Heliyon 9 (2023) e17542

Contents lists available at ScienceDirect

Heliyon

journal homepage: www.cell.com/heliyon

Impact of pre-procedural diastolic blood pressure on major adverse cardiovascular events in non ST-segment elevation myocardial infarction patients following revascularization

Xiong Wang [1], Jingtang Hu [1], Peng Wang [1], Haifeng Pei [**], Zhen Wang [*]

Department of Cardiology, The General Hospital of Western Theater Command, Chengdu 610083, China

ARTICLE INFO

Keywords:
Diastolic blood pressure
Major adverse cardiovascular events
Non ST-Segment elevation myocardial infarction
Percutaneous coronary intervention

ABSTRACT

Previous reports have observed a consistent J-shaped relationship between cardiac events and diastolic blood pressure (DBP). However, the EPHESUS study clearly showed that myocardial reperfusion abolished the J-shaped association, suggesting a different association pattern after revascularization. Therefore, in this study, we investigated the different patterns in which DBP affects cardiovascular risk in non ST-segment elevation myocardial infarction (NSTEMI) patients after revascularization, which may benefit the risk stratification for NSTEMI patients. We obtained the NSTEMI database from the Dryad data repository and analyzed the association between preprocedural DBP and long-term major adverse cardiovascular events (MACEs) in 1486 patients with NSTEMI following percutaneous coronary intervention (PCI). Multivariate regression models were used to assess the impact of DBP on outcomes in an adjusted fashion according to DBP tertiles. The *p* value for the trend was calculated using linear regression. When examined as a continuous variable, a multivariate regression analysis was repeated. Pattern stability was verified by interaction and stratified analyses. The median (interquartile range) age of the patients was 61.00 (53.00–68.00) years, and 63.32% were male. Cardiac death showed a graded increase as the DBP tertile increased (p for trend = 0.0369). When examined as a continuous variable, a 1 mmHg increase in DBP level was associated with an 18% higher risk of long-term cardiac death (95% CI: 1.01–1.36, p = 0.0311) and a 2% higher risk of long-term all-cause death (95% CI: 1.01–1.04; p = 0.0178). The association pattern remained stable when stratified by sex, age, diabetes, hypertension, and smoking status. An association between low DBP and higher cardiovascular risk was not observed in our study. We showed that higher preprocedural DBP increased the risk of long-term cardiac death and all-cause death in patients with NSTEMI following PCI.

1. Introduction

Acute myocardial infarction (AMI) is the most common cardiovascular disease and a major cause of morbidity and mortality worldwide [1]. Among patients with AMI, non ST-segment elevation myocardial infarction (NSTEMI) is approximately twice as

* Corresponding author.
** Corresponding author.
E-mail addresses: web2010@foxmail.com (H. Pei), xzwz2022@163.com (Z. Wang).
[1] Xiong Wang, Peng Wang, and Jingtang Hu have contributed equally to this work as co-first authors.

https://doi.org/10.1016/j.heliyon.2023.e17542
Received 7 January 2023; Received in revised form 13 June 2023; Accepted 20 June 2023
Available online 21 June 2023

common as ST-segment elevation myocardial infarction (STEMI) [2]. Despite advancements in medical interventions and public awareness, the incidence of NSTEMI has been increasing over the past decade [3,4,5]. With respect to prognosis, although patients with NSTEMI appear to have lower short-term mortality than those with STEMI, with the extension of follow-up time, the mortality rate of NSTEMI patients has caught up with or even exceeded the mortality rate of STEMI patients [6,7,8]. This can be explained by differences in baseline patient characteristics, including older age in the NSTEMI population, but more importantly by improper risk stratification for NSTEMI patients [9].

The efficacy of an invasive strategy with revascularization is well established in patients with NSTEMI [10]. The improved outcome is, however, increasing the risk of subsequent cardiovascular events [11,12]. The identification of factors associated with a high risk of adverse events in post-AMI patients is essential for improving treatment and follow-up strategies [13]. However, information on these risk factors is currently limited.

In the Global Registry of Acute Coronary Events risk prediction tool, systolic blood pressure (SBP) was listed as one of nine factors that independently predicted death and the combined endpoint in the initial 6 months after admission [14]. With the reduction of SBP, hospital mortality increases significantly [14,15,16,17]. Additionally, several studies have previously demonstrated an inverse link between increasing SBP at admission and the risk of adverse cardiovascular outcome [18,19,20,21]. This can be explained by the fact that an increase in SBP is accompanied by an increase in coronary artery perfusion [21]. However, myocardial perfusion is critically dependent on diastolic blood pressure (DBP), as 85% of left ventricular perfusion occurs during diastole [22]. A J-shaped relationship between DBP and cardiovascular outcomes has been described in the Framingham population, in patients with hypertension and coronary artery disease, and those with a high cardiovascular risk after cardiovascular events or with peripheral arterial disease, with a particularly high risk at lower DBP [23,24,25]. However, the Eplerenone Post-Acute Myocardial Infarction Heart Failure Efficacy and Survival Study (EPHESUS) trial found a different pattern: after AMI, patients with heart failure exhibited a higher cardiovascular risk at low DBP, but after reperfusion, this elevated risk at low DBP was abolished [22]. This suggests that the effect of DBP on patients after revascularization may differ from that previously recognized.

Therefore, in this study, we analyzed the correlation between preprocedural DBP and long-term major adverse cardiovascular events (MACEs) in patients with NSTEMI following percutaneous coronary intervention (PCI) to critically investigate the different patterns in which DBP affects the cardiovascular risk in patients after revascularization.

