

DANPACE: The Danish multicenter randomised trial on AAIR versus DDDR pacing in sick sinus syndrome

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on behalf of the DANPACE investigators*

Conflicts of interest

- Jens Cosedis Nielsen has received speakers fees and/or consultant honoraries from Medtronic, St Jude Medical, Biotronik, Astra-Zeneca, and Sanofi-Aventis.

DANPACE investigators

Steering Committee (numbers of patients included):

- Henning Rud Andersen (chairman) and Jens Cosedis Nielsen (co-chairman), Aarhus University Hospital, Skejby (337);
- Poul-Erik Bloch-Thomsen, Gentofte Hospital (180);
- Søren Højberg, Bispebjerg Hospital (121);
- Mogens Møller, Odense University Hospital (114);
- Thomas Vesterlund, Aalborg Hospital (111);
- Dorthe Dalsgaard, Herning Hospital (108);
- Tonny Nielsen, Esbjerg Hospital (77);
- Mogens Asklund, Kolding Hospital (72);
- Elsebeth Vibeke Friis, Haderslev Hospital (70);
- Per Dahl Christensen, Viborg Hospital (56);
- Erik Hertel Simonsen, Hillerød Hospital (47);
- Ulrik Hedegaard Eriksen, Vejle Hospital (39);
- Gunnar Vagn Hagemann Jensen, Roskilde Hospital (28);
- Jesper Hastrup Svendsen, Rigshospitalet (24).

From United Kingdom:

- William D. Toff (UK coordinating investigator), J. Douglas Skehan, Kieran Brack, Glenfield Hospital, Leicester (8);
- Craig Barr, Andreas Tselios, Nicola Gordon, Russells Hall Hospital, Dudley (6);
- John Cleland, Andrew Clark, Sarah Hurren, Castle Hill Hospital, East Cottingham (3);
- David McEneaney, Andrew Moriarty, Anne Mackin, Craigavon Area Hospital, Craigavon (2);
- Arif Ahsan, Jane Burton, Ruth Oliver, Nottingham City Hospital (2),
- Barry Kneale, Lynda Huggins, Worthing Hospital (2).

From Canada:

- Jeffrey S. Healey, Hamilton (8).

Background

- In patients with sick sinus syndrome (SSS) bradycardia can be treated with any pacemaker: AAIR, VVIR, or DDDR.
- VVIR pacing increases atrial fibrillation as compared with physiological pacing (DDDR or AAIR), and VVIR pacing was associated with increased mortality as compared with AAIR pacing in one small trial.¹
- Ventricular pacing has been found to cause ventricular desynchronisation with lowering of LVEF and left atrial dilatation, resulting in heart failure and atrial fibrillation.

¹: Andersen HR et al., Lancet 1997

Aim

- To compare AAIR and DDDR pacing in SSS.
- Primary endpoint:
 - Death from any cause.
- Secondary endpoints:
 - Paroxysmal atrial fibrillation (at planned follow-up)
 - Chronic atrial fibrillation
 - Stroke
 - Heart failure
 - Pacemaker reoperation

Statistics

- 1,900 patients.
- Followed for in mean 5.5 years.
- Identify a 6% absolute difference in mortality.
- Power 80%, overall $\alpha=0.05$.
- Intention to treat.

- Two planned interim analyses after 1/3 and 2/3 of the expected number of deaths.

