

# Assessment of Coronary Artery Disease in Non-Valvular Atrial Fibrillation: Is This Light at the End of the Tunnel?

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**Abstract:** Non-valvular atrial fibrillation (NVAf) is the most common sustained arrhythmia worldwide, and is associated with significant morbidity and mortality. Increasing life expectancy, coupled with a surge in comorbidity burden, has resulted in a sharp increase in NVAf prevalence over the last three decades. Coronary artery disease (CAD) is an important and clinically relevant risk factor of AF. Concomitant CAD has significant implications for AF management and is a major determinant of the overall outcomes. Shared risk factors, a common pathophysiological basis, and heightened thrombogenesis culminating in cardiovascular adverse events, highlight the close association between the two. The clinical course of AF is worse when associated with CAD, resulting in poor heart rate control, increased propensity to develop stroke and myocardial infarction, increased likelihood of acute presentation with hemodynamic collapse and pulmonary edema, increased bleeding tendencies, and poor response to ablation therapies. Emerging research highlighting the significant role of underlying CAD as an independent predictor of thromboembolic risk has paved the way for the adoption of CAD beyond prior myocardial infarction into the symbol “V” of the CHA2DS2-VASc score. In our opinion, elderly patients aged >65 years with AF, with a history of one or more cardiovascular comorbidities, or evidence of atherosclerosis in other vascular beds should warrant a closer look and a dedicated effort to look for associated CAD. This would allow for a more holistic and comprehensive approach to patients with AF and ultimately help reduce the disease burden and improve the overall outcomes.

**Keywords:** atrial fibrillation, AF, coronary artery disease, CAD, inflammation, endothelial dysfunction, pathophysiology, catheter ablation, stroke, CHA2DS2VASc score, coronary artery calcium score

## Introduction

Non-valvular atrial fibrillation (NVAf) remains the commonest sustained arrhythmia worldwide and accounts for significant morbidity and mortality.<sup>1–3</sup> Apart from being a major risk factor for ischemic stroke, AF is unequivocally associated with excess heart failure, limb ischemia, myocardial infarction and dementia.<sup>4–6</sup> Furthermore, there is a 3-fold increased likelihood of sudden and non-sudden cardiac death among patients with AF compared with those without AF.<sup>7,8</sup> Increasing life expectancy, coupled with a surge in comorbidity burden, has resulted in a sharp increase in NVAf prevalence in both the developed and developing world over the last three decades. Indeed, the burden on the healthcare system is enormous, and the situation is expected to worsen by 2050, when the lifetime risk of AF is expected to be approximately 1 in 3 beyond 40 years of age.<sup>1</sup>

Early diagnosis by screening high-risk populations, timely institution of pharmacotherapy to control heart rate and prevent stroke, and aggressive control and management of risk factors are key to improving outcomes and reducing the disease burden.<sup>1,9,10</sup> The most recent AF guidelines by the ACC/AHA/ACCP/HRS published in 2023 clearly highlight the need for lifestyle changes and risk factor modification as key pillars not only to prevent the progression of AF and the development of AF-related complications, but also to prevent its onset.<sup>9</sup> Guidelines emphasize the management of

obesity, smoking, excessive alcohol consumption, control of blood pressure and blood sugar, physical activity, and appropriate treatment of cardiovascular diseases including heart failure and coronary artery disease (CAD).