2. Methods

2.1. Data source and study population

The study data were obtained from the Dryad data repository at http://datadryad.org/ with https://doi.org/10.5061/dryad.13d31. As previously described, the study was a prospective cohort study involving 2533 patients treated with at least one drug-eluting stent who completed long-term follow-up documentation [median of 29.8 months (quartiles, 25.6–34 months)] [26]. The ethics committee of The First Affiliated Hospital of Zhengzhou University approved this study, and all participants provided written informed consent. The *Helsinki Declaration* was strictly adhered to in this study to protect the patients' privacy. Data collection, analysis, and reporting with respect to the patients was completely anonymized.

In our primary analyses, we included only cases of NSTEMI (1486 patients were included and 10 patients were excluded for missing DBP values) (Fig. 1). The variables used in the database were as follows: age, sex, DBP, SBP, body mass index (BMI), heart rate, smoking status, heart failure, atrial fibrillation, previous myocardial infarction, chronic obstructive pulmonary disease, hypertension, diabetes, PCI, coronary artery bypass graft surgery, creatinine, uric acid, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, triglycerides, total cholesterol, left ventricular ejection fraction, type of lesion, medication, and MACEs.

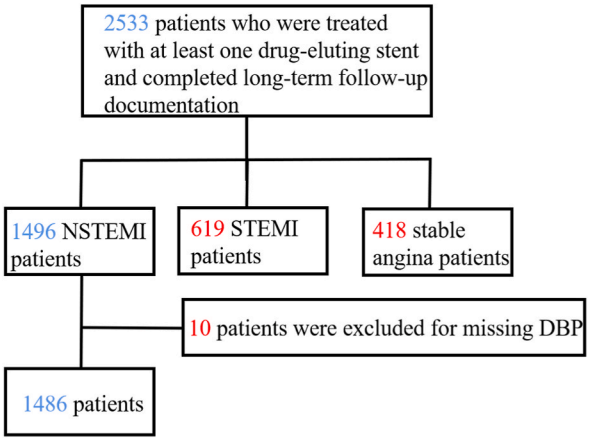

Fig. 1. Study flowchart. NSTEMI: non ST-segment elevation myocardial infarction; STEMI: ST-segment elevation myocardial infarction; DBP: diastolic blood pressure.

2.2. Exposure variables and outcome

We divided the 1486 patients included in the study into three groups (<72 mmHg, 72–79 mmHg, and >79 mmHg) according to the tertiles of pre-procedural DBP. The primary outcome was MACEs, including angina, revascularization, AMI, cardiac death, and all-cause death within the follow-up period.

2.3. Statistical analysis

Data are presented as median and interquartile range [IQR] for non-normally distributed continuous variables and as counts and percentages for categorical variables. Normality tests were conducted using the Shapiro–Wilk test. Baseline characteristics and MACEs were stratified according to DBP tertiles. Proportions according to tertiles were compared using the chi-squared test. The *p* value for the trend was calculated using linear regression. Both non-adjusted and multivariate adjusted models (variables adjusted for age, sex, SBP, and diabetes) were applied to evaluate the association between DBP and MACEs. Interaction and stratified analyses were conducted according to age (≦70 and > 70 years), sex (male and female), diabetes, hypertension, and smoking status. All analyses were performed using the statistical software packages R (http://www.R-project.org, The R Foundation) and EmpowerStats (http://www.empowerstats.com, X&Y Solutions, Inc., Boston, MA, USA). A two-sided significance level of 0.05 was used to evaluate statistical significance.

3. Results

A total of 1486 eligible patients were included in this analysis. The median (IQR) age was 61.00 (53.00–68.00) years, 63.32% were male, and 30.30% were smokers. A total of 825 (55.29%) patients were diagnosed with hypertension and 319 (21.55%) were diagnosed with diabetes.

The baseline characteristics according to DBP tertiles are shown in Table 1. Those in the highest tertile of DBP were significantly more likely to be younger (*p* for trend = 0.0054) and have a higher heart rate (*p* for trend = 0.0030) and BMI (*p* for trend = 0.0049).

Table 1
Baseline characteristics according to tertiles of DBP.

