

International Study of Comparative
Health Effectiveness with Medical and
Invasive Approaches- Chronic Kidney
Disease Trial

ISCHEMIA-CKD

Background

- 17% of US population (~26 million) have CKD¹
- By 2030 >2 million people with ESRD and many more with CKD projected²
- ~500 million worldwide with CKD
- ESRD and CKD associated with high risks of death from CAD³
- CKD patients are 5-10 times more likely to die than to develop ESRD

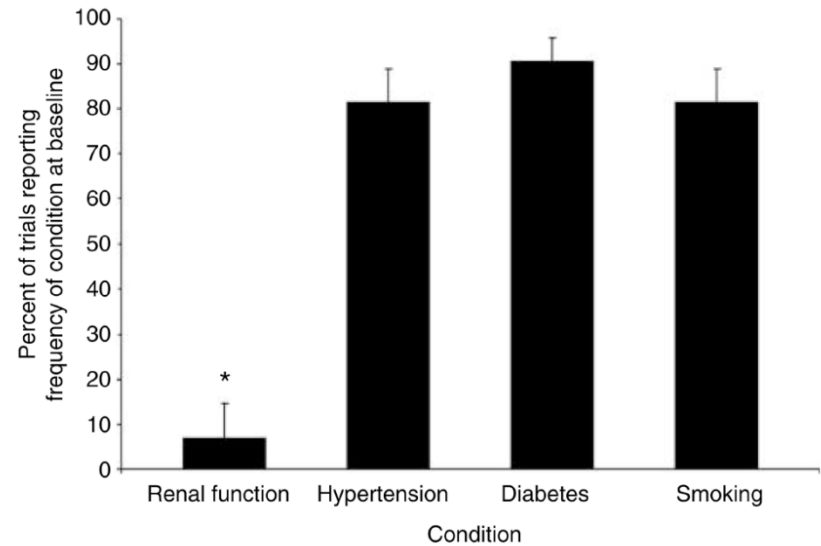
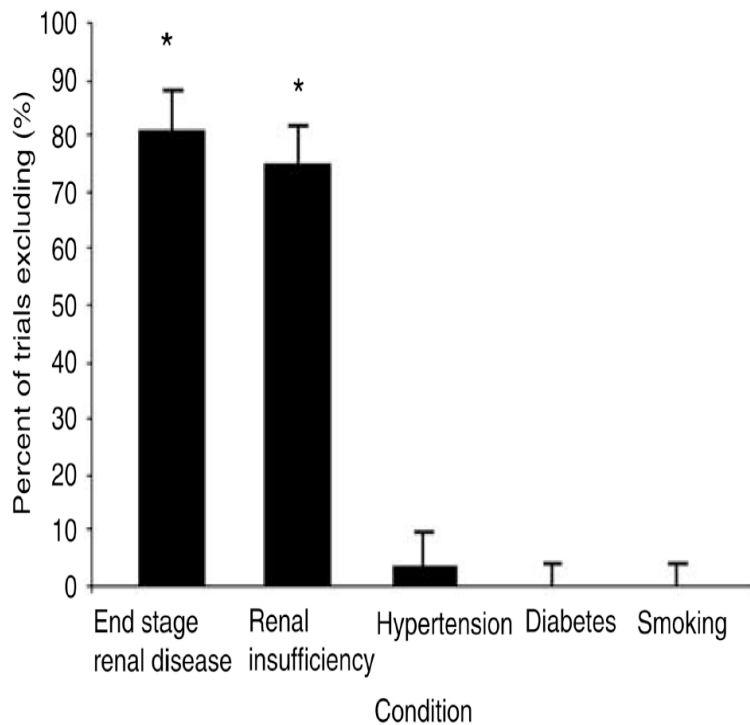
¹ 1999--2004 NHANES data

