# OUTCOMES OF CORONARY ANGIOPLASTY IN DIABETIC PATIENTS – A RETROSPECTIVE STUDY

Galla Raghu Kishore, Chandragiri Susmitha, PV Rao

*ABSTRACT*

***Aims:*** *We want to study the effect of diabetes Mellitus (DM) on the outcomes in patients with coronary artery disease (CAD) undergoing percutaneous coronary intervention (PCI) comparing those with non diabetics, with reference to gender.*

***Methods:*** *We retrospectively evaluated the consecutive patients undergoing PCI either with acute coronary syndrome (ACS) or chronic stable angina (CSA) in our institute between March 2014 to March 2015. We followed them up to one year for the major cardiovascular events (MACES) and other complications. We compared the rate of events between diabetic and non diabetic patients along with gender subgroups and tested for the significance.*

***Results:*** *In 645 patients undergone PCI in our institute, 326(50.5%) were diabetics, of them 104(31.9%) were females. Patients with diabetes with CAD were older with more incidence of hypertension and kidney derangement than non diabetics. History of CAD and previous procedure are definitely more in diabetics as is multi vessel disease (p=0.02) and LV dysfunction (p=0.003).Total number of patients presenting with complications within one year of PCI is 18(0.02%).Of them 14 are males and 4 are females,14 were diabetics and 4 were non diabetics. There was no statistical significance in the outcomes between female & males (p=0.7), diabetics females & diabetic males (p=0.48) and non diabetics females & nondiabetic males(p=0.7).Male patients with diabetes had significantly more complications than non diabetic males (p=0.05) but there is no significant difference between diabetic and non diabetic females (p=0.59).*

***Conclusion:*** *Patients with DM undergoing PCI had more complications than non diabetics with significant difference between male diabetics and non diabetic males. This difference is not significant between diabetic and non diabetic females.*

*KEY WORDS: Diabetes, Percutaneous Coronary intervention - PCI, Females.*

Article received on 25 March2016, published on 30 April 2016.

Galla Raghu Kishore[1]; Chandragiri Susmitha[2], PV Rao [3].
[1] DM student, Department of Cardiology,NIMS,India
[2] DM student, Department of Nephrology, NIMS, India
[3] Professor of Endocrinology (Retd)
Corresponding author: Galla Raghu Kishore ,
Email: raghukishoregalla@gmail.com

## INTRODUCTION

The prevalence of diabetes is rising worldwide reaching epidemic proportions[1].Diabetic patients have a greater burden of atherogenic risk factors than nondiabetic patients, including hypertension, obesity, dyslipidemia, insulin resistance and elevated levels of plasma fibrinogen[2].Patients with diabetes have higher incidence of coronary artery disease and high rate of complications before and after revascularization procedures. The National Cholesterol Education Program report from the United States and guidelines from Europe consider type 2 diabetes to be a coronary artery disease (CAD) equivalent, placing it in the highest risk category for CAD[3]. It is estimated that more than 50% of adult diabetics have significant coronary atherosclerosis, prevalence 10 times greater than that of the general population, which is about 2%-4% and 15-25% of patients who undergo percutaneous or surgical coronary angioplasty are diabetics[4].Cardiovascular mortality in all age groups and for both sexes rises equivalently with DM or a history of myocardial infarction (MI) both are profoundly synergistic[5].There is a recent trend towards coronary artery disease affecting young generation and the major risk factor being diabetes. Furthermore, in patients with DM there is two to four fold increased risk of mortality after MI, and worse overall long-term prognosis with CAD[6,7].During the past decade, there is much advancement in both percutaneous coronary intervention (PCI) and surgical techniques to improve methods of coronary revascularization. Although these advancements have improved outcomes in diabetic patients, this population still experiences significantly worse outcomes compared with the general population[8], and the optimal revascularization strategy in diabetic patients remains unclear. Gender differences in CAD and its outcomes do exist in diabetic patients with females are more aged with more

comorbidities and a high in patient mortality than male patients[9].

