

Relationship between coronary artery disease and atrial fibrillation still unclear

To the editor Bidirectional relationships have been suspected to exist between atrial fibrillation (AF) and heart failure, thromboembolism, renal dysfunction, and coronary artery disease (CAD).¹ Also, CAD and AF share similar clinical risk factors including obesity, smoking, low physical activity, hypertension, diabetes, and sleep apnea.² Previous experimental animal studies indicated that acute ischemia is associated with higher atrial vulnerability contributing to AF development.³ Nevertheless, we could not confirm this hypothesis in our study and found that AF prevalence was higher in patients with coronary artery sclerosis rather than CAD (Supplementary material, *Figure S1*).⁴ We also found that neither CAD origin nor its extent were associated with prevalent AF in our cohort.

With great interest, we read the article by Tomaszuk-Kazberuk et al⁵ confirming our findings. However, there are some issues that we feel should be highlighted and discussed here. First, it was intriguing and slightly confusing to us that the authors showed a lower risk of chronic coronary syndromes (CCS) in patients with hypertension, diabetes, hyperlipidemia, heart failure, and renal dysfunction despite higher prevalence of these comorbidities observed in CCS. Second, it is unclear how medical CCS treatment with statins, angiotensin-converting enzyme inhibitors, or angiotensin II receptor blockers modulated the findings because of their pleiotropic effects.⁵ In our study, we found that drug use was significantly higher in patients with clinically relevant CAD compared with those with normal vessels or noncritical CAD (59.1%, 22.8%, and 18.1%, respectively).⁴ Finally, in contrast to the study by Tomaszuk-Kazberuk et al,⁵ we analyzed differences in AF prevalence among 3 groups: individuals with normal (unobstructed) coronary vessels, coronary artery sclerosis, and clinically relevant CAD (defined as coronary artery stenosis $\geq 75\%$). Despite our hypothesis of a (monotonic) relationship between AF and angiographic coronary artery status, we found the highest AF prevalence in patients with coronary artery sclerosis, and—paradoxically—in CAD.⁴

Nevertheless, both analyses from the Leipzig Heart Study and the Białystok Coronary Project

reported the same key findings.^{4,5} We agree with the authors that the main results could be partly explained by the similarity of the clinical presentations of CAD and AF. Chest pain, dyspnea, anxiety—or even elevated levels of biomarkers—are common in both CAD and AF paroxysms. We suspect that these clinical signs and symptoms in patients with AF biased physicians' decision, favoring the indication for coronary angiography, which eventually showed normal or only sclerotic coronary arteries. Importantly, both conditions—CAD and AF—share not only various clinical risk factors but are also supposed to have common underlying pathomechanisms such as inflammation. Nevertheless, despite higher interleukin-6 levels in patients with critical CAD in our study, we observed that adjustment for inflammatory markers did not change the results regarding the association between CAD and AF.

In summary, two large observational studies reported similar results contradicting previous hypotheses that AF prevalence is higher in patients with CAD. Further longitudinal studies with deeper phenotyping, eg, assessment of myocardial vitality, should further clarify the relationship between CAD and AF.

SUPPLEMENTARY MATERIAL

Supplementary material is available at www.mp.pl/paim.

ARTICLE INFORMATION

AUTHOR NAMES AND AFFILIATIONS Jelena Kornej, Markus Scholz, Timm Seewöster (JK: National Heart, Lung, and Blood Institute's Framingham Heart Study, Framingham, Massachusetts, United States; Sections of Cardiovascular Medicine and Preventive Medicine, Boston Medical Center, Boston University School of Medicine, Boston, Massachusetts, United States; LIFE—Leipzig Research Center of Civilization Diseases, Leipzig University, Leipzig, Germany; MS: LIFE—Leipzig Research Center of Civilization Diseases, Leipzig University, Leipzig, Germany; Institute for Medical Informatics, Statistics and Epidemiology, Leipzig University, Leipzig, Germany; TS: Heart Center at University of Leipzig, Department of Electrophysiology, Leipzig, Germany)

CORRESPONDENCE TO Timm Seewöster, MD, Heart Center Leipzig at University of Leipzig, Department of Electrophysiology, Strümpellstraße 39, 04289 Leipzig, Germany, phone: +49 341 865 1431, email: t.seewoester@yahoo.de

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REFERENCES

- 1 Kornej J, Börschel CS, Benjamin EJ, Schnabel RB. Epidemiology of atrial fibrillation in the 21st century: novel methods and new insights. *Circ Res*. 2020; 127: 4-20. [↗](#)
- 2 Benjamin EJ, Muntner P, Alonso A, et al. Heart disease and stroke statistics-2019 update: a report from the American Heart Association. *Circulation*. 2019; 139: e56-e528.
- 3 Nishida K, Qi XY, Wakili R, et al. Mechanisms of atrial tachyarrhythmias associated with coronary artery occlusion in a chronic canine model. *Circulation*. 2011; 123: 137-146. [↗](#)
- 4 Kornej J, Henger S, Seewöster T, et al. Prevalence of atrial fibrillation dependent on coronary artery status: insights from the LIFE-Heart Study. *Clin Cardiol*. 2020; 43: 1616-1623. [↗](#)
- 5 Tomaszuk-Kazberuk A, Koziński M, Kuźma Ł, et al. Atrial fibrillation is more frequently associated with nonobstructive coronary lesions: the Białystok Coronary Project. *Pol Arch Intern Med*. 2020; 130: 1029-1036. [↗](#)

