Original Research Article

The association between 24-h blood pressure variability and major adverse cardiac events (MACE) in hospitalized patients with acute myocardial infarction:a prospective study

Comment [RK1]: Full form (Hour) maybeused in title

Abstract :

Acute myocardial infarction (AMI) is major cardiovascular disease that causes high morbidity and mortality. In AMI, ischemia and necrosis affected some cardiomyocytes leading to a decrease in myocardial contractility which is followed by an acute proinflammation reaction and increased sympathetic tone. Meanwhile, high blood pressure variability (BPV) causing an increased left ventricular workload, heart rate, myocardial oxygen demand and induces proinflammation and endothelial dysfunction. Therefore a high BPV and its associated pathological effects are likely to aggravate the physiological function of the heart and affect the emergence of acute cardiac complications in AMI[1]. Patients Blood pressure variability (BPV) has been mainly studied through the prism of congestive heart failure (CHF) and hypertension, but not in the setting of an acute coronary syndrome (ACS). This study aims to investigate the association between short-term BPV and major adverse cardiac events (MACE) in AMI patients. This prospective study included 74 patients that were hospitalized in the cardiology department in ARRAZI hospital MOHAMED VI , MARRAKECH between September 2022 and February 2023, by using weighted standard deviation of 24-hour ambulatory blood pressure monitoring readings.

Results :

The average systolic BPV value which was calculated as standard deviation (SD) and average real variability (ARV) was more important in the MACE group than in the non-

MACE group. Systolic SD and systolic ARV in the MACE group were 12,78 mmHg and11,61 mmHg respectively. In the non-MACE group, systolic SD and systolic ARV were 10.45mmHg and 7,23 mmHg respectively. There was no significant association between BPV and MACE. However, there were significant differences between systolic ARV in patients with hypertension who experienced MACE and patients without hypertension who experienced MACE, unlike patients who didn't expreienced MACE for whom the ARV was nearly the same for patient with and without HBP .

Conclusion :

The BPV of AMI patients who experience MACE was higher than that of non-MACE AMI patients. There was no significant association between BPV and MACE during the acute phase of AMI, however the BPV was significantly more important for HBP patient who experienced MACE, which leads us to think that the screening of BPV in HBP patient may by a predictive factor for the development of MACEs.

Keywords: acute coronary syndrome, ambulatory BP monitoring, blood pressure variability, major adverse cardiac events (MACE)

Comment [RK2]: Spell check

Introduction :

Hypertension and its effect on target organ damage have been extensively established in clinical practice. Overall, each increase in systolic blood pressure (SBP) of 20 mm Hg (or each 10-mm Hg increase in diastolic blood pressure [DBP]) doubles the risk of a fatal coronary event and stroke[2]

Blood pressure (BP) variability is a dynamic phenomenon including short-, medium-, and long-term fluctuations as a result of complex interactions between behavioral, humoral, and neural central or reflex influences. The magnitude of such fluctuations is dependent on several variables including BP status (ie, normotension vs hypertension), changes in blood plasma volume, preload and afterload variations, respiratory cycles, use of antihypertensive medications, and the individual response to a variety of daily life stimuli such as physical activity, mental stress, duration/quality of sleep, smoking, alcohol consumption, seasonal variations in outdoor temperature, and other physiological and pathological factors.[1] Currently, blood pressure variability (BPV) is considered a novel risk factor for cardiovascular disease. It can be estimated by different blood pressure (BP) devices (mainly ambulatory BP monitoring [ABPM]) using different calculation and statistical methods (mainly weighted standard deviation or average real variability)[2]

On the other hand, patients with acute coronary syndrome (ACS) often show vasomotor instability, which increases the tendency of exaggerated responses to antihypertensive treatment, with BP fluctuating up and down early during ACS management.[3]

However, the prognostic impact of in-hospital BP variability on major adverse cardiac events (MACE) and clinical outcomes in other high cardiovascular risk patients is unclear. The aim of the present study was to assess the relationship between in-hospital BP variability and MACE in patients with acute myocardialinfraction .