² Gilbertson et al. J Am Soc Nephrol 2003;14:F-PO881

³ Go et al. N Engl J Med 2004;351:1296–1305

CKD Patients are Underrepresented in Clinical Trials

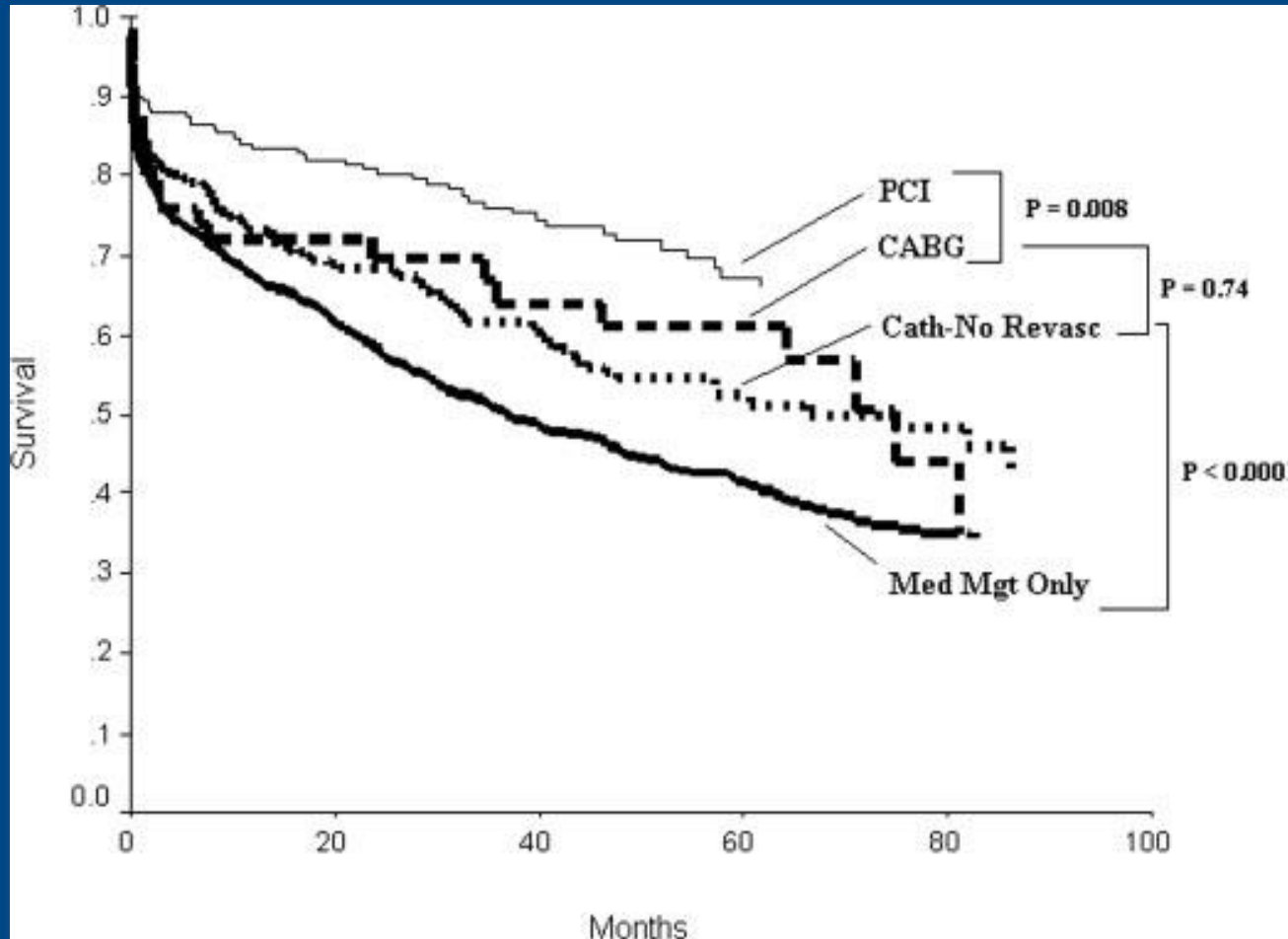
The exclusion of patients with chronic kidney disease from clinical trials in coronary artery disease



