HHS Public Access

Author manuscript

Int J Cardiol. Author manuscript; available in PMC 2020 October 15.

Published in final edited form as:

Int J Cardiol. 2019 October 15; 293: 197–202. doi:10.1016/j.ijcard.2019.05.064.

Incidence, Determinants and Impact of Acute Kidney Injury in Patients with Diabetes Mellitus and Multivessel Disease undergoing Coronary Revascularization: Results from the FREEDOM Trial

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Abstract

Background—The incidence and prognostic significance of acute kidney injury (AKI) in patients with diabetes mellitus and multivessel coronary artery disease undergoing coronary revascularization is not well known. The current analysis included patients randomized to PCI vs. CABG as part of the FREEDOM trial. We sought to examine the impact of AKI and its predictors in diabetic patients with multivessel coronary artery disease undergoing PCI vs. CABG.

Methods—We conducted a pre-specified subgroup analysis of the FREEDOM trial to examine the incidence, correlates and impact of AKI according to revascularization strategy. AKI predictors were identified using multivariable logistic regression and associations between AKI and outcomes were examined using Cox regression. The primary endpoint was the composite occurrence of all-cause death, stroke or myocardial infarction at 5 years of follow-up.

Results—AKI occurred more frequently in patients following CABG (15.6%) compared with PCI (9.1%) (P<0.001). AKI was associated with a higher risk for major cardiovascular events

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(MACE) at 5 years (34.6% vs. 20.5%, p<0.001), an effect that remained large and significant irrespective of CABG (HR=2.18 95% CI 1.44–3.31, p=<0.001) or PCI (HR=2.08 95% CI 1.35–3.21, p<0.0001). There was a non-significant interaction (p-value = 0.89) between the revascularization method and AKI, supporting that AKI is a significant risk factor in both revascularization methods.

Conclusions—Although risk for AKI was higher in patients undergoing CABG, the impact of AKI on MACE was substantial irrespective of revascularization strategy. Preventive strategies to identify patients at risk for AKI are warranted to mitigate the long-term effects of this complication.

Keywords

AKI; diabetes mellitus; revascularization; kidney injury; complications

Introduction

Acute Kidney Injury (AKI) is a common complication following cardiovascular procedures. It is associated with increased risk for short and long term adverse events as well as increased costs.[1–5] In addition, it predicts the future development of chronic kidney disease (CKD). [6, 7]

AKI following percutaneous coronary intervention (PCI) is associated with contrast dye as well as other risk factors.[8–10] AKI following coronary artery bypass surgery (CABG) is associated with preoperative, intraoperative, and postoperative factors.[11, 12] Irrespective of revascularization strategy, one of the main risk factors for AKI is prior renal dysfunction and diabetes mellitus.[13] Among diabetic patients, up to 25% of individuals may manifest some degree of renal impairment.[14] In subgroup analysis (non-randomized) of the ACUITY study, diabetic patients with acute coronary syndrome and multivessel disease treated with PCI had less acute kidney injury but greater need for repeat revascularization at one year.[15] To date, the rates of AKI following PCI versus CABG in patients with diabetes mellitus have never been evaluated in a randomized study. The current analysis included patients randomized to PCI vs. CABG as part of the FREEDOM trial.[16] We sought to examine the incidence, predictors and impact of AKI in diabetic patients with multivessel coronary artery disease undergoing PCI vs. CABG.

Methods

Patient Selection and Randomization

Detailed study methods and primary results of the FREEDOM trial have been previously reported.[16] In brief, the study enrolled patients with diabetes and angiographically confirmed multivessel coronary artery disease with a stenosis of more than 70% in two or more major epicardial vessels involving at least two separate coronary-artery territories and without left main coronary stenosis. For the present analysis, we excluded patients on chronic dialysis therapy. Randomization was conducted in a 1:1 ratio with the use of permuted blocks with dynamic balancing within each study center. A core laboratory

reading of all qualifying angiograms was conducted at the Cardiovascular Research Foundation in New York.

Revascularization and Pharmacologic Therapy

Sirolimus-eluting and paclitaxel-eluting stents were the predominant types of drug-eluting stents that were used in the trial, according to the timing of the study. The study protocol recommended that only one type of drug-eluting stent should be used in a given patient. A newer generation of drug-eluting stents could be used in the trial as long as they were approved for use. Dual antiplatelet therapy with aspirin and clopidogrel was recommended for at least 12 months after stent implantation. Arterial revascularization was encouraged for patients randomized to CABG.

