Original Research Article

Uncontrolled Hypertension as a Risk for Coronary Artery Disease: Patient Characteristics and the Role of Physician Intervention

Abstract:

Objective: Our research was designed to evaluate the association of uncontrolled hypertension with coronary artery disease and analyze the role of intervention in preventing CAD mortality ratio.

Methodology: This case controlled single-center study was conducted in department of Medicine, Peoples University of Medical and Health Sciences Nawabshah Pakistan from January 2020 to September 2021. In this study, BP screening was done among the adult population aged 50 years or over. All the recruited patients of coronary artery disease were divided into two main groups for a clinical trial; case (identified cases of uncontrolled hypertension) and the control group (without history of cardiovascular disorders and used medication for hypertension). For evaluating physician intervention, both groups were divided into two main groups for treatments; the standard Bp control (having <140 mm Hg SBP level) and the intensive blood pressure control (whose SPB <120 mm Hg). we used BP-lowering medication which adjusted the systolic blood pressure around 135–139 mm Hg in the standard group and less than 120 in intensive group.

Results: Overall the female prevalence was comparatively high (63.2%) than males (37%). No significant differences were found in the baseline characteristics of participants. In 42% of cases, we found coronary artery calcification. Univariate logistic analysis of our study demonstrates the association of CAD with age, smoking, and BMI. We also found a positive association of CAD with higher CRP, and uncontrolled hypertension.

Conclusion: Our study observed a significant association between uncontrolled hypertension and coronary artery disease. The results of our study concluded that interventions in terms of BP control might be affected due to pre-existing cardiovascular diseases. However, intensive BP treatment would help to reduce the mortality ratio of CAD patients.

Keywords:

Uncontrolled blood pressure, coronary artery disease, Systolic blood pressure, intervention group, case controlled.

Introduction:

Hypertension is one of the challenging issue of modern world which causes high prevalence of morbidity and mortality worldwide. Generally affecting more than one billion world population is affecting with hypertension including both developing and and developed countries. Overall 9.4 million hypertension related deaths were reported every year[1]. According to the medical 2025 becomes worsen year with 1.7 billion expected young deaths due to hypertension. In low-income countries, annually 6 million hypertensive deaths are reported every year[2]. Underdeveloped countries are the most easy target of hypertension disease due to unhygienic and poor diet plans with less awareness[3]. Currently 2/3rd hypertensive patients live in underdeveloped countries[3]. Disease burden of the poor countries increased due to high prevelance of hypertension. Usually, female population is more prone to the hypertension. Almost 6.8% female population suffered from cardiovascular diseases due to high prevelance of hypertension as compared to men (3.4%)[4]. In the past variety of researches were produced to demonstrate the association of elevated blood pressure with coronary artery disease (CAD)[1,2,3,4]. These results demonstrate that hypertension is the most prevalent disorder among 30% to 70% of individuals with pre-existing CAD[5]. A previous study reported an increased mortality ratio in patients aged 40-69 years after observing a 20mm Hg rise in systolic blood pressure and a 10 mm Hg rise in diastolic blood pressure (DBP) among patients with ischemic heart disease[6]. However, a reduction in SBP level may contribute to lowering the risk of deaths among cardiovascular patients[7]. Our research was designed to evaluate the association of uncontrolled hypertension with coronary artery disease and analyze the role of intervention in preventing CAD mortality ratio.

Methodology:

This case controlled single-center study was conducted in department of Medicine, Peoples University of Medical and Health Sciences Nawabshah Pakistan from January 2020 to 2021. In this study, BP screening was done among the adult population aged 50 years or over. Before initiating the research, ethical approval was obtained from the hospital research ethics committee and research was conducted by following Helsinki principles. All the participants were well-known about the objectives and nature of the research. Written and verbal consent were obtained from every participant. Hypertensive patients were defined as those whose systolic blood pressure $\geqslant$140 mm Hg and $\geqslant$90 mm Hg with or without antihypertensive treatment. Patients who filled the written consent form were included for further observations.

