ČKS BRNO 2023

MANIFEST-PF
Registrační studie: *jednoroční sledování*

Prof. MUDr. Petr Neužil, CSc., FESC

•

Kardiocentrum Nemocnice Na Homolce

Praha

The *MANIFEST-PF* Cooperative

Physicians & Centers-1

Petr Neuzil, Jan Petru, V.Reddy, Mohit Turagam	Homolka Hospital, Prague, Czech Republic
Boris Schmidt, Julian Chun	MVZ CCB Frankfurt und Main-Taunus GbR, Germany
Tobias Reichlin, Lauren Roten, Thomas Kueffer	Inselspital – Bern University Hospital, Switzerland
Kars Neven, Anna Füting, Gilbert Rahe	Witten/Herdecke University, Witten, Germany
Andreas Metzner, Marc Lemoine	University Medical Center Hamburg-Eppendorf, Germany
Jim Hansen, Martin Ruwald	Herlev-Gentofte University Hospital, Hellerup, Denmark
Yuri Blaauw, Bart Mulder	University Medical Center Groningen, Netherlands
Philippe Maury, Anne Rollin	University Hospital Rangueil, Toulouse, France
Thomas Arentz, Heiko Lehmann	Universitätsklinikum Freiburg, Germany
Philipp Sommer, Thomas Fink	Ruhr-University Bochum, Bad Oeynhausen, Germany
Ante Anic, Zrinka Jurisic	University Hospital Center Split, Split, Croatia
Frederic Anselme, Corentin Chaumot	Rouen Hospital, Rouen, France

The *MANIFEST-PF* Cooperative

Physicians & Centers-2

Serge Boveda, Raquel Adelino	Clinique Pasteur, Toulouse, France
Thomas Deneke, Karin Nentwich	Heart Center Bad Neustadt, Germany
Stephan Willems, Melanie Gunawande	Asklepios Hospital St.Georg, Hamburg, Germany
Pepijn van der Voort, Alexandre Ouss	Catharina Ziekenhuis Eindhoven, The Netherlands
Roland Tilz, Bettina Kirstein	University Heart Center, Lubeck, Germany
Moritoshi Funasako, Petr Neuzil	Neuron Medical, Brno, Czech Republic
Daniel Scherr, Martin Manninger	Medical University of Graz, Austria
Reza Wakili, Jan-Eric Bohnen	University Duisburg-Essen, Germany
Daniel Steven, Arian Sultan	Heart Center University Hospital of Cologne, Germany
Josef Kautzner, Petr Peichl	IKEM, Prague, Czech Republic
Johan Vijgen, Pieter Koopman	Jessa Hospitals, Hasselt, Belgium
Pierre Jais, Nicolas Derval	IHU LIRYC, CHU Bordeaux, University of Bordeaux, France

PFA Safety in the "Real World"

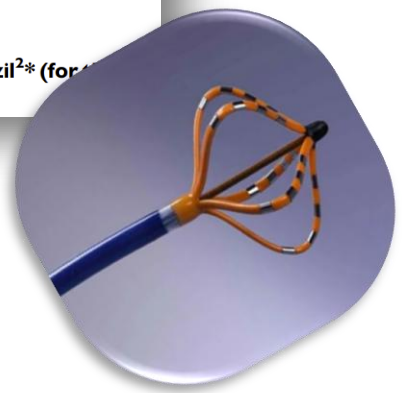
MANIFEST-PF Survey Outcomes

ESC European Society of Cardiology
Europace (2022) **00**, 1–11
https://doi.org/10.1093/europace/euac050

CLINICAL RESEARCH

Multi-national survey on the methods, efficacy, and safety on the post-approval clinical use of pulsed field ablation (*MANIFEST-PF*)

Emmanuel Ekanem[1], Vivek Y. Reddy[1,2], Boris Schmidt[3], Tobias Reichlin[4], Kars Neven[5,6], Andreas Metzner[7], Jim Hansen[8], Yuri Blaauw[9], Philippe Maury[10,11], Thomas Arentz[12], Philipp Sommer[13], Ante Anic[14], Frederic Anselme[15], Serge Boveda[16,17], Tom Deneke[18], Stephan Willems[19], Pepijn van der Voort[20], Roland Tilz[21,22,23], Moritoshi Funasako[2,24], Daniel Scherr[25], Reza Wakili[26], Daniel Steven[27], Josef Kautzner[28], Johan Vijgen[29], Pierre Jais[6], Jan Petru[2], Julian Chun[3], Laurent Roten[4], Anna Füting[5,30], Andreas Rillig[7], Bart A. Mulder[9], Arne Johannessen[8], Anne Rollin[10], Heiko Lehrmann[12], Christian Sohns[13], Zrinka Jurisic[14], Arnaud Savoure[15], Stephanes Combes[16,17], Karin Nentwich[18], Melanie Gunawardene[19], Alexandre Ouss[20], Bettina Kirstein[21,22,23], Martin Manninger[25], Jan-Eric Bohnen[26], Arian Sultan[27], Petr Peichl[28], Pieter Koopman[29], Nicolas Derval[6], Mohit K. Turagam[1], and Petr Neuzil[2]* (for MANIFEST-PF Cooperative)