DBP	1st Tertile (<72 mmHg)	2nd Tertile (72–79 mmHg)	3rd Tertile (>79 mmHg)	p for trend
n	482	322	682	
AGE, yrs, Median (IQR)	62.50 (53.00–70.00)	61.00 (54.25–68.00)	60.00 (52.00–67.00)	0.0054
Male, n (%)	310 (64.32%)	200 (62.11%)	431 (63.20%)	0.6989
SBP, mmHg, Median (IQR)	83.50 (75.25–106.75)	90.00 (80.00–119.50)	120.00 (86.00–140.00)	<0.0001
DBP, mmHg, Median (IQR)	65.00 (60.00–69.00)	76.00 (74.00–77.00)	84.00 (80.00–90.00)	<0.0001
Heart rate, beats/min, Median (IQR)	70.00 (62.00–78.00)	71.00 (64.00–79.75)	72.00 (65.00–80.00)	0.0030
BMI, kg/m2, Median (IQR)	23.51 (21.26–26.14)	23.67 (21.30–26.40)	24.49 (22.32–26.79)	0.0049
Smoker, n (%)	147 (30.50%)	94 (29.19%)	210 (30.79%)	0.9118
Heart failure, n (%)	61 (12.66%)	41 (12.77%)	85 (12.50%)	0.9368
Atrial fibrillation, n (%)	4 (0.83%)	3 (0.93%)	12 (1.76%)	0.1707
OMI, n (%)	26 (5.39%)	14 (4.35%)	29 (4.25%)	0.3635
COPD, n (%)	5 (1.04%)	1 (0.31%)	5 (0.73%)	0.5571
Hypertension, n (%)	238 (49.38%)	175 (54.52%)	412 (60.41%)	0.0002
Diabetes, n (%)	105 (21.78%)	74 (23.05%)	140 (20.53%)	0.6037
Prior PCI, n (%)	50 (10.40%)	24 (7.45%)	40 (5.87%)	0.0046
Prior CABG, n (%)	6 (1.24%)	3 (0.93%)	9 (1.32%)	0.9058
Creatinine, μmol/L, Median (IQR)	69.00 (59.00–83.00)	68.00 (55.00–81.25)	68.00 (56.10–79.00)	0.8008
Uric acid, μmol/L, Median (IQR)	299.00 (248.00–348.75)	288.50 (239.00–349.50)	291.00 (244.00–354.00)	0.9845
Triglyceride, mmol/L, Median (IQR)	1.47 (1.09–2.26)	1.71 (1.24–2.35)	1.67 (1.21–2.41)	0.1810
Total cholesterol, mmol/L, Median (IQR)	4.16 (3.52–5.00)	4.15 (3.50–4.94)	4.26 (3.57–4.93)	0.5135
HDL-C, mmol/L, Median (IQR)	1.08 (0.91–1.29)	1.06 (0.88–1.24)	1.02 (0.86–1.22)	0.0032
LDL-C, mmol/L, Median (IQR)	2.59 (1.98–3.27)	2.60 (1.97–3.24)	2.63 (2.05–3.27)	0.7986
LVEF, %, Median (IQR)	63.00 (61.00–66.00)	63.00 (60.00–65.00)	63.00 (60.00–66.00)	0.3852
Multivessel disease, n (%)	102 (21.16%)	74 (22.98%)	169 (24.78%)	0.1499
Left main disease, n (%)	18 (3.73%)	11 (3.42%)	19 (2.79%)	0.1767
Chronic total occlusion, n (%)	34 (7.05%)	36 (11.18%)	64 (9.38%)	0.1756
Aspirin, n (%)	475 (98.55%)	319 (99.07%)	673 (98.68%)	0.8460
Clopidogrel, n (%)	461 (95.64%)	306 (95.03%)	657 (96.33%)	0.5831
Beta-blocker, n (%)	321 (66.60%)	229 (71.12%)	502 (73.61%)	0.0097
ACEI	251 (52.07%)	169 (52.48%)	356 (52.20%)	0.9671
Calcium-channel blocker, n (%)	140 (29.05%)	86 (26.71%)	228 (33.43%)	0.1074
Statin, n (%)	448 (92.95%)	300 (93.17%)	643 (94.28%)	0.3582

DBP: diastolic blood pressure; IQR: interquartile range; SBP: systolic blood pressure; BMI: body mass index; OMi: old myocardial infarction; COPD: chronic obstructive pulmonary disease; PCI: percutaneous coronary intervention; CABG: coronary artery bypass graft surgery; HDL-C: high density lipoprotein cholesterol; LDL-C: low density lipoprotein cholesterol; LVEF: left ventricular ejection fraction; ACEI: angiotensin-converting enzyme inhibitors.

Additionally, they were more likely to have history of hypertension (p for trend = 0.0002) and use of beta-blockers (p for trend = 0.0097), whereas those in the lowest tertile of DBP were more likely to have a history of PCI (p for trend = 0.0046) and higher high-density lipoprotein cholesterol levels (p for trend = 0.0032).

We used a multivariate linear regression model to evaluate the relationship between preprocedural DBP and long-term MACEs. The fully adjusted models are presented in Table 2 and Fig. 2. There were no significant differences in angina, revascularization, AMI, and all-cause death when examined by DBP tertiles. However, cardiac death showed a graded increase as the DBP tertile increased (p for trend = 0.0369).

When examined as a continuous variable, the univariate and fully adjusted multivariate linear regression models are shown in Table 3. In the univariate model, DBP was a significant independent predictor of angina, revascularization, and cardiac death; for every 1 mmHg increase in DBP, the risk of angina increased by 1% (95% CI: 1.00–1.02, p = 0.0120), the risk of revascularization increased by 2% (95% CI: 1.00–1.04: p = 0.0101), and the risk of cardiac death increased by 9% (95% CI: 1.05–1.12: p < 0.0001). However, in the fully adjusted multivariate model, DBP predicted the risk of cardiac death and all-cause death; for every 1 mmHg increase in DBP, the risk of cardiac death increased by 18% (95% CI: 1.01–1.36; p = 0.0311) and the risk of all-cause death increased by 2% (95% CI: 1.01–1.04; p = 0.0178).

To verify the stability of the relationship between preprocedural DBP and long-term MACEs, we performed interaction and stratified analyses (Table 4). When the stratification factor was set as sex, age, diabetes, hypertension, or smoking status, preprocedural DBP significantly predicted cardiac death. Interestingly, the effect value was higher in patients with diabetes (1.24 *vs.* 1.07, interaction p-value = 0.0031) and smokers (1.17 *vs.* 1.07, interaction p-value = 0.0437). Contrastingly, the relationship between preprocedural DBP and all-cause death was stable in all stratifications and preprocedural DBP significantly predicted all-cause death.

