2017 CST-Astellas Canadian Transplant Fellows Symposium

Pre-Transplant Cardiovascular Assessment

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Solid Organ Transplantation:
Having the Heart to Go Through With It

September 25, 2017

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Advanced Heart Failure/Transplantation
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Disclosures

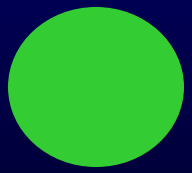
- Novartis
  - Clinical trials, honoraria
- Servier
  - Consultant fees

Game Plan

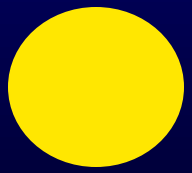
- Why are we concerned about cardiovascular disease in this population?
- How do we risk stratify patients prior to transplantation?
- When is further evaluation appropriate?
- What can we do with the results?

For Your Consideration

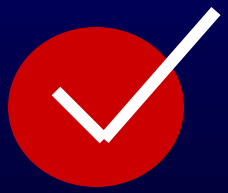
- 55 M, etoh cirrhosis, evaluated for liver transplantation
  - prior myocardial infarction, EF 45%
  - using nitro spray daily for the last month; now having typical chest pain with *any* activity



Good to go
I'd bet the farm on it



Definitely Maybe
Further evaluation required

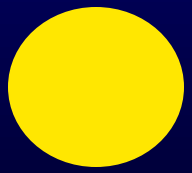


Nope
Cardiac risk prohibitive for now

For Your Consideration

- 32 F, 1˚ pulmonary arterial hypertension NYD evaluated for lung transplantation
  - Moderate RVH, normal LV function on echo
  - Previously competitive swimmer
  - No other co-morbidities

Good to go
I'd bet the farm on it



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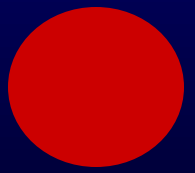
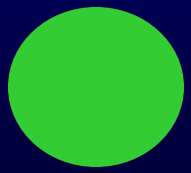


Nope
Cardiac risk prohibitive for now

For Your Consideration

- 48 F, diabetic nephropathy, on IHD x 4 years, evaluated for renal transplantation
  - Obese, history of hypertension, prior TIA
  - Very SOB when walking stairs in her apartment



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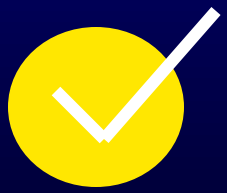

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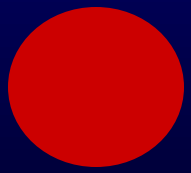
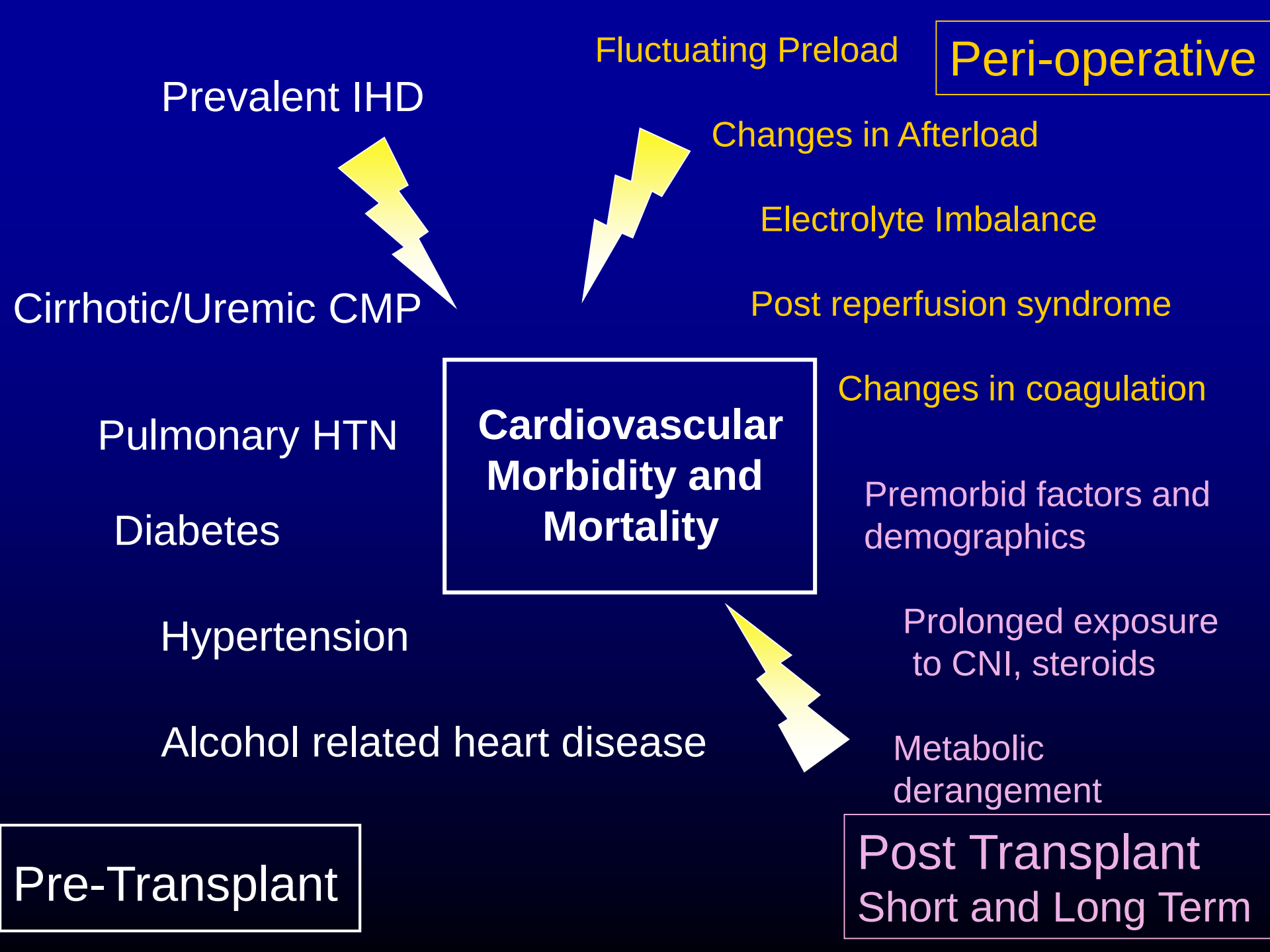


Nope
Cardiac risk prohibitive for now

Real life risk

- Cardiovascular complications are a key contributor to perioperative mortality
- Rates of death or life-threatening cardiac complication with any surgery ~5-8% *(range: 1-25%)*

- Depends on:
  - Type of surgery
  - Underlying patient clinical risk profile


Fluctuating Preload
Peri-operative
Prevalent IHD
Changes in Afterload
Electrolyte Imbalance
Cirrhotic/Uremic CMP
Post reperfusion syndrome
Changes in coagulation
Pulmonary HTN
Cardiovascular Morbidity and Mortality
Premorbid factors and demographics
Diabetes
Prolonged exposure to CNI, steroids
Hypertension
Alcohol related heart disease
Metabolic derangement
Pre-Transplant
Post Transplant
Short and Long Term