24 centers in Europe

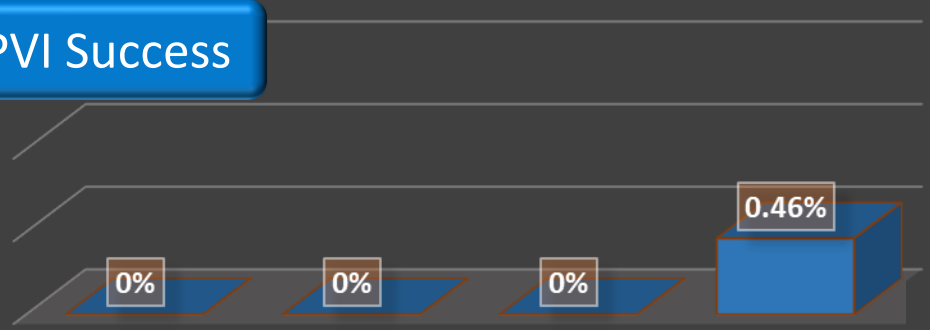
90 Operators

1,758 Patients

99.9% Acute PVI Success

Limitations

1. *Center*-level survey
2. No long-term efficacy



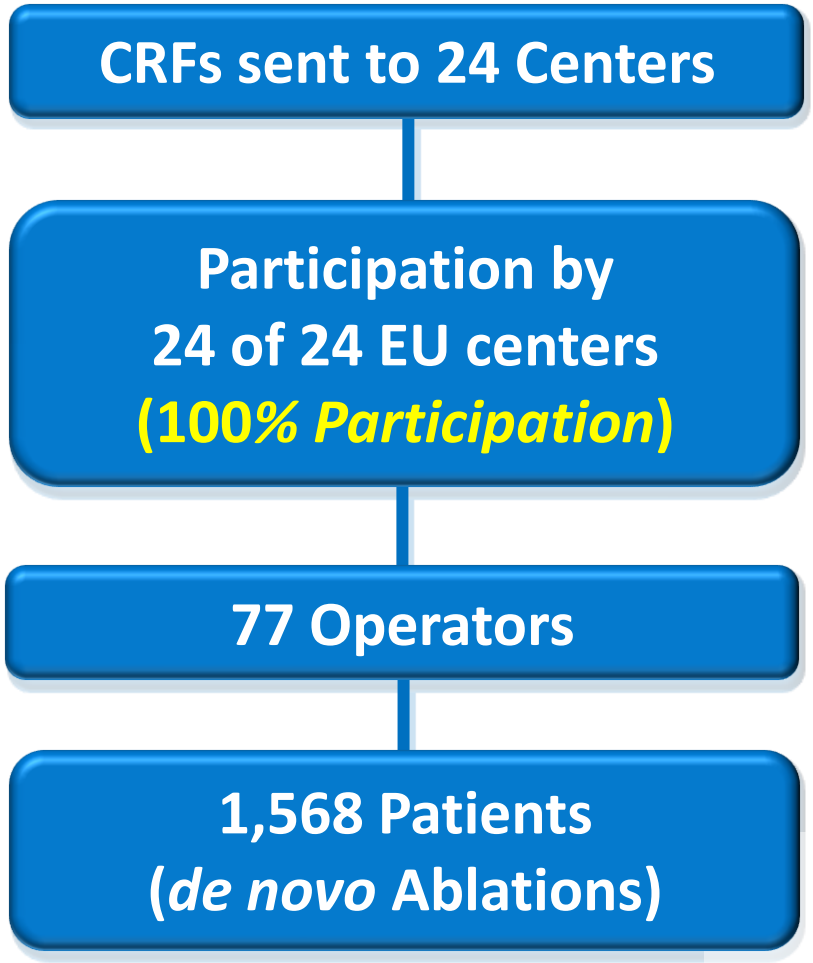
PFA-Specific AEs

E.Ekanem, VY.Reddy, B.Schmidt, et al, *Europace* 24:1256–1266 (2022)

MANIFEST-PF Registry

Rationale & Design

- Retrospective study including all Post-CE Mark PFA cases after March 1, 2021 (up to May 30, 2022)
  - All **consecutive** patients undergoing PFA
  - Only First-time AF ablation procedures
- ***Patient-level*** data was acquired & analyzed
- Approved by the EC at Homolka Hospital, Prague
- Primary Effectiveness Outcome:
  - Freedom from AF/AFL/AT recurrence ≥30 sec (post 3-mo blanking period)
  - Follow-up per usual center practice
- Secondary Effectiveness Outcomes:
  - Freedom from AF/AFL/AT (post 3-mo blanking) + freedom from **class I/III AADs** + **redo ablation**
- Safety Data
  - Acute & Chronic major & minor adverse events



MANIFEST-PF: Results

Baseline Patient Characteristics - 1

	Patients w/ available data	Value (%)
Age (mean ± SD)	1,568 (100%)	**64.5 ± 11.5**
Female (%)	1,568 (100%)	**553 (35%)**
Body Mass Index (kg/m2) (mean ± SD)	1,554 (99.1%)	**28 ± 5**
AF Type (%)		
Paroxysmal	1,568 (100%)	**1021 (65%)**
Persistent	1,568 (100%)	**498 (32%)**
Long-standing persistent	1,568 (100%)	**49 (3%)**
Comorbidities		
CHA_2DS_2-VASc (mean ± SD)	1,568 (100%)	**2.2 ± 1.6**
Atrial flutter (%)	1,235 (78.8%)	**158 (12.8%)**
Coronary artery disease (%)	1,235 (78.3%)	**167 (13.5%)**
Diabetes (%)	1,568 (100%)	**196 (12.5%)**
Hypertension (%)	1,568 (100%)	**959 (61.1%)**
Heart failure (%)	1,568 (100%)	**226 (14.4%)**
Sleep apnea (%)	1104 (70.4%)	**102 (9.2%)**
Prior stroke/TIA (%)	1568 (100%)	**97 (6.2%)**

MANIFEST-PF: Results

Baseline Patient Characteristics - 2

	Patients w/ available data	Value (%)
Echocardiographic parameters		
LVEF (%) (median, IQR)	1,381 (88.1%)	**60 (55 – 64)**
LA diameter (mm) (median, IQR)	1,220 (77.8%)	**42 (39 – 46)**
Medications		
Class I AADs (%)	1,566 (99.9%)	**343 (21.9%)**
Class III AADs (%)	1,567 (99.9%)	**279 (17.8%)**

MANIFEST-PF: Results

Procedural Characteristics - 1

	Patients w/ available data	Value (%)
Ablation Lesion Sets		
Pulmonary vein isolation (%)	1,568 (100%)	**1,568 (100%)**
Acute success (%)	1,568 (100%)	**1,556 (99.2%)**
Additional non-PV ablation (%)	1,568 (100%)	**359 (22.8%)**
LA posterior wall ablation (%)	1,568 (100%)	173 (11%)
"Roof" line (%)	1,568 (100%)	21 (1.3%)
Mitral line (%)	1,568 (100%)	37 (2.4%)
CTI ablation (%)	1,568 (100%)	84 (5.4%)
Other ablation (%)	1,568 (100%)	44 (2.8%)
Energy used to perform Non-PV ablation		
Pulsed Field energy	359 (100%)	305 (85%)
Radiofrequency	359 (100%)	54 (15%)

MANIFEST-PF: Results

Procedural Characteristics - 2

	Patients w/ available data	Value (%)
Endotracheal intubation (%)	1,568 (100%)	**317 (20%)**
Electroanatomical mapping (%)	1,568 (100%)	**457 (29%)**
ICE Imaging (%)	1,234 (79%)	**407 (33%)**
Fluoroscopy time (min) (median, IQR)	1,521 (97.0%)	**12 (7 – 19)**
Procedure time (min) (median, IQR)	1,540 (98.2%)	**61 (40 – 90)**
Same day discharge (%)	1234 (78.7%)	**101 (6.4%)**

MANIFEST-PF: Results

Follow-Up Details

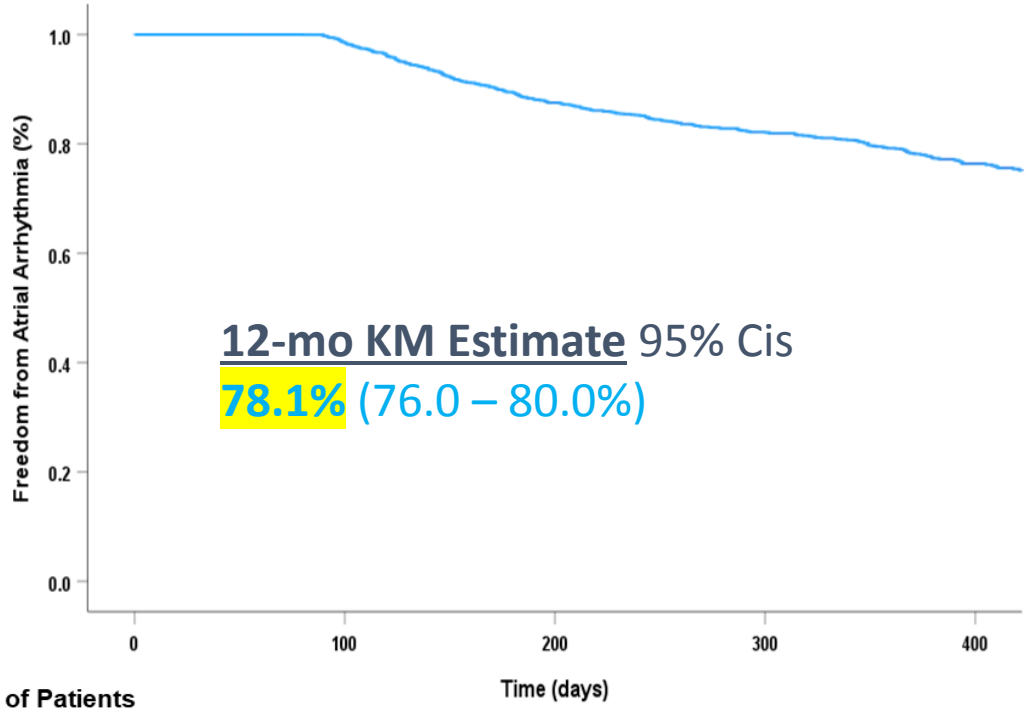
	N=1,568
Follow up duration, days (median, IQR)	367 (289 – 421)
No. of follow up 24-hour Holter monitors (median, IQR)	2 (1 – 3)
No. of follow up visits (median, IQR)	3 (2 – 3)
No. of Patients Receiving Class I/III AADs at 12 mo *	168 (10.7%)
Time to AF/AFL recurrence, days (median, IQR)	180 (129 – 266)
Redo-ablation (%)	148 (9.3%)

