

Special issue on atrial fibrillation

This issue of *Acta Cardiologica* is devoted to atrial fibrillation (AF). AF is the most common sustained arrhythmia, increases with age, and presents with a wide spectrum of symptoms and severity [1–5]. AF is categorised into paroxysmal, persistent, and permanent, requiring highly individualised management approaches.

Patients with type 2 diabetes are at high risk of developing arrhythmias, especially AF and atrial flutter (AFL). Metformin, the first line oral antidiabetic agent, is not known to be associated with an increase or a decrease risk of cardiac arrhythmias. Conversely, a higher risk of arrhythmias has been attributed to sulphonylureas. New antidiabetic medications have emerged during the last decades (dipeptidyl peptidase-4 inhibitors (DPP-4is or gliptins), glucagon-like peptide-1 receptor agonists (GLP-1RAs), sodium-glucose cotransporter type 2 transporter inhibitors (SGLT2is or gliflozins); their cardiovascular safety have been investigated in several large prospective placebo-controlled cardiovascular outcome trials [6]. In their metanalysis, Boulmpou et al. showed that the use of GLP-1RAs does not significantly affect the risk for major cardiac arrhythmias in patients with type 2 diabetes mellitus [7]. The life expectancy of individuals with human immunodeficiency virus (HIV) has markedly improved over the past few decades. HIV infection has been shown to be independently associated with an increased risk of AF, particularly with low CD4+ cell count and high viral load [8]. In their study, Antwi-Amoabeng et al. explored the relationship between HIV and AF (31,224 HIV-positive with AF) using ICD-9-CM codes to identify AF patients from the US National Inpatient Sample (NIS) between 2005 and 2015. The prevalence of HIV among patients with AF increased between 2005 and 2015. As compared to HIV-negative individuals with AF, a diagnosis of HIV was associated with increased inpatient mortality, length of stay, and cost of care (Figure 1) [9].

AF and myocardial infarction (MI) share multiple cardiovascular risk factors, such as high body mass index, hypertension and diabetes mellitus, coexistence of AF and MI is very common (Figure 2) [10].

In their study, Wu et al. reported that AF represents an independent risk factor for new-onset MI in an industrial population of North China (Figure 3) [6].

AF presents a 5-fold increase of the risk for ischaemic stroke and 20–30% of ischaemic strokes appear to be directly associated with AF. Both the prevalence of AF and the related stroke risk increase markedly in the elderly [4,5]. Silent cerebral infarction (SCI) has been linked to

subsequent symptomatic stroke, psychiatric disorders (i.e. depression), cognitive dysfunction, dementia, and death [2]. SCI can be identified by means of imaging modalities as gold standard tests, but an acute event can also be detected by serum neuron specific enolase (NSE). NSE concentrations are significantly correlated with stroke severity and outcome [2]. Treatment with an oral anti-coagulant (OAC) reduces the risk for stroke effectively. Vitamin K antagonists (VKAs), such as warfarin have been the mainstay for stroke prevention in AF patients for several decades. They proved to be superior to antiplatelet agents therapy regarding stroke prevention. Currently, direct (D) OACs, with a more favourable benefit/risk ratio, have widely replaced warfarin for stroke prevention and are recommended as first-line OAC in patients with AF [4]. Goksuluk et al. examined the impact of OAC on the prevalence of SCI, identified by an NSE level >12 ng/ml, in 197 consecutive patients with non-valvular AF [11]. Interestingly, they showed that DOACs were associated with significantly reduced SCIs compared with warfarin, probably due to more effective and consistent therapeutic level of anticoagulation. Comparative fracture risk for DOACs and VKAs among patients with AF remains unclear. In their metanalysis concerning 477821 patients from 22 studies which met the including criteria, Yang et al. showed that DOACs were associated with a significantly lower risk of any fracture and osteoporotic fracture compared to warfarin. This benefit was also observed in specific DOACs types such as dabigatran, rivaroxaban and apixaban [12].

