



ATRIAL FIBRILLATION MANAGEMENT

2021 Executive Summary

**Overview of Atrial Fibrillation Management
and Treatment Outcomes**



The management of atrial fibrillation focuses on effectively and safely controlling the irregular heart rhythm, improving symptoms, and reducing key complications based on shared decision-making between healthcare professionals and patients.

WHAT IS ATRIAL FIBRILLATION AND WHY IS IT IMPORTANT?

Atrial fibrillation (AF) is characterized by an irregular and often fast heartbeat that results in uncoordinated contraction of the top 2 chambers of the heart (ie, atria).¹

AF can be categorized into several types:^{2,3}

First-diagnosed AF: AF that has not been diagnosed before, regardless of how long it has been present for.

Paroxysmal AF: Occasional AF that stops ≤ 7 days with or without intervention.

Persistent AF: Continuous AF that lasts longer than 7 days.

Early Persistent AF: Continuous AF that lasts 7 days to 3 months.

Long-standing Persistent AF: Continuous AF that lasts >12 months when a rhythm control therapy has been adopted.

Permanent AF: Represents a therapeutic attitude, where the presence of AF is accepted by the patient and physician, and no more attempts will be made to restore or maintain sinus rhythm. If a rhythm control strategy is adopted, then the arrhythmia would be reclassified to "long-standing persistent AF".

Risk factors for AF include:



LIFESTYLE FACTORS

Obesity⁴⁻⁷, smoking³, alcohol consumption^{3, 7-8}



OTHER CONDITIONS

High blood pressure⁷, heart failure⁹⁻¹⁴, history of heart attack^{9,15}, coronary artery or other heart disease^{5,9}



NON-MODIFIABLE FACTORS

Older age^{3,16}, family history or other genetic factors^{9, 17-18}, male sex^{3, 9, 16}

Early detection and diagnosis of AF may help improve patient outcomes, since a long history and duration of AF have been associated with recurrence.¹⁹⁻²²



15%-30%

OF PATIENTS EXPERIENCE
NO SYMPTOMS (i.e. silent AF)²³



1 in 5
PATIENTS PROGRESS
IN 1 YEAR²⁴⁻²⁷



PAROXYSMAL
AF

PERSISTENT
AF

Patients with AF have an increased risk for life-threatening complications and other diseases:²⁸

5x

Increase heart failure



2.4x

Increase stroke



2x

Increase cardiovascular mortality



- AF worsens quality of life for patients and caregivers.²⁹⁻³⁴
- AF increasingly places a **critical financial burden** on the healthcare system, costing **€660-€3,286 million annually across European countries**.³⁵⁻³⁹

The 2020 (ESC)/ (EACTS) guidelines on the management of AF and the 2017(HRS)/ (EHRA)/(ECAS)/ (APHRS)/ (SOLAECE) expert consensus statement on catheter and surgical ablation of AF recommend an integrated management strategy to reduce mortality, tailor management to patient preferences, and reduce hospitalizations.

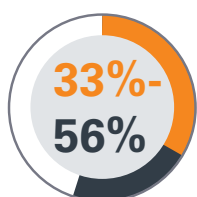
The ABC pathway for integrated AF patient management includes:³

- A** – Anticoagulation/Avoid stroke
- B** – Better symptom control
- C** – Comorbidities/Cardiovascular risk factor management

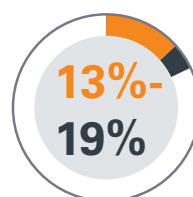
- Education and screening programs aimed at **increasing awareness and diagnosis of AF are critical to reducing the risk of stroke and death** in patients with undiagnosed AF.^{40, 41}
 - Ideally, patients will recognize AF symptoms and contact their clinicians when symptoms arise.⁴²
- **Early treatment of AF is important**, as it may improve patient life expectancy and quality of life.^{77, 78}

Antiarrhythmic drug (AAD) therapy is moderately effective. It is commonly associated with treatment withdrawals, however, it has been shown to improve quality of life, and is affordable in the short term.

With drug therapy treatment:



of patients are in
**NORMAL SINUS
RHYTHM
AT 1 YEAR⁴³**



of patients
**WITHDRAW FROM
TREATMENT DUE TO
ADVERSE EVENTS⁴³**



of patients
**IMPROVEMENT
IN QUALITY OF
LIFE⁴⁴**

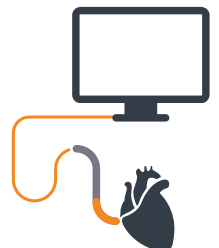
Catheter ablation is highly effective, associated with a low rate of ablation-related adverse events, and has been shown to reduce the rate of AF-related complications. It has also been shown to improve quality of life, and reduce resource utilization.

With catheter ablation treatment:



94%
of patients are **FREE FROM ARRHYTHMIA RECURRENCE**
AT 1 YEAR⁴⁵⁻⁵⁴

1.8% of patients experience
AN ABLATION-RELATED ADVERSE EVENT⁵⁵



IMPROVEMENT IN QUALITY OF LIFE⁵⁶



Catheter ablation is more effective than drug therapy, has a low chance of AF-related complications, has significantly greater improvement in quality of life, and is less costly over the long term.



improvement in survival
FREE FROM ATRIAL ARRHYTHMIA
over **4 years** after ablation⁵⁵



Similarly
LOW

RATES OF AF-RELATED COMPLICATIONS^{55, 57-58}



Death



Stroke



Cardiac arrest



Cardiovascular hospitalization

Patients with **paroxysmal AF** who undergo catheter ablation are almost **10 TIMES LESS LIKELY TO PROGRESS TO PERSISTENT AF** than **those on AADs**^{*59}

*(HR 0.11; 95% CI 0.025-0.483; p=0.0034.)

■ MANAGEMENT OF AF PATIENTS

Therapeutic goals of the ABC pathway for integrated care of patients with AF are to reduce the risk of stroke, reduce symptoms of AF, and manage cardiovascular risk factors and comorbidities.³

WHAT IS THE GOAL OF AF MANAGEMENT?

