Implantable cardiac monitors in high-risk post-infarction patients with cardiac autonomic dysfunction and moderately reduced left ventricular ejection fraction – A randomized trial

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for the SMART-MI investigators

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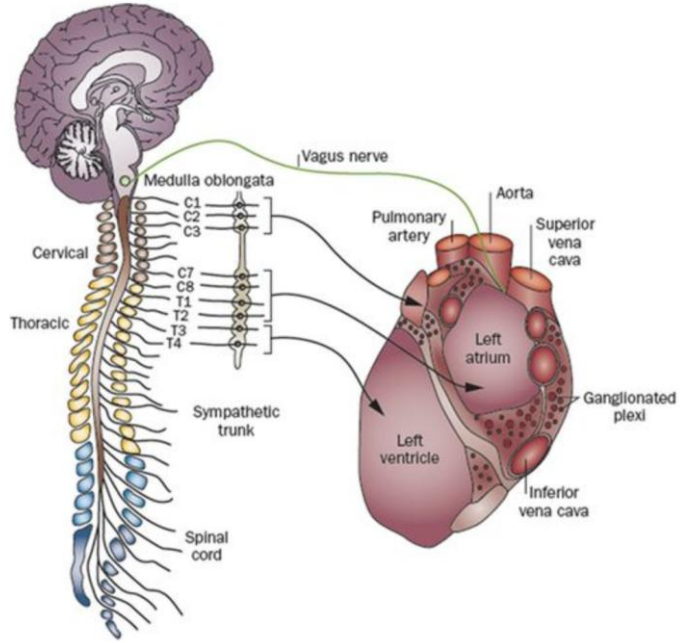
Background

- Most cardiovascular complications after myocardial infarction (MI) occur in patients with left ventricular ejection fraction (LVEF) >35%[1]
- A MI can cause profound damage to the autonomic nervous system at various levels of the cardiac neuroaxis[2]
- Cardiac autonomic dysfunction after MI is associated with poor prognosis, irrespective of LVEF
- Cardiovascular complications may be preceded by subclinical arrhythmic events[3]
- Early detection of these arrhythmias by telemedical monitoring may identify patients at very high risk for impending complications



[1]ISAR RISK, Eur Heart J 2009
[2]Circulation Research 2014
[3]CARISMA-ICM, Circulation 2010

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Hypothesis

Telemedical monitoring with implantable cardiac monitors (ICMs) is superior to conventional follow-up in early detection of serious arrhythmic events (SArE) in post-MI patients with cardiac autonomic dysfunction and LVEF 36-50%

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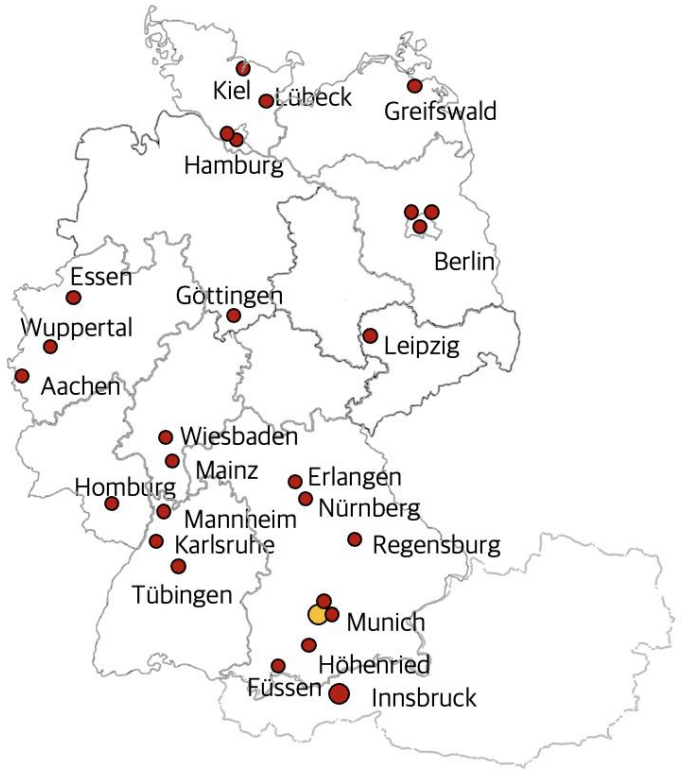
Study design

