Supraventricular Arrhythmias.
Management in Elderly.
State of knowledge.

Bratislava, 1st July, 2016
Daniel Lighezan, FESC
NMN - The Latest Anti-Aging Drug to be Tried on Humans

Posted on June 23, 2016, 6 a.m. in Anti-Aging Research Science | Anti-Aging | Diabetes

Researchers are planning to test nicotinamide mononucleotide (NMN) on a small group of 10 healthy people.

Nicotinamide mononucleotide (NMN), a compound that has shown to slow the aging process in animals, is now going to be used in a clinical study to test its safety and effectiveness in humans. Keio University's Research Ethics Committee is going to explore the appropriateness of the idea, and if the plan is accepted, Washington University in St. Louis and Keio University will begin this study in Japan next month. The researchers will then give the compound, nicotinamide mononucleotide to ten healthy people and study whether NMN can improve bodily functions. A research group including Prof. Shinichiro Imai of Washington University found NMN could potentially extend people’s life spans by activating a gene known for its anti-aging effects called sirtuin. Sirtuins are able to silence certain genes, including ones that promote aging. When mice were given NMN, it was found that the compound can reverse age-related eyesight and metabolism deteriorations. “We’ve confirmed a remarkable effect in the experiment using mice, but it’s not clear yet how much [the compound] will affect humans,” Imai said. “We’ll carefully conduct the study, which I hope will result in important findings originating in Japan.” Next fiscal year, the government will contribute full-fledged support to anti-aging studies, promoting research in this field and benefiting the NMN clinical trial.
Introduction

- Most cardiac arrhythmias in the elderly are the consequence of:
  - hypertension
  - coronary artery disease
  - Heart failure......

- Problems of the cardiovascular system that are related to ageing:
  - vascular stiffness
  - a reduced adrenergic cardiovascular response,
  - an increased dependency on the atrial contribution to left ventricular diastolic filling,
  - a greater likelihood of coronary artery disease
  - are all factors that exacerbate the symptoms and worsen the prognosis when arrhythmias appear
In the elderly, arrhythmias are a significant cause of:
- falls,
- physical disability,
- frequent hospital admissions.

With the exception of atrial fibrillation and flutter, the remaining supraventricular tachycardias do not adversely affect the patient’s prognosis.
Background

- SVT is a common clinical condition that occurs in persons of all age groups, and treatment can be challenging.

- **SVT in general is any tachyarrhythmia that requires atrial and/or atrioventricular (AV) nodal tissue for its initiation and maintenance.** It is usually a narrow-complex tachycardia that has a regular, rapid rhythm; exceptions include atrial fibrillation (AF) and multifocal atrial tachycardia (MAT). Aberrant conduction during SVT results in a wide-complex tachycardia.

- The most common mechanism identified is reentry.
Classification

Depending on the site of origin of the dysrhythmia, SVT may be classified as an atrial or AV tachyarrhythmia.

**Atrial tachyarrhythmias include the following:**
- Sinus tachycardia
- Inappropriate sinus tachycardia (IST)
- Sinus nodal reentrant tachycardia (SNRT)
- Atrial tachycardia
- Multifocal atrial tachycardia
- Atrial flutter
- Atrial fibrillation

**AV tachyarrhythmias include the following:**
- AV nodal reentrant tachycardia (AVNRT)
- AV reentrant tachycardia (AVRT)
- Junctional ectopic tachycardia (JET)
- Nonparoxysmal junctional tachycardia (NPJT)
Etiology

- SVT and paroxysmal SVT are triggered by a reentry mechanism. This may be induced by premature atrial or ventricular ectopic beats. Other triggers include hyperthyroidism and stimulants, including caffeine, drugs, and alcohol.

- It is also common in patients with previous myocardial infarction, mitral valve prolapse, rheumatic heart disease, pericarditis, pneumonia, chronic lung disease, and current alcohol intoxication.
Atrial tachyarrhythmias
Sinus Tachycardia

- Sinus tachycardia is the most common regular SVT. It has an accelerated sinus rate that is a physiologic response to a stressor. It is characterized by a heart rate faster than 100 beats per minute (bpm) and generally involves a regular rhythm with p waves before all QRS complexes.

- Underlying physiologic stresses such as hypoxia, hypovolemia, fever, anxiety, pain, hyperthyroidism, and exercise usually induce sinus tachycardia.

- Certain drugs, such as stimulants (eg, nicotine, caffeine), medications (eg, atropine, salbutamol), recreational drugs (eg, cocaine, amphetamines, ecstasy), and hydralazine, can also induce the condition. Treatment involves addressing the basic underlying stressor.
Inappropriate sinus tachycardia

- IST is an accelerated baseline sinus rate in the absence of a physiologic stressor. In this situation, healthy adults may have an elevated resting heart rate and an exaggerated heart rate response to even minimal exercise. This tachyarrhythmia is observed most commonly in young women without structural heart disease.

