Catheter Ablation vs. Risk Factor Modification with Antiarrhythmic Drugs to Treat Atrial Fibrillation – the PRAGUE-25 Study

Pavel Osmancik[1], Tomas Roubicek[2], Stepan Havranek[3], Jan Chovancik[4], Veronika Bulkova[5], Dalibor Herman[1], Martin Matoulek[3], Vladimir Tuka[3], Ivan Ranic[4], Jana Hozmanova[1], Marek Hozman[1], Lucie Znojilova[1], Adam Latinak[2], Jan Pidhorodecky[2], Milan Dusik[3], Jan Simek[3], Otakar Jiravsky[4], Bogna Jiravska – Godula[4], Frantisek Lehar[5], Michal Cernosek[5], Hana Zelinkova[6], Jiri Jarkovsky[6], Klara Benesova[6]

1. Cardiocenter, Third Faculty of Medicine, Charles University Prague and University Hospital Kralovske Vinohrady, Prague, Czech Republic
2. Dept. of Cardiology, Regional Hospital Liberec, Czech Republic
3. Cardiocenter, 2nd internal clinic – Cardiology and Angiology, Charles University, General Faculty Hospital, Prague Czech Republic
4. Department of Cardiology, Cardiocenter, Hospital Podlesí a.s., Trinec, Czech Republic
5. Dept of Cardiology, Neuron Medical Center, Hospital Brno, Czech Republic
6. Masaryk University, Institute of Biostatistics and Analyses, Czech Republic.

Background

- Obesity is a very important risk factor of AF, and an increase of body mass index (BMI) by 5 points is associated with a 19-29% increase in the incidence of AF
- Obesity was very prevalent in RCT comparing catheter ablation with medical treatment
  - CABANA, EARLY-AF (both ablation vs. antiarrhythmics): median BMI 30 kg/m^2
  - ADVENT (thermal vs. non-thermal ablation): median 28.5 kg/m

Background

- Catheter ablation was superior in AF treatment if compared with AADs
  - ***AF freedom on AAD was present at 1 year in 40-45% of patients*** (40.8% CABANA, 45% STOP-AF, and 52% [95%CI 47-57%] in metaanalysis of AAD studies)
  - ***AF freedom with CA was present in 55-70% of patients*** (63.6% CABANA, or 57% [95%CI 50-64%] in metaanalysis of CA vs. AAD studies)

➢ AAD treatment was NOT supported by LFM in the conservative (AAD) arms in ANY study comparing CA vs. AAD

Background and hypothesis

- Weight loss, an increase in physical activity and reduced alcohol consumption (lifestyle modification, LFM, or risk factor modification) have been associated with improved SR maintenance

  LEGACY study: LFM in patients with BMI > 27 kg/m^2 resulted in significant AF freedom without catheter ablation or antiarrhythmic drugs according to the achieved weight loss

  - > 10% of body weight => 45.4% AF freedom
  - 3-9% of body weight => 22.2% AF freedom
  - < 3% of body weight => 13.4% of patients

- **<u>Hypothesis & clinical question</u> of the study: in obese AF patients, LFM could significantly augment the effect of antiarrhythmic drug medication, and this combination could be <u>non-inferior</u> to catheter ablation**

Methods

- Randomized, multicenter, investigator – initiated, non-inferiority trial comparing the effect of catheter ablation with treatment based on lifestyle modification in combination with antiarrhythmic drugs in obese AF patients (clinicaltrials.gov, NCT04011800)

- Supported by the research grant of the Ministry of Health Czech Republic (Czech Health Research Council, NU21-02-00388)

Inclusion, Exclusion criteria and Randomization

Inclusion criteria

- symptomatic AF
- BMI $\geq$ 30 and $\leq$ 40 kg/m^2

Exclusion criteria

- History of AF-induced cardiomyopathy, LV EF $\leq$ 40%, BMI > 40
- contraindication to AADs, age > 75 years, significant limitations that could affect physical activity

RANDOMIZATION (1/1)

- Catheter ablation (CA) group
- LFM-AAD group (lifestyle modification + AADs)
  - Stratified by BMI, AF type, age