4. Discussion

In this study, we investigated the different patterns in which DBP affects cardiovascular risk in patients after revascularization. Our results showed a graded increase in the risk of long-term cardiac death as the preprocedural DBP tertile increased above 72 mmHg in patients with NSTEMI. When examined as a continuous variable and fully adjusted for patient characteristics—including age—more significant results were observed, and pre-procedural DBP predicted long-term cardiac death and all-cause death. Moreover, the results were still significant in the interaction and stratified analyses, and the effect values were higher in patients with diabetes and smokers. These findings suggest that preprocedural DBP critically affects MACEs in patients with NSTEMI following PCI; thus, preprocedural DBP should be included in the risk stratification of NSTEMI patients following PCI.

About 3 decades ago, Farnett et al. concluded that there was a consistent J-shaped relationship between cardiac events and DBP [27]. Since then, the J-curve phenomenon has been observed in several large trials of normotensive and hypertensive patients [23–25, 28–33]. The J-curve may be explained by three pathophysiological mechanisms: (1) low DBP could compromise coronary perfusion and cause cardiac ischemia; (2) low DBP could result from an increase in pulse pressure, reflecting stiffness of large arteries; and (3) low DBP could be a sign of underlying chronic illness, thereby increasing risk [33]. Therefore, low DBP essentially reduces coronary perfusion. Effective myocardial perfusion pressure, the difference between DBP and left ventricular filling, can be adjusted by coronary autoregulation in ischemia or increased workload conditions and may potentially impact outcomes due to ischemia or impaired left ventricular function [34]. In healthy dogs, a perfusion pressure as low as 35 mmHg is sufficient to maintain coronary perfusion; however, this might change when coronary artery stenoses are present [35]. The EPHESUS study clearly showed that myocardial reperfusion in patients after AMI with heart failure abolished the J-shaped association [22]. Additionally, low DBP in a population where obstructive coronary artery disease was excluded showed no evidence of a J-curve in the DBP risk association [36]. Simultaneously, our results did not show that low preprocedural DBP in NSTEMI patients following PCI is associated with a higher risk of MACEs.

Our findings revealed the predictive value of high preprocedural DBP for long-term cardiac death and all-cause death in patients with NSTEMI after PCI. Unsurprisingly, we observed a higher effect value between patients with diabetes and smokers with cardiac death. Diabetes and smoking are two of the most powerful risk factors for adverse cardiovascular events [37,38]. It is well known that age has a strong influence on all-cause death, although the association between higher pre-procedural DBP and long-term all-cause death was not significant in the univariate model; after adjusting for age, the result changed. Additionally, when stratified by patient characteristics, including sex, age, diabetes, hypertension, and smoking, the significant association persisted.

Our findings are limited to patients with NSTEMI treated with drug-eluting stents. Further, the assessment of the effects of

Table 2
MACEs stratified by tertiles of diastolic blood pressure.

DBP	1st Tertile (<72 mmHg)	2nd Tertile (72–79 mmHg), β (95%CI) p-value	3rd Tertile (>79 mmHg), β (95%CI) p-value	p for trend
Angina	Reference	1.30 (0.93, 1.83) 0.1260	1.06 (0.78, 1.44) 0.7136	0.7041
Revascularization	Reference	1.01 (0.59, 1.75) 0.9593	1.02 (0.63, 1.64) 0.9414	0.9415
AMI	Reference	0.63 (0.29, 1.34) 0.2290	0.87 (0.47, 1.59) 0.6422	0.6297
Cardiac death	Reference	2.91 (0.53, 16.08) 0.2210	4.76 (1.03, 21.97) 0.0456	0.0369
All cause death	Reference	1.42 (0.81, 2.51) 0.2199	1.41 (0.85, 2.34) 0.1889	0.1850

All adjusted for age, gender, MACEs: major adverse cardiovascular events; SBP and diabetes. DBP: diastolic blood pressure; AMI: Acute myocardial infarction.