- The underlying mechanism of IST may be hypersensitivity of the sinus node to autonomic input or an abnormality within the sinus node and/or its autonomic input. P wave morphology is normal on ECG and it is a diagnosis of exclusion.
Sinus nodal reentrant tachycardia

- SNRT is frequently confused with IST. SNRT is due to a reentry circuit, either in or near the sinus node. Therefore, it has an abrupt onset and offset. The heart rate is usually 100-150 bpm, and electrocardiographic tracings usually demonstrate a normal sinus P wave morphology.
Atrial tachycardia

- is an arrhythmia originating in the atrial myocardium. Enhanced automaticity, triggered activity, or reentry may result in this rare tachycardia

- The heart rate is regular and is usually 120-250 bpm. The P-wave morphology is different from the sinus P waves and is dependent on the site of origin of the tachycardia

- Because the arrhythmia does not involve the AV node, nodal blocking agents, such as adenosine and verapamil, are usually unsuccessful in terminating this arrhythmia. Atrial tachycardia has also been associated with digoxin toxicity via the triggered mechanism
Multifocal atrial tachycardia

- is a tachyarrhythmia that arises within the atrial tissue; it is composed of 3 or more P-wave morphologies and heart rates. This arrhythmia is fairly uncommon; it is typically observed in elderly patients with pulmonary disease. The heart rate is greater than 100 bpm, and electrocardiographic findings typically include an irregular rhythm, which may be misinterpreted as atrial fibrillation (see the image below). Treatment involves correcting the underlying disease process.

- Magnesium and verapamil may sometimes be effective
Atrial flutter

- is a **tachyarrhythmia arising above the AV node with an atrial rate of 250-350 bpm**. The mechanism behind atrial flutter is generally reentrant in nature. Typically, counterclockwise atrial flutter is due to a **macroreentrant right atrial circuit**. It is commonly observed in patients with any of the following conditions:
  - Ischemic heart disease
  - Myocardial infarction
  - Cardiomyopathy
  - Myocarditis
  - Pulmonary embolus
  - Toxic ingestion (e.g., alcohol)
  - Chest trauma
Atrial Fibrillation

- is an extremely common arrhythmia arising from chaotic atrial depolarization. The atrial rate is usually 300-600 bpm, while the ventricular rate may be 170 bpm or more. Electrocardiographic findings characteristically include an irregular rhythm with fibrillatory atrial activity.
AV tachyarrhythmias
AV nodal reentrant tachycardia

- One of the common causes of paroxysmal SVT is AVNRT. AVNRT is diagnosed in 50-60% of patients who present with regular narrow QRS tachyarrhythmia and is often in people older than 20 years.
AV reentrant tachycardia

- AVRT is another common form of paroxysmal SVT. The incidence rate of AVRT in the general population is 0.1-0.3%. AVRT is more common in males than in females (male-to-female ratio of 2:1), and patients with AVRT commonly present at a younger age than do patients with AVNRT. AVRT is associated with the Ebstein anomaly, although most patients with AVRT do not have evidence of structural heart disease.

- AVRT results from the presence of 2 or more conducting pathways; specifically, the AV node and 1 or more bypass tracts. In a normal heart, only a single route of conduction is present. Conduction begins at the sinus node, progresses to the AV node, and then to the bundle of His and the bundle branches. However, in AVRT, 1 or more accessory pathways connect the atria and the ventricles. The accessory pathways may conduct impulses in an anterograde manner, a retrograde manner, or both.
A reentry circuit may also be established by a premature impulse traveling in an anterograde manner through a manifest accessory pathway and in a retrograde manner through the AV node; this is called antidromic AVRT. While the orthodromic AVRT is typically a narrow-complex tachycardia, antidromic AVRT inscribes a bizarre, wide-complex tachycardia.
Junctional ectopic tachycardia and nonparoxysmal junctional tachycardia

- JET and NPJT are rare; they presumably arise because of increased automaticity, triggered activity, or both. They are usually observed following valvular surgery, after myocardial infarction, during active rheumatic carditis, or with digoxin toxicity. These tachycardias are also observed in children following congenital heart surgery. Electrocardiographic findings include a regular narrow QRS complex, although P waves may not be visible. Patients with AV dissociation have also been described.
The distribution of arrhythmias for catheter ablation in elderly patients varied from centre to centre
- atrioventricular nodal re-entrant tachycardia ablations in 18.8% (in 48 centres),
- accessory pathway ablations 7.2% (47 centres),
- his bundle ablations (for rate control) 17.0% (48 centres),
- AF ablations 18.6% (46 centres),
- atrial tachycardia/flutter ablations 27.7% (49 centres)
- ventricular arrhythmia ablations in 10.7% (48 centres), respectively.

There was no age limit for supraventricular tachycardia ablation in most centres. On the contrary, the age limit was set for complicated ablation procedures in many centres.
Atrial Fibrillation
a degenerative condition of ‘old age’ (?)
This arrhythmia is associated with the following conditions:

- Hypertension
- Ischemic heart disease
- Thyrotoxicosis
- Alcohol intoxication
- Pericarditis
- Mitral valve prolapse and other disorders of the mitral valve
- Rheumatic heart disease
- Digitalis toxicity
Peripheral arterial disease is associated with an increased risk of atrial fibrillation in the elderly

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Epidemiology

- There has been a worldwide increase in the ageing population
- 25 to 30 million in Europe by 2050
- Age is the most significant risk factor for AF
- Diseases with increased incidence in elderly:
  - Heart failure
  - Stroke
  - Diabetes
  - Atherosclerosis
  - Cancer
  - Vascular dementia
  - Alzheimer’s disease
  - Parkinsonism
  - Arthritis
Age and Atrial Fibrillation

- The prevalence of AF shows a strong age dependence varying from 0.5% in patients aged <40 years to 5% in patients aged >65 years and nearly 10% amongst octogenarians.
- Both the Framingham Heart Study and the Rotterdam Study estimated that the lifetime risk for development of AF in adults >40 years and at the age of 55 years respectively to be approximately 1 in 4.
- The Cardiovascular Health Study:
  - a large population study of 5201 elderly adults showed an incidence of 17.6 and 42.7 events per 1000 person-years amongst men aged 65 to 74 years and 75 to 84 years, respectively, whereas amongst women
  - the incidences were 10.1 and 21.6.