Patients aged 50 or above with an increased risk of cardiovascular events were included. We excluded all patients with a medical history of diabetes mellitus and chronic kidney disease. Furthermore, patients with prior stroke, myocardial infraction, congestive heart failure were also excluded from the research.

All the recruited patients of coronary artery disease were divided into two main groups for a clinical trial; case (identified cases of uncontrolled hypertension) and the control group (without history of cardiovascular disorders and used medication for hypertension). Trained physicians of the hospital to measure blood pressure with standardized protocol by using automatic devices. Patients were asked to sit in a seated position for three BP measurements. All the BP measurements were 65 seconds apart. In the controlled group, we assured that the blood pressure of recruited participants ranges under 160/100. Coronary artery calcification (CAC) was identified by performing a CT scan of the case group. Agatston score was used to analyze CAC regression analysis. This score was then subdivided into five categories for analyzing low to severe coronary atherosclerosis. For evaluating physician intervention, both groups were divided into two main groups for treatments; the standard Bp control (having <140 mm Hg SBP level) and the intensive blood pressure control (whose SPB <120 mm Hg). We used ACE inhibitors (20 mg lisinopril tablet as BP-lowering medication) which adjusted the systolic blood pressure around 135–139 mm Hg in the standard group and less than 120 in intensive group. This tablet were given to patients after the 2 BP measurements and CT scan. Patients with a history of coronary artery bypass grafting and having a history of percutaneous coronary intervention were defined under the category of coronary revascularization. Primary outcomes of the research targeted composite events of myocardial infarction, heart failure, stroke, and cardiovascular death whereas events like hypotension, electrolyte abnormality, and bradycardia were also recorded. Patients were followed for 3 months for calculating mean SBP and DBP values. Demographic information including age, sex, smoking status of patients, body mass index, fasting plasma glucose levels, lipoprotein cholesterol, and triglycerides were recorded for statistical analysis[8,9].

We used SPSS 23.0 for statistical analysis. Mean and standard deviations were used for measuring continuous variables whereas Chi- square and student t-test was used for measuring categorical variables. For analysing the difference between two groups we used student t-test. Multivariate logistic regression with a 95% confidence interval for adjusted odds ratios was used to determine risk factors of hypertension associated with CAD.

Results:

This case-controlled trial study recruited 147 patients with hypertension. Among these patients, 49 had coronary artery disorder whereas the remaining ninety-eight were non CAD patients. Overall the female prevalence was comparatively high (63.2%) than males (37%). No significant

differences were found in the baseline characteristics of participants (Table 1). CT scan was performed in the uncontrolled hypertensive group for coronary artery calcification. One of the patients had obesity so we failed to achieve CAC data of that patient. In 42% of cases, we found coronary artery calcification. Univariate logistic analysis of our study demonstrates the association of CAD with age, smoking, and BMI. We also found a positive association of CAD with higher CRP, and uncontrolled hypertension (Table 2). After a median follow-up of 6 months, we found that intensive BP treatment is highly associated with a low probability of mortality but enhances the risk of stroke. In patients, without CAD we found that intensive BP treatment decreased the risk of myocardial infarction, and heart failure than standard treatment (Table 4).

Table 1: Demographic and clinical characteristics of recruited patients[9]

Variables	Control group (General population) n=98 (66.6%)	Case group (uncontrolled hypertension) n= 49 (33.3%)	All subjects N= 147	p-value
Age	55±5	52±15	54±10	0.08
Sex				1.0
Male	36 (37%)	18 (37%)	54 (37%)	
Female	62 (63%)	31 (63.2%)	93 (63.2%)	
Diastolic blood pressure (mm Hg)	81±9	95±14	86±12	<0.001
Systolic blood pressure (mm Hg)	132±14	155±30	140±23	<0.001
Blood pressure ⩾160/100 mm Hg	0	22 (45%)	22 (15%)	<0.001
Blood pressure ⩾140/90 and <160/100 mm Hg	34 (35%)	20 (41%)	54 (37%)	

