Vorhofflimmern und Schlaganfall –
Ablation, Antikoagulation,
Vorhofohrverschluß –
was wann wann für wen?

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Incidence of Atrial Fibrillation, Standard population of industrialised countries

> 60 years 5 %
> 70 years 7-8 %
> 80 years 10 %
Atrial Fibrillation and Mortality

• Mortality is at least 3 times higher in AF patients as compared to non AF patients
• This is mainly due to stroke and due to bleedings from oral anticoagulation
• No major difference in stroke rate between PAF, PsAF, LsAF
• AF patients are more likely to develop dementia*

Atrial Fibrillation, Categories

- Paroxysmal Atrial Fibrillation ( > 30 sec)
- Persistent Atrial Fibrillation ( > 7 days)
- Long standing persistent Atrial Fibrillation ( > 6 months)
- Permanent Atrial Fibrillation ( > 12 months)
Etiology of Atrial Fibrillation
multiple factors

- Mechanical stress / La dilatation
- Genetic alterations
- Atrial fibrosis
- Inflammation
- Autonomic hyperactivation
- Macroneference
AF disease progression without ablation during several years:

Paroxysmal AF  Persistent AF  Long standing AF

β-Blockers  Cardioversion  Amiodarone  Cardioversion  Cardioversion
How about AF symptoms during disease progression?

(fast and irregular heart beat, breathing problems, exercise insufficiency)

- Usually high symptom level in some patients with PAF and PsAF
- Often low symptom level in patients with LsAF
AF, Treatment Goals

• No stroke
• No dementia
• No symptoms
• No disease progression
Therapy of AF

- OAK / LAA Occlusion
- Drugs
- Cardioversion
- Ablation
Orale Antikoagulation

- Cumarine:
  - Coumadin (Warfarin)
  - Phenprocoumon (Falithrom/Marcumar)

- Direct Oral Anticoagulants (DOAK’s)
  a) Faktor 10a Antagonists
    - Apixaban (Eliquis),
    - Rivaroxaban (Xarelto)
  b) Thrombininhibitoren
    - Dabigatran (Pradaxa)
Plasmatische Gerinnung
DOAK´s vs. Warfarin

- RELY (Dabigatran)
- ARISTOTLE (Apixaban)
- ROCKET AF (Rivaroxaban)


RELY, intracerebral bleeding
Case 1

- 70 years, male
- Paroxysmal atrial fibrillation (PAF)
- No heart failure
- Does not want to take vitamin K antagonists because he is lazy

- What do you do?
- You are not lazy but your drug budget is stressed...
Case 1

- Still VKA
- Change to DOAK
- LAA occlusion
Left Atrial Appendage Occlusion
Watchman device

- Reduces stroke rate similar to warfarin (PROTECT-AF non inferiority trial)

Amplatzer™ Cardiac Plug
Watchman device, Protect AF Trial – long term follow up

Primary efficacy endpoint: Stroke, CV death (& unknown), Systemic embolism

All cause mortality
Case 2

• 76 years, male
• Ex professional cyclist, still 3 times per week on the bike
• Permanent atrial fibrillation (PmAF)
• LA 60mm, EF 65%, LVEDV 420ml, SV 273ml
• Resting heart rate 28´min, up to 8 s asystoly, does not want to take VKA any longer because he is afraid of injuries when falling off his bike

- What to do?
Case 2, cyclist 76 years

• Continue VKA
• Change to DOAK
• LAA occlusion

• Catheter ablation of atrial fibrillation yes/no
• Pacemaker yes/no
Therapy of AF - Drugs

- Metoprolol / Bisoprolol
- Amiodarone / Dronedarone
- Flecainid / Propafenone
Cardioversion

• First episode of paroxysmal or persistent atrial fibrillation

• Post ablation
Case 3

• 43 years, male
• Bus driver
• Paroxysmal atrial fibrillation (PAF) since 36 hours after excessive drinking
• EF normal, LA normal