- The SAFE study which was a UK-based multicentre randomised control trial of elderly (≥65 years) patients with AF showed an overall prevalence of 7.2% and 10.3% in those aged 75 years and older, 1.6% yearly incidence of new AF.

Incidence of AF with Age

Prevalence of atrial fibrillation in four population-based surveys; Epidemiology of arrhythmias and conduction disorders in older adults.

Chow GV1, Marine JE, Fleg JL.
Atrial Fibrillation, Age and Sex

There is an increase in the number of people with Atrial Fibrillation as age increases.

- Men
- Women
Management objectives in AF

- Rate control
- Prevention of TE
- Rhythm control
Recent-onset AF

Haemodynamic instability

yes

Emergency

Elective

no

Patient/physician choice

electrical

Structural heart disease

severe

Intravenous ibutilide
d
Intravenous amiodarone

Moderate

Intravenous flecainide
d propafenone
d vernakalant
d
Intravenous amiodarone

None

Pill-in-the-pocket (high dose oral)
d flecainide propafenone

pharmacological

Intravenous flecainide propafenone vernakalant

Intravenous amiodarone

Intravenous amiodarone

Pill-in-the-pocket technique – preliminary assessment in a medically safe environment and then used by the patient in the ambulatory setting.

*ibutilide should not be given when significant left ventricular hypertrophy (≥1.4 cm) is present.

Vernakalant should not be given in moderate or severe heart failure, aortic stenosis, acute coronary syndrome or hypotension. Caution in mild heart failure.

*Pill-in-the-pocket* technique – preliminary assessment in a medically safe environment and then used by the patient in the ambulatory setting.
Management in Patients with newly discovered AF

- Recent onset AF
  - Hemodynamic Instability
    - Yes: Emergency
    - No: TE risk assessment and rate control vs rhythm control should be considered
      - Elective
      - Pharmacologic Cardioversion
  - Electrical Cardioversion
Management objectives in AF

Rate control

AF

Prevention of TE

Rhythm control
Pharmacologic management in Patients with newly discovered AF

Newly Discovered AF

Paroxysmal

No therapy needed unless symptoms (e.g., hypotension, HF, angina)

Anticoagulation as needed

Persistent

Rate control and anticoagulate as needed

Consider antiarrhythmic drug therapy

Cardioversion

Long-term antiarrhythmic drug therapy unnecessary

Accept permanent AF

Anticoagulation and rate control as needed
Atrial fibrillation-rate vs rhythm control

**AFFIRM: All-Cause Mortality**

- **Rate**
- **Rhythm**

- \( p=0.078 \) unadjusted
- \( p=0.068 \) adjusted

<table>
<thead>
<tr>
<th>Rhythm N</th>
<th>Rate N</th>
</tr>
</thead>
<tbody>
<tr>
<td>2033</td>
<td>2027</td>
</tr>
<tr>
<td>1932</td>
<td>1925</td>
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<tr>
<td>1807</td>
<td>1825</td>
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<td>1316</td>
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</tr>
<tr>
<td>780</td>
<td>774</td>
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<tr>
<td>255</td>
<td>236</td>
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</table>

Choice of Oral Antiarrhythmic Drug

- Minimal or no structural heart disease
  - Treatment of underlying condition and prevention of remodelling – ACE-I / ARB / statin
    - HHD
      - No LVH
        - dronedarone / flecainide / propafenone / sotalol
        - amiodarone
    - LVH
      - dronedarone
      - amiodarone

- Significant structural heart disease
  - CHD
    - sotalol
  - HF
    - amiodarone

ACE-I = angiotensin-converting enzyme inhibitor; ARB = angiotensin-receptor blocker; HHD = hypertensive heart disease; CHD = coronary heart disease; HF = heart failure; LVH = left ventricular hypertrophy. NYHA = New York Heart Association.
# Oral Antiarrhythmic Drugs

## Recommendations for oral antiarrhythmic agents

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>Class</th>
<th>Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dronedarone is recommended in patients with recurrent AF as a moderately effective antiarrhythmic agent for the maintenance of sinus rhythm.</td>
<td>I</td>
<td>A</td>
</tr>
<tr>
<td>Short-term (4 weeks) antiarrhythmic therapy after cardioversion may be considered in selected patients e.g., those at risk for therapy associated complications.</td>
<td>IIb</td>
<td>B</td>
</tr>
<tr>
<td>Dronedarone is not recommended in patients with permanent AF.</td>
<td>III</td>
<td>B</td>
</tr>
</tbody>
</table>
Choice of antiarrhythmic drugs

- Adverse effects may occur when antiarrhythmic drugs are administered to patients older than 75 years.

- Several antiarrhythmic drugs would raise concern related to prescription to elderly patients with arrhythmias:
  - flecainide in 26 (52.0%) centres,
  - amiodarone in 15 (30.0%) centres,
  - digitalis in 13 (26.0%) centres,
  - dronedarone in 11 (22.0%) centres,
  - β-blocker in 9 (18.0%) centres,
  - calcium channel blocker in 8 centres (16.0%),
  - adenosine in 4 (8.0%),
  - and none of above drugs were concerned in 12 (24.0%) centres.