Data from 86 trials randomizing 411 633 subjects

Majority (~80%) of CAD trials exclude CKD/ESRD patients

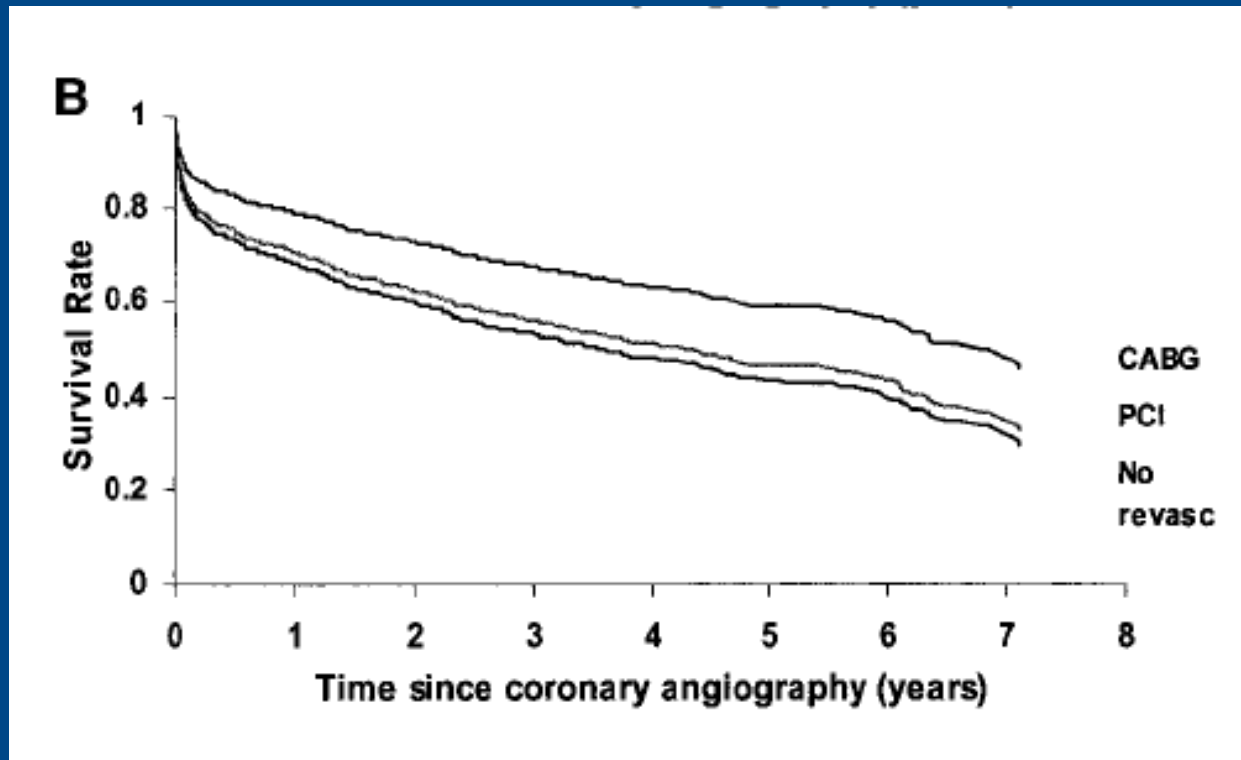
Revasc vs. Medical Therapy: Mortality



ACS patients with CKD (eGFR <60 or on HD)