- Investigator-initiated, randomized, multicentre study
- 33 tertiary centres in Germany and Austria
- Funded by the German Center for Cardiovascular Research (DZHK) and the Medtronic Bakken Research Centre
- Enrolment from May 2016 and February 2021
- Coordination, ECG and ICM core labs by the Munich University Hospital



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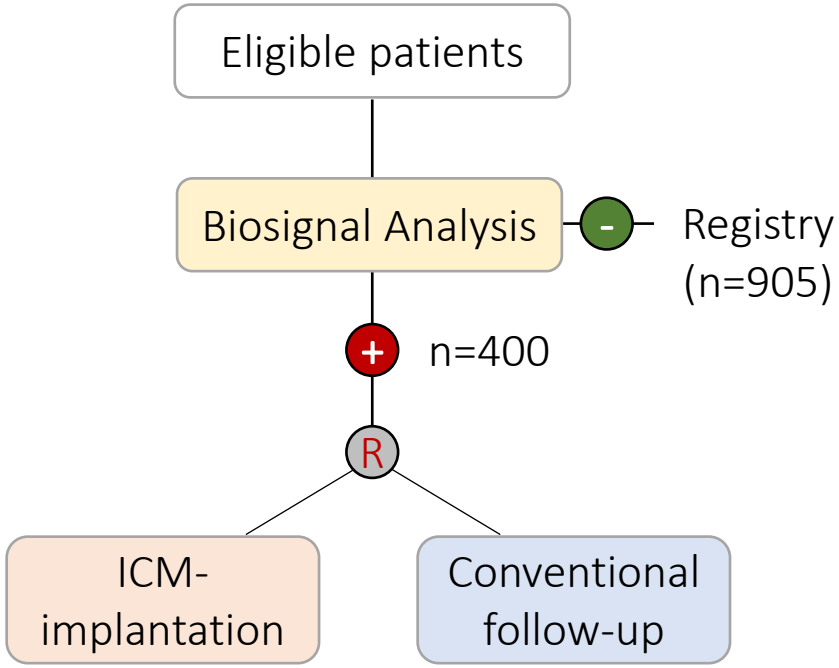
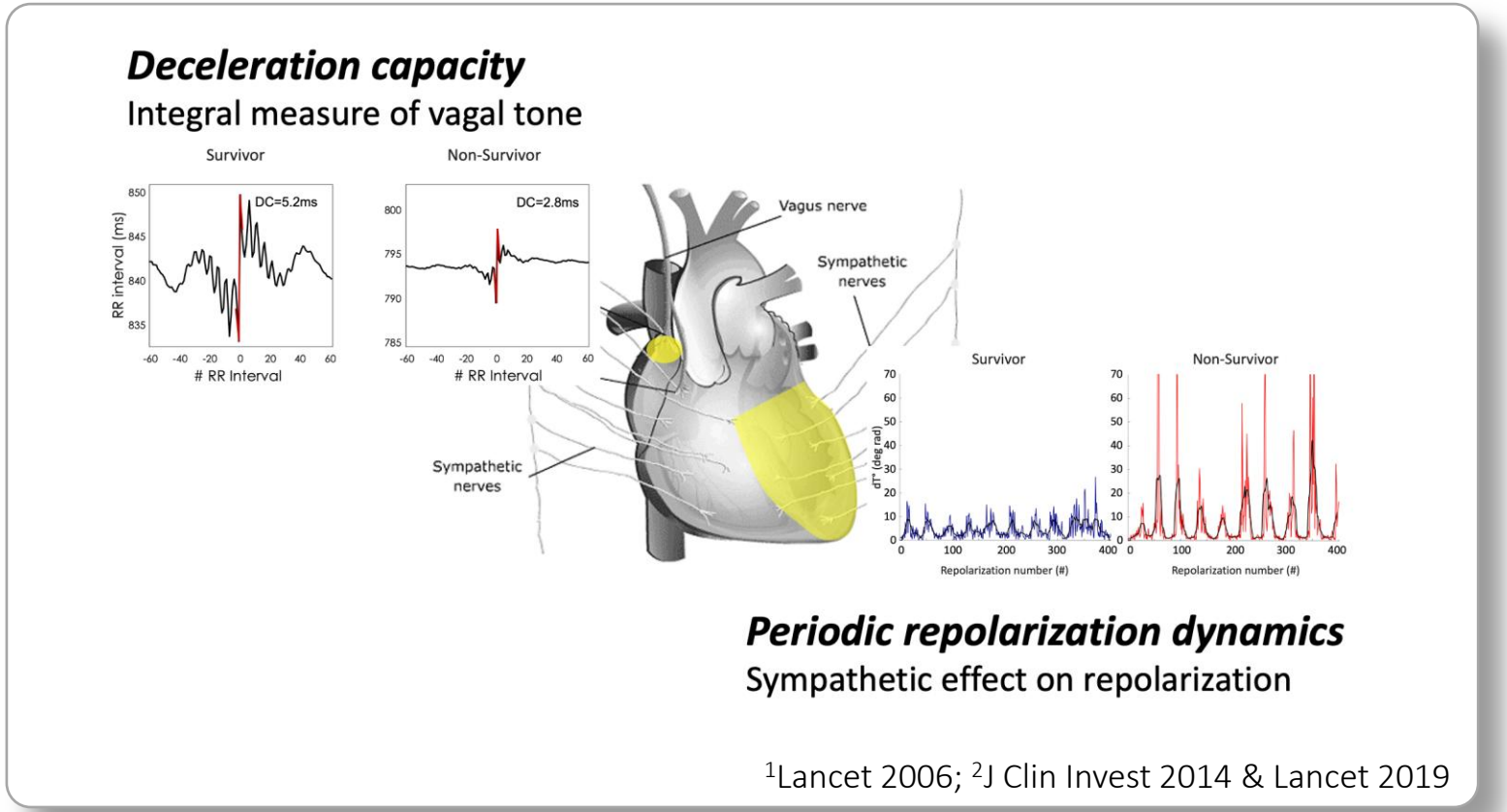
Study participants & procedures





