

Coronary artery disease, arterial stiffness, and myocardial work: what is the role of diabetes in this vicious circle?

To the editor We really appreciated the results of the observational study conducted by Dziarmaga et al,¹ who demonstrated a significant negative correlation between the echocardiographic parameters of myocardial work and arterial stiffness among patients with stable coronary artery disease (CAD). A closer look at participants' characteristics reveals that 27% of them had concomitant diabetes, all on metformin-based antidiabetic regimen, while one-third of them received insulin treatment.

Of note, as previously reported,² CAD represents the major contributor of the cardiovascular disease burden in patients with diabetes. Therefore, there is an absolute need for prognostic markers, such as arterial stiffness, for the risk stratification and therapeutic management of diabetic patients. It has been established that patients with diabetes have increased arterial stiffness compared with the general population, with a strong and significant relationship both with micro- and macrovascular complications.³

Recently, Tadic et al⁴ showed in a cross-sectional study that diabetes additionally affects myocardial work in hypertensive patients, with glycated hemoglobin representing an independent variable, significantly correlating with the global myocardial work index and constructive work.

Therefore, we would be interested in a subanalysis of the results presented by Dziarmaga et al¹ according to patients' diabetic status at baseline, as it would add further knowledge, despite the relatively small sample size. The identification of such an association would be of great interest, as it might guide antidiabetic treatment, particularly since recent data have suggested that newer antidiabetic drugs with established cardiovascular benefits have beneficial effects both on arterial stiffness and myocardial work indices.⁵ Further larger studies are needed to shed light on that association and its implications in clinical practice.

ARTICLE INFORMATION

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CONFLICT OF INTEREST None declared.

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HOW TO CITE Patoulias D, Papadopoulos C, Doumas M. Coronary artery disease, arterial stiffness, and myocardial work: what is the role of diabetes in this vicious circle? *Kardiol Pol.* 2021; 79: 360. doi:10.33963/KP.15891

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Authors' reply We are grateful to Patoulias et al¹ for their interest in our work,² as well as valuable and inspiring comments. Strong clinical and observational evidence shows that patients with diabetes are at risk of developing

TABLE 1 Clinical data and parameters describing left ventricular function, including myocardial work, in coronary artery disease patients with or without diabetes. The comparison was performed using the nonpaired *t* test. All methodological details are shown in the study by Dziarmaga et al.²

Parameter	No diabetes (n = 65)	Diabetes (n = 24)	P value
Age, y	63.52 (8.44)	62.89 (11.65)	0.78
HR, bpm	68.02 (10.6)	70.03 (12.12)	0.45
SBP, mm Hg	129.13 (14.69)	134.76 (17.11)	0.13
DBP, mm Hg	76.24 (9.41)	74.63 (18.05)	0.59
PWV, m/s	8.49 (3.1)	9.17 (3.8)	0.4
LVEF, %	60.84 (12.42)	57.24 (13.06)	0.23
E/e'	7.97 (1.97)	12.01 (5.81)	<0.001
GWE, mm Hg%	91.85 (4.42)	87.69 (7.37)	0.002
GCW, mm Hg%	2044.15 (524.71)	1832.76 (640.69)	0.12
GCWW, mm Hg%	144.97 (78.88)	180.7 (127.15)	0.12
GWI, mm Hg%	1823.65 (449.98)	1583.36 (539.96)	0.04

Data are presented as mean (SD).

Abbreviations: E/e', the ratio between early mitral inflow velocity and mitral annular early diastolic velocity; GCW, global myocardial constructive work; GWE, global myocardial work efficiency; GWI, global myocardial work index; GWW, global myocardial wasted work; LVEF, left ventricular ejection fraction; PWV, pulse wave velocity

and faster progression of cardiovascular disease with severe complications, including premature death.^{3,4}

We utterly agree with Patoulias et al¹ that reliable predictive tools for risk stratification, therapeutic management, and clinical monitoring would be of great practical relevance and exploitable in many patients with diabetes. However, it remains unclear whether such solutions should employ the measurement of arterial stiffness, myocardial work, or other methods. From the theoretical angle, such techniques should have a clear physiological and clinical explanation. From the practical point of view, such procedures should be noninvasive, reproducible, with established and accepted cutoff values, easily applicable, and, if possible, not expensive.

The measures of arterial stiffness or myocardial work are attractive candidates that meet both theoretical and practical requirements. The clinical value of arterial stiffness has been studied for over 40 to 50 years. It has established a strong position in evaluating the cardiovascular system, particularly in risk prediction in various groups of patients, including those with diabetes.^{3,4} Preliminarily, as for myocardial work analysis, the quantification of left ventricular pressure-strain loops was doable only with the invasive approach.⁵ However, since the advent of strain and strain rate analysis by Russel et al,⁵ it has been possible to estimate myocardial work entirely noninvasively.

The history of the noninvasive approach to the quantification of myocardial work has spanned approximately 8 years. Nevertheless,

its practical application with the commercially available methodology is even younger. There is a gradually increasing number of studies using that method, and some of them investigate the influence of impaired glucose metabolism or diabetes on left ventricular function.

Our observational study² demonstrated that patients with coronary artery disease and increased arterial stiffness present with worse left ventricular function measured by myocardial work indices. As noted by Patoulias et al,¹ more than a quarter of our study patients had diabetes. The authors have raised an interesting issue as to how diabetes might have influenced our findings. We followed their suggestion and explored it in a subanalysis (TABLE 1), which we discuss below.

Patients with CAD and diabetes had significantly increased E/e' and reduced global myocardial work efficiency and global myocardial work index. However, diabetes showed no significant contribution after adding as a covariate to the models for either global myocardial work efficiency or global myocardial work index, or global myocardial constructive work, or global myocardial wasted work (*P* value for diabetes contribution between 0.64 and 0.92).

This subanalysis showed that CAD patients with diabetes have worse diastolic function and myocardial work efficiency and index than those without diabetes. However, no remarkable influence of diabetes after adjustment for other clinical variables might suggest the lack of any significant effect. However, the latter finding should be interpreted with caution. The number

of study patients with and without diabetes was relatively low to consider those findings reliable.

We are aware that more individuals should be enrolled to answer the critical question about the effects of diabetes on myocardial work in patients with CAD. It also deserves to be investigated whether hypoglycemic therapy might influence myocardial work and other indices of left ventricular function in this population.

ARTICLE INFORMATION

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CONFLICT OF INTEREST None declared.

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HOW TO CITE Dziarmaga M, Minczykowski A, Zwanzig M, et al. Coronary artery disease, arterial stiffness, and myocardial work: what is the role of diabetes in this vicious circle? Authors' reply. *Kardiol Pol.* 2021; 79: 360-362. doi:10.33963/KP.15892

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