Methods

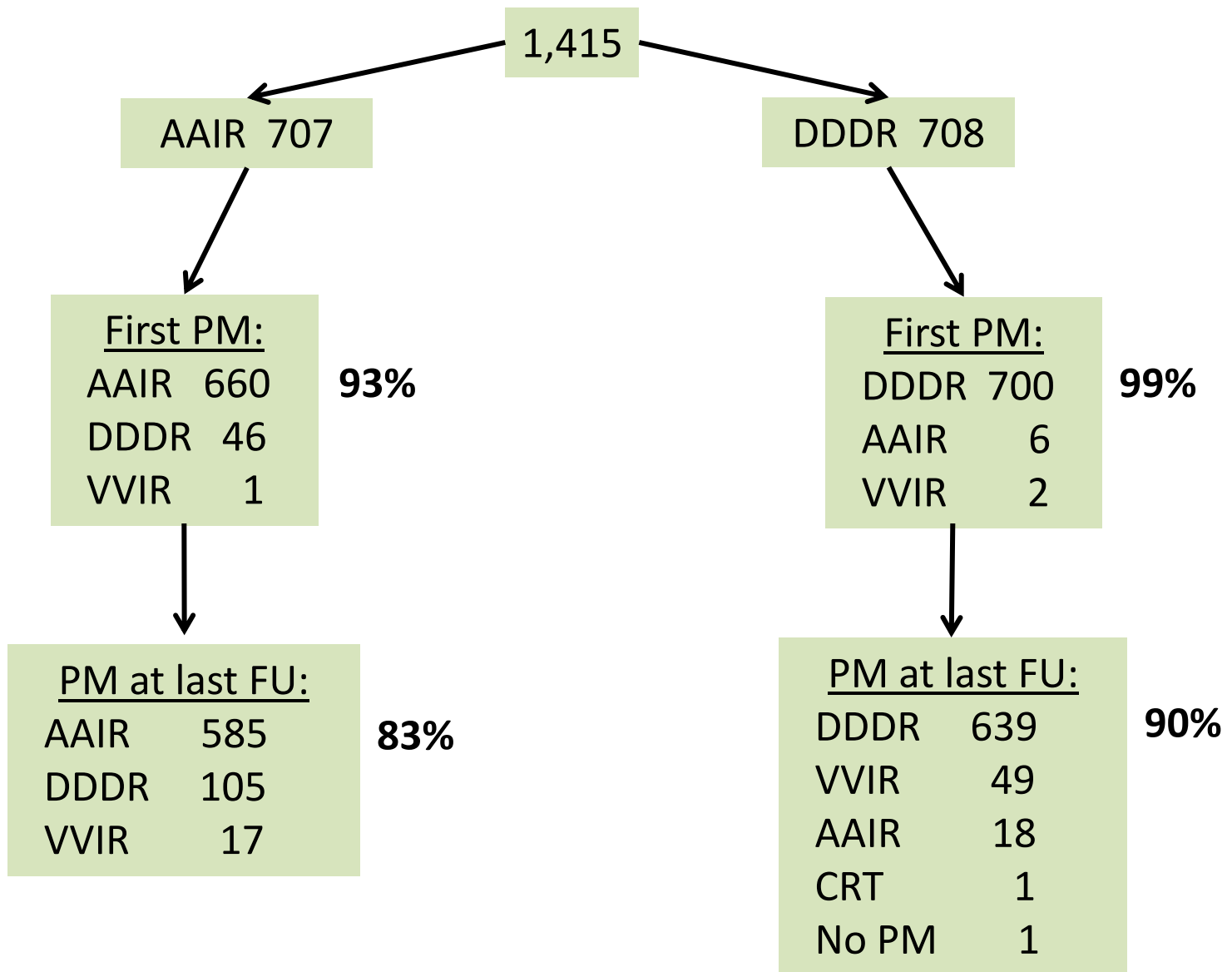
- Randomised controlled trial.
- Inclusion criteria:
 - symptomatic bradycardia and documented sinus-pause >2s or sinus bradycardia <40bpm >1 minute whilst awake,
 - PR-interval ≤ 0.22 s (age 18-70 years) or PR-interval ≤ 0.26 s (age ≥ 70 years),
 - QRS width <0.12s.
- Exclusion criteria:
 - AV block,
 - bundle branch block,
 - persistent atrial fibrillation >12 months,
 - atrial fibrillation with QRS rate <40 bpm for ≥ 1 min or pauses >3s,
 - a positive test for carotid sinus hypersensitivity.

Pacemaker programming

- Rate adaptive function was active
- Lower rate 60 bpm
- Upper rate 130 bpm

- DDDR:
 - Paced AV-interval ≤ 220 ms
 - Sensed AV-interval ≤ 200 ms.
 - Rate-adaptive shortening of the AV-interval.

