prognostic Value of Stress Testing in Patients Assessed for Kidney Transplantation

	RR for MI in 8 Studies	RR for Cardiac Death in 12 Studies
Postitive Test*	2.7 (1.3-6.0)	2.9 (1.7-5.1)

*Myocardial perfusion studies and dobutamine stress echocardiography.

CG Rabbat, et al. *J Am Soc Nephrol* 2003; 14:431

Pre-Transplant Prediction of >70% Lesions

Study	Diab	N	Test	CAD	Sens	Spec	PPV	NPV
Marwick 1990	56%	45	MPS	31%	0.29	0.68	0.29	0.68
Boudreau 1990	100%	80	MPS	53%	0.86	0.79	0.82	0.83
Vandenberg 1996	100%	41	MPS	39%	0.63	0.76	0.63	0.24
Vandenberg 1996	100%	35	MPS	40%	0.50	0.67	0.50	0.67
Dahan 1998	23%	60	MPS	22%	0.92	0.89	0.71	0.98
Herzog 1999	78%	50	DSE	32%	0.75	0.76	0.60	0.87
Worthley 2003	78%	40	MPS	38%	0.87	0.88	0.81	0.92
de Lima 2003	--	89	DSE	38%	0.44	0.87	0.53	0.60
de Lima 2003	--	102	MPS	23%	0.35	0.76	0.72	0.68
Sharma 2005	39%	125	DSE	29%	0.89	0.94	0.86	0.95
Ferreira 2007	27%	148	DSE	--	0.71	0.85	--	--
Mean	67%	74	--	35%	0.66	0.80	0.65	0.74
Median	78%	60	--	35%	0.71	0.79	0.67	0.76

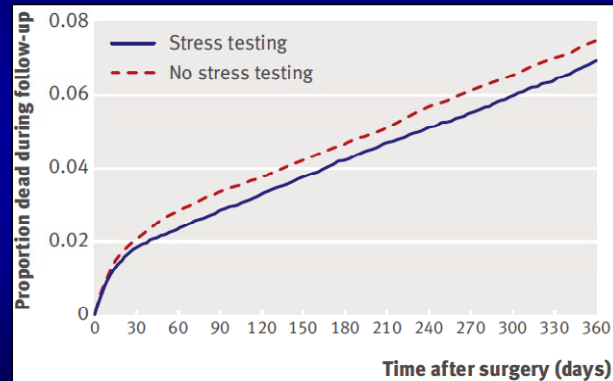
Pre-Transplant Prediction of >70% Lesions: MPS versus DSE

Study	Diab	N	Test	CAD	Sens	Spec	PPV	NPV
Mean	48%	103	DSE	33%	0.70	0.86	0.66	0.81
Median	39%	107	DSE	32%	0.73	0.86	0.60	0.87
Mean	76%	58	MPS	35%	0.63	0.78	0.64	0.71
Median	89%	45	MPS	38%	0.63	0.76	0.71	0.68

**Do screening and
revascularization lead to
better outcomes?**

Non-Invasive Cardiac Stress Testing before Elective Major Non-Cardiac Surgery

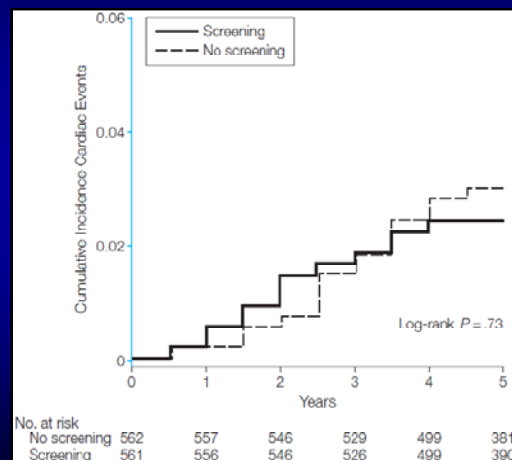
Acute care hospitals in Canada
1994-2004
Population (N=271,082):
Age ≥ 40
Elective non-cardiac surgery
Intermediate to high risk
23,991 (8.9%) underwent testing