The impact of physiological changes associated with age on the pharmacokinetic and pharmacodynamic properties of drugs can be considerable.

This is especially so for those drugs that are principally renally excreted and/or are nephrotoxic.

These drugs typically have a narrow therapeutic range and dose adjustment may be required to avoid drug accumulation and toxicity.

Reliance on the serum creatinine concentration is inappropriate in the elderly patient population and may lead to dosing errors and avoidable toxicity.

More accurate methods of assessment of renal function are readily available.
Antiarrhythmic drugs

- Treatment in elderly is also particularly challenging due to:
  - lack of good hemodynamic reserves
  - frequency of electrolyte disturbance
  - high prevalence of coronary disease

- Following Adverse Drug Reaction due to decreased clearance:
  - hypotension
  - light-headedness, seizures
  - confusion
  - slurred speech
Physiologic Changes of Aging Affecting Absorption

- Physiologic change
  - Decreased gastric acidity
  - Decreased gastrointestinal blood flow
  - Delayed gastric emptying
  - Slowed intestinal transit time

- General clinical effect
  - None on passive diffusion or bioavailability for most drugs
  - Decreased active transport: Decreased bioavailability for some drugs
  - Decreased first-pass effect: Increased bioavailability for some drugs
Physiologic Changes of Aging Affecting Distribution

- Decreased Total body water
  - Increased Plasma Conc. of water soluble drugs
  - Lower doses are required: Lithium, digoxin, ethanol, etc

- Decreased Lean body mass
  - Increased Volume Distribution, Longer ($t_{1/2}$) of water soluble drugs
  - Accumulation into fat of lipid soluble drugs: Benzos, etc

- Decreased Serum Albumin
  - Increased unbound fraction of highly protein bound drugs
  - Binds acidic drugs: warfarin, phenytoin, digitalis, etc

- Decreased Alpha1 Acid glycoprotein
  - Increased unbound fraction of highly protein bound drugs
  - Binds basic drugs: lidocaine and propranolol, etc
Aging Effects on Hepatic Metabolism

- Metabolic clearance of drugs by the liver may be reduced due to:
  - decreased hepatic blood flow
  - decreased liver size and mass

- **Examples**: morphine, meperidine, metoprolol, propranolol, verapamil, amitriptyline, nortriptyline
Major Reasons for Adverse Drug Reactions in the Elderly

- Positive relationship between number of drugs taken and incidence
- Overall incidence is estimated to be at least twice that in the younger population
- Prescribing errors
  - Polypharmacy
  - Drug interactions with other prescriptions
  - Unawareness of age related physiologic changes
- Drug usage errors
  - “Hidden ingredients”: OTCs
Pharmacodynamic changes in elderly

- Pharmacodynamic changes in the elderly have been less extensively studied
- Evidence of enhanced end-organ responsiveness or “sensitivity” to medications with aging
- Enhanced “sensitivity” may be due
  - Changes in receptor affinity
  - Changes in receptor number
  - Post-receptor alteration
  - Age-related impairment of homeostatic mechanisms
    - Example: decreased baroreceptor reflexes
Management objectives in AF

- Rate control
- Prevention of TE
- Rhythm control
Established stroke risk factors

High-Risk Factors
- Mitral stenosis
- Prosthetic heart valve
- History of stroke or TIA

Moderate-Risk Factors
- Age > 75 years
- Hypertension
- Diabetes mellitus
- Heart failure or ↓ LV function

Less Validated Risk Factors
- Age 65–75 years
- Coronary artery disease
- Female gender
- Thyrotoxicosis
### Stroke risk stratification in non valvular AF

<table>
<thead>
<tr>
<th>Definition and Scores for CHADS$_2$ and CHA$_2$DS$_2$-VASc</th>
<th>Score</th>
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</thead>
<tbody>
<tr>
<td><strong>CHADS$_2$</strong></td>
<td></td>
</tr>
<tr>
<td>Congestive HF</td>
<td>1</td>
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<tr>
<td>Hypertension</td>
<td>1</td>
</tr>
<tr>
<td>Age $\geq$75 y</td>
<td>1</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>1</td>
</tr>
<tr>
<td>Stroke/TIA/TE</td>
<td>2</td>
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<tr>
<td><strong>Maximum score</strong></td>
<td>6</td>
</tr>
<tr>
<td><strong>CHA$_2$DS$_2$-VASc</strong></td>
<td></td>
</tr>
<tr>
<td>Congestive HF</td>
<td>1</td>
</tr>
<tr>
<td>Hypertension</td>
<td>1</td>
</tr>
<tr>
<td>Age $\geq$75 y</td>
<td>2</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>1</td>
</tr>
<tr>
<td>Stroke/TIA/TE</td>
<td>2</td>
</tr>
<tr>
<td>Vascular disease (prior MI, PAD, or aortic plaque)</td>
<td>1</td>
</tr>
<tr>
<td>Age 65–74 y</td>
<td>1</td>
</tr>
<tr>
<td>Sex category (i.e., female sex)</td>
<td>1</td>
</tr>
<tr>
<td><strong>Maximum score</strong></td>
<td>9</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>CHA$_2$DS$_2$-VASc Score</th>
<th>Stroke Risk %</th>
</tr>
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<tbody>
<tr>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>1</td>
<td>1.3</td>
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<tr>
<td>2</td>
<td>2.2</td>
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<tr>
<td>3</td>
<td>3.2</td>
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<td>4</td>
<td>4.0</td>
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<td>5</td>
<td>6.7</td>
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<td>6</td>
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<td>7</td>
<td>9.6</td>
</tr>
<tr>
<td>8</td>
<td>12.5</td>
</tr>
<tr>
<td>9</td>
<td>15.2</td>
</tr>
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# Has-Bled Score