* Data available in 1,145 of 1,568 patients (73%)

MANIFEST-PF: Primary Outcome

Kaplan-Meier Analysis: Freedom from AF/AFL/AT

Full Cohort

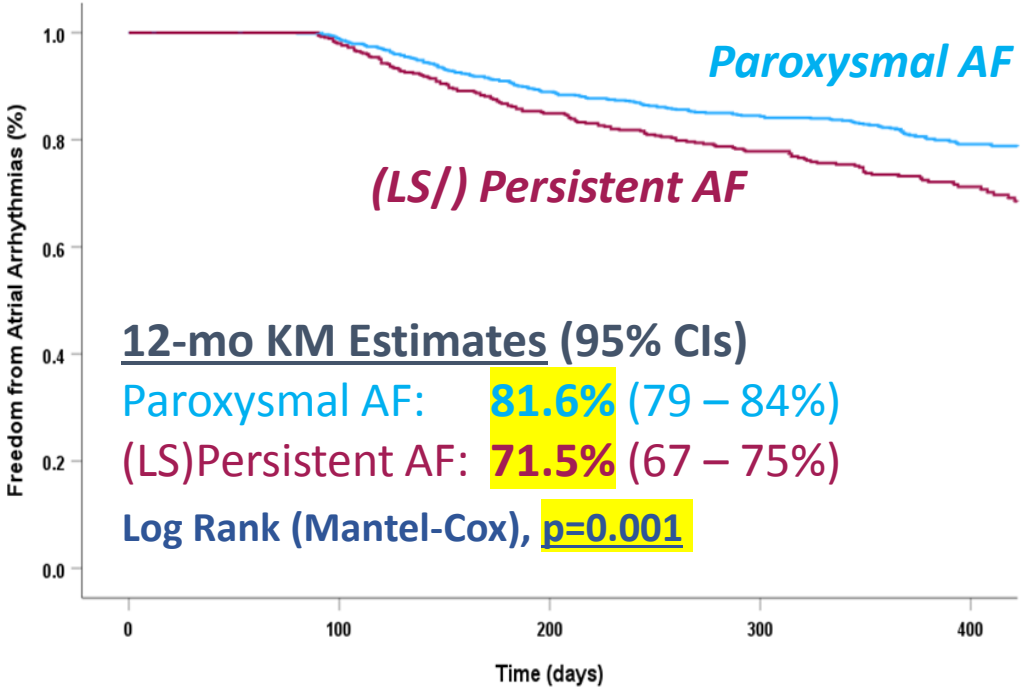


12-mo KM Estimate 95% Cis

78.1% (76.0 – 80.0%)

No. of Patients				
1,568	1,529	1,223	993	435

By AF Subtype



12-mo KM Estimates (95% CIs)

Paroxysmal AF: **81.6%** (79 – 84%)

(LS)Persistent AF: **71.5%** (67 – 75%)

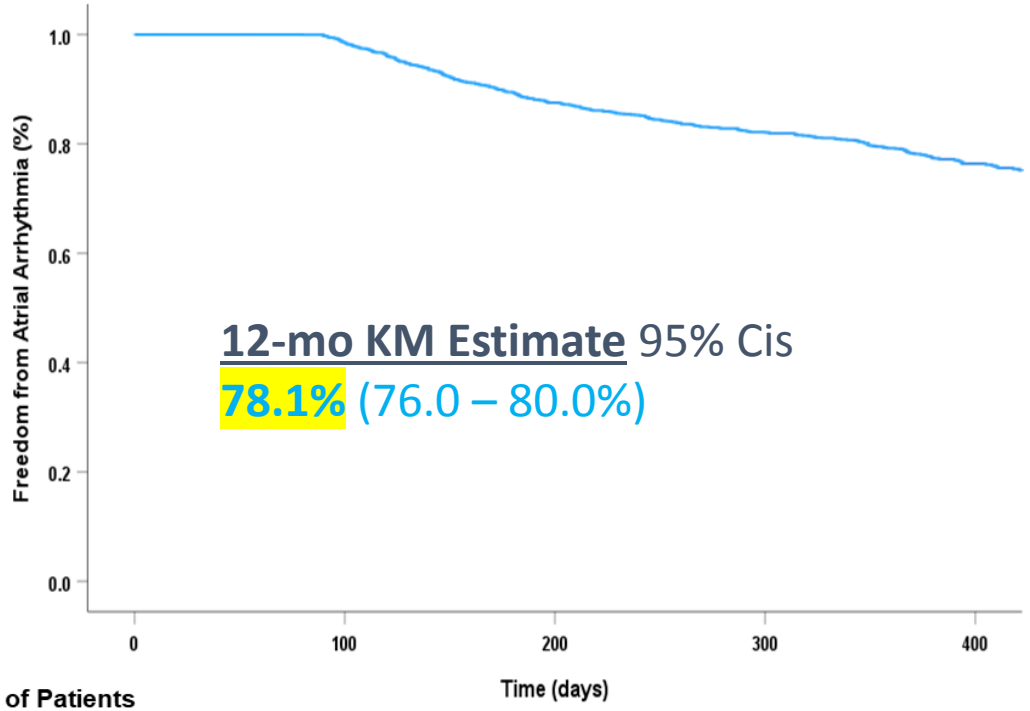
Log Rank (Mantel-Cox), p=0.001

No. of Patients					
Paroxysmal AF	1,021	995	809	657	282
Persistent AF	547	534	414	336	153

MANIFEST-PF: Primary Outcome

Kaplan-Meier Analysis: Freedom from AF/AFL/AT

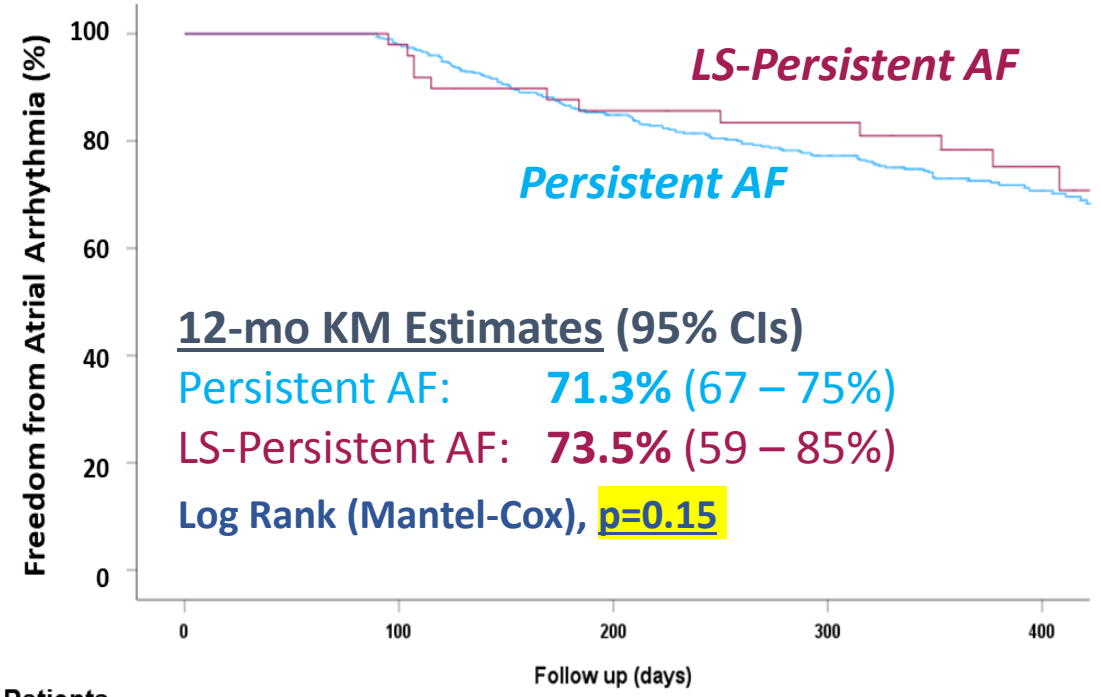
Full Cohort



12-mo KM Estimate 95% Cis
78.1% (76.0 – 80.0%)