PATIENTS AND METHODS

2.1. Patient selection

Patients with ACS were included in the study if they met the following criteria: (1) they presented with typical anginal pain lasting for >30 minutes; (2) there was ST-segment elevation or depression of at least 1 mm in at least two contiguous electrocardiography leads or new onset of complete left bundle branch block; and (3) they had positive troponin elevation. **Exclusion criteria** :were morbid obesity or handicap that inhibited the ability of ABPM placement, chronic obstructive airway disease, clinical hemodynamic or electrical instability, chronic renal impairment (estimated glomerular filtration rate <60 mL/min), history of secondary hypertension, or congestive heart failure.

2.2. Study design

Comment [RK3]: type of studydetails ? – short duration to be a prospective study – elaborate on : Were the sutdy participants followed up over a period of time ? if so duration/ No. Of observation

Between September 2022 and february 2023, 121 patients were hospitalized in the cardiology department in ARRAZI hospital ,CHU MOHAMED VI , MARRAKECH, for ACI. We were not able to offer the ABPM to 41 patients for logistical reasons (eg : not enough time to prepare the protocol, lack of devices, study staff unavailable). Of the 80 patients who were offered the ABPM, 6 were unable to complete the study (recently experienced unusual chest pain or due a technical problem) These 6 patients were excluded because they did not complete the ABPM, leaving 74 participants for this analysis .

2.3. Study population

We enrolled 74 consecutive patients who fulfilled the inclusion and exclusion criteria for this study. Demographic characteristics, medical history, and smoking status were assessed. We measured weight, resting BP, and heart rate. All patients included in the study were treated according to the recent European Society of Cardiology guidelines for the management of ST-segment elevation myocardial infarction (STEMI)[4] and

non-STEMI.[5] After the initial event, all patients received acetyl salicylic acid (150 or 75 mg/d) indefinitely, clopidogrel (75 mg/d), and other medications, including β-blockers, angiotensin-converting enzyme inhibitors, nitrates, and statins, were prescribed according to standard guidelines. In the present study, diabetes mellitus was defined as having a fasting glucose level ≥126 mg/dL and/or a glycated hemoglobin level ≥6.5% (in National Glycohemoglobin Standardization Program units) or being treated with one or more antidiabetic medications. Hyperlipidemia was defined as having a total cholesterol level ≥240 mg/dL or being treated with one or more antihyperlipidemic medications. A history of cardiovascular disease was defined as having had one or more of the following: angina pectoris, myocardial infarction, heart failure, aortic dissection, or stroke. Chronic kidney disease was defined as estimated glomerular filtration rate (<60 mL/min/1.73 m^2) Current smoking was defined as smoking at the time of study enrollment or within the prior year.

2.4. Ambulatory BP monitoring

All 74 patients were fitted with the ABPM devices (Contec model ABPM 50, Germany and Reynolds ABPM) for 24 hours within the first 7 days after cardiac care unit admission. The device was programmed to obtain BP readings at 15-minute intervals during the day (8 AM–8 PM) and at 30-minute interval during the night (8 PM–8 AM). Mean SBP, DBP, mean arterial pressure, and BP load values were obtained for the full 24-hour, daytime, and nighttime periods.[6] Hypertension was diagnosed when office SBP was ≥140 mm Hg and/or DBP was ≥90 mm Hg on at least two separate occasions, or by a previous diagnosis of hypertension with current antihypertensive medication use. The criteria for good-quality ABPM to be included in the study were the following: Approximately 75% to 80% valid readings should be obtained .

2.5. Calculation of BPV indices

BPV index :

BPV index was defined as the weighted standard deviation (SD) of 24-hour BP, daytime BP, and nighttime BP (SBP and DBP). As measures of short-term reading-to-reading BPV, we used the SD over 24 hours weighted for the time interval between consecutive

readings (SD_{24}) and the average of the daytime and nighttime SDs weighted for the duration of the daytime and nighttime interval (SD_{dn}). The SD_{dn} is the mean of day and night SD values corrected for the number of hours included in each of these two periods, according to the following formula: SD_{dn} = ([day SD × hours included in the daytime] + [night SD × hours included in the nighttime])/(hours included in daytime+nighttime).This method removes the influence of the day-night BP difference from the estimate of BPV.