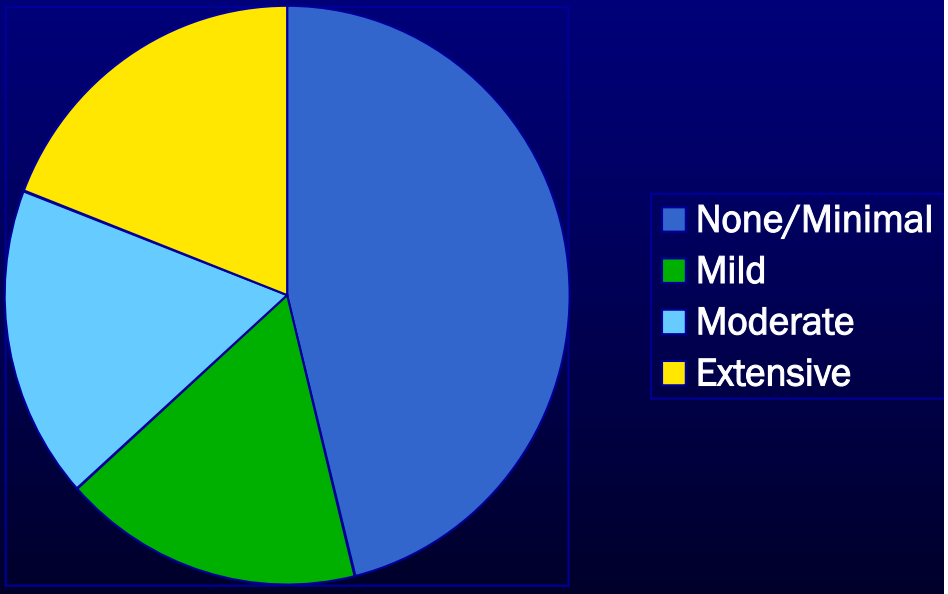
Pre-existing Cardiac Risk Factors in End-stage Organ Failure

	Liver	Heart	Kidney
Hypertension	*22%*	50%	60%
Hyperlipidemia	*17%*	10-30%	70-100%
Diabetes	*16%*	17-29%	30-40%
Smoking	*53%*	50-75%	24-35%

Bart et al. JACC 1997;30:1002
Donovan et al. Transplantation 1996

Prevalence of CAD: Pre-Liver Tx Population

- Framingham calculator underestimates risk
- Contemporary estimates ~ 25-30% angiographic stenosis (>50%) in transplant candidates
  - Majority asymptomatic



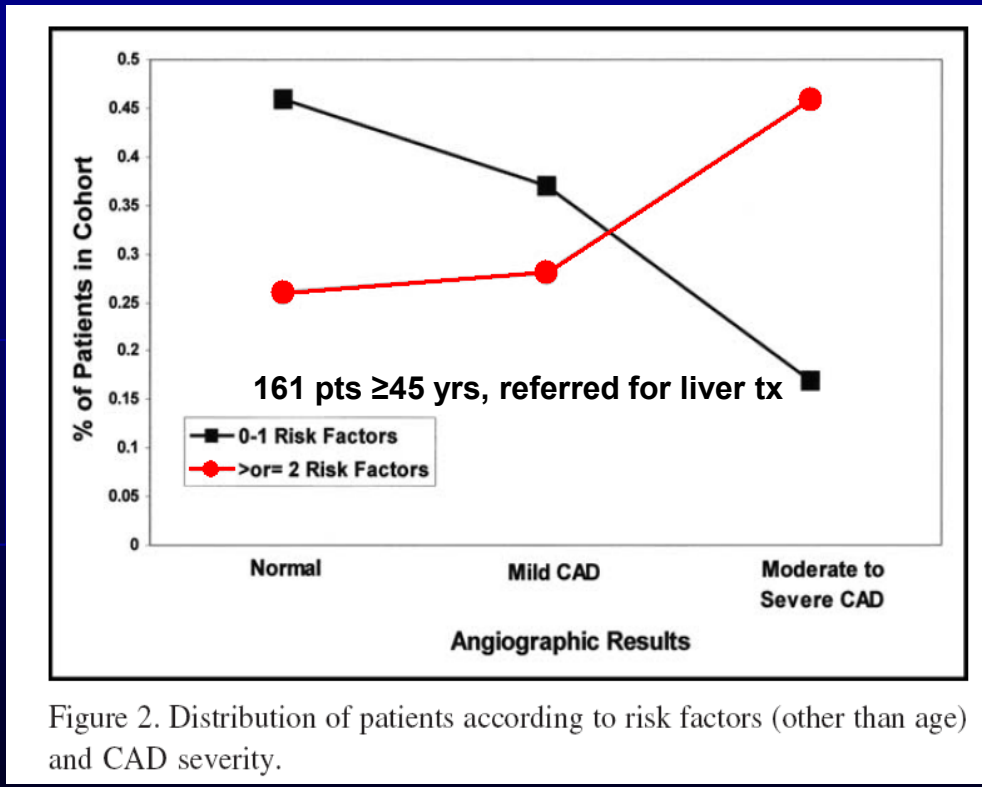


Figure 2. Distribution of patients according to risk factors (other than age) and CAD severity.

Tiukinhoy-Laing et al Am J Cardiol 2006
McAvoy et al Liver Transpl 2008

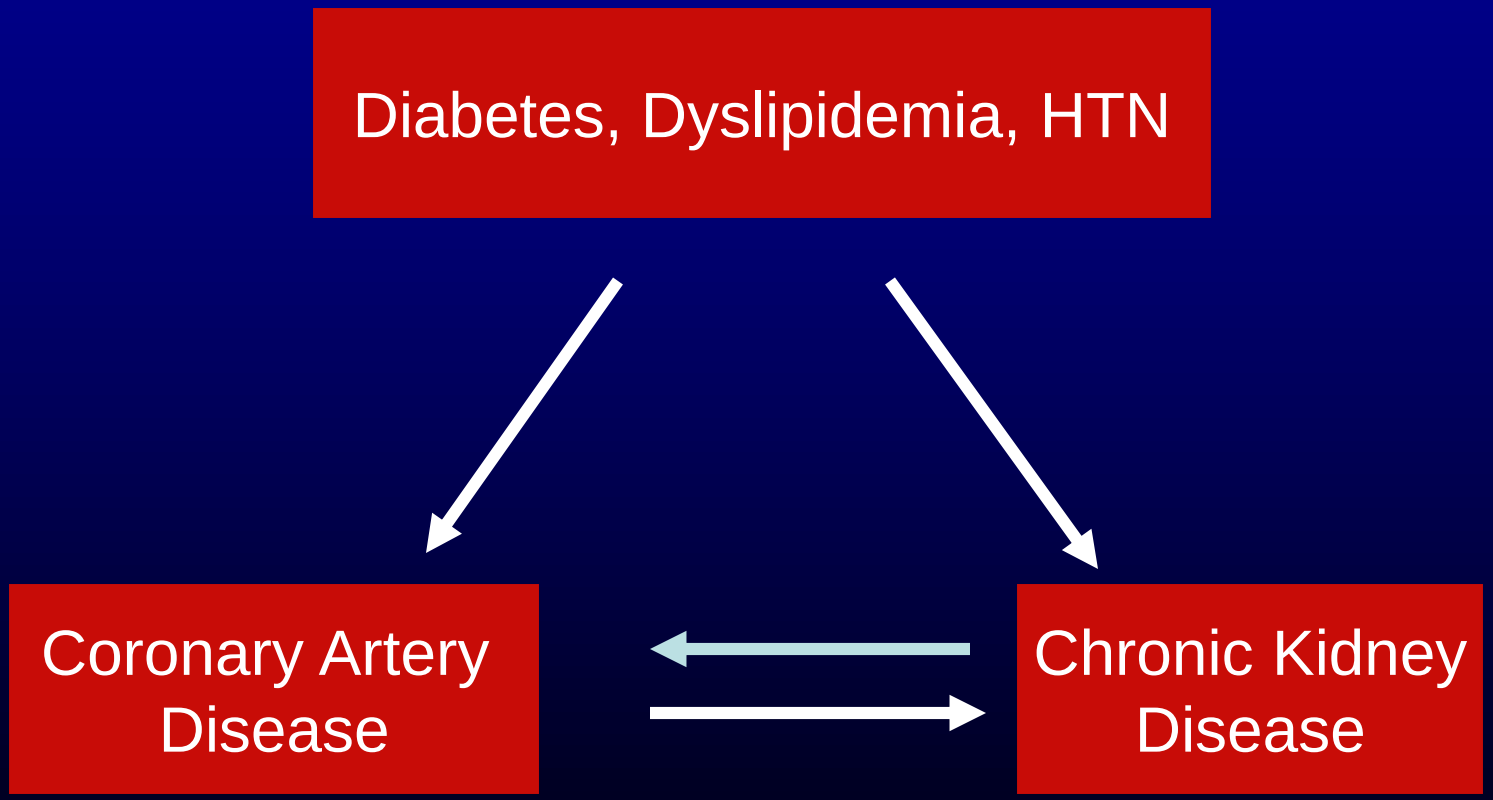
Why it Matters: Prognostic Impact of CAD in Liver Transplantation

