**Introduction:**

Cardiovascular disease remains the leading cause of death for patients on dialysis. [1] Coronary artery disease and myocardial infarction remain important co-morbidities even after successful kidney transplant [2]. A prior study reported trends in outcome of post-transplant patients with ST elevation myocardial infarction (STEMI) [3]. However, trends and outcome of post-kidney transplant patients who present with non ST elevation myocardial infarction (NSTEMI) in the contemporary era are lacking. Thus, we analyzed a national database to report trends and outcome of kidney transplant recipients who present with NSTEMI in the United States.

**Methods:**

**Overview of Data**

The Healthcare Cost and Utilization project (HCUP) is the most comprehensive source of non-federal hospital care data. HCUP enables researchers, insurers, policymakers and others to study health care delivery and patient outcomes over time, and at the national, regional, State, and community levels [4]. The National (Nationwide) In-patient Sample (NIS) is a complex stratified sample comprising 20% of all hospital admissions in the United States. In 2018, 47 states and the District of Columbia contribute data to HCUP, representing more than 95% US population.

**Study Population**

We queried the NIS database to identify adult (> 17years) admissions for the primary diagnosis of NSTEMI (410.71) between January 2007 and September 2015. From these admissions, we isolated patients with prior kidney transplant (V42.0) who were not currently on hemodialysis (39.95) or peritoneal dialysis (54.98). This methodology has been implemented in prior studies with the NIS data to identify kidney transplant recipients with functioning graft [3]. We excluded patients who has chronic kidney disease (CKD; 585.1 – 585.5 & 585.9). Thus, our final study cohort consisted of adult patients in two groups (KTx – kidney transplant with functioning graft) and non-CKD (those without documented CKD) admitted to US non-federal hospitals with the primary diagnosis of NSTEMI between January 2007 and September 2015. Figure 1 provides the cohort selection flowchart. We utilized International Classification of Diseases, Ninth Edition, Clinical Modification (ICD- 9 CM) diagnosis and procedure codes to define clinical conditions and procedures performed during hospital stay. A detailed overview of codes used for each condition is provided in the online supplement.

We identified the following demographic characteristics for each patient: age, gender, weekday vs weekend admission and conventional Elixhauser co-morbidities provided by HCUP. Atrial fibrillation, history of coronary artery bypass grafting (CABG) or percutaneous intervention (PCI), prior myocardial infarction, smoking and anemia were abstracted using ICD-9 CM codes. Patient`s race was identified as Caucasian, African American, Hispanic or Others (comprising Asian, Pacific Islander etc). Primary insurance payee was identified as either Medicare, Medicaid, Private commercial insurance or self-pay. The NIS data further provides hospital characteristics for each admission. US is divided into 4 census regions: Northeast, West, Mid-west and South. Within each region, depending upon location and presence of a teaching program, hospitals are stratified as rural, urban teaching and urban non-teaching centers. Also within each region, patients are stratified into quartiles based on their zip-code adjusted median household income.

Using ICD-9 procedure (PCS) codes we identified those patients who underwent coronary angiography during the index admission. We further also identified those patients who had percutaneous intervention (PCI) or coronary artery bypass grafting (CABG).

The primary end-point of the study was determining trends for intervention (either PCI or CABG) in renal transplant recipients presenting with NSTEMI. Secondary end-points studied include in-hospital mortality, length of hospital stay. We also constructed logistic regression models to compare rates of coronary angiography/PCI/CABG and in-hospitlal mortality between KTx vs. non-CKD patients.

**Statistical Analysis**

The data is a stratified complex sample; appropriate clustering variable (HOSPID), strata variable (NIS\_STRATUM) and discharge weights (DISCWT) are provided in the data file. We used the complex survey method commands (PROC SURVEYFREQ & PROC SURVEYMEANS) available in SAS 9.4 (Statistical Analysis System, Cary, NC, 2016) to generate weighted estimates. Unadjusted Odds Ratio (uOR) and their 95% confidence limits (CL) were calculated from the derived contingency tables. Continuous variables are presented as mean (standard error) while categorical variables are reported as percentage (standard error). We used the students `t` test and Pearson Chi square tests to compare continuous and categorical data between the two cohorts (KTx and NKF). We used PROC SURVEYLOGISTIC with appropriate clustering to determine adjusted odds` for receiving intervention, either PCI or CABG in the renal transplant cohort. Co-variates included in the model were patient age, gender, co-morbidities i.e., heart failure, diabetes mellitus, complicated diabetes mellitus, hypertension (with and without complications), obesity, AIDS and frailty. We also included other patient risk factors i.e. prior history of PCI, CABG, prior stroke and presence of AICD. We calculated robust standard errors that correct for presence of dependence inherent within survey samples. Statistical significance of co-variates in the model was obtained with the non-parametric type 3 F-test. Results of PROC SURVEYLOGISTIC provides adjusted Odds` Ratio (aOR) with their 95% CL.