Thrombus formation in the left atrium (LA) with ensuing embolism in the cerebral circulation is deemed to be the cause of stroke [13]. LA appendage (LAA) thrombi is the source of 90% of left-sided cardiac thrombi in patients with AF [4]. Few data are however available regarding the prevalence of LA thrombi in AF patients treated with DOACs. In their study, Angelini et al. evaluated the prevalence and predictors of LA/LAA thrombi in 352 consecutive patients with non-valvular AF treated with DOACs [14]. A LA/LAA thrombus was detected by transesophageal echocardiography in 27 (7.7%) patients. Predictors of LA/LAA thrombi were a CHA₂DS₂-VASc score > 3 and obesity. In their letter to the Editor, Murat et al. underscored that the predictors and prevalence of LA/LAA thrombus in AF patients varies widely, mainly due to differences in patient risk profiles, comorbidities, kidney function, CHA₂DS₂-VASc score, LA structure and functions, LAA characteristics and DOACs types and doses. Pooled evaluations of these factors would be important

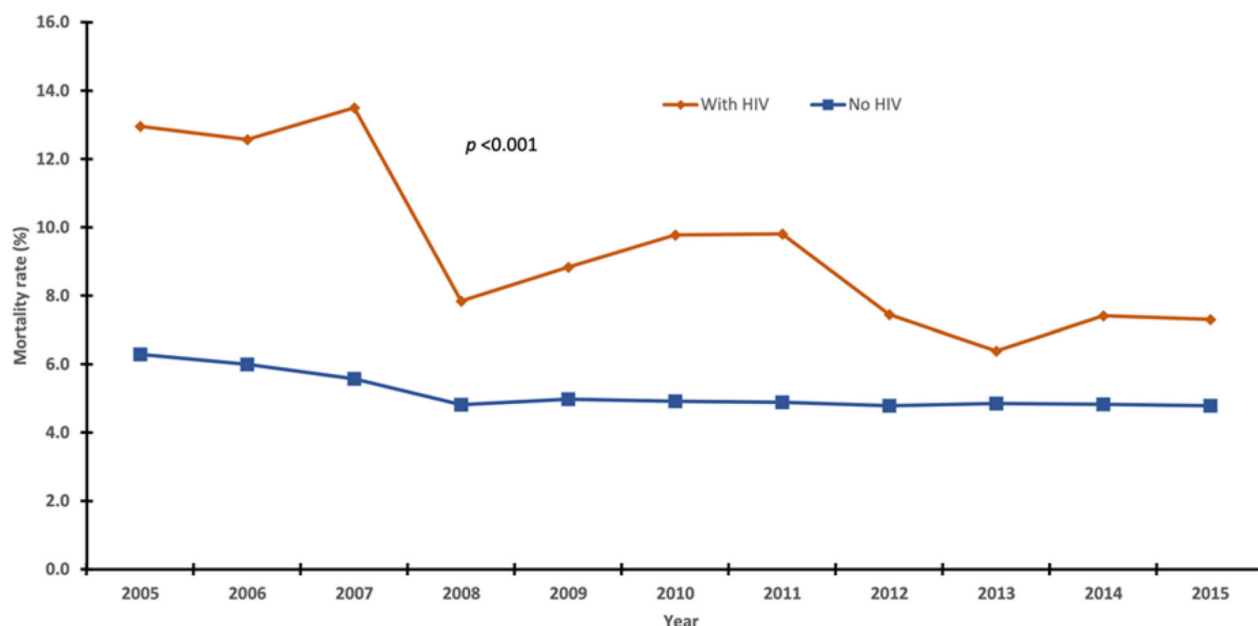


Figure 1. Ten-year trend comparison in in-hospital mortality in atrial fibrillation hospitalisations with and without HIV [9].

