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Nocturnal Dipping Status in Ischemic Heart Disease Patients and Its Correlation with Coronary Angiography

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ABSTRACT

Background: Loss of nocturnal dipping, diagnosed by Ambulatory Blood Pressure Monitoring (ABPM), has been associated with adverse cardiovascular events. But its precise relationship with pattern of coronary artery involvement is not known. Aims and Objectives: To find out any association between pattern of coronary artery involvement and nocturnal non-dipping, and to assess the relation between cardiovascular risk factors and non-dipping among stable ischemic heart disease patients undergoing planned coronary angiography. Results: Final sample size was 426. 68.08% patients were non-dippers. On uni-variate analysis, dyslipidemia, smoking and class of angina were significantly associated with nocturnal non-dipping. On multivariate analysis, it was observed that nocturnal non-dipping was associated with diabetes and smoking. Moreover, proportion of patients having multivessel and/or left main coronary artery involvement was more among non-dippers than dippers. Conclusion: Nocturnal non-dipping may be associated with more severe coronary artery disease.

Keywords: ABPM; Multivessel disease; Non-dipper; Stable Ischemic Heart Disease

INTRODUCTION

Ambulatory blood pressure monitoring (ABPM) was shown to be superior to office BP as a predictor of future cardiovascular events, mainly because it reflects the overall status of BP over different times of the day and night. [1] Failure to exhibit dipping at night (non-dippers), or rise in BP at night (risers) portends an increased risk of adverse cardiac events. [2] There is a linear and inverse relationship between cardiovascular mortality and the nocturnal decline in BP, which was independent of the overall BP load during 24 h and other cardiovascular risk factors. [3] One study suggested a relationship between nondipping and coronary artery disease. [4] The OPERA study showed a relation between carotid intimamedia thickness (IMT) and non-dipper, again pointing towards increased atherosclerotic risk. [5]

Another study in post myocardial infarction (MI) patients demonstrated role of ABPM in predicting cardiac death and heart failure. [6] Diabetic nephropathy patients with high nocturnal systolic blood pressure variability were shown to be at greater risk of significant coronary artery disease. [7] A few studies other have attempted to correlate the nocturnal non-dipping with extent and severity of CAD [8, 9] Such studies are limited in number and lacking in the Indian subcontinent. In this context, the present study was conducted among stable ischemic heart disease patients admitted at a tertiary care facility for planned coronary angiogram, to see if there is any association of night time BP by ABPM with conventional cardiovascular risk factors, as also

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find out whether there is any relation between dipping status and severity of coronary involvement.

MATERIALS AND METHODS:

This was a observational, cross-sectional study which included all stable ischemic heart disease (SIHD) patients aged less than 75 years, admitted in the cardiology ward of a tertiary care hospital in eastern India during the specified study period of six months (April 2019-September 2019). All patients were planned for coronary angiography for different indications. Patients with significant autonomic dysfunction (sustained drop of systolic BP ≥ 20 mm of Hg or Diastolic BP≥10 mm of Hg within 3 minutes of standing from supine position with heart rate<15beats/min), increase in renal dysfunction(eGFR<60ml/min), hepatic dysfunction, active infection, clinically or hemodynamically unstable patients and those who did not give informed consent were excluded. Sample size calculation was done using the formula

 $(z_{\alpha})^2$ pq/L², where z_{α} =1.96, p=expected proportion of abnormal ambulatory BP, L=relative precision. Taking p as 50%, L as 10% of p, i.e. 5, the estimated sample size came to be roughly 384. A total of 517 individuals were screened during the specified study period. History, physical examination, baseline electrocardiogram, echocardiogram, routine blood tests and bedside evaluation for significant autonomic dysfunction were done in all patients. Ultimately 426 patients satisfied the inclusion and exclusion criteria. Out of 91 patients who were excluded, 59 did not give consent for angiography, 29 patients had did not give consent for the study, and remaining three had history of postural hypotension. All 426 patients were subjected to ABPM (Meditech), as also coronary angiography (Siemens Artis).

Definitions:

Hypertension was defined as per ESC 2018 criteria.

For ABPM, night time was taken as 10pm to 7am.

Dipper: ratio of night time and day time mean SBP 0.8-0.9 or night time fall 10%-20%

Non-dippers: ratio of night time and day time mean SBP 0.9-1 or night time fall <10%

Extreme dippers: ratio of night time and day time mean SBP<0.8 or night time fall >20%.

Risers: Ratio of night time and day time mean SBP >1

Single vessel disease: presence of \geq 50% diameter luminal narrowing in one of the three major epicardial vessel systems.

Double-vessel disease: presence of \geq 50% diameter luminal narrowing in two of the three major epicardial vessel systems.

Triple-vessel disease: presence of $\geq 50\%$ diameter luminal narrowing in all three major epicardial vessel systems or in the left anterior descending and proximal circumflex arteries in patients with nondominant right coronary arteries⁽¹³⁹⁾

We considered two categories of night time BP response as per ABPM: "total dippers" (comprising dippers and extreme-dippers) and total "non-dippers" (comprising non-dippers and risers).

Data were recorded in a pre-designed, pre-tested semi-structured schedule, then entered into a Microsoft Office Excel worksheet (2007) and later the spreadsheets were used for analyses. Statistical analysis was done using SPSS© version 20.0. For descriptive statistics, mean and standard deviation were used for continuous variables, while number and percentages were used in case of categorical variables. For inferential statistics, various tests of significance were used according to the type of variable. Informed consent was mandatory for all clearance participants. The study got from Institutional Ethics Committee.