Baseline examinations

- performed in all patients during 4 weeks after randomization

  - CardioPulmonary Exercise Test (CPET, VO2 max)
  - 7-day ECG Holter recording
  - Echocardiography
  - Blood biochemistry (HbA1c, lipids, NT-proBNP, CRP)
  - Quality of life assessment (AFEQT questionnaire)

Trial procedures – catheter ablation arm

- Catheter ablation (PVI or PVI + additional ablation lesions in non-paroxysmal AF patients)
- Procedures scheduled within 6 weeks after randomization
- Catheter ablation using radiofrequency or pulsed-field energy

Trial procedures – LFM-AAD arm

- Targeted weight reduction and exercise program directed by teams of dietary specialists and physiotherapists (not by cardiologists)

- Goals: i) ***a decrease of 10% of the initial body weight, ii) an increase in physical activity, iiii) a decrease in alcohol intake***

- Initial consultation with nutritionists and physioterapists within 4 weeks, low calorie diet, individual exercise program based om CPET results (in-person and phone consultation, OBEFIS mobile application)

- The choice of AADs during the first months after randomization with possible uptitration till the end of blanking period (IC AAD preferred, amiodarone only as third-line choice only)

Trial outcomes

PRIMARY OUTCOME:

absence of any atrial tachyarhythmia (AF, atrial flutter, atrial tachycardia) lasting > 30 sec during the one year of follow-up after the blanking period

- Outpatient visits scheduled every 3 months since the start of treatment
- Seven-day Holter recording every 3 months in the first year, and every six months later

SECONDARY OUTCOMES (all between baseline and 12 months)

- AF burden
- Peak VO2 uptake at CPET
- AFEQT score
- Metabolic parameters (HbA1C, lipids, NT-proBNP, CRP)