Randomisation and pacing mode



Baseline Characteristic	AAIR (N=707)	DDDR (N=708)	p-value
Female gender no. (%)	472 (66.8)	441 (62.3)	0.08
Age (years, mean±SD)	73.5 ±11.2	72.4 ±11.4	0.054
Brady-tachy syndrome no. (%)	303 (42.9)	318 (44.9)	0.44
Hypertension	241 (34.1)	239 (33.8)	0.90
Previous myocardial infarction no. (%)	94 (13.3)	90(12.7)	0.74
Diabetes no. (%)	68 (9.6)	72 (10.2)	0.73
Previous transient cerebral ischemia no. (%)	35 (5.0)	37 (5.2)	0.81
Previous stroke no. (%)	61 (8.6)	53 (7.5)	0.43
Left ventricular ejection fraction reduced (< 50%) no. (%)	59 (10.6)	54 (9.5)	0.55
Left ventricular end-diastolic diameter (mm, mean±SD)	47.7 ± 7.3	47.8 ± 7.3	0.45
Left atrial diameter (mm, mean±SD)	39.3 ± 6.5	38.8 ± 6.4	0.23
Symptoms before pacemaker no. (%)			
Syncope	359 (50.8)	349 (49.3)	0.58
Dizzy spells	597 (84.4)	587 (82.9)	0.44
Heart failure	86 (12.2)	79 (11.2)	0.56
≥2 of the above three symptoms	317 (44.8)	291 (41.1)	0.16
Medication at randomization no. (%)			
Anticoagulation	108 (15.3)	89 (12.6)	0.14
Aspirin	369 (52.2)	361 (51.1)	0.67
Sotalol	43 (6.1)	44 (6.2)	0.91
Beta-blocker other than sotalol	159 (22.5)	132 (18.7)	0.08
Calcium-channel blocker	137 (19.4)	142 (20.1)	0.75
Digoxin	73 (10.3)	62 (8.8)	0.32
Amiodarone	25 (3.5)	24 (3.4)	0.88
Class I Antiarrhythmics	14 (2.0)	20 (2.8)	0.30
Angiotensin-converting-enzyme inhibitors	160 (22.6)	170 (24.0)	0.53
Diuretics	304 (43.0)	263 (37.2)	0.03
New York Heart Association functional class no. (%)			0.33
I	503 (71.4)	522 (73.9)	
II	172 (24.4)	158 (22.4)	
III	29 (4.1)	24 (3.4)	
IV	0	2 (0.3)	
Wenckebach block point (≥100 bpm, %)	611 (94.1)	581 (91.6)	0.08
Treated as randomized	660 (93.4)	700 (98.9)	<0.001