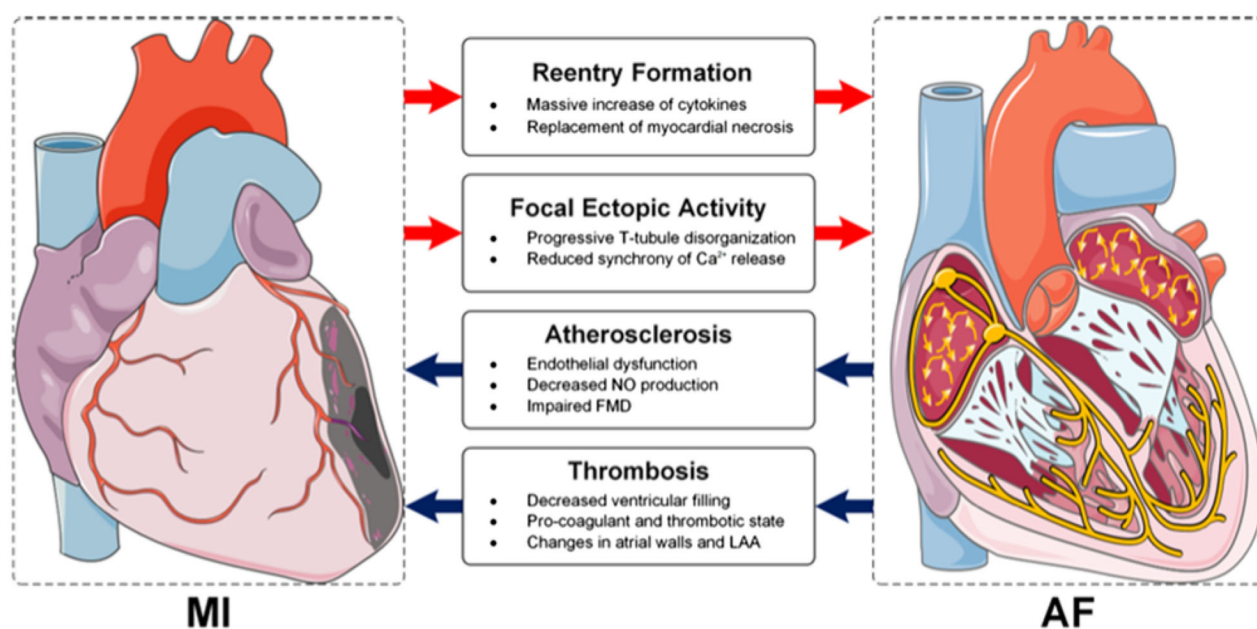


Figure 2. Mechanisms of MI and AF aggravate each other. MI: myocardial infarction; AF: atrial fibrillation. NO: nitric oxide; FMD: flow-mediated dilation; LAA: left atrial appendage. The red arrows indicate the mechanisms of MI aggravate and exacerbate AF, and the blue arrows indicate the mechanisms of AF aggravate and exacerbate MI [10].

to improve pre-procedural patient management and post-procedure patient follow-up [15].

Cardiopulmonary exercise testing (CPET) is a significant tool for evaluating exercise capacity in various cardiovascular conditions, quantifying symptoms and predicting outcomes. In patients with AF, CPET seems to hold a clinically important predictive value for future cardiovascular event. CPET helps phenotype AF populations, evaluates exercise capacity after cardioversion or catheter ablation, and assesses heart rate response to exercise; peak VO_2 and VE/VCO_2 , commonly measured indices

during CPET, could also serve as prognostic tools in patients with AF [16]. Beyond the usual methods, including transmitral flow and changes in LA area and volume, novel techniques such as tissue Doppler imaging (TDI) and strain imaging provide more accurate estimation of LA function. LA strain is correlated with LA fibrosis in patients with AF, is significantly reduced in those with prior stroke, and predicts subsequent stroke [5]. The CHARGE-AF and the CHA_2DS_2 -VASc risk scores are used for AF risk prediction, though the CHARGE-AF performed better. Both scores did not include evaluation of LA