No. of Patients					
	1,568	1,529	1,223	993	435

Non-Paroxysmal AF Subtypes



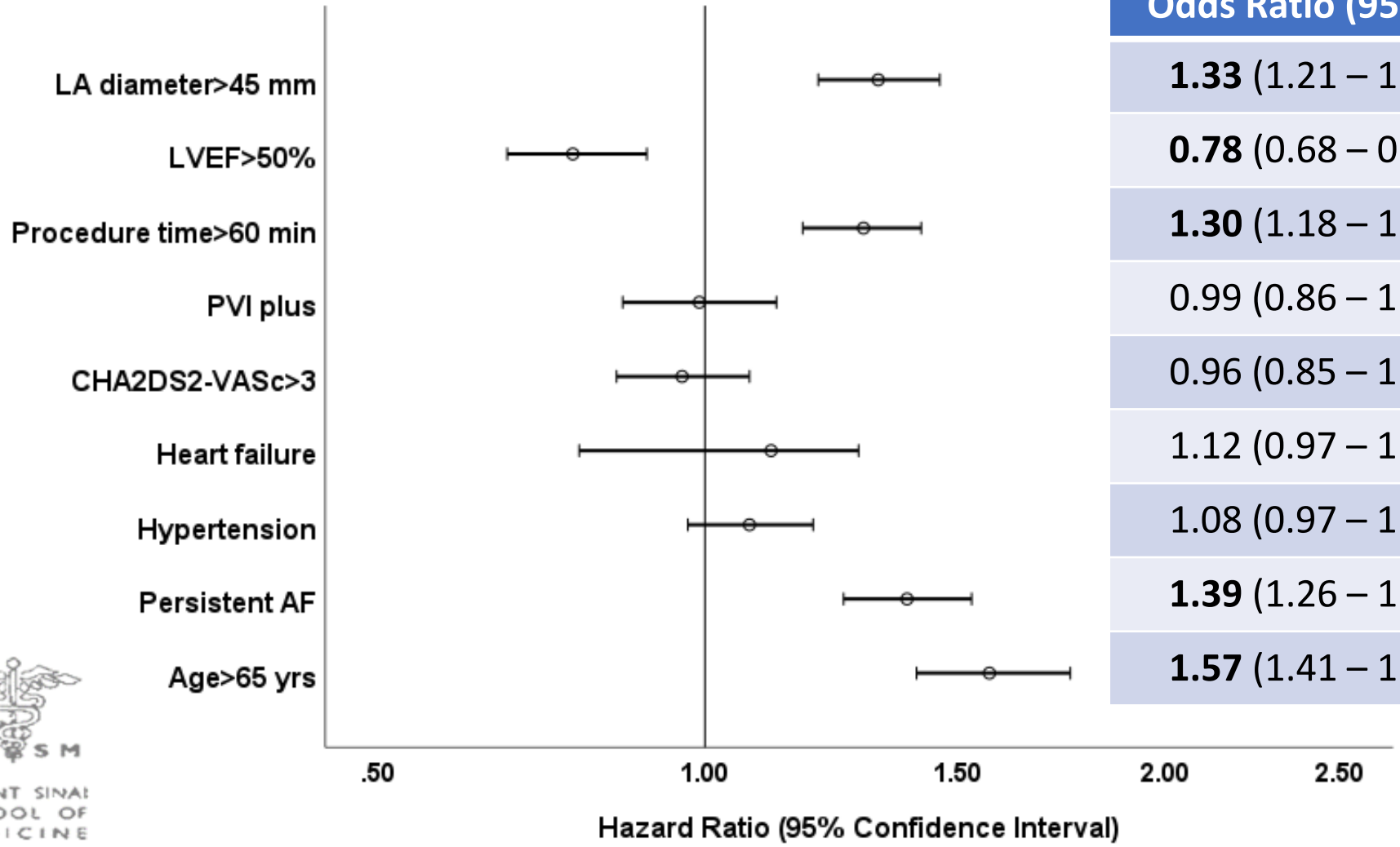
12-mo KM Estimates (95% CIs)
Persistent AF: **71.3%** (67 – 75%)
LS-Persistent AF: **73.5%** (59 – 85%)
Log Rank (Mantel-Cox), p=0.15

No. of Patients					
Persistent AF	498	487	374	299	133
LS-Persistent AF	49	47	40	37	20