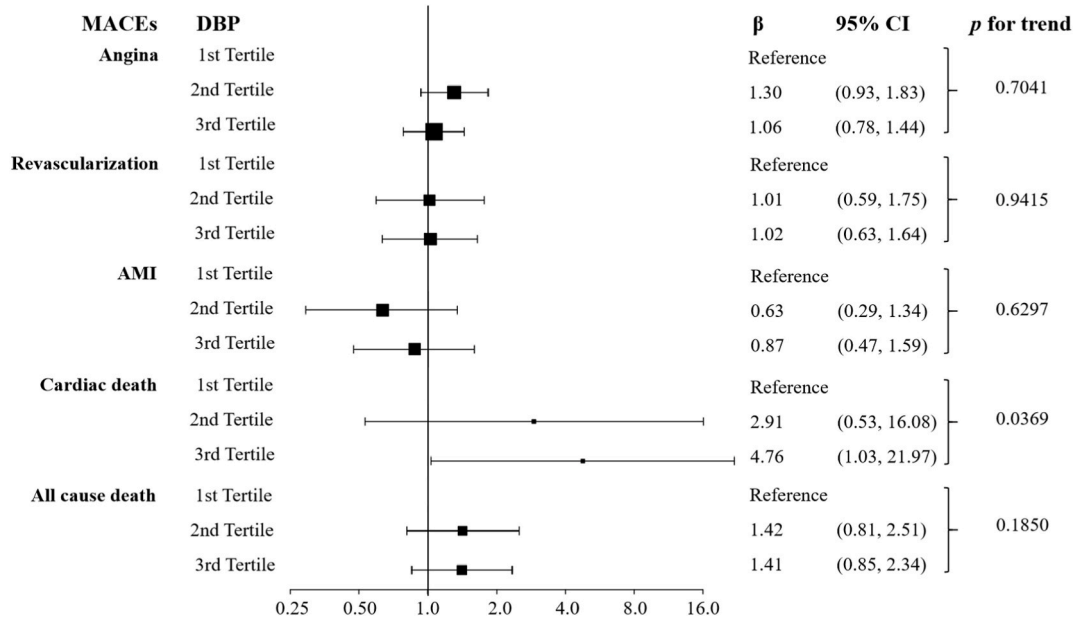

Fig. 2. MACEs stratified by tertiles of diastolic blood pressure. MACEs: major adverse cardiovascular events; DBP: diastolic blood pressure; AMI: Acute myocardial infarction.

Table 3
Pre-procedural DBP as a predictor of cardiac death and all cause death as a continuous variable.

	Univariable			Multivariable (fully adjusted)		
	β	95% CI	*p*-value	β	95% CI	*p*-value
Angina	1.01	(1.00, 1.02)	0.0120	1.00	(0.98, 1.02)	0.7495
Revascularization	1.02	(1.00, 1.04)	0.0101	1.01	(0.97, 1.02)	0.6718
AMI	1.01	(0.99, 1.03)	0.2062	0.99	(0.96, 1.02)	0.6007
Cardiac death	1.09	(1.05, 1.12)	<0.0001	1.18	(1.01, 1.36)	0.0311
All cause death	1.01	(1.00, 1.03)	0.1463	1.02	(1.01, 1.04)	0.0178

Multivariable model adjusted for age, gender, SBP, diabetes, heart rate, BMI, beta blockers, and HDL-C. DBP: diastolic blood pressure; AMI: Acute myocardial infarction.

preprocedural DBP on MACEs in these patients was a secondary analysis. This exploratory analysis assumed a quadratic relationship between preprocedural DBP and outcomes. Furthermore, a single pre-procedural blood pressure measurement only provides a snapshot of the hemodynamics and cannot reflect the real status of blood pressure. Besides, the importance of reperfusion in influencing the relationship between DBP and clinical outcomes needs to be further evaluated in future studies.

In conclusion, NSTEMI patients who underwent PCI with a high preprocedural DBP had an increased risk of long-term cardiac and all-cause death. Our findings support the current guidelines, suggesting lower DBP boundaries for revascularization in high-risk patients [39].

Author contribution

Xiong Wang, Zhen Wang, and Haifeng Pei: Conceived and designed the experiments; Analyzed and interpreted the data; Wrote the paper.

Jingtang Hu, Peng Wang: Analyzed and interpreted the data; Wrote the paper.

Data availability statement

Data will be made available on request.

Additional information

No additional information is available for this paper.

Table 4
Effect of pre-procedural DBP on cardiac death and all cause death in participants with gender, age, history of diabetes, history of hypertension and smoking status.

Cardiac death				
	β	95% CI	p-value	Interaction p-value
Gender				
female	1.07	(1.02, 1.13)	0.0062	0.2487
male	1.11	(1.06, 1.17)	<0.0001	
Age				
≦70 years old	1.08	(1.03, 1.13)	0.0015	0.2085
>70 years old	1.13	(1.06, 1.22)	0.0006	
Diabetes				
Yes	1.24	(1.11, 1.39)	0.0002	0.0031
No	1.07	(1.03, 1.12)	0.0006	
Hypertension				
Yes	1.10	(1.05, 1.16)	<0.0001	0.6370
No	1.09	(1.03, 1.15)	0.0033	
Smoker				
Yes	1.17	(1.07, 1.27)	0.0002	0.0437
No	1.07	(1.02, 1.12)	0.0031	
All cause death				
Gender				
female	1.02	(0.99, 1.05)	0.1877	0.5982
male	1.03	(1.01, 1.06)	0.0113	
Age				
≦70 years old	1.02	(0.99, 1.05)	0.1643	0.2956
>70 years old	1.04	(1.01, 1.07)	0.0094	
Diabetes				
Yes	1.03	(1.00, 1.07)	0.0427	0.6023
No	1.02	(1.00, 1.05)	0.0420	
Hypertension				
Yes	1.02	(1.00, 1.05)	0.0695	0.4318
No	1.04	(1.01, 1.07)	0.0177	
Smoker				
Yes	1.03	(1.00, 1.07)	0.0310	0.5173
No	1.02	(1.00, 1.05)	0.0942	

All adjusted for age, gender, SBP, diabetes. DBP: diastolic blood pressure.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgments

The study was supported by the project of Administration of Traditional Chinese Medicine of Sichuan Province, China (2021MS493); Incubation Projects of Hospital Management of the General Hospital of the Western Theater Command (No. 2021-XZYG-C42) and National Natural Science Foundation of China (No.81970241).