<table>
<thead>
<tr>
<th>CHA\textsubscript{2}DS\textsubscript{2}-VASc</th>
<th>Score</th>
<th>HAS-BLED</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Congestive heart failure/LV dysfunction</td>
<td>1</td>
<td>Hypertension i.e. uncontrolled BP</td>
<td>1</td>
</tr>
<tr>
<td>Hypertension</td>
<td>1</td>
<td>Abnormal renal/liver function</td>
<td>1 or 2</td>
</tr>
<tr>
<td>Aged ≥75 years</td>
<td>2</td>
<td>Stroke</td>
<td>1</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>1</td>
<td>Bleeding tendency or predisposition</td>
<td>1</td>
</tr>
<tr>
<td>Stroke/TIA/TE</td>
<td>2</td>
<td>Labile INR</td>
<td>1</td>
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<tr>
<td>Vascular disease [prior MI, PAD, or aortic plaque]</td>
<td>1</td>
<td>Age (e.g. &gt;65)</td>
<td>1</td>
</tr>
<tr>
<td>Aged 65-74 years</td>
<td>1</td>
<td>Drugs (e.g. concomitant aspirin or NSAIDSs) or alcohol</td>
<td>1</td>
</tr>
<tr>
<td>Sex category [i.e. female gender]</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Maximum score</strong></td>
<td><strong>9</strong></td>
<td></td>
<td><strong>9</strong></td>
</tr>
</tbody>
</table>
### Recommendations for prevention of thromboembolism in non-valvular AF - general

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>Class</th>
<th>Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antithrombotic therapy to prevent thromboembolism is recommended for all patients with AF, except in those patients (both male and female) who are at low risk (aged &lt;65 years and lone AF), or with contraindications.</td>
<td>I</td>
<td>A</td>
</tr>
<tr>
<td>The choice of antithrombotic therapy should be based upon the absolute risks of stroke/thromboembolism and bleeding and the net clinical benefit for a given patient.</td>
<td>I</td>
<td>A</td>
</tr>
<tr>
<td>The CHA₂DS₂-VASc score is recommended as a means of assessing stroke risk in non-valvular AF.</td>
<td>I</td>
<td>A</td>
</tr>
<tr>
<td>Female patients who are aged &lt;65 and have lone AF (but still have a CHA₂DS₂-VASc score of 1 by virtue of their gender) are low risk and no antithrombotic therapy should be considered.</td>
<td>IIa</td>
<td>B</td>
</tr>
</tbody>
</table>
Choice of Anti-coagulant

- Includes rheumatic valvular AF, hypertrophic cardiomyopathy, etc.

** Antiplatelet therapy with aspirin plus clopidogrel, or – less effectively – aspirin only, may be considered in patients who refuse any OAC

Atrial fibrillation

- Yes
  - Valvular AF*
    - No (i.e. non-valvular AF)
      - Yes
        - < 65 years and lone AF (including females)
          - Yes
            - No antithrombotic therapy
          - No
            - Assess risk of stroke (CHA₂DS₂-VASc score)
              - 0
                - Oral anticoagulant therapy
                  - NOAC
              - 1**
                - Oral anticoagulant therapy
                  - NOAC
              - ≥2
                - Oral anticoagulant therapy
                  - NOAC

** Oral anticoagulant therapy

- NOAC
- VKA


www.escardio.org/guidelines
## Common NOAC’s

<table>
<thead>
<tr>
<th>Drug characteristics</th>
<th>Dabigatran (RE-LY)⁷⁰,⁷¹</th>
<th>Rivaroxaban (ROCKET-AF)³</th>
<th>Apixaban (ARISTOTLE)⁴</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mechanism</strong></td>
<td>Oral direct thrombin inhibitor</td>
<td>Oral direct factor Xa inhibitor</td>
<td>Oral direct factor Xa inhibitor</td>
</tr>
<tr>
<td><strong>Bioavailability, %</strong></td>
<td>6</td>
<td>60–80</td>
<td>50</td>
</tr>
<tr>
<td><strong>Time to peak levels, h</strong></td>
<td>3</td>
<td>3</td>
<td>3</td>
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<tr>
<td><strong>Half-life, h</strong></td>
<td>12–17</td>
<td>5–13</td>
<td>9–14</td>
</tr>
<tr>
<td><strong>Excretion</strong></td>
<td>80% renal</td>
<td>2/3 liver, 1/3 renal</td>
<td>25% renal, 75% faecal</td>
</tr>
<tr>
<td><strong>Dose</strong></td>
<td>150 mg b.i.d.</td>
<td>20 mg o.d.</td>
<td>5 mg b.i.d.</td>
</tr>
<tr>
<td><strong>Dose in renal impairment</strong></td>
<td>110 mg b.i.d.</td>
<td>15 mg o.d. (if CrCl 30-49 mL/min)</td>
<td>2.5 mg b.i.d.</td>
</tr>
<tr>
<td><strong>Special considerations</strong></td>
<td>Intestinal absorption is pH-dependent and is reduced in patients taking proton pump inhibitors</td>
<td>Higher levels expected in patients with renal or hepatic failure</td>
<td>Increased risk of bleeding in patients taking verapamil/amiodarone/quinidine/ketoconazole</td>
</tr>
</tbody>
</table>
Last Intake before elective Surgery