This study is mainly aimed to evaluate the outcomes of PCI in diabetic patients comparing those who are non diabetics and to see if there is any significant difference in outcomes and complication between these two subgroups especially with reference to the gender.

## MATERIALS & METHODS

We have retrospectively analyzed the data of 645 patients presenting with obstructive CAD undergoing PCI in the Nizam's Institute of Medical Sciences, Hyderabad, India between March 2014 to March 2015.We included both the stable and unstable coronary artery disease patients in our study. We excluded patients with significant renal, hepatic & other systemic dysfunction and patients who are in severe cardiogenic shock.

Institutional ethical guidelines were followed. Informed consent was taken from all the patients before inclusion into the study. All patients were evaluated after a detailed history, physical examination, and appropriate investigations. Demographic and clinical characteristics of patients were documented. Blood samples were collected at baseline and at 8–12 h and 18–24 h after the procedure, and were analyzed in a core biochemistry laboratory. The biochemical parameters are repeated at 15 days and 6 months and clinically followed up to one year.

All patients were pre-treated with oral aspirin and Clopidogrel or Prasugrel or Ticagrelor 2–6 h prior to the procedure and glycoprotein IIb/IIIa inhibitor or bivaluridin is used in accordance with the discretion of the operator. PCI done through radial or femoral route were included. All patients undergoing PCI were given 70 IU/kg unfractionated heparin before PCI, while drug eluting stents were deployed in all the patients. Dual antiplatelet therapy was recommended post-PCI at least for 1 year.

All the patients were classified according to their angiographic profile as single vessel disease (>70% lesion involving one epicardial coronary artery) or multi vessel disease (>70% stenosis in 2 or more epicardial coronary arteries).Angiographic success was defined as residual coronary artery stenosis < 50% after balloon angioplasty or < 20% after stent implantation with normal TIMI grade 3 flow .ECGs were taken immediately after the procedure and after 24 hours to look for any fresh changes. Cardiac enzymes were sent after 12 and 24 hours to rule out any procedure related complications, recurrent MI or acute stent thrombosis. Additional ECGs or cardiac enzymes were performed in patients complaining of chest pain after the procedure.

FOLLOW UP: All the patients were followed up to one year. Biochemical parameters and echocardiography were performed at 15 days and one year. The events and complications occurred during the follow up were noted and clinical records were reviewed whenever necessary. MACE was defined as a composite of death from any cause, MI, and the need for repeat revascularization (new PCI or coronary revascularization surgery). These patients are divided into diabetic and non diabetic sub groups and most of the baseline demography, risk factors, biochemical variables, clinical and angiographic profiles and complications were compared between these.

STATISTICAL ANALYSIS: Data analysis was performed using Minitab version 16 software. The frequency of abnormal results were determined for each marker and compared by the *Fisher's exact test*. Continuous variables were expressed as mean ± SD and were compared by the ANOVA test. Categorical variables were compared using chi-square test. Results with a p value $<0.05$ is considered to be significant.

## RESULTS

Totally 645 patients presenting with Coronary artery disease undergoing PTCA between March 2014 to March 2015 were included in the study. Total number of patients undergoing PTCA included in the study is 645. 121(18.8%) patients presented with Myocardial infarction (STEMI/NSTEMI), 162 (25.1%) patients with unstable angina and 362 (56.1%) patients with CSA. Patients having history of prior myocardial infarction in 45 (6.9%), PCI in 123(19%) and prior CABG in 31(4.8%) of patients.429 (66.51%) patients were hypertensives and 326 (50.54%) were diabetics. M:F 2.9:1. The demographic features of these patient details were given in Table 1.

Out of them 104 (31.9%) patients were females. Patients with diabetes with CAD were older with more incidence of hypertension and kidney derangement than non

diabetics. History of CAD and previous procedure are definitely more in diabetics as is LV dysfunction (p=0.003).