Although the incidence of AF and CAD increases with advancing age, there is a much stronger association between AF and CAD beyond senescence. The risk of CAD (encompassing both obstructive and non-obstructive CAD) in the general population is estimated to be approximately 11–16%.<sup>11,12</sup> In contrast, the prevalence of CAD in AF patients is estimated to be 3–4 times higher than that in the general population.<sup>13</sup> In the recent dedicated prospective study by Sharma YP et al, CAD was present in 70% of all patients with AF undergoing angiography. Amongst these majority had obstructive CAD (46%) highlighting the significant association between the two.<sup>14</sup> The results were in sync with a previous study by Nucifora G et al wherein 82% of all AF patients had underlying CAD on computed tomography coronary angiography and amongst them 41% had obstructive CAD again reinforcing the close link between AF and CAD.<sup>15</sup> Steensig et al also indicated the need for further evaluation of the relationship between AF and CAD and in their report on AF patients, spanning over 8 years and enrolling 96430 patients, they concluded that majority of AF patients had underlying CAD (59% of the cohort) when evaluated by angiography.<sup>16</sup> Shared risk factors, a common pathophysiological basis, and heightened thrombogenesis culminating in cardiovascular adverse events, highlight the close association between the two.<sup>13,17,18</sup> Furthermore, effective control and management of either one often leads to a reduced burden on the other. Similarly, the disease course is more aggressive when the two coexist than when they occur in isolation. For instance, when AF complicates CAD, it has been observed that there is a greater extent and complexity of CAD, as reflected by higher syntax scores. This often leads to adverse outcomes, with an increased likelihood of heart failure, ventricular arrhythmia, and cardiac death.<sup>19,20</sup> Likewise, the clinical course of AF worsens with the concomitant development of CAD. This often manifests in the form of poor heart rate control, increased propensity to develop stroke and myocardial infarction, acute presentation with hemodynamic collapse and pulmonary oedema, increased likelihood of bleeding complications and poor response to ablation therapies.<sup>21–23</sup> Hence, given the implications of underlying CAD in AF, this makes a strong case for the active diagnosis and management of CAD in patients with AF.

## Implications of Underlying CAD on Thromboembolic Risk

Consistent evidence supports the concept of increased burden of AF amongst those with concomitant CAD compared to AF in the absence of CAD. However, the concept has only recently been translated into clinical practice, as exemplified by alterations in the CHA2DS2-VASc score. The CHA2DS2-VASc score since its first description in 2001 has been validated across the globe for predicting not only the risk of stroke but also poor overall outcomes and mortality among patients with AF.<sup>24</sup> Previously, the symbol “V” in the score stood for vascular disease which encompassed only a history or documented prior myocardial infarction, presence of aortic atheroma/plaque and the presence of significant peripheral arterial disease in any of the major vascular beds. Accordingly, this did not account for the presence of significant underlying CAD alone beyond previous myocardial, as a risk factor for stroke and overall outcomes. However, the results of large prospective studies and their accompanying editorials, clearly indicated that underlying CAD was a strong predictor of increased thrombogenicity throughout the vascular system and poorer overall outcomes in AF patients. In particular, large studies by Shi et al<sup>25</sup> and Steensig et al<sup>16</sup> are fundamental to our understanding of the impact of CAD on AF. In their independent investigations, they concluded that CAD, as identified by coronary angiography, was the strongest predictor of stroke beyond all other components of the CHA2DS2-VASc score.<sup>26</sup> Furthermore, they demonstrated that stroke risk was less dependent on traditional risk factors, but more so on coronary anatomy and the extent of CAD. These studies along with others over the last decade by Rasmussen et al<sup>27</sup> and Anandasundaram et al<sup>28</sup> paved the way for adoption of underlying CAD beyond prior myocardial infarction into the symbol “V” of the CHA2DS2-VASc score. This was reflected for the first time in the European Society of Cardiology (ESC) 2020 guidelines for AF management.<sup>29</sup> The concept has gained acceptance most prominently in Europe, as highlighted by a recent survey conducted by the European Heart Rhythm Association, wherein almost 80% of all practicing cardiologists were aware of underlying CAD as a component of the CHA2DS2-VASc score and applied it in their clinical practice.<sup>30</sup>

