Compliance of Secondary Prevention Strategies in Coronary Artery Disease Patients with and without Diabetes Mellitus – A Cross-Sectional Analytical Survey from Kerala, India

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Abstract

Context: There is limited data related to compliance of secondary prevention strategies for coronary artery diseases (CAD) among patients with and without diabetes. **Objectives:** The objective was to compare compliance to secondary prevention strategies for CAD including smoking cessation, weight management, blood pressure (BP) control, Low density lipoprotein (LDL) cholesterol control and adequate physical activity between patients with and without diabetes. **Settings and Design:** This is a hospital-based cross-sectional analytical study. **Methods and Materials:** The study questionnaire was used to collect data through interviews of CAD patients. Compliance to secondary prevention strategies was documented using European Society of Cardiology guidelines. **Statistical Analysis:** We used modified Poisson model to estimate adjusted prevalence ratios (Adj. PR) for estimating compliance. **Results:** Among 1,206 participants with CAD, 609 (50.5%) had diabetes. The Adj. PR s for three targets – smoking cessation (Adj. PR 1.01, 95% CI 0.97, 1.06, P 0.50), ideal BMI (Adj. PR 0.99, 95% CI 0.92, 1.09, P 0.99) and adequate physical activity (Adj. PR 1.12, 95% CI 0.97, 1.29, P 0.12) showed no significant difference between the groups. There was poor BP control in patients with diabetes compared to those without the same (Adj. PR 0.19, 95% CI 0.15, 0.23, $P < 0.0001$). LDL cholesterol control was better in patients with diabetes in comparison to those without the same (Adj. PR 1.19, 95% CI 1.08, 1.31, P 0.0005). **Conclusion:** The compliance for secondary prevention of CAD among patients with diabetes is similar to those without diabetes except for poor control of hypertension and better control of LDL cholesterol.

Keywords: Compliance, coronary artery disease, diabetes mellitus, myocardial infarction, secondary prevention

INTRODUCTION

Coronary artery disease (CAD) develops as a consequence of decline in myocardial perfusion over a period of time.[1] Currently, CAD constitutes one-third to half of the cardiovascular diseases (CVD).[1] CVDs account for 17.9 million deaths (31% of all deaths) worldwide.[2,3] Approximately, three-fourths of the global CVD deaths are reported from low- and middle-income countries. Diabetes mellitus (DM) is one of the major risk factors for CAD.[2] Recent studies report that 9.3% of adults among the world population have diabetes.[4,5]

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Previous evidence suggests that those with Type 2 diabetes have risks of death and cardiovascular events two to four times higher than the general population.[6] Findings from Framingham Heart Study reported that the attributable risk of CVD caused by T2DM had an increase from 5.4 to 8.7% over a period of two decades.[7] A recently published longitudinal study in T2DM patients for a period of 10 years reported that the hazard ratio for CVD death showed a constant increase every year.[8]

Currently, guidelines are available for each level of CVD prevention.[9,10] Several studies have shown that proper implementation of secondary prevention strategies improved CAD outcomes in patients with diabetes.[11-14] Compliance to secondary prevention strategies for CAD among low resource countries is a less explored area that needs more attention.

There is an excellent opportunity to attenuate the excess CVD risk associated with Type 2 diabetes by adhering to contemporary evidence-based treatment.[15] The results from the recently published Swedish national diabetes register that collected data from 2,71,174 diabetic patients with Type 2 diabetes sheds light into the scope of this prevention strategy.[15] The researchers examined whether the excess risk of death and cardiovascular events seen among patients with Type 2 diabetes can be reduced or eliminated by strict compliance to the risk factor control. They concluded that strict control of risk factors can significantly minimize the risk of death from any cause and even reverse the excess risk for myocardial infarction among patients with diabetes when compared to those without the same.[15]

The current scenario of compliance to secondary prevention strategies among CAD patients with diabetes hailing from low-resource countries is unknown. Such information needs to be documented for better secondary prevention of CAD among those with documented diabetes from these countries. The primary objective of this study was to compare the compliance to secondary prevention strategies for CAD including smoking cessation, ideal body weight management, blood pressure (BP) control, LDL cholesterol control and adequate physical activity between CAD patients with and without diabetes from Kerala, India and to report the adjusted prevalence ratios. The secondary objective was to compare the cardiovascular drug therapy profile between CAD patients with and without diabetes.