Statistical rationale and methods

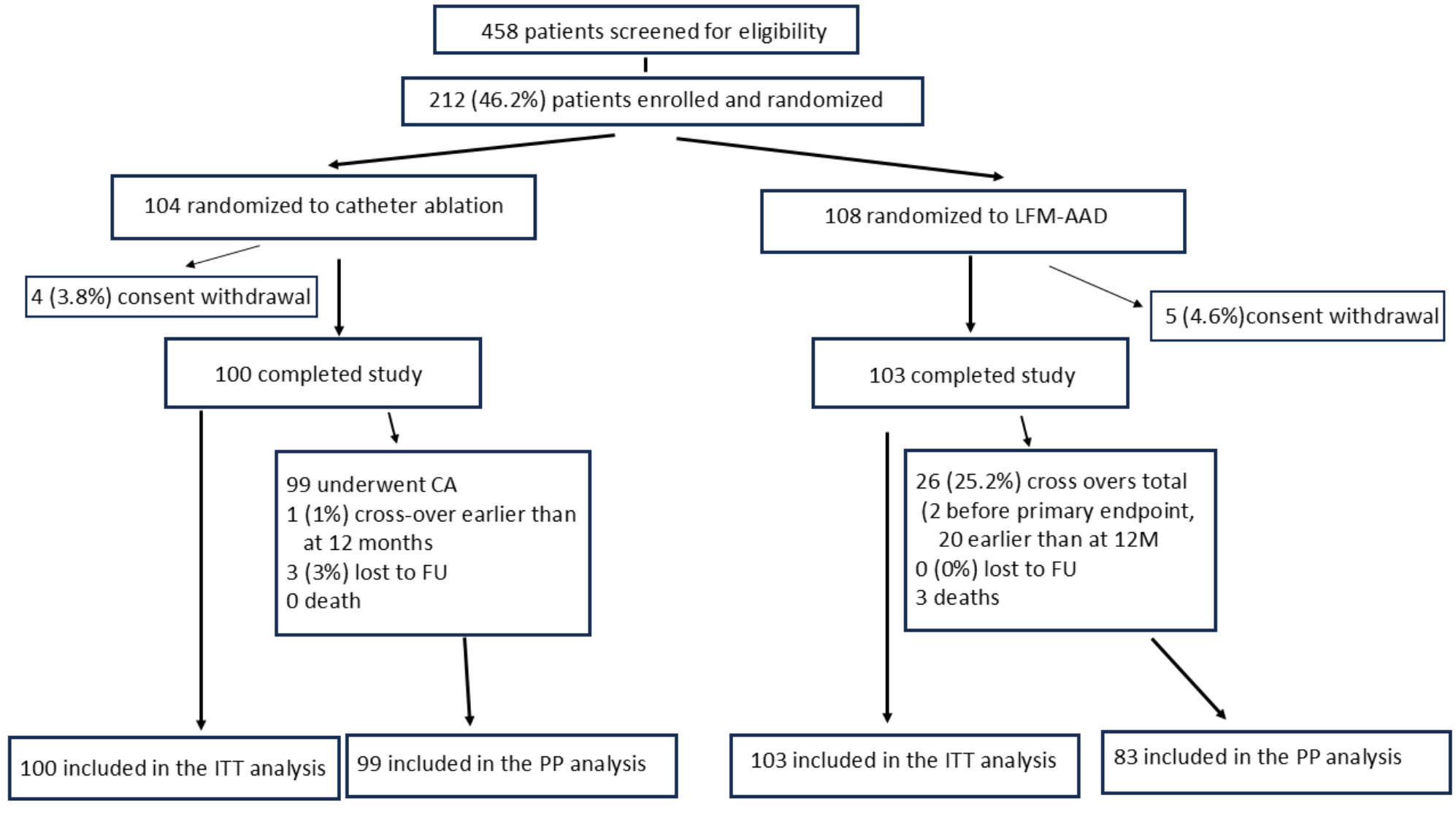
Expected AF freedom

- 60% patients after cathteter ablation
- 65% patients in LFM-AAD arm

NIM: 12% (studies comparing AAD vs placebo, one-year AF freedom in placebo arms in 24.9% of patients (95%CI 15-34%)

- ➢ 80% power, alpha 5%, NIM 12%: 202 patients to enroll (expected 10% drop-out, 212 patients to enroll)
- ➢ ITT and PP analyses

Study flow chart (CONSORT)



Patient characteristics

	CA arm (n = 100)	LFM+AAD arm (n=103)
Age – yr	60 ± 8	60 ± 9
Male sex – No (%)	68 (68.0 %)	71 (68.9 %)
Body weight – kg	110 ± 15	109 ± 17
Body mass index	**35.0 ± 2.9**	**34.9 ± 3.2**
Paroxysmal AF	**56 (56.0 %)**	**57 (55.3 %)**
Persistent AF	39 (39.0 %)	41 (39.8 %)
Long-lasting persistent AF	5 (5.0 %)	5 (4.9 %)
Heart failure – No (%)	13 (13.0 %)	11 (10.7 %)
Hypertension – No (%)	84 (84.0 %)	86 (83.5 %)
Diabetes mellitus – No(%)	19 (19.0 %)	30 (29.1 %)
Coronary artery disease – No (%)	8 (8.0 %)	6 (5.8 %)
CHA_2DS_2-VASc score	**2.0 ± 1.2**	**2.0 ± 1.2**
Pacemaker – No (%)	3 (3.0 %)	1 (1.0 %)

Catheter ablation group (n=100)

- 99 patients underwent the procedure (1 early cross over)
- CA using radiofrequency energy in 48 and pulsed-field energy in 51 patients
- All patients = pulmonary vein isolation, additional lesions in 35 (35.4%) patients

Procedural major complications: 1 (1%) patient – TIA

Re-do ablations or AADS during FU: 7 (7%) patients redo-ablation, and 16 (16%) on AADs, all due to AF recurrences

Body weight: -0.35 kg (±4.78) at 12 months, - 0.08 kg (±5.96) at 24 months

LFM-AAD group (n=103)

significant body weight reduction during follow-up

- **At 12 months: −6.37 ± 7.94 kg, p < 0.001**
- **At 24 months: -6.29 ± 8.80 kg, p< 0.001**

AAD use:

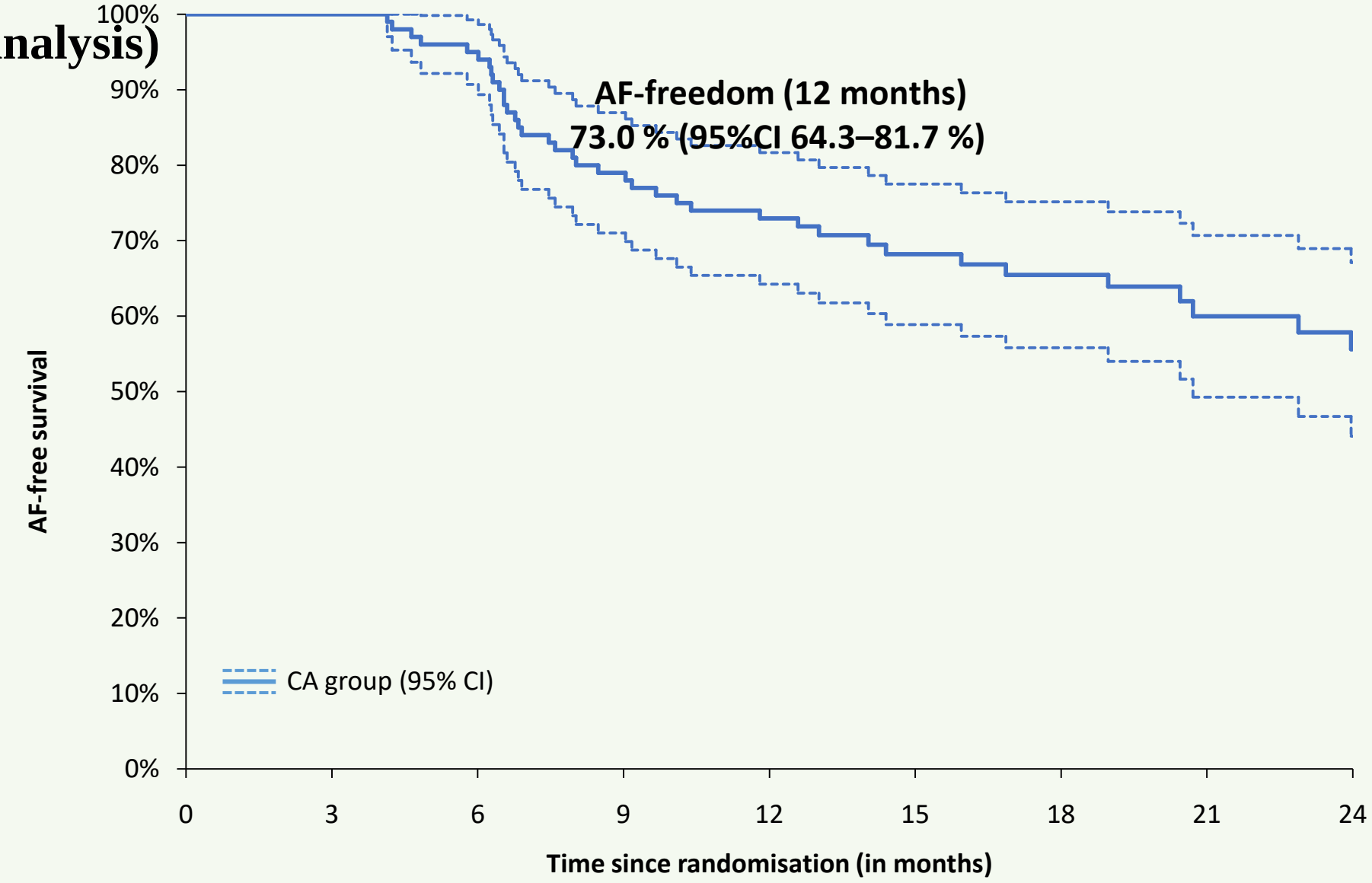
- At 3 months: 97 (95.1%) patients
- At 12 months: 66 (66.7%) patients

Cross-over: 25 patients (23 AFTER AF recurrence)

Major complications: 4 patients (3 syncope, 1 sudden cardiac death)

