PRELIMINARY REPORT

Journal of General and Family Medicine WILEY

Paradoxical high augmentation index in females with diabetes mellitus

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Abstract
The relationship between diabetes mellitus (DM) and augmentation index (AIx) remains unclear. We conducted an observational cross-sectional study. Subjects were patients who underwent coronary angiography. We examined the relationship between high AIx and several factors. The total number of diabetic patients was 144, and median AIx was 0.256. In diabetic patients, the significant relationship between female gender and high AIx (median cut-off value, ≥0.256) was found by the multivariate logistic analysis (adjusted odds ratio = 2.888; 95% confidence interval: 1.032-8.081). The significant relationship between female gender and high AIx was found in patients with DM.

KEYWORDS
augmentation index, diabetes mellitus, female gender

1 | INTRODUCTION

Compared with patients with diabetes mellitus (DM) who have normal blood pressure, concomitant hypertension in patients with DM is known to increase all-cause mortality or cardiovascular events.[1] In daily clinical practice, peripheral blood pressure is measured at the brachial artery. However, pathophysiologically, central arterial pressure is a better predictor of cardiovascular events than peripheral blood pressure because central arterial pressure is measured closer to the heart.[2] Actually, the augmentation index (AIx), which is calculated from the central arterial pressure waveform, is reported to be an excellent predictor for mortality or cardiovascular events.[3] However, the association between DM and AIx remains unclear. Although some previous studies have showed that DM was associated with high AIx,[4,5] other studies have reported no association.[6] In this study, we investigated the relationship between DM and AIx.

2 | METHODS

This study was subanalysis of our previous report.[7] We conducted an observational cross-sectional study at Juntendo University and St. Luke's International Hospital in Tokyo, Japan. Subjects were patients who underwent coronary angiography from January to September 2013. This study was approved by the Institutional Ethics Committee of each hospital. We investigated clinical background of patients with DM. To examine relationship between high AIx (median cut-off value, ≥0.256) and several factors in diabetic patients, we conducted the multivariate logistic analysis. We also evaluated relationship between high AIx (median cut-off value, ≥0.319) and several factors in nondiabetic patients.

We enrolled consecutive patients who underwent a scheduled coronary angiography and central pressure recordings. In this study, the exclusion criteria were patients with inadequate coronary

TABLE 1 Association between the clinical factors and high AIx

Multivariate logistic regression analysis			
	OR	95% CI	P Value
Age	1.022	0.984-1.062	.258
Female gender	2.888	1.032-8.081	.043*
Hypertension	0.922	0.271-3.140	.897
Dyslipidemia	1.680	0.572-4.936	.345
eGFR	1.005	0.993-1.018	.414
Aspirin	2.600	1.116-6.058	.027*
Statin	0.860	0.344-2.153	.860
RAS-I	2.316	1.028-5.218	.043*
CCB	1.437	0.626-3.299	.392

eGFR = estimated glomerular filtration rate, RAS-I = renin angiotensin system inhibitors, CCB = calcium channel blocker, CI = confidence interval, OR = odds ratio, *means statistically significant.

angiographic information, and those whose arterial pressure waveforms could not be properly measured were excluded. Central arterial pressure waveform analysis was performed on a printed paper by two experienced cardiologists who were blinded to the characteristics of the patients. The central arterial pressure was measured at four points in accordance with our previous study[7]: P0, diastolic pressure; P1, reflection pressure; P2, peak systolic pressure; P3, dicrotic notch pressure (incisura).[8] Augmentation pressure was defined as the difference between P1 and P2, and AIx was calculated by dividing augmentation pressure by pulse pressure (P2-P0). AIx was calibrated for a heart rate of 75 bpm.

3 | RESULTS

The total number of diabetic patients was 144, and mean age was 68.3±10.1 (SD). There were 119 male and 25 female patients. Mean AIx was 0.255±0.214, and median AIx was 0.256. 84.7% of the cases had hypertension. 74.3% of the cases had dyslipidemia. 38.9% of the cases had history of coronary revascularization (percutaneous coronary intervention or coronary artery bypass grafting). The significant relationship between female gender and high AIx was found by the multivariate logistic analysis (Table 1).

The total number of nondiabetic patients in this study was 260. There were 194 male and 66 female patients. In nondiabetic patients group, female gender was not significantly associated with high AIx (adjusted odds ratio = 0.714; 95% confidence interval: 0.369-1.379).

4 | DISCUSSION

We showed the significant relationship between female gender and high AIx. This finding was contradictory to our expectation of a strong relationship between male patients and high AIx because
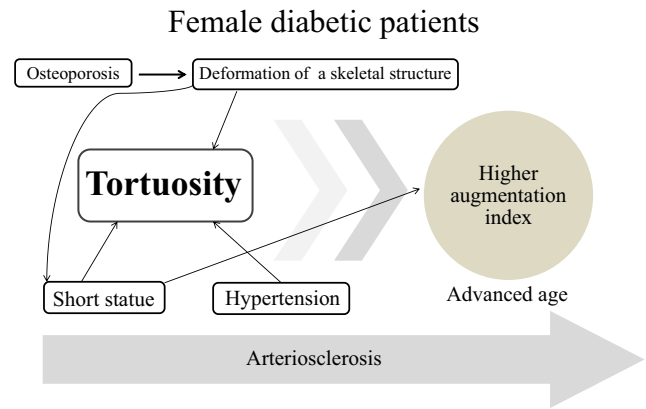
FIGURE 1 Hypothetical association between high augmentation index and female gender in diabetic patients

arteriosclerosis occurs more often in men. Factors other than arteriosclerosis can be closely associated with high AIx in female. We hypothesized that arterial tortuosity could be responsible for high AIx. Reportedly, arterial tortuosity develops with aging,[9] and Cha et al.[10] pointed female gender as one of the predictors for severe tortuosity of the right subclavian artery. Anatomical abnormality can be responsible for the increase in reflective wave because aged females tend to develop tortuosity. Figure 1 shows our hypothetical association between high AIx and females with DM. Females with DM tends to develop complicated osteoporosis that can cause skeletal deformation or decreased height through compression fracture. Aging, female gender, short stature, and long-standing hypertension, when combined, are factors that can lead to arterial tortuosity.

There are several limitations to this study. First, the sample size of this study was small. Especially, the number of female diabetic patients was 25, which was not large enough to support the study results. Second, the causal relationship could not be clarified because of the nature of the study design. Third, although we hypothesized that tortuosity was the cause of high AIx, we did not directly evaluate the relationship between tortuosity and AIx. We should have compared the vessel characteristics between diabetic and nondiabetic patients. Future studies to verify the relationship between tortuosity and AIx should be conducted.

5 | CONCLUSION

We showed the significant relationship between female gender and high AIx. Factors other than arteriosclerosis such as skeletal deformation or arterial tortuosity can be closely associated with high AIx in female diabetic patients.

CONFLICTS OF INTEREST

The authors have stated explicitly that there are no conflicts of interest in connection with this article.

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