## Impact of Underlying CAD on AF Related Complications

### Stroke

In contrast to previous beliefs and recommendations, for instance, in 2006, the American Heart Association/American College of Cardiology guidelines labelled underlying CAD as a “weak or less validated risk factor for stroke”. However, this soon changed, with evidence accumulating in support of CAD as an independent predictor of thromboembolism and stroke after adjusting for confounding variables.<sup>31</sup> Apart from the prominent studies by Shi et al and Steensig et al, as highlighted above, other prospective studies have further consolidated the significant contribution of CAD to future stroke among patients with AF. Notably, Hillerson et al demonstrated that incidental coronary artery calcium (in the absence of symptoms of ischemia) detected by chest computed tomography was an independent predictor of both future stroke and overall mortality at one year.<sup>32</sup> The findings of this study were replicated in a large American cohort of patients with AF who underwent routine cardiac computed tomography prior to pulmonary vein isolation. In this study, Wang et al demonstrated an abnormal coronary artery calcium (CAC) score was present in 62% of all AF patients in their cohort. CAC was strongly linked to not only future stroke but also overall major adverse cardiovascular events (MACE) and death. In addition, they highlighted that the incorporation of CAC into the CHA2DS2-VASc score could help reclassify 20% of all patients with AF who would benefit from the addition of aspirin and statins to reduce morbidity and mortality.<sup>33</sup>

### Acute Coronary Syndrome (ACS)

The bidirectional relationship between CAD and AF is well established and highlighted by common pathophysiological mechanisms, with endothelial dysfunction and inflammation being dominant factors.<sup>13</sup> This vicious cycle results in accelerated atherosclerosis and thrombogenicity throughout the vasculature. Although AF is independently associated with ACS, irrespective of prior CAD, the risk is greatly increased once underlying CAD is present. In a large, multi-center Chinese cohort comprising 6403 patients with AF, underlying CAD was the strongest predictor of future ACS.<sup>34</sup> In another recent prospective study, Batta et al highlighted an increased risk of ACS in AF patients over a 24 month period. Furthermore, their analysis demonstrated that underlying CAD and an increased initial C-reactive protein level were the main determinants of the development of ACS in their cohort, again highlighting the significant role of inflammation in these patients.<sup>35</sup>

### Heart Failure

Although heart failure and AF share a mutually dependent relationship with onset of one increasing the likelihood of developing the other. Presence of underlying CAD in AF can hasten the onset of heart failure and accelerate its progression.<sup>36–38</sup> Overall, AF is more prevalent in any heart failure that occurs in the background of underlying CAD than in non-ischemic cardiomyopathy. Heart failure in AF when occurring in CAD patients is often more difficult to treat, complicated by higher ventricular rates, greater elevation in pulmonary pressure, higher prevalence of ventricular arrhythmias, and less response to medical therapy than in the absence of CAD.<sup>39,40</sup> Although higher ventricular rates seen in patients with AF can lead to reduced diastolic filling, myocardial ischemia, and dysfunction, even in those with normal coronary arteries, the effects are more pronounced in patients with underlying CAD with poor tolerability to fast heart rates and a greater degree of subsequent increase in left ventricular end-diastolic pressure and pulmonary wedge pressure culminating in heart failure.<sup>13</sup>

## Impact of Underlying CAD on Outcomes Following Catheter Ablation for AF

Another important aspect of AF management in recent years has been early rhythm control, particularly via catheter ablation (CA). Multicentric large randomized trials clearly indicate that CA not only improves symptomatology among patients with AF but also has a beneficial effect on left ventricular filling pressures and function, stroke and dementia risk, and overall mortality.<sup>41,42</sup> The most recent 2023 ACC/AHA/ACCP/HRS guidelines for AF management have stressed early rhythm strategy (mainly via CA) and highlighted the importance of maintaining sinus rhythm and reducing AF duration.<sup>9</sup> As expected, CA received a class I recommendation for rhythm/rate control in selected individuals with