Outcomes and Definitions

The primary outcome was a composite of death from any cause, nonfatal myocardial infarction and nonfatal stroke (major adverse cardiovascular events [MACE]), as previously defined. Glomerular filtration rate was estimated (eGFR) using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation.[17] CKD was defined as an eGFR < 60 ml/min/1.73m^2 in accordance with National Kidney Foundation guidelines. AKI was determined using the AKI network (AKIN) criteria [18], and defined as an absolute increase of at least 0.3mg/dl or a 50% relative increase, compared with admission creatinine. AKI was calculated using baseline and post-procedure (within 3 days of procedure) creatinine results. All patients were followed until death, last known contact or study end, whichever came first.

Statistical Analysis

Baseline clinical and procedural characteristics were compared between AKI groups stratified by revascularization strategy (CABG and PCI) using the Student's t-test for continuous and fisher exact test for categorical variables, respectively. Multivariable logistic regression was used to identify factors that predict AKI including all subjects, and within PCI and CABG groups. Sex and age were included regardless of their significance. All other variables were selected using stepwise regression with an entry and stay p-values of 0.30 and 0.20 respectively. Further, variables were excluded using backward elimination until all p-values were 0.10 or less. Rates of adverse events were expressed as Kaplan-Meier estimates of time to first event and compared across groups using the log-rank test. Within each revascularization group, hazard ratios for adverse events associated with AKI (versus no AKI) were generated using Cox proportional hazards regression with adjustment for the following covariates: gender, age, insulin use, history of MI, clinical presentation (stable angina / acute coronary syndrome), SYNTAX score, current smoking status, EuroSCORE, LVEF (left ventricular ejection fraction), eGFR, contrast load, and history of PVD (peripheral vascular disease). Formal interaction testing between the main effects of AKI versus no AKI and CABG versus PCI was performed on each individual endpoint. To account for reverse causation, a landmark analysis was conducted with Cox regression models for both MACE (major adverse cardiovascular events) and mortality after excluding events or censoring that happened in the first 30 days. In addition, the proportional hazard assumption was tested for the primary endpoint (MACE) within PCI and CABG group, and

it holds within each group. A p value of less than 0.05 was considered statistically significant. All the analysis was done with SAS program (version 9.4).

Results

The present cohort included 1692 patients (Appendix Figure 1). Two hundred and eight patients (12.3%) developed AKI following their procedures. AKI was more common in patients following CABG (15.6%) compared with PCI (9.1%) (P<0.001). The occurrence of more advanced AKI (stage 2 or 3) was more frequent in patients undergoing CABG (3.4% vs. 1.7%, p=0.03). Baseline clinical and procedural characteristics are presented in Tables 1 and 2 and in Appendix Tables 1 and 2, respectively.

There was a difference in the clinical characteristics of patients that developed AKI in the 2 treatment groups. In the PCI group, insulin dependent DM and stable angina as an indication for PCI were associated with AKI. In the CABG group, patients with AKI were older, had PVD, were treated with clopidogrel and insulin, had lower eGFR values and higher EuroSCORE values, had a complication following their CABG and required at least one blood transfusion.

Most parameters were well balanced between PCI and CABG. SYNTAX and EuroSCORE scores were similar irrespective of revascularization strategy in both groups. Revascularization was complete in the majority of patients with no significant differences between CABG and PCI groups (Table 2).

In the multivariable analysis of the overall cohort, higher BMI, insulin use, CABG and PVD were associated with higher risk of AKI, while statins and higher eGFR values were associated with decreased risk of AKI (Table 3a). In the PCI group, insulin use and stable disease were predictors of AKI (Table 3b). In the CABG group, higher BMI, clopidogrel and insulin use were associated with AKI while statins and higher eGFR values were protective of AKI (Table 3c). In an analysis of AKI incidence by eGFR values, AKI was less common in the PCI group in all patient groups (until eGFR 15ml/min/1.73m^2) (Table 4)

AKI was associated with longer hospital stay for PCI (4.0 vs. 2.6 days, p=0.01) and CABG (11.6 vs. 8.4 days, p<0.001). AKI was a significant predictor of outcome at 5 years in both the PCI and CABG groups (Table 5). Unadjusted rates of all events, with the exception of stroke, were significantly higher in the presence of AKI. After multivariable adjustment, associations remained significant for all-cause mortality, cardiac mortality, myocardial infarction, major bleeding and MACE in the PCI group. In the CABG group, AKI was associated with increased rates of all-cause mortality, cardiac and non-cardiac mortality, major bleeding and MACE. The risk of AKI was associated with a doubling of the risk of MACE and almost three times increase in all-cause mortality at 5 years.

Kaplan Meier curves at 5 years are presented for the entire cohort (Appendix Figure 2), PCI group (Appendix Figure 3) and CABG group (Appendix Figure 4). In a landmark analysis, patients surviving the first 30 days, AKI was still associated with increased risk of death and MACE at 5 years in all groups (Appendix Table 3). In addition, there was an interaction between the incidence of AKI and baseline renal function with lower eGFR values having

higher incidence of AKI (Appendix Table 3). AKI was associated with increased MACE regardless of the revascularization method (PCI/CABG). There was a non-significant interaction (p-value = 0.89) between the revascularization method and AKI, supporting that AKI is a significant risk factor in both revascularization methods.