References

[1] G. A. Roth, G. A. Mensah, C. O. Johnson, G. Addolorato, E. Ammirati, L. M. Baddour, N. C. Barengo, A. Z. Beaton, E. J. Benjamin, C. P. Benziger, A. Bonny, M. Brauer, M. Brodmann, T. J. Cahill, J. Carapetis, A. L. Catapano, S. S. Chugh, L. T. Cooper, J. Coresh, M. Criqui, N. DeCleene, K. A. Eagle, S. Emmons-Bell, V. L. Feigin, J. Fernandez-Sola, G. Fowkes, E. Gakidou, S. M. Grundy, F. J. He, G. Howard, F. Hu, L. Inker, G. Karthikeyan, N. Kassebaum, W. Koroshetz, C. Lavie, D. Lloyd-Jones, H. S. Lu, A. Mirijello, A. M. Temesgen, A. Mokdad, A. E. Moran, P. Muntner, J. Narula, B. Neal, M. Ntsekhe, D. O. G. Moraes, C. Otto, M. Owolabi, M. Pratt, S. Rajagopalan, M. Reitsma, A. Ribeiro, N. Rigotti, A. Rodgers, C. Sable, S. Shakil, K. Sliwa-Hahnle, B. Stark, J. Sundstrom, P. Timpel, I. M. Tleyjeh, M. Valgimigli, T. Vos, P. K. Whelton, M. Yacoub, L. Zuhlke, C. Murray, V. Fuster, Global burden of cardiovascular diseases and risk factors, 1990-2019: update from the GBD 2019 Study, J. Am. Coll. Cardiol., 25 (76) 2982, https://doi. 10.1016/j.jacc.2020.11.010.

[2] B. C. Case, C. Yerasi, Y. Wang, B. J. Forrestal, J. Hahm, S. Dolman, W. S. Weintraub, R. Waksman, Admissions rate and timing of revascularization in the United States in patients with non-ST-elevation myocardial infarction, Am. J. Cardiol. (134) 24, https://doi. 10.1016/j.amjcard.2020.08.010.

[3] S. Khera, D. Kolte, W. S. Aronow, C. Palaniswamy, K. S. Subramanian, T. Hashim, M. Mujib, D. Jain, R. Paudel, A. Ahmed, W. H. Frishman, D. L. Bhatt, J. A. Panza, G. C. Fonarow, Non-ST-elevation myocardial infarction in the United States: contemporary trends in incidence, utilization of the early invasive strategy, and in-hospital outcomes, J. Am. Heart Assoc., 4(3) https://doi. 10.1161/JAHA.114.000995.

[4] S.M. Jennings, K. Bennett, M. Lonergan, E. Shelley, Trends in hospitalisation for acute myocardial infarction in Ireland, Heart 17 (98) (1997-2008) 1285, https://doi.org/10.1136/heartjnl-2012-301822.

[5] Y. Kim, Y. Ahn, M. C. Cho, C. J. Kim, Y. J. Kim, M. H. Jeong, Current status of acute myocardial infarction in Korea, Korean J. Intern. Med. 1 (34) 1, https://doi. 10.3904/kjim.2018.381.

[6] X. Han, L. Bai, M. H. Jeong, J. H. Ahn, D. Y. Hyun, K. H. Cho, M. C. Kim, D. S. Sim, Y. J. Hong, J. H. Kim, Y. Ahn, Higher long-term mortality in patients with non-ST-elevation myocardial infarction than ST-elevation myocardial infarction after discharge, Yonsei Med. J., 5 (62) 400,https://doi. 10.3349/ymj.2021.62.5.400.

[7] C. J. Terkelsen, J. F. Lassen, B. L. Norgaard, J. C. Gerdes, T. Jensen, L. B. Gotzsche, T. T. Nielsen, H. R. Andersen, Mortality rates in patients with ST-elevation vs. non-ST-elevation acute myocardial infarction: observations from an unselected cohort, Eur. Heart J., 1(26) 18, https://doi. 10.1093/eurheartj/ehi002.

[8] Y. Hao, J. Liu, J. Liu, N. Yang, S. J. Smith, Y. Huo, G. C. Fonarow, J. Ge, K. A. Taubert, L. Morgan, M. Zhou, Y. Xing, C. S. Ma, Y. Han, D. Zhao, Sex differences in in-hospital management and outcomes of patients with acute coronary syndrome, Circulation, 15 (139) 1776,https://doi. 10.1161/CIRCULATIONAHA.118.037655..

[9] A. Mitsis, F. Gragnano, Myocardial infarction with and without ST-segment elevation: a contemporary reappraisal of similarities and differences,Curr. Cardiol. Rev., 4 (17) e1507044971, https://doi. 10.2174/1573403X 16999201210195702.

[10] B. C. Case, W. S. Weintraub, Non-ST-segment-elevation myocardial infarction: when is rapid revascularization critical? J. Am. Heart Assoc., 19 (10)e23645, https://doi. 10.1161/JAHA.121.023645.

[11] Global, regional, and national incidence, prevalence, and years lived with disability for 301 acute and chronic diseases and injuries in 188 countries, 1990-2013: a systematic analysis for the Global Burden of Disease Study, Lancet 9995 (386) (2013) 743, https://doi.org/10.1016/S0140-6736(15)60692-4.

[12] S. Johansson, A. Rosengren, K. Young, E. Jennings, Mortality and morbidity trends after the first year in survivors of acute myocardial infarction: a systematic review, Bmc Cardiovasc Disor, 1 (17) 53,https://doi. 10.1186/s12872-017-0482-9.

[13] V. Kyto, T. Prami, H. Khanfir, P. Hasvold, E. Reissell, J. Airaksinen, Usage of PCI and long-term cardiovascular risk in post-myocardial infarction patients: a nationwide registry cohort study from Finland, Bmc Cardiovasc Disor, 1 (19) 123,https://doi. 10.1186/s12872-019-1101-8.

