

New onset of chest pain: the importance of remote monitoring

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Introduction

Left ventricular (LV) dysfunction is found in about 20-30% of patients with atrial fibrillation (AF). Conversely, AF occurrence can deteriorate LV function determining severe LV dysfunction.¹ Moreover, symptoms of heart failure (HF) like dyspnoea or chest pain may be related to AF occurrence without more specific symptoms like palpitations.¹ Finally, devices like implantable cardioverter-defibrillator (ICD) may register atrial high-rate episodes (AHREs), which can last for more than 5 or 6 min and are also called subclinical AF. The clinical management of these episodes is still controversial. Rhythm vs. rate control strategies is still a matter of debate. Evidences regarding the use of oral anticoagulation in patients with AHRE are scarce. Therefore, AF needs to be confirmed either by surface electrocardiogram (ECG) or by intracardiac electrograms.

Case presentation

A 64-year-old Caucasian man, with history of hypertension and previous subclinical myocardial infarction 10 years before (he was treated with single coronary artery bypass graft: left internal mammalian artery on left anterior descending artery), was admitted to our emergency department for aborted sudden cardiac death related to ventricular fibrillation. A dual chamber ICD (Biotronik Iforia 3 DR-T) was implanted in secondary prevention (*Figure 1*).² LV ejection fraction was 44%. The ICD was routinely checked after the implant, and the patient received remote monitoring (RM) system.³ Five years later, AHRE was detected by RM, and the patient was called for an outpatient visit (*Figure 2*). Atrial fibrillation episode was discovered lasting for more than 24h and the patient was complaining for occurrence of dyspnoea and chest pain but he was not feeling palpitation or rhythm irregularity. An echocardiogram was repeated and LV ejection fraction felt

down to 30% and mild left atrial dilatation was found. The patient was hospitalized for initial HF symptoms and suspect angina. A coronary angiography showed patency of the bypass graft and no critical stenosis on native coronary arteries. The first therapeutic action was to start antithrombotic therapy with rivaroxaban.¹ The thrombo-embolic risk of the patient was classified as high with a CHA₂DS₂-VASc score of 4. The second action was to choose between rhythm or rate control strategy. Initially a rate control approach was followed, starting treatment with beta-blocker (bisoprolol 10 mg/day). However, after 3 months, patient was still complaining of symptoms, mainly fatigue, dyspnoea, and chest pain during stress. Since the lack of improvement in symptoms, we decided to switch to a rhythm control strategy.¹ Amiodarone therapy was started, and an internal electrical cardioversion from the device was performed restoring sinus rhythm (*Figure 3*).



Figure 1 Dual chamber implantable cardioverter-defibrillator with atrial and ventricular lead.