RESULTS:

Mean age of the study population was 53.42 years [S.D. 7.58; range 29-74 years], with male preponderance. Dyslipidemia was the most commonly present risk factor (45.07%), followed by smoking (42.97%). Majority were non-dippers/risers (290; 68.08%), and angiography revealed multivessel CAD in most of the patients (313; 73.47%). [Table 1] Left main involvement was noticed in 49 patients. Taking the dipping status as the dependent variable, on uni-variate analysis, it was observed that diabetes, dyslipidemia, smoking and class of angina were significantly associated with nocturnal nondipping/rising. On logistic regression analysis, by ENTER method, it was observed that diabetes and smoking were significantly associated with nocturnal

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non-dipping/rising. [Table 2] Further, it was noticed that dipping status was significantly associated with pattern of coronary artery involvement, and nondippers/risers had greater percentage of multivessel CAD and/or left main disease, compared to dippers. [Table 3]

DISCUSSION:

The study showed that among patients with stable ischemic heart disease, nocturnal dipping status was associated with diabetes and dyslipidemia. Loss of nocturnal dipping was significantly associated with multivessel coronary artery disease and/or left main involvement.

Studies from various parts of the world have attempted to find a relation between coronary artery disease and nocturnal dipping status. Sherwood A et al found an association between CAD and nocturnal non-dipping among post-menopausal women of United States. [8] Yan B et al showed that reverse dipping was associated with stable coronary artery disease. [9] Viera AJ et al conducted a prospective study among American young adults who underwent ABPM, and observed that higher coronary calcium score after 10 to 15 years of follow up was associated with both extreme dipping and non-dipping in an 'U'-shaped fashion. [10]De la Sierra A, et al were of the opinion that non-dipping was more closely associated with CAD than nocturnal hypertension. [11] A recent study from Italy showed that reverse dipping was associated with stroke more frequently than non-dipping and dipping. [12] Among chronic kidney disease patients, it was noticed that coronary artery calcium was associated with nocturnal dipping status. [13] Mousa T et al have also found that larger number of patients with CAD were non-dippers, as compared to persons without CAD. [14]

Fewer studies have been conducted to find an association between pattern of coronary artery involvement and dipping status. Pierdomenico SD et al did not find any association between pattern of coronary involvement and dipping status, unlike this study where a tendency towards multivessel disease was found in non-dippers. [15]

Conclusion: The present study has limitations as it was a single centre study with a relatively small sample size. However, it indicated the possibility of association of more severe CAD in patients with nondipping. Moreover, a few predictors of non-dipping like diabetes and smoking were found. Further studies with greater number of patients are necessary to correlate severity of CAD with nocturnal dipping status.

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Variable	Frequency (%)		
Age			
< 50	155(36.48)		
≥50	271(63.62)		
Gender			
Male	290 (68.08)		
Female	136 (31.92)		
Religion			
Hindu	265(62.21)		
Muslim	161(37.79)		
Hypertension			
Present	129(30.28)		
Absent	297(69.72)		
Diabetes			
Present	111(26.06)		

 Table 1: Demographic and clinical profile of the study population (n=426)

Absent	315(73.94)
Dyslipidemia	
Present	192(45.07)
Absent	234(54.93)
Smoking	
Present	183(42.96)
Absent	243(57.04)
Angina class	
CCS2	222(52.11)
CCS3/CCS4	204(47.89)
LVEF	
< 40%	162(38.03)
\geq 40%	264(61.97)
Dipping pattern on ABPM	
Extreme dippers	47(11.03)
Dippers	89(20.89)
Non-dippers	230(53.99)
Risers	60(14.08)
Pattern of coronary involvement	
Normal coronaries / Minor CAD	37(8.69)
SVCAD	76(17.84)
DVCAD	154(36.15)
TVCAD and/or LMCAD	159(37.32)

N.B.: Total dippers: 136 (31.92%); Total non-dippers:290 (68.08%)

Risk factor	Total dippers (136)	Total non- dippers (290)	OR (95% C.I.)	Adjusted OR (95% C.I.) **
Age				
<50	52	103	1	
≥ 50	84	187	1.12(0.74-1.71)	
Gender				
Male	94	196	1	
Female	42	94	1.07(0.69-1.67)	
Hypertension				
Absent	100	197	1	
Present	36	93	1.31(0.83-2.06)	
Diabetes				
Absent	114	201	1	1
Present	22	89	2.29(1.36-3.86)	1.47(1.08-5.42)
Dyslipidemia				
Absent	101	133	1	1
Present	35	157	3.41(2.17-5.33)	2.49(0.96-6.54)
Smoking				
Absent	105	138	1	1
Present	31	152	3.73(2.35-5.92)	2.31(1.57-7.59)
Class of angina				
CCS 2	117	105	1	1
CCS 3/CCS 4	19	185	10.85(6.31-18.63)	7.76(0.84-35.75)
LVEF				
<40%	51	111	1.03(0.68-1.57)	
\geq 40%	85	179	1	

 Table 2: Effect of different parameters on dipping status [n=426]

Note: **Logistic regression analysis ENTER method; dependent variable- dipping status; only significant variables entered; Nagelkerke R square-0.402

	Normal coronaries / Minor CAD	SVCAD	DVCAD	TVCAD and/or LMCAD	p value
Totaldippers(136)	29	39	40	28	<0.0001
Total non-dippers (290)	8	37	114	131	
Total	37	76	154	159	

Table 3: Relation between dipping status and pattern of coronary artery involvement [n=426]

N.B.: Chi square: 67.39, degrees of freedom: 3