MANIFEST-PF: Results

Risk factors for Primary Efficacy Failure

Multivariable Logistic Regression

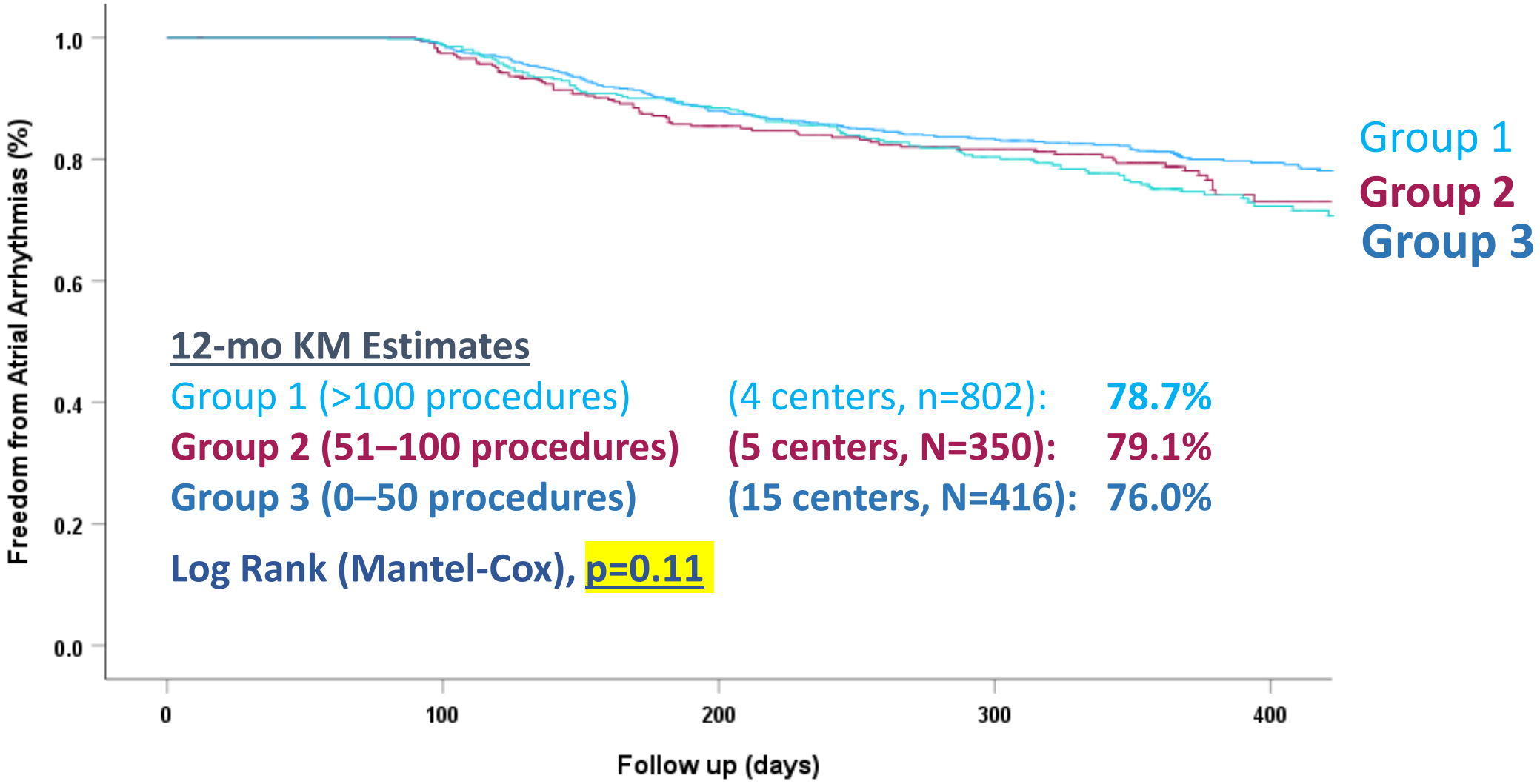


Odds Ratio (95% CI)	P-value
1.33 (1.21 – 1.46)	**<0.001**
0.78 (0.68 – 0.90)	**<0.001**
1.30 (1.18 – 1.43)	**<0.001**
0.99 (0.86 – 1.13)	0.92
0.96 (0.85 – 1.08)	0.52
1.12 (0.97 – 1.29)	0.10
1.08 (0.97 – 1.20)	0.14
1.39 (1.26 – 1.53)	**<0.001**
1.57 (1.41 – 1.76)	**<0.001**

MSSM
MOUNT SINAI SCHOOL OF MEDICINE

Results: Freedom from AF/AFL/AT

Outcomes by Center Volumes



12-mo KM Estimates

Group 1 (>100 procedures)	(4 centers, n=802):	**78.7%**
Group 2 (51–100 procedures)	**(5 centers, N=350):**	**79.1%**
Group 3 (0–50 procedures)	**(15 centers, N=416):**	**76.0%**

Log Rank (Mantel-Cox), p=0.11

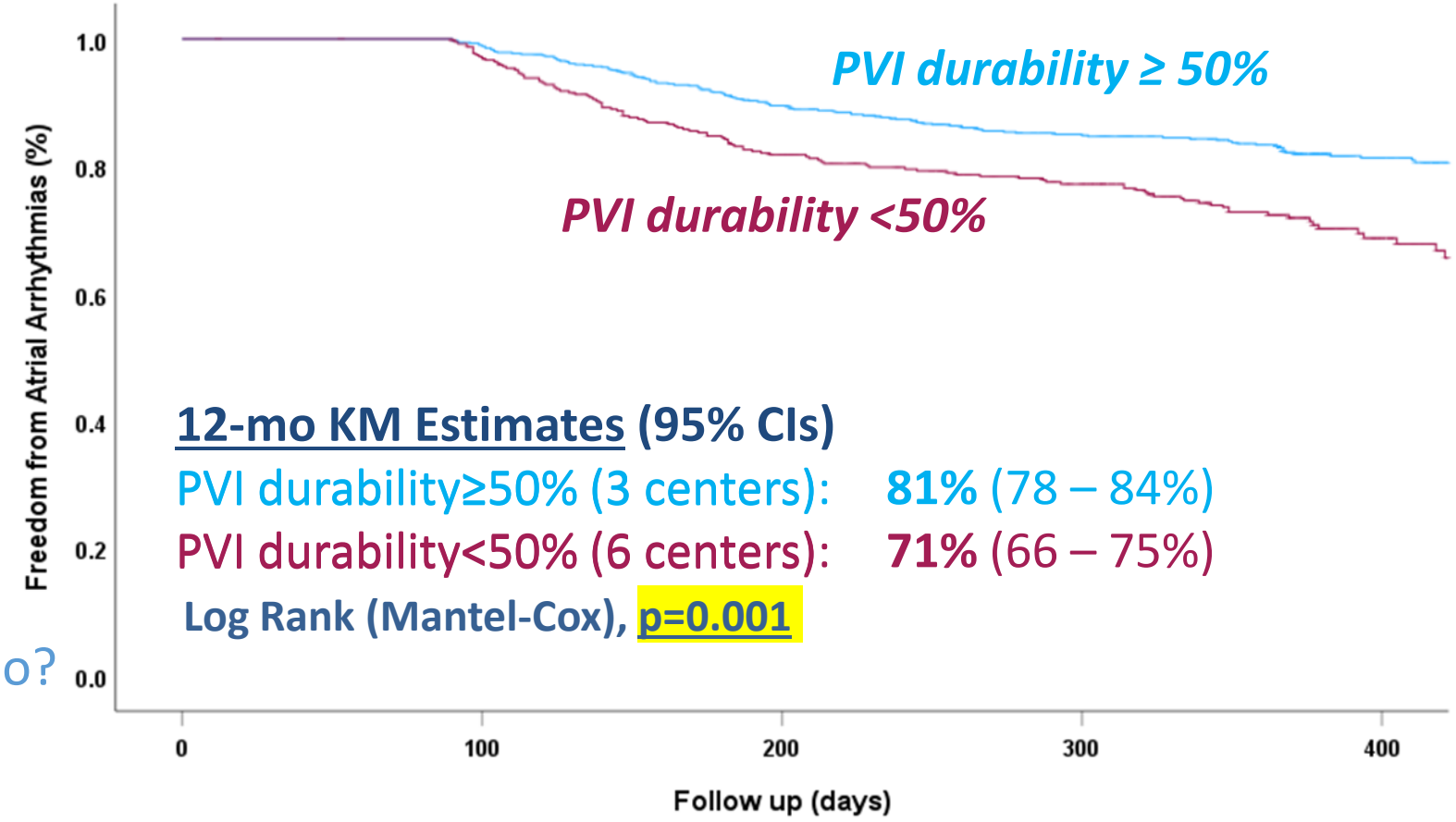
Results: Freedom from AF/AFL/AT

Based on Center-Level PVI Durability at Redo Ablation

PVI Durability in Redo Cases

- Redo in **9.3%** pts (148 of 1,568)
- Durable PVI seen in:
  - **72.1%** of PVs (427 of 592)
  - **45.2%** of pts with all PVs durably isolated (67 of 148)

- *Post Hoc* Analysis: Outcomes by center-level PVI durability at redo?
  - Only centers with > 5 redo cases



12-mo KM Estimates (95% CIs)

PVI durability≥50% (3 centers): **81%** (78 – 84%)