[1]Lancet 2006; [2]J Clin Invest 2014 & Lancet 2019

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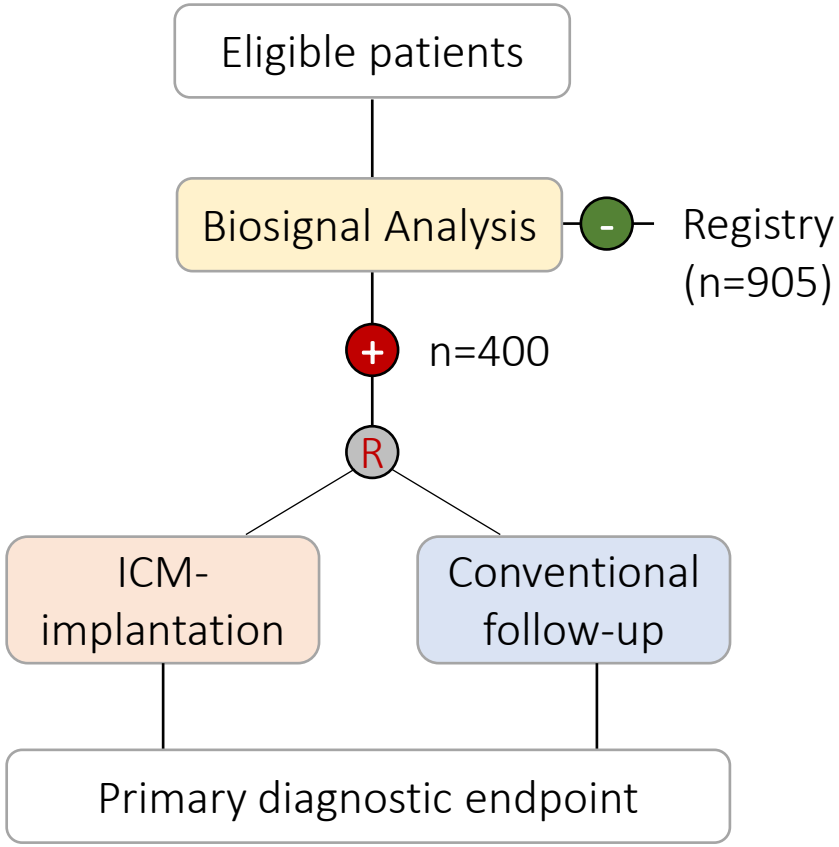
Study participants & procedures