DN Wijeyesundera, et al. *BMJ* 2010; 340:b5526

The Detection of Ischemia in Asymptomatic Diabetics (DIAD) study

1123 asymptomatic patients
Type 2 diabetes
Age 50-75
Enrolled 2000-2007
Randomized to MPS screening
Primary Endpoint: Death or AMI
(2.9% in 4.8 years of follow-up)



DIAD Study Group *JAMA* 2009;301:1547

Optimal Medical Therapy with or without PCI for Stable Coronary Disease

COURAGE
2,287 patients with CAD
Randomized to PCI
Post hoc analysis:
320 with eGFR<60 mL/min/1.73m²

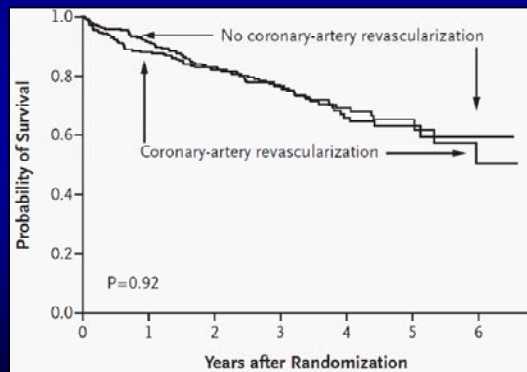
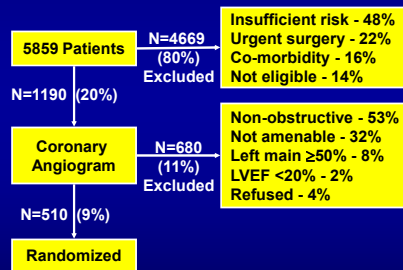
Primary end point predictors (Cox regression analysis)

Variable	HR (95% CI)	p Value
Percutaneous coronary intervention versus optimal medical therapy	1.05 (0.09–1.16)	0.36
Chronic kidney disease	1.48 (1.15–1.90)	0.002
Age (per year)	1.01 (1.00–1.02)	0.05
Men	1.27 (1.09–1.48)	0.003
Race/ethnicity (white)	1.01 (0.87–1.16)	0.94
Previous myocardial infarction	1.21 (1.09–1.35)	<0.001
No. of diseased vessels	1.26 (1.10–1.45)	0.001
Left ventricular ejection fraction	0.99 (0.98–0.99)	0.04
Diabetes mellitus	1.21 (1.09–1.34)	<0.001
Veterans Affairs	1.26 (0.91–1.74)	0.17
Canadian	0.88 (0.63–1.22)	0.43
Previous coronary artery bypass grafting	1.12 (0.97–1.29)	0.14

No interactions of above variables with treatment were significant (lowest p = 0.06).

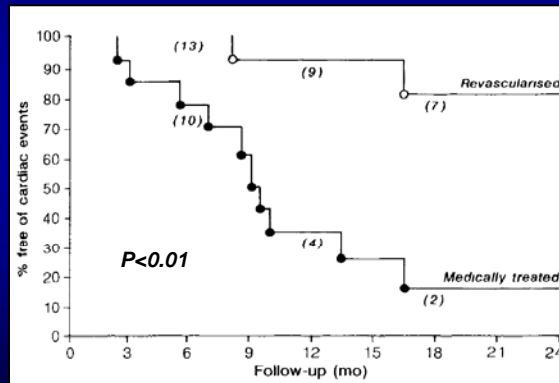
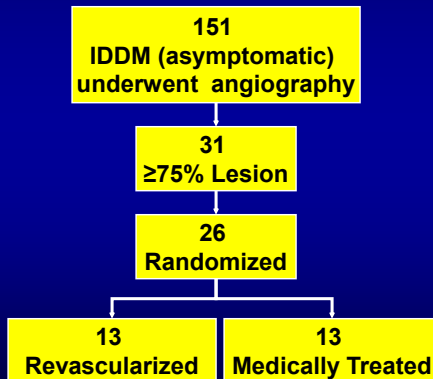
JA Seldis, et al. *Am J Cardiol* 2009;104:1647