AF over and above medical therapy. However, on a closer look, there is clear evidence supporting reduced efficacy, increased adverse outcomes and increased recurrence following CA in AF patients having underlying obstructive CAD compared to those without CAD. Furthermore, in a recent prospective propensity score-matched cohort study, CA failed to meet the primary composite endpoint of stroke, acute coronary syndrome, bleeding, and overall death in patients with underlying stable CAD, highlighting the complexities in managing AF in patients with underlying CAD.<sup>43</sup> This underlines the fact that ischemia at the microvascular level remains one of the most crucial factors involved in the initiation and propagation of AF, and that unless ischemia is dealt with first, electrical remodeling via CA is unlikely to lead to sustained improvement in AF burden and its overall impact. Further validation of these statements came when Hiraya et al undermined the importance of managing ischemia in AF. In their prospective study over a period of eight years, AF patients with significant CAD (>70% stenosis in any one major coronary bed) had a much higher risk of recurrence after CA (56% vs 39%;  $p<0.001$ ). In addition, significant CAD was an independent predictor of AF recurrence in the multivariate analysis. Furthermore, they demonstrated the impact of myocardial revascularization via percutaneous coronary intervention (PCI) on the outcomes following CA. Patients who underwent PCI had a much lower rate of recurrence following CA than those who were treated with medical therapy alone (38% vs 72%;  $p<0.001$ ).<sup>44</sup> Their findings were confirmed in an independent observation by Chen et al, wherein they not only demonstrated the association between CAD and AF recurrence post-CA but also reiterated the positive impact of revascularization on reducing the AF burden, AF-related complications, and recurrence of AF post-CA over a 24-month period.<sup>45</sup> Recently, Guo et al demonstrated worse clinical outcomes in AF patients with concomitant CAD undergoing CA independent of the AF recurrence/burden, further highlighting the complex nature and crosstalk between AF and CAD and the need to further explore their relationship in an effort to reduce overall morbidity and mortality.<sup>46</sup>

These developments support an active effort to unmask underlying CAD among AF patients with cardiovascular comorbidities or evidence of atherosclerosis in other vascular beds. In turn, this would allow for early and aggressive risk factor modification and treatment of underlying CAD, resulting in a reduction in the overall impact and burden of AF.

## Role of Unmasking CAD in AF Management

Despite the increased prevalence and significant implications of underlying CAD in patients with AF, current guidelines do not advocate the routine assessment of CAD in ambulatory patients with AF who do not have clear signs and symptoms suggestive of underlying ischemia. In our opinion, this statement downplays the importance of concomitant CAD as a bystander in AF without much clinical relevance. Indeed, our arguments, along with emerging research with each passing day, clearly highlight the strong link between AF and CAD and stress the impact of underlying CAD on treatment strategies and outcomes at all stages of AF management. According to a recent study by Fernandes et al, the authors concluded that actively looking for CAD in asymptomatic AF patients via cardiac computed tomography angiography helped initiate aspirin and statin therapy in 25% of patients and modified the statin intensity in another 17%.<sup>47</sup> Their findings are relevant as statins have consistently shown to not only to reduce cardiovascular morbidity and mortality, but also in regards to AF, have shown to reduce the incidence and burden of AF, reduce MACE and overall mortality in AF patients.<sup>48,49</sup> Regarding the addition of aspirin to oral anticoagulants in AF patients with underlying systemic atherosclerosis, Heo et al demonstrated reduced overall all-cause mortality compared to those who were on oral anticoagulants alone.<sup>50</sup> Although in their cohort they primarily recruited patients post stroke, the same can be extrapolated to other vascular territories as atherosclerosis is usually a systemic process. Furthermore, unmasking of underlying CAD in patients with AF often leads to alterations in the choice of rate-controlling drugs, antihypertensive drugs, and anti-diabetic drugs, with a tendency to use agents with proven benefits in CAD.<sup>13,51–55</sup> This is expected to translate into net clinical benefit for patients with AF. Although one certainly should not receive a message that we advocate the indiscriminate use of coronary angiography/CAC scoring in all AF patients, there is certainly a large group of patients with AF who otherwise do not have symptoms of CAD but have comorbidities or predisposing conditions that make them susceptible to CAD. In particular, elderly patients aged >65 years with AF, with a history of one or more cardiovascular comorbidities, or evidence of atherosclerosis in other vascular beds should warrant a closer look and a dedicated effort to look for associated CAD. This would allow for a more holistic and comprehensive approach to patients with AF and ultimately help reduce the disease burden and improve the overall outcomes.