2.6. Outcome ascertainment

All patients were followed up for an average of 7 days during their hospital stay. Clinical outcome was evaluated through the monitoring of major adverse cardiac events (MACE) occurring at any time during in-hospital follow-up. Only the most serious event of MACE was used to calculate the cumulative MACE per patient according to the following sequence: death >shock>cerebrovascular stroke>heart failure>hypertensive crisis>life-threatening arrhythmia. Death was defined as all-cause death at follow-up. Heart failure during follow-up was defined as either the presence of rales in more than one third of the lung fields that did not clear with coughing or evidence of pulmonary edema on chest x-ray.[5]Cardiogenic shock was defined by sustained low BP with tissue hypoperfusion.[7] Cerebrovascular stroke, either ischemic or hemorrhagic, was defined as poor blood flow to the brain resulting in cell death.[8] Hypertensive crisis was defined as severely elevated BP >180/110 mm Hg in the sitting of ACS.[9] Life-threatening arrhythmias included ventricular tachycardia, ventricular fibrillation, and complete heart block.[10]

RESULTS

Of the 74 patients in the sample population, 35,13% had STEMI and 64,8% had NSTEMI. Most of the AMI patients were male(59,4%), with a mean age of 58,2 years. The youngest patient was 38 years old and the oldest was 81 years old. Smoking is the most common risk factor, followed by high blood pressure, diabetes mellitus, and chronic kidney disease. MACE was obtained in 13 patients consisting of three patients with

Comment [RK4]: Past tense

malignant arrhythmias, seven patients with acute heart failure, two patients with cardiac arrest, and three patients with cardiogenic shock

Table1features of the 74 patients

Comment [RK5]: Description of the Variables & proportions maybeexpanded / explainedwell for betterunderstanding by the reader
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Variable

Sex,n (%)	
Male	44(59,4%)
Female	30(40,5%)
Age	58,2
Diabetesmellitus	33(44%)
Hypertension	40(54%)
Dyslipidemia	
Smoking,n(%)	54(59%)
ChronicKidneydisease	4(5,4%)
Previouscardiovasculardisease	12(16,2%)
MACE	13(17,56%)
AMI STEMI/NSTEMI	8(10,8%)/5(6,75%)
Systolicblood pressure(mmHg)	113,4
Distolicblood pressure(mmHg)	68,2
SD-SBP	11,615
SD-DBP	7,76
ARV-SBP	9,42
ARV-DBP	6,70

The mean of 24-hours systolic and diastolic blood pressure values were 113,4mmHg and 68,2 mmHg, respectively. The 24-hours systolic-diastolic BPV (SD-BPV/SD-DBP) and the systolic-diastolic ARV (ARV-SBP/ARV-DBP) were 11,615 mmHg, 7,76 mmHg, 9.42mmHg, 6,70 mmHg respectively). The mean value of systolic BPV in the group with

MACE (SD-SBP and ARV-SBP) was higher than the group without MACE. However, there was no significant relationship between VTD and the incidence of MACE.
The relationship between BPV and MACE was not significant :

Patients with MACEs:

Table2 MACE 's patients blood pressure features

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SD-SBP	**12,78**
SD-DBP	8,695
ARV-SBP	11,61
ARV-DBP	7,81

Patients withoutMACEs :

Table3 Non MACE's patients blood pressure features

Comment [RK7]: , symbol can bereplacewithdecimal point

SD-SBP	**10,45**
SD-DBP	6,84
ARV-SBP	7,23
ARV-DBP	5,6

As shown in Table4 , the mean BPV in AMI patients with high blood pressure was significantly higher than in patients without HBP

Table4 BPV in patients with and without HBP

BPV	Patients with HBP	Patients without HBP
SD-SBP	12,42	10,8
SD-DBP	9,22	6,3
ARV-SBP	11	7,84

ARV-DBP	7,47	5,93

As shown in Table5 the mean BPV in AMI patients with hypertension who experienced MACE was significantly higher than in patients without hypertension who experienced MACE

Comment [RK8]: Test of signifiance & at whatlevel ?

Table5 BPV in AMI patients with and without HBP experienced MACE

Comment [RK9]: Spell check

BPV	**Patients with HBP**	**Patients without HBP**
SD-SBP	14,2	11,2
SD-DBP	10,18	7,21
ARV-SBP	12,63	10,59
ARV-DBP	9,29	6,33

While The BPV in AMI patients who didn't experienced MACE was nearly the same in patients with or withoutHBP .

