Optimal Timing of Ventricular Arrhythmia Ablation After Myocardial Infarction and Potential Role of Programmed Ventricular Stimulation: Systematic Review and Meta-analysis

Prana Jagannatha, MD

Udayana University Hospital, Bali, Indonesia

Korean Heart Rhythm Society
COI Disclosure

Prana Jagannatha, MD:

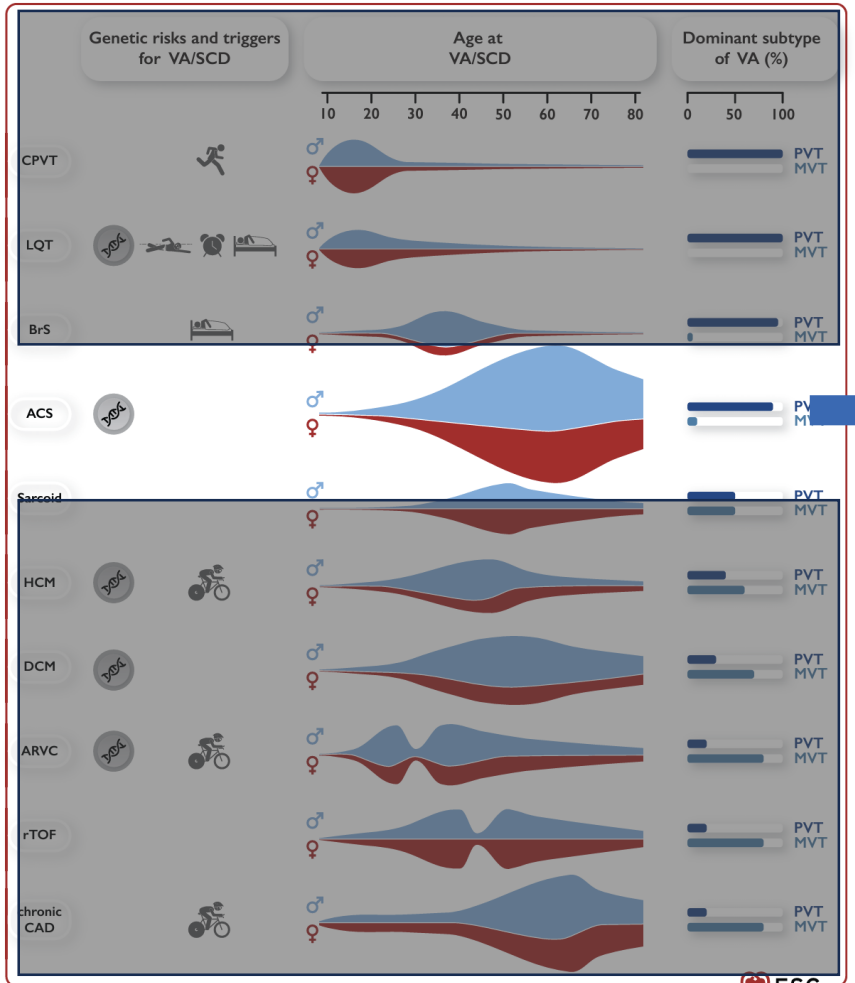
The authors have no financial conflicts of interest to disclose concerning the presentation

BACKGROUND

ESC European Society of Cardiology

European Heart Journal (2022) **43**, 3997–4126
https://doi.org/10.1093/eurheartj/ehac262

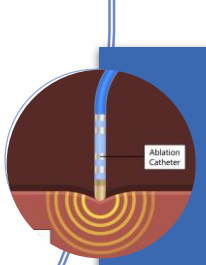
ESC GUIDELINES



Risk stratification and primary prevention of SCD		
In patients with syncope and previous STEMI, PES is indicated when syncope remains unexplained after non-invasive evaluation.[146,584]	I	C
ICD therapy is recommended in patients with CAD, symptomatic heart failure (NYHA class II–III), and LVEF ≤35% despite ≥3 months of OMT.[354,356]	I	A
ICD therapy should be considered in patients with CAD, NYHA class I, and LVEF ≤30% despite ≥3 months of OMT.[354]	IIa	B
ICD implantation should be considered in patients with CAD, LVEF ≤40% despite ≥3 months of OMT, and NSVT, if they are inducible for SMVT by PES.[355]	IIa	B
Secondary prevention of SCD and treatment of VAs		
ICD implantation is recommended in patients without ongoing ischaemia with documented VF or haemodynamically not-tolerated VT occurring later than 48 h after MI.[349–351]	I	A
Catheter ablation should be considered in patients with CAD and recurrent, symptomatic SMVT, or ICD shocks for SMVT despite beta-blockers or sotalol treatment.[471]	IIa	C
In patients with CAD eligible for ICD implantation, catheter ablation may be considered just before (or immediately after) ICD implantation to decrease subsequent VT burden and ICD shocks.[484,485,582,583]	IIb	B

VT: ↑ Risk of morbidity & mortality

ICD : Painful → ↓ QoL



VT ablation : mainstay therapy for the treatment of VT storm and drug refractory

Preventive ablation vs Defereed ablation?