## Conclusions

The relationship between AF and CAD is bidirectional, complex, and mutual with significant negative implications for the overall cardiovascular system. These two conditions share common risk factors and are closely linked at the pathophysiological level. Therefore, treating these patients in isolation is inappropriate and inadequate. Indeed, our arguments clearly highlight the strong link between AF and CAD, and stress the impact of underlying CAD on treatment strategies and outcomes at all stages of AF management. Using this perspective paper, we make our stance on a dedicated attempt to unmask concomitant CAD in patients with AF who are at risk for atherosclerotic vascular disease, independent of symptoms of ischemia.

## Disclosure

The author(s) report no conflicts of interest in this work.

## References

1. Linz D, Gawalko M, Betz K, et al. Atrial fibrillation: epidemiology, screening and digital health. *Lancet Reg Health.* 2024;37.
2. Huang B, Li M, Lip GY. The burden of atrial fibrillation related to metabolic risks: different countries and territories, yet the same challenges. *Eur Heart J Qual Care Clin Outcome.* 2024;qcae037.
3. Vad OB, Paludan-Müller C, Diederichsen SZ, Olesen MS. Tackling a growing healthcare challenge: atrial fibrillation epidemiology, prevention, and underlying causes. *Lancet Reg Heal.* 2024;37.
4. Bizhanov KA, Abzaliev KB, Baimbetov AK, Sarsenbayeva AB, Lyan E. Atrial fibrillation: epidemiology, pathophysiology, and clinical complications (literature review). *J Cardiovasc Electrophysiol.* 2023;34(1):153–165. doi:10.1111/jce.15759
5. Wu J, Nadarajah R. The growing burden of atrial fibrillation and its consequences. *BMJ.* 2024;385.
6. Batta A, Sharma YP, Hatwal J, Panda P, Kumar BGV, Bhogal S Predictors of dementia amongst newly diagnosed non-valvular atrial fibrillation patients. *Indian Heart J* 2022;74(6):505–509. doi:10.1016/j.ihj.2022.11.009
7. Chen LY, Sotoodehnia N, Bůžková P, et al. Atrial fibrillation and the risk of sudden cardiac death: the atherosclerosis risk in communities study and cardiovascular health study. *JAMA Intern Med.* 2013;173(1):29–35. doi:10.1001/2013.jamainternmed.744
8. Waldmann V, Jouven X, Narayanan K, et al. Association between atrial fibrillation and sudden cardiac death: pathophysiological and epidemiological insights. *Circ Res.* 2020;127(2):301–309. doi:10.1161/CIRCRESAHA.120.316756
9. Joglar JA, Chung MK, Armbuster AL, et al. 2023 ACC/AHA/ACCP/HRS guideline for the diagnosis and management of atrial fibrillation: a report of the American College of Cardiology/American Heart Association Joint Committee on clinical practice guidelines. *Circulation.* 2024;149(1):e1–156. doi:10.1161/CIR.0000000000001193
10. Li M, Shi J, Chu M, et al. Screening for atrial fibrillation by village doctors in rural areas of China: the Jiangsu province rural community AF project. *Vasc Health Risk Manag.* 2022;18:757–766. doi:10.2147/VHRM.S379182
11. Sarebanhassanabadi M, Mirjalili SR, Marques-Vidal P, Kraemer A, Namayandeh SM. Coronary artery disease incidence, risk factors, awareness, and medication utilization in a 10-year cohort study. *BMC Cardiovasc Disord.* 2024;24(1):101. doi:10.1186/s12872-024-03769-3