- Historically associated with 50% mortality within 3yrs post tx
- Approx 20-25% in contemporary era

- Improvements in screening and management likely to be offset by transplantation of higher risk patients

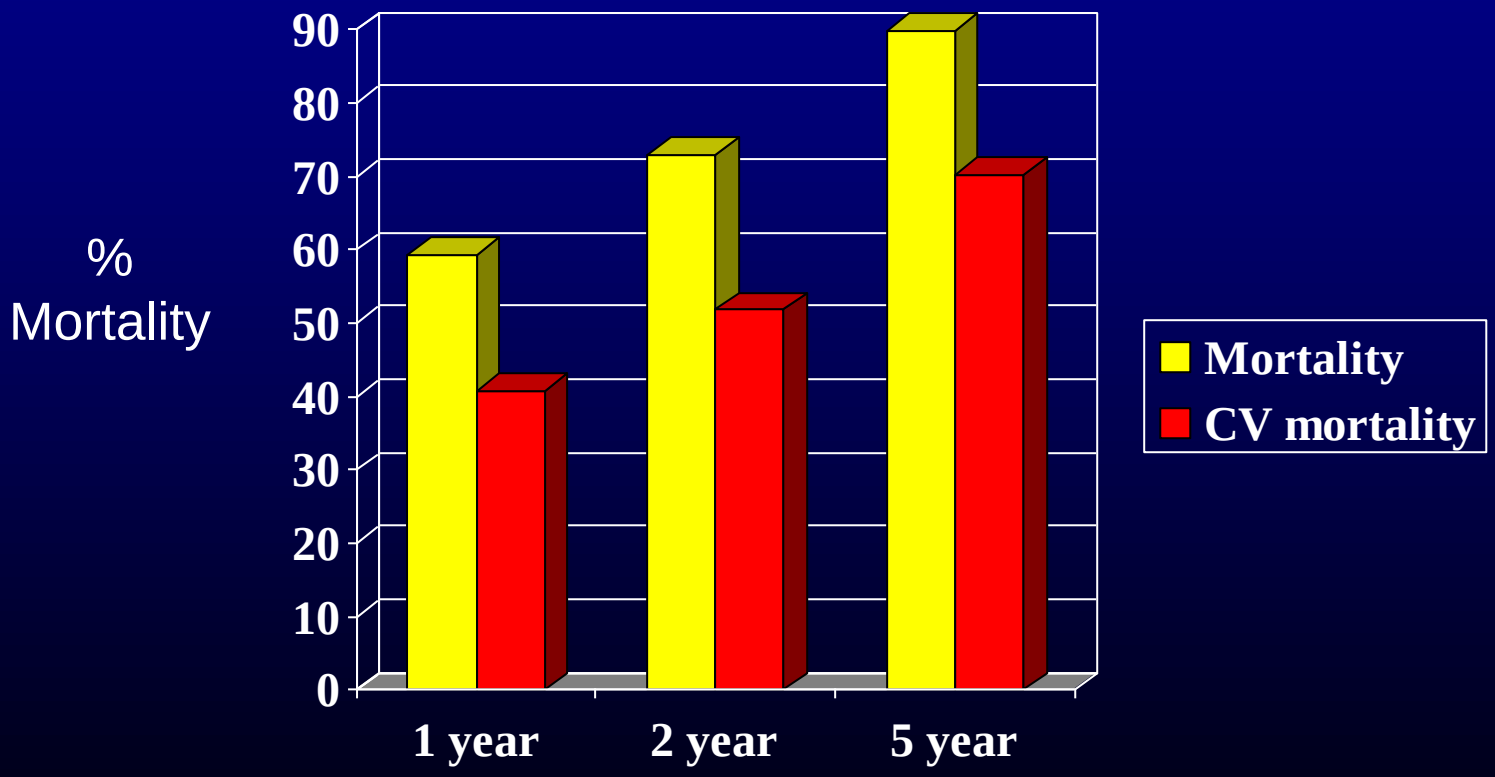
Plotkin et al, Liver Transpl Surg, 1996
Diedrich et al, Transplant Proc 2008
Pruthi et al, Liver Transpl, 2001

Coronary Artery Disease and CKD



Poor Prognosis of Cardiac Disease in Dialysis Patients

34,189 patients on long-term dialysis
1977-1995 - US Renal Data System



Herzog et al NEJM 1998

Long Term Effect of Heart Disease in Renal Transplant Patients

- Heart disease is the most common cause of death
  - 60% of deaths due to cardiovascular disease
- Incidence of MI >10% by 3 years post tx
  - Previous coronary disease increases the risk

Shirali et al, Clin J Am Soc Nephrol 2008
Jardine et al, Am J Kidney Dis 2005
Lentine et al, J Am Soc Nephrol 2005