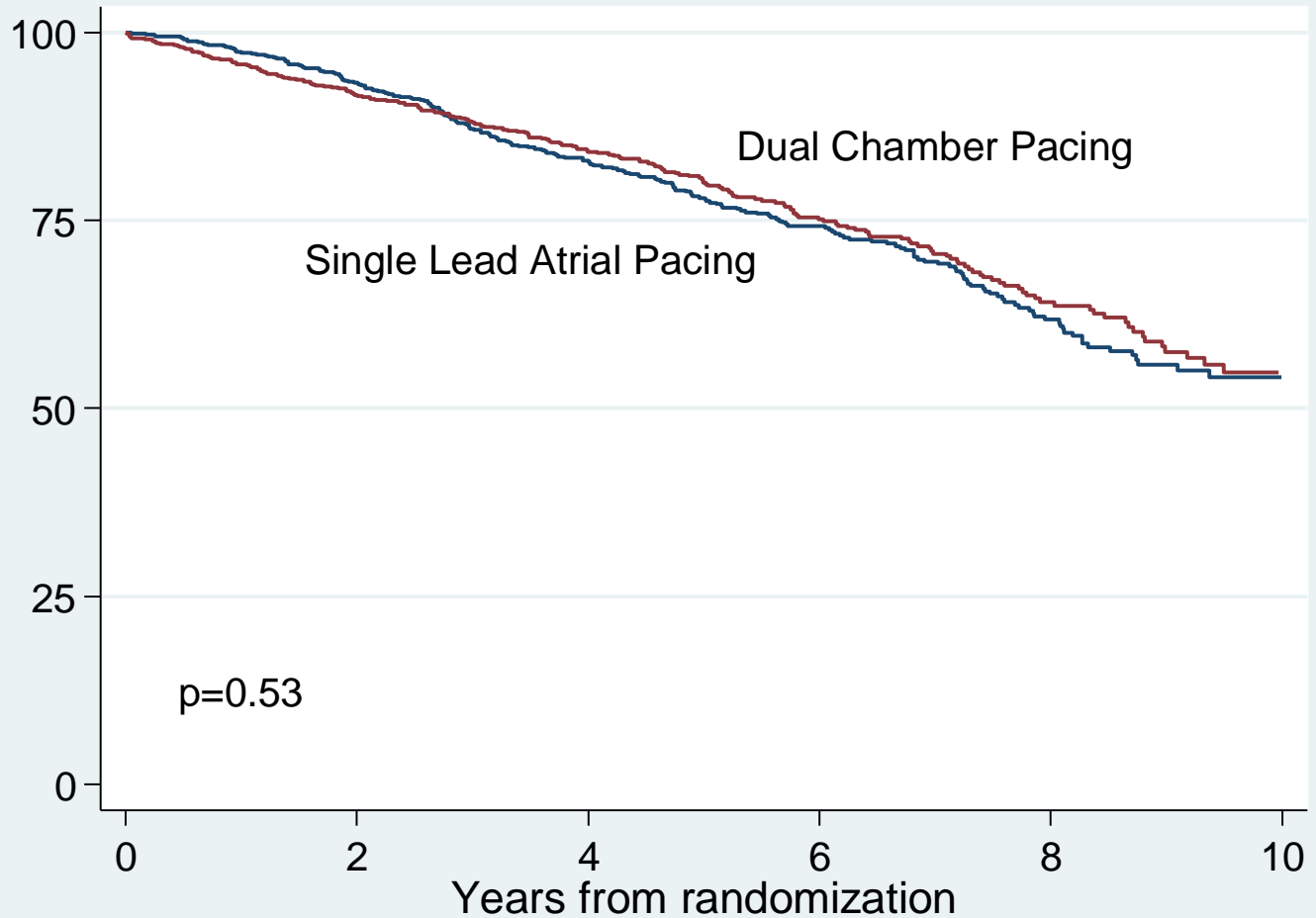


Results

- Follow-up 5.4 ± 2.6 years
- No patients lost for follow-up
- Pacing in the atrium:
 - AAIR group: $58 \pm 29\%$
 - DDDR group: $59 \pm 31\%$