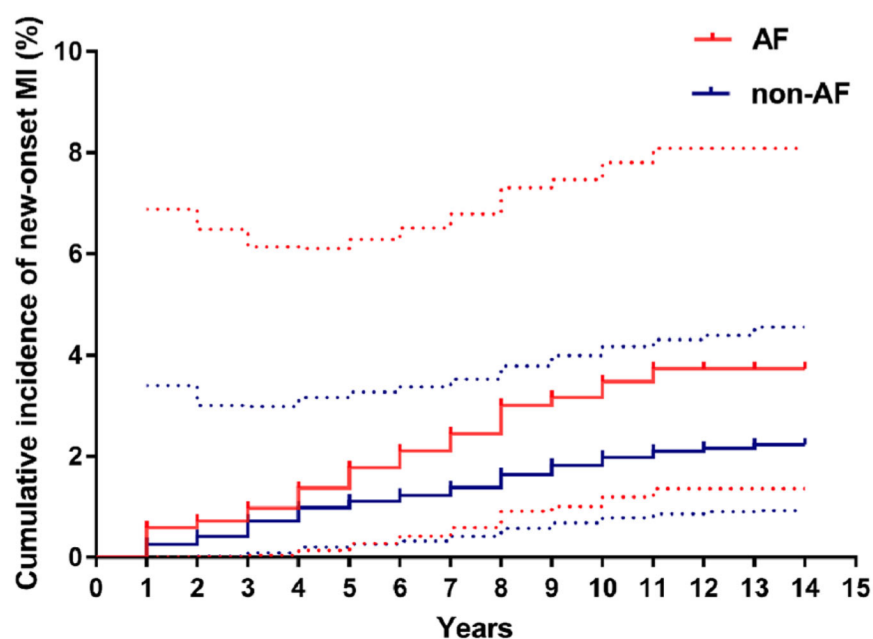


Figure 3. Cumulative incidence of new-onset MI. MI: myocardial infarction; AF: atrial fibrillation; Non-AF: without AF. Dotted line indicates the 95% confidence interval [10].

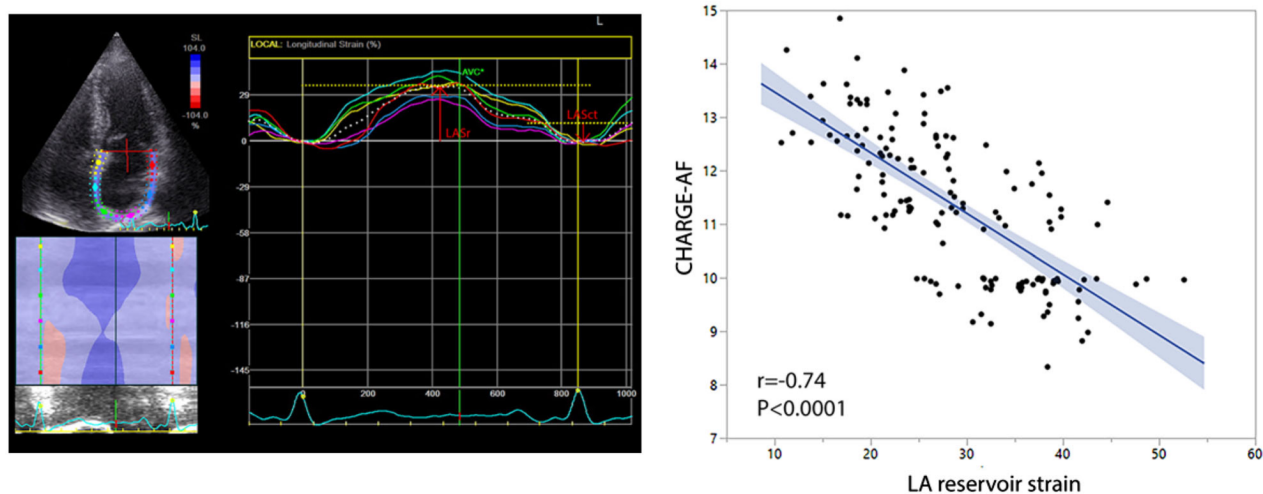


Figure 4. Left. Example of the LA strain measurements: LASr = peak systolic strain – strain value at end-diastole. LASct = strain value at end-diastole (by definition zero) – value at onset of atrial contraction. Right. Correlation of CHARGE-AF risk score and LASr: Good correlation between LASr and CHARGE-AF score [17].

function. In their study concerning 148 patients, Tan et al. showed that LA longitudinal strain derived from 2D speckle tracking echocardiography was highly correlated with CHARGE-AF risk score and may be used as a parameter to predict atrial myopathy and hence AF risk (Figure 4) [17]. Left atrial function deteriorates immediately following AF ablation and partially recovers in early follow-up but remains abnormal in the majority of patients [18].

There are two fundamental approaches to the management of AF: re-establishing and maintaining sinus rhythm (rhythm control); and controlling ventricular rate with atrioventricular node blocking agents (rate control).