KHRS 2023

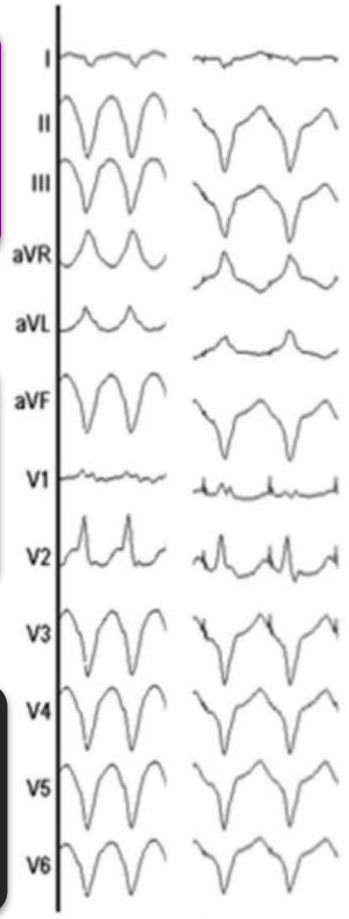
BACKGROUND

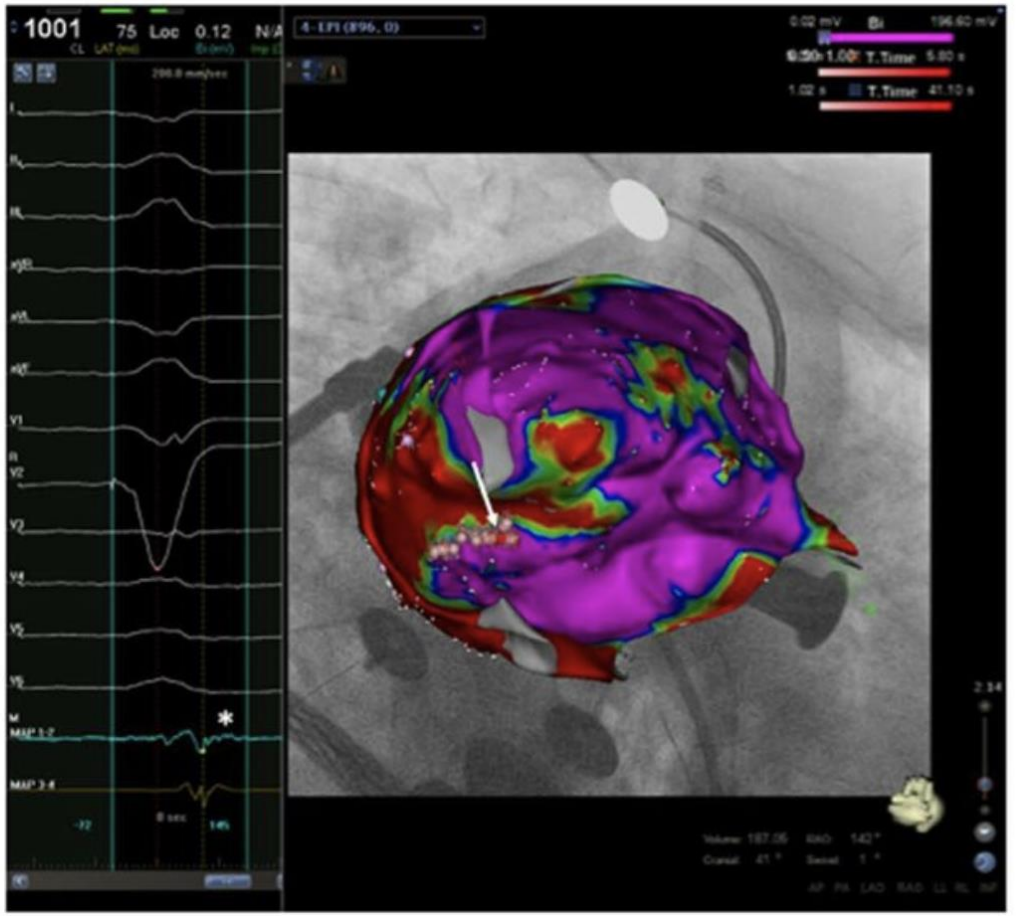
Programmed Ventricular Stimulation :

Are all patients suitable for prophylactic VT ablation ?

PVS: Limited evidence for risk stratification post MI

Aim : evaluate optimal timing of VAs ablation & putative role of PVS stratification





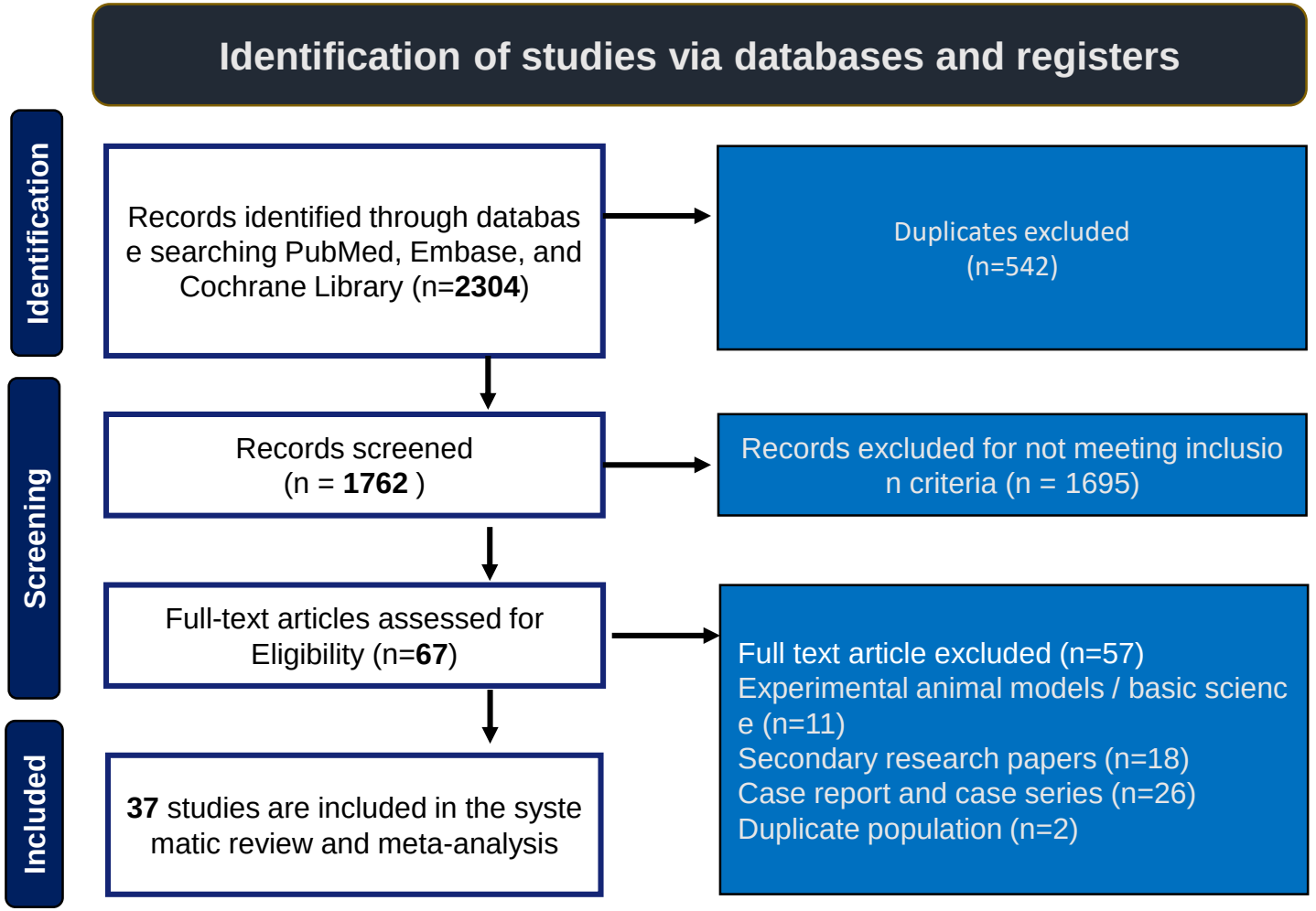
METHODS

Inclusion criteria

- •RCT for ablation outcome and Cohort study for PVS outcomes
- •Population : Adult human patients who underwent treatment of VT post MI
- •Intervention: ICD + early ablation or Assessing the use of PVS post MI
- •Control : ICD implantation alone as initial strategy
- •When assessing PVS, provides Tp, Tn, Fp, Fn values
- •Provide any outcomes of present study

Exclusion criteria

- • Experimental animal models / basic science
- • Secondary research papers
- • Case report and case series
- • Duplicate population

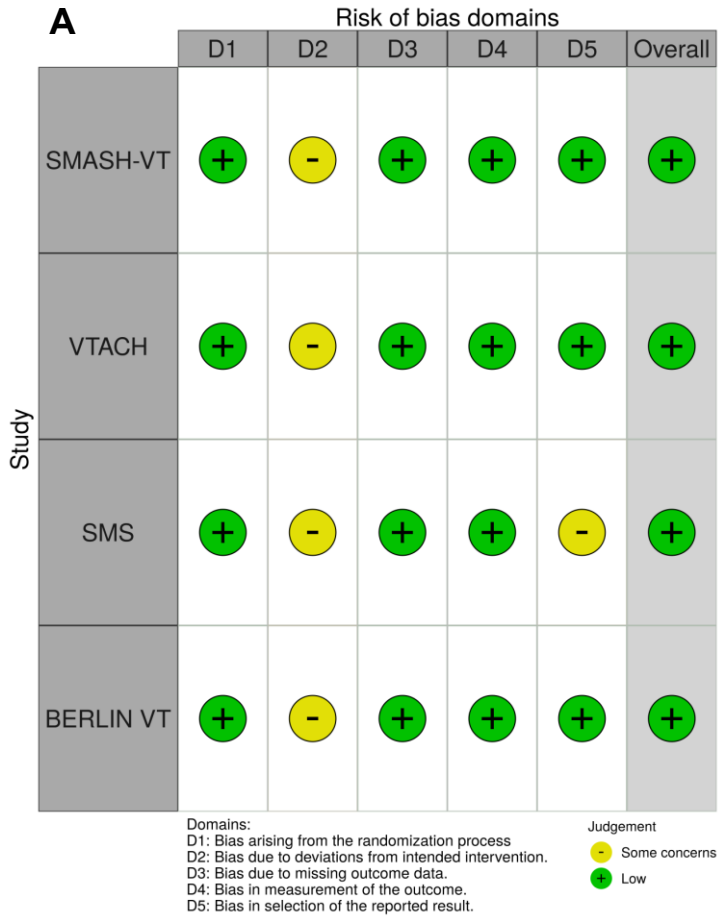


- **Primary outcomes**: ICD therapy, appropriate shock, VT storm, PVS predictive value
- **Secondary outcomes**: Complication rate, mortality, SF-36 Quality of life changes