12. Kumar AS, Sinha N. Cardiovascular disease in India: a 360 degree overview. *Med J Armed Forces India.* 2020;76(1):1–3. doi:10.1016/j.mjafi.2019.12.005
13. Batta A, Hatwal J, Batta A, Verma S, Sharma YP. Atrial fibrillation and coronary artery disease: an integrative review focusing on therapeutic implications of this relationship. *World J Cardiol.* 2023;15(5):229–243. doi:10.4330/wjc.v15.i5.229
14. Sharma YP, Batta A, Makkar K, et al. Angiographic profile and outcomes in persistent non-valvular atrial fibrillation: a study from tertiary care center in North India. *Indian Heart J.* 2022;74(1):7–12. doi:10.1016/j.ihj.2021.12.010
15. Nucifora G, Schuijff JD, Tops LF, et al. Prevalence of coronary artery disease assessed by multislice computed tomography coronary angiography in patients with paroxysmal or persistent atrial fibrillation. *Circ Cardiovasc Imaging.* 2009;2(2):100–106. doi:10.1161/CIRCIMAGING.108.795328
16. Steensig K, Olesen KK, Thim T, et al. Should the presence or extent of coronary artery disease be quantified in the CHA2DS2-VASc score in atrial fibrillation? A report from the Western Denmark heart registry. *Thromb Haemost.* 2018;118(12):2162–2170. doi:10.1055/s-0038-1675401
17. Yuan S, Lin A, Qiang HQ, Burgess S, Larsson SC. Circulating interleukins in relation to coronary artery disease, atrial fibrillation and ischemic stroke and its subtypes: a two-sample Mendelian randomization study. *Int J Cardiol.* 2020;313:99–104. doi:10.1016/j.ijcard.2020.03.053
18. Ding WY, Protty MB, Davies IG, Lip GY. Relationship between lipoproteins, thrombosis, and atrial fibrillation. *Cardiovasc Res.* 2022;118(3):716–731. doi:10.1093/cvr/cvab017
19. Motloch LJ, Reda S, Larbig R, et al. Characteristics of coronary artery disease among patients with atrial fibrillation compared to patients with sinus rhythm. *Hellenic J Cardiol.* 2017;58(3):204–212. doi:10.1016/j.hjc.2017.03.001
20. Brezinov OP, Vorotilina N, Vasilenko L, Kogan Y, Lev EI, Laish-Farkash A. Coronary artery disease among patients admitted with atrial fibrillation and chest pain. *Coron Artery Dis.* 2023;34(2):96–101. doi:10.1097/MCA.0000000000001206
21. Shakeel I, Sharma H, Hodson J, et al. Prevalence and impact of concomitant atrial fibrillation in patients undergoing percutaneous coronary intervention for acute myocardial infarction. *J Clin Med.* 2024;13(8):2318. doi:10.3390/jcm13082318
22. Hammoudeh A, Badaineh Y, Tabbalat R, et al. The intersection of atrial fibrillation and coronary artery disease in middle Eastern patients. analysis from the Jordan atrial fibrillation study. *Glob Heart.* 2024;19(1). doi:10.5334/gh.1312
23. Saglietto A, Varbella V, Ballatore A, Xhakupi H, Ferrari GMD, Anselmino M. Prognostic implications of atrial fibrillation in patients with stable coronary artery disease: a systematic review and meta-analysis of adjusted observational studies. *Rev Cardiovasc Med.* 2021;22(2):439–444. doi:10.31083/j.rcm2202049
24. Gage BF, Van Walraven C, Pearce L, et al. Selecting patients with atrial fibrillation for anticoagulation: stroke risk stratification in patients taking aspirin. *Circulation.* 2004;110(16):2287–2292. doi:10.1161/01.CIR.0000145172.55640.93