We created a time dependent model for these outcomes and presented the results (Hazard ratio over time) in the appendix figure 5. In both PCI and CABG group, in the first months AKI group subjects were at higher risk of all-cause death or cardiac death, but the effect size decreases dramatically in the first year.

Discussion

The main findings of the present study include: 1. AKI is a more frequent complication after CABG versus PCI in patients with underlying DM and multivessel CAD; 2. Risk factors of AKI were largely distinct according to revascularization strategy, suggesting that underlying mechanisms for AKI might differ in patients undergoing CABG versus PCI; and 3. The impact of AKI on both ischemic and hemorrhagic complications is large and significant irrespective of revascularization strategy. To the best of our knowledge, these data represent the largest comparative evaluation of AKI in patients with diabetes mellitus treated by CABG or PCI.

In a post-hoc analysis of the ACUITY study, Ben-Gal et al.[15] previously reported AKI rates of 13.4% versus 33.6% ($p<0.001$) among patients with NSTE-ACS and DM undergoing PCI and CABG respectively. Analogously, Warren et al.[19] also reported an approximate 30% incidence of AKI in a pooled analysis of randomized trials involving ACS patients. Chang et al. reported higher AKI rates in the CABG group compared with PCI ranging from 6–20%.[20]. In the EXCEL study, randomizing patients with left main disease to PCI vs. CABG, AKI (using a 0.5mg/dl cutoff or dialysis) was found to be more common in the CABG group (2.5% vs. 0.6%, $p<0.001$). [21]

In contrast, we observed lower rates of AKI among those receiving CABG and PCI, differences that might be attributable to the inclusion of a more stable population in FREEDOM compared with earlier reports as well as to variations in the definitions of AKI across studies. In addition, our study was the only one that randomized patients with diabetes and multivessel disease to one of the two revascularization strategies. Notwithstanding these differences in absolute rates, however, we also found that relative risk for AKI was approximately 2-fold higher among those receiving CABG. [15] These findings were consistent across different eGFR baseline values. AKI was associated with adverse outcomes regardless of revascularization strategy. Despite the higher AKI rates in the CABG population, overall, AKI didn’t change the beneficial effect of CABG in this patient population.

Several studies have identified correlates of AKI that correspond to patient (age, sex, risk factors), procedural (contrast volume, intra aortic balloon pump use, urgency) and laboratory biomarkers (serum creatinine, serum glucose).[1, 11] Consistent with these earlier reports we also found that BMI, renal dysfunction, statin use, PVD and insulin-requiring DM were

contributors to AKI in the overall FREEDOM cohort. However, when examined by revascularization approach, only insulin-requiring DM emerged as a common and significant determinant of AKI among those treated with PCI and CABG. This finding highlights and reinforces the prognostic relevance of advanced DM as an important risk marker for subsequent renal dysfunction. The lack of overlap in other parameters suggests variability in the underlying pathophysiology or mechanisms leading to AKI among patients treated with CABG versus PCI. Increases in BMI, for example, were inversely related to AKI in CABG-treated patients whereas no such association was observed in the PCI population. It is plausible that the physiologic insult with CABG versus PCI is much greater in lower BMI compared with higher BMI patients, thereby accounting for this observation.[22]

In both CABG and PCI populations, AKI is associated with increased risks for death, MI as well as heart failure. [23] In addition, AKI has been to be associated with increased risk of kidney disease progression in PCI and CABG.[6, 7] Consistent with these earlier reports, we also observed excess risk among those with versus without AKI irrespective of revascularization strategy. While absolute rates of adverse events were higher among those treated with PCI, relative risks associated with AKI were comparable between groups with no evidence of interaction between AKI status and randomized treatment. Importantly, we also found that patients with AKI were at significantly higher risk for bleeding, highlighting that morbidity in patients with AKI extends to both ischemic and hemorrhagic complications. Giacoppo et al. previously reported similar associations in a post-hoc analysis of ACS patients undergoing PCI, results that we now extend to more stable patients treated with both CABG and PCI. [1] As post-procedural events might also lead to AKI, we performed a landmark analysis to account for such reverse causality, with results that were consistent with our primary findings. In aggregate our results, combined with earlier observations, highlight that risk after AKI is substantial and durable over time.