} P=0.52
- Pacing in the ventricle:
 - DDDR group: $65 \pm 33\%$

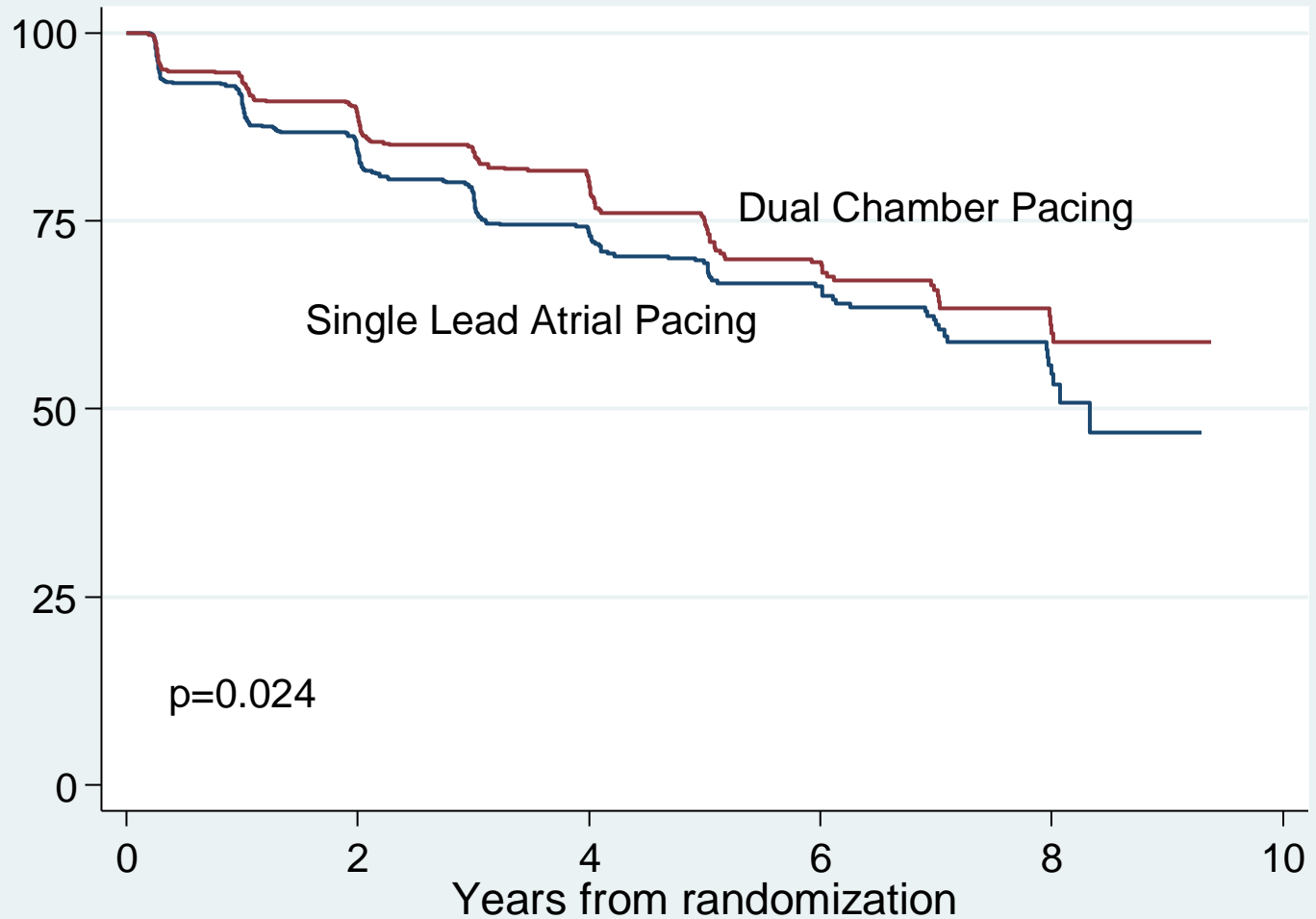
Survival



No. at Risk

Single Lead	707	648	466	298	147	25
Dual Chamber	708	629	462	287	136	24

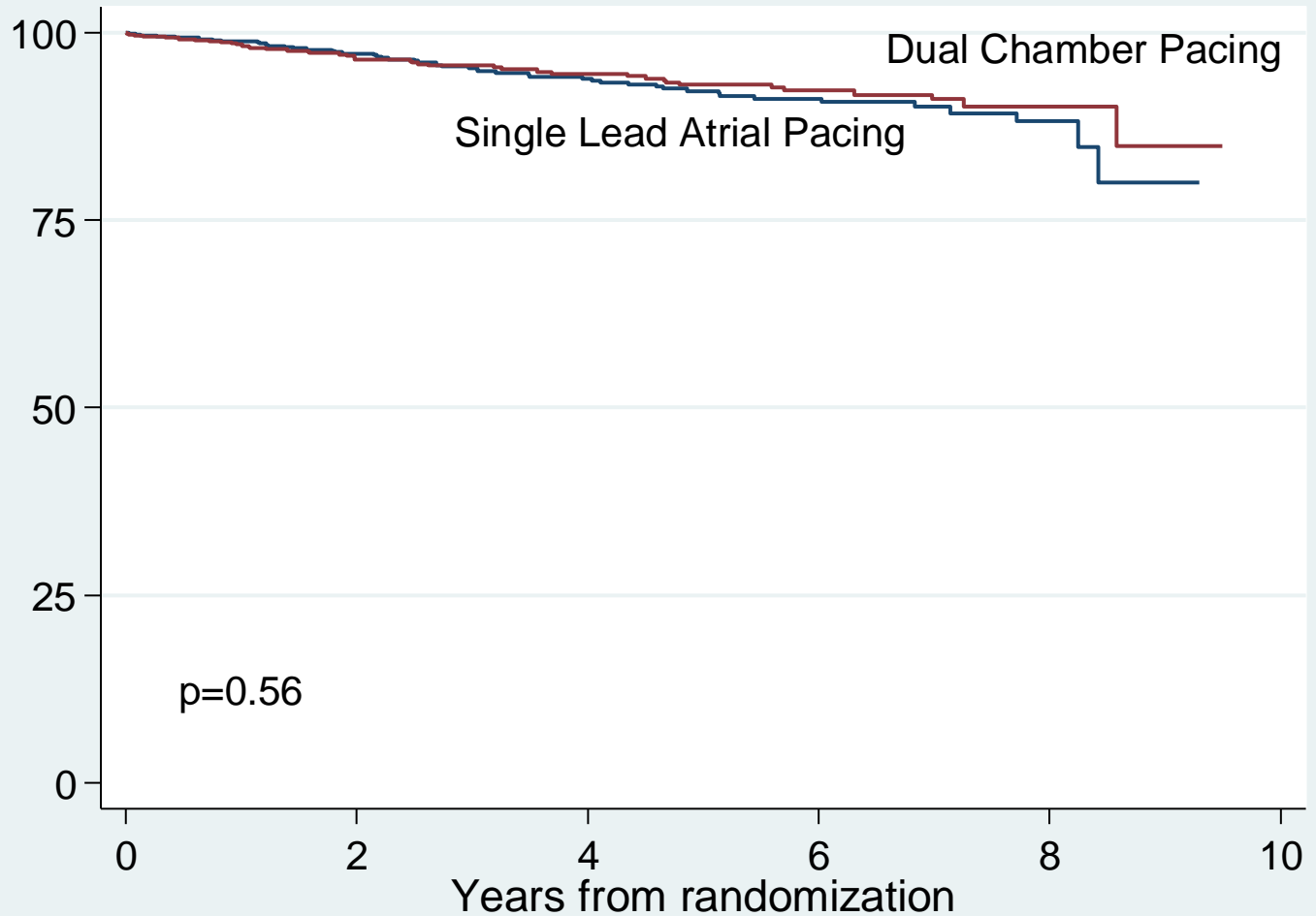
Atrial fibrillation



No. at Risk

Single Lead	707	498	301	157	47	0
Dual Chamber	708	504	330	158	52	0

Stroke



No. at Risk

Single Lead 707

571

383

225

68

0

Dual Chamber 708

550