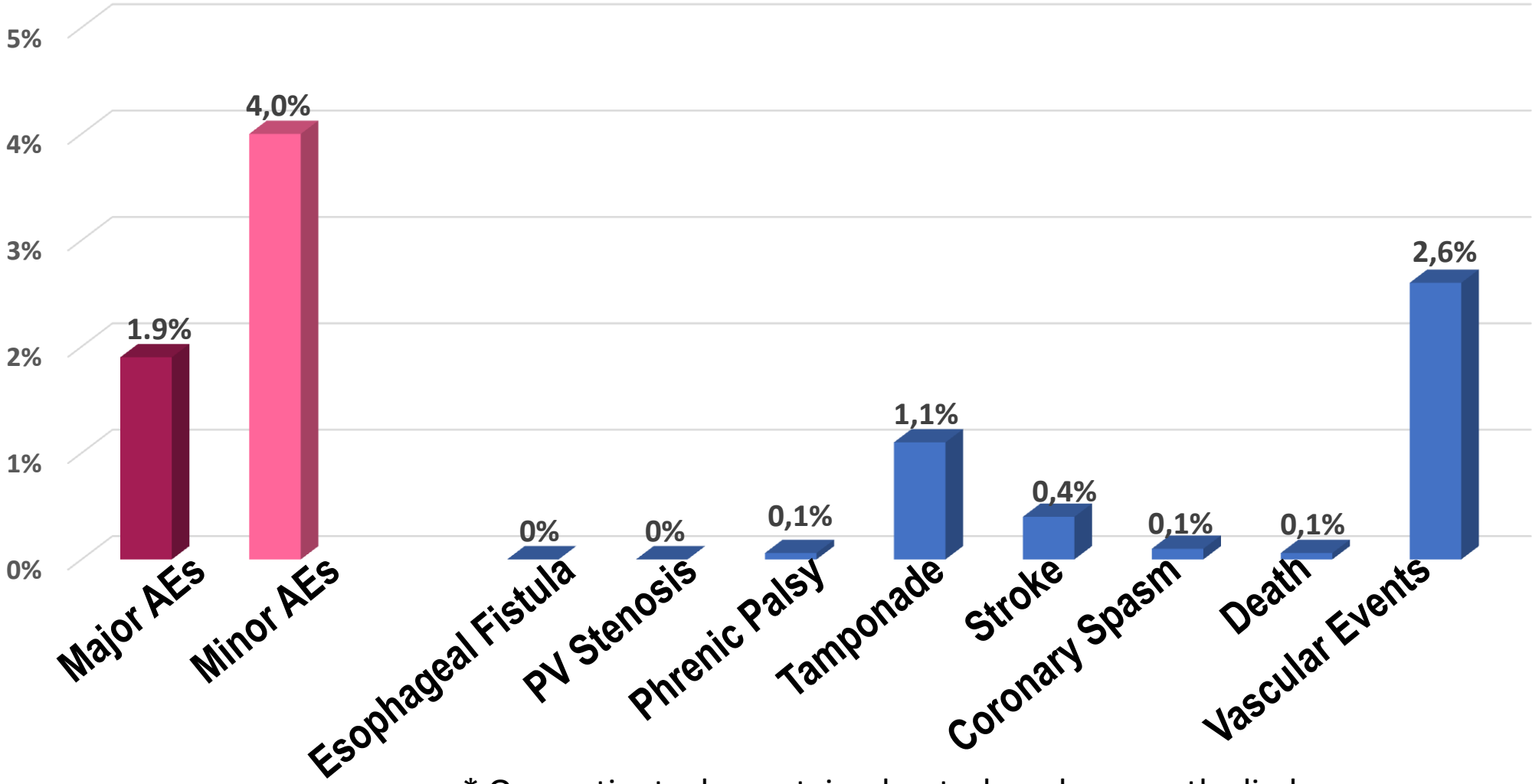
PVI durability<50% (6 centers): **71%** (66 – 75%)

Log Rank (Mantel-Cox), p=0.001

No. of Patients					
PVI durability ≥ 50%	699	688	591	481	242
PVI durability <50%	398	380	299	252	83

MANIFEST-PF: Safety Results

Adverse Events

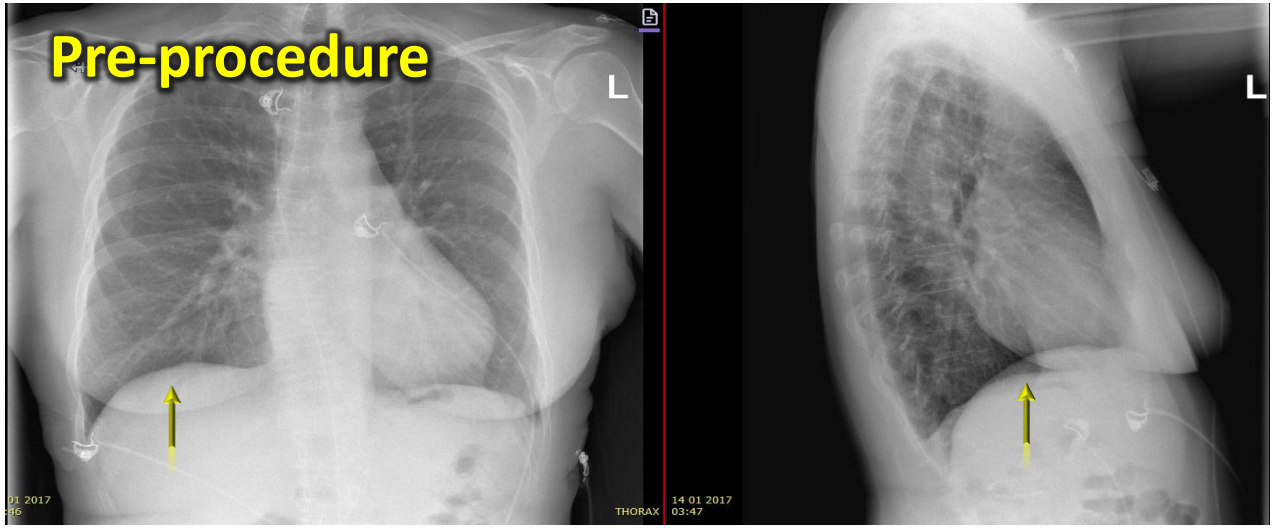


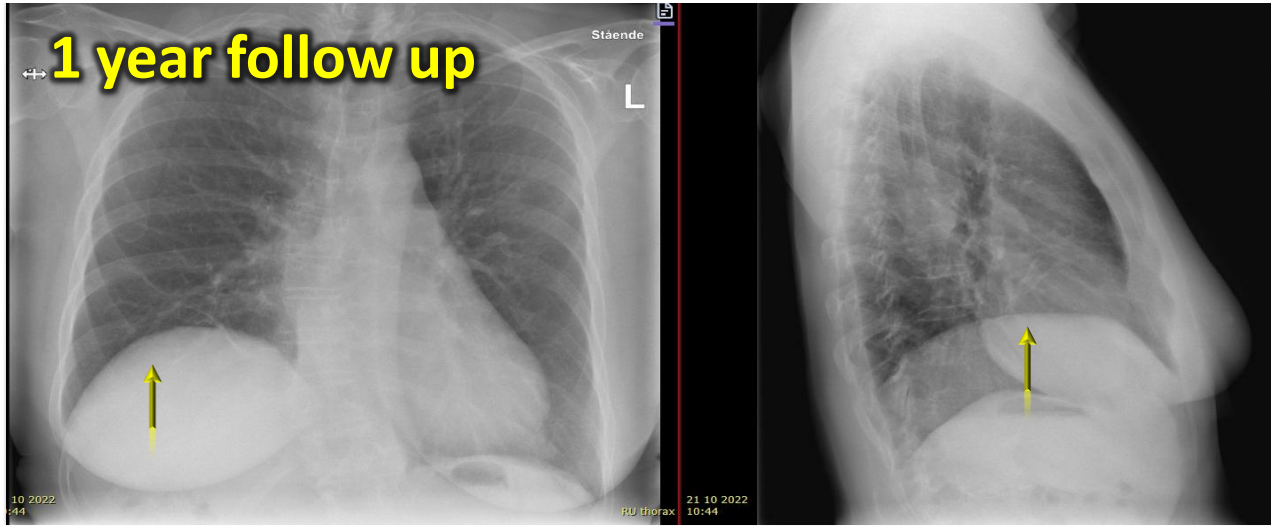
* One patient who sustained a stroke subsequently died.