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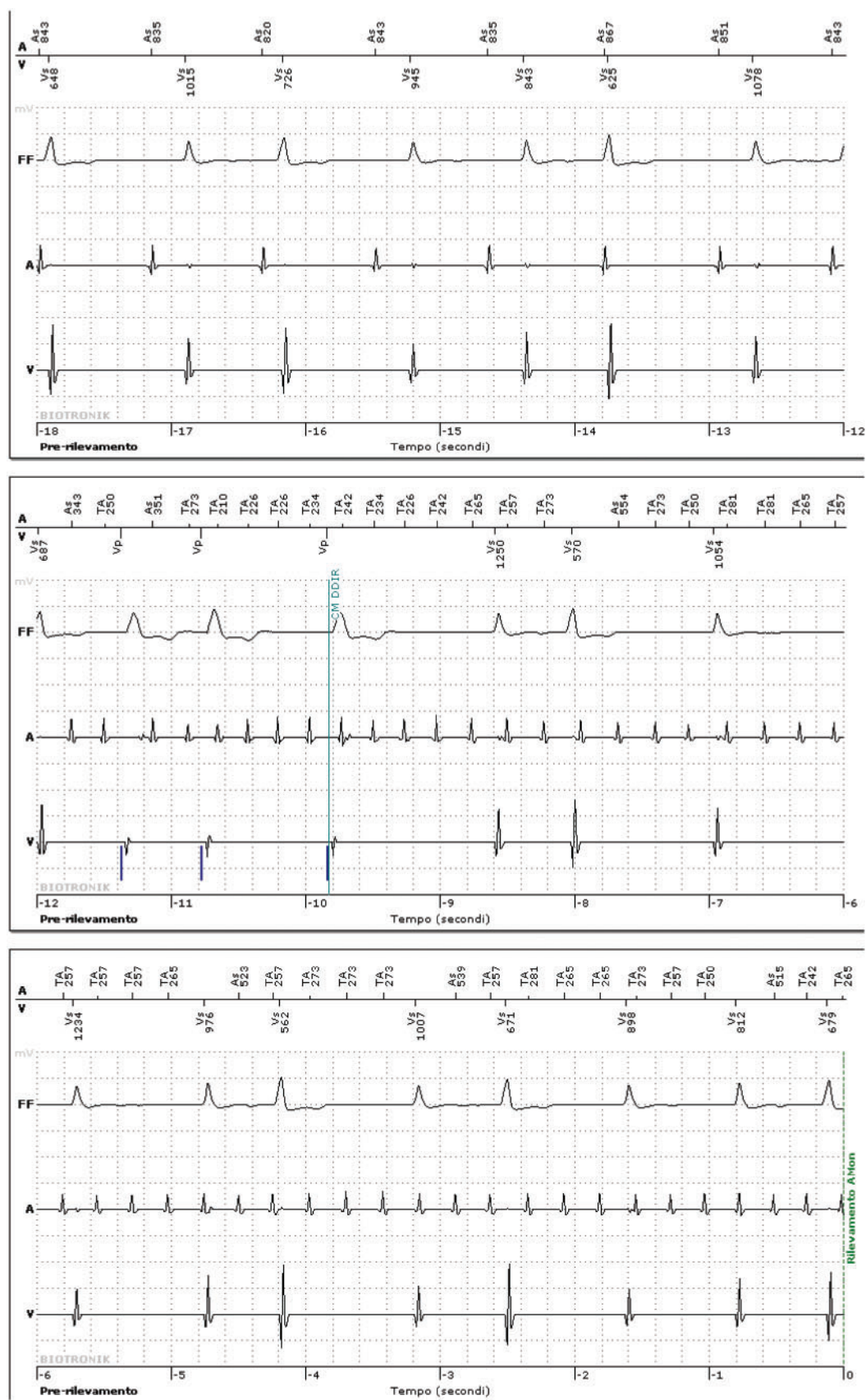


Figure 2 Atrial fibrillation episode detected with remote monitoring. In the upper intracardiac electrogram (EGM) strip sinus rhythm is still present, in the other two EGM strips atrial fibrillation is present since the atrial channel (A) shows much more waves than ventricular channel (V).