- AF is associated with an **increased risk of stroke** compared to patients in sinus rhythm.¹¹
- The presence of cardiovascular risk factors **significantly impact the lifetime risk** of developing AF.³
- The ABC pathway has been shown **to significantly lower the risk** of all-cause death, composite outcome of stroke/major bleeding/cardiovascular death and first hospitalization, rates of cardiovascular events, and health-related costs than usual care.³

TREAT AF: THE ABC PATHWAY

The Atrial fibrillation Better Care (ABC) pathway streamlines integrated care for patients with AF and involves **anticoagulation/avoidance of stroke (A)**, **better symptom management (B)**, and **cardiovascular and comorbidity optimization (C)**.



NEW
ESC 2020³

HOW IS THE PATIENT WITH AF TREATED?

Current treatment options recommended for managing AF include:

RATE CONTROL THERAPIES



PHARMACOLOGICAL

Beta blockers or non-dihydropyridine calcium channel antagonists, digitalis glycosides, or amiodarone



SURGICAL

AV node ablation with pacemaker implantation

RHYTHM CONTROL THERAPIES

RHYTHM CONTROL THERAPIES FOR AN EPISODE OF AF

Electrical and pharmacological cardioversion

LONG-TERM RHYTHM CONTROL THERAPIES



PHARMACOLOGICAL



CATHETER ABLATION



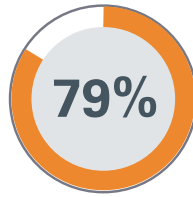
SURGICAL

■ MANAGEMENT OF AF PATIENTS

RATE CONTROL THERAPIES

are effective at lowering and controlling heart rate in patients with AF,

with as many as



of patients in the target heart rate range of **60-100 BEATS PER MINUTE.**⁷⁹

Over the long-term:

RHYTHM CONTROL THERAPIES

that include AADs and catheter ablation are

the most common methods for **CONTROLLING AF**, effectively preventing recurrence in



as many as **94%** of patients OVER **1-YEAR**^{3, 45-50}

Guidance on the delivery of good care to patients with AF are available from the 2020 ESC/EACTS guidelines and 2017 HRS/EHRA/ECAS/APHRS/SOLAECE expert consensus statement.

WHAT ARE THE RECOMMENDATIONS FOR MANAGING A PATIENT WITH AF?

The 2020 ESC/EACTS Guidelines recommend a structured approach to the diagnosis, characterization, and treatment of AF, known as the Confirm and Characterise To Atrial fibrillation Better Care (CCTo ABC) pathway.³

CCTO ABC

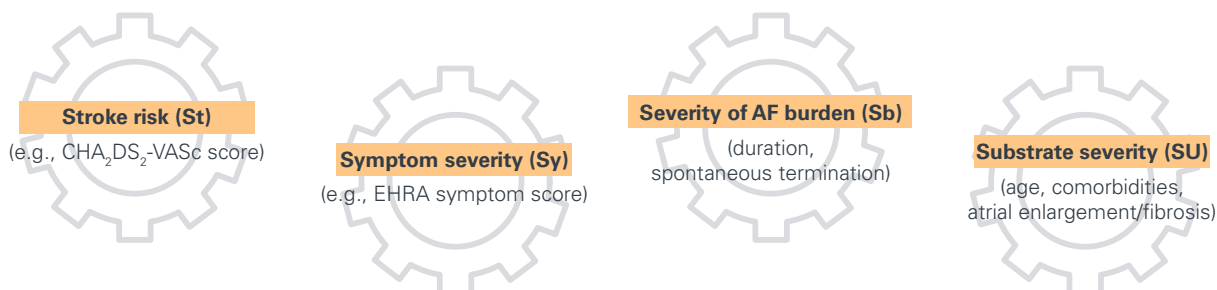
Confirm AF

NEW
ESC 2020³

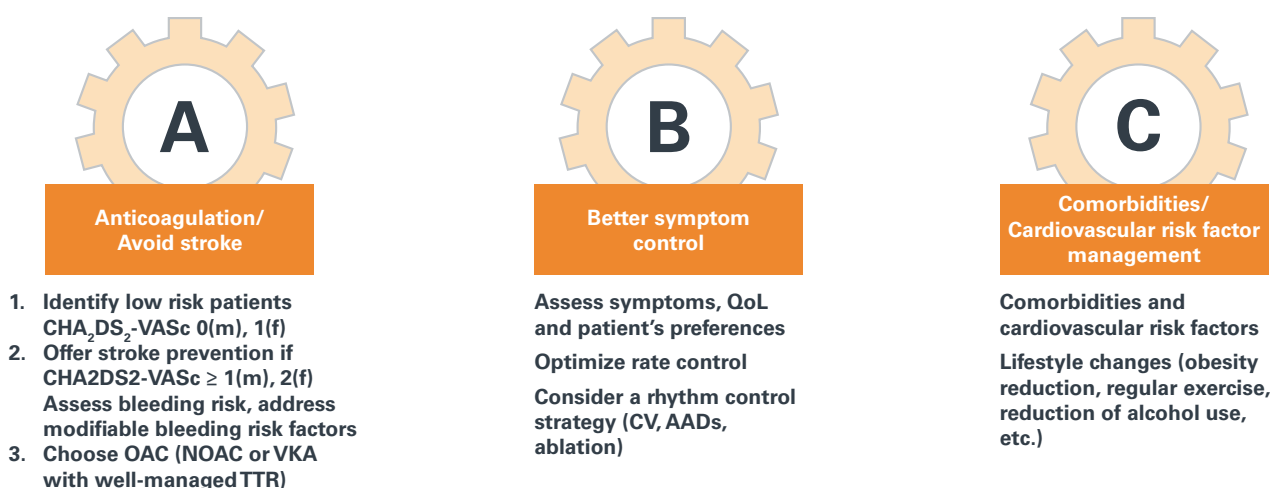


A 12-lead ECG or a rhythm strip showing AF pattern for ≥ 30s.