- ICM-implantation (Reveal LINQ, Medtronic) and connection to Carelink system
- Daily data transmission to ICM core lab in Munich
- Predefined SArE reported to study centres within 48h
- Response to SArE at discretion of treating physicians
- Median follow-up 21 months (IQR 11–34)

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Endpoints

- **Primary composite endpoint: Serious arrhythmic events (SArE)**
  - Atrial fibrillation (AF) ≥6min[1]
  - AV block ≥IIb[2]
  - Fast non-sustained VT (CL ≤320ms for ≥ 40 beats)[3] / sustained VT/VF

- **Secondary endpoints (selection)**
  - Death
  - Major adverse cardiac and cerebrovascular events (MACCE)

[1] ASSERT, NEJM 2012; [2]CARISMA, Circulation 2010; [3]ADVANCE III, JAMA 2013

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Patients' characteristics and treatments

	ICM group (N=201)	Control group (N=199)
Age (years)	64 (57-73)	65 (57-73)
Females (%)	24%	15%
CHA_2DS_2-VASc	3 (2–4)	3 (2–4)
STEMI (vs. NSTEMI)	61%	57%
LVEF (%)	45 (40-48)	45 (40-48)
PCI	100%	99%
Aspirin	98%	97%
P2Y12 inhibitor	100%	100%
Betablocker	95%	89%
RAS inhibition	97%	93%
Statins	95%	98%

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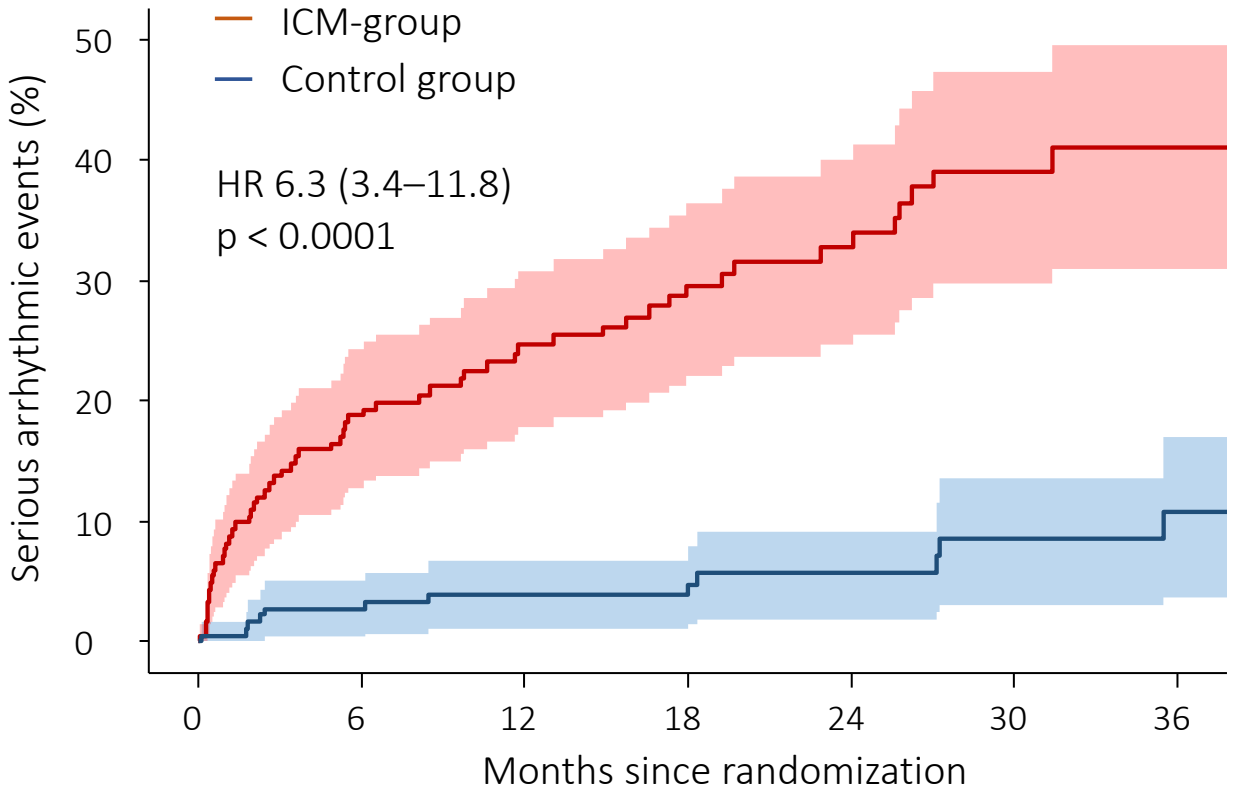
Primary efficacy endpoint



