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CRC Rotation
IRB proposal
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Title: Short and Long Term Incidence of Nephropathy and Risk Factors for Nephropathy after Coronary Artery Bypass Grafting or Drug-Eluting Stent Implantation for Multi-Vessel (2 and 3 Vessel) Coronary Artery Disease in Patients with Normal Baseline Serum Creatinine and those with Elevated Baseline Serum Creatinine Levels

Study Description:

1. Study Purpose and Rationale:

Coronary artery disease (CAD), or atherosclerotic heart disease, is the end result of the accumulation of atheromatous plaques within the walls of the coronary arteries that supply the myocardium with oxygen and nutrients. Coronary artery bypass surgery (CABG) and percutaneous coronary intervention (PCI) with stent placement are two common techniques to treat CAD in an attempt to prolong life. However, both procedures have several complications. Acute kidney injury (AKI) is a prevalent complication of both cardiac surgery and cardiac catheterization (Wang, Asrith). AKI is a serious complication as it can generate extra costs, it can lead to necessitate dialysis, and it can also increase the odds of death. While several recent studies have shown that long-term survival appears to be better with CABG than PCI in patients with Chronic Renal Failure, it is unclear if this affect is present in those without kidney disease (Ashrith, Sunagawa, Wang). It is also unclear whether there is a difference in the incidence of AKI between the two interventions, and whether this might account for survival changes.

It is well established that iodinated contrast medium that is used in cardiac catheterizations can cause renal damage, which ranges from a transient elevation of the serum creatinine (SCr) concentration to permanent renal failure (Abe, Caixeta). In fact, contrast induced nephropathy (CIN) is the third leading causes of all hospital-acquired renal insufficiency (Abe). The incidence of CIN varies greatly among various studies and to date, the some of the important known risk factors include preexisting renal insufficiency, older age, female gender, race, anemia, heart failure, diabetes (Sidhu, Chong).

It has also been seen that cardiac surgery can cause renal damage, also ranging from a transient elevation of the SCr concentration to permanent renal failure (Modine, Sirvinskas, Medalion, Nakatsu). The reasons for renal dysfunction include renal hypo-perfusion, non-pulsatile flow, hypothermia, microembolism, and stimulation of the inflammatory response during cardiopulmonary bypass (Rodrigues). Within CABG, whether or not the person is on-pump versus off-pump can also be a factor in the development of AKI (Loganathan, Machado, Brushi).

Unfortunately, many aspects of AKI literature remain controversial and without consensus, making direct comparisons difficult (Asrith, Sunagawa). Previous literature from the Contrast-Induced Nephropathy Consensus Panel had defined AKI in PCI as an increase in SCr >25% over baseline and/or a rise in SCr >0.5 mg/dl within 48 hours.

However, recently, the Acute Kidney Injury Network (AKIN) (www.AKINet.org) has proposed a definition of AKI based on the RIFLE classification (Risk, Injury, Failure, Loss, and End-Stage Kidney disease), which describes overall AKI as an increase in SCr of>0.3mg/dl, increase of 50% of baseline SCr, or reduction in urine output (<0.5ml/kg/hr) within 48 hours. This study will use the latter criteria as the standard to measure AKI in both CABG and PCI. We will also define nephropathy as a decrease in GFR from one stage to another (>90, 60-89, 30-59, 15-29, <15).

Patients undergoing 2 vessel or 3 vessel disease (>70% stenosis) interventions (PCI or CABG) will be included in this study and data will be collected from the first 48 hours, 168 hours (7days) post procedure, at the 1 month time point, at the 6 month time point, and at the 1 year time point.

Since baseline demographics may play a role in the development of nephropathy, baseline variables will be determined (see below for listing). Since it is highly well established that those already with preexisting kidney disease are at higher risk for developing AKI, this study will divide patients into those with normal baseline SCr <1.5 mg/dL and those with some renal impairment, baseline SCr>1.5.

This study seeks to 1) determine the incidence of nephropathy after CABG or PCI 2) to compare the incidence of nephropathy between CABG and PCI 3) determine major risk factors for nephropathy.