<table>
<thead>
<tr>
<th>Dabigatran</th>
<th>Apixaban–Edoxaban–Rivaroxaban</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>No important bleeding risk and/or adequate local haemostasis possible: perform at trough level (i.e. ≥12 or 24 h after last intake)</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Low risk</strong></td>
<td><strong>High risk</strong></td>
</tr>
<tr>
<td>CrCl ≥80 mL/min</td>
<td>≥24 h</td>
</tr>
<tr>
<td>CrCl 50–80 mL/min</td>
<td>≥36 h</td>
</tr>
<tr>
<td>CrCl 30–50 mL/min(^a)</td>
<td>≥72 h</td>
</tr>
<tr>
<td>CrCl 15–30 mL/min(^a)</td>
<td>≥96 h</td>
</tr>
<tr>
<td>CrCl &lt;15 mL/min</td>
<td>Not indicated</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>High risk</strong></td>
<td><strong>Low risk</strong></td>
</tr>
<tr>
<td></td>
<td>≥24 h</td>
</tr>
<tr>
<td></td>
<td>≥24 h</td>
</tr>
<tr>
<td></td>
<td>≥48 h</td>
</tr>
<tr>
<td></td>
<td>≥48 h</td>
</tr>
</tbody>
</table>

- **No official indication for use**

**There is no need for pre-operative bridging with LMWH/UFH**

Bold values deviate from the common stopping rule of ≥24 h low risk, ≥48 h high risk.
Low risk: with a low frequency of bleeding and/or minor impact of a bleeding; high risk with a high frequency of bleeding and/or important clinical impact.
CrCl, creatinine clearance.
\(^a\) Many of these patients may be on the lower dose of dabigatran (i.e. 110 mg BID) or apixaban (i.e. 2.5 mg BID), or have to be on the lower dose of rivaroxaban (i.e. 15 mg OD) or edoxaban (i.e. 30 mg OD).
Bleeding Risk

Bleeding while using a NOAC

- Inquire about last NOAC intake
- Blood sample to determine creatinine (clearance), hemoglobin and WBC
- Inquire lab on possibility for rapid coagulation assessment

Mild bleeding

- Delay or discontinue next dose
- Reconsider concomitant medication

Moderate severe bleeding

Supportive measures:

- mechanical compression
- endoscopic hemostasis if gastro-intestinal bleed
- surgical hemostasis
- fluid replacement (colloids if needed)
- RBC substitution if needed
- fresh frozen plasma (as plasma expander)
- platelet substitution (if platelet count ≤60x10^9/L)

For dabigatran:

- maintain adequate diuresis
- consider hemodialysis
- consider idarucizumab 5g IV (approval pending)
- (charcoal haemoperfusion?)

Life-threatening bleeding

- For dabigatran-treated patients: idarucizumab 5g IV

Otherwise, consider:

- PCC (e.g. Beriplex®, CoFact®) 50 U/kg; +25 U/kg if indicated
- aPCC (Feiba®) 50 U/kg; max 200 U/kg/day
- (rFVIIa (NovoSeven®) 90 μg/kg no data about additional benefit )

Heidbuchel 2016
Anticoagulant therapy in elderly-EHRA survey

- Long-term anticoagulant therapy
  - 62% - VKA
  - 38% - NOAC

- After radiofrequency ablation
  - 76% - VKA
  - 22% - NOAC
  - 2% aspirin

Anticoagulation in Elderly

- Management of heart rhythm disorders in elderly patients (>75 years old) is influenced by geriatric pathophysiologic factors
- 50 centers, 20 countries
- Anticoagulant use in patients with atrial fibrillation EHRA survey 2
  - 19.2% are not anticoagulated with AVK, nor NOACs

Reasons not to anticoagulate-EHRA survey

- High risk bleeding 72%
- Choice/family choice 48%
- Altered kidney function 32%
- Altered liver function 14%
- Question deemed irrelevant 4 centers 8%

Elderly and glomerular filtration rate

Table 26. Prevalence of GFR Categories in Adults

<table>
<thead>
<tr>
<th>GFR mL/min/1.73 m²</th>
<th>Age Group (y)</th>
<th>20–39</th>
<th>40–59</th>
<th>60–69</th>
<th>≥70</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥90</td>
<td></td>
<td>86.0%</td>
<td>55.7%</td>
<td>38.5%</td>
<td>25.5%</td>
</tr>
<tr>
<td>60–89</td>
<td></td>
<td>13.7%</td>
<td>42.7%</td>
<td>53.8%</td>
<td>48.5%</td>
</tr>
<tr>
<td>30–59</td>
<td>—a</td>
<td>1.8%</td>
<td>7.1%</td>
<td>24.6%</td>
<td></td>
</tr>
<tr>
<td>15–29</td>
<td>—a</td>
<td>—a</td>
<td>—a</td>
<td>1.3%</td>
<td></td>
</tr>
</tbody>
</table>

N (millions): 82 55 20 20

GFR estimated from serum creatinine using MDRD Study equation based on age, gender, race and calibration for serum creatinine. Data from NHANES III (1988–1994). N = 15,000. Based on one-time assessment of estimated GFR.

* Fewer than 20 cases; data not considered reliable.