Authors' reply We thank Kornej et al for their comments. Chronic coronary syndromes (CCS) represent the major cause of death worldwide, and atrial fibrillation (AF) deteriorates the quality of life and prognosis in patients with CCS. Kornej et al contrasted 2 large studies that contradict previous hypotheses that the incidence of AF is higher in patients with CCS.^{1,2}

Indeed, Kornej et al¹ studied a large sample size of patients with invasively confirmed coronary status and advanced phenotyping of the study cohort using clinical, echocardiographic, and laboratory data. In the Białystok Coronary Project, our main conclusion was consistent with the results of Kornej et al,¹ but we respectfully suggest that our detailed results have been misinterpreted. In our analysis, the absence of diseases such as chronic heart failure (odds ratio [OR], 0.68; 95% CI, 0.56–0.83; $P < 0.001$) and other classic risk factors for CCS such as hypertension (OR, 0.68; 95% CI, 0.56–0.82; $P < 0.001$), chronic kidney disease (OR, 0.79; 95% CI, 0.66–0.94; $P < 0.001$), and diabetes (OR, 0.69; 95% CI, 0.59–0.81; $P < 0.001$) increased the probability of developing nonsignificant atherosclerotic lesions in epicardial coronary arteries. Consequently, patients with these comorbidities were at higher risk of CCS.

The study protocols used in both cohorts differed, but, in our opinion, it is worth noting that, similar to the LIFE Heart Study, the severity of coronary artery disease was correlated with the presence of AF. Comparing the groups of patients with and without AF, the percentage of patients with 2-vessel and 3-vessel coronary artery disease was higher in the group without CCS. Interestingly, our cohorts did not differ in terms of age, and a similar proportion of CCS was reported in both groups (40.4% versus 40.1%), although marked differences between the incidence of AF were evident (6.9% versus 20.2%).^{1,2} We also found no significant differences with regard to the prevalence of classic risk factors for AF. This fact seems to be even more alarming when considering sex distribution in the study cohorts (female sex, 45% vs 34%).

Pathophysiological mechanisms such as inflammation and oxidative stress represent the underlying causes of both AF and CCS. Our hypothesis on the difference in the prevalence of AF in both study cohorts may be due to the burden of nonclassic risk factors such as air pollution or socioeconomic factors. In our previous studies, we demonstrated the impact of air pollution on both the incidence of acute coronary syndromes (ACS)³ and deaths from any cardiac causes.⁴

Decision making on patient selection for coronary angiography in the setting of AF is more difficult than in patients without AF.⁵ Hence, further prospective evaluation of this population is also necessary. Our study cohort was followed up for a relatively long period of time, a median (interquartile range) of 2616 (1849–3649) days. In the followed-up group of patients with AF, as many as 557 deaths (37.4%) were recorded, 26% of which were coded as ACS. In the group of patients without AF, the death rate was 19.4%, only 14.5% of which was due to ACS. Hence, the progression of coronary artery disease was observed during long-term follow-up, which may have serious health implications for patients with AF.

ARTICLE INFORMATION

AUTHOR NAMES AND AFFILIATIONS Łukasz Kuźma, Anna Tomaszuk-Kazberuk, Marek Koziński, Gregory Y. H. Lip (ŁK: Department of Invasive Cardiology, Medical University of Białystok, Białystok, Poland; AT-K: Department of Cardiology, Medical University of Białystok, Białystok, Poland; MK: Department of Cardiology and Internal Medicine, Medical University of Gdańsk, Gdynia, Poland; GYHL: Liverpool Center for Cardiovascular Science, University of Liverpool and Liverpool Heart and Chest Hospital, Liverpool, United Kingdom; Aalborg Thrombosis Research Unit, Department of Clinical Medicine, Aalborg University, Aalborg, Denmark)

CORRESPONDENCE TO Prof. Anna Tomaszuk-Kazberuk, MD, PhD, Department of Cardiology, Medical University of Białystok, ul. M. Skłodowskiej-Curie 24A, 15-276 Białystok, Poland, phone: +48 85 746 86 56, email: a.tomaszuk@poczta.fm

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REFERENCES

- 1 Kornej J, Henger S, Seewöster T, et al. Prevalence of atrial fibrillation dependent on coronary artery status: Insights from the LIFE-Heart Study. *Clin Cardiol*. 2020; 43: 1616-1623. [↗](#)
- 2 Tomaszuk-Kazberuk A, Koziński M, Kuźma Ł, et al. Atrial fibrillation is more frequently associated with nonobstructive coronary lesions: the Białystok Coronary Project. *Pol Arch Intern Med*. 2020; 130: 1029-1036. [↗](#)
- 3 Kuźma Ł, Pogorzelski S, Struniawski K, et al. Effect of air pollution on the number of hospital admissions for acute coronary syndrome in elderly patients. *Pol Arch Intern Med*. 2020; 130: 38-46.
- 4 Kuźma Ł, Struniawski K, Pogorzelski S, et al. Gender differences in association between air pollution and daily mortality in the capital of the green lungs of Poland-population-based study with 2 953 000 person-years of follow-up. *J Clin Med*. 2020; 9: 2351. [↗](#)
- 5 Tomaszuk-Kazberuk A, Nikas D, Lopatowska P, et al. Patients with atrial fibrillation and chronic kidney disease more often undergo angioplasty of left main coronary artery – a 867 patient study. *Kidney Blood Press Res*. 2018; 43: 1796-1805. [↗](#)