[14] B. Elbarouni, S. G. Goodman, R. T. Yan, R. C. Welsh, J. M. Kornder, J. P. Deyoung, G. C. Wong, B. Rose, F. R. Grondin, R. Gallo, M. Tan, A. Casanova, K. A. Eagle, A. T. Yan, Validation of the Global Registry of Acute Coronary Event (GRACE) risk score for in-hospital mortality in patients with acute coronary syndrome in Canada, Am. Heart J., 3 (158) 392,https://doi. 10.1016/j.ahj.2009.06.010.

[15] K. A. Fox, O. H. Dabbous, R. J. Goldberg, K. S. Pieper, K. A. Eagle, F. Van de Werf, A. Avezum, S. G. Goodman, M. D. Flather, F. J. Anderson, C. B. Granger, Prediction of risk of death and myocardial infarction in the six months after presentation with acute coronary syndrome: prospective multinational observational study (GRACE), BMJ Br. Med. J. (Clin. Res. Ed.), 7578 (333) 1091,https://doi. 10.1136/bmj.38985.646481.55.

[16] S. G. Goodman, W. Huang, A. T. Yan, A. Budaj, B. M. Kennelly, J. M. Gore, K. A. Fox, R. J. Goldberg, F. J. Anderson, The expanded Global Registry of Acute Coronary Events: baseline characteristics, management practices, and hospital outcomes of patients with acute coronary syndromes, Am. Heart J., 2 (158) 193, https://doi. 10.1016/j.ahj.2009.06.003.

[17] K. A. Fox, S. G. Goodman, W. Klein, D. Brieger, P. G. Steg, O. Dabbous, A. Avezum, Management of acute coronary syndromes. Variations in practice and outcome; findings from the Global Registry of Acute Coronary Events (GRACE), Eur. Heart J., 15 (23) 1177,https://doi. 10.1053/euhj.2001.3081.

[18] D. Roth, R. Van Tulder, B. Heidinger, H. Herkner, W. Schreiber, C. Havel, Admission blood pressure and 1-year mortality in acute myocardial infarction, Int. J. Clin. Pract., 8 (69) 812 https://doi. 10.1111/ijcp.12588.

[19] G. Shlomai, E. Kopel, I. Goldenberg, E. Grossman, The association between elevated admission systolic blood pressure in patients with acute coronary syndrome and favorable early and late outcomes, J. Am. Soc. Hypertens., 2 (9) 97,https://doi. 10.1016/j.jash.2014.11.005.

[20] J. S. Park, K. S. Cha, D. Shin, D. S. Lee, H. W. Lee, J. H. Oh, J. H. Choi, H. C. Lee, T. J. Hong, S. H. Lee, J. S. Kim, Y. H. Park, J. H. Kim, K. J. Chun, M. H. Jeong, Y. Ahn, S. C. Chae, Y. J. Kim, Prognostic significance of presenting blood pressure in patients with ST-elevation myocardial infarction undergoing percutaneous coronary intervention, Am. J. Hypertens., 6 (28) 797, https://doi. 10.1093/ajh/hpu230.

[21] J. Pei, X. Wang, Z. Xing, P. Chen, W. Su, S. Deng, X. Hu, Association between admission systolic blood pressure and major adverse cardiovascular events in patients with acute myocardial infarction, PLoS One, 6 (15) e234935 https://doi. 10.1371/journal.pone.0234935.

[22] M. Bohm, J. P. Ferreira, F. Mahfoud, K. Duarte, B. Pitt, F. Zannad, P. Rossignol, Myocardial reperfusion reverses the J-curve association of cardiovascular risk and diastolic blood pressure in patients with left ventricular dysfunction and heart failure after myocardial infarction: insights from the EPHESUS trial, Eur. Heart J.,17 (41) 1673, https://doi. 10.1093/eurheartj/ehaa132.

[23] S. S. Franklin, S. S. Gokhale, V. H. Chow, M. G. Larson, D. Levy, R. S. Vasan, G. F. Mitchell, N. D. Wong, Does low diastolic blood pressure contribute to the risk of recurrent hypertensive cardiovascular disease events? The Framingham Heart Study, Hypertension, 2 (65) 299,https://doi. 10.1161/HYPERTENSION.AHA.114.04581.

[24] E. Vidal-Petiot, I. Ford, N. Greenlaw, R. Ferrari, K. M. Fox, J. C. Tardif, M. Tendera, L. Tavazzi, D. L. Bhatt, P. G. Steg, Cardiovascular event rates and mortality according to achieved systolic and diastolic blood pressure in patients with stable coronary artery disease: an international cohort study, Lancet, 10056 (388) 2142, https://doi. 10.1016/S0140-6736(16)31326-5.

[25] M. Bohm, H. Schumacher, K. K. Teo, E. M. Lonn, F. Mahfoud, J. Mann, G. Mancia, J. Redon, R. E. Schmieder, K. Sliwa, M. A. Weber, B. Williams, S. Yusuf, Achieved blood pressure and cardiovascular outcomes in high-risk patients: results from ONTARGET and TRANSCEND trials, Lancet, 10085 (389) 2226,https://doi. 10.1016/S0140-6736(17)30754-7.