The clinical relevance of our findings is highlighted by the frequent occurrence of AKI, coupled with the significant impact of AKI on complications, length of stay and on subsequent cardiovascular risk. Due to recent advances in the field as well as physician awareness, AKI rates have decreased over recent years in patients treated by PCI. [24] Patients treated with LVEDP guided saline treatment or forced diuresis have lower AKI rates.[25–27] In addition, high dose statins have been associated with reduced rates of AKI following PCI[28] in some studies, but not in all studies.[29] Blood transfusions have been associated to be associated with AKI (adjusted odds ratio, 4.87 [4.71–5.04].[8] A restrictive blood transfusion strategy might improve PCI outcomes by reducing the risk of AKI. Admission hyperglycemia (above 200mg/dl) is associated with increased AKI risk (OR = 2.46, 95% CI 1.16–5.28; p = 0.018).[9] Biomarkers can also be used to predict AKI. In one study, Neutrophil/lymphocyte ratio, above 6.5, was associated with AKI in PCI patients. [30] Therefore, careful planning and treatment prior to PCI might reduce the risk of developing AKI.

The results of the current study should be interpreted within the context of several important limitations, the most relevant of which may be the mild- moderate level of renal impairment present in our cohort as the mean eGFR was ~ 70 ml/min/1.73 m^2. Therefore, the rates of AKI in patients with more severe CKD might be higher. Second, we did not measure urinary

output and therefore we may have underestimated the true incidence of AKI. Third, as with any subgroup analysis, our results should be considered hypothesis-generating and require confirmation in a larger dedicated study involving prevention of AKI patients alone. Lastly, pre procedural hydration protocol was not standardized and therefore might also affect our results.

In conclusion, these findings from the FREEDOM trial demonstrate that AKI is more common after CABG compared with PCI. Different risk factors are associated with AKI after each procedure suggesting different mechanisms of harm. However AKI does not influence the overall benefit of CABG over PCI in reducing 5-year CV events. Larger, prospective studies are warranted to confirm our findings and to evaluate targeted techniques in reducing AKI for patients undergoing PCI or CABG.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

Funding

Supported by grants (U01 01HL071988 and 01HL092989) from the NHLBI. Cordis, Johnson & Johnson, and Boston Scientific provided the stents; Eli Lilly provided abciximab and an unrestricted research grant; and Sanofi-Aventis and Bristol-Myers Squibb provided clopidogrel.

Abbreviations

AKI	Acute Kidney Injury
CABG	Coronary Artery Bypass Grafting
PCI	Percutaneous coronary intervention
MACE	Major Cardiovascular events
eGFR	Estimated glomerular filtration rate

References

[1]. Giacoppo D, Madhavan MV, Baber U, Warren J, Bansilal S, Witzenbichler B, et al. Impact of Contrast-Induced Acute Kidney Injury After Percutaneous Coronary Intervention on Short- and Long-Term Outcomes: Pooled Analysis From the HORIZONS-AMI and ACUITY Trials. Circulation Cardiovascular interventions. 2015;8:e002475. [PubMed: 26198286]

[2]. Elmistekawy E, McDonald B, Hudson C, Ruel M, Mesana T, Chan V, et al. Clinical impact of mild acute kidney injury after cardiac surgery. The Annals of thoracic surgery. 2014;98:815–22. [PubMed: 25086946]

[3]. Mangano CM, Diamondstone LS, Ramsay JG, Aggarwal A, Herskowitz A, Mangano DT. Renal dysfunction after myocardial revascularization: risk factors, adverse outcomes, and hospital resource utilization. The Multicenter Study of Perioperative Ischemia Research Group. Annals of internal medicine. 1998;128:194–203. [PubMed: 9454527]

[4]. Hobson CE, Yavas S, Segal MS, Schold JD, Tribble CG, Layon AJ, et al. Acute kidney injury is associated with increased long-term mortality after cardiothoracic surgery. Circulation. 2009;119:2444–53. [PubMed: 19398670]

[5]. Dasta JF, Kane-Gill SL, Durtschi AJ, Pathak DS, Kellum JA. Costs and outcomes of acute kidney injury (AKI) following cardiac surgery. Nephrology, dialysis, transplantation : official publication of the European Dialysis and Transplant Association - European Renal Association. 2008;23:1970–4.

[6]. Ishani A, Nelson D, Clothier B, Schult T, Nugent S, Greer N, et al. The magnitude of acute serum creatinine increase after cardiac surgery and the risk of chronic kidney disease, progression of kidney disease, and death. Archives of internal medicine. 2011;171:226–33. [PubMed: 21325112]

[7]. James MT, Ghali WA, Tonelli M, Faris P, Knudtson ML, Pannu N, et al. Acute kidney injury following coronary angiography is associated with a long-term decline in kidney function. Kidney international. 2010;78:803–9. [PubMed: 20686453]

[8]. Karrowni W, Vora AN, Dai D, Wojdyla D, Dakik H, Rao SV. Blood Transfusion and the Risk of Acute Kidney Injury Among Patients With Acute Coronary Syndrome Undergoing Percutaneous Coronary Intervention. Circulation Cardiovascular interventions. 2016;9.