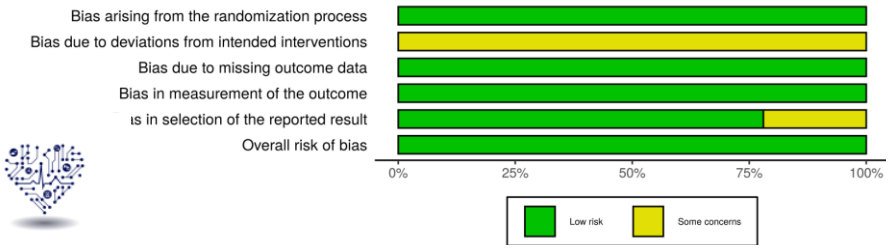
KHRS 2023

RESUTS

A



B



C

Study	Selection				Comparability		Outcome			Total
	1	2	3	4	1	2	1	2	3	
Marchlinski, 1983	★	★	★	★	-	-	★	★	★	7
Roy, 1985	★	★	★	★	-	-	-	★	★	6
P Santarelli, 1985	★	★	★	★	-	-	-	★	★	6
Kuck 1986	★	★	★	★	-	-	★	★	★	7
Gonzales 1988	★	★	★	★	-	-	-	-	★	5
Dennis, 1988	★	★	★	★	-	-	-	-	★	5
Cripps, 1989	★	★	★	★	-	-	-	-	★	5
Bhandari, 1989	★	★	★	★	-	-	-	★	★	6
Lesaka, 1990	★	★	★	★	★	-	-	★	★	7
Richards, 1991	★	★	★	★	-	-	-	★	★	6
Bourke, 1991	★	★	★	★	-	-	-	★	★	6
Nogami, 1991	★	★	★	★	-	-	-	★	★	6
Bhandari, 1992	★	★	★	★	-	-	-	★	★	6
Hueb, 1992	★	★	★	★	-	-	-	★	★	6
Pedretti, 1992	★	★	★	★	-	-	★	★	★	7
Brembilla-Perrot, 1995	★	★	★	★	-	-	-	★	★	6
Zoni-Berisso,1996	★	★	★	★	-	-	-	★	★	6
Andresen, 1999	★	★	★	★	-	-	★	★	★	7
Buxton, 2000	★	★	★	★	-	-	-	-	★	5
Schmitt, 2001	★	★	★	★	-	-	-	-	★	5
Fuenmayor, 2004	★	★	★	★	-	-	-	-	★	5
Reviele, 2005	★	★	★	★	-	-	-	★	★	6
Daubert, 2006	★	★	★	★	★	-	-	★	★	7
De Ferrari, 2007	★	★	★	★	-	-	-	★	★	6
Hukuri, 2009	★	★	★	★	-	-	-	★	★	6
Belhessen, 2009	★	★	★	★	-	-	★	★	★	7
Constantini, 2009	★	★	★	★	-	-	-	-	★	5
Kumar, 2010	★	★	★	★	-	-	-	-	★	5
Zaman, 2014	★	★	★	★	-	-	-	-	★	5
Gatzoulis,2019	★	★	★	★	-	-	-	★	★	6

RESUTS & DISCUSSION

Study ID	Year, region	Group	No. of patients	Age (y)	Male sex (n)	LVEF (%)	LVEF >30%	Amiodarone	B-Blocker	Follow-up time (month)
SMASH-VT	2007, US	Ablation + ICD	64	67 ± 9	59	30.7 ± 9.5	37	0	60	22.5
		ICD only	64	66 ± 10	52	32.9 ± 8.5	30	0	63	
VTACH	2010, Europe	Ablation + ICD	52	67.7 ± 8.3	50	34 ± 9.1	20	18	39	22.5
		ICD only	55	64.4 ± 8.2	50	34.1 ± 8.8	23	19	41	
SMS	2017, Europe	Ablation + ICD	54	68.4 ± 7.7	47	32 ± 6.9	22	16	49	27
		ICD only	57	65.9 ± 8.4	46	30.4 ± 7.3	27	20	52	
BERLIN VT	2020, Europe	Ablation + ICD	246	67.1	223	34.9	156	65	206	24
		ICD only	259	65.6	224	35.2	163	61	215	

CONT . . .

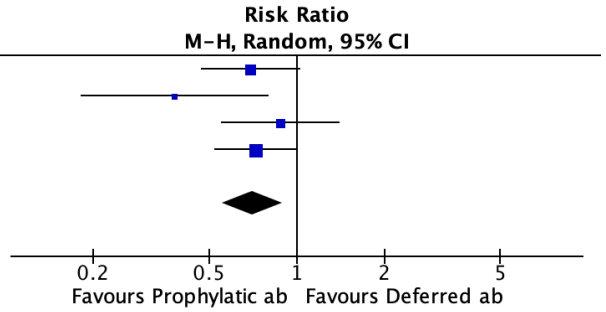
Study ID	No. of patients	Age (y)	Male sex (n)	LVEF (%)	Amiodarone	B-Blocker	Follow-up time (month)
Andresen, 1999	146	55	120	41.1 ± 12.3	NA	NA	24
Belhessen, 2009	154	59.5 ± 12	132	40.7 ± 9.5	NA	NA	36
Bhandari, 1989	75	61,5	68	38.1 ± 8.5	21	20	36
Bhandari, 1992	86	66 ± 10	70	34 ± 9.1	0	0	12
Bourke, 1991	1209	66 ± 10	882	34.1 ± 8.8	123	56	24
Brembilla-Perrot, 1995	440	63.4	321	42 ± 8.9	19	89	24.4
Buxton, 2000	1750	67 ± 9	1072	38.4 ± 7.3	NA	MA	28
Constantini, 2009	566	66 ± 10	321	34.9	34	90	36.2
Cripps, 1989	75	67.7 ± 8.3	51	35.2	0	75	33
Daubert, 2006	593	64.4 ± 8.2	284	44	38	123	36
De Ferrari, 2007	105	68.4 ± 7.7	72	30.7 ± 9.5	8	89	24
Dennis, 1988	338	65.9 ± 8.4	221	42.9 ± 8.5	31	239	18
Fuenmayor, 2004	50	67.1	38	34 ± 9.1	10	30	18
Gatzoulis,2019	575	65.6	302	34.1 ± 8.8	32	321	12
Gonzales 1988	84	60.3	58	42 ± 3.9	8	50	12
Hueb, 1992	27	62.3 ± 11.3	19	30.4 ± 7.3	NA	NA	12
Hukuri, 2009	345	66.3 ± 15	298	34.9	NA	NA	24
Kuck 1986	18	66 ± 10	9	35.2	NA	NA	24
Kumar, 2010	360	66 ± 10	184	39.7 ± 9.5	NA	NA	36
Lesaka, 1990	133	63.4	98	35.9 ± 8.5	NA	NA	33
Marchlinski, 1983	41	67 ± 9	32	34 ± 9.1	NA	NA	36
Nogami, 1991	32	66 ± 10	19	36.1 ± 8.8	NA	NA	24
P Santarelli, 1985	50	67.7 ± 8.3	33	32 ± 6.9	8	18	18
Pedretti, 1992	37	64.4 ± 8.2	22	30.4 ± 7.3	2	30	18
Reviele, 2005	76	68.4 ± 7.7	39	34.9	11	60	NA
Richards, 1991	361	65.9 ± 8.4	182	35.2	NA	NA	12
Roy, 1985	150	67.1	87	44	20	87	12
Schmitt, 2001	98	65.6	67	42	0	0	24
Zaman, 2014	290	60.3	120	38	37	100	24
Zoni-Berisso,1996	93	62.3 ± 11.3	75	39	0	93	12