[26] H. M. Yao, Y. D. Wan, X. J. Zhang, D. L. Shen, J. Y. Zhang, L. Li, L. S. Zhao, T. W. Sun, Long-term follow-up results in patients undergoing percutaneous coronary intervention (PCI) with drug-eluting stents: results from a single high-volume PCI centre, BMJ Open, 8 (4) e4892 https://doi. 10.1136/bmjopen-2014-004892.

[27] L. Farnett, C. D. Mulrow, W. D. Linn, C. R. Lucey, M. R. Tuley, The J-curve phenomenon and the treatment of hypertension. Is there a point beyond which pressure reduction is dangerous? JAMA, J. Am. Med. Assoc., 4 (265) 489.

[28] M. L. Bots, J. C. Witteman, A. Hofman, P. T. de Jong, D. E. Grobbee, Low diastolic blood pressure and atherosclerosis in elderly subjects. The Rotterdam study, Arch. Intern. Med., 8 (156) 843.

[29] R. J. Glynn, C. U. Chae, J. M. Guralnik, J. O. Taylor, C. H. Hennekens, Pulse pressure and mortality in older people, Arch. Intern. Med., 18 (160) 2765 https://doi. 10.1001/archinte.160.18.2765.

[30] R. Pastor-Barriuso, J. R. Banegas, J. Damian, L. J. Appel, E. Guallar, Systolic blood pressure, diastolic blood pressure, and pulse pressure: an evaluation of their joint effect on mortality, Ann. Intern. Med., 9 (139)731, https://doi. 10.7326/0003-4819-139-9-200311040-00007.

[31] A. Zanchetti, L. Hansson, D. Clement, D. Elmfeldt, S. Julius, T. Rosenthal, B. Waeber, H. Wedel, Benefits and risks of more intensive blood pressure lowering in hypertensive patients of the HOT study with different risk profiles: does a J-shaped curve exist in smokers? J. Hypertens., 4 (21) 797,https://doi. 10.1097/00004872-200304000-00024.

[32] S. E. Lee, H. Y. Lee, H. J. Cho, W. S. Choe, H. Kim, J. O. Choi, E. S. Jeon, M. S. Kim, K. K. Hwang, S. C. Chae, S. H. Baek, S. M. Kang, D. J. Choi, B. S. Yoo, K. H. Kim, M. C. Cho, J. J. Kim, B. H. Oh, Reverse J-curve relationship between on-treatment blood pressure and mortality in patients with heart failure, JACC-Heart Fail, 11 (5) 810 https://doi. 10.1016/j.jchf.2017.08.015.

[33] F. H. Messerli, G. Mancia, C. R. Conti, A. C. Hewkin, S. Kupfer, A. Champion, R. Kolloch, A. Benetos, C. J. Pepine, Dogma disputed: can aggressively lowering blood pressure in hypertensive patients with coronary artery disease be dangerous? Ann. Intern. Med., 12 (144) 884,https://doi. 10.7326/0003-4819-144-12-200606200-00005.

[34] N. Westerhof, C. Boer, R. R. Lamberts, P. Sipkema, Cross-talk between cardiac muscle and coronary vasculature, Physiol. Rev., 4 (86) 1263 https://doi. 10.1152/physrev.00029.2005.

[35] J. J. Canty, Coronary pressure-function and steady-state pressure-flow relations during autoregulation in the unanesthetized dog, Circ. Res., 4(63) 821, https://doi. 10.1161/01.res.63.4.821.

[36] G. C. Roush, A. Zubair, K. Singh, W. J. Kostis, D. A. Sica, J. B. Kostis, Does the benefit from treating to lower blood pressure targets vary with age? A systematic review and meta-analysis, J. Hypertens., 8 (37) 1558,https://doi. 10.1097/HJH.0000000000002079.

[37] B. A. Bergmark, B. M. Scirica, P. G. Steg, C. L. Fanola, Y. Gurmu, O. Mosenzon, A. Cahn, I. Raz, D. L. Bhatt, Blood pressure and cardiovascular outcomes in patients with diabetes and high cardiovascular risk, Eur. Heart J., 24 (39) 2255, https://doi. 10.1093/eurheartj/ehx809.

[38] A. Timmis, P. Vardas, N. Townsend, A. Torbica, H. Katus, D. De Smedt, C.P. Gale, A.P. Maggioni, S.E. Petersen, R. Huculeci, D. Kazakiewicz, R.V. de Benito, B. Ignatiuk, Z. Raisi-Estabragh, A. Pawlak, E. Karagiannidis, R. Treskes, D. Gaita, J.F. Beltrame, A. McConnachie, I. Bardinet, I. Graham, M. Flather, P. Elliott, E. A. Mossialos, F. Weidinger, S. Achenbach, European Society of Cardiology: cardiovascular disease statistics, Eur. Heart J. 8 (43) (2021) 716, https://doi.org/10.1093/eurheartj/ehab892.

[39] F.J. Neumann, M. Sousa-Uva, A. Ahlsson, F. Alfonso, A.P. Banning, U. Benedetto, R.A. Byrne, J.P. Collet, V. Falk, S.J. Head, P. Juni, A. Kastrati, A. Koller, S. D. Kristensen, J. Niebauer, D.J. Richter, P.M. Seferovic, D. Sibbing, G.G. Stefanini, S. Windecker, R. Yadav, M.O. Zembala, ESC/EACTS Guidelines on myocardial revascularization, Eur. Heart J. 2 (40) (2018) 87, https://doi.org/10.1093/eurheartj/ehy394.