Restoration of sinus rhythm with regularisation of the heart's rhythm improves cardiac hemodynamics and exercise tolerance. By maintaining the atrial contribution to cardiac output, symptoms of heart failure and overall quality of life can improve. Currently the backbone of most catheter ablation techniques is to target the pulmonary veins (PVs) in order to achieve their electrical isolation and maintain sinus rhythm. Additional techniques may be used to ablate non-PV triggers and candidate atrial sites considered responsible for maintaining AF. A left atrial anterior isthmus line is usually added in the setting of atrial segmentation in persistent AF or in the

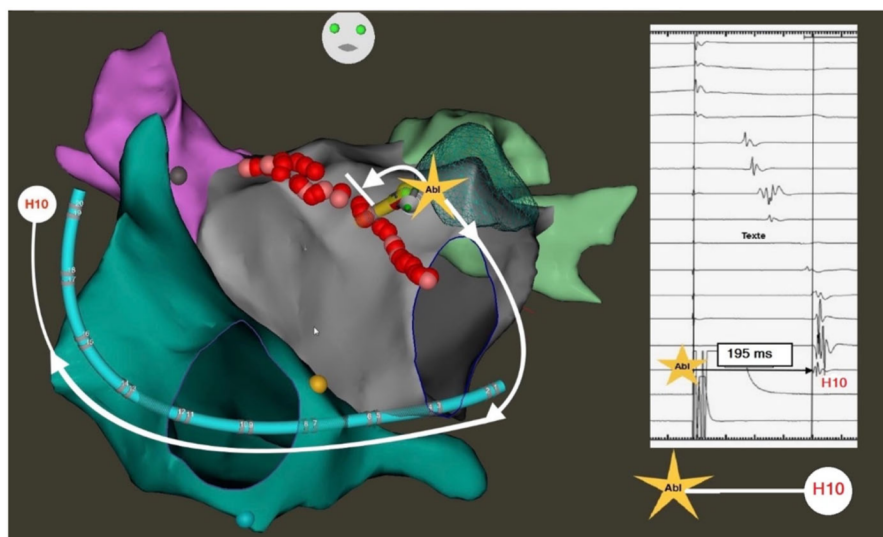


Figure 5. Virtual anatomical view of the ablation catheter positioning and the way the depolarisation wave must travel when pacing from beyond the anterior isthmus line (ABL-H10) if isthmus block is complete (195 ms). The right inset illustrates the recordings of the multipolar catheter bipoles from H1 (at the top) to H10 and the time spent from the pacing stimulus towards H10. RA: right atrium; LA: left atrium; LAIL: left anterior isthmus line [19].

presence of a perimitral flutter. A commonly described endpoint for successful ablation of AF is bidirectional block of the four pulmonary veins. Through an image focus, De Roy et al. illustrated, with a new pacing technique, a fast and easy way of validation of completeness of bidirectional block, after having performed an anterior isthmus line (Figure 5) [19].

Percutaneous LAA closure is recognised as an alternative to long-term anticoagulation for stroke prevention in patients with non-valvular AF and contraindication to systemic OAC. The Amplatzer Amulet and Watchman devices are the two most frequently used devices for percutaneous LAA closure globally. The new generation of WATCHMAN device, the WATCHMAN FLX™, is designed to treat a wider range of LAA anatomies and sizes compared to the previous iteration, the WATCHMAN 2.5™. In their case series presentation, Salaun et al. elegantly illustrated the interest of using the WATCHMAN 2.5™ device to facilitate procedural success despite challenging LAA anatomies [20]. The new Amulet Amplatzer™ Steerable Delivery Sheath is designed to improve ease-of-use in both simple and challenging LAA anatomies. Such steerability may enable successful endovascular closure of greater proportion of LAA and potentially reduce procedural times and complication with complex cases. Selvais et al. reported an interesting case of complex chicken wing LAA where the use of this new steerable sheath had facilitated access to the LAA and co-axial alignment of the sheath for optimal device implantation [21]. Among other things, leadless pacemakers may be suitable for patients with permanent AF in case of barriers to superior venous access or specific and complex anatomic considerations [22].

Disclosure statement

No potential conflict of interest was reported by the author(s).