Prevalence of CAD: Pre-Lung Tx Population

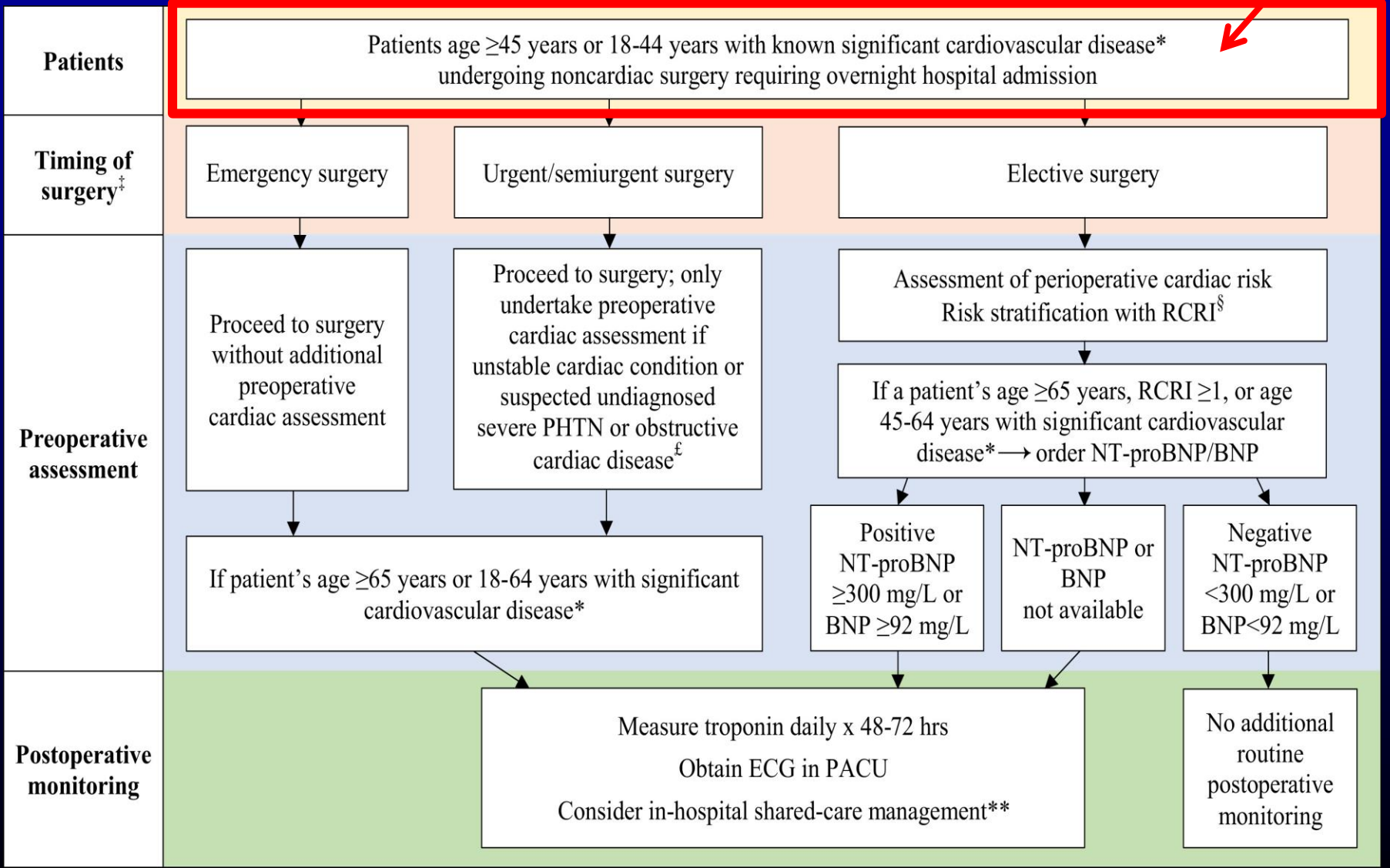
- Approaches ~20% in patients >50 yrs
- Non invasive study accuracy not well described
- Low threshold for angiography in patients >50yrs or multiple RFs

Assessing Patients for Surgery

Canadian Cardiovascular Society's Guideline Algorithm

High proportion of transplant candidates

Duceppe et al, Can J Cardiol 2016



Assessing Patients for Surgery
-A Practical Approach-

Step 1

Rule out active cardiac conditions

- Unstable coronary disease
- Decompensated heart failure
- Severe obstructive cardiac disease
  - Aortic stenosis, mitral stenosis
  - HCM with severe obstruction
  - Pulmonary arterial hypertension

Do not proceed until definitively treated or optimized with clinical stability

Assessing Patients for Surgery
-A Practical Approach-

Step 2

Identify and quantify the risk of CV complications in adults >45 years or those with cardiovascular disease

Revised Cardiac Risk Index: 6 independent risk factors validated for adults undergoing non-cardiac surgery

- *Heart Failure*
- *Ischemic heart disease*
- *History of stroke*
- ***Chronic kidney disease***
- ***Diabetes on insulin***
- ***High risk/major surgery***

Risk Factors	Incidence of Complications
0	< 4%
1	6%
2	10%
3 or more	15+%

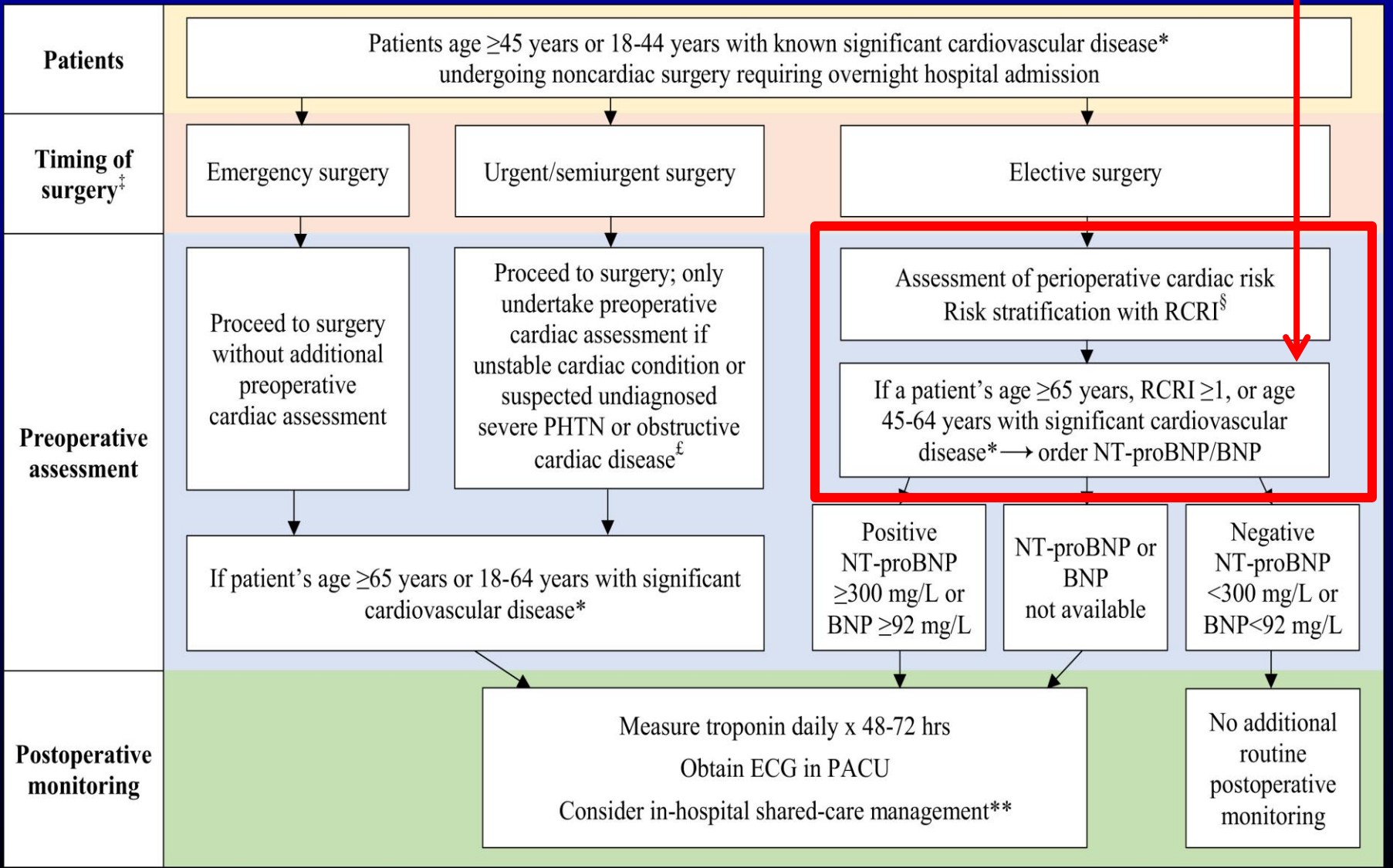
Lee et al, Circulation 1999

A few clinical risk stratification methods are available

Assessing Patients for Surgery
Guideline Algorithm (Revised)

