Συμπεράσματα από τις πρόσφατες πρόσφατες μελέτες κατάλυσης της κολπικής μαρμαρυγής

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ΓΝΑ «Ο ΕΥΑΓΓΕΛΙΣΜΟΣ»
Catheter ablation of AF: what about hard end-points?

- Mortality
- Stroke
- HF hospitalizations
The CABANA trial

Patient Randomization

Subjects 2204

Ablation Therapy 1108

- Ablated 1006 (90.8%)
  - repeat ablation 215 (19.4%)
- Not ablated 102 (9.2%)

Completed FU 1002 (90.4%) 48.9 mo

Drug Therapy 1096

- Drug Treated 1092 (99.6%)
  - rhythm control 953 (87.2%)
  - rate control only 126 (11.5%)
- Cross Over Ablated 301 (27.5%)

Completed FU 966 (88%) 48.2 mo

Crossovers

Douglas Packer, HRS 2018
The CABANA trial: Crossovers

• Crossover was common with 9.2% of patients in the ablation arm not undergoing the procedure and 27.5% of those in the drug therapy arm ultimately undergoing ablation.

• Both of these factors would be expected to ”dilute” any treatment benefit produced by ablation.

• The trial did not actually compare ablation vs. drugs as was intended but rather it compared the strategy of ablation vs. initial medical therapy with ablation for recurring symptoms.
Is the CABANA landmark AF study on catheter ablation a positive or negative study?

"Unbelievable! Electrophysiologists Embrace 'Alternative Facts"

- Milton Packer, MD's editorial in MedPage Today, May 16, 2018

"AFib Ablation Outperforms Drugs in CABANA Trial"

- Cardiovascular Business, May 10, 2018

"CABANA: Ablation Disappoints for AF vs Drugs, Questions Remain"

- Medscape Medical News, May 10, 2018
Is the CABANA a landmark trial ???

Too many limitations …

• Study design was problematic for a landmark trial (the crossovers should have been avoided).

• Patients with different types of AF (paroxysmal, persistent, and long-standing persistent) were included for analysis.

• Different ablation strategies: clinicians used their preferred ablation catheter and had their choice of therapy—PVI or WACA, with or without additional ablations in other areas of the heart.

• Is the CABANA already an old trial with respect to the technology used (old catheters without contact information).

• The benefit of this kind of evidence-based medicine is to provide clarity to clinicians faced with decisions to make in daily practice, but CABANA, so far, has generated confusion, not confidence.

• The CABANA investigators presented several ‘alternative’ analyses, which totally undermined the integrity of the trial's randomization process.

• Can “real world” data answer some of these questions???
The CABANA trial: Intention-to-treat analysis

Primary Endpoint (Death, Disabling Stroke, Serious Bleeding, or Cardiac Arrest) (ITT)

Ablation vs. Drug
Hazard ratio: 0.86 (95% CI, 0.65–1.15)
P=0.303

Douglas Packer, HRS 2018
The CABANA trial: Intention-to-treat analysis

47% reduction in recurrent AF episodes with ablation compared to drug therapy

Douglas Packer, HRS 2018
The CABANA trial: Catheter ablation is the most effective way to control AF

Douglas Packer, HRS 2018
A 27% reduction in the primary endpoint and 40% mortality risk reduction was present when patients actually underwent ablation (treatment received).

Douglas Packer, HRS 2018
Why do we pursue rhythm control?

• Mortality benefit
  • AFFIRM
  • DIAMOND
  • CHF-STAT
  • QUEBECCOHORT

• Reduced risk of stroke
  • ATHENA
  • QUEBECCOHORT

• The CABANA trial showed a 47% reduction in recurrent AF episodes with ablation compared to drug therapy, and therefore the mortality and stroke benefits were more or less expected.
The CABANA trial: Subgroup analysis

- Subgroup analysis indicated that patients younger than 65 years seemed to show a benefit from ablation, while patients older than 75 showed little benefit.

- Patients with heart failure seemed to particularly derive benefit, which goes along with the results of the CASTLE- AF trial.

Douglas Packer, HRS 2018
Catheter ablation was associated with significantly lower mortality and ischemic stroke:

- 4169 ablation cases and 4169 weighted-matched controls.
- Mean follow-up period of 3.6±0.9 years.
- Catheter ablation was associated with significantly lower mortality (HR=0.59; ischemic stroke (HR=0.68); and hemorrhagic stroke (HR=0.36) compared with controls.

Circ Arrhythm Electrophysiol. 2018;11:e005739.
Catheter Ablation of Atrial Fibrillation in Patients With Heart Failure
The CASTLE AF trial

• HF patients (EF<35%) were randomized to either conventional treatment according to current guidelines for AF in heart failure (n=184) or to a catheter-ablation protocol using pulmonary-vein isolation (n=179), after a run-in of 5 weeks to optimize heart-failure therapy.
• They were followed at 3, 6, 12, 24, 36, 48, and 60 months.
• Mean age in both groups was about 64 years, the majority of patients were in NYHA class 2, and most patients had persistent or long-standing persistent AF.
• About 70% of both groups had an ICD, and the remainder a CRT-D.
The CASTLE AF trial: major findings

Death or Hospitalization for Worsening Heart Failure

Hazard ratio, 0.62 (95% CI, 0.43–0.87)
P=0.007 by Cox regression
P=0.006 by log-rank test

Death from Any Cause

Hazard ratio, 0.53 (95% CI, 0.32–0.86)
P=0.01 by Cox regression
P=0.009 by log-rank test

Hospitalization for Worsening Heart Failure

Hazard ratio, 0.56 (95% CI, 0.37–0.83)
P=0.004 by Cox regression
P=0.004 by log-rank test

The CASTLE AF trial: major findings

• There was a 47% reduction in cardiovascular mortality in the catheter group. The mortality effect of ablation vs conventional care became evident at about 3 years;

• In the catheter ablation group, 60% improved their ejection fraction by more than 35%;

• After 5 years, 60% of the ablation group were in normal sinus rhythm compared to only 22% receiving conventional drug therapy;

• Heart failure hospital admissions improved immediately within 6 months of the ablation.

The CASTLE AF trial: mortality benefit

• The magnitude of mortality benefit (47%) exceeds that of any known HF therapy.

• Angiotensin receptor-neprilysin inhibitor drugs reduce mortality by 35%; ICDs and β-blockers do so by 30%.

• This is an astonishing benefit size.
Improvement of Ejection Fraction: No more heart failure???

• One of the most astounding statistic of CASTLE-AF was that 60% of patients improved their ejection fraction by 35% after their catheter ablation.

• That kind of improvement means that many patients no longer suffered from heart failure.

• This is an amazing development in medicine.
The CASTLE AF trial: important limitations

- A “protected” study: highly selected population
- Unblinded nature of treatment assignments (underperformance of the medical arm)
- Patients enrolled in the medical arm had higher rates of diabetes, more use of digoxin, and a greater incidence of ischemic cardiomyopathy.
- CASTLE-AF enrolled patients with failed (or unwanted) medical therapy to an arm of more medical therapy.
Catheter Ablation of Atrial Fibrillation in Patients With Heart Failure
A Meta-analysis of Randomized Controlled Trials

• Compared with drug therapy:
  • AF ablation reduced all-cause mortality (9.0% vs. 17.6%; risk ratio [RR], 0.52 [95% CI, 0.33 to 0.81] and HF hospitalizations (16.4% vs. 27.6%; RR, 0.60 [CI, 0.39 to 0.93]).
  • Ablation improved left ventricular ejection fraction (LVEF) (mean difference, 6.95% [CI, 3.0% to 10.9%]), 6-minute walk test distance (mean difference, 20.93 m [CI, 5.91 to 35.95 m]), peak oxygen consumption (VO2max) (mean difference, 3.17 mL/kg per minute [CI, 1.26 to 5.07 mL/kg per minute]), and quality of life.

Original Research

Ablation of Atrial Fibrillation in Patients with Heart Failure: Reversal of Atrial and Ventricular Remodelling

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CLINICAL INVESTIGATIONS

Predictors of arrhythmia recurrence in patients with heart failure undergoing left atrial ablation for atrial fibrillation

Predictors of arrhythmia recurrence in patients with heart failure undergoing left atrial ablation for atrial fibrillation

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Background: Atrial fibrillation (AF) ablation is increasingly used in patients with reduced left ventricular ejection fraction (LVEF). The aim of the present study was to evaluate the long-term results of a single radiofrequency catheter ablation procedure in heart failure (HF) patients with AF.

Hypothesis: We tested the hypothesis that left atrial ablation is an effective therapeutic modality in patients with heart failure.

Methods: Our study included HF patients with LVEF <50% who underwent catheter ablation for AF at our department between January 2010 and March 2017. All patients underwent our institution's protocol for follow-up post-ablation.

Results: The study enrolled a total of 38 patients (mean age, 54.1 ± 12.2 years; 28 [73.7%] males; mean LVEF, 38.2% ± 6.3%). After a mean follow-up period of 38.2 months (range, 5–92 months), 28 patients (73.7%) were free from arrhythmia recurrence. In multivariate analysis, early arrhythmia recurrence (P = 0.03) and amiodarone antiarrhythmic drug administration (P = 0.003) remained independent predictors of arrhythmia recurrence.

Conclusions: The main findings of this study are that (1) a single radiofrequency catheter ablation procedure is an effective and safe modality for AF in patients with concomitant HF; (2) after a mean 3.3 years of follow-up, 73.7% of HF patients remained in sinus rhythm; and (3) early arrhythmia recurrence was a significant predictor of arrhythmia recurrence after the blanking period.

- 38 pts (ICM, NICM)
- Mean LVEF 38.2%
- After a mean 3.3 years of follow-up, 73.7% of HF patients remained in SR.
- EAR and the use of amiodarone before the procedure were significant predictors of arrhythmia recurrence after the blanking period.
- A single AF catheter ablation procedure is an effective and safe modality in HF patients with AF.
New data regarding on AF mapping and ablation:

- the quality of lesions and the durability of PVI
- the biophysics of RF ablation
- the accuracy of LA electroanatomical mapping
- the impact of “diseased” LA on AF ablation outcomes
- the effect of substrate modification targeting specific electrograms on persistent AF ablation outcomes
Evaluation of a Strategy Aiming to Enclose the Pulmonary Veins With Contiguous and Optimized Radiofrequency Lesions in Paroxysmal AF: The CLOSE protocol

- Ablation index (AI) (Carto System, Biosense Webster).
- AI is a novel marker of ablation lesion quality that incorporates power, CF, and time in a weighted formula and was found to accurately estimate ablation lesion depth in preclinical studies.
- RF was delivered until an AI of >400 at the posterior wall/roof and >550 at the anterior wall.
Survival Plots for Patient Subgroups

- Freedom from documented AF/AT/AFL in patients off ADT (n=104): 91.3%
- Freedom from documented AF/AT/AFL in patients without arrhythmia during the 3 months blanking (n=114): 95.6%
- Freedom from documented AF/AT/AFL in patients on ADT (n=26): 96.2%
- Freedom from documented AF/AT/AFL in patients with arrhythmia during the 3 months blanking (n=16): 68.8%
Use of Ablation Index-Guided Ablation Results in High Rates of Durable Pulmonary Vein Isolation and Freedom From Arrhythmia in Persistent AF: The PRAISE Study Results

- 40 consecutive patients with persistent AF underwent AI-guided PVI with target values of 550 for anterior and 400 for posterior left atrial regions, followed by a protocol-mandated repeat procedure after 2 months.
- Late PV reconnection was identified in only 7% of PVs.
- At 12 months, 38/40 (95%) patients were in sinus rhythm, with 4 (10%) patients having AADs.
High-Power and Short-Duration Ablation for Pulmonary Vein Isolation Biophysical Characterization

- 20 swines
- Step 1 compared 3 HP-SD ablation settings: 90 W/4 s, 90 W/6 s, and 70 W/8 s in a thigh muscle preparation. Ablation at 90 W/4 s was identified as the best compromise.
- In step 2, a total of 174 single ablation applications were performed in the beating heart and resulted in 3 (1.7%) steam-pops, all occurring at catheter-tissue interface temperature >85°C. Additional 233 applications at 90 W/4 s and temperature limit of 65°C were applied without steam-pop.
- Step 3 compared the presence of gaps and lesion transmurality in atrial lines and pulmonary vein isolation between HP-SD (90 W/4 s, T < 65°C) and standard (25 W/20 s) ablation.

J Am Coll Cardiol EP 2018
Activation Mapping With Integration of Vector and Velocity Information: "coherent mapping"

Circ Arrhythm Electrophysiol. 2018;11:e006536.
High density mapping. How can we improve the accuracy?

• We tested the accuracy of a new mapping algorithm with contact information (TPI, CARTO, BW).

• A more specific delineation of LA fibrosis may be produced using multipolar catheters with contact information, through elimination of false positive annotated mapping points due to low contact.

Asvestas et al. PACE 2019
The existence of LA voltage areas < 0.4 mV more than 10% of the total LA surface area predicts arrhythmia recurrence following PVI for paroxysmal AF.
Targeted ablation of specific electrogram patterns in low voltage areas after PVI in persistent AF: Termination to an organized rhythm reduces AF recurrence.

Efremidis et al. JCE 2018
“Don’t believe everything you read (in the EP literature) or at least (don’t believe) the interpretation of the results and conclusions drawn. It is not etched in stone (like the Ten Commandments).”
—Mark Josephson, 1978

Thank you very much for your attention
High-Power and Short-Duration Experimental studies

• Porcine model: The time to create a 4-mm-deep lesion was >20 sec for 20-W ablations and only 6–7 seconds for 50-W ablations.

• Sheep model: Examined 50- and 60-W ablations for 5 sec vs conventional 40-W ablations for 30 seconds delivered at a contact force of 10g in an in vitro and in vivo sheep model. 50- and 60-W ablations for 5 sec achieved transmural lesions and were safer than 40-W ablations for 30 seconds. The incidence of steam pops was 8% in the 40-W/30-sec ablations vs. none in the 50- and 60-W ablations for 5 sec.