Characterise AF (the 4S-AF scheme)



Treat AF: The ABC pathway



■ MANAGEMENT OF AF PATIENTS

1 Integrated Management of AF & Collaborative Decision Making

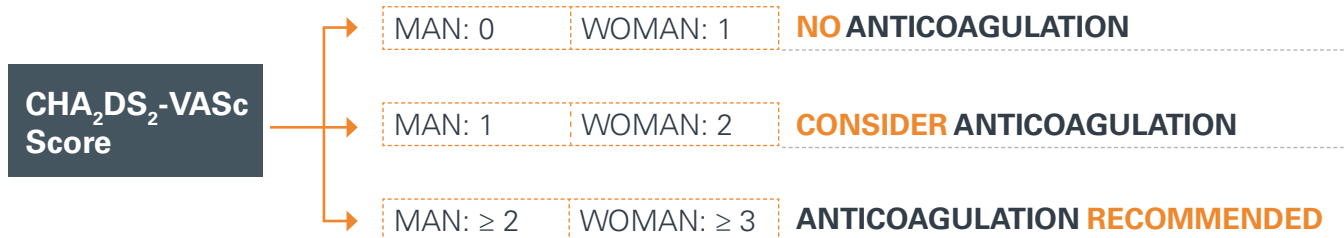
NEW
ESC 2020³

Following the diagnosis of AF, guidelines recommend an integrated and structured approach to patient care and AF management that involves multidisciplinary teams of cardiologists and electrophysiologists, non-specialist healthcare professionals, and allied health professionals, and places patients and their carers in a central role in decision-making.³

Physicians are recommended to optimize shared decision making about specific AF treatment option(s) in consideration by:³

- Informing patient about advantages/ limitations and benefits/risks associated with options being considered
- Discussing potential burden of treatment with patient and include patient's perspective of treatment burden in the treatment decision

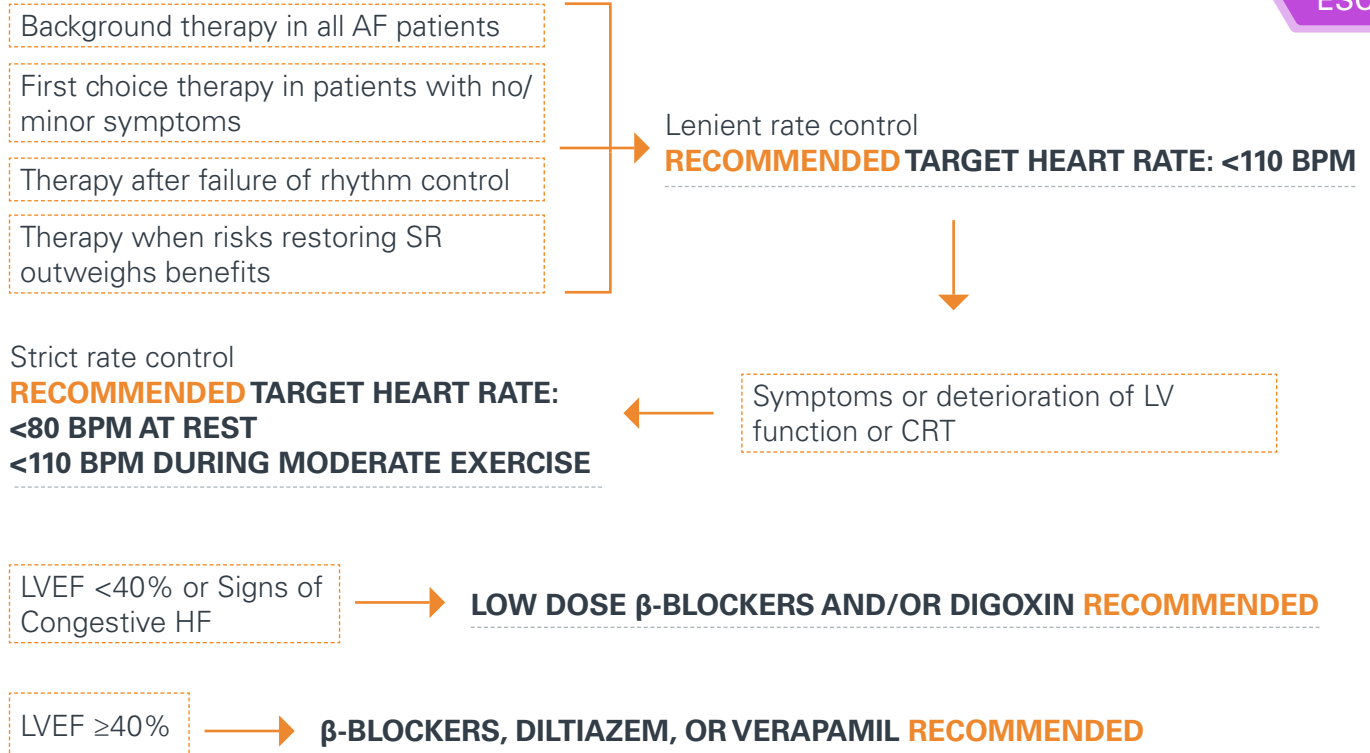
2 Oral Anticoagulation Therapy for Stroke Prevention in Patients with AF³



■ MANAGEMENT OF AF PATIENTS

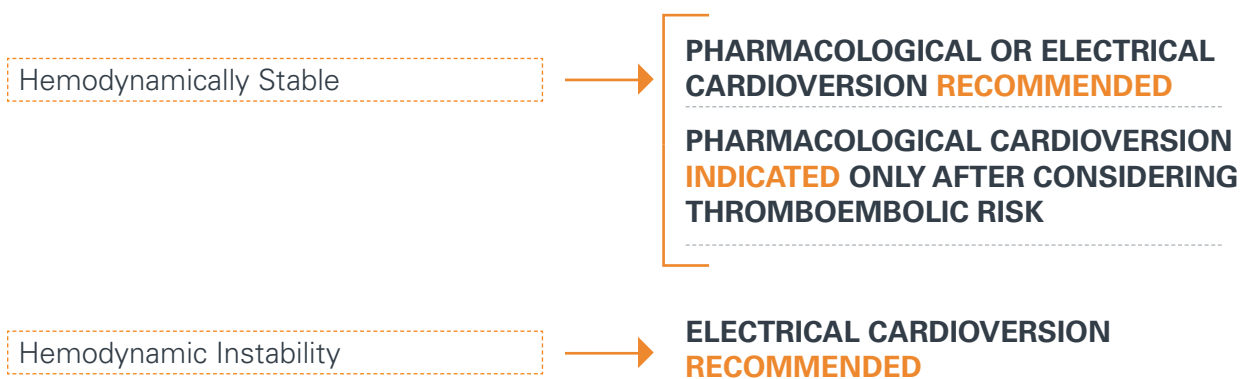
3 Rate Control Therapy to Lower and Control Heart Rate and Improve Symptoms of AF³