High proportion of transplant candidates

Duceppe et al, Can J Cardiol 2016



Assessing Patients for Surgery
-A Practical Approach-

Step 3

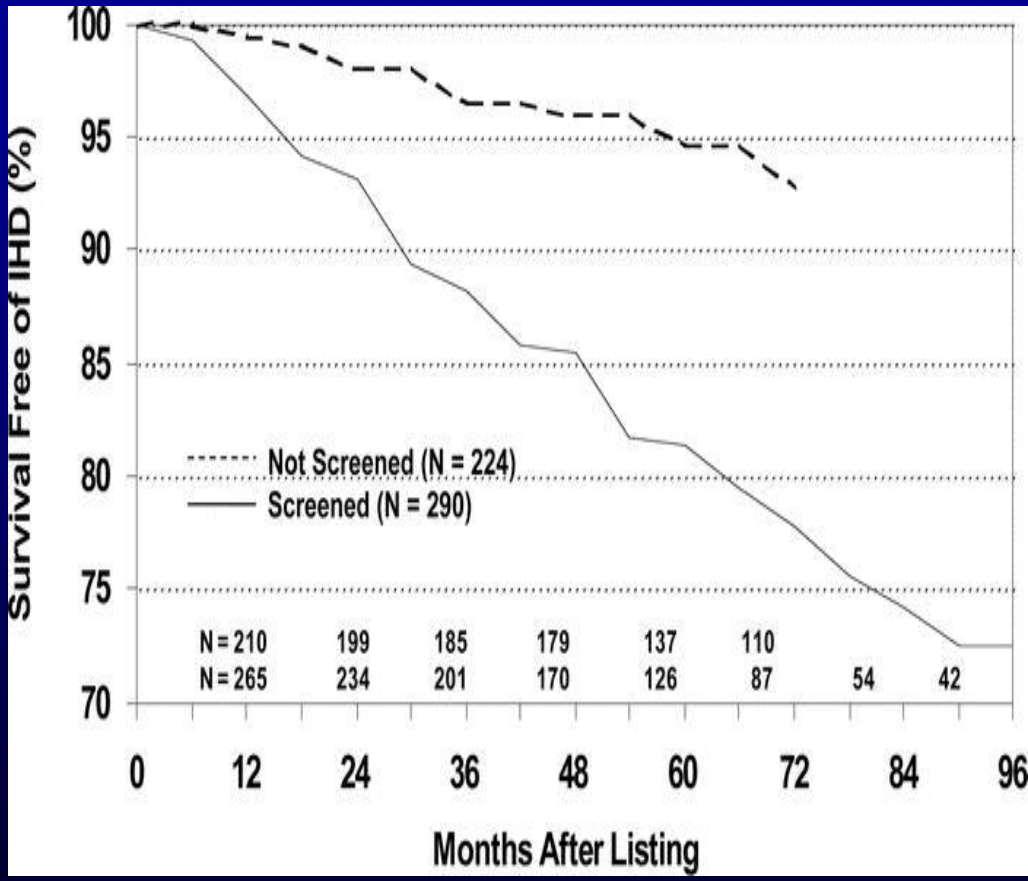
Determine if further cardiac evaluation is required

Intrathoracic / intra-abdominal transplant candidates usually have one indication for further evaluation:

- Revised Cardiac Risk Index ≥1, or
- Established cardiovascular disease
- Age >65

Purpose of Proceeding with Cardiac Evaluation

- Provide information re: **risk of surgery *and* long-term morbidity and mortality**
- Monitor for risk at surgery
  - Increase precautions
- Intervention pre – transplant
  - Medical – PCI
  - Surgical
- Target for aggressive risk factor reduction post transplant



Screened if: IHD, DM, Prior IHD, risk factors

Kasiske et al, Transplantation 2005

Consider the Options for further Evaluation: Biomarker Measurement*

Test Result for Natriueretic Peptide	Risk estimate (%)	95% CI for risk estimate
NT pro BNP < 300 ng/L or BNP < 92 ng/L	5	4%-6%
NT pro BNP >300 ng/L or BNP >92 ng/L	22	19%-25%

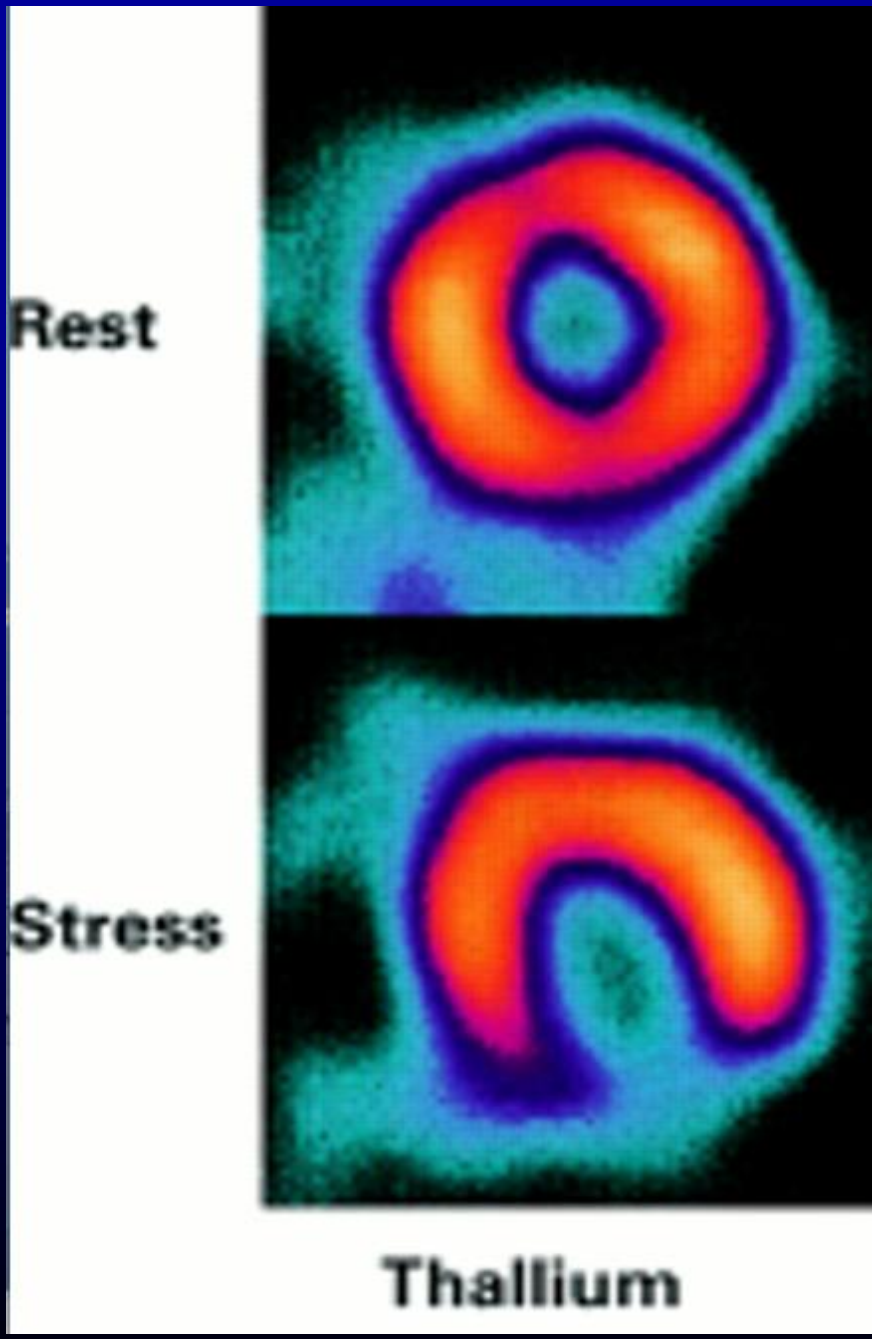
Risk of death/MI 30 days post operatively based on natriuretic peptide measurement