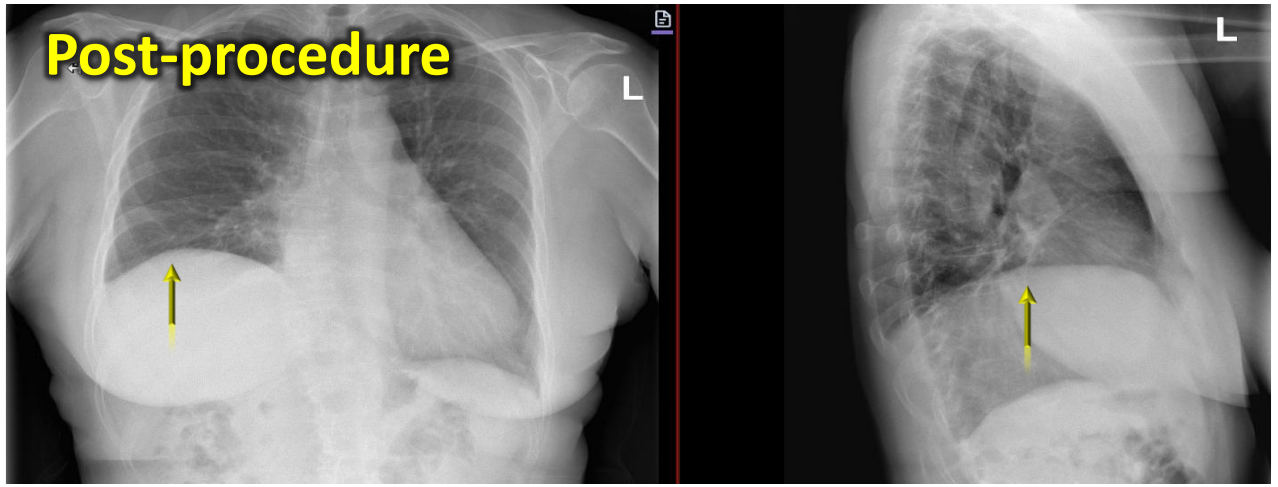
† Defined as persisting beyond hospital discharge.

Phrenic Nerve Palsy Case

Serial X-Ray Imaging







Conclusions

In an unselected population undergoing first-ever AF ablation in routine practice, using the pentaspline PFA catheter:

- One-year Freedom from AF/AFL/AT was good (78%)
  - Efficacy better for Paroxysmal AF (82%) than Persistent AF (71%)
  - Efficacy sensitive to PVI durability

- Despite first use of a novel PFA catheter, Good safety profile:
  - C/w preferential tissue ablation (no esophageal damage, or PV stenosis)
  - However, 1 patient sustained phrenic nerve injury beyond hospitalization
  - No Late Complications

Limitations

- Retrospective study

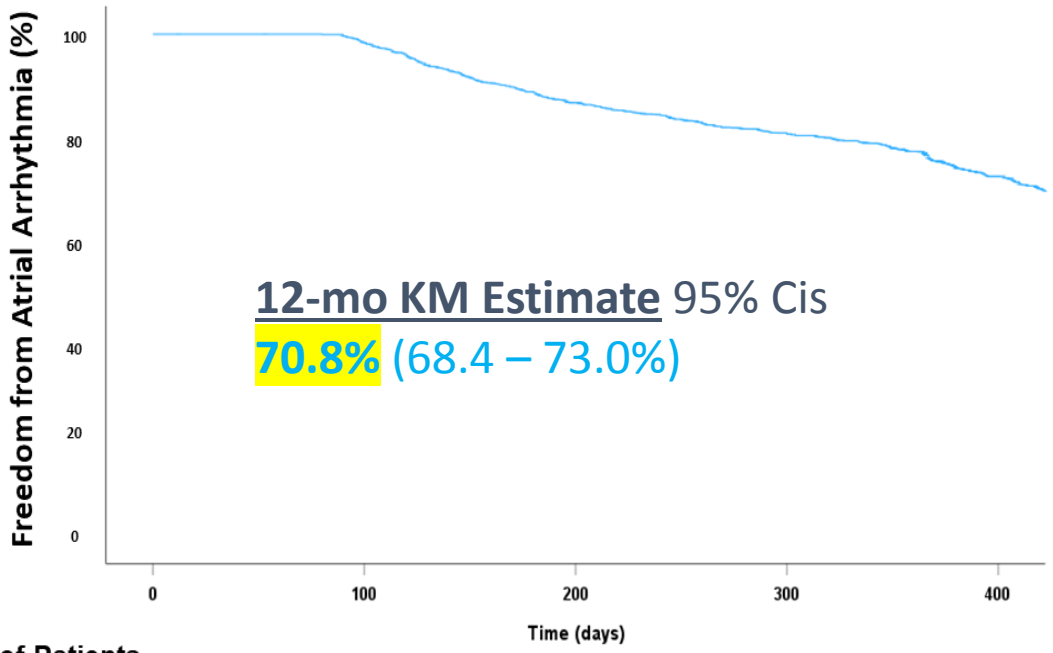
- Efficacy results:
  - Variability in frequency and/or intensity (eg, ±Holters) of f/u
  - *Durability of PVI is unknown (as well as other lesions sets)*

- Safety results:
  - Little data on safety of lesion sets beyond PVI
  - What happens when >10,000 pts are treated?

MANIFEST-PF: Secondary Outcome

Freedom from AF/AFL/AT *or* AADs *or* Redo Ablation

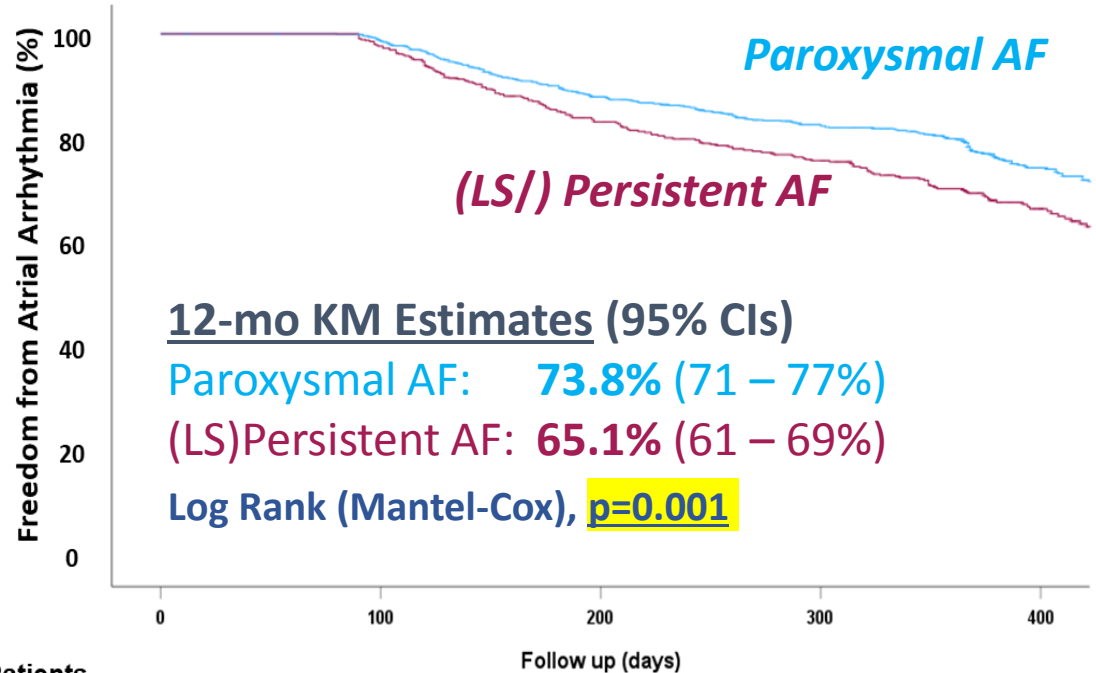
Full Cohort



12-mo KM Estimate 95% Cis
70.8% (68.4 – 73.0%)