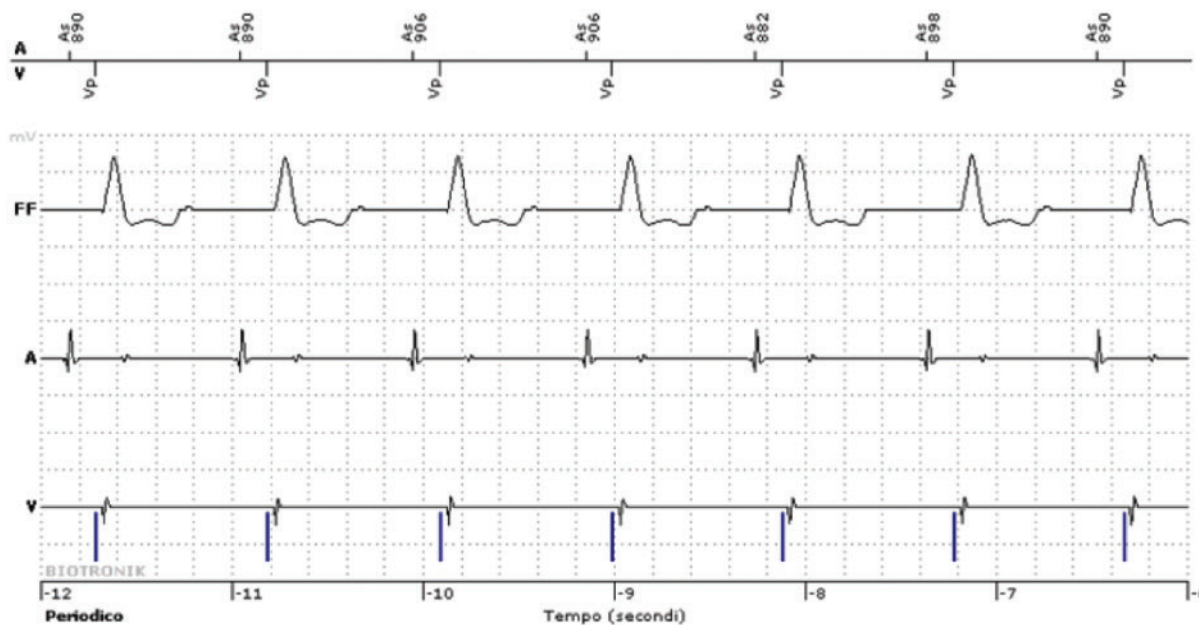


Figure 3 Sinus rhythm was restored: the relationship between atrial (A) and ventricular (V) signals is 1:1.

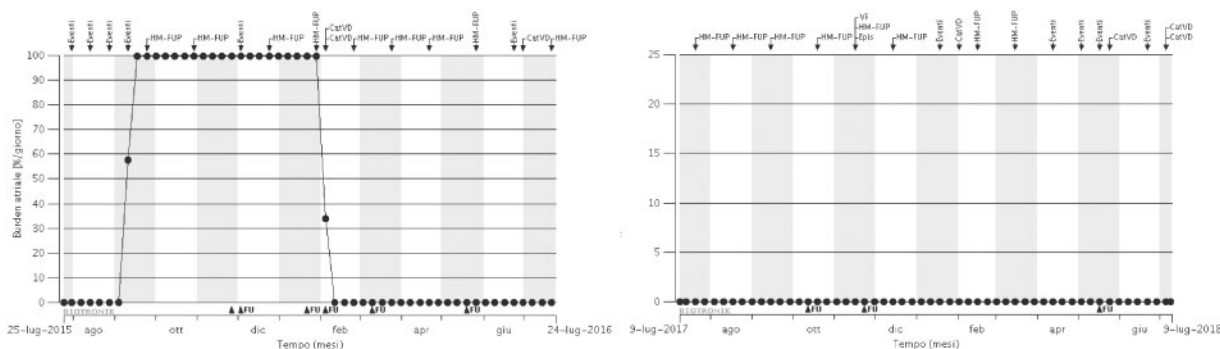


Figure 4 Atrial fibrillation burden is shown. In particular, in September 2015 AF burden is 100% until February 2016. Before and after this period atrial fibrillation burden is 0% and in 2018 atrial fibrillation burden is still 0% confirming that the patient is still in sinus rhythm.

At 1-month follow-up after electrical cardioversion, the patient was feeling better, no more chest pain, fatigue, or dyspnoea were reported. An echocardiogram performed after 60 days showed an improved LV function with an ejection fraction of 38%. After 3 years of follow-up, AF burden was still 0% and no more AHREs episodes were detected from the ICD, and the patient was in New York Heart Association (NYHA) functional Class I (Figure 4).

Discussion

Atrial fibrillation and HF frequently coexist in the same patient, often negatively promoting the course of each other. Dyspnoea or chest pain without more specific arrhythmic symptoms may delay the diagnosis of AF in HF patients. Given the poor outcomes in patients with HF who developed AF, a prompt diagnosis and therapy could be of paramount importance in these patients.

Cardiac implantable electronic devices (CIEDs) with an atrial lead or dipole for sensing allow continuous monitoring of atrial rhythm potentially highlighting AHRE that enable early detection of AF. Prior studies have demonstrated that the detection of AHRE correlates with electrocardiographic documentation of AF.^{4,5}

Atrial fibrillation can affect HF triggering inappropriate shocks, precipitating HF, and increasing the risk of thrombo-embolic stroke. The principal benefits of RM are early arrhythmia detection associated with a prompt clinical management and patient continuous monitoring allowing patient-tailored strategy of treatment.^{6,7} The Home Guide Registry demonstrated that automatic RM allows early detection of AF with high sensitivity and appropriate reaction to optimize medical treatment.⁸ Useful and detailed information about AF episodes such as arrhythmia recurrences and burden, number and duration of the episodes, mean and maximum ventricular rate are stored differently in CIEDs according to the manufacturer.