**Shown to provide best incremental risk prediction*

Duceppe et al, Can J Cardiol 2016

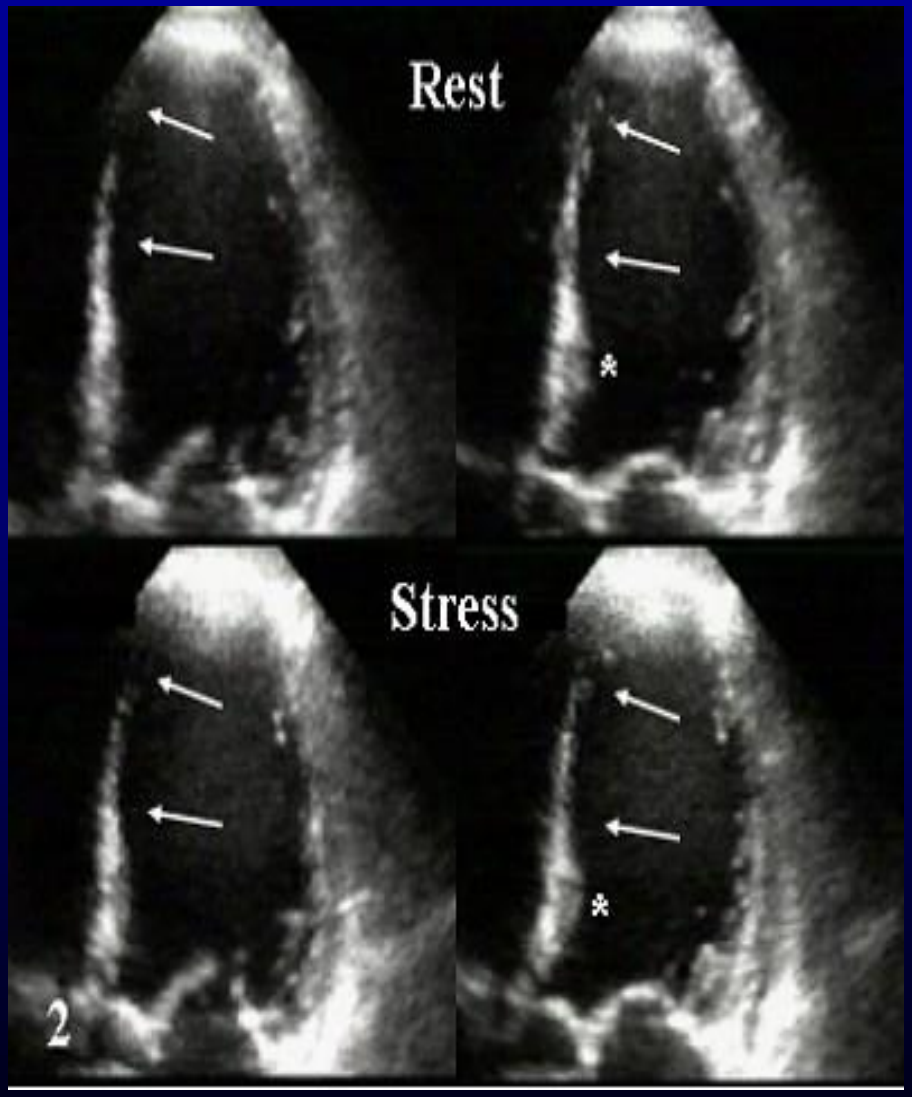
Other options for further Evaluation:
Myocardial Perfusion Imaging

- Radio-labeled substance (thallium or MIBI) injected during rest and during exercise or pharmacologic stress
  - Taken up by myocardium proportionally to blood flow
  - Identifies regions of inadequate perfusion



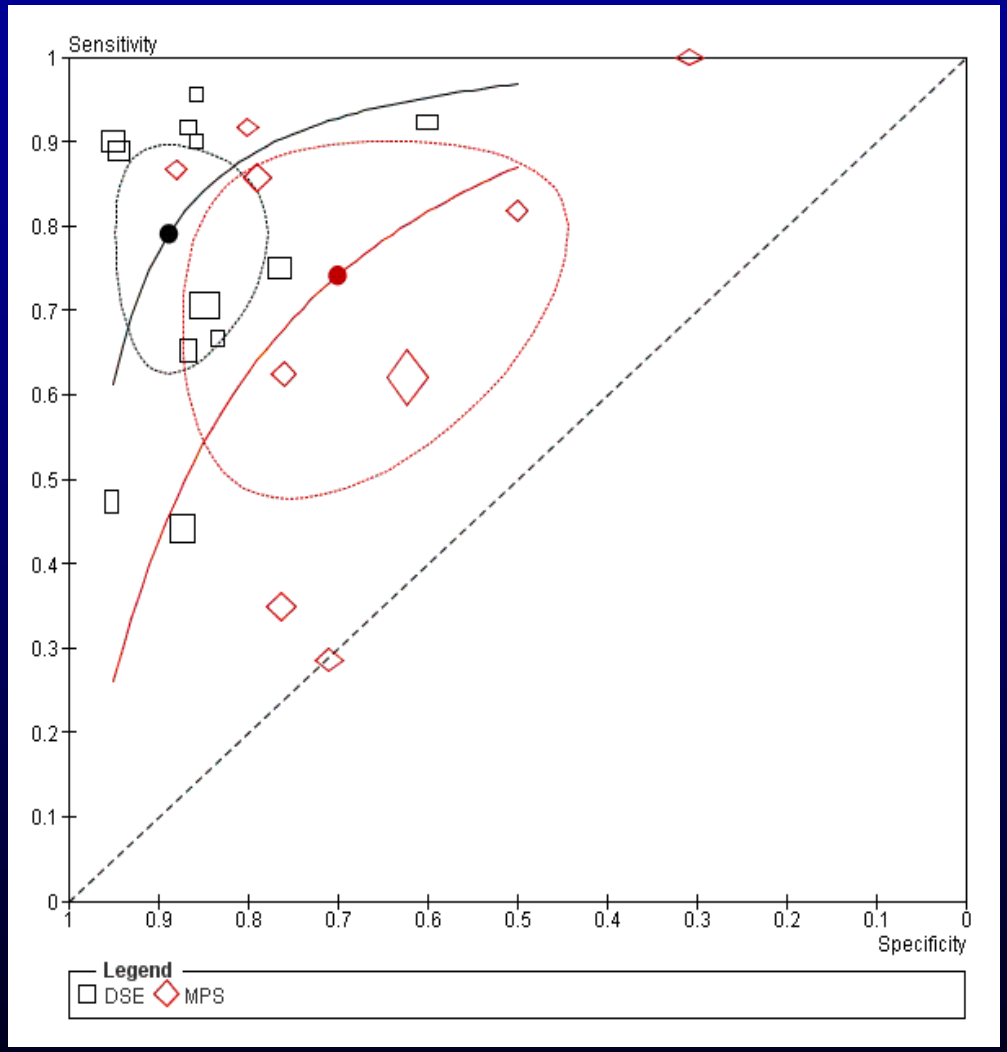
Other options for further Evaluation: **Stress Echo Imaging**