Coronary Revascularization before Elective Major Vascular Surgery



EO McFalls, et al. *New Eng J Med* 2004; 351:2795

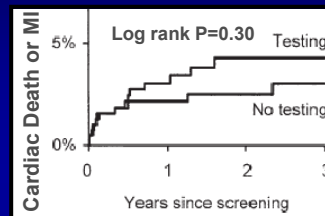
Coronary Revascularization in IDDM Patients with Chronic Renal Failure



CL Manske, et al. *Lancet* 1992; 340:998

Dutch Echocardiographic Cardiac Risk Evaluation Applying Stress Echo Study (DECREASE II)

770 elective non-cardiac vascular surgery
 All had 1 or 2 risk factors
 All had beta-blocker therapy (heart rate 60-65)
 Of 386 randomized to testing
 12 (3.1%) were revascularized



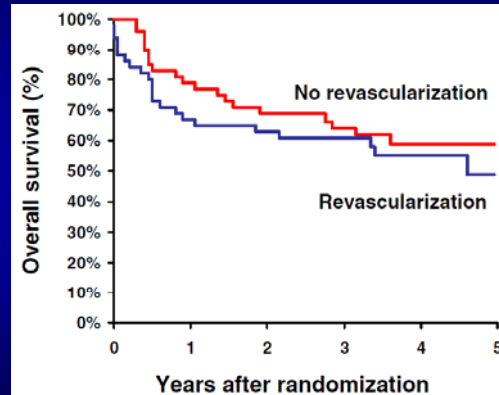
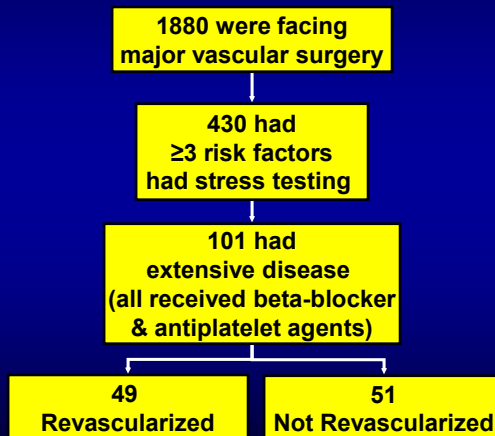
Outcomes at 30 Days

	All-Cause Death	Cardiac Death	MI	Cardiac Death or MI*
Testing N=386	15 (3.9%)	6 (1.6%)	7 (1.8%)	9 (2.3%)
No testing N=384	8 (2.1%)	2 (0.5%)	5 (1.3%)	7 (1.8%)

*Primary endpoint = Cardiac Death or MI at 30 days

D Poldermans, et al. *J Am Col Cardiol* 2006; 48:964

Dutch Echocardiographic Cardiac Risk Evaluation Applying Stress Echo Study (DECREASE V)



D Poldermans, et al. *J Am Coll Cardiol* 2007;49:1763
O Shouten, et al. *Am J Cardiol* 2009;103:897

Proportion Screened Who Underwent Pre-Transplant Revascularization

3.2% (3/95)

MS Lewis, et al., *Am J Cardiol* 2002; 89:847

2.9% (5/174)

AD Patel, et al., *Am J Cardiol* 2003; 92:146

9.0% (26/290)

BL Kasiske, et al., *Transplantation* 2005; 80:814

5.7% (17/300)

RK Patel *Am J Transplant* 2008; 8:1673

6.2% (40/644)