[9]. Shacham Y, Gal-Oz A, Leshem-Rubinow E, Arbel Y, Keren G, Roth A, et al. Admission Glucose Levels and the Risk of Acute Kidney Injury in Nondiabetic ST Segment Elevation Myocardial Infarction Patients Undergoing Primary Percutaneous Coronary Intervention. Cardiorenal medicine. 2015;5:191–8. [PubMed: 26195971]

[10]. Shacham Y, Steinvil A, Arbel Y. Acute kidney injury among ST elevation myocardial infarction patients treated by primary percutaneous coronary intervention: a multifactorial entity. Journal of nephrology. 2016;29:169–74. [PubMed: 26861658]

[11]. Yi Q, Li K, Jian Z, Xiao YB, Chen L, Zhang Y, et al. Risk Factors for Acute Kidney Injury after Cardiovascular Surgery: Evidence from 2,157 Cases and 49,777 Controls - A Meta-Analysis. Cardiorenal medicine. 2016;6:237–50. [PubMed: 27275160]

[12]. Pannu N, Graham M, Klarenbach S, Meyer S, Kieser T, Hemmelgarn B, et al. A new model to predict acute kidney injury requiring renal replacement therapy after cardiac surgery. CMAJ : Canadian Medical Association journal = journal de l'Association medicale canadienne. 2016;188:1076–83.

[13]. Girman CJ, Kou TD, Brodovicz K, Alexander CM, O'Neill EA, Engel S, et al. Risk of acute renal failure in patients with Type 2 diabetes mellitus. Diabetic medicine : a journal of the British Diabetic Association. 2012;29:614–21. [PubMed: 22017349]

[14]. Baber U, Farkouh ME, Arbel Y, Muntner P, Dangas G, Mack MJ, et al. Comparative efficacy of coronary artery bypass surgery vs. percutaneous coronary intervention in patients with diabetes and multivessel coronary artery disease with or without chronic kidney disease. European heart journal. 2016;37:3440–7. [PubMed: 27572072]

[15]. Ben-Gal Y, Mohr R, Feit F, Ohman EM, Kirtane A, Xu K, et al. Surgical versus percutaneous coronary revascularization for multivessel disease in diabetic patients with non-ST-segment-elevation acute coronary syndrome: analysis from the Acute Catheterization and Early Intervention Triage Strategy trial. Circulation Cardiovascular interventions. 2015;8.

[16]. Farkouh ME, Domanski M, Sleeper LA, Siami FS, Dangas G, Mack M, et al. Strategies for multivessel revascularization in patients with diabetes. The New England journal of medicine. 2012;367:2375–84. [PubMed: 23121323]

[17]. Levey AS, Stevens LA, Schmid CH, Zhang YL, Castro AF 3rd, Feldman HI, et al. A new equation to estimate glomerular filtration rate. Ann Intern Med. 2009;150:604–12. [PubMed: 19414839]

[18]. Levin A, Warnock DG, Mehta RL, Kellum JA, Shah SV, Molitoris BA, et al. Improving outcomes from acute kidney injury: report of an initiative. American journal of kidney diseases : the official journal of the National Kidney Foundation. 2007;50:1–4. [PubMed: 17591518]

[19]. Warren J, Mehran R, Baber U, Xu K, Giacoppo D, Gersh BJ, et al. Incidence and impact of acute kidney injury in patients with acute coronary syndromes treated with coronary artery bypass grafting: Insights from the Harmonizing Outcomes With Revascularization and Stents in Acute Myocardial Infarction (HORIZONS-AMI) and Acute Catheterization and Urgent Intervention Triage Strategy (ACUITY) trials. American heart journal. 2016;171:40–7. [PubMed: 26699599]

[20]. Chang TI, Leong TK, Boothroyd DB, Hlatky MA, Go AS. Acute kidney injury after CABG versus PCI: an observational study using 2 cohorts. Journal of the American College of Cardiology. 2014;64:985–94. [PubMed: 25190232]

[21]. Stone GW, Sabik JF, Serruys PW, Simonton CA, Genereux P, Puskas J, et al. Everolimus-Eluting Stents or Bypass Surgery for Left Main Coronary Artery Disease. The New England journal of medicine. 2016;375:2223–35. [PubMed: 27797291]

[22]. Lagny MG, Jouret F, Koch JN, Blaffart F, Donneau AF, Albert A, et al. Incidence and outcomes of acute kidney injury after cardiac surgery using either criteria of the RIFLE classification. BMC nephrology. 2015;16:76. [PubMed: 26025079]

[23]. Olsson D, Sartipy U, Braunschweig F, Holzmann MJ. Acute kidney injury following coronary artery bypass surgery and long-term risk of heart failure. Circulation Heart failure. 2013;6:83–90. [PubMed: 23230310]

[24]. Amin AP, Salisbury AC, McCullough PA, Gosch K, Spertus JA, Venkitachalam L, et al. Trends in the incidence of acute kidney injury in patients hospitalized with acute myocardial infarction. Archives of internal medicine. 2012;172:246–53. [PubMed: 22332157]

[25]. Brar SS, Aharonian V, Mansukhani P, Moore N, Shen AY, Jorgensen M, et al. Haemodynamic-guided fluid administration for the prevention of contrast-induced acute kidney injury: the POSEIDON randomised controlled trial. Lancet (London, England). 2014;383:1814–23.