- Usually dobutamine required to reach target heart rate
- Highly dependent on images taken
- High prevalence of chronotropic incompetence



Exercise or dobutamine used for stress

Accuracy of non-invasive tests in pre-kidney transplant evaluation*



Cochrane review of 22 studies

Compared DSE and MPS to Angiography for diagnosis of CAD

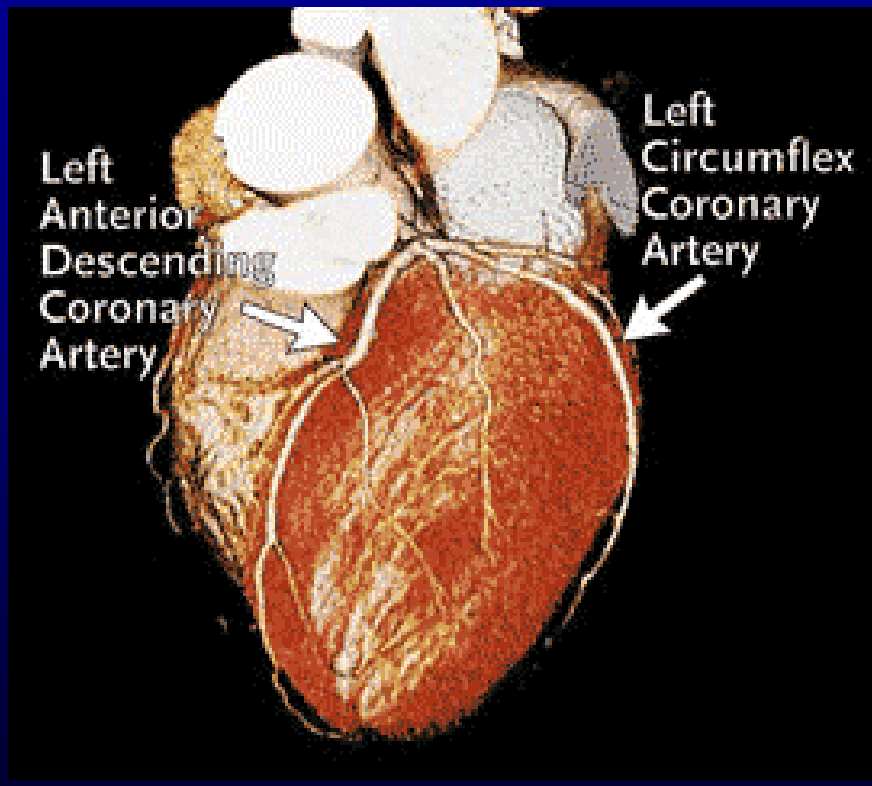
	sensitivity	specificity
DSE:	0.79	0.89
MPS:	0.74	0.70

DSE = dobutamine stress echo
MPS = myocardial perfusion studies

Wang et al, Cochrane Database Syst Rev, 2011

Other Options for further Evaluation: CT Angiography

- Non-invasive with test accuracy >95%
- May increase total radiation dose
- Contrast load may be significant
- Not a functional test
- Can identify higher risk subgroups but shown to *significantly overestimate* surgical risk

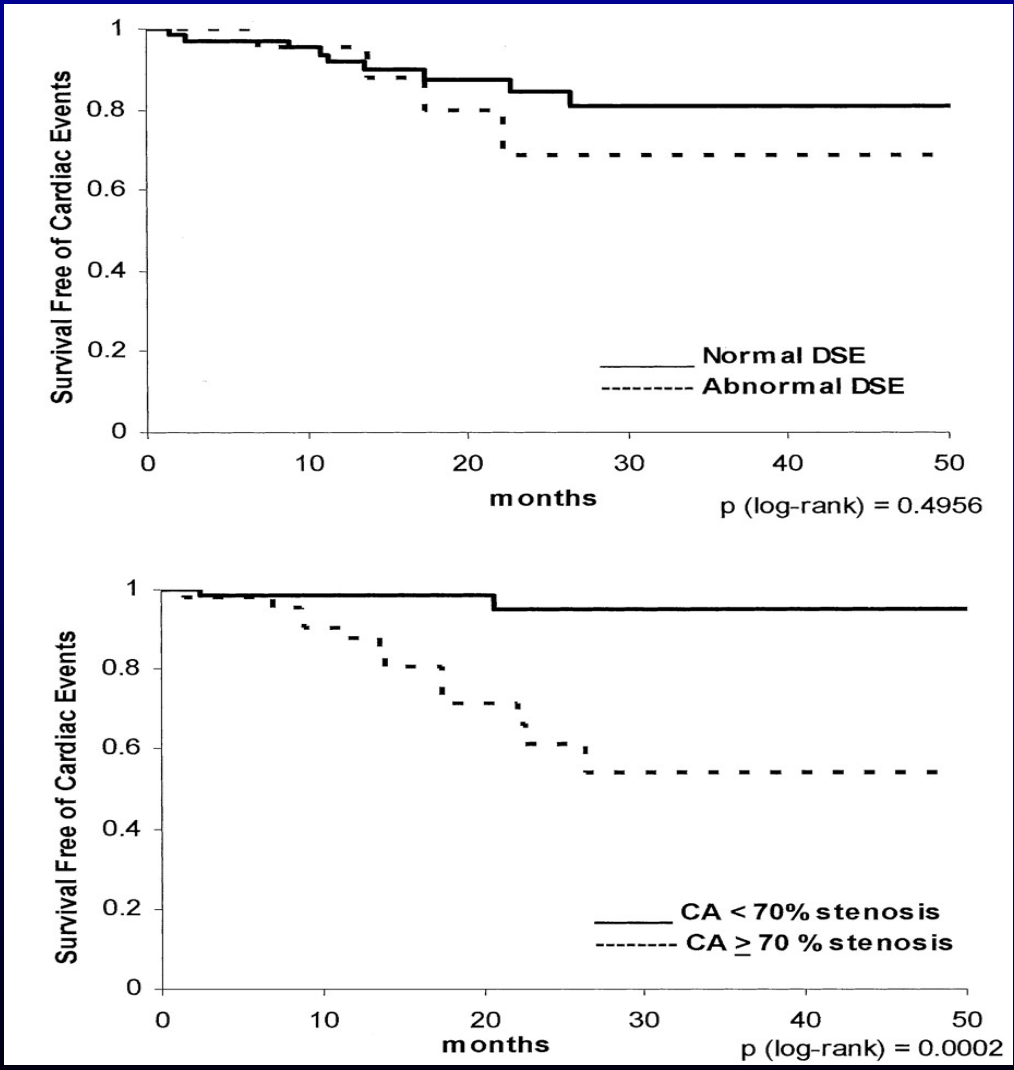


What about coronary angiography for direct assessment of coronary disease?