METHODOLOGY

The current study is an analytical cross-sectional survey. The study settings were two tertiary care centers and two cardiology clinics in the Ernakulam district of the state of Kerala, India. The study period was 2 years (January 2017-January 2019).

The sample size was calculated on the basis of Euroaspire IV data published by Gyberg *et al*.[16] They reported that 28% of CAD patients with diabetes had their LDL below the recommended cut-off of <70 mg/dL according to the guidelines published by the joint task force of the European Society of Cardiology and other societies on CVD prevention in clinical practice.[10] The corresponding figure for patients without diabetes was 16%. We used the patient LDL target compliance for computing sample size since it was the target applicable to all the patients. The minimum sample size needed for the study was 400 with a desired CI of 95 and 80% power. We then inflated the sample size to 1,206 to account for the missing data and non-availability of LDL testing data in a subset of recruited patients.

The sampling technique used was convenient consecutive sampling. The patients who were under follow up for CAD were consecutively recruited from the study institutions. The CAD was defined in our study according to the Sheridan review.[17]

The inclusion criteria used were (a) confirmed CAD patients with follow up period ranging from 1 to 6 years at the time of recruitment (b) age between 30 and 80 years (c) residing in Ernakulam district (d) patients who were able to comprehend Malayalam or English language. The exclusion criterion was concomitant chronic diseases like malignancy, chronic liver disease, end-stage chronic kidney disease and stroke.

The data were collected using a structured questionnaire designed to capture information regarding sociodemographic details, clinical history, comorbid conditions, details of primary event, biochemical parameters, details of current medications and details about self-reported physical activity.

The initial version was prepared in English after several discussions with all the investigators. This version was then tested in 50 patients who visited the outpatient department of the cardiology division at the host institution. We removed redundant questions and modified several questions as per patient feedback during this testing. The final English version was approved by all the investigators. The approved version was later translated to Malayalam and back translated to English by two separate language specialists. The original English version and the back translated version were later compared for concurrence and necessary modifications were done in consensus with all the investigators.

Compliance to the secondary prevention strategies for CAD were documented as per the ESC guidelines published in 2016.[10] For BMI classification, we used WHO BMI classification scale.[18] The cut-offs used for defining compliance to secondary prevention strategies for CAD is presented as Appendix 1. The socioeconomic status (SES) was classified according to Kuppuswamy's socioeconomic scale (2018).[19] SES was classified into low (<10), middle (11-25) and high (26-29) using the scores derived from this scale.

Statistical analysis

We used SAS Version 9.4 for Windows (SAS Institute, Cary, North Carolina, USA) for conducting the statistical analysis.

Categorical variables are summarized as proportions and continuous variables as means (+/−SD) or medians (Q1-Q3) according to their distributions. We used the Chi-square test to do bivariate comparisons. We used the modified Poisson model to estimate the adjusted prevalence ratios (Adj. PR) for compliance to secondary prevention strategies. The prevalence ratios were adjusted for age, sex, place of residence, socioeconomic status, insurance status and type of treatment taken. We reported the Adj. PR with their 95% confidence intervals.

Ethical approval
The study was approved by the institutional ethics committee (IRB-AIMS-2017-125). We obtained written informed consent from study participants before data collection. Confidentiality was maintained throughout the study.