25. Shi B, Liu D, Wang Q, et al. Relationship among atrial fibrillation, the CHA<sub>2</sub>DS<sub>2</sub>-VASc score and ischaemic stroke in patients with coronary artery disease: a propensity score matching study in Hebei, China. *BMC Cardiovasc Disord.* 2021;21(1):1–10. doi:10.1186/s12872-021-02276-z
26. Steensig K, Olesen KK, Thim T, et al. CAD is an independent risk factor for stroke among patients with atrial fibrillation. *J Am Coll Cardiol.* 2018;72(20):2540–2542. doi:10.1016/j.jacc.2018.08.1046
27. Rasmussen LH, Larsen TB, Due KM, Tjønneland A, Overvad K, Lip GY. Impact of vascular disease in predicting stroke and death in patients with atrial fibrillation: the Danish diet. *Cancer Health Cohort Study J Thromb Haemost.* 2011;9(7):1301–1307. doi:10.1111/j.1538-7836.2011.04308.x
28. Anandasundaram B, Lane D, Apostolakis S, Lip G. The impact of atherosclerotic vascular disease in predicting a stroke, thromboembolism and mortality in atrial fibrillation patients: a systematic review. *J Thromb Haemost.* 2013;11(5):975–987. doi:10.1111/jth.12177
29. Hindricks G, Potpara T, Dagres N, et al. 2020 ESC guidelines for the diagnosis and management of atrial fibrillation developed in collaboration with the European Association for Cardio-Thoracic Surgery (EACTS) The Task Force for the diagnosis and management of atrial fibrillation of the European Society of Cardiology (ESC) Developed with the special contribution of the European Heart Rhythm Association (EHRA) of the ESC. *Eur Heart J.* 2021;42(5):373–498.
30. Zhang J, Lenarczyk R, Marin F, et al. The interpretation of CHA<sub>2</sub>DS<sub>2</sub>-VASc score components in clinical practice: a joint survey by the European Heart Rhythm Association (EHRA) Scientific Initiatives Committee, the EHRA Young Electrophysiologists, the association of cardiovascular nursing and allied professionals, and the European Society of Cardiology Council on Stroke. *EP Eur.* 2021;23(2):314–322.
31. Lip GY. Coronary artery disease and ischemic stroke in atrial fibrillation. *Chest.* 2007;132(1):8–10. doi:10.1378/chest.07-0500
32. Hillerson D, Wool T, Ogunbayo GO, Sorrell VL, Leung SW. Incidental coronary artery calcification and stroke risk in patients with atrial fibrillation. *Am J Roentgenol.* 2020;215(2):344–350. doi:10.2214/AJR.19.22298
33. Wang TKM, Chan N, Cremer PC, et al. Incorporating coronary calcification by computed tomography into CHA<sub>2</sub>DS<sub>2</sub>-VASc score: impact on cardiovascular outcomes in patients with atrial fibrillation. *EP Eur.* 2021;23(8):1211–1218.
34. Kotalczyk A, Guo Y, Fawzy AM, Wang Y, Lip GY. Outcomes in elderly Chinese patients with atrial fibrillation and coronary artery disease. A report from the Optimal Thromboprophylaxis in Elderly Chinese Patients with Atrial Fibrillation (ChiOTEAF) registry. *J Arrhythmia.* 2022;38(4):580–588. doi:10.1002/joa3.12744
35. Batta A, Hatwal J, Panda P, Sharma Y, Wander GS, Mohan B. Impact of initial high sensitivity C-reactive protein on outcomes in nonvalvular atrial fibrillation: an observational study. *Future Cardiol.* 2024;1–9.
36. Krummen DE. Atrial fibrillation and heart failure—identification of patients at risk. *Circ J.* 2016;80(3):587–589.
37. Boriani G, Vitolo M, Mei DA, et al. Asymptomatic vs. symptomatic atrial fibrillation: clinical outcomes in heart failure patients. *Eur J Intern Med.* 2024;119:53–63. doi:10.1016/j.ejim.2023.09.009
38. Llargo JT, Bailén MC, Aumente JMS, et al. Incidence and prediction of hospitalization for heart failure in patients with atrial fibrillation: the REFLEJA scale. *Rev Esp Cardiol Engl Ed.* 2024.