Table 1: Shows the baseline demographic characteristics of the study population.

| Parameters | Value |
|---|---|
| Age (years) | 57.69 ± 11.06 |
| Male(%) | 478 (74.10) |
| Hypertension (%) | 429(66.51) |
| Smoking (%) | 162(25.11) |
| Diabetes mellitus (%) | 326(50.54) |
| MI (%) | 121(18.75) |
| Unstable angina | 162(25.11) |
| Chronic stable angina (%) | 362(56.12) |
| Left ventricular dysfunction (%) | 216(33.48) |
| Previous PCI (%) | 123(19.06) |
| Prior CABG (%) | 31(0.04) |
| Prior MI (%) | 45(0.06) |

Non diabetics were presented more commonly with MI whereas diabetics were presented with unstable angina or CSA (Table 2).

Table 2: Showing demographic, clinical & biochemical parameters of diabetics vs non diabetics

| Parameter | Diabetics (n=326) | Non diabetics (n=319) | p value |
|---|---|---|---|
| Age(yrs) | 58.6 ± 10.1 | 56.6 ± 12.01 | 0.02 |
| HTN | 291(89.3%) | 138(43.3%) | 0.00 |
| Females | 104(62.3%) | 63(37.7%) | - |
| Hb | 12.8 ± 2.2 | 13.19 ± 2.15 | 0.02 |
| S.Creat. | 1.3 ± 0.4 | 1.19 ± 0.27 | 0.00 |
| Previous PCI | 80(24.5%) | 43(13.5%) | 0.00 |
| Previous CABG | 23(7.1%) | 8(2.5%) | 0.006 |
| Prior MI | 29(8.9%) | 16(4.9%) | 0.052 |
| LV dys. | 127(38.9%) | 89(27.1%) | 0.003 |
| Diagnosis<br>MI<br>USA<br>CSA | <br>51(15.6%)<br>87(26.7%)<br>188(57.7%) | <br>70(21.3%)<br>75(22.8%)<br>174(52.9%) | <br>0.04<br>0.35<br>0.4 |

In Table 3 PCI details were given. Total no of lesions treated in DM were 440 and in non-diabetics were 401. Multi vessel disease is significantly high in Diabetics (p=0.002).

Table 3: Comparing of Angiographic profile of the diabetic and non diabetic subgroups.

| Variables | DM | Non DM | p value |
|---|---|---|---|
| Target vessel<br>Single vessel<br>Two vessels<br>Multi vessel PCI | <br>221(67.8%)<br>96(29.4%)<br>09(2.8%) | <br>237(74.3%)<br>82(25.7%)<br>00 | <br>0.07<br>0.3<br>0.002 |
| Type of target lesion<br>A<br>B<br>C | <br>209<br>90<br>26 | <br>221<br>81<br>17 | <br>0.2<br>0.5<br>0.2 |
| Mean Stent len.(mm) | 21.5± 10.6 | 21.8 ± 8.9 | 0.6 |
| Mean stent dia.(mm) | 2.98 ± 0.82 | 3.04 ± 0.96 | 0.4 |
| Mean no of stents | 1.43 | 1.36 | 0.5 |
| Use of Gp IIb/IIIa I | 36 | 30 | 0.5 |

Total number of patients presenting with complications within one year of PCI is 18(0.02%).Of them 14 are males and 4 are females. 5 patients presented with angina, 7 patients developed stent thrombosis, 3 patients had CCF, 1 patient developed Contrast induced nephropathy (CIN) and 2 patients died during this period of follow up. Of the 18 patients presented with complications 12 patients are having diabetes, 10 are males and 2 are females. Out of 6 patients presented with complications 4 were males and 2 were females. There was no statistical significance in the outcomes between female & males (p=0.7), diabetics females & diabetic males (p=0.4) and non diabetics females & nondiabetic males(p=0.7) (Table 4).