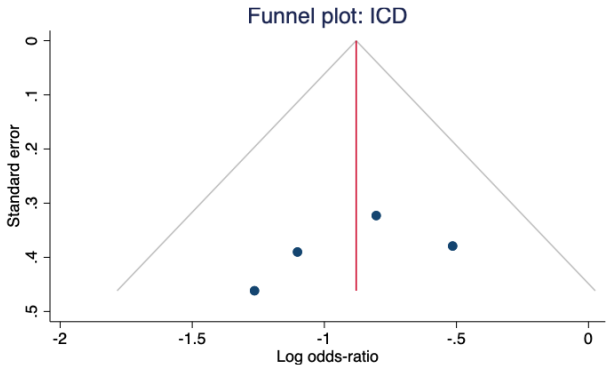
RESUTS & DISCUSSION

A. ICD THERAPY

Study or Subgroup	Prophylatic ablation Events	Total	Deferred ablation Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
BERLIN VT	25	73	39	79	29.4%	0.69 [0.47, 1.02]
SMASH-VT	8	64	21	64	9.8%	0.38 [0.18, 0.80]
SMS	20	54	24	57	22.3%	0.88 [0.55, 1.40]
VTACH	26	52	38	55	38.5%	0.72 [0.52, 1.00]
Total (95% CI)		**243**		**255**	**100.0%**	**0.70 [0.55, 0.89]**
Total events	79		122			

Heterogeneity: Tau² = 0.01; Chi² = 3.68, df = 3 (P = 0.30); I² = 18%
Test for overall effect: Z = 2.91 (P = 0.004)

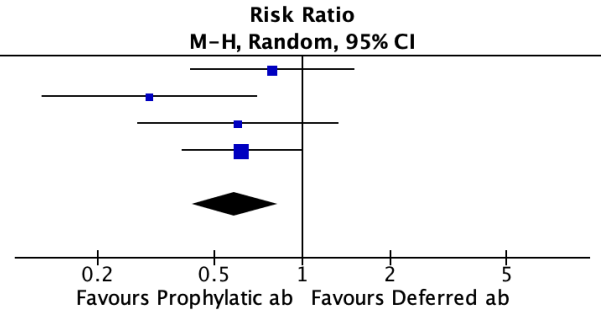


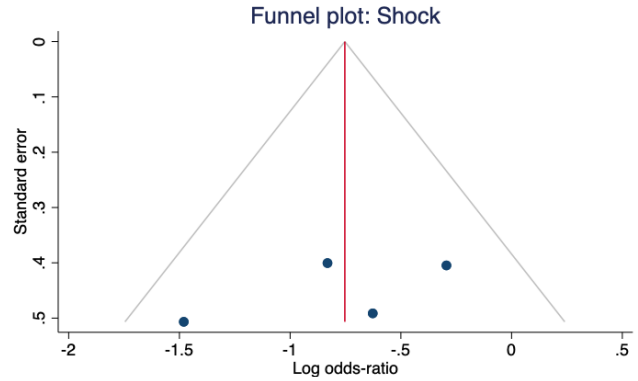


B. APPROPRIATE SHOCK

Study or Subgroup	Prophylatic ablation Events	Total	Deferred ablation Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
BERLIN VT	13	76	18	83	24.7%	0.79 [0.42, 1.50]
SMASH-VT	6	64	20	64	15.0%	0.30 [0.13, 0.70]
SMS	8	54	14	57	17.1%	0.60 [0.28, 1.32]
VTACH	17	52	29	55	43.2%	0.62 [0.39, 0.99]
Total (95% CI)		**246**		**259**	**100.0%**	**0.59 [0.42, 0.82]**
Total events	44		81			

Heterogeneity: Tau² = 0.01; Chi² = 3.34, df = 3 (P = 0.34); I² = 10%
Test for overall effect: Z = 3.09 (P = 0.002)

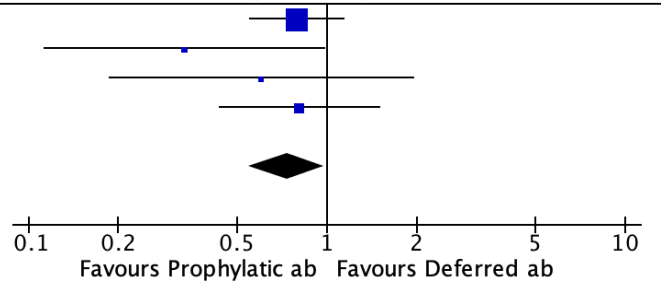


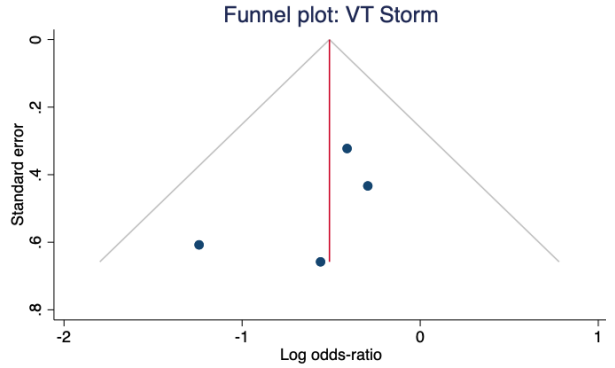


C. VT STORM

Study or Subgroup	Experimental Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
BERLIN VT	29	76	40	83	64.2%	0.79 [0.55, 1.14]
SMASH-VT	4	64	12	64	7.3%	0.33 [0.11, 0.98]
SMS	4	54	7	57	6.2%	0.60 [0.19, 1.94]
VTACH	13	52	17	55	22.4%	0.81 [0.44, 1.50]
Total (95% CI)		**246**		**259**	**100.0%**	**0.73 [0.55, 0.98]**
Total events	50		76			