References

- [1] Lancellotti P, Cosyns B. Highlights of acta cardiologica, acta cardiologica. *Acta Cardiol.* 2022;77(6):469–470.
- [2] Tufano A, Lancellotti P. Atrial cardiomyopathy: pathophysiology and clinical implications. *Eur J Intern Med.* 2022;101:29–31.
- [3] Claeys MJ, Bondue A, Lancellotti P, et al. Summary of 2020 ESC guidelines on non-STE ACS, adult congenital heart disease, sports cardiology and atrial fibrillation. *Acta Cardiol.* 2022;77(10):864–872.
- [4] de Vries TAC, Hemels MEW, Cools F, et al. Characteristics of patients with atrial fibrillation prescribed edoxaban in Belgium and The Netherlands: insights from the ETNA-AF-Europe study. *Acta Cardiol.* 2021;76(4):431–439.
- [5] Lancellotti P, Galderisi M. Prediction of ischaemic stroke in non-valvular atrial fibrillation if advanced echocardiography plays the game. *Eur Heart J.* 2018;39(16):1426–1428.
- [6] Scheen AJ. Glucose-lowering agents and risk of cardiac arrhythmias. *Acta Cardiol.* 2023;78(3):377–378.
- [7] Boulmpou A, Patoulias D, Papadopoulos CE, et al. Meta-analysis of cardiovascular outcome trials assessing the impact of glucagon-like peptide-1 receptor agonists on major cardiac arrhythmias. *Acta Cardiol.* 2022;14:1–6.
- [8] Imberti JF, Vitolo M, Boriani G. Atrial fibrillation and HIV: a new association requiring pathophysiological and outcome studies. *Acta Cardiol.* 2023;78(3):379–381.
- [9] Antwi-Amoabeng D, Ghuman J, Sathappan S, et al. Influence of HIV on in-hospital outcomes in patients with atrial fibrillation. *Acta Cardiol.* 2023;78(3):349–356.
- [10] Wu J, Hou Q, Han Q, et al. Atrial fibrillation is an independent risk factor for new-onset myocardial infarction: a prospective study. *Acta Cardiol.* 2023;78(3):341–348.
- [11] Goksuluk H, Ozyuncu N, Duzen IV, et al. Comparison of frequency of silent cerebral infarction as assessed by serum

- neuron specific enolase in patients with non-valvular atrial fibrillation: warfarin versus direct oral anticoagulant. *Acta Cardiol.* 2023;78(3):320–326.
- [12] Yang N, Zhao Y, Bai Z, et al. The association of non-vitamin K antagonist oral anticoagulants vs. warfarin and the risk of fractures for patients with atrial fibrillation: a systematic review and meta-analysis. *Acta Cardiol.* 2023;78(3):298–310.
- [13] Velayutham R, Parale C, Anantharaj A. Pinball thrombi in the left atrium. *Acta Cardiol.* 2023;78(3):369–370.
- [14] Angelini F, Bocchino PP, Peyracchia M, et al. Prevalence and predictors of left atrial thrombosis in atrial fibrillation patients treated with non-vitamin K antagonist oral anticoagulants. *Acta Cardiol.* 2023;78(3):290–297.
- [15] Murat S, Murat B, Gorenk B. Predictors of left atrial thrombosis in atrial fibrillation patients treated with direct oral anticoagulants. *Acta Cardiol.* 2023;78(3):371.
- [16] Boulmpou A, Teperikidis E, Papadopoulos CE, et al. The role of cardiopulmonary exercise testing in risk stratification and prognosis of atrial fibrillation: a scoping review of the literature. *Acta Cardiol.* 2023;78(3):274–287.
- [17] Tan TS, Korkmaz K, Akbulut IM, et al. Association between CHARGE-AF risk score and LA mechanics: LA reservoir strain can be a single parameter for predicting AF risk. *Acta Cardiol.* 2023;78(3):311–319.
- [18] Zhong XF, Liu DS, Zheng YQ, et al. Left atrial reservoir and pump function after catheter ablation with persistent atrial fibrillation: a two-dimensional speckle tracking imaging study. *Acta Cardiol.* 2023;78(3):331–340.
- [19] De Roy L, Dechaux D, Deceuninck O. Atrial fibrillation ablation and anterior isthmus line: a simple and precise method for validation of bidirectional block. *Acta Cardiol.* 2023;78(3):364–366.
- [20] Salaun E, Bernier M, Paradis JM, et al. Watchman 2.5TM versus watchman FLXTM device in atypical left atrial anatomies: old fashion never dies. *Acta Cardiol.* 2023;78(3):372–376.
- [21] Selvais N, Leduc N, Ben Yedder M, et al. Use of the novel amplatzer steerable sheath for percutaneous closure of a complex chicken-wing left atrial appendage. *Acta Cardiol.* 2023;78(3):367–368.
- [22] Lancini D, Smith C, Elkhateeb O, et al. Leadless micra pacemaker implantation in patient with previous senning procedure for Dextro-Transposition of the great arteries. *Acta Cardiol.* 2023;78(3):357–361.

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