Table 4: Details of outcomes at one year.

| Complications | Females | Males | p value |
|---|---|---|---|
| Total outcomes (n=18) | 4(2.3%) | 14(2.9%) | 0.7 |
| Diabetics (n=12) | 2(1.1%) | 10(2.1%) | 0.4 |
| Non diabetics (n=6) | 2(1.2%) | 4(0.8%) | 0.7 |

Table 5: Results of Chi Square analysis for outcomes .

| Variables | Disease | No of pts | Outcomes | $X^2$ value | RR | 95% CI | p value |
|---|---|---|---|---|---|---|---|
| Male | DM | 222 | 10 | 3.68 | 2.9 | 0.85 to 11.51 | 0.05 |
| | Non DM | 256 | 4 | | | | |
| Female | DM | 104 | 2 | 0.29 | 0.59 | 0.05 to 5.97 | 0.6 |
| | Non DM | 63 | 2 | | | | |

With the Chi square test, there was a significant difference between diabetics and non diabetic male patients in view of complications and male patients with diabetes are at a significantly higher risk of complications after PCI than those not having diabetes. Whereas, this is not true for females (Table 5).

Two patients died, both of them were diabetics. Mortality rate was 0.6% without statistical difference between diabetics and non diabetics (p=0.2).

## DISCUSSION

Diabetic patients currently comprises of approximately one-fourth to one third of patients referred for PCI{10]. Diabetic patients experience worse outcomes than nondiabetic patients undergoing either coronary artery bypass grafting (CABG) or PCI.

When matched for other patient characteristics, diabetic patients have more extensive and diffuse CAD[11]. The higher risk of complications also persists after PCI, where higher rates of acute MI and repeat revascularization were reported in diabetes patients[12,13]. Data from large populations of diabetic patients in the National Heart, Lung, and Blood Institute Dynamic Registry[14,15] showed that despite comparable acute procedural results, diabetic patients have lower long-term survival rates, and increased rates of re-infarction and target lesion revascularization compared with nondiabetic patients. Kip et al[12], in the National Heart, Lung, and Blood Institute Dynamic Registry, the results of balloon angioplasty were specifically compared between 281 diabetics and 1833 non-diabetics. The diabetics were older, had more comorbidity, were more often women, and had more extensive and diffuse coronary disease. The initial angiographic success rate and degree of revascularization (complete vs incomplete) were similar, but the incidence of the endpoint formed by mortality, infarction, or the need for urgent revascularization during hospitalization was 11% in diabetics and only 6.7% in non-diabetics (P<0.01), The mortality and incidence of infarction in the hospital phase were greater in diabetics, especially diabetic women, who had a mortality of 8%. The long-term evolution was clearly unfavorable in diabetics: the adjusted mortality at 9 years was twice as high in diabetics (36% vs 18%; RR, 1.82; 95% CI, 1.41- 2.34), the incidence of infarction was 60% higher (29% vs 19%), and the need for new revascularization procedures was greater in diabetics (33% more required new angioplasty and 19% more needed coronary surgery in the follow-up than in non-diabetics). In our study half of the patients underwent PCI are diabetics and the two groups are almost equally numbered with differences in baseline characteristics. Diabetic patients when compared with non diabetics, are more older (58.63 ± 10.14 vs 56.66 ± 12.01) ,had more incidence of Hypertension (89.26% vs 43.26%), less mean hemoglobin (12.80 ± 2.23 vs 13.19 ± 2.15), more renal dysfunction (Serum Creatinine 1.32 ± 0.36 vs 1.19 ± 0.27) and significantly more incidence of LV dysfunction (38.95% vs 27.05%, p=0.003). History of previous revascularization by either PCI or CABG is also more in diabetics 31.58% vs 15.97 % (p=0.00 for PCI and p=0.006 for CABG) in non-diabetics. History of previous MI is 8.89% in diabetics vs 4.86% in non-diabetics (p=0.05). Diabetics were presented more frequently with unstable angina and chronic stable angina (84.35% vs 75.68%) while myocardial infarction is more in non-diabetics (21.27% vs 15.64%). Analysis of the angiographic profile revealed that diabetics have more incidence of multi vessel disease (32.20% vs 24.92% p=0.002), with more number of complex (B & C) lesions (35.58% vs 29.78%) and more mean number of stents per patient (1.43 vs 1.36) than the non diabetic sub group. All the patients who underwent triple vessel PCI (n=9) were diabetics.