Cath and revascularization associated with better outcomes

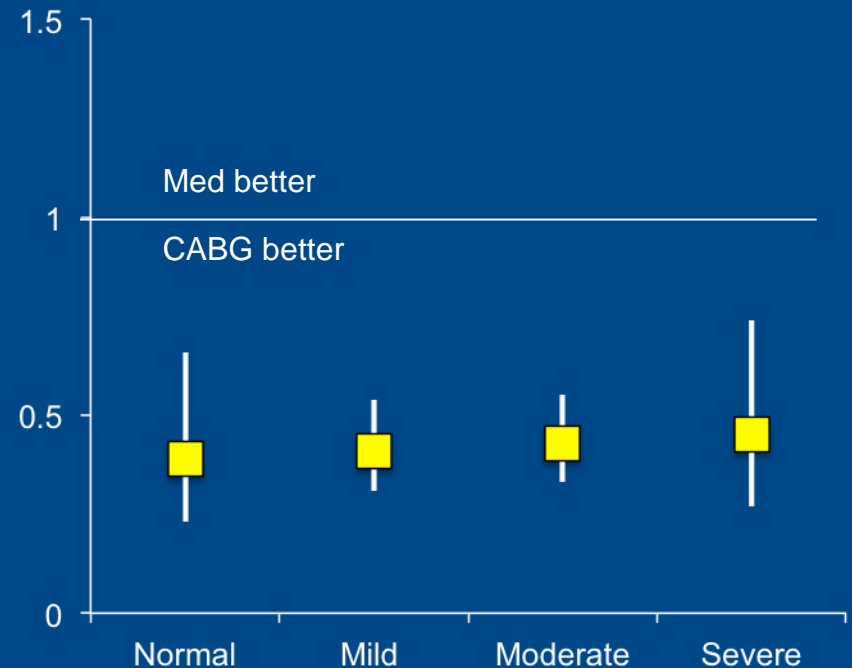
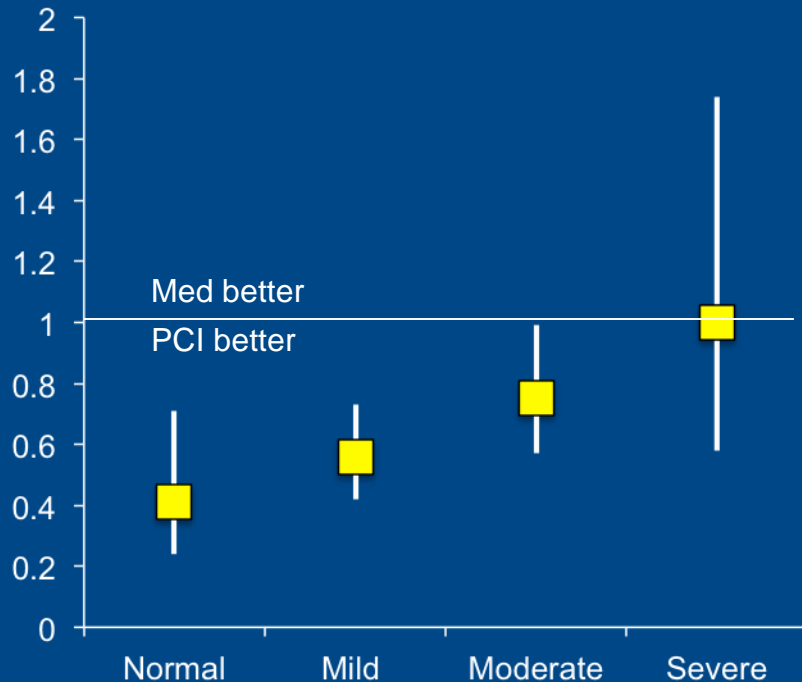
Revasc vs. Medical Therapy: Mortality



APPROACH Registry: 750 non-dialysis dependent CKD patients with or without ACS undergoing cardiac cath

Better outcomes with CABG when compared with PCI or no revasc

Revasc vs. Medical Therapy: Mortality



4584 patients with clinically significant CAD from Duke Database
Lower mortality with PCI (vs. Med) not significant with severe CKD.
However, CABG with lower mortality vs. Med across all CKD stages