NEW
ESC 2020³



4 Acute Rhythm Control Therapy to Restore Normal Sinus Rhythm³

NEW
ESC 2020³

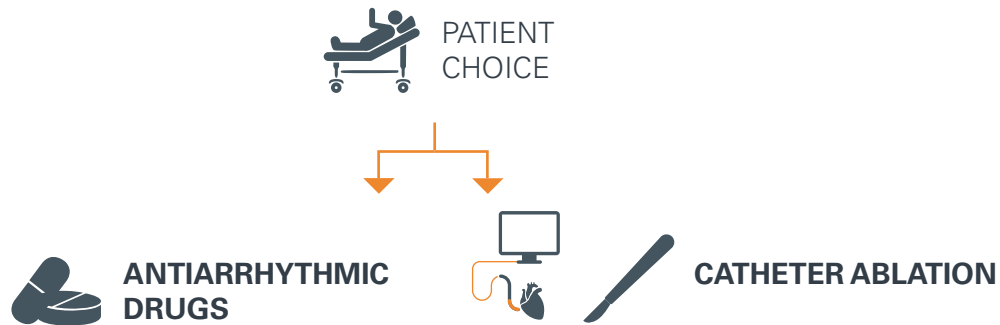


■ MANAGEMENT OF AF PATIENTS

5 Rhythm Control Therapy for Reducing AF-related Symptoms and Improving Quality of Life³

NEW
ESC 2020³

- Guidelines recommend that decision to treat with AADs, catheter ablation, and/or surgical ablation include patient choice.^{2,3}
- The choice of AADs needs to consider the presence of comorbidities, cardiovascular risk, potential for proarrhythmia, toxic effects, symptom burden, and patient preference.²



NEW
ESC 2020³

Symptomatic AF

Paroxysmal

Persistent without
recurrence risk factors

Persistent with
recurrence risk factors

**First line therapy
(Before AADs - Class I
or III)**

CONSIDER CATHETER ABLATION*

**Refractory/intolerant
to ≥ 1 AADs
(Class I or III)**

CATHETER ABLATION RECOMMENDED

**Refractory/intolerant
to ≥ 1 β-blocker**

CONSIDER CATHETER ABLATION

*In rare individual circumstances, catheter ablation may be carefully considered as first-line therapy for persistent with recurrent risk factors

Special populations

All AF - First-line

LV dysfunction when
tachycardia-induced
cardiomyopathy is
highly probable

CATHETER ABLATION RECOMMENDED

HF with reduced LVEF

CONSIDER CATHETER ABLATION

Surgical ablation of AF

CONSIDER CONCOMITANT AF ABLATION IN PATIENTS UNDERGOING CARDIAC SURGERY, BALANCING THE BENEFITS OF FREEDOM FROM ATRIAL ARRHYTHMIAS AND THE RISK FACTORS FOR RECURRENCE (LEFT ATRIAL DILATATION, YEARS IN AF, AGE, RENAL DYSFUNCTION, AND OTHER CV RISK FACTORS).

AF recurrence after catheter ablation

CONSIDER SHORT-TERM AAD THERAPY TO PREVENT EARLY RECURRENCE AFTER CATHETER ABLATION

CONSIDER CATHETER ABLATION WHEN FIRST CATHETER ABLATION IMPROVED SYMPTOMS

Implementation of guideline recommendations for the management of individual patients with AF is **needed to improve patient outcomes and reduced healthcare costs**; however, **adherence to guidelines is modest worldwide**.³

Antiarrhythmic drug therapy is an integral part of maintaining sinus rhythm after cardioversion²

WHAT IS THE IMPACT OF ANTIARRHYTHMIC DRUG THERAPY IN MANAGING AF?

Antiarrhythmic drug therapy is fairly safe, cost effective and affordable in the short term but can be costly over the long term. Although moderately effective at maintaining normal sinus rhythm, it is effective at controlling symptoms of AF and improving patient quality of life.

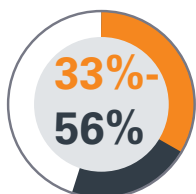
- Choice of AAD is primarily guided by safety considerations, namely the risk of proarrhythmia and organ toxicity:³

As patients are ultimately responsible for taking their medication, placing patients in a central role in the decision-making process is recommended to improve patient compliance and reduce the risk of the clinical consequences of AF.³

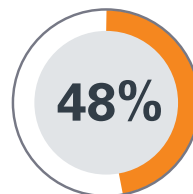
CLINICAL IMPACT

Antiarrhythmic drug therapy is fairly safe and moderately effective at maintaining normal sinus rhythm; its impact on consequences such as stroke, heart failure and mortality have been demonstrated in a limited number of studies.

AADs are moderately effective:



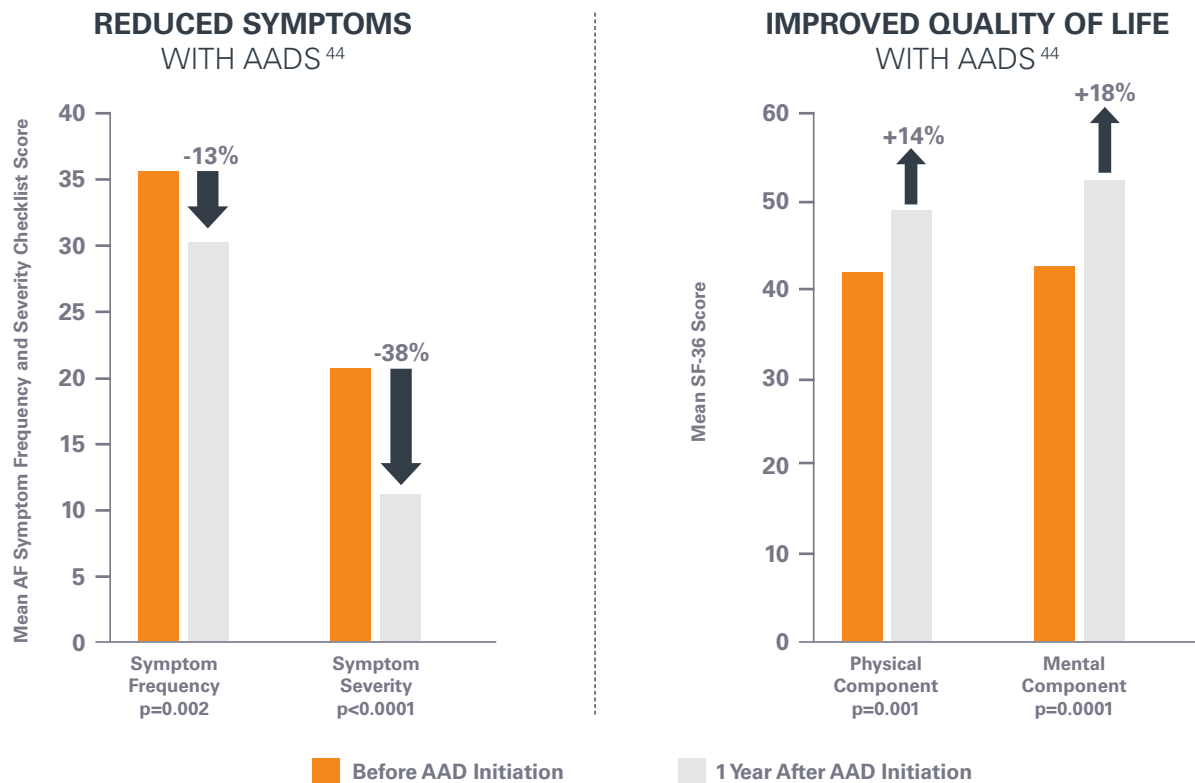
rate for **maintaining normal sinus rhythm** at 1 year.⁴³



of patients with AF are **not well managed on AADs**.⁶²

PATIENT IMPACT

Antiarrhythmic drug therapy is effective at controlling symptoms of AF and significantly improves patient quality of life.



Abbreviations: AAD = antiarrhythmic drug; AF = atrial fibrillation; SF-36 = Short Form 36 questionnaire. Source: Jais et al. (2008)

ECONOMIC IMPACT

Antiarrhythmic drug therapy is cost effective and affordable in the short term, but can be costly over the long term.

- Several studies show that AADs are cost effective, with key drivers including **reduced adverse events, stroke and mortality**.⁶³⁻⁶⁵

Initial cost of AAD treatment is **LOW**

however

LENGTH of treatment is **INDEFINITE** and the **cumulative cost** of AADs

INCREASES 28% ANNUALLY over 9 years*⁶⁶

- Cost of AAD therapy is influenced by its **toxicity level** and **effectiveness in restoring sinus rhythm** and **reducing the risk of AF-related consequences**.^{65, 67-72}

*From one study performed in France; data were limited for other European countries.

Catheter ablation is a well-established treatment for the prevention of AF recurrence that is used to create small scars on targeted parts of heart tissue that block the abnormal electrical signals causing the arrhythmia.^{2, 3}

WHAT IS THE IMPACT OF CATHETER ABLATION IN MANAGING AF?

Catheter ablation is highly effective at maintaining sinus rhythm and controlling symptoms, has a low rate of complications, reduces patient risk of AF-related complications and significantly improves patient quality of life. It has been proven to be cost effective by reducing the need for unplanned medical visits and overall healthcare cost.

Common ablation strategies include isolation of the pulmonary veins and the creation of specific lines of lesions within the left atrium.³

Upon deciding that rhythm control is required for long-term management of AF, it is important to discuss the efficacy and complication rates of AF catheter ablation and AADs with patients.³

CLINICAL IMPACT

Catheter ablation is highly effective at maintaining sinus rhythm, is associated with a low rate of adverse events and reduced patient risk of AF-related complications, including stroke, dementia, heart failure, and mortality.

- Catheter ablation is effective in eligible patients with AF, with recent studies reporting high rates of freedom from atrial arrhythmias at one year after a single procedure with advanced catheter ablation technology:



UP TO
94%

PAROXYSMAL
AF⁴⁵⁻⁵⁰



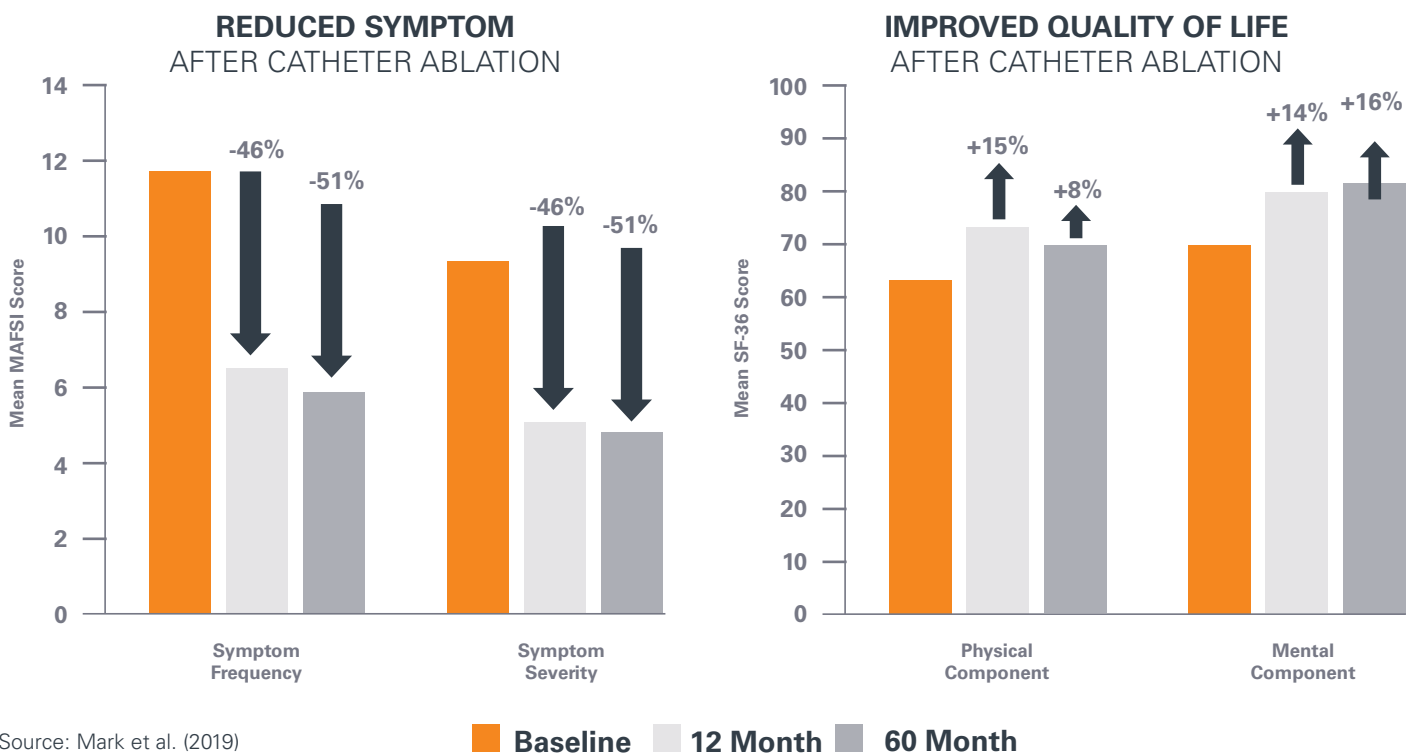
UP TO
83%

PERSISTENT
AF^{45, 48, 51-54}

PATIENT IMPACT

Catheter ablation is highly effective at controlling symptoms of AF and significantly improves patient quality of life.

- **Reductions** in symptom severity and improvements in quality of life after catheter ablation of AF are **maintained over long-term follow-up**.⁵⁶



Source: Mark et al. (2019)

ECONOMIC IMPACT

Catheter ablation is cost effective: it reduces the need for unplanned medical visits, additional treatments to control AF, and subsequent treatment for long-term consequences of AF, in turn, reducing overall healthcare cost.

CATHETER ABLATION
reduces the need for
unplanned medical visits

by up to
80%

as compared to
before ablation*⁷³

*at 2 years based on evidence outside of Europe

■ COMPARISON OF TREATMENTS

Recent studies have examined the comparative clinical and cost effectiveness of catheter ablation and drug therapy, including rate and rhythm control drugs, over long-term follow-up.

WHAT IS THE IMPACT OF CATHETER ABLATION COMPARED TO DRUG THERAPY IN MANAGING AF?

Several studies have shown that catheter ablation is significantly more effective than AADs at preventing recurrence of atrial arrhythmias with a similar rate of complications.

CLINICAL IMPACT

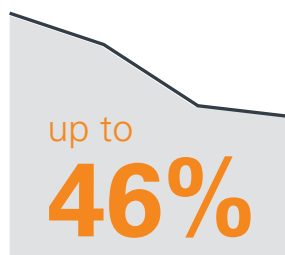
Catheter ablation is more effective in preventing recurrence, complications, and progression of AF than drug therapy, with a similar rate of adverse events.

The **CABANA** trial found that **CATHETER ABLATION** was more **EFFECTIVE** at preventing recurrence of AF



improvement in survival **FREE FROM ATRIAL ARRHYTHMIA** over **4 years** compared to drug therapy⁵⁵

CATHETER ABLATION was also associated with



reductions in the probability of **AF-RELATED complications**^{**}



Death



Stroke



Cardiac arrest



Cardiovascular hospitalization

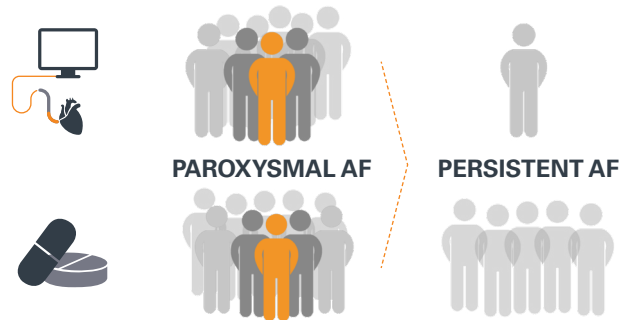
compared to drug therapy over 7-years follow-up.⁷⁴

* (hazard ratio [HR] 0.52; 95% confidence interval [CI] 0.45-0.60; p<0.001)

** 46% cardiac arrest, 41% stroke, 33% death, 17% cardiovascular hospitalization

■ COMPARISON OF TREATMENTS

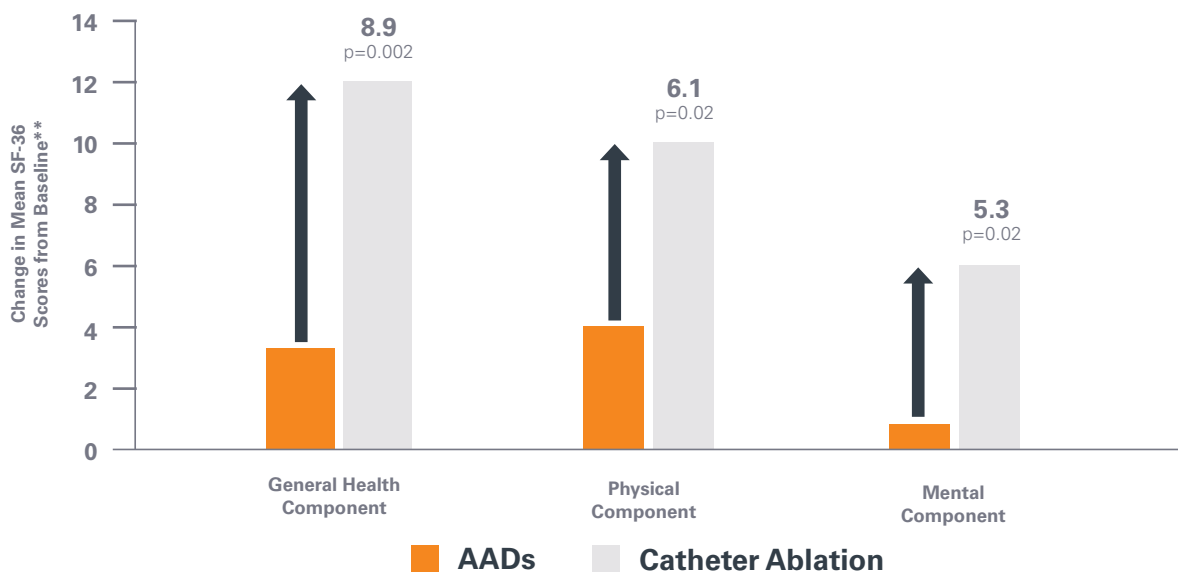
The **ATTEST randomized controlled** trial found that patients receiving ablation, with **paroxysmal AF** are almost **10 TIMES LESS LIKELY TO PROGRESS TO PERSISTENT AF** than **those on AADs***⁵⁹