ICM	201	145	104	76	57	37	25
Control	199	177	139	110	84	57	41

60 SArE

- 43 AFiB
- 10 AVB ≥IIb
- 7 VT/VF

12 SArE

- 11 AFiB
- 1 VT/VF

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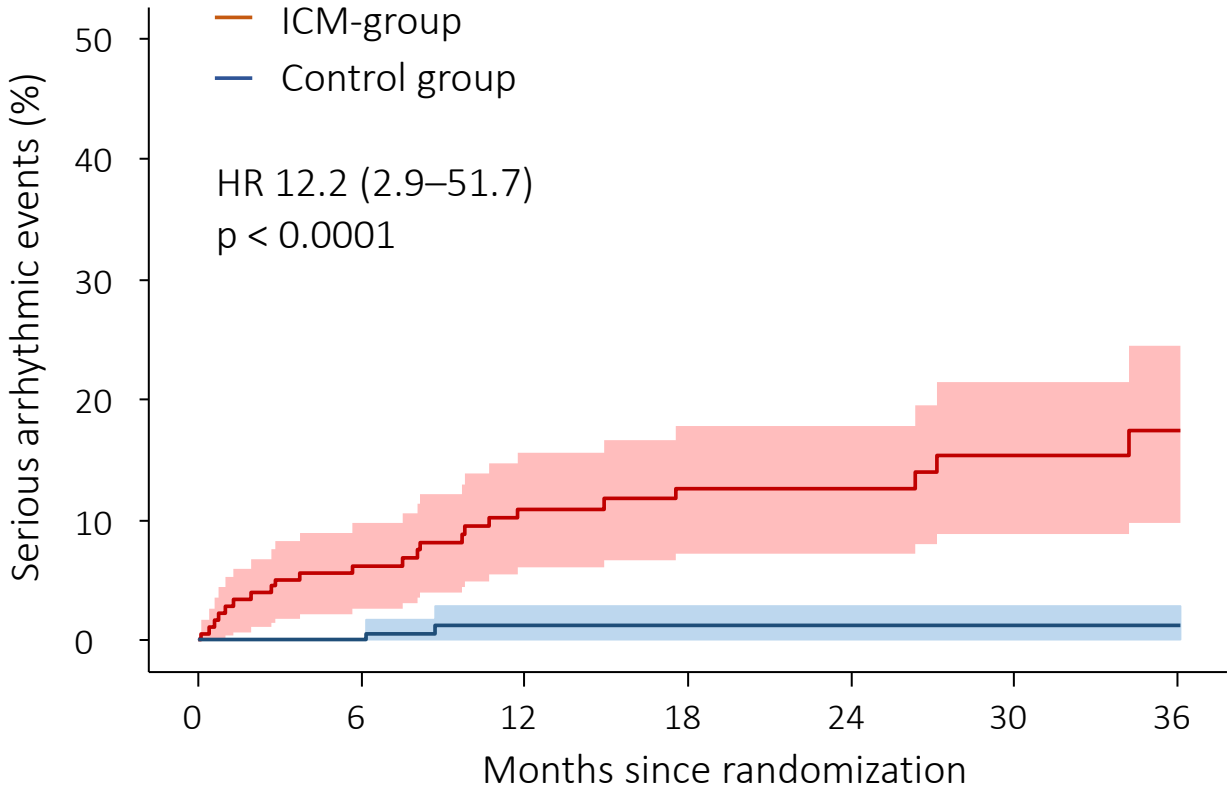
Exploratory analysis: SArE excluding AFiB