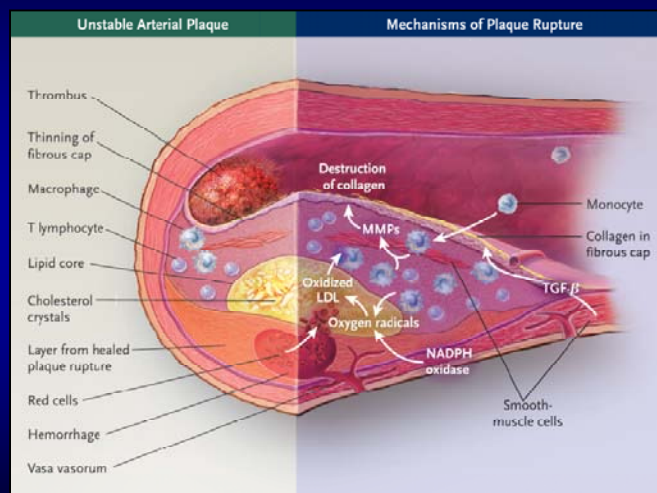
LJ Hickson *Am J Transplant* 2008;8:2352

9.5% (1,228/12,876)

KL Lentine, et al., *CJASN* 2008 3:1115

Should we be surprised if screening and preemptive revascularization don't improve outcome?

Role of Plaque Rupture in CAD Events



DD Heistad. *New Engl J Med* 2003; 349:2285

What do guidelines say?

Guidelines for CAD Screening and Prevention

AST 2001

High-risk → stress test
Diabetes
Prior IHD
≥2 traditional risk factors
Positive test → anigography
Critical lesions → revascularize

Am J Transplant 2001;1:S3

KDOQI 2005

Annual stress tests in wait-listed patients who have:
Diabetes
Prior IHD, PVD or EF≤40%
≥2 traditional risk factors

Am J Kidney Dis 2005;45:S1

AHA/ACC CABG 2004

Class I
Significant left main stenosis
Left main equivalent
3 vessel disease, esp. if LVEF<50%
Class IIa
Can be beneficial in proximal LAD
with 1-2 vessel CAD

Circulation 2004;110:e340

AHA/ACC 2007

Intermediate Risk Surgery
≥1 Risk Factor

No Symptoms
Functional Capacity ≥4 METS

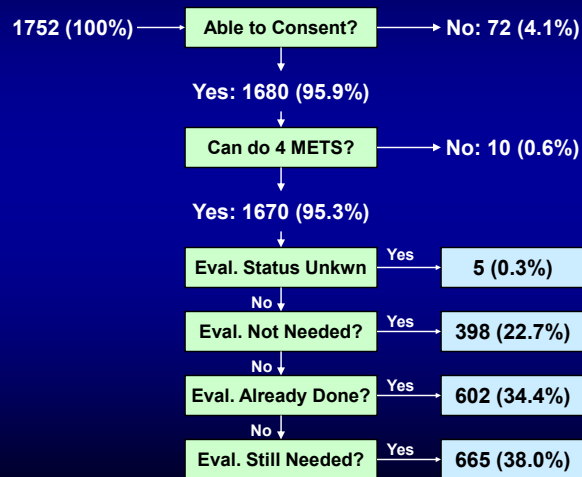
Yes
Proceed to Surgery

No/Unknown
Surgery with HR Control
Stress testing "if it will change
management" (Class IIb)