39. Pallisgaard JL, Lindhardt TB, Staerk L, et al. Thiazolidinediones are associated with a decreased risk of atrial fibrillation compared with other antidiabetic treatment: a nationwide cohort study. *Eur Heart J Cardiovasc Pharmacother.* 2017;3(3):140–146.
40. Dziewięcka E, Gliniak M, Winiarczyk M, et al. The burden of atrial fibrillation and its prognostic value in patients with dilated cardiomyopathy. *Pol Heart J Kardiologia Pol.* 2020;78(1):37–44. doi:10.33963/KP.15046
41. Marrouche NF, Brachmann J, Andresen D, et al. Catheter ablation for atrial fibrillation with heart failure. *N Engl J Med.* 2018;378(5):417–427. doi:10.1056/NEJMoa1707855
42. Kirchhof P, Camm AJ, Goette A, et al. Early rhythm-control therapy in patients with atrial fibrillation. *N Engl J Med.* 2020;383(14):1305–1316. doi:10.1056/NEJMoa2019422
43. Cui Y, Dong J, Du X, et al. Comparison of prognosis and outcomes of catheter ablation versus drug therapy in patients with atrial fibrillation and stable coronary artery disease: a prospective propensity-score matched cohort study. *Clin Cardiol.* 2021;44(10):1422–1431. doi:10.1002/clc.23699
44. Hiraya D, Sato A, Hoshi T, et al. Impact of coronary artery disease and revascularization on recurrence of atrial fibrillation after catheter ablation: importance of ischemia in managing atrial fibrillation. *J Cardiovasc Electrophysiol.* 2019;30(9):1491–1498. doi:10.1111/jce.14029
45. Chen X, Zhao J, Zhu K, Qin F, Liu H, Tao H. The association between recurrence of atrial fibrillation and revascularization in patients with coronary artery disease after catheter ablation. *Front Cardiovasc Med.* 2021;8:756552. doi:10.3389/fcvm.2021.756552
46. Guo F, Li C, Chen C, et al. Impact of coronary artery disease on the outcomes of catheter ablation in patients with atrial fibrillation. *Braz J Cardiovasc Surg.* 2022;38:381–388.
47. Fernandes S, Cruz I, Faria R, et al. Impact of coronary artery calcium score screening on cardiovascular risk stratification of patients with atrial fibrillation undergoing ablation. *Cardiology.* 2023;148(5):427–433. doi:10.1159/000532018
48. Andelova K, Bacova BS, Sykora M, Hlivak P, Barancik M, Tribulova N. Mechanisms underlying antiarrhythmic properties of cardioprotective agents impacting inflammation and oxidative stress. *Int J Mol Sci.* 2022;23(3):1416. doi:10.3390/ijms23031416
49. Tseng CH, Chung WJ, Li CY, et al. Statins reduce new-onset atrial fibrillation after acute myocardial infarction: a nationwide study. *Medicine.* 2020;99(2):e18517. doi:10.1097/MD.00000000000018517
50. Heo J, Lee H, Lee IH, et al. Combined use of anticoagulant and antiplatelet on outcome after stroke in patients with nonvalvular atrial fibrillation and systemic atherosclerosis. *Sci Rep.* 2024;14(1):304.
51. Bocchino PP, Angelini F, Toso E. Atrial fibrillation and coronary artery disease: a review on the optimal use of oral anticoagulants. *Rev Cardiovasc Med.* 2021;22(3):635–648. doi:10.31083/j.rcm2203074
52. Mascarenhas L, Downey M, Schwartz G, Adabag S. Anti-arrhythmic effects of metformin. *Heart Rhythm O2.* 2024;5(5):310–320. doi:10.1016/j.hroo.2024.04.003
53. Han X, Liu Y, Li G, Tse G, Liu T. A narrative review on prediabetes or diabetes and atrial fibrillation: from molecular mechanisms to clinical practice. *Heart Mind.* 2023;7(4):207–216. doi:10.4103/hm.HM-D-23-00028
54. Batta A, Hatwal J. Atrial fibrillation and prediabetes: a liaison that merits attention! *World J Diabetes.* 2024;15(7):1645. doi:10.4239/wjd.v15.i7.1645
55. Sarkar A, Fanous KI, Marei I, et al. Repurposing metformin for the treatment of atrial fibrillation: current insights. *Vasc Health Risk Manag.* 2024;20:255–288. doi:10.2147/VHRM.S391808

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