Blood pressure <140/90 mm Hg	64 (65%)	7 (14%)	71 (48%)	
Antihypertensive treatment	24 (24%)	38 (83%)	62 (43%)	<0.001
No. of antihypertensive drugs	2 (1-4)	0	0 (0–2)	<0.001
Body mass index (kg m−2)	28.5±4.7	28.8±4.9	28.6±4.7	0.2
Triglycerides (mmol l−1)	1.6±1.4	1.4±0.7	1.5±1.2	0.4
Total cholesterol (mmol l−1)	5.5±0.9	5.1±1.0	5.4±1.0	0.01
HDL cholesterol (mmol l−1)	1.5±0.5	1.5±0.9	1.5±0.6	0.6
LDL cholesterol (mmol l−1)	3.3±0.9	3.0±1.0	3.2±1.0	0.045
Estimated GFR (ml min per 1.73 m2)	89±18	78±18	85±19	<0.001
Creatinine (µmol l−1)	69±13	80±17	73±16	<0.001
C-reactive protein (mg l−1)	2.0 (0.9–4.0)	2.5 (1.0–4.8)	2.1 (1.0–4.0)	0.2
CAC score >399 U	2 (2%)	7 (14%)	9 (6%)	0.007
CAC score >99 U	11 (11%)	14 (29%)	25 (17%)	0.008
CAC score >9 U	23 (24%)	21 (43%)	44 (30%)	0.007
CAC score >0 U	37 (38%)	25 (51%)	62 (42%)	

CAC score = 0 U	60 (62%)	24 (49%)	84 (58%)	0.1
Median CAC score (U)	0 (0–9)	4 (0–145)	0 (0–38)	0.04
Active smoking	22 (22%)	11 (22%)	33 (22%)	1.0

Table 2: Multivariate logistic regression analysis for prediction of CAD[9]

Risk Factors	Odd ratios	p- value
Age (per year)		
Uncontrolled hypertension	3.9 (1.6–9.1)	0.002
Active smoking	3.2 (1.2–8.5)	0.02
CRP (per mg l−1)	1.08 (1.01–1.15)	0.03
Body mass index (per kg m−2)	1.11 (1.01–1.21)	0.02

Table 3: Primary outcomes of intensive versus standard Bp treatment[8]

Outcomes	Intensive BP treatment n= 25	Standard BP treatment n= 24	Adjusted Model		Unadjusted Model	
			Hazard ratio (95% C.I)	P value	Hazard ratio (95% C.I)	P value
Primary outcome	12.9%	12.0%	1.05 (0.76–1.46)	0.87	1.04 (0.76–1.44)	0.90
All-cause death	5.0%	7.7%	0.60 (0.37–0.96)	0.03	0.62 (0.39–0.98)	0.04
CVD death	2.1%	2.6%	0.75 (0.35–	0.47	0.77 (0.37–	0.49

			1.63)		1.62)	
Myocardial infarction	5.1%	4.8%	1.05 (0.62–1.75)	0.87	1.03 (0.62–1.72)	0.90
Stroke	3.2%	1.5%	2.08 (0.94–4.58)	0.07	2.03 (0.93–4.46)	0.08
Heart failure	2.6%	3.9%	0.61 (0.32–1.17)	0.14	0.62 (0.33–1.18)	0.15
ACS	3.4%	2.7%	1.22 (0.64–2.35)	0.55	1.20 (0.63–2.31)	0.58

Table 4: Safety events of treatment[8]

Safety events	Intensive BP treatment	Standard BP treatment	Hazard ratio	p-value
Hypotension	4.8%	2.4%	2.00 (1.06–3.79)	0.03
Bradycardia	4.3%	3.6%	1.12 (0.63–1.98)	0.71
Syncope	2.4%	3.1%	0.73 (0.37–1.47)	0.38
Acute kidney injury	6.1%	4.3%	1.39 (0.82–2.33)	0.22
Electrolyte abnormality	5.3%	2.2%	2.38 (1.25–4.56)	0.01
Serious adverse events	54.7%	53.1%	1.03 (0.88–1.20)	0.73
Injurious fall	3.1%	2.4%	1.21 (0.60–2.43)	0.59