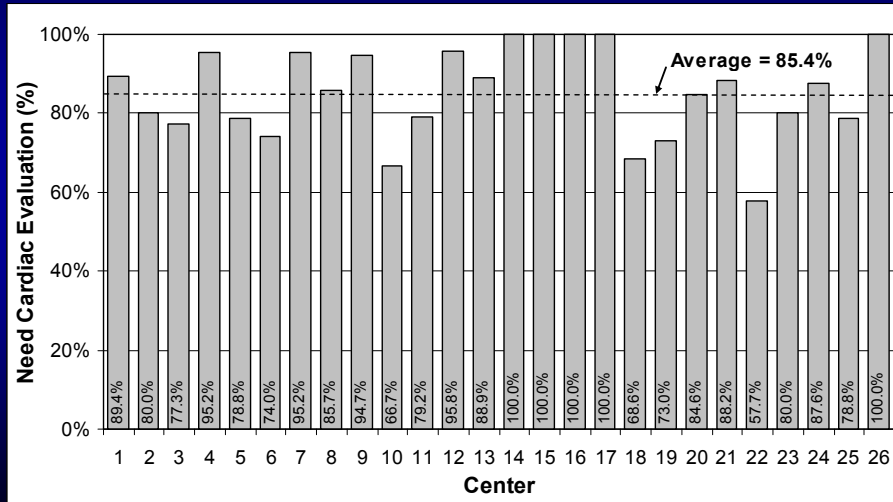
J Am Col Cardiol 2007;50:1707

Can we do a randomized controlled trial?

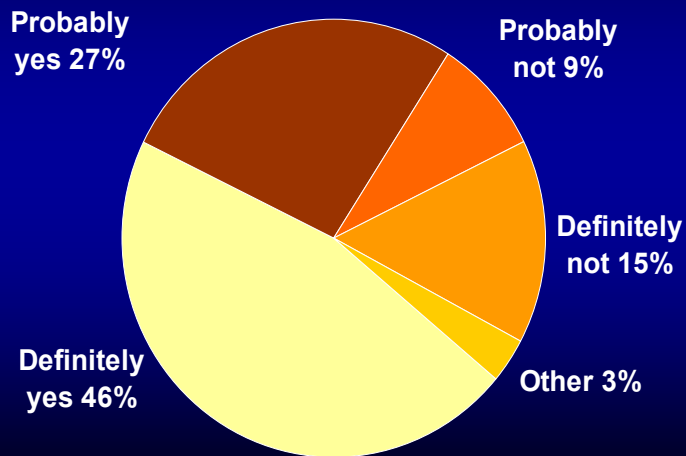
The Coronary Screening for Kidney Transplantation (COST) Study



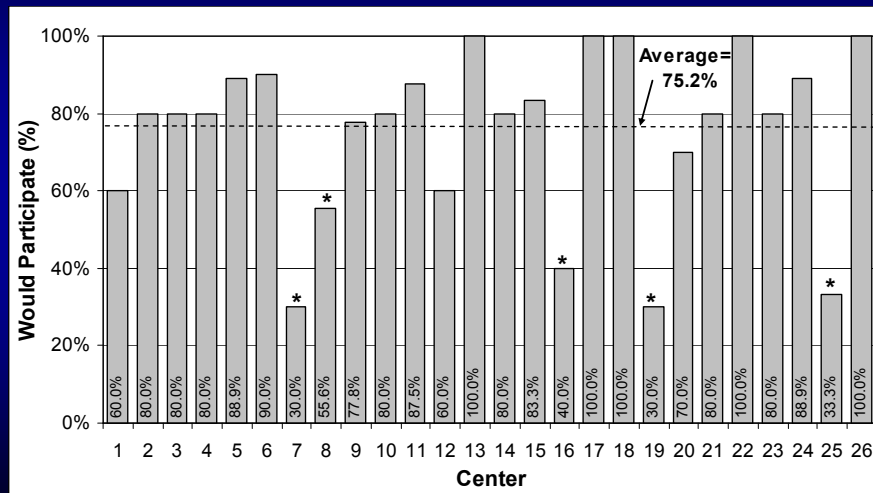
Proportion Needing Coronary Evaluation



Results of Interviews in 241 Candidates: “If the study were held today would you participate?”