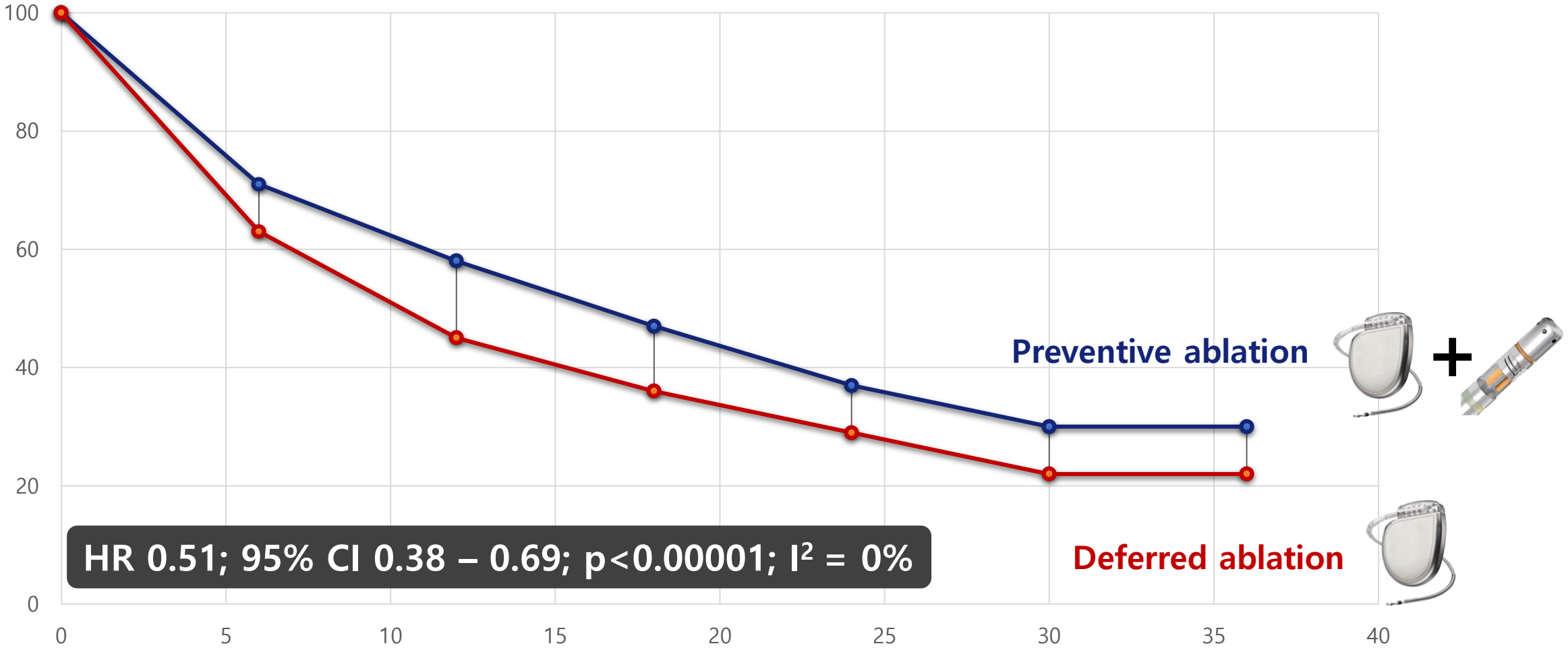
Heterogeneity: Tau² = 0.00; Chi² = 2.52, df = 3 (P = 0.47); I² = 0%
Test for overall effect: Z = 2.08 (P = 0.04)