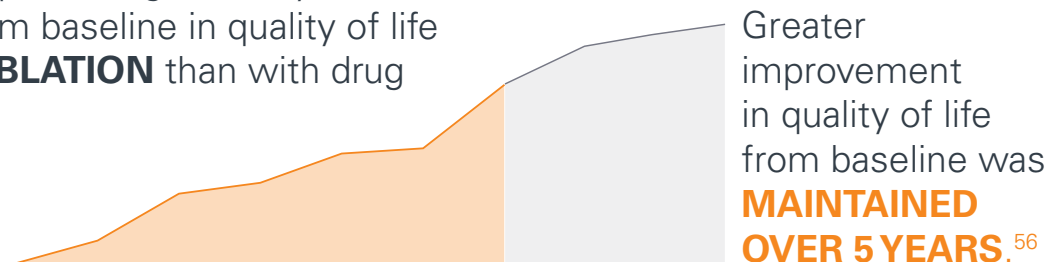
PATIENT IMPACT

Catheter ablation of AF results in a significantly greater improvement in patient quality of life than drug therapy.

- The CAPTAF trial reported a **significantly** and **clinically** relevant **greater improvement** from baseline in patient-reported quality of life with catheter ablation than AADs at 1 year.⁵⁸



The CABANA trial reported significantly **GREATER IMPROVEMENT** from baseline in quality of life **WITH CATHETER ABLATION** than with drug therapy at 1 year.



* (HR 0.11; 95% CI 0.02-0.48; p=0.0034)

**As measured by the SF-36 described in Section 4C.

Abbreviations: AAD = antiarrhythmic drug; CAPTAF = Catheter Ablation compared with Pharmacological Therapy for Atrial Fibrillation; SF-36 = Short Form 36 questionnaire. Source: Blomstrom-Lundqvist et al. (2019)

■ COMPARISON OF TREATMENTS

ECONOMIC IMPACT

Catheter ablation is cost effective compared to antiarrhythmic drugs for the long term treatment of patient with AF.

- A UK database analysis found that catheter ablation treatment was associated with reduced resource utilization compared to drugs over 1 year (excluding the 3 month blanking period).⁷⁶



51% REDUCTION
IN CARDIOVASCULAR-
RELATED OUTPATIENT VISITS
($p < 0.001$)



38% REDUCTION
IN INPATIENT ADMISSIONS
FOR HEART FAILURE
($p = 0.0318$)

- Despite the initial investment, costs become favorable for catheter ablation at 5 years after the initial ablation procedure when compared to antiarrhythmic drugs.⁶⁶

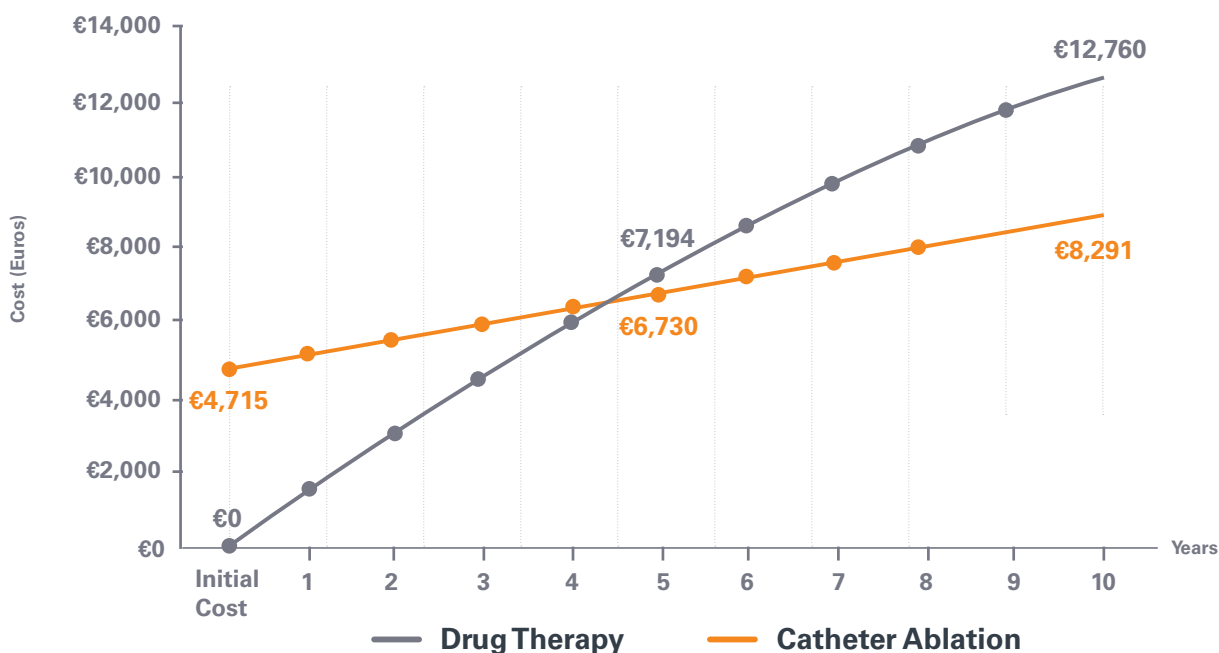


PROJECTING COSTS
TO 10 YEARS AFTER
ABLATION*



catheter ablation was
associated with a
35% SAVINGS
IN COSTS COMPARED TO
DRUG THERAPY⁶⁶

CUMULATIVE COSTS OF PAROXYSMAL AF TREATMENT OVER 10 YEARS



*Study performed in France; data were limited for other European countries.