Center Variation in Respondents Who Said They Would Participate



Sample Size Estimation

- ❖ For time from randomization to a major adverse cardiac event (MACE), to detect a relative risk (RR) with power of 80%:

For RR=1.30, we would need **N=1,700**

For RR=1.25, we would need **N=2,500**

For RR=1.20, we would need **N=3,900**

What We Learned from COST

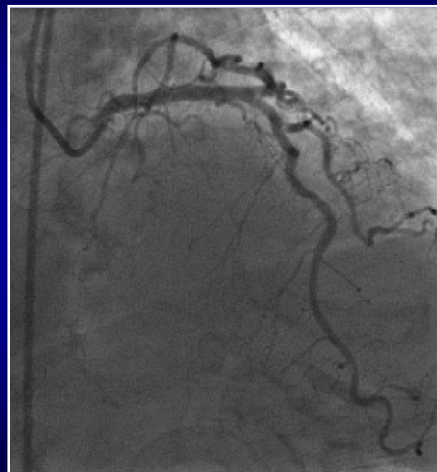
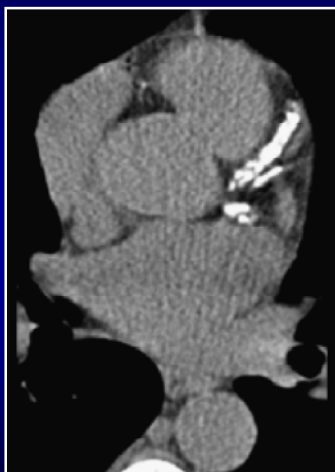
- ❖ ~75% are screened for CHD
- ❖ ~50% already had cardiac evaluation
- ❖ ~50% had no potential living donor
- ❖ ~75% would likely agree
- ❖ Barriers likely would include:
 - Language
 - Evaluations completed beforehand!
 - “Buy-in” from IRBs and key personnel



“What doesn’t kill you, makes you a burden.”

**Are there more effective
screening tests?**

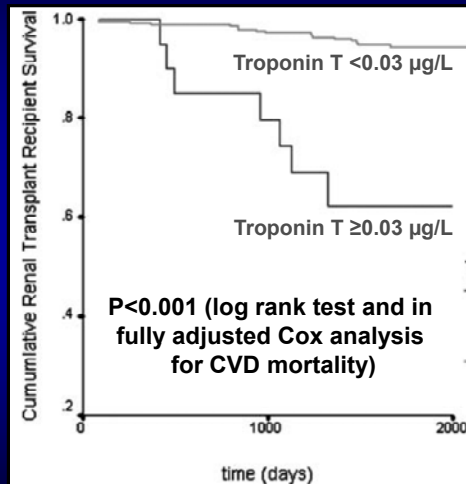
Coronary Calcification and CAD



LL Tong, et al. *Hemodial Int* 2008;12:16

Troponins and CVD Deaths

N= 372 cross-section
Mean time posttransplant = 7 y
Follow-up median = 4.8 y
Troponin T <0.03 µg/L, death
17/351 (4.8%) from CVD
25/351 (7.1%) non-CVD
7/351 (2.0%) unknown cause
Troponin T ≥0.03 µg/L, death
7/21 (33.3%) from CVD
3/21 (14.3%) non-CVD
2/21 (9.5%) unknown cause



GM Connelly, et al., *Nephrol Dial Transplant* 2008; 23:1019

Reasons to Screen for CAD before Kidney Transplantation

- ❖ Fix coronary arteries to:
 - reduce morbidity & mortality ?
 - “protect the kidney” ?
- ❖ Identify high-risk patients to:
 - exclude from transplant ?
 - manage risk factors ?

What is optimal medical management?

Optimal Medical Management before and after Kidney Transplantation

- ❖ Transplant early
- ❖ Smoking abstinence
- ❖ Treat hypertension ?
- ❖ Treat dyslipidemias ?
- ❖ Control diabetes ?
- ❖ Diet and exercise ?

Thank you!