What to do?
Case 3

- 43 years, male
- Bus driver
- Paroxysmal atrial fibrillation (PAF) since 36 hours after excessive drinking
- EF normal, LA normal

What to do?
TEE / cardioversion / 3 month OAK
**Case 4**

- 63 years, female
- Pulmonary vein isolation because of persistent atrial fibrillation 2 month ago
- Cardioversion day 2, cardioversion day 10, now again PsAF since two weeks

- What to do?
Case 4, 63 years, female, post ablation

- TEE/CV
- Change to frequency control
- Need to know more
Cardioversion

- Post ablation:
  How many electrical cardioversions should be applied for repetitive recurrences of atrial arrhythmias following ablation of persistent atrial fibrillation?

Figure 3 Kaplan–Meier estimate of the time to restoration of sinus rhythm for three consecutive months after ablation.

Figure 2 Distribution of the patients according to the number of electrical cardioversions applied in the patients with or without an ablation failure. ECs, electrical cardioversions.
How many ECs should be applied for repetitive recurrences of atrial arrhythmias?

Table 2 Predictors of ablation failure (n = 40)

<table>
<thead>
<tr>
<th>Variables</th>
<th>Univariate</th>
<th></th>
<th>Multivariate</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Age &gt;65 years</td>
<td>0.78 (0.34 – 1.63)</td>
<td>0.53</td>
<td>2.16 (0.49 – 15.77)</td>
<td>0.36</td>
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<tr>
<td>Female</td>
<td>0.95 (0.41 – 2.05)</td>
<td>0.91</td>
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<tr>
<td>Body mass index &gt;25 kg/m²</td>
<td>1.37 (0.70 – 2.71)</td>
<td>0.36</td>
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<tr>
<td>Long-standing persistent AF</td>
<td>2.85 (1.14 – 12.6)</td>
<td>0.049</td>
<td></td>
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<tr>
<td>Duration of AF of &gt;5 years</td>
<td>1.35 (0.69 – 2.85)</td>
<td>0.39</td>
<td></td>
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</tr>
<tr>
<td>Number of failed AADs of ≥2</td>
<td>1.49 (0.67 – 4.07)</td>
<td>0.37</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>1.51 (0.78 – 3.06)</td>
<td>0.23</td>
<td></td>
<td></td>
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<tr>
<td>Diabetes</td>
<td>1.13 (0.52 – 2.35)</td>
<td>0.75</td>
<td></td>
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<tr>
<td>Structural heart disease</td>
<td>0.77 (0.17 – 2.27)</td>
<td>0.66</td>
<td></td>
<td></td>
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<tr>
<td>Left ventricular ejection fraction &lt;50%</td>
<td>1.15 (0.53 – 2.41)</td>
<td>0.7</td>
<td></td>
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</tr>
<tr>
<td>Left atrial diameter &gt;45 mm</td>
<td>1.37 (0.71 – 2.70)</td>
<td>0.35</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Left atrial volume &gt;90 mL</td>
<td>1.46 (0.76 – 2.89)</td>
<td>0.26</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean diameter of the PVs &gt;20mm</td>
<td>0.92 (0.43 – 1.86)</td>
<td>0.82</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Atypical PV anatomy</td>
<td>1.07 (0.45 – 2.37)</td>
<td>0.87</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Interleukin-6 &gt; 7.0 pg/mL</td>
<td>1.25 (0.65 – 2.44)</td>
<td>0.51</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Time to early recurrence of AF of ≥10 days</td>
<td>0.87 (0.43 – 1.69)</td>
<td>0.69</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number of electrical cardioversions of ≥3</td>
<td>12.2 (4.24 – 60.67)</td>
<td>&lt;0.0001</td>
<td>11.32 (3.83 – 58.22)</td>
<td>0.0019</td>
</tr>
</tbody>
</table>