Catheter ablation can be more clinically and cost effective when compared to drug therapy for the treatment of patients with AF.^{55, 57-59,66, 74}



94%

of patients are

FREE FROM ARRHYTHMIA RECURRENCE

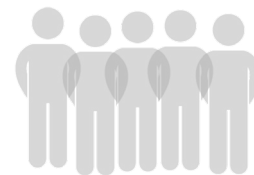
AT 1 YEAR⁴⁵⁻⁵⁴



PAROXYSMAL AF

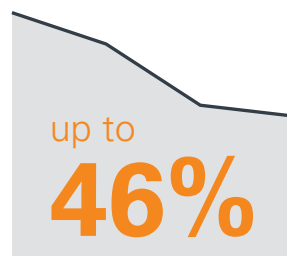


PERSISTENT AF



Patients with **paroxysmal AF** who undergo catheter ablation are almost **10 TIMES LESS LIKELY TO PROGRESS TO PERSISTENT AF** than **those on AADs**^{*59}

CATHETER ABLATION
was also associated with



significant reductions
in the probability of **AF-RELATED complications**



Death



Stroke



Cardiac arrest



Cardiovascular hospitalization

compared to drug therapy over 7-years follow-up.⁷⁴

AF can be effectively and safely treated with rhythm control therapies; overall disease management focuses on controlling the irregular heart rhythm, improving symptoms, and reducing key complications based on shared decision-making between healthcare professionals and patients.

NEW
ESC 2020³

- Many patients are unaware that **AF is a life-threatening condition**, therefore, programs that increase knowledge and diagnosis of AF are important tools that can:
 - **Reduce the risk of stroke and death** in patients with undiagnosed AF.^{13, 14}
 - **Lead to early treatment of AF** that may increase patient life expectancy and quality of life.^{16, 17}
- **Patient values** need to be considered in treatment decision making and incorporated into the AF management pathways; the structured assessment of PRO measures is an important element to document and measure treatment success.³
- The **ABC pathway** streamlines integrated care of AF patients across healthcare levels and among different specialities.³
- The primary indication for rhythm control using cardioversion, AADs, and/or catheter ablation is **reduction in AF-related symptoms and improvement of QoL**.³
- Catheter ablation is a well-established treatment for prevention of AF recurrences. When performed by appropriately trained operators, **catheter ablation is a safe and superior alternative to AADs** for maintenance of sinus rhythm and symptom improvement.³
- **Identification and management of risk factors and concomitant diseases** is an integral part of the treatment of AF patients.³
- **Major health modifiers causing AF**
 - What are the major the mechanisms causing AF in individual patients with pre-existing conditions (eg, cardiac structural remodelling, heart failure)?
 - How do education interventions translate into actual behavioural change in patients and physician that leads to improvements in clinical management and outcomes, especially in the multi-morbid AF patient?
- **Implementation of digital technologies for screening, diagnosis, and risk stratification in the AF patient**
 - How will new techniques for digital ECG analysis (eg, machine learning and artificial intelligence) and new technologies (eg, wearables and injectables) for detection and diagnosis of AF help to personalize therapy and stratify risk to the AF patient?
 - Which patient groups would benefit most from these new techniques and new technologies for the detection and diagnosis of AF?
- **Type of AF**
 - Recent data suggests that paroxysmal AF is not one entity and that according to the pattern, type of therapy and outcome may differ. Can paroxysmal AF be further classified?

The 2020 ESC/EACTS guidelines for the management of AF highlights key areas of future research including the following:³

NEW
ESC 2020³

■ AF catheter ablation technique

- What is the best approach to safely and expeditiously achieve permanent pulmonary vein isolation in a single procedure?
- Does ablating additional targets improve outcomes of AF catheter ablation?

■ Outcome of AF catheter ablation

- What is the value of early AF ablation in preventing AF progression?
- What is the optimal outcome measure (eg, AF 30 sec, AF burden, etc.) for AF-related outcome?
- How much reduction in AF burden is needed to achieve an effect on hard endpoints, including survival, stroke, and comorbidity?
- What is the main mechanism of PVI translating into freedom of AF?
- What is the potential effect of cardiac structure and function on the likelihood of success of AF ablation?
- What is the effect of AF catheter ablation on clinical outcomes, including death, stroke, serious bleeding, AF recurrence, QoL, and cardiac arrest?
- What is relationship between the degree of atrial dilation/fibrosis and successful AF ablation?
- What is the impact of specific components of structural heart disease, including left atrial structure/function, left ventricular function, etc. on:
 - the success of AF catheter ablation?
 - the likelihood of AF recurrence?

■ Who may benefit less from AF catheter ablation

- There are gaps in knowledge about subgroups of patients who may benefit less from AF catheter ablation, including:
 - Persistent and long-standing persistent AF
 - Patients with enlarged atrial size and/or atrial fibrosis
 - Patients with atypical atrial flutter
 - Patients with risk factors of AF recurrence, including obesity or sleep apnea

■ Personalized therapy

- Can improved assessment of the pathophysiological process involved in the individual patient through the use of clinical characteristics, blood biomarkers, and non-invasive substrate determination (ie, echo/MRI/CT) improve personalized therapy (eg, selection of rhythm control, treatment of risk factors and comorbidities, type of AAD, atrial ablation, and which type/techniques used for AF)?

1. Iazzo PA (2015). Handbook of Cardiac Anatomy, Physiology and Devices. Springer Science and Business Media, LLC: Switzerland.
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3. Hindricks G, Potpara T, Dagres N, Arbelo E, Bax JJ et al. (2020) 2020 ESC Guidelines for the diagnosis and management of atrial fibrillation developed in collaboration with the European Association of 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. *European Heart Journal*.
4. Naser N, Dilic M, Durak A, Kulic M, Pepic E et al. (2017) The Impact of Risk Factors and Comorbidities on The Incidence of Atrial Fibrillation. *Mater Sociomed* 29 (4): 231-236.
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