RESUTS & DISCUSSION

3 Year Survival from VT (ICD therapy)

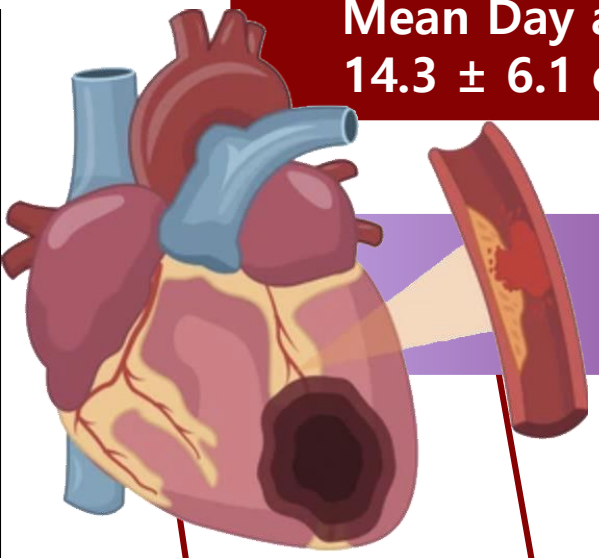


KHRS 2023

RESUTS & DISCUSSION

Pathophysiology of VAs post-MI

Mean Day ablation attempt post MI:
14.3 ± 6.1 day

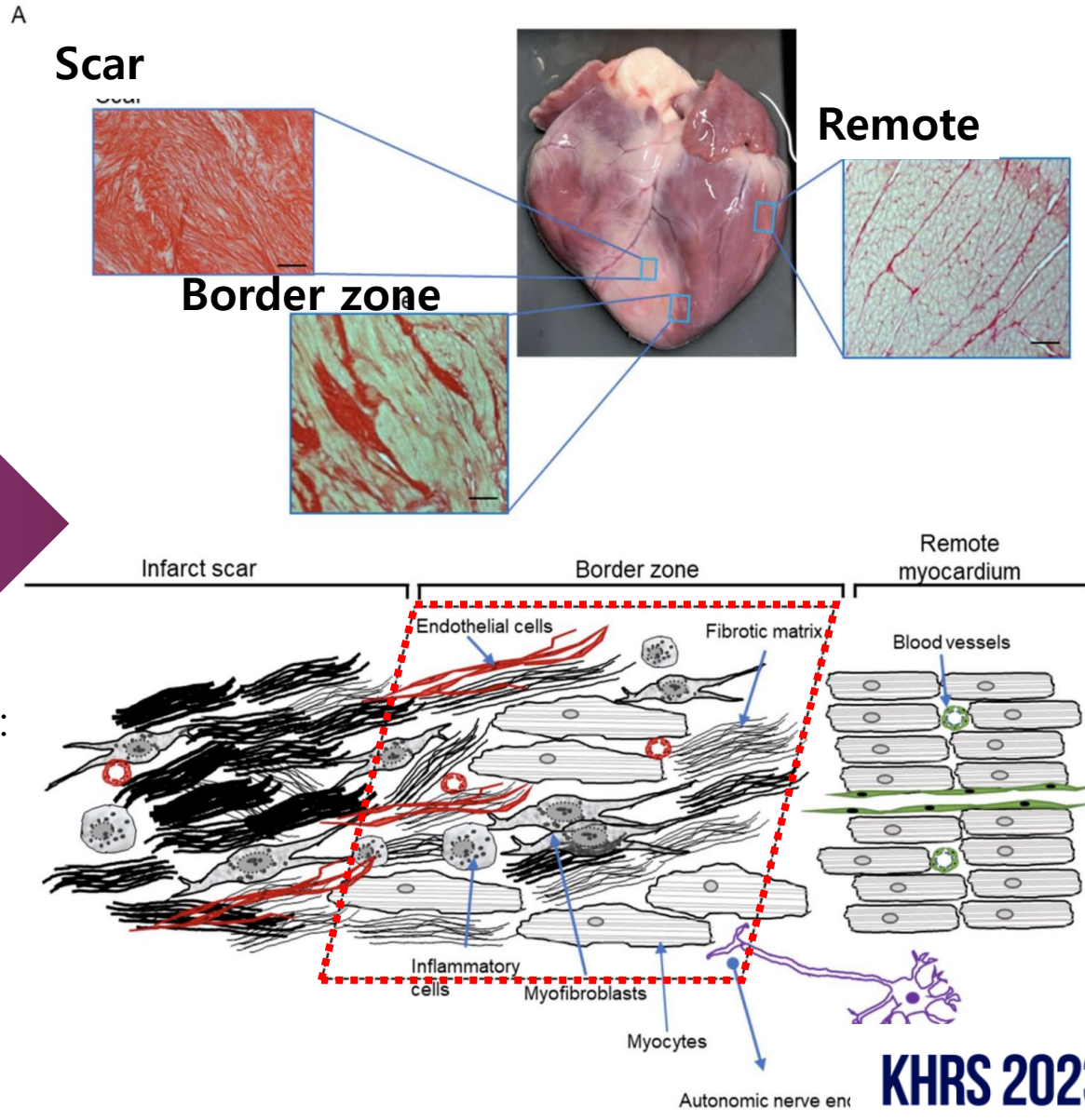


Post infarct

Chronic phase (day > 30) :
Remodelling

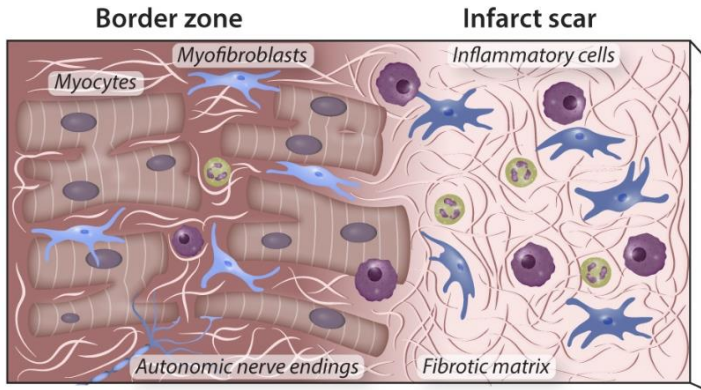
Intermediate phase (day 7-30) :
fibrosis replacement

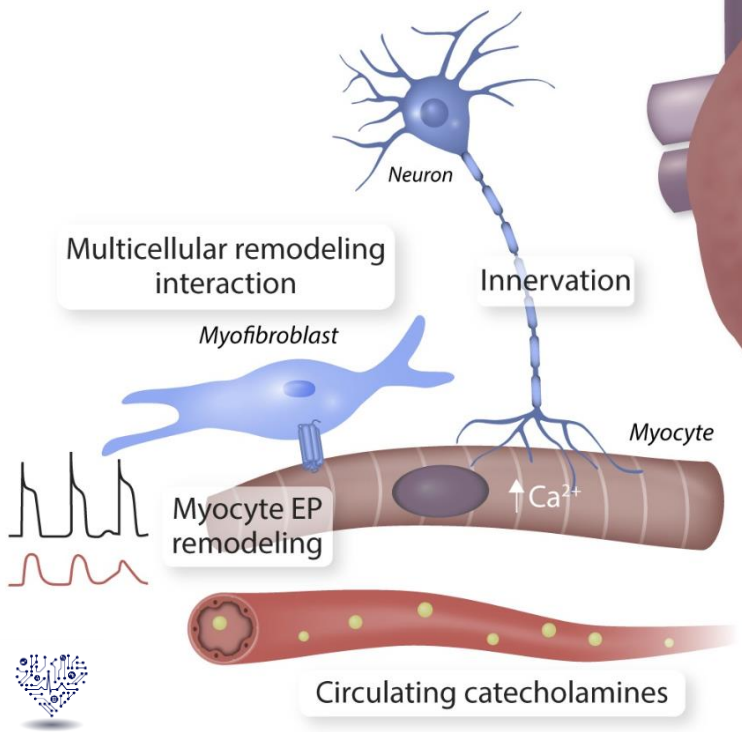
Initial phase (day 1-5) :
cell death & inflamation