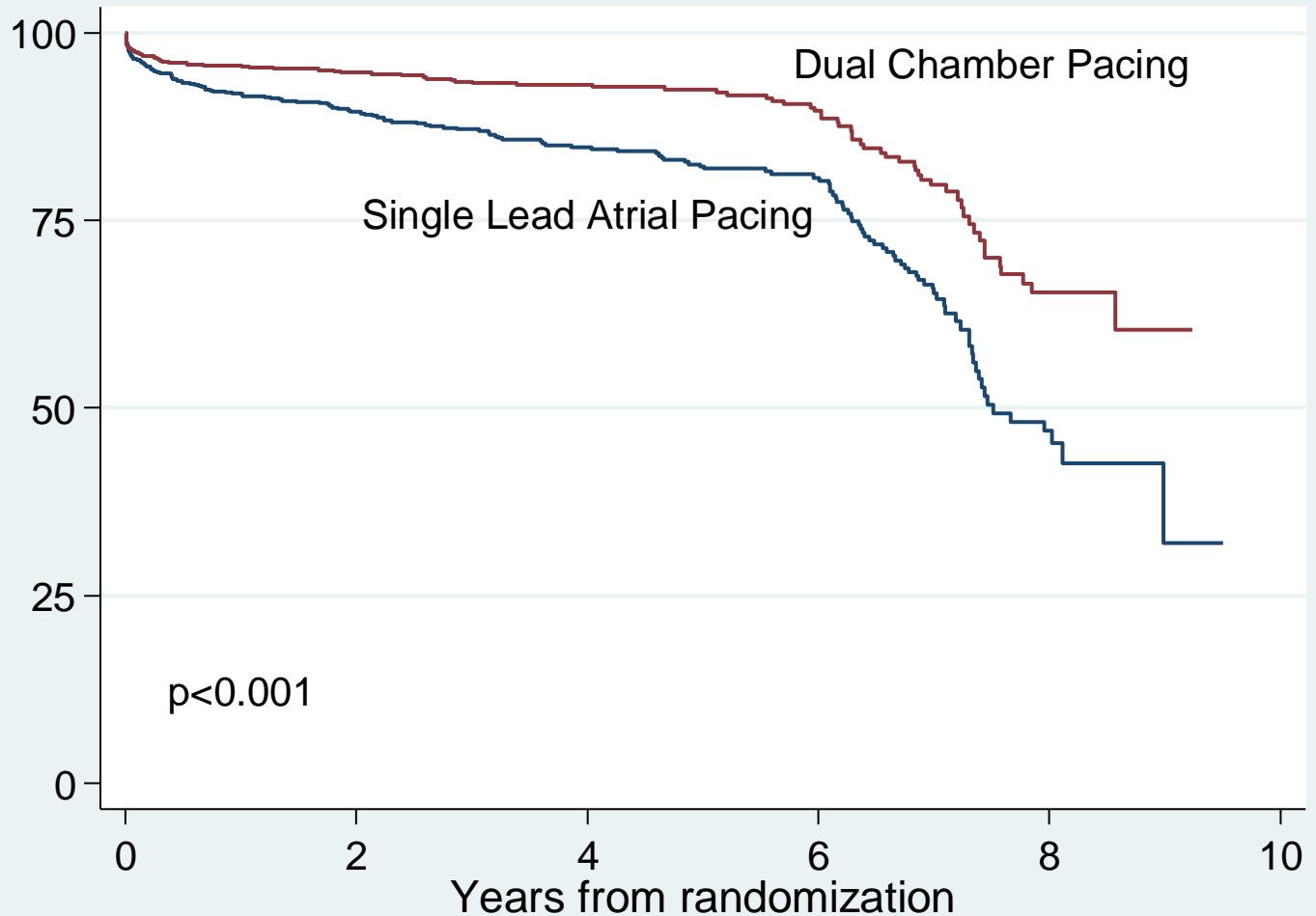
391

215

73

0

Reoperation



No. at Risk

Single Lead 707

527

340

196

33

0

Dual Chamber 708

534

377

198

44

0

Heart failure

- NYHA class at last FU: $p=0.43.$
- Diuretics at last follow-up: $p=0.89.$
- Hospitalization for heart failure: $p=0.90.$

Clinical Outcomes – Multivariate analysis

	Adjusted HR	95% CI	P-value
Death	0.94	0.77-1.14	0.52
Paroxysmal AF	1.24	1.01-1.52	0.042
Chronic AF	1.01	0.74-1.39	0.93
Stroke	1.05	0.70-1.59	0.80
Reoperation	2.00	1.54-2.61	<0.001

Conclusions

- No difference in survival between AAIR and DDDR pacing in SSS.
- Risk of reoperation is doubled with AAIR pacing.
- Paroxysmal atrial fibrillation is more common in AAIR pacing.
- DDDR pacing with an AV interval ≤ 220 ms is the preferred pacing mode for SSS.
- AAIR pacing should no longer be used.

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