



## Editorial

## In-hospital pulse pressure variability: A novel marker of cardiovascular risk among patients with coronary artery disease undergoing percutaneous coronary intervention?



## ARTICLE INFO

## Keywords

Pulse pressure  
Cardiovascular  
Coronary artery disease  
Percutaneous coronary intervention

## 1. Manuscript text

Elevated systolic and diastolic blood pressure (BP) are major risk factors for cardiovascular events [1,2]. Pulse pressure (PP), the difference between systolic and diastolic BP, is also a predictor of cardiovascular events [3]. Among individuals with established coronary artery disease, PP is associated with increased risk of cardiovascular outcomes even after adjusting for systolic or diastolic BP [4]. This association has been usually explained by the fact that greater PP values reflect increased stiffness of large arteries, an acknowledged contributor to atherosclerosis [5].

Previous post-hoc analysis of randomized clinical trials demonstrated that there is a J-curve between systolic and diastolic BP and adverse cardiovascular outcomes in patients with cardiovascular disease, including those with coronary artery disease [6]. For this reason, current hypertension guidelines recommend that office systolic and diastolic BP should not be reduced to levels below 120 mmHg and 70 mmHg, respectively, in individuals with high cardiovascular risk [7]. Interestingly, a J-curve association with cardiovascular events was also reported for PP in high-risk patients, even though the mechanisms underlying this relationship are still uncertain [6].

In this issue of the journal, Nochioka et al. reported the findings of a retrospective observational study in a large Japanese cohort (n = 8708) of patients with acute and chronic coronary artery syndrome who were hospitalized and underwent percutaneous coronary intervention (PCI) [8]. The researchers evaluated whether changes in PP measured at two time points (before PCI and at hospital discharge) would have prognostic value and expanded the current knowledge by showing a U-shape relationship between the incidence rates of major adverse cardiac or cerebrovascular events and in-hospital PP change, even after adjusting for several confounders. These findings align with former data showing that in-hospital systolic BP variability predicted cardiovascular events

and kidney function decline among 226 patients who underwent elective PCI for stable coronary artery disease [9]. More importantly, the work by Nochioka et al. raises the assumption that PP variability and control during hospitalization might have clinical and prognostic value for patients undergoing PCI regardless of having acute or chronic coronary artery syndrome. These findings are very interesting and the authors should be praised for their insightful analysis. Nevertheless, some aspects of the study deserve further comments.

The authors properly suggested that PP change could be a marker of BP day-to-day BP variability, which is an acknowledged predictor of cardiovascular outcomes [10,11], therefore providing a potential explanation for the association between PP change and subsequent cardiovascular events. However, the mechanisms underlying in-hospital PP changes were not apparent in their analysis. Previous studies demonstrated that coronary artery disease patients may experience either improvement or impairment of left ventricular (LV) function following PCI [12]. Because decreases in LV function can lead to BP reductions [7], it is possible that some patients with PP changes might have experienced variation in LV function throughout hospitalization. Although the authors adjusted their analyses by LV ejection fraction and brain natriuretic peptide levels, it was not clear in the protocol when these measures were performed during the in-hospital period. Additional information on this topic could be useful to evaluate the exact influence of LV function on the presented results.

The researchers stated in the Methods Section that BP was measured according to usual practices before PCI and at discharge, but was not standardized. This lack of standardization might have also contributed to generate PP variation. It is acknowledged that BP measured by the oscillometric and auscultatory methods yields different PP values [13], while one isolated BP measurement usually overestimates the obtained BP value due to the white-coat effect when compared with several BP measurements [7]. In addition, patients with postural hypotension, who

DOI of original article: <https://doi.org/10.1016/j.ijcha.2024.101430>.

<https://doi.org/10.1016/j.ijcha.2024.101445>

Received 7 June 2024; Accepted 9 June 2024

Available online 15 June 2024

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intrinsically have higher risk of future cardiovascular events [7], may exhibit greater BP levels in supine position than in sitting position [14]. Therefore, differences in the devices used to measure BP, the number of BP measurements and the position of the patient during BP measurement at each time point could have led to PP variation throughout hospitalization.

Some relevant limitations of the study were acknowledged by the authors. First, data on valvular diseases and antihypertensive treatment during hospitalization, which could be confounders when assessing the prognostic value of PP, were not available. Second, the retrospective design limited the ability to establish causality between PP change and outcomes. Third, the studied sample solely comprised Japanese patients, raising the supposition that the findings may not be generalizable to other ethnic populations. Conversely, additional points are worth mentioning. Although the results demonstrated a robust U-shaped association between PP change and cardiovascular outcomes, it is still uncertain whether this association remained significant after adjusting for systolic or diastolic BP at discharge or for systolic or diastolic BP variation during hospitalization. In addition, the incremental value of in-hospital PP change in predicting cardiovascular events beyond established prognostic factors [15] and systolic or diastolic BP values was not evaluated.

Despite the above considerations, the study by Nochioka et al. [8] deserves to be highlighted because it provides novel evidence that in-hospital PP variability might have clinical value for patients with acute and chronic coronary artery syndrome undergoing PCI. New research is needed to validate these findings and to establish the incremental value of PP change in predicting cardiovascular events beyond established prognostic factors in this population.

#### Sources of Funding

The study was supported by the Brazilian National Council for Scientific and Technological Development (CNPq; grant 310869/2021-8 for Dr. Nadruz).

#### 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.

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