If the reliability of RM for AF early detection, notification and quantification is well established,⁹⁻¹¹ evidences regarding the use of this technology for early anticoagulation are less clear.¹²⁻¹⁵ Ongoing clinical trials will probably better clarify the benefit of oral anticoagulation in patients with AHRE [Apixaban for the Reduction of Thrombo-Embolic in Patients With Device-Detected Sub-clinical Atrial Fibrillation (ARTESIA) and Non-vitamin K antagonist Oral anticoagulations in patients with Atrial High-rate episodes (NOAH-AFNET)].

In our patient, rhythm control strategy showed better results compared to rate control strategy to control symptoms, in particular chest pain during stress.

Guidelines suggest that HF patients with AF and severe symptoms may benefit from rhythm control therapy in addition to rate control.¹ Several studies and meta-analysis tried to compare rhythm vs. rate control strategy in patients with HF.¹⁶⁻¹⁹ Although no significant reduction of mortality rate, hospitalization, or thromboembolism was found with rhythm control strategy, persistence of sinus rhythm improves LV function, exercise capacity, and quality of life.^{18,20,21}

Once the rhythm control strategy was chosen for our patient, the use of a new oral anticoagulant allowed a quicker elective cardioversion compared to vitamin K antagonist (VKA).

In patients undergoing electrical cardioversion, long-term novel oral anticoagulant (NOAC) therapy showed similar results on thrombo-embolic risk prevention compared to warfarin.²²⁻²⁴ Moreover, the predictable pharmacokinetics and pharmacodynamics of NOACs allows a more rapid and reliable time to cardioversion without any delay to achieve stable therapeutic international normalized ratio (INR) values as it often the case with VKA strategy.²²

In conclusion, RM by CIEDs allows early detection of arrhythmia episodes in HF patients even in the absence of clear symptoms. Continuous monitoring enables physician to tailor arrhythmia management and treatment in these patients.

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References

- Kirchhof P, Benussi S, Kotecha D, Ahlsson A, Atar D, Casadei B, Castella M, Diener HC, Heidbuchel H, Hendriks J, Hindricks G, Manolis AS, Oldgren J, Popescu BA, Schotten U, Van Putte B, Vardas P, Agewall S, Camm J, Baron EG, Budts W, Carerj S, Casselman F, Coca A, De CR, Deftereos S, Dobrev D, Ferro JM, Filippatos G, Fitzsimons D, Gorenek B, Guenoun M, Hohnloser SH, Kolh P, Lip GY, Manolis A, McMurray J, Ponikowski P, Rosenhek R, Ruschitzka F, Savelieva I, Sharma S, Suwalski P, Tamargo JL, Taylor CJ, Van GIC, Voors AA, Windecker S, Zamorano JL, Zeppenfeld K. 2016 ESC Guidelines for the management of atrial fibrillation developed in collaboration with EACTS. *Eur Heart J* 2016;**37**:2893-2962.
- Priori SG, Blomstrom-Lundqvist C, Mazzanti A, Blom N, Borggrefe M, Camm J, Elliott PM, Fitzsimons D, Hatala R, Hindricks G, Kirchhof P, Kjeldsen K, Kuck KH, Hernandez-Madrid A, Nikolaou N, Norekval TM, Spaulding C, Van Veldhuisen DJ; ESC Scientific Document Group. 2015 ESC Guidelines for the management of patients with ventricular arrhythmias and the prevention of sudden cardiac death: the Task