126 transplant candidates with risk factors for coronary disease

Combination of stress Imaging and coronary angiography

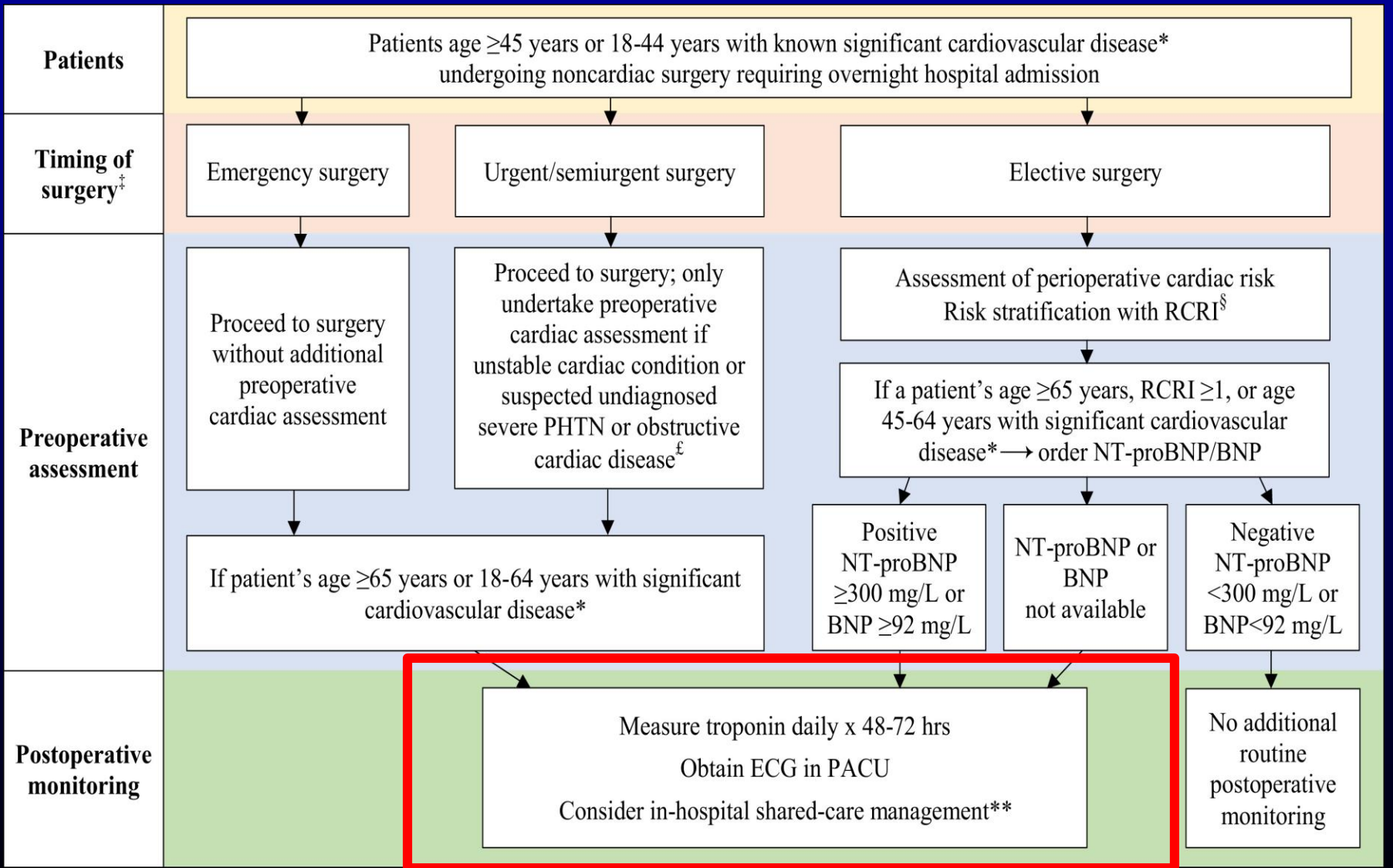
Coronary angio strongest predictor of major cardiovascular events



De Lima et al, Hypertension 2003

Ok…so what should we do with the results?

Duceppe et al, Can J Cardiol 2016



Why not revascularize routinely?

510 pts undergoing high-risk surgery

Randomized to medical Rx vs revascularization (60% PCI, 40% CABG)

Excluded pts with L main stenosis, LVEF <20%, severe aortic stenosis

McFalls et al, N Engl J Med 2004

Other considerations for risk reduction perioperatively

Intervention	Management
ASA	Stop 3 days prior to OR if possible
Beta blocker	Continue if already taking (unless bp low) Do not initiate to reduce events
ACEI/ARB	Stop 24h prior to OR if possible
Statin	Continue
$Alpha_2$ agonist	Do not initiate to reduce events
Calcium channel blocker	Do not initiate to reduce events
Smoking cessation	Discuss and initiate plan >4 weeks prior if possible

Duceppe et al, Can J Cardiol 2016

How does all this apply to transplant surgery?

- It depends!
- If the objective is just to get the patient through surgery…applying guidelines is a reasonable evidence based approach
- But, considering longer term outcomes, optimal use of organs and allograft survival, additional considerations may apply

What do I do?
Caution! Evidence-free opinion follows:

- Guideline based risk assessment
- Use multiple modalities to assess risk and potential burden of cardiac disease
- Define coronary anatomy if evidence of ischemia
- Lower threshold for intervention depending on type of transplant surgery and potential for demand ischemia
- Communicate cardiac prognosis (as best I can) to the referring team

Other Key Cardiac Issues

- LV dysfunction and HF
  - Uremic CMP
  - Cirrhotic CMP with impaired contractile reserve

- Pulmonary hypertension in non-lung tx candidates
  - RVSP by echo alone inadequate for assessment
    - If >40mmHg, should trigger right heart cath
  - **High** mortality if mean PA pressure >35-50mmHg

Other Key Cardiac Issues

- PFO
  - Risk of paradoxical emboli
- QT prolongation

Summary

- Cardiovascular co-morbidity is highly prevalent in this population
- Majority of transplant candidates require evaluation of cardiovascular risk
- Clinical characteristics and non-invasive testing can adequately risk stratify most patients
  - BNP
  - Functional testing or coronary anatomy assessment
- High risk patients may be appropriate for invasive testing
  - Optimal medical therapy is indicated in all cases
  - Intervention/revascularization is indicated in select cases