RESULTS
Baseline characteristics of study population
We approached 1,230 patients with documented CAD and recruited a total of 1,206 patients for the study. All the consented 1,206 patients were included in the final analysis. The details of the baseline characteristics of the study population are shown in Table 1. Among the

patients, 879 (72.9%) were males and 767 (63.6%) were from rural areas. Majority of the patients were from middle socioeconomic status (n = 742, 61.5%). The mean age of the study population was 61.3 (9.6) years. Among the recruited participants, 609 (50.5%) reported a diagnosis of diabetes. The mean age of the patients with diabetes and without diabetes were 62.4 (8.9) years and 60.2 (10.1) years, respectively. The insurance coverage for diabetic patients with CAD was 36.1% and that of non-diabetic patients was 36.2%.

The proportion of patients with hypertension, dyslipidemia, current smoking and current alcohol use among patients with CAD and diabetes were 56.5, 46.6, 1.8 and 8.5%, respectively. The corresponding values for those without diabetes were 49.1, 43.6, 2.8 and 6.9%, respectively. The proportion of patients with ST elevation myocardial infarction (STEMI, NSTEMI), unstable angina and effort angina in the diabetes group were 33.3, 23.5, 22.0 and 21.2%, respectively. The corresponding values for patients without diabetes were 29.5, 23.8, 20.8 and 25.9%, respectively. There was no significant difference for CAD types between patients with and without diabetes (χ^2 4.576, *P* 0.2056).

Among patients with diabetes, the most common treatment modality reported was percutaneous transluminal coronary angioplasty (PTCA) (55.9%) followed by medical therapy

Table 1: Baseline characteristics of study population			
Variables	Overall *n* (%)	Diabetics *n* (%)	Non-diabetics *n* (%)	*P*
Overall	1206 (100%)	609 (50.5)	597 (49.5)	
Sex				
Male	879 (72.9)	432 (70.9)	447 (74.9)	0.1239
Female	327 (27.1)	177 (29.1)	150 (25.1)	
Place of residence				
Urban	439 (36.4)	232 (38.1)	207 (34.7)	0.2168
Rural	767 (63.6)	377 (61.9)	390 (65.3)	
Socioeconomic status				
High	44 (3.6)	28 (4.6)	16 (2.7)	0.0239
Middle	742 (61.5)	388 (63.7)	354 (59.3)	
Low	420 (34.8)	193 (31.7)	227 (38.0)	
Insurance				
Yes	436 (36.2)	220 (36.1)	216 (36.2)	0.9838
Co-morbidities				
Hypertension	637 (52.8)	344 (56.5)	293 (49.1)	0.0099
Dyslipidemia	544 (45.1)	284 (46.6)	260 (43.6)	0.2821
Smoking*	28 (2.3)	11 (1.8)	17 (2.8)	0.2299
Alcohol intake	93 (7.7)	52 (8.5)	41 (6.9)	0.2768
CAD Subtypes				
STEMI**	379 (31.4)	203 (33.3)	176 (29.5)	0.2056
NSTEMI[#]	285 (23.6)	143 (23.5)	142 (23.8)	
Unstable Angina	258 (21.4)	134 (22.0)	124 (20.8)	
Effort Angina	284 (23.5)	129 (21.2)	155 (25.9)	
Treatment taken				
Medical therapy alone	357 (29.7)	173 (28.4)	184 (30.8)	0.2744
Angioplasty	679 (56.3)	341 (55.9)	338 (56.6)	
CABG[##]	170 (14.1)	95 (15.6)	75 (12.6)	

*Current smokers only. **ST elevation myocardial infarction, [#]Non-ST elevation myocardial infarction, [##]Coronary arteries bypass graft

alone (28.4%) and CABG (15.6%). Corresponding values for the same treatment modalities in the group without diabetes were 56.6, 30.8 and 12.6, respectively. There was no significant difference for CAD types between the two groups (χ^2 2.586, P 0.2744).

Compliance to secondary prevention strategies

The compliance to secondary prevention strategies for CAD patients with diabetes as well as those without diabetes is presented in Table 2. Among the strategies, smoking cessation (94.9% vs 92.9%, P 0.3756), ideal BMI (63.4% vs 64.2%, P 0.77) and adequate self-reported physical activity (39.9% vs 38.53%, P 0.62) showed no significant differences between CAD patients with and without diabetes. The compliance to LDL control was better among CAD patients with diabetes compared to those without the same (42.9% vs 29.9%, P 0.0001). On the contrary, BP control was worse among CAD patients with diabetes compared to those without the same (12.6% vs 67.8%, P 0.0001).