- Force for the Management of Patients with Ventricular Arrhythmias and the Prevention of Sudden Cardiac Death of the European Society of Cardiology (ESC) Endorsed by: Association for European Paediatric and Congenital Cardiology (AEPC). *Eur Heart J* 2015;**36**:2793-2867.
- Hindricks G, Taborsky M, Glikson M, Heinrich U, Schumacher B, Katz A, Brachmann J, Lewalter T, Goette A, Block M, Kautzner J, Sack S, Husser D, Piorowski C, Sogaard P; IN-TIME Study Group*. Implant-based multiparameter telemonitoring of patients with heart failure (IN-TIME): a randomised controlled trial. *Lancet* 2014;**384**:583-590.
 - Pollak WM, Simmons JD, Interian A Jr, Atapattu SA, Castellanos A, Myerburg RJ, Mitrani RD. Clinical utility of intraatrial pacemaker stored electrograms to diagnose atrial fibrillation and flutter. *Pacing Clin Electrophysiol* 2001;**24**:424-429.
 - Purerfellner H, Gillis AM, Holbrook R, Hettrick DA. Accuracy of atrial tachyarrhythmia detection in implantable devices with arrhythmia therapies. *Pacing Clin Electrophysiol* 2004;**27**:983-992.
 - Ono M, Varma N. Remote monitoring to improve long-term prognosis in heart failure patients with implantable cardioverter-defibrillators. *Expert Rev Med Devices* 2017;**14**:335-342.
 - Ricci RP. Disease management: atrial fibrillation and home monitoring. *Europace* 2013;**15**: i35-i39.
 - Ricci RP, Morichelli L, D'Onofrio A, Calo L, Vaccari D, Zanolto G, Curris A, Buja G, Rovai N, Gargaro A. Effectiveness of remote monitoring of CIEDs in detection and treatment of clinical and device-related cardiovascular events in daily practice: the HomeGuide Registry. *Europace* 2013;**15**:970-977.
 - Amara W, Montagnier C, Cheggour S, Boursier M, Gully C, Barnay C, Georger F, Deplagne A, Fromentin S, Mlotek M, Lazarus A, Taieb J; SETAM Investigators. Early detection and treatment of atrial arrhythmias alleviates the arrhythmic burden in paced patients: the SETAM study. *Pacing Clin Electrophysiol* 2017;**40**:527-536.
 - Rosier A, Mabo P, Temal L, Van Hille P, Dameron O, Deleger L, Grouin C, Zweigenbaum P, Jacques J, Chazard E, Laporte L, Henry C, Burgun A. Personalized and automated remote monitoring of atrial fibrillation. *Europace* 2016;**18**:347-352.
 - Zoppo F, Facchin D, Molon G, Zanolto G, Catanzariti D, Rossillo A, Baccillieri MS, Menard C, Comisso J, Gentili A, Grammatico A, Bertaglia E, Proclemer A. Improving atrial fibrillation detection in patients with implantable cardiac devices by means of a remote monitoring and management application. *Pacing Clin Electrophysiol* 2014;**37**:1610-1618.
 - Doliwa Sobocinski P, Anggardh Rooth E, Frykman Kull V, von Arbin M, Wallen H, Rosenqvist M. Improved screening for silent atrial fibrillation after ischaemic stroke. *Europace* 2012;**14**:1112-1116.
 - Gladstone DJ, Sharma M, Spence JD; EMBRACE Steering Committee and Investigators. Cryptogenic stroke and atrial fibrillation. *N Engl J Med* 2014;**371**:1260.
 - Kirchhof P, Lip GY, Van Gelder IC, Bax J, Hylek E, Kaab S, Schotten U, Wegscheider K, Boriani G, Brandes A, Ezekowitz M, Diener H, Haegeli L, Heidbuchel H, Lane D, Mont L, Willems S, Dorian P, Aunes-Jansson M, Blomstrom-Lundqvist C, Borenstein M, Breitenstein S, Brueckmann M, Cater N, Clemens A, Dobrev D, Dubner S, Edvardsson NG, Friberg L, Goette A, Gulizia M, Hatala R, Horwood J, Szumowski L, Kappenberger L, Kautzner J, Leute A, Lobban T, Meyer R, Millerhagen J, Morgan J, Muenzel F, Nabauer M, Baertels C, Oeff M, Paar D, Polifka J, Ravens U, Rosin L, Stegink W, Steinbeck G, Vardas P, Vincent A, Walter M, Breithardt G, Camm AJ. Comprehensive risk reduction in patients with atrial fibrillation: emerging diagnostic and therapeutic options—a report from the 3rd Atrial Fibrillation Competence Network/European Heart Rhythm Association Consensus Conference. *Europace* 2012;**14**:8-27.
 - Martin DT, Bersohn MM, Waldo AL, Wathen MS, Choucair WK, Lip GY, Ip J, Holcomb R, Akar JG, Halperin JL; IMPACT Investigators. Randomized trial of atrial arrhythmia monitoring to guide anticoagulation in patients with implanted defibrillator and cardiac resynchronization devices. *Eur Heart J* 2015;**36**:1660-1668.
 - Chatterjee S, Sardar P, Lichstein E, Mukherjee D, Aikat S. Pharmacologic rate versus rhythm-control strategies in atrial fibrillation: an updated comprehensive review and meta-analysis. *Pacing Clin Electrophysiol* 2013;**36**:122-133.
 - Di Biase L, Mohanty P, Mohanty S, Santangeli P, Trivedi C, Lakkireddy D, Reddy M, Jais P, Themistoclakis S, Dello Russo A, Casella M, Pelargonio G, Narducci ML, Schweikert R, Neuzil P, Sanchez J, Horton R, Beheiry S, Hongo R, Hao S, Rossillo A, Forleo G, Tondo C,