<u>Baseline variables</u> to be assessed include prior to procedure:

Age
Gender
Race
Hemoglobin Levels
Clotting Times
    Prothrombin (PT)
    Partial Thromboplastin time (PTT)
    INR
Diabetes Mellitus
    Fasting blood glucose level greater than 126 mg/dL
    Taking glucose lowering medications.
    Insulin Requirements
Blood Pressure
    Systolic BP
    Hypertension (SBP>140)
    Hypotension (SBP <100)
Hyperlipidemia
    HDL
    LDL
    Triglycerides
COPD
Current tobacco use
Current alcohol use
Body Mass Index (BMI < or > 30)
    Waist Circumference

Urea
Creatinine Levels and GFR; using the 4 variable MDRD equation
- Normal Creatinine; SCr<1.5
- Elevated Creatinine; SCr>1.5
- Normal GFR; >60
- Abnormal GFR; <60
- Use of hemodialysis

Troponin Levels
Creatinine Kinase (CK)
EKG Changes (ST deviations)
TIMI Risk score
Canadian Cardiovascular Society Angina Class
NY Heart Association Congestive Heart Failure Class
Prior MI
Prior PCI
Prior CABG
History of Neoplasm
Left Ventricular Ejection Fraction (LVEF)
Peripheral Vascular Disease
Medications
- Aspirin
- Antithrombin
- Anticoagulation
- Antiplatelet
- Statins
- Beta Blockers
- ACE Inhibitors/ARBs
- NSAIDs

Procedure Techniques will be noted:
On-pump vs. off pump CABG
Duration of surgery
Use of saline hydration
Use of N-acetylcysteine
Quantity of contrast (type)

Outcomes to be followed up to 168 hours post procedure, at 1 month, at 6 months, and at 12 months:
Creatinine
Creatinine Kinase
Urea
Microalbuninuria
GFR (>90, 60-89, 30-59, 15-29, <15)
Use of hemodialysis
Length of Hospital Stay
Death – Cardiac Death, NonCardiac Death, Bleeding Death

2. Study Design and Statistical Procedures: This is a retrospective cohort study which will include collection of clinical data from all patients admitted to Columbia University Hospital who underwent PCI or CABG from 2000 to 2010. Continuous data will be reported as a mean value +/- SD. Categorical data will be presented as absolute values and percentages. Comparison of continuous variables will be performed by student's t-test; while chi-square and Fisher's exact tests will be performed for comparison of categorical variables. In order to control for multiple factors, multivariate analysis of variance, linear and logistical regression may also be needed.

As prior studies have shown that those with abnormal kidney functions are more predisposed to further kidney damage; two groups will be created; those with normal renal function, baseline SCr<1.5 mg/dL will be placed in the Normal category and those with impaired renal function, SCr>1.5 will be placed in the impaired group.

Our Null Hypothesis is that at one week, one month, 6 months, and one year, kidney function and patient survival do not differ between those who underwent CABG and PCI. Prior studies report 5-15% (estimate average of 10%) AKI post-procedure in those with normal SCr and higher rates of AKI (20-50%; estimated average of 30%) post procedure in those with abnormal kidney function. We project that in order to detect a 5% difference in AKI rates, we will need n = 738, or approximately 800 patients, in the CABG and 800 patients in the PCI arms with normal SCr; while we will need n=1442, or approximately 1500 patients, in the CABG and 1500 patients in the PCI arms with abnormal SCr, for 80% power to detect a 5% difference at an alpha <0.05.

3. Study Procedures: Charts of patients treated be either CABG or PCI at Columbia University between 2000 and 2010 qualify for this review. This is a retrospective cohort study that will require going through patient's electronic medical records to extract the data points. Patient's date of death will be confirmed using the Social Security Death Index. No new procedures need to be performed on the patient's studied.

4. Study Drugs or Devices: None, not applicable

5. Study Questionnaires: None, not applicable

6. Study Subjects: We will include all patients who have undergone multi-vessel (2 or 3) PCI or CABG at Columbia University between 2000 and 2010. Pt will have 2 or 3 vessel disease defined as CAD with >70% stenosis (Wang).

7. Recruitment: None, not applicable

8. Confidentiality of Study Data: All data will be collected from patient charts and stored on a 128-bit encrypted password-protected Excel file that is accessible only to the researchers involved. The database will not include individually identifiable data for confidentiality purposes. A randomly assigned number will replace patients' identification. The key linking patient identity to the data number will be maintained

separately by the Principal Investigator on a different password-protected computer. Once data collection is complete, all identifiers will be destroyed at the earliest opportunity.

9. Potential Risks: There are no identifiable physical or emotional risks to the study participants. As this is a retrospective chart review, the only risk is the possibility of loss of confidentiality. However, this is unlikely due to the measures already in place to safeguard patient identity.

10. Potential Benefits: This study offers no direct benefit to the patients whose charts are being reviewed. However, study results may yield improvement in future care of patients with atherosclerosis deciding between CABG and PCI.

11. Alternatives: None, not applicable

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