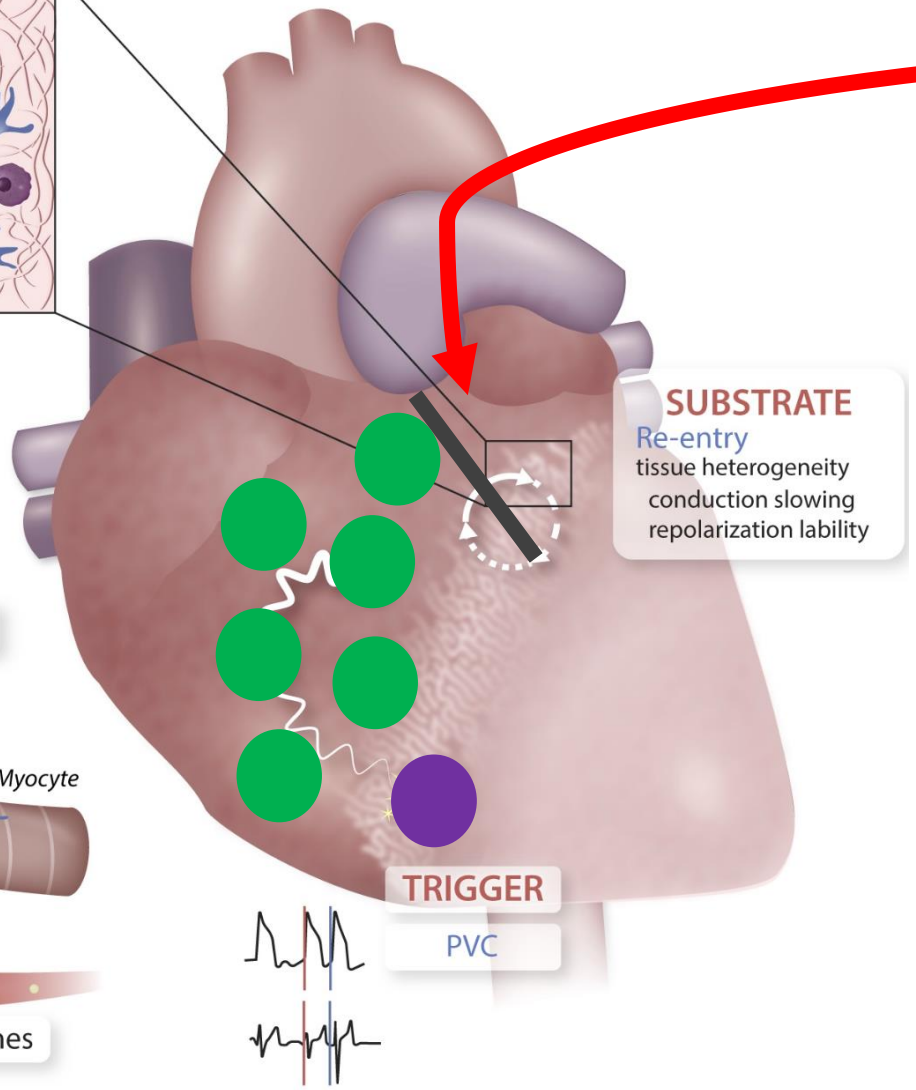


KHRS 2023

RESUTS & DISCUSSION







Catheter ablation

1. Bidirectional block of critical isthmuses
2. Homogenisation of the substrate
3. Elimination of triggering PVC focus

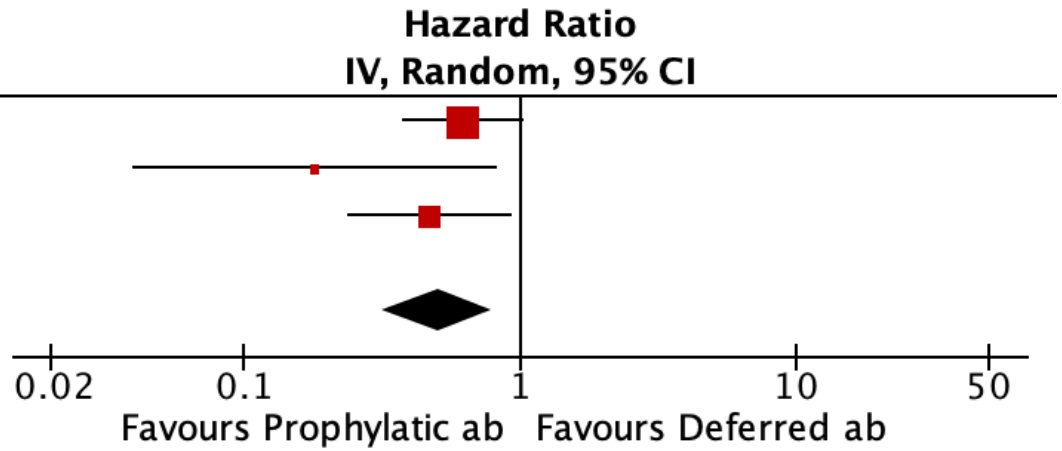
RESUTS & DISCUSSION

Subgroup analysis of population with LVEF >30% :

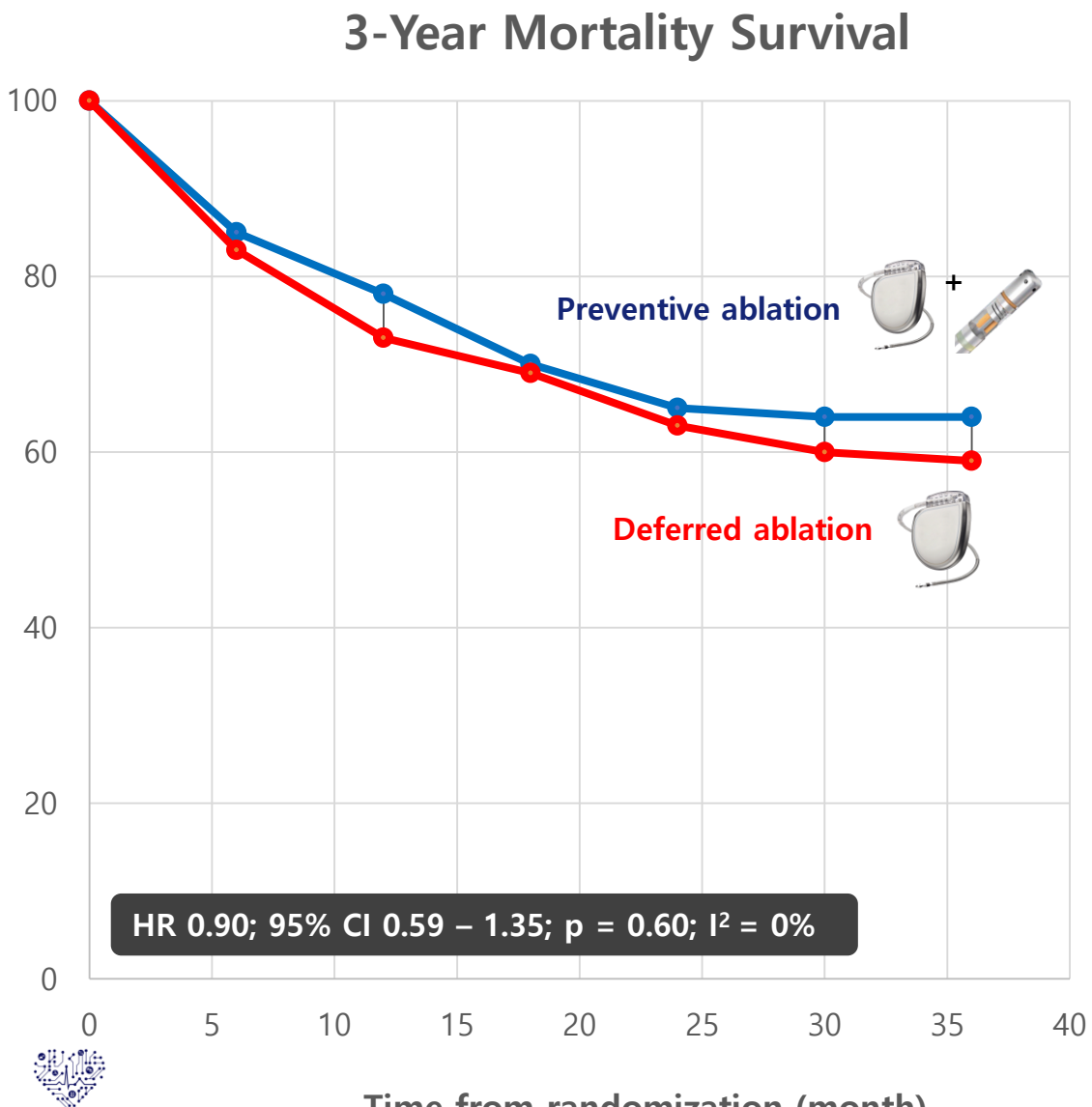
Study or Subgroup	log[Hazard Ratio]	SE	Weight	Hazard Ratio IV, Random, 95% CI
BERLIN VT	-0.478	0.2498	55.6%	0.62 [0.38, 1.01]
SMASH-VT	-1.7148	0.7674	8.8%	0.18 [0.04, 0.81]
VTACH	-0.755	0.3429	35.7%	0.47 [0.24, 0.92]
Total (95% CI)			**100.0%**	**0.50 [0.32, 0.80]**

Heterogeneity: $Tau^2 = 0.04$; $Chi^2 = 2.49$, df = 2 (P = 0.29); $I^2 = 20\%$

Test for overall effect: Z = 2.93 (P = 0.003)



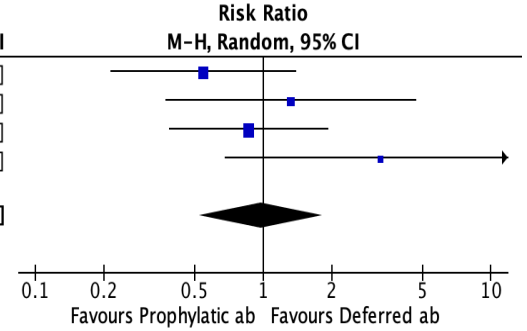
RESUTS & DISCUSSION



Mortality:

Study or Subgroup	Prophylatic ablation Events	Total	Deferred ablation Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
BERLIN VT	6	64	11	64	30.2%	0.55 [0.21, 1.39]
SMASH-VT	5	52	4	55	19.4%	1.32 [0.38, 4.66]
SMS	9	54	11	57	36.9%	0.86 [0.39, 1.92]
VTACH	6	76	2	83	13.5%	3.28 [0.68, 15.74]
Total (95% CI)		**246**		**259**	**100.0%**	**0.98 [0.52, 1.82]**
Total events	26		28			

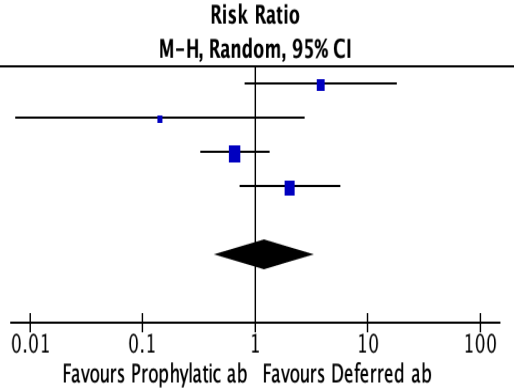
Heterogeneity: $Tau^2 = 0.11$; $Chi^2 = 4.09$, df = 3 (P = 0.25); $I^2 = 27\%$
Test for overall effect: Z = 0.07 (P = 0.94)