ISCHEMIA-CKD



Patients with site determined ischemia⁺ and eGFR <30 or on dialysis¹

No waiting for core lab confirmation of ischemia

No CCTA

RANDOMIZE

Simplified criteria for ETT/expanded def of ischemia

INVASIVE Strategy
OMT² + Cath +
Optimal Revascularization

CONSERVATIVE Strategy
OMT² alone
Cath reserved for OMT failure

Average 3 Years of Follow-up
Primary Endpoint: Composite of Death and MI

¹ Low probability of significant left main disease based on assessment per PI

² OMT=Optimal medical therapy

+See MOO 06.2.2 Screening for Advanced CKD Patients

Major Inclusion/Exclusion Criteria

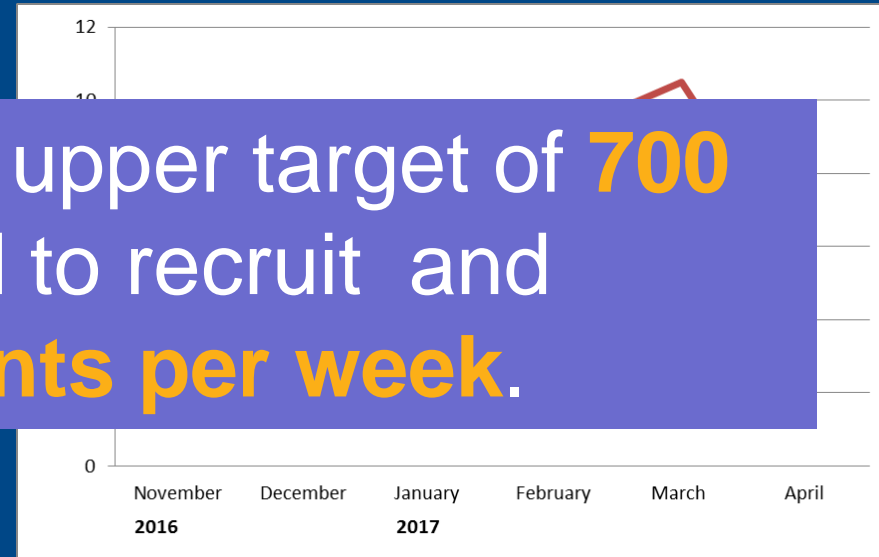
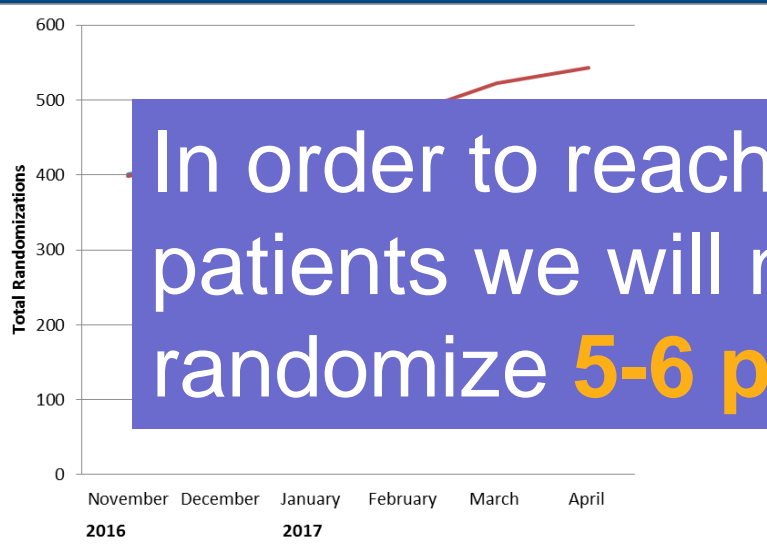
Major Inclusion Criteria

- Site-determined ischemia⁺ on an ischemia test
- eGFR <30 or on dialysis

Major Exclusion Criteria

- LVEF < 35%
- Acute coronary syndrome within the previous 2 months
- PCI within the previous 12 months
- Prior CABG unless the anatomy is found to be suitable for complete revascularization

Randomization Trends last 6 months



In order to reach the upper target of **700** patients we will need to recruit and randomize **5-6 patients per week**.

Eligibility of Patients on List for Renal Transplant

Patients on the renal transplantation list may be particularly suitable for the trial because:

- The average wait time for renal transplantation is ~5-7 years. Most patients can be enrolled into the trial and still go on to receive renal transplantation.
- There is a 50% chance of not receiving cath and thus preventing exposure to contrast.
- Participants randomized to the CON arm (optimal medical therapy only) can cross over to cath closer to the time of renal transplantation, if cath is the standard of care prior to renal transplant.
- Patients with CKD have increased risk of restenosis and need for repeat revascularization after PCI or CABG. If the usual practice is for CKD patients to undergo cath when they are listed, they may need another cath prior to their renal transplant in 5-7 years. It may therefore be best to allow them to participate in the trial and revascularize closer to transplantation

Impact of Revascularization on Outcome Prior to Non- Cardiac Surgery (including renal transplant): Review of Evidence

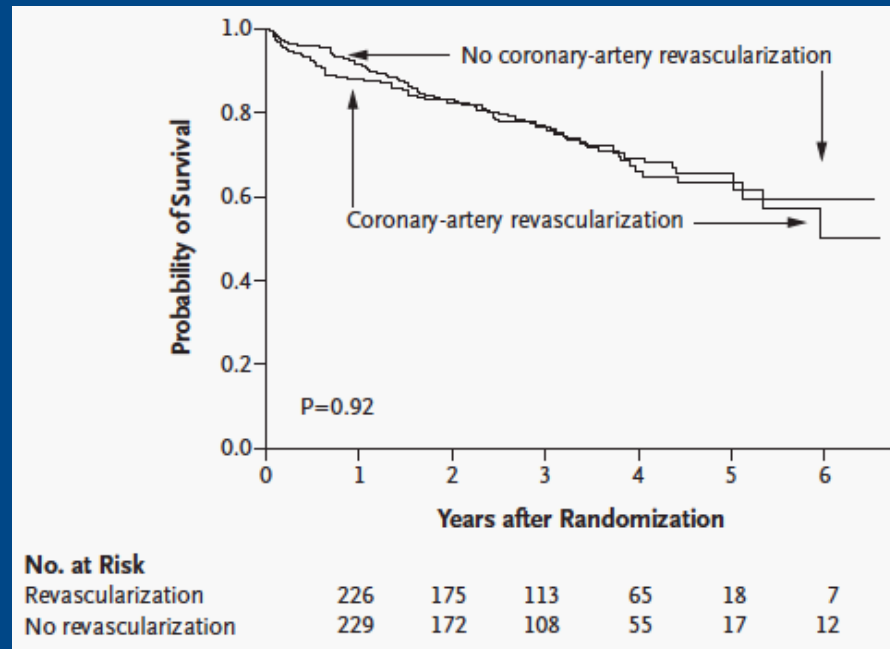
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Coronary-Artery Revascularization before Elective Major Vascular Surgery