[26]. Chorin E, Ben-Assa E, Konigstein M, Rofe MT, Hochstadt A, Galli N, et al. Prevention of post procedural acute kidney injury in the catheterization laboratory in a real-world population. International journal of cardiology. 2017;226:42–7. [PubMed: 27783968]

[27]. Putzu A, Boscolo Berto M, Belletti A, Pasotti E, Cassina T, Moccetti T, et al. Prevention of Contrast-Induced Acute Kidney Injury by Furosemide With Matched Hydration in Patients Undergoing Interventional Procedures: A Systematic Review and Meta-Analysis of Randomized Trials. JACC Cardiovascular interventions. 2017;10:355–63. [PubMed: 28231903]

[28]. Han Y, Zhu G, Han L, Hou F, Huang W, Liu H, et al. Short-term rosuvastatin therapy for prevention of contrast-induced acute kidney injury in patients with diabetes and chronic kidney disease. Journal of the American College of Cardiology. 2014;63:62–70. [PubMed: 24076297]

[29]. Sarma A, Cannon CP, de Lemos J, Rouleau JL, Lewis EF, Guo J, et al. The incidence of kidney injury for patients treated with a high-potency versus moderate-potency statin regimen after an acute coronary syndrome. Journal of the American Heart Association. 2014;3:e000784. [PubMed: 24786143]

[30]. Arbel Y, Shacham Y, Ziv-Baran T, Laufer Perl M, Finkelstein A, Halkin A, et al. Higher neutrophil/lymphocyte ratio is related to lower ejection fraction and higher long-term all-cause mortality in ST-elevation myocardial infarction patients. Can J Cardiol. 2014;30:1177–82. [PubMed: 25154806]

Highlights

- The current analysis included patients randomized to PCI vs. CABG as part of the FREEDOM trial.
- AKI occurred more frequently in patients following CABG (15.6%) compared with PCI (9.1%) (P<0.001).
- AKI was associated with a higher risk for major cardiovascular events (MACE) at 5 years (34.6% vs. 20.5%, p<0.001).
- Risk Factors for AKI were different in PCI vs. CABG, suggesting different mechanisms.

Table 1.

Baseline Clinical Characteristics by Treatment Modality and Renal Function

	PCI			CABG		
	AKI N=79	**No AKI N=789**	**P-value**	**AKI N=129**	**No AKI N=695**	**P-value**
Age (± SD)	64.2±9.5	63.0±8.9	0.24	64.5±8.8	62.5±9.0	0.02
Male Gender, n (%)	57 (72.2)	574 (72.8)	0.90	93 (72.1)	480 (69.1)	0.53
BMI (± SD)	30.4±6.4	29.5±5.2	0.25	30.6±5.8	29.7±5.2	0.07
Current Smoker, n (%)	11 (13.9)	112 (14.2)	>0.99	20 (15.5)	119 (17.1)	0.70
Hypertension, n (%)	66 (83.5)	663 (84.0)	0.87	117 (90.7)	584 (84.0)	0.06
Dyslipidemia, n (%)	63 (79.7)	666 (84.4)	0.26	104 (80.6)	589 (84.7)	0.24
History of myocardial infarction, n (%)	26 (32.9)	196 (24.8)	0.14	35 (27.1)	178 (25.6)	0.74
PVD, n (%)	12 (15.2)	77 (9.8)	0.17	20 (15.5)	63 (9.1)	0.04
Type of diabetes (Type 1)	8 (10.1)	25 (3.2)	0.01	7 (5.4)	28 (4.0)	0.48
CKD	26 (32.9)	182 (23.1)	0.05	50 (38.8)	158 (22.7)	0.0002
Admission Medications						
Aspirin, n (%)	73 (92.4)	718 (91.0)	0.84	119 (92.2)	627 (90.2)	0.62
Beta-blockers, n (%)	58 (73.4)	601 (76.2)	0.58	99 (76.7)	519 (74.7)	0.66
Statins, n (%)	60 (75.9)	656 (83.1)	0.12	100 (77.5)	586 (84.3)	0.07
Clopidogrel, n (%)	14 (17.7)	214 (27.1)	0.08	38 (29.5)	131 (18.8)	0.01
Insulin, n (%)	37 (46.8)	259 (32.8)	0.02	57 (44.2)	198 (28.5)	<0.001
Anticoagulants, n (%)	9 (11.4)	131 (16.6)	0.26	24 (18.6)	99 (14.2)	0.23
Nitrates, n (%)	31 (39.2)	317 (40.2)	0.90	53 (41.1)	258 (37.1)	0.43
ACEI/ARB, n (%)	54 (68.4)	512 (64.9)	0.62	86 (66.7)	448 (64.5)	0.69
Laboratory results						
Glycated Hemoglobin (g/l)	8.0±1.6	7.7±1.8	0.17	7.6±1.4	7.7±1.7	0.25
eGFR (ml/min/1.73m^2)	71.8±28.0	76.3±20.5	0.17	68.5±24.0	76.1±19.4	<0.001
LVEF	57.3±11.9	58.4±11.5	0.43	58.5±13.6	58.9±11.1	0.70
Clinical Presentation						
STEMI, n (%)	3 (3.8)	57 (7.2)	0.35	7 (5.4)	41 (5.9)	>0.99
NSTEMI, n (%)	13 (16.5)	202 (25.6)	0.08	33 (25.6)	168 (24.2)	0.74
Stable angina, n (%)	63 (79.7)	530 (67.2)	0.02	89 (69.0)	486 (69.9)	0.84