Similar results were reported by Schomig et al[16] in a retrospective review of more than 20,000 patients undergoing PCI from 1980 to 1999. During this period, in-hospital mortality in diabetic patients undergoing PCI

nearly doubled in both the elective (0.8% versus 1.4%; P<0.001) and emergent (6.9% versus 12.7%; P<0.001) settings. In various trials and registries like Stein (Emory)[17], CABRI[18], EAST[19], BARI[20], DUKE University[21] diabetics is consistently associated with multi vessel disease, more complications and revascularization rates as well as higher mortality than their non diabetic counterparts. In one year follow up in our study totally 18 patients were presented with complications, of them 14 (77.77%) were diabetics. In them 8 patients presented with MACEs including 2 deaths and 6 stent thrombosis needing emergency revascularization. Of these 8 patients presented with MACEs 6 patients were diabetics (75%) including the 2 patient who died.

Diabetes portends adverse outcome irrespective of the revascularization strategy chosen. Diabetes is an independent risk factor for increased early and late mortality in patients treated with CABG[22.23]. In a review of 9920 patients with diabetes and 2278 patients without diabetes from a single centre over 15 years, Calafiore et al[24] revealed lower survival rates in diabetic patients versus nondiabetic patients at five-year (78%versus 88%) and 10-year (50% versus 71%) follow-up. In a large cohort using clinical data from a registry of 130,985 PCI procedures in Belgium, from January 2006 to February 2011. Compared to males, females were significantly older (70.3 vs. 64.8 years), and were more frequently diabetic or hypertensive. Unadjusted in-hospital mortality rates were higher in females versus males (2.5% for women and 1.6% for men, p<0.0001). After multivariable analysis, female gender remained an independent predictor of mortality (odds ratio 1.35, 95% CI: 1.22-1.49, p < 0.0001) after multivariable adjustment[9]. Latest PROMISE trail by Hemal K et al [25] also showed some of the similar features of our study like women were older (62.4 years of age vs. 59.0 years of age) and were more likely to be hypertensive (66.6% vs. 63.2%), dyslipidemic (68.9% vs. 66.3%), and to have a family history of premature CAD (34.6% vs. 29.3) (all p values < 0.005). Women were less likely to smoke (45.6% vs. 57.0%; p < 0.001), although their prevalence of diabetes was similar to that in men (21.8% vs. 21.0%; p = 0.30). Women were less likely to have a positive test (9.7% vs. 15.1%; p < 0.001). Although univariate predictors of test positivity were similar, in multivariable models, age, body mass index, and Framingham risk score were predictive of a positive test in women, whereas Framingham and Diamond and Forrester risk scores were predictive in men.

Even though all older studies have demonstrated higher event rates, there is change in this tendency now. In the recently published CONFIRM (Coronary CT Angiography Evaluation for Clinical Outcomes: An International Multicenter) registry[26], 5,632 patients (mean age 60.2 ± 11.8 years, 36.5% women) were followed for 5 years. Obstructive CAD was more prevalent in men (42% vs. 26%; p < 0.001), whereas women were more likely to have normal coronary arteries (43% vs. 27%; p < 0.001). There were a total of 798 incident MACE events. After adjustment, there was a strong association between increased MACE risk and non obstructive CAD (HR: 2.16 for women, 2.56 for men; p < 0.001 for both), obstructive 1-vessel CAD (HR: 3.69 and 2.66; p < 0.001), 2-vessel CAD (HR: 3.92 and 3.55; p < 0.001), and 3-vessel/left main CAD (HR: 5.94 and 4.44; p < 0.001). Further exploratory analyses of atherosclerotic burden did not identify sex-specific patterns predictive of MACE. Similarly in our study also we didn't find any statistical significance in the outcomes between female & males (p=0.7), diabetics females & diabetic males (p=0.48) and non diabetics females & nondiabetic males (p=0.7).Male patients with diabetes had significantly more complications than non diabetic males (p=0.05) but there is no significant difference between diabetic and non diabetic females (p=0.59). So it is evident from our study that there was no gender difference between men and women even with or without diabetes in view of outcomes. But significantly worse outcomes are observed in diabetic men than non diabetic men in our study which is not so in females.