To study change in trends from 2007 to 2015, we first obtained weighted estimates for each year and then created an ordinal s x 2 table. The Cochran Armitage test z score was used to obtain a one-sided p-value to determine if the change observed over time is statistically significant. To determine whether the presence of prior renal transplant was associated with receipt of revascularization (PCI or CABG), we developed a hierarchical model with hospital identifier (HOSPID) as the random effect and other co-variates as fixed effect.

All results apart from trend analyses are reported as two-tailed at the 95% confidence level.

**Results:**

HCUP reported average 36,847,467 admissions per year between 2007 and 2015. From this cohort, we eventually identified xxx adult admissions with NSTEMI between January 2007 and September 2015. We further excluded xxx with chronic renal failure; thus our final cohort consists of 3,660,015 patients (post renal transplant = 7923 patients, normal renal function = 3,652,092 patients) admitted with NSTEMI during the study period. Figure 1 provides the cohort selection flowchart.

Patients in the renal transplant cohort were younger (mean age 60.65 vs 68.72 years; p < 0.001) and more likely to be males (63.68% vs 56.08%, p < 0.001). Diabetes mellitus (32.35 % vs 30.06%; p = 0.04) and complicated hypertension (76.72% vs 70.49%; p < 0.001) was higher in the renal transplant cohort. Both cohorts had equal probability of patients with prior myocardial infarction (10.01% vs 10.35%; p = 0.64) or prior PCI (11.64% vs 11.35%; p=0.71). Table 1 provides a comparison of co-morbidities and baseline characteristics in the two cohorts.

**Revascularization**

Overall, 58.01(57.27 – 58.76) % had coronary angiography during hospitalization. Among them, 30.2 (29.65 – 30.76) % had PCI while 8.5(8.25 – 8.73) % underwent CABG. Angiography rates were 58.03(57.29 – 58.77) % and 51.66(49.16 – 54.15) % among patients with non-CKD and renal transplant recipients respectively [aOR 0.53(0.47 – 0.59); p < 0.001] . Renal transplant recipients were 39% less likely to receive revascularization [ aOR 0.61(0.54 – 0.68); p < 0.001]. Renal transplant recipients were also less likely to receive either PCI [aOR 0.70(0.62 – 0.78); p < 0.001] or CABG [aOR 0.60(0.49 – 0.73); p < 0.001] during this hospital stay.

In-hospital mortality among renal transplant recipients [5.28(4.17 – 6.39) %] was similar to patients with normal renal function [uOR 1.04(0.83 – 1.30); p = 0.70]. Renal transplant recipients had a longer hospital stay [ 6.69 (6.27 – 7.10) days; p < 0.001] when compared to patients with normal renal function. Congestive heart failure at admission increased mortality [aOR 1.65(1.02 – 2.68); p = 0.03].

Would add trends in cor angio/PCI/CABG and mortality in KTx and non-CKD groups and also report in a supplemental table ORs for comparison for cor angio/PCI/CABG and mortality by year in the 2 groups.

1. Add comorbidities = fluid/ elec, PVD,
2. Trends in intervention according to year in renaltx patients
3. Trends for cor revasc in renal tx cohort
4. Mortality trends in renal tx cohort ; aOR for mortality in renal tx cohort.

References:

1. System, U.S.R.D., *USRDS annual data report: Epidemiology of kidney disease in the United States*. 2018 Bethesda, MD.

2. Kahn, M.R., et al., *Coronary artery disease in a large renal transplant population: implications for management.* Am J Transplant, 2011. **11**(12): p. 2665-74.

3. Gupta, T., et al., *Management and Outcomes of ST-Segment Elevation Myocardial Infarction in US Renal Transplant Recipients.* JAMA Cardiol, 2017. **2**(3): p. 250-258.

4. *Agency for Healthcare Research and Quality - Advancing Excellence in Health Care*. 2018 December 2018 [cited 2018 12/31/2018]; Available from: <https://www.ahrq.gov/data/hcup/index.html>.