BMI- Body Mass Index, PCI- percutaneous coronary intervention, CABG- coronary artery bypass grafting, STEMI – ST elevation myocardial infarction, TIA- transient ischemic attack, PVD- peripheral vascular disease, ACEI- Angiotensin converting enzyme inhibitors; ARB - Angiotensin receptor blocker, CTO- chronic total occlusion

Table 2.

Baseline Procedural Characteristics by Treatment Modality and Renal Function

	PCI			CABG		
	AKI N=79	**No AKI N=789**	**P-value**	**AKI N=129**	**No AKI N=695**	**P-value**
Risk Scores						
EuroSCORE	3.0±2.9	2.6±2.2	0.28	3.3±3.5	2.6±2.2	0.04
SYNTAX score	27.2±9.7	26.1±8.4	0.25	25.4±8.1	26.1±8.9	0.45
Number of lesions	3.2±1.3	3.0±1.3	0.32	-	-	-
CTO	32/442 (7.2)	252/4610 (5.5)	0.13	41/741 (5.5)	236/4172 (5.7)	>0.99
Bifurcation	95/441 (21.5)	1038/4609 (22.5)	0.68	149/739 (20.2)	856/4153 (20.6)	0.81
Staged procedures	2.6±1.7	2.5±1.1	0.91	-	-	-
Number of lesions stented	3.4±1.4	3.6±1.4	0.20	-	-	-
Surgery off pump	-	-	-	22 (17.1)	126 (18.1)	0.90
Number of graft vessels	-	-	-	2.8±0.7	2.9±0.8	0.14
Number of IMA	-	-	-	1.1±0.5	1.1±0.4	0.51
Complete revascularization	69 (87.3)	699 (88.6)	0.71	113 (87.6)	629 (90.5)	0.34
Contrast Volume (cc)	347.4±164. 0	317.3±156.0	0.11			
IMA (Yes/No)	-	-	-	122 (94.6)	660 (95.0)	0.83
Double IMA (Yes/No)	-	-	-	19 (14.7)	76 (10.9)	0.23
Transfusions at Discharge	-	-	-	-	-	-
At least one PRBC Transfusion	3 (3.8)	23 (2.9)	0.72	50 (38.8)	187 (26.9)	0.01
At least one Platelet Transfusions	0 (0.0)	11 (1.4)	0.61	12 (9.3)	34 (4.9)	0.06
At least one FFPs Transfusions	0 (0.0)	4 (0.5)	>0.99	12 (9.3)	44 (6.3)	0.25
At least one Whole Blood Transfusions	0 (0.0)	2 (0.3)	>0.99	7 (5.4)	18 (2.6)	0.09
Complications at discharge for patients who underwent CABG						
Complications occur during or following the CABG procedure	-	-	-	51 (39.5)	134 (19.3)	<0.001
Arrhythmia: SVT	-	-	-	19 (14.7)	61 (8.8)	0.05
Atria Fibrillation	-	-	-	11 (8.5)	40 (5.8)	0.22
Arrhythmia: VT	-	-	-	3 (2.3)	8 (1.2)	0.39
Other Arrhythmia	-	-	-	17 (13.2)	39 (5.6)	0.004
Repeat Sternotomy for Bleeding	-	-	-	8 (6.2)	16 (2.3)	0.04
Deep Sternal Wound Infection	-	-	-	3 (2.3)	12 (1.7)	0.72
Sepsis or Endocarditis	-	-	-	6 (4.7)	5 (0.7)	0.003
GI Bleeding, Perforation or Infarction	-	-	-	2 (1.6)	2 (0.3)	0.12
Respiratory Failure	-	-	-	9 (7.0)	9 (1.3)	<0.001
Post Procedure Hospital Stay (± SD)	4.0±4.5	2.6±3.1	0.01	11.6±9.3	8.4±6.8	<0.001

CTO- chronic total occlusion

Table 3:

Variables associated with the development of AKI in multivariable regression models **A**- Association of AKI and predictor variables in the entire cohort. **B**- Association of AKI and predictor variables for subjects who underwent PCI procedure. **C**- Association of AKI and predictor variables for subjects who underwent CABG procedure.