No. of Patients					
	1,568	1,529	1,223	993	435

By AF Subtype



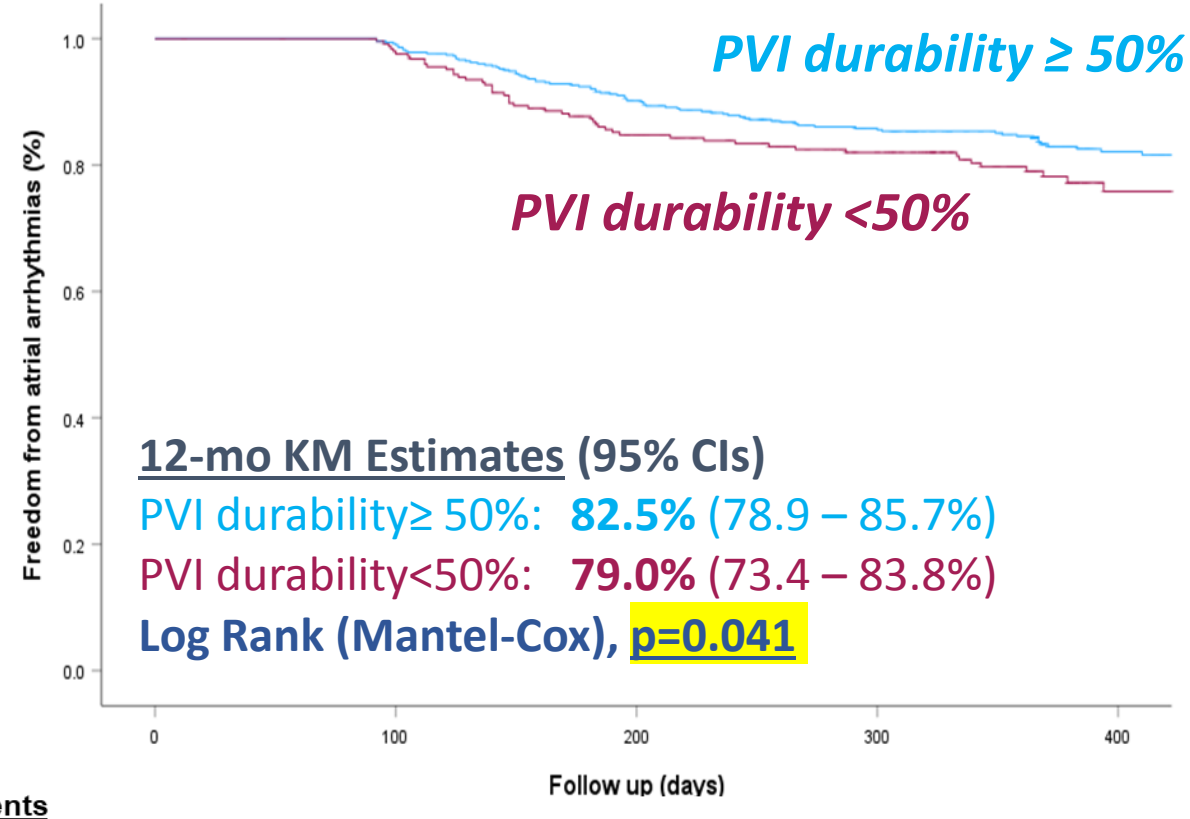
12-mo KM Estimates (95% CIs)
Paroxysmal AF: **73.8%** (71 – 77%)
(LS)Persistent AF: **65.1%** (61 – 69%)
Log Rank (Mantel-Cox), p=0.001

No. of Patients					
Paroxysmal AF	1,021	995	809	657	282
Persistent AF	547	534	414	336	153

Results: Freedom from AF/AFL/AT

Based on Center-Level PVI Durability at Redo Ablation

Paroxysmal AF



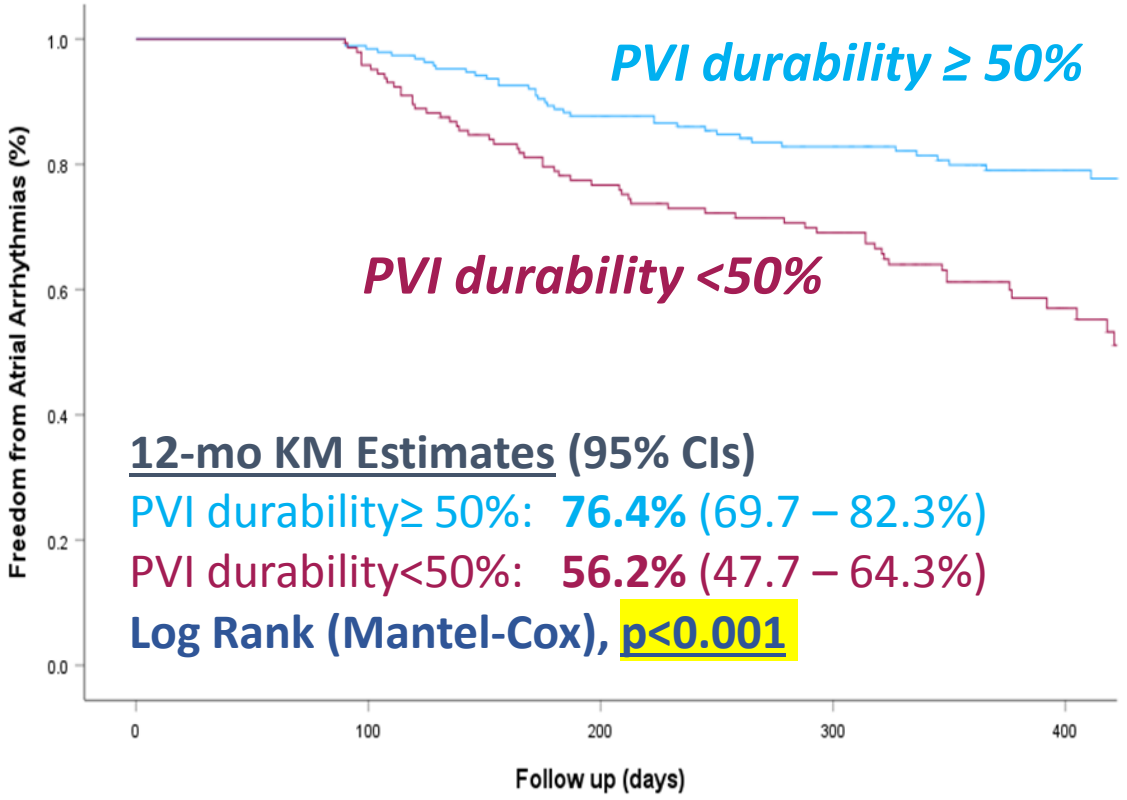
12-mo KM Estimates (95% CIs)

PVI durability≥ 50%: **82.5%** (78.9 – 85.7%)

PVI durability<50%: **79.0%** (73.4 – 83.8%)

Log Rank (Mantel-Cox), p=0.041

Persistent AF



12-mo KM Estimates (95% CIs)

PVI durability≥ 50%: **76.4%** (69.7 – 82.3%)

PVI durability<50%: **56.2%** (47.7 – 64.3%)

Log Rank (Mantel-Cox), p<0.001

No. of Patients										
PVI durability≥ 50%	508	500	432	357	177	191	188	159	123	64
PVI durability<50%	252	242	196	166	50	146	137	103	86	32