Figure 1: Relationship of estimated glomerular filtration rate (eGFR) as derived by the MDRD formula to age*

* A: median (50% of subjects have eGFR above this line); B: 80% of subjects have eGFR above this line; C: 97.5% of subjects have eGFR above this line. These reference lines are derived from over 300,000 presentations to a large private pathology service, with exclusion of creatinine results lying outside a Gaussian distribution for each age decade (personal communication, Ken Sikaris, Chemical Pathologist, Melbourne Pathology Service, VIC).

Renal Function Impact on NOAC Half Lives

<table>
<thead>
<tr>
<th>renal function</th>
<th>dabigatran</th>
<th>rivaroxaban</th>
<th>apixaban</th>
<th>edoxaban</th>
</tr>
</thead>
<tbody>
<tr>
<td>CrCl &gt; 80 mL/min</td>
<td>12-17 h</td>
<td>5-9 h (young)</td>
<td>11-13 h (elderly)</td>
<td>12 h</td>
</tr>
<tr>
<td>CrCl 50-80 mL/min</td>
<td>=17 h</td>
<td>=8.7 h</td>
<td>=14.6 h</td>
<td>=8.6 h</td>
</tr>
<tr>
<td>CrCl 30-50 mL/min</td>
<td>=19 h</td>
<td>=9.0 h</td>
<td>=17.6 h</td>
<td>=9.4 h</td>
</tr>
<tr>
<td>CrCl 15-30 mL/min</td>
<td>=28 h</td>
<td>=9.5 h</td>
<td>=17.3 h</td>
<td>=16.9 h</td>
</tr>
<tr>
<td>CrCl ≤ 15 mL/min</td>
<td>No data</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
</tbody>
</table>

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
Hein Heidbuchel, Peter Verhamme, Marco Alings, et al

<table>
<thead>
<tr>
<th>Antiarrhythmic drugs:</th>
<th>Via</th>
<th>Dabigatran</th>
<th>Apixaban</th>
<th>Edoxaban</th>
<th>Rivaroxaban</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amiodarone</td>
<td>moderate P-gp competition</td>
<td>+12-60%</td>
<td>No PK data</td>
<td>+40%</td>
<td>Minor effect (use with caution if CrCl &lt;50 ml/min)</td>
</tr>
<tr>
<td>Digoxin</td>
<td>P-gp competition</td>
<td>No effect</td>
<td>No data yet</td>
<td>No effect</td>
<td>No effect</td>
</tr>
<tr>
<td>Diltiazem</td>
<td>P-gp competition and weak CYP3A4 inhibition</td>
<td>No effect</td>
<td>+40%</td>
<td>No data yet</td>
<td>Minor effect (use with caution if CrCl 15-50 ml/min)</td>
</tr>
<tr>
<td>Dronedarone</td>
<td>P-gp competition and weak CYP3A4 inhibition</td>
<td>+70-100% (US: 2 x 75 mg if CrCl 30-50 ml/min)</td>
<td>No PK or PD data; caution</td>
<td>+85% (Reduce NOAC dose by 50%)</td>
<td>Moderate effect but no PK or PD data; caution and try to avoid</td>
</tr>
<tr>
<td>Quinidine</td>
<td>P-gp competition</td>
<td>+53%</td>
<td>No data yet</td>
<td>+77% (No dose reduction required by label)</td>
<td>Extent of increase unknown</td>
</tr>
<tr>
<td>Verapamil</td>
<td>P-gp competition (and weak CYP3A4 inhibition)</td>
<td>+12-180% (reduce NOAC dose and take simultaneously)</td>
<td>No PK data</td>
<td>+53% (SR) (No dose reduction required by label)</td>
<td>Minor effect (use with caution if CrCl 15-50 ml/min)</td>
</tr>
</tbody>
</table>

**Red:** contra-indicated/not recommended. **Orange:** reduce dose (from 150 mg BID to 110 mg BID for dabigatran; from 20 to 15 mg OD for rivaroxiban; from 5 mg BID to 2.5 mg BID for apixaban). **Yellow:** consider dose reduction if two or more ‘yellow’ factors are present.
Patients with no anticoagulation in AF according to the specialty of the doctor who treated them

- Surgeon: 100%
- Neurologist: 100%
- Family Doctor: 81.3%
- Generalist: 68.8%
- Emergencist: 54.5%
- Cardiologist: 20.6%

Selection criteria for catheter ablation of AF

- **Technically it can be performed in almost anyone .... but it’s primarily indicated for symptom control not for prognosis!**

  - **Best results** - No structural heart disease & paroxysmal AF
    Serious complications = 1-2% per procedure
    Success = 85% with 1-2 procedures

  - **Less predictable results** – persistent AF & dilated LA / LVH
    Success = 70% with 1-2 procedures

  - **Research procedures** – paroxysmal or persistent AF in
    CCF / HCM or chronic persistent AF (> 12 mths)
### Table 1

Clinical efficacy and complication rates of AF ablation.