A			
	Parameter	**OR (95% CI)**	**P-value**
	BMI	1.03 (1.01,1.06)	0.02
	eGFR	0.99 (0.98,1)	0.01
	PVD	1.58 (1.03,2.44)	0.04
	Statins	0.61 (0.43,0.88)	0.01
	Insulin	1.82 (1.33,2.48)	<0.001
	PCI vs CABG	0.51 (0.38,0.69)	<0.001
B			
	Parameter	**OR (95% CI)**	**P-value**
	Insulin	1.88 (1.17,3.03)	0.01
	Stable coronary heart disease vs ACS	1.96 (1.1,3.46)	0.02
C			
	Parameter	**OR (95% CI)**	**P-value**
	BMI	1.04 (1,1.08)	0.04
	eGFR	0.98 (0.97,1)	0.004
	PVD	1.73 (0.97,3.07)	0.06
	Statins	0.59 (0.36,0.96)	0.04
	Clopidogrel	1.89 (1.21,2.94)	0.005
	Insulin	1.86 (1.24,2.79)	0.003

Table 4

Rates of AKI by baseline eGFR values.

		PCI (N=868)		CABG (N=824)	
		AKI N=79	**P-value**	**AKI N=129**	**P-value**
GFR Categories	**GFR ml/min/1.73 m^2**		0.03*		0.001*
1: Normal or high	≥90	16 (6.5%)		23 (11.1%)	
2: Mildly decreased	60–89	37 (8.9%)		56 (13.7%)	
3A: Mildly to moderately decreased	45–59	13 (9.8%)		32 (22%)	
3B: Moderately to severely decreased	30–44	11 (18.9%)		13 (27%)	
4: Severely decreased	15–29	1 (12.5%)		5 (38%)	
5: Kidney failure	<15	1		0	

Table 5.

Rates of Adverse Events* by AKI and Adjusted Hazard Ratios (aHR) The models were adjusted for age, gender, syntax score, BMI, insulin use, current smoking, history of MI, PVD, and hypertension, ACS/stable coronary heart disease, aspirin, clopidogrel, eGFR, EUROSCORE and LVEF.

	PCI					CABG					P-Interaction
	AKI (N=79)	No AKI (N=789)	P-value (log-rank)	aHR (95% CI)	p-value	AKI (N=129)	No AKI (N=695)	P-value (log-rank)	aHR (95% CI)	p-value	
Death, n (%)	20 (29.8)	79 (14.6)	<0.001	2.38 (1.38,4.13)	0.002	26 (23.7)	44 (7.9)	<0.001	3.67 (2.18,6.18)	<0.001	0.27
Cardiac Death, n (%)	16 (25.5)	49 (9.5)	<0.001	3.10 (1.62,5.91)	<0.001	16 (13.3)	27 (4.9)	<0.001	3.59 (1.85,6.96)	<0.001	0.78
Non-Cardiac Death, n (%)	4 (5.8)	30 (5.6)	0.45	1.39 (0.46,4.15)	0.56	10 (12.0)	17 (3.2)	<0.001	3.87 (1.66,9.05)	0.002	0.21
Myocardial Infarction, n (%)	17 (28.3)	73 (12.5)	<0.001	2.36 (1.32,4.21)	0.004	8 (7.0)	30 (5.0)	0.26	1.61 (0.72,3.60)	0.25	0.44
Stroke, n (%)	1 (1.5)	16 (2.4)	0.70	0.52 (0.07,4.07)	0.53	7 (6.2)	26 (4.9)	0.28	1.47 (0.62,3.53)	0.38	0.54
Major Bleeding, n (%)	10 (16.6)	50 (7.3)	0.02	2.27 (1.13,4.58)	0.02	14 (14.0)	40 (6.3)	0.02	1.90 (0.99,3.66)	0.05	0.64
MACE, n (%)	30 (43.1)	148 (24.6)	<0.001	2.08 (1.35,3.21)	<0.001	33 (29.2)	92 (15.9)	<0.001	2.18 (1.44,3.31)	<0.001	0.89

AKI – Acute kidney Injury; HR – hazard ratio; CI – confidence interval; MACE – major adverse cardiovascular events.

*Event rates expressed as Kaplan-Meier estimates at 5 years.