Discussion:

In this case-control study, we observed a significant association between uncontrolled hypertension and coronary artery disease. In our study, we found an increased prevalence of CT-detected coronary artery calcification. These results are in correspondence to the previous study of Allen[10] in which he observed a clear association of uncontrolled hypertension and coronary artery calcification. The significant results were found due to adjustment of cardiovascular risk factors including lipid parameters. The median CAC score and level of hypertension in the different categories of CAC in our study were comparable to the previous study of Heinz recall study[11]. Heinz's study found similar parameters in stage 1-2 hypertension patients. We observed that CAC is an independent predictor of cardiovascular events as found in other studies[12,13,14]. But these results are in contradiction to the large cohort study in which they failed to analyze all clinical outcomes due to interventions that allow CAC screening[15]. The hypothesis claims that lipid-lowering therapy reduced the risk of cardiovascular events in hypertensive patients[16], however, our study was independent of lipid parameters.

Our results also indicate that cardiovascular diseases highly affect the clinical outcomes of BP treatment. Intensive BP treatment reduced the risk of cardiovascular events in patients without CAD but failed to achieve any successful outcomes in CAD patients. However, intensive treatment reduced cardiovascular deaths in CAD patients without affecting any clinical outcomes. We observed a high probability of stroke in CAD patients during intensive BP treatment. The risk of stroke was also high in revascularization. However, in non-CAD hypertensive patients targetted systolic blood pressure 120 mm Hg reduced the clinical outcomes. The study of Attar et al[17]., observed successful outcomes of intensive BP treatment for primary prevention of cardiovascular disease and observed reduced mortality in high-risk CVD patients. In contradiction, the study of Sleight[18] found no outcome at < 130 SBP level.

In hypertensive cardiovascular patients, optimal BP targets remain controversial. A variety of studies related to CAD were produced in past but they ignored SBP targets. The international study conducted by Pepine et al[19]., suggested low SBP is more effective than antihypertensive drug class in patients aged 50 or above. Bangalore study suggested SBP below 140 mm Hg for better clinical outcomes in hypertensive CAD patients. On the other hand, the findings of network meta-analysis conducted in 2017 recommended SBP target be to <130 mm Hg in adults[20,21, 22]. Usually, in CAD patients with hypertension, diastole causes coronary perfusion so DBP attain focus in recent years. One of the secondary analyses observed a J-shaped association between BP and cardiovascular events. They observed prominent J-curved in diastole than in systole. Many researchers reported a high potential of tolerating low levels of DBP in patients with coronary revascularization[20,24]. The other study suggested that a DPB level is lower than 70 mm Hg could be dangerous for patients with unstable angina[25]. Comparing these results of DBP with our study we observed that DBP around 65 mm Hg will be safe and did not increase CVD events.

Regardless of antihypertensive treatment, our study observed lower DBP levels in patients with a history of coronary revascularization. This happened due to poor arterial elasticity and atherosclerotic lesions in patients with revascularization. Loss of arterial elasticity leads to DBP decline and auto-regulatory process of the coronary circulation[26]. Regarding the cardiovascular risk factors including cholesterol, heart rate was better controlled in CAD than others.

Limitations of the study:

For this study we measured blood pressure with manually operated semi-automatic devices in control group which gave higher readings than the case group. This was the major limitation of study resulting in lower observed difference in both group. Due to this we observed a huge affect on systolic blood pressure in regression model. The percentage of hypertension patients with cardiovascular disorders was very small which affect our statistical analysis. Furthermore, we excluded patients with a history of diabetes mellitus or stroke, so our study conclusions may not apply to other subsets of patients. We recommend that further studies should be produced and carefully interpreted to validate these results.

Conclusion:

Our study observed a significant association between uncontrolled hypertension and coronary artery disease. The results of our study concluded that interventions in terms of BP control might be affected due to pre-existing cardiovascular diseases. However, intensive BP treatment would help to reduce the mortality ratio of CAD patients.

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