We have limitations to this study. 1) It is a study based on retrospective analysis of the data from a single center which is prone to different bias and not a randondamized control trial so that we can't draw any conclusions from the study. 2) We didn't compared the risk of smoking vs nonsmokers as the most of the smokers are males in India and there is a clear gender difference which may lead to bias.

## CONCLUSION

In conclusion, diabetic patients undergoing PCI were more aged with more number of comorbidities like

anemia and renal dysfunction. They had extensive CAD, complex lesions, more number of stents per patient, history of previous MI and more number of repeated revascularizations. Multivessel disease and LV dysfunction were significantly higher in diabetic patients than non diabetics. There was no significant difference in complications between the diabetic males and females, non diabetic males and females as well as diabetic female and non diabetic female sub groups. But there is a significant difference between complications in male diabetics than male non diabetic subgroup with diabetic males experiencing significantly more complications than males not having diabetes. So it is reasonable to conclude that the gender difference in outcomes follow PCI was not significant.

**REFERENCES:**

1) Danaei G, Finucane MM, Lu Y, et al. National, regional, and global trends in fasting plasma glucose and diabetes prevalence since 1980: systematic analysis of health examination surveys and epidemiological studies with 370 country-years and 2.7 million participants. Lancet.2011; 378:31–40.

2) Hammound T, Tanguay JF, Bourassa MG. Management of coronary artery disease: Therapeutic options in patients with diabetes. *J Am CollCardiol 2000;36:355-65.*

3) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults. Executive Summary of the Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). *JAMA 2001;285:2486-97.*

4) Fein F, Scheur J. Heart diseases in diabetes mellitus: theory and practice. En: Rifkin H, Porte D Jr, editors. New York: Elsevier,1990; 812-23.

5) Schramm TK, Gislason GH, Kober L, et al. Diabetes patients requiring glucose-lowering therapy and nondiabetics with a prior myocardial infarction carry the same cardiovascular risk: a population study of 3.3 million people. Circulation.2008; 117:1945–1954.

6) Aronson D, Rayfield EJ, Chesebro JH. Mechanisms determining course and outcome of diabetic patients who have had acute myocardial infarction. Ann Intern Med. 1997; 126:296–306.

7) Donahoe SM, Stewart GC, McCabe CH, et al. Diabetes and mortality following acute coronary syndromes. JAMA.2007; 298:765–775.

8) Tanveer A, Khan PV, Sellke FW. Cardiac surgery and diabetes mellitus. In: Johnstone MT, Veves A, eds. Diabetes and Cardiovascular Disease, 2nd edn. Totowa: Humana Press, 2005.

9) Impact of gender difference in hospital outcomes following percutaneous coronary intervention. Results of the Belgian Working Group on Interventional Cardiology (BWGIC) registry.Lempereur M[1], Magne J, Cornelis K, Hanet C, Taeymans Y, Vrolix M, Legrand V EuroIntervention. 2014 Dec 23.pii:20130526-01.

10) Van Belle E, Périé M, Braune D, et al. Effects of coronary stenting on vessel patency and long-term clinical outcome after percutaneous coronary revascularization in diabetic patients. *J Am CollCardiol 2002;40:410-7.*

11) Kip KE, Faxon DP, Detre KM, Yeh W, Kelsey SF, Currier JW. Coronary angioplasty in diabetic patients. The National Heart, Lung, and Blood Institute Percutaneous Transluminal Coronary Angioplasty Registry. *Circulation 1996;94:1818-25. (Comment in1996;94:1804-6).*

12) Mehran R, Dangas GD, Kobayashi Y, et al. Short- and long term results after multivessel stenting in diabetic patients. *J Am CollCardiol 2004; 43:1348–1354.*

13) Garg P, Normand SL, Silbaugh TS, et al. Drug-eluting or bare metal stenting in patients with diabetes mellitus: Results from the Massachusetts data analysis center registry. *Circulation 2008; 118:2277–2285.*

14) Stein B, Weintraub WS, Gebhart SP, et al. Influence of diabetes mellitus on early and late outcome after percutaneous transluminal coronary angioplasty. *Circulation 1995;91:979-89.*