23 SArE

- 14 AVB ≥IIb
- 9 VT/VF

2 SArE

- 2 VT/VF

ICM	201	165	122	93	72	53	39
Control	199	182	142	113	84	58	43

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Diagnostic and therapeutic interventions

	ICM group (n=201)	Control group (n=199)	*P*-value
ICD-implantation	13	5	0.056
Pacemaker implantation	6	0	0.041
EP study	12	3	0.019
Catheter ablation	10	3	0.051
Revascularization	40	43	0.37
Initiation of OAK for AF	37*	11	<0.001

* median AF duration 4.5 hours

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Secondary clinical endpoints

	ICM (n=201)	Control (n=199)	Hazard Ratio (95% CI)	*P*-value
Clinical endpoints				
Death	11	9	1.3 (0.5-3.1)	0.580
MACCE	25	26	1.0 (0.6-1.8)	0.910

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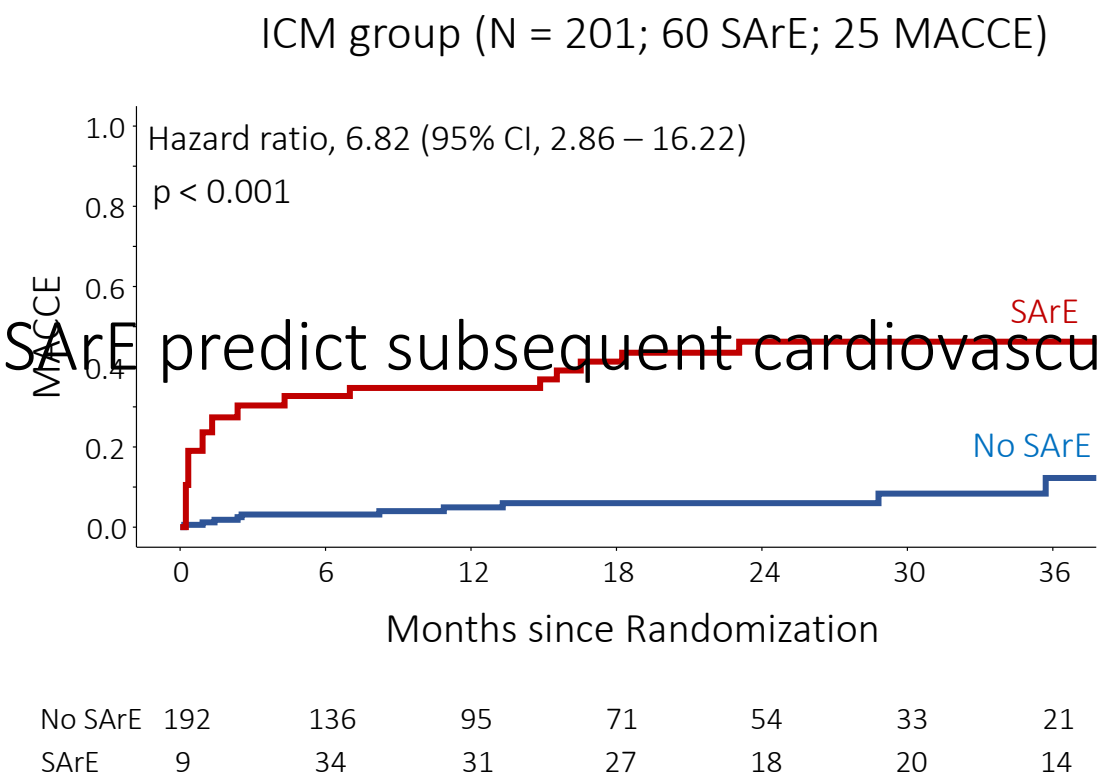
Time dependent Cox regression analysis

Do ICM-detected SArE predict subsequent cardiovascular complications ?