OR, odds ratio; CI, confidence interval; AF, atrial fibrillation; AADs, antiarrhythmic drugs; PV, pulmonary vein.
Ablation of Atrial Fibrillation

1. Pulmonary vein isolation (RF, Cryo, PVAC, nMARQ)
   Ganglionated plexus ablation

2. Additional substrate modification of LA:
   - Linear Lesions
   - CAFE Ablation
   - Ganglionated Plexus Ablation

3. Rotor Ablation
Diagram of the Sites of 69 Foci Triggering Atrial Fibrillation in 45 Patients

Ostial PVI
Ostial PVI

Obsolet because of Pulmonary vein stenosis
Antral PVI
Antral Pulmonary Vein Isolation
Cryoballon PVI
Effect on the Connective Tissue Matrix

RF Lesion at 1 Week (canine model)
+70° C • 50 W • 60 seconds

Cryolesion at 1 Week (canine model)
-75° C • 1 x 4 minutes

Hemorrhage Still Present
Fibrosis Started

16x

Disrupted Endocardium
Thrombus Present

Minimal Thrombus
Endocardium Intact

Fibrosis Complete
Well Demarcated

PVAC (pulmonary vein ablation catheter) PVI

Ablation Frontiers / Medtronic
Incidence of Asymptomatic Intracranial Embolic Events After Pulmonary Vein Isolation Comparison of Different Atrial Fibrillation Ablation Technologies in a Multicenter Study


Post-procedure magnetic resonance imaging detected a single new embolic lesion in 2 of 27 patients in the irrigated RF group (7.4%) and in 1 of 23 in the cryoballoon group (4.3%). However, in the PVAC group 9 of 24 patients (37.5%) demonstrated $2.7 \pm 1.3$ new lesions each ($p = 0.003$ for the presence of new embolic events among the 3 groups).
nMARQ PVI
nMARQ PVI
AF triggers from the pulmonary veins – why?

Human intrinsic cardiac nervous system, location of ganglionated plexus

Gross and Microscopic Anatomy of the Human Intrinsic Cardiac Nervous system,

J.A. Armour et al

The Anatomical Record 247:289-298 (1997)
RF Ganglionated plexus ablation

Zhang et al.,

3D EnSite NavX Map combined with CT scan
Case 5

- 83 years, female, biological age 73
- Hypertension
- No heart failure in sinus rhythm NYHA 0
- Exercise insufficiency under paroxysmal atrial fibrillation several hours a day, EHRA III-IV
- LA 45mm

- What to do?
Case 5, 83 years, female, PAF EHRA III

- Amiodarone / Dronedarone
- Catheter ablation

If yes:
- Standard antral RF pulmonary vein isolation
- RF GPA
- Cryoballon ablation
- nMARQ
- PVAC
Ablation of Atrial Fibrillation

1. Pulmonary vein isolation (RF, Cryo, PVAC, nMARQ)
   Ganglionated plexus ablation

2. Additional substrate modification of LA:
   - Linear Lesions
   - CAFE Ablation
   - Ganglionated Plexus Ablation

3. Rotor Ablation
Antral PVI + Linear Lesions

Roof Line

Bottom Line
Roof Line
Antral PVI + Linear Lesions

Roof Line

Bottom Line
Antral PVI + Linear Lesions

- Roof Line
- Bottom Line
- Mitral Isthmus Line posterior right
- Mitral Isthmus Line posterior left
Posterior Mitral Isthmus Line
Antral PVI + CAFE
(=Complex Atrial Fractionated Electrogramms)
Antral PVI + Lines + CAFE
Antral PVI + GPA
(= Ganglionated Plexus Ablation)

Katritsis et al, 
*Autonomic Denervation Added to Pulmonary Vein Isolation for Paroxysmal Atrial Fibrillation: A Randomized Clinical Trial* 

Zhou et al, 
*A meta-analysis of the comparative efficacy of ablation for atrial fibrillation with and without ablation of the ganglionated plexi.* 
Cryoballon PVI, both balloons