Table6 BPV in AMI patients who didn't experienced MACE with and without histoiry of HBP

BPV	**Patients with HBP**	**Patients without HBP**
SD-SBP	10,72	10,18
SD-DBP	7,13	6,55
ARV-SBP	7,34	7,12
ARV-DBP	5,75	5,45

However the BPV was significantly more important for HBP patient who experienced MACE than HBP patients didn't experienced MACE : SD-SBP (14,2 +versus 10,72 %) and ARV-SBP (12,63 versus 7,34 %), on the other hand , for patients with no history of HBP there was no significant difference in BPV between the one who experienced MACE and the one who didn't .

Discussion :

The high incidence of AMI in older and males may be due to an increased incidence of smoking in moroccan men ,metabolic diseases, such as hypertension and diabetes[11].

The ACCESS (2012) found that the mean age of acute coronary syndromes (ACS) patients ware 59 years, and 76% were male[12]; these demographics are almost the same as those in the present study.

Comment [RK10]: Past tense

The incidence of MACE in this study was 17,56%. This result is higher than that of previous studies conducted atCiptoMangunkusumo National Hospital in 2019[1] and Anastasia et al. (2019)[13] studies on ACS patient populations and found that 15,8% and 11.9%, respectively had MACE.

-In the last few years ,very few studies has investigate the impact of BPV measured by ABPM in patients with ACS .

The BP fluctuation and variability during ACS has been presented as a finding during management of these critically ill patients.[3]

Therefore, in our study, we investigated the impact of BPV analysis using ABPM during first 7 days of admission as a new risk factor for in-hospital MACE.

Comment [RK11]: reconsidersentanceas third party

-The average BPV value in the present study was slightly lower than the value identified by Harefa (2021), who studied The association between 24-h blood pressure variability and major adverse cardiac events (MACE) in hospitalized patients with acute myocardial infarction: a retrospective cohort study.[1]

-In Cesare Cuspidi ' study[14] and Harefa .[1]during the 7-day observation period, MACEs occurred in respectfully 37% and 15 ,83% patients versus 17,56 % in our study ,wich is in the same line .

-The mean SD-SBP and SD-DBP in Harefa's study were 11.98 ± 4.68 mmHg and 8.82 ± 3.63mmHg, respectively. Meanwhile, systolic and diastolic ARV was 9.36 ± 3.48

mmHg and 7.73 ± 2.98 mmHg, respectively. Our study results and Harefa 's are very close ,wich may be due to a similar patients managements and close monitoring of BP in the intensive care unit

Comment [RK12]: Spell check

Hassan et al. (2017), conducted a prospective cohort study with 200 samples and found a significant correlation between a high BPV and the incidence of MACE in AMI patients who were observed for the first seven days of hospitalization. In Hassan's study, a weighted standard deviation of blood pressure (wSD-BP) and the standard deviation of the 24-hour systolic-diastolic blood pressure (SD-SBP/SD-DBP) was used to measure BPV. Hassan et al. found a significant correlation between the high wSD-BP group (>12.6mmHg) and the high SD-SBP group (>13.5 mmHg) and the incidence of MACE (r=0.56, *p*=0.003)[15]. The contribution by Hassan and colleagues adds a piece of information on the relationship between short-term BP variability and cardiovascular complications in the setting of ACS, a clinical condition in which many factors may contribute to acutely alter physiological BP variability.. The present study findings indicate that BPV and MACE did not have a significant relationship in the first seven days of AMI patient hospitalization. However, the average BPV value in the MACE group was higher than in the non-MACE group. The result is in line with the finding in Hassan et al study [14]and Harefa .[1].

The non-significance relationship between BPV and MACE found in the present study could be due to the study population, which was smaller than the one Hassan and all refers to, but also due to various cardiovascular risk factors. The BPV characteristics in each comorbid disease affected the average BPV of the entire study population and affected the relationship between BPV and MACE.

Conclusion :

BPV could be an important risk factor for in-hospital MACE in patients with ACS with either STEMI or non-STEMI especially in patients with a history of HBP,which leads us to think that the screening of BPV in HBP patient may be very useful in predicting ofMACE .

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Comment [RK13]: Vancouver style of referencingmaybeconsidered

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