15) Laskey WK, Selzer F, Vlachos HA, et al. Comparison of in-hospital and one-year outcomes in patients with and without diabetes mellitus undergoing percutaneous catheter intervention (from the National Heart, Lung, and Blood Institute Dynamic Registry).*Am J Cardiol 2002;90:1062-7.*

16) Schomig A, Schmitt C, Dibra A, et al. One year outcomes with abciximab vs. placebo during percutaneous coronary intervention after pre-treatment with clopidogrel. *Eur Heart J 2005;26:1379.*

17) Stein B, Weintraub WS, Gebhart SSP, Cohen-Bernstein CI, Grosswald R, Liberman HA, et al. Influence of diabetes mellitus on early and late outcome after percutaneous transluminal coronary angioplasty. *Circulation 1995;91:979-89.*

18) Kurbaan A, Bawker TJ, Ilsley CD, Sigwart U, Rickards AF, on behalf of the CABRI investigators. Difference in the mortality of the CABRI diabetic and nondiabetic populations and its relation to coronary artery disease and the revascularization mode. *Am J Cardiol 2001;87:947-50.*

19) King SB III, Kosinki AS, Guyton RA, Lembo NJ, Weintraub WS, for the Emory Angioplasty versus Surgery Trial. Eight-year mortality in the Emory Angioplasty versus Surgery Trial (EAST). *J Am Coll Cardiol 200;35:1116-21.*

20) The BARI investigators. Seven-year outcome in the bypass angioplasty revascularization investigation (BARI) by treatment and diabetic status. *J Am Coll Cardiol 2000;35:1122-9.*

21) Barsness GW, Peterson ED, Ohman EM, Nelson CL, DeLong ER, Reves JG, et al. Relationship between diabetes mellitus and long-term survival after coronary bypass and angioplasty. *Circulation 1997;96:2551-6*

22) Marso SP, Giorgi LV, Johnson WL, et al. Diabetes mellitus is associated with a shift in the temporal risk profile of in hospital death after percutaneous coronary intervention: An analysis of 25,223 patients over 20 years. *Am Heart J 2003;145:270-7.*

23) Smith LR, Harrell FE Jr, Rankin JS, et al. Determinants of early versus late cardiac death in patients undergoing coronary artery bypass graft surgery. *Circulation 1991;84(5 Suppl):III245-53.*

24) Calafiore AM, Di Mauro M, Di Giammarco G, et al. Effect of diabetes on early and late survival after isolated first coronary bypass surgery in multivessel disease. *J Thorac Cardiovasc Surg 2003; 125:144-54.*

25) Kshipra Hemal , Neha J. Pagidipati, MD, MPH,, Adrian Coles, PD, Rowena J. Dolor, MD, MHS, Daniel B. Mark, MD, MPH, Patricia A. Pellikka, MD, Hoffmann, MD, MPH, Sheldon E. Litwin, MD. Sex Differences in Demographics, Risk Factors, Presentation, and Noninvasive Testing in Stable Outpatients With Suspected Coronary Artery Disease Insights From the PROMISE Trial. *J Am Coll Cardiol,Cardiovascular imaging, 2016;9,4:337.346.*

26) Joshua Schulman-Marcus, MD; Bríain ó Hartaigh, PhD; Heidi Gransar, MS; Fay Lin, MD[a]; Valentina Valenti, MD; Iksung Cho, MD; Daniel Berman, MD; Tracy Callister, MD, Augustin DeLago, MD; Martin Hadamitzky, MD; Joerg Hausleiter, MD; Mouaz Al-Mallah, MD; Matthew Budoff, MD, Philipp Kaufmann, MD[h]; Stephan Achenbach, MD[i]; Gilbert Raff, MD[i]; Kavitha Chinnaiyan, MD[i]Sex-Specific Associations Between Coronary Artery Plaque Extent and Risk of Major Adverse Cardiovascular Events: The CONFIRM Long-Term Registry. *J Am Coll Cardiol Img. 2016;9(4):364-372.*