- Burkhardt JD, Haissaguerre M, Natale A. Ablation versus amiodarone for treatment of persistent atrial fibrillation in patients with congestive heart failure and an implanted device: results from the AATAC Multicenter Randomized Trial. *Circulation* 2016;**133**:1637-1644.
18. Ahn J, Kim HJ, Choe JC, Park JS, Lee HW, Oh JH, Choi JH, Lee HC, Cha KS, Hong TJ, Kim YH. Treatment strategies for atrial fibrillation with left ventricular systolic dysfunction—meta-analysis. *Circ J* 2018;**82**:1770-1777.
 19. Caldeira D, David C, Sampaio C. Rate vs rhythm control in patients with atrial fibrillation and heart failure: a systematic review and meta-analysis of randomised controlled trials. *Eur J Intern Med* 2011;**22**:448-455.
 20. Hunter RJ, Berriman TJ, Diab I, Kamdar R, Richmond L, Baker V, Goromonzi F, Sawhney V, Duncan E, Page SP, Ullah W, Unsworth B, Mayet J, Dhinoja M, Earley MJ, Sporton S, Schilling RJ. A randomized controlled trial of catheter ablation versus medical treatment of atrial fibrillation in heart failure (the CAMTAF trial). *Circ Arrhythm Electrophysiol* 2014;**7**:31-38.
 21. MacDonald MR, Connelly DT, Hawkins NM, Steedman T, Payne J, Shaw M, Denvir M, Bhagra S, Small S, Martin W, McMurray JJ, Petrie MC. Radiofrequency ablation for persistent atrial fibrillation in patients with advanced heart failure and severe left ventricular systolic dysfunction: a randomised controlled trial. *Heart* 2011;**97**:740-747.
 22. Cappato R, Ezekowitz MD, Klein AL, Camm AJ, Ma CS, Le Heuzey JY, Talajic M, Scanavacca M, Vardas PE, Kirchhof P, Hemmrich M, Lanius V, Meng IL, Wildgoose P, van Eickels M, Hohnloser SH; X-VerT Investigators. Rivaroxaban vs. vitamin K antagonists for cardioversion in atrial fibrillation. *Eur Heart J* 2014;**35**:3346-3355.
 23. Diener HC, Aisenberg J, Ansell J, Atar D, Breithardt G, Eikelboom J, Ezekowitz MD, Granger CB, Halperin JL, Hohnloser SH, Hylek EM, Kirchhof P, Lane DA, Verheugt FWA, Veltkamp R, Lip GYH. Choosing a particular oral anticoagulant and dose for stroke prevention in individual patients with non-valvular atrial fibrillation: Part 1. *Eur Heart J* 2017;**38**:852-859.
 24. Heidbuchel H, Verhamme P, Alings M, Antz M, Diener HC, Hacke W, Oldgren J, Sinnaeve P, Camm AJ, Kirchhof P; ESC Scientific Document Group. Updated European Heart Rhythm Association practical guide on the use of non-vitamin-K antagonist anticoagulants in patients with non-valvular atrial fibrillation: executive summary. *Eur Heart J* 2017; **38**:2137-2149.