Complication:

Study or Subgroup	Prophylatic ablation Events	Total	Deferred ablation Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
BERLIN VT	7	76	2	83	22.3%	3.82 [0.82, 17.84]
SMASH-VT	0	64	3	64	9.5%	0.14 [0.01, 2.71]
SMS	10	54	16	57	37.1%	0.66 [0.33, 1.32]
VTACH	9	46	5	52	31.1%	2.03 [0.73, 5.64]
Total (95% CI)		**240**		**256**	**100.0%**	**1.20 [0.43, 3.33]**
Total events	26		26			

Heterogeneity: $Tau^2 = 0.61$; $Chi^2 = 7.81$, df = 3 (P = 0.05); $I^2 = 62\%$
Test for overall effect: Z = 0.34 (P = 0.73)



KHRS 2023

RESUTS & DISCUSSION

Recommendations	Class[a]	Level[b]
Risk stratification and primary prevention of SCD		
In patients with syncope and previous STEMI, PES is indicated when syncope remains unexplained after non-invasive evaluation.[146,584]	I	C
ICD therapy is recommended in patients with CAD, symptomatic heart failure (NYHA class II–III), and LVEF ≤35% despite ≥3 months of OMT.[354,356]	I	A
ICD therapy should be considered in patients with CAD, NYHA class I, and LVEF ≤30% despite ≥3 months of OMT.[354]	IIa	B
ICD implantation should be considered in patients with CAD, LVEF ≤40% despite ≥3 months of OMT, and NSVT, if they are inducible for SMVT by PES.[355]	IIa	B
In patients with CAD, prophylactic treatment with AADs other than beta-blockers is not recommended.[556,578,579]	III	A
Secondary prevention of SCD and treatment of VAs		
ICD implantation is recommended in patients without ongoing ischaemia with documented VF or haemodynamically not-tolerated VT occurring later than 48 h after MI.[349–351]	I	A
In patients with CAD and recurrent, symptomatic SMVT, or ICD shocks for SMVT despite chronic amiodarone therapy, catheter ablation is recommended in preference to escalating AAD therapy.[471]	I	B

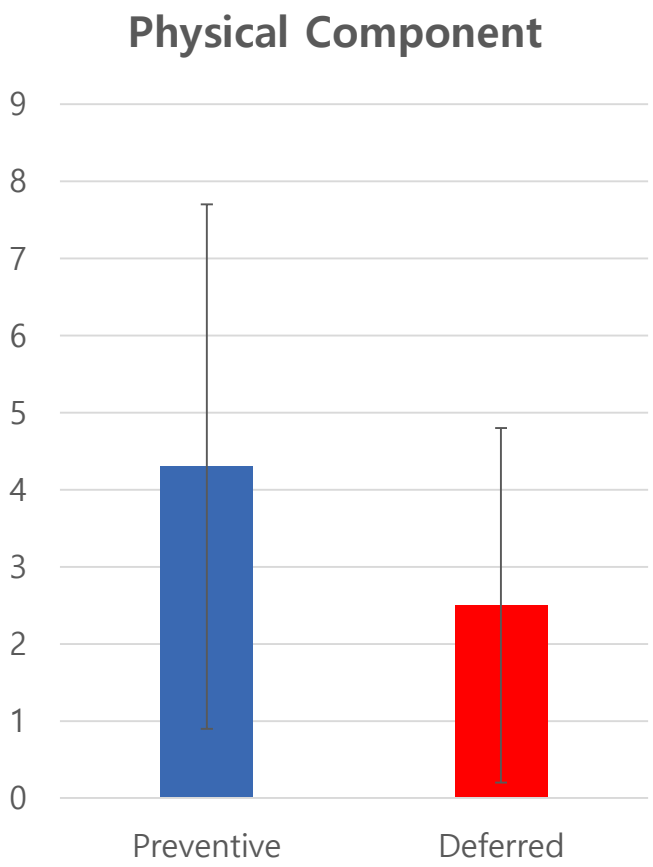
Study, year, country, type of study	Type of prevention: primary/secondary, inclusion and exclusion criteria[a]	Control[b]	No. of patients in study (ICD group, control group), enrollment (E), follow-up (FU)	Conclusion: ICD patients' QoL compared to control group			LOE/ study quality[c]
				Worse	Neutral	Better	
Schron et al. (23) 2002 USA Multicenter RCT (AVID)	Prevention: sec. Inclusion: VF or symptomatic VT (including sustained VT resulting in syncope or sustained VT in the setting of LVEF ≤ 40% and clinically important symptoms of hemodynamic compromise), survival of at least 1 year Exclusion: n.r.	Med. (antiarrhythmic drugs)	800 (416, 384) E: n.r. FU: 12 months		✓		2b–
				"ICD and AAD (antiarrhythmic drugs) therapy are associated with similar alterations in self-perceived QoL over 1-year follow-up"			
Leosdottir et al. (28) 2006 Iceland Cross-sectional study	Prevention: n.r. Inclusion: all ICD patients living in Iceland at the beginning of 2002 Exclusion: not able to complete questionnaires due to mental or physical disabilities (assessed by caring physician)	PM	108 (41, 67) E: 2002–2003 FU: n.a.		✓		4+
				"ICD patients had a comparable QoL with pacemaker recipients and were not more likely to suffer from anxiety, depression, or general psychiatric distress"			
Newall et al. (29) 2007 New Zealand Cross-sectional study	Prevention: n.r. Inclusion: ≥18 years, able to comprehend English Exclusion: taking antidepressant medications for pre-existing depression	PM	95 (46, 49) E: 2005 FU: n.a.		✓		4+
				"Quality-of-life scores were normal for all ICD patients with respect to both mental and physical component scores, and not different from the pacemaker group"			
Czosek et al. (31) 2012 USA Multicenter cross-sectional study	Prevention: prim. and sec. Inclusion: children between 8 and 18 and their parents Exclusion: n.r.	PM	173 (40, 133) E: 2004–2008 FU: n.a.		✓		4–
				"Patient- and parent-proxy-reported QOL is significantly affected by the presence of cardiac rhythm devices and is worsened in those patients with CHD (congenital heart disease) and ICD systems as opposed to pacing systems"			
Duru et al. (27) 2001 Switzerland Cross-sectional study	Prevention: n.r. Inclusion: 40–70 years, first pectoral implantation of ICD or PM Exclusion: n.r.	PM	152 (76, 76) E: 1993–1999 FU: n.a.		✓		4–
				"There was no difference between the three groups (ICD with experienced shock, ICD without experienced shock, PM), with respect to scores on any aspect of the HAD and SF-36"			
Redhead et al. (30) 2010 UK Cross-sectional study	Prevention: sec. Inclusion: first ICD implanted between April 2004 and March 2007 after MI Exclusion: n.r.	PM & Oth. (49 patients: PM, 50 patients: angioplasty, and 50 patients: catheter ablation for drug-resistant atrial fibrillation)	249 (100, 149) E: 2010 FU: n.a.		✓		4+
				"Mean scores for each assessment were similar for each group"			
Kamphuis et al. (25) 2002 The Netherlands Observational study	Prevention: n.r. Inclusion: survived an out-of-hospital cardiac