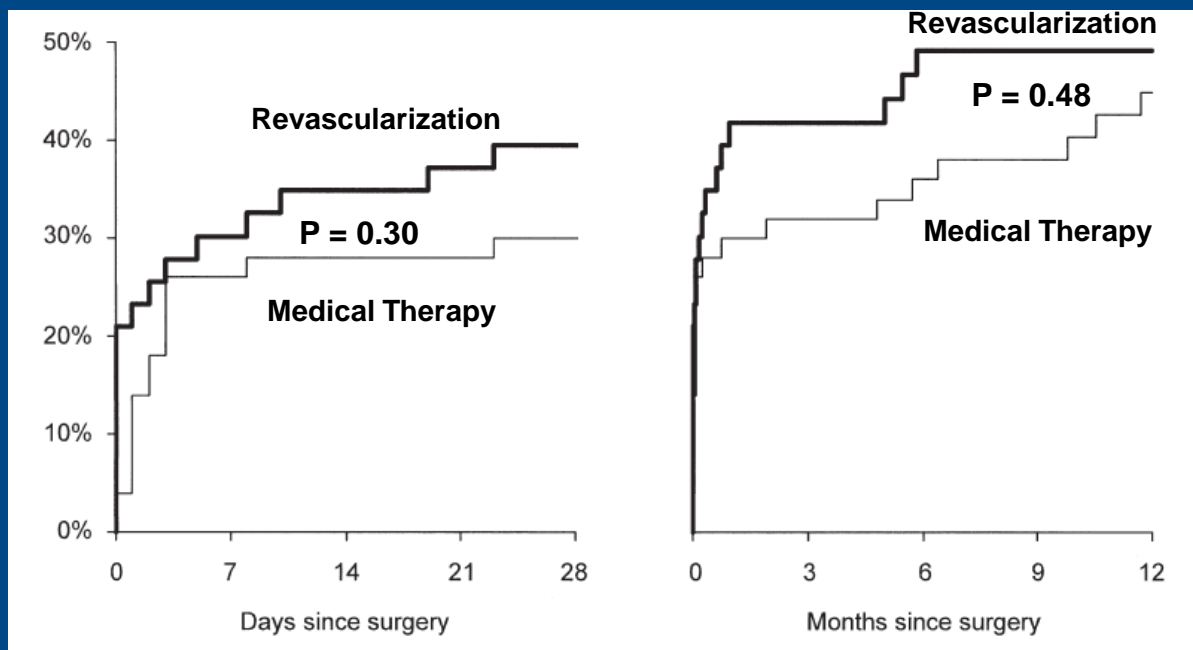


No benefit of revascularization prior to major vascular surgery

N Engl J Med 2004;351:2795-804

A Clinical Randomized Trial to Evaluate the Safety of a Noninvasive Approach in High-Risk Patients Undergoing Major Vascular Surgery

The DECREASE-V Pilot Study



- Patients with extensive stress-induced ischemia (5 segments or 3 walls)
- 46% with Angina
- Preoperative coronary revascularization in high-risk patients was not associated with an improved outcome (numerically higher events)

J Am Coll Cardiol 2007;49:1763–9

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

There is no evidence to support prophylactic preoperative percutaneous revascularization in patients with asymptomatic ischemia or stable angina

Summary

- Exponential increase in cardiovascular events in patients with CKD who have SIHD
- Majority of CV trials exclude patients with CKD
 - Most treatment decisions are extrapolated from cohorts without CKD
- ISCHEMIA-CKD will be the largest treatment strategy trial in these patients
- For more information:
 - www.ischemiackd.org