Event rates according to the Simon and Makuch method

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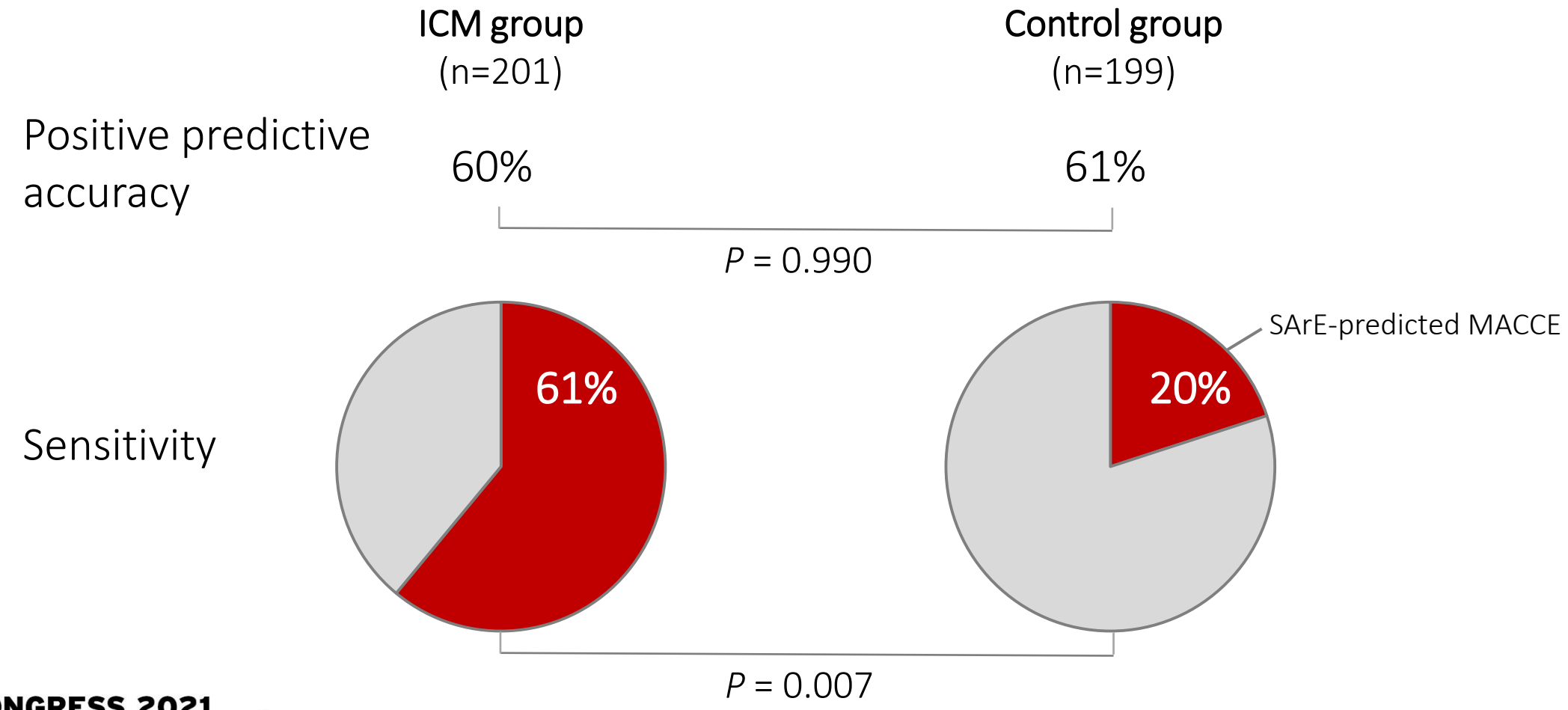
SArE as predictors of subsequent MACCE



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Limitations

- SMART-MI is a *diagnostic* study not powered to detect differences in clinical outcomes (small sample size, short follow-up)
- Therefore, no conclusions can be drawn about whether early detection of and response to prognostically relevant SArE leads to better outcomes

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Conclusions

- Post-MI patients with cardiac autonomic dysfunction and LVEF 36-50% develop a high number of subclinical brady- and tachyarrhythmic SArE that can be effectively detected by telemonitoring with ICMs.
- ICM-detected SArE are highly predictive of subsequent cardiovascular complications.
- Early detection of subclinical SArE may open a window of opportunity for preemptive interventions.
- Future studies powered for clinical endpoints are needed.

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Thanks to all SMART-MI investigators

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Thank you for your attention.