We estimated the prevalence ratios of five secondary prevention targets – smoking cessation, ideal body weight based on BMI, BP control, LDL cholesterol control and adequate self-reported physical activity by comparing patient groups with and without diabetes. These Adj. PR were computed after adjusting for possible confounders including age, gender, place of residence, SES, insurance status and type of treatment for CAD. The details are presented in Table 3. Three targets – smoking cessation, ideal BMI and adequate physical activity showed no significant difference between the groups. There was poor BP control for the group with diabetes in comparison to the group without the same (Adj. PR 0.19, 95% CI 0.15, 0.23, $P < 0.0001$). On the contrary, LDL cholesterol control was better for patients with diabetes compared to those without the same (Adj. PR 1.19, 95% CI 1.08, 1.31, P 0.0005).

Profile of cardiovascular drug therapy – overall and by diabetic status

The details of the cardiovascular drug therapy are available in Table 4. The most common drug group prescribed overall was antiplatelets/anticoagulants (96%) followed by lipid lowering drugs (89.4%) and beta blockers (68.2%). We compared the use of cardiovascular drugs between CAD patients with and without diabetes. The use of antiplatelets/

anticoagulants (96.1% vs 95.9%, P 0.8594), statins (88.3% vs 90.5%, P 0.2151) and calcium channel blockers (19.0% vs 16.6%, P 0.2763) were similar in both the groups. The use of RAAS (42.0% vs 33.3%, P 0.0018), diuretics (14.1% vs 10.2%, P 0.0384) and beta blockers (72.1% vs 64.2%, P 0.0032) were significantly higher in patients with diabetes [Table 4].

Discussion

The current study compares the compliance to five independent secondary prevention strategies related to CAD between patients with and without diabetes hailing from Kerala, India. The state of Kerala in India has a peculiar combination of better healthcare indices and a high prevalence of CAD and its risk factors together with a high prevalence of diabetes.[20,21] Krishnan *et al.* reported in 2016 that the age adjusted prevalence of confirmed CAD was 3.5% in Kerala. The prevalence of diabetes reported in this study was 15% for the state.[21]

Approximately half of the 1,206 CAD patients recruited in the study had a documented diagnosis of diabetes. The prevalence of hypertension was significantly higher among patients with diabetes compared to those without the same (56.5% vs 49.1%, P 0.0099). The prevalence for dyslipidemia was similar in both the groups.

The profile of CAD subtypes appeared to be similar between the two groups with the dominant type being ST elevation myocardial infarction (STEMI) in both groups. The type of treatment also appeared to be similar between two groups with PTCA as the most prescribed treatment in patients with and without diabetes.

Among the prevention strategies, smoking cessation, weight management and physical activity showed no significant difference between the groups on adjusted comparisons as suggested by the reported prevalence ratios. Those with diabetes showed better compliance to LDL cholesterol (Adj. PR 1.19) and poor compliance to BPcontrol (Adj. PR 0.19) when compared to those without diabetes.

Our study used the cutoffs proposed by the European Society of Cardiology guidelines for secondary prevention of CAD which was published in 2016.[10] Two studies had earlier examined the

Table 2: Compliance to secondary prevention targets among CAD patients with and without diabetes

Target components	Diabetes		Non-diabetes		*P*
	Total *n*	Compliance *n* (%)	Total *n*	Compliance *n* (%)	
Smoking* Cessation (prior smokers)	215	204 (94.9)	241	224 (92.9)	0.3756
Body mass index (18.5-24.99)	609	386 (63.4)	597	383 (64.2)	0.77
Blood pressure control (140/90 for all)	609	380 (62.4)	597	405 (67.8)	0.0493
Blood pressure control** (130/80 for DM & 140/90 for Non-DM)	609	77 (12.6)	597	405 (67.8)	0.0001
Low density lipoprotein Level (<70 mg/dL)***	412	177 (42.9)	398	119 (29.9)	0.0001
Physical activity level (150 min/week)****	609	243 (39.90)	597	230 (38.53)	0.62