Case 6

- 68 years, female
- Hypertrophic obstructive cardiomyopathy (HOCM), post TASH
- LA 58mm, EF 70%, EDV 60ml, ESV 42ml, SV 18ml
- MI II°
- NYHA II in sinus rhythm
- Now persistent atrial fibrillation, EHRA IV

What to do?
Case 6, 68 years, female, HOCM, PsAF

- Frequency control
- Catheter ablation

If catheter ablation:
- RF PVI + lines
- RF PVI + CAFE
- RF PVI + GPA
- Two cryoballoons
## AF ablation success rate

<table>
<thead>
<tr>
<th>Type</th>
<th>Success Rate</th>
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<tbody>
<tr>
<td>PAF</td>
<td>70 – 92%</td>
</tr>
<tr>
<td>PsAF</td>
<td>50 – 72%</td>
</tr>
<tr>
<td>LsAF</td>
<td>30 – 60%</td>
</tr>
</tbody>
</table>

drops rapidly with disease progression

Pokushalv et al. Europace 2010:12,342-46  
Boersma et al. Heart Rhythm 2008:5,1635-42  
Pappone et al. JACC 2003:42,185-197  
Nademane K et al. JACC 2004:43,2044-53  
Kottkamp H et al. JACC 2004:44,869-877  
Haissaguerre M et al. JCE 2005:16,1125-1137
Disease progression of AF

Paroxysmal AF
Persistent AF
Long standing AF

Increasing Structural Changes
- LA dilatation
- Atrial fibrosis
- Autonomic hyperactivation
- Genetic alterations

Decreasing ablation succes rate
- 70%
- 50%
- 30%

Symptoms
Ablation of Atrial Fibrillation

1. Pulmonary vein isolation (RF, Cryo, PVAC, nMARQ)
   Ganglionated plexus ablation

2. Additional substrate modification of LA:
   - Linear Lesions
   - CAFE Ablation
   - Ganglionated Plexus Ablation

3. Rotor Ablation
Fokal Impulse and Rotor Mapping (FIRM)
Roof rotor was stable during WACA, until eliminated during roof ablation.

Freedom from Atrial Fibrillation

Ablation Through Rotor or Focal Source

Ablation Not Through Rotor or Focal Source (all had PVI still)

Narayan et al., On-Treatment Analysis of CONFIRM. J Am Coll Cardiol. 2013
PRECISE-PAF, Rotor Ablation Without PVI

- HRS Late Breaking Clinical Trial (May 2013)
- Prospective Design In 31 PAF Patients (Persistent AF excluded)
- 5 clinical sites
- Veins confirmed ‘open’ at procedure end
- Implanted Loop Recorders In 64%, OR

Short Ablation Time (mean 17 min)

Results Similar to CONFIRM without PVI

Precise Rotor Elimination without Concomitant pulmonary vein Isolation for Successful Elimination of Paroxysmal Atrial Fibrillation (PRECISE-PAF): Narayan et al - Late Breaking Clinical Trial Presentation at 2013 Annual Scientific Sessions of the Heart Rhythm Society
Have we been targeting the wrong organ?

Pokushalov et al,
A Randomized Comparison of Pulmonary Vein Isolation With Versus Without Concomitant Renal Artery Denervation in Patients With Refractory Symptomatic Atrial Fibrillation and Resistant Hypertension
J Am Coll Cardiol. 2012;60(13):1163-1170

Ralph J. Verdino
Catheter Ablation for the Treatment of Atrial Fibrillation - Have We Been Targeting the Wrong Organ?□, Am Coll Cardiol. 2012;60(13):1171-1172
Summary / Take home messages

- Think of DOAK’s / LAA Occlusion
- Ablate early but do not ablate PmAF
- PVI or GPA with PAF
- PVI + Substrate Modification with PsAF
- Cardiovert up to three times post ablation
- Be ready for new techniques...
Vielen Dank für Ihre Aufmerksamkeit!