<table>
<thead>
<tr>
<th>Author</th>
<th>Patients (Age range in years)</th>
<th>AF type (Paroxysmal, persistent, chronic)</th>
<th>Mean follow-up (Months)</th>
<th>Clinical efficacy of ablation</th>
<th>Major complication</th>
<th>Ref.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hsieh et al.</td>
<td>37 (72 ± 4)</td>
<td>Paroxysmal</td>
<td>52 ± 6</td>
<td>81%</td>
<td>0%</td>
<td>19</td>
</tr>
<tr>
<td>Corrado et al.</td>
<td>174 (77 ± 6)</td>
<td>Paroxysmal 55 % Persistent 45%</td>
<td>20 ± 14</td>
<td>73 - 80%</td>
<td>1%</td>
<td>27</td>
</tr>
<tr>
<td>Zado et al.</td>
<td>948 (&lt;65)</td>
<td>Paroxysmal 65%</td>
<td>27 ± 13</td>
<td>89%</td>
<td>1.6%</td>
<td>20</td>
</tr>
<tr>
<td></td>
<td>185 (65-75)</td>
<td>Paroxysmal 62%</td>
<td></td>
<td>84%</td>
<td>1.7%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>32 (≥75)</td>
<td>Paroxysmal 53%</td>
<td></td>
<td>86%</td>
<td>2.9%</td>
<td></td>
</tr>
<tr>
<td>Leong-Sit et al.</td>
<td>232 (&lt;45)</td>
<td>Paroxysmal 71%</td>
<td>32 ± 20</td>
<td>87%</td>
<td>0</td>
<td>21</td>
</tr>
<tr>
<td></td>
<td>438 (45-54)</td>
<td>Paroxysmal 62%</td>
<td>31 ± 19</td>
<td>88%</td>
<td>1.7%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>570 (55-64)</td>
<td>Paroxysmal 66%</td>
<td>28 ± 17</td>
<td>88%</td>
<td>1.4%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>308 (≥65)</td>
<td>Paroxysmal 63%</td>
<td>28 ± 17</td>
<td>82%</td>
<td>2.6%</td>
<td></td>
</tr>
<tr>
<td>Traub et al.</td>
<td>45 (&lt;70)</td>
<td>Paroxysmal</td>
<td>19</td>
<td>80%</td>
<td>4.4%</td>
<td>22</td>
</tr>
<tr>
<td></td>
<td>15 (≥70)</td>
<td></td>
<td>23</td>
<td>60%</td>
<td>6.7%</td>
<td></td>
</tr>
<tr>
<td>Bunch et al.</td>
<td>717 (&lt;80)</td>
<td>Paroxysmal 46%</td>
<td>12</td>
<td>75%</td>
<td>0.7%</td>
<td>30</td>
</tr>
<tr>
<td></td>
<td>35 (≥80)</td>
<td>Paroxysmal 54%</td>
<td></td>
<td>78%</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Santangeli et al.</td>
<td>2651 (&lt;80)</td>
<td>Paroxysmal</td>
<td>18±6</td>
<td>71%</td>
<td>0</td>
<td>25</td>
</tr>
<tr>
<td></td>
<td>103 (≥80)</td>
<td></td>
<td></td>
<td>69%</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Radiofrequency catheter ablation of AF in older patients. Outcomes & Complications

<table>
<thead>
<tr>
<th></th>
<th>≤ 65 years</th>
<th>65-75 years</th>
<th>&gt; 75 years</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>91</td>
<td>88</td>
<td>61</td>
<td>---</td>
</tr>
<tr>
<td>Persistent AF</td>
<td>24%</td>
<td>34%</td>
<td>66%*</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>Major complications</td>
<td>1%</td>
<td>1%</td>
<td>0%</td>
<td>NS</td>
</tr>
<tr>
<td>Minor complications</td>
<td>4%</td>
<td>5%</td>
<td>5%</td>
<td>NS</td>
</tr>
<tr>
<td>SR without AARx</td>
<td>94%*</td>
<td>84%</td>
<td>61%</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>Hospital attendances Pre- vs Post-ablation</td>
<td>22 / 3</td>
<td>26 / 4</td>
<td>20 / 2</td>
<td>&lt; 0.01</td>
</tr>
</tbody>
</table>

Patients > 75 years: AF < 1 hour + AARx = 82%
Atrial Fibrillation-AV node ablation and implantation of a pacemaker

Alternative strategies in the elderly are AV node (AVN) ablation plus pacemaker placement. In the PABA-CHF study\textsuperscript{[13]} in a relatively young population (mean age 60 ± 8 years) pulmonary-vein isolation was superior to AVN ablation with biventricular pacing in patients with heart failure who had drug-refractory AF. Hsieh \textit{et al.}\textsuperscript{[14]} compared the long-term results (>4 years) of 71 elderly patients (>65 years old) with medically refractory paroxysmal AF who were assigned to either AVN ablation plus single-chamber (VVI or VVIR) pacemaker, versus pulmonary vein isolation, AF was better controlled in the group with AVN ablation and pacemaker placement than in the group with AF ablation (100% vs 81%, P = 0.013). Most other outcome variables favored the AF ablation.
Dr. Heimlich, 96, Saves Choking Woman With Namesake Maneuver

By Barbara Goldberg

May 31, 2016

- (Reuters) - Dr. Henry Heimlich, the 96-year-old Cincinnati surgeon credited with inventing the lifesaving technique named for him, used it for the first time this week to save a fellow senior center resident who was choking on a hamburger, a center spokesman said on Friday.

- Heimlich, who in multiple national television appearances had demonstrated the technique commonly known as the "Heimlich Maneuver" to dislodge food from an airway, had never employed it in an emergency, said spokesman Ken Paley.

- But on Monday, Heimlich was sitting at a communal dining table at Cincinnati's Deupree House, an upscale senior living center where he lives, and noticed fellow resident Patty Ris, 87, in distress while eating an open-faced hamburger.

- "I sort of felt wonderful about it, just having saved that girl," Heimlich said.
Thank You!