*215 diabetic patients and 241 non-diabetic patients were former smokers. **<130/80 mm Hg for diabetics, <140/90 mm Hg for non-diabetics. ***LDL data was available for 810 patients only. ****150 minutes or more of moderate to severe intensity physical activity/week

compliance to secondary prevention strategies based on these guidelines stratified by diabetic status.[16,22] This enables us to compare the compliance to secondary prevention approaches between CAD patients with diabetes to those without diabetes. In the Euroaspire V study, good control of LDL (less than 70 mg/dL) was reported among 37% of CAD patients with diabetics and among 25% of CAD patients without diabetics suggesting better control for LDL cholesterol among CAD patients with diabetes compared to CAD patients without the same.[22] Our study too reported exactly similar patterns of LDL control in CAD patients with diabetes (42.9%) faring better than those without diabetes (29.9%). In addition, the LDL control in the current study appears to be slightly better than that reported by Euroaspire for both groups.[22]

Euroaspire V also reported the proportion of CAD patients with good BP control separately for individuals with diabetes (<130/80 mm Hg) and those without diabetes (<140/90 mm Hg). The corresponding values were 25% for patients with diabetes and 64% for those without the same.[22] These values suggest poor control of BP among CAD patients with diabetes (as per suggested cutoffs) when compared to those without diabetes. Similarly, poor control of BP among CAD patients with diabetes (12.6%) compared to their counterparts without diabetes (67.8%) was reported by the current study as well.

The Euroaspire study also reported that 55% of CAD patients with diabetes had BP below 140/90 mm Hg.[22] The corresponding value from the present study was 64%. Only one in eight CAD patients with diabetes in the present study reported ideal BP control. This value suggests a dismal picture

of extremely poor BP control among CAD patients with diabetes from this part of the world. This is much worse than one in four reported from Euroaspire for the same category.[22]

The recently published Swedish diabetic cohort study sheds light into the scope of mortality and morbidity reduction that can be achieved by good risk factor control among patients with diabetes.[15] This cohort study confirms the fact that the number of risk factors controlled at diagnosis are prognostic of later cardiovascular events in those with diabetes. Among patients with diabetes who had all five variables (glycated hemoglobin, LDL cholesterol, albuminuria, smoking and BP) within target ranges, the hazard ratio for death from any cause, as compared with controls, was 1.06 (95% CI 1.00-1.12) suggesting the excellent mortality reduction from good control of the risk factors mentioned above.[15] The corresponding HR for acute myocardial infarction (MI) was 0.84 (95% CI, 0.75-0.93) leading to an actual reversal of excess cardiovascular risk from diabetes.[15] Similar benefits were seen for stroke (HR 0.95, 95% CI, 0.84-1.07).[15] Our study as well as Euroaspire V seems to suggest that the most difficult to control among the risk factors is BP for CAD patients with diabetes.[22] This also suggests that an opportunity to minimize the excess risk for all-cause mortality as well as that of acute MI and stroke is yet to be utilized in full among CAD patients with diabetes.

The compliance to smoking cessation appears to be excellent in both the groups. The ideal weight target performance appears to be modest in the two groups with approximately two out of three reporting within the ideal weight category. Self-reported physical activity cuts a sorry figure in both the groups with less than half reporting ideal physical activity levels and suggests the need for tremendous improvement in this area.

The profile of cardiovascular drug therapy appears to be different between the both groups. The different types of CAD-related drugs taken by the study population were antiplatelets, lipid-lowering drugs, renin angiotensin aldosterone system inhibitors (RAAS), calcium channel blockers (CCBs), diuretics and betablockers (BBs). Among the six groups of drugs listed, three groups showed significantly higher prescriptions among CAD patients with diabetes compared to CAD patients without the same. These were RAAS (42.0 vs 33.3%), diuretics (14.1% vs 10.2%) and betablockers (72.1% vs 64.2%). It is worth noting that despite prescribing more antihypertensives, those with diabetes still

Table 3: Adjusted Prevalence ratios* of individual prevention strategies among patients with and without diabetes

Secondary prevention targets	Prevalence ratio	92% CI	*P*
Smoking cessation	1.01	0.97-1.06	0.50
Blood pressure control	0.19	0.15-0.23	<0.0001
Weight management	0.99	0.92-1.09	0.99
LDL control	1.19	1.08-1.31	0.0005
Adequate physical activity	1.12	0.97-1.29	0.12

*Prevalence ratios reported after adjusting for age, sex, place of residence, socioeconomic status, insurance status and type of treatment taken

Table 4: Comparison of cardiovascular drug therapy in patients with and without diabetes

Cardiovascular Medicine	Overall (1206) *n* (%)	Diabetics (609) *n* (%)	Non-diabetics (597) *n* (%)	*P*
Antiplatelets/anticoagulants	1158 (96.0)	585 (96.1)	573 (95.9)	0.8594
Lipid lowering drugs (statins)	1078 (89.4)	538 (88.3)	540 (90.5)	0.2151
Renin angiotensin aldosterone system inhibitors	455 (37.7)	256 (42.0)	199 (33.3)	0.0018
Calcium channel blockers	215 (17.8)	116 (19.0)	99 (16.6)	0.2763
Diuretics	147 (12.2)	86 (14.1)	61 (10.2)	0.0384
Betablockers	822 (68.2)	439 (72.1)	383 (64.2)	0.0032

had higher BP, which highlights the difficulty encountered in achieving tight BP targets in this group.

The ESC guidelines on cardiovascular disease prevention emphasizes the role of strict risk factor control for better outcomes among CAD patients with and without diabetes.[10] The guidelines state that lifestyle management in the form of diet control and enhanced physical activity targeting an ideal weight range should be central in the management of CAD patients with and without diabetes.[10] Along with lifestyle interventions, reductions in BP and cholesterol should be targeted as strictly as possible.[10] A recent meta-analysis of randomized trials of BP-lowering agents among patients with DM highlights the benefits of strict control of BP for reducing cardiovascular events.[23] The meta-analysis documented significant reductions in all-cause mortality, cardiovascular events, CAD events, stroke, heart failure, retinopathy, new or worsening albuminuria and renal failure. A systolic target <140 mm Hg lessened the risk of all-cause mortality and most separate outcomes mentioned above. Further reductions in the risk for albuminuria, retinopathy and stroke were achieved with a systolic target <130 mm Hg. The overall survival remained the same with both targets.[23] It should also be noted that CAD patients with diabetes have a vascular risk well in excess of those with CAD without diabetes. The former group also has a substantially lower life expectancy than the latter.[24] The current scenario of compliance to secondary prevention approaches for CAD in India is suboptimal with significant scope for improvement.[25] There is also a need for interventions targeting improvement in quality of life among CAD patients under secondary prevention in India.[26]

Globally, sizable reductions in CVD mortality in patients with diabetes have occurred due to better management of risk factors.[10] Unfortunately, these benefits are partly offset by the steady increase in prevalence of diabetes worldwide.[10] Efforts aimed at reducing the global incidence of diabetes may be helpful in this regard and may reduce the pressures on all healthcare systems globally.

Conclusion

The compliance achieved in risk factors modifications for secondary prevention of CAD among CAD patients with Type 2 diabetes is similar to those without diabetes except for BP control. CAD patients with diabetes showed better control for LDL cholesterol compared to those without the same. The antihypertensive use was higher in those with diabetes but control of BP remained suboptimal in both the groups. BP control was worse among CAD patients with diabetes compared to those without the same. Efforts to improve management of BP among CAD patients with diabetes needs to be implemented given the scope of morbidity and mortality reduction from such measures.

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Conflicts of interest

There are no conflicts of interest.

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