Primary outcome

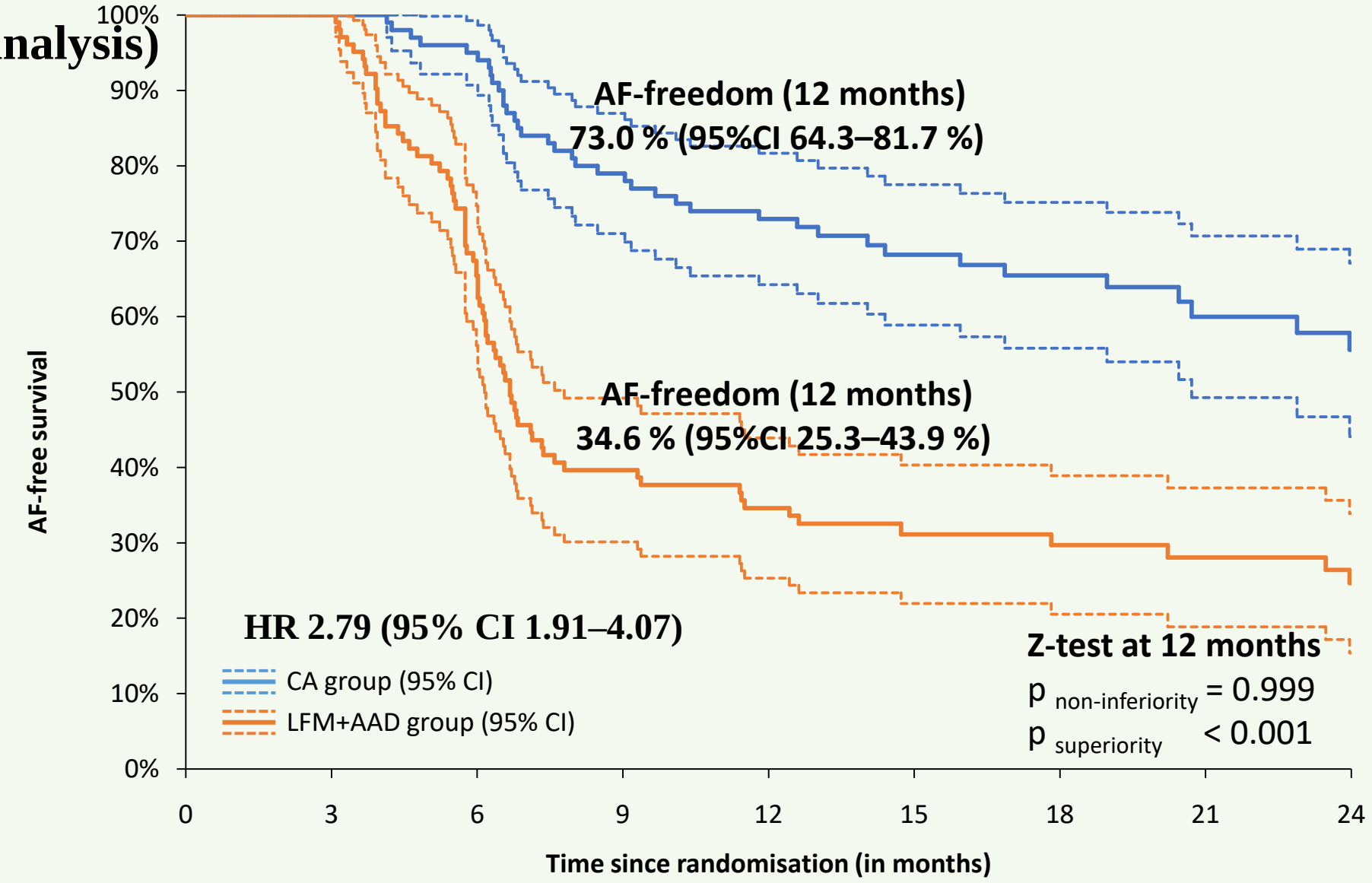
(ITT analysis)



No. at risk:									
CA	100	100	95	79	71	52	47	30	25
LFM+AAD	103	103	66	40	34	22	21	17	14

Primary outcome

(ITT analysis)



No. at risk:									
CA	100	100	95	79	71	52	47	30	25
LFM+AAD	103	103	66	40	34	22	21	17	14

Secondary outcomes (12 months, ITT)

	CA arm (n=100)		within-group comparison (baseline – 12month)	LFM-AAD arm (n=103)		within-group comparison (baseline – 12 month)	Between-groups comparison at 12 months (individual differences)
	baseline	**12 months**	**p**	**Baseline**	**12 months**	**p**	**p**
HbA1c (mmol/L)	39.6 ± 9.8	41.6 ± 11.2	***0.048***	40.7 ± 7.1	39.6 ± 8.0	***<0.001***	**<0.001**
Triglycerides (mmol/L)	1.86 ± 1.20	1.71 ± 1.29	*0.21*	1.79 ± 0.87	1.50 ± 0.73	***<0.001***	0.08
Cholesterol (mmol/L)	4.52 ± 1.12	4.28 ± 0.96	*0.10*	4.46 ± 1.13	4.29 ± 1.10	*0.09*	0.79
CRP (mmol/L)	4.59 ± 4.82	3.77 ± 4.31	*0.12*	4.34 ± 4.18	3.67 ± 3.87	***0.009***	0.40
VO2 max (ml/kg/min)	17.90±4.57	18.05±4.74	*0.90*	19.09±5.07	20.38±5.81	***0.028***	0.13
AF burden (%)	31.1±42.6	12.1±31.2	***<0.001***	35.9±44.1	22.1±37.2	***0.001***	0.17
NT-pro BNP (pg/mL)	506 ± 566	284 ± 463	***<0.001***	495 ± 548	342 ± 412	***0.001***	0.21
AFEQT	68.6 ± 19.9	86.2±14.3	***<0.001***	72.7±18.9	85.4±15.4	***<0.001***	0.14

Conclusion

- LFM is associated with significant metabolic, functional improvement and with a decrease in AF burden

- with regard to SR maitenance, treatment strategy based on LFM-AADs was inferior to catheter ablation

Study limitations:

- Planned weight loss of >10% of body weight was not achieved, GLP-1 agonists not systematically used, no continuous ECG (ILR) monitoring

Acknowledgement

Cardiocenter, 3rd Faculty of Medicine, Charles University Prague and University Hospital Kralovske Vinohrady, Prague
Pavel Osmancik, MD, PhD, Dalibor Herman, MD, PhD, Marek Hozman, MD, PhD, Jana Hozmanova, MSc, Lucie Znojilova, MSc, Petr Stros, MD, Karol Curila, MD, PhD, Ondrej Sussenbek, MD, Zuzana Carna, MD

Cardiocenter, 2nd Internal clinic – Cardiology and Angiology, Charles University, General Faculty Hospital, Prague
Stepan Havranek, MD, PhD, Martin Matoulek, MD, PhD, Vladimir Tuka, MD, PhD, Milan Dusik, MD, PhD, Jan Simek, MD, PhD, Kristyna Souza-Lopez, MSc, Eva Farnikova, Ondrej Kade, MSc, Pavel Kraus, MSc

Dept. of Cardiology, Regional Hospital Liberec, Liberec
Tomas Roubicek, MD, PhD, Adam Latinák, MD, Jan Pidhorodecky, MD, Sylvie Stregl – Hruskova, Daniela Chovancekova, Petra Bredova

Department of Cardiology, Cardiocenter, Hospital Podlesí a.s., Trinec
Jan Chovancik, MD, PhD, Ivan Ranic, MD, Otakar Jiravsky, MD, Bogna Jiravska – Godula, MD, Barbora Ryskova, Marketa Sikorova

Neuron Medical Center, Hospital Brno, Brno
Veronika Bulkova, MSc, PhD, Martin Fiala, MD, PhD, Frantisek Lehar, MD, Michal Cernosek, MD, Simona Perinkova, Robert Prosecky, Lenka Slobodnikova

Masaryk University, Institute of Biostatistics and Analyses, Brno
Klara Benesova, MSc, Hana Zelinkova, MSc, Jiri Jarkovsky, MSc, PhD

Osmancik P, Roubicek T, Havranek S, Chovancik J, Bulkova V, Herman D, Matoulek M, Tuka V, Ranic I, Hozmanova J, Hozman M, Znojilova L, Latinak A, Pidhorodecky J, Dusik M, Simek J, Jiravsky O, Jiravska-Godula B, Lehar F, Cernosek M, Hejdukova Z, Zelinkova H, Jarkovsky J, Benesova K. Catheter Ablation vs Lifestyle Modification With Antiarrhythmic Drugs to Treat Atrial Fibrillation: PRAGUE-25 Trial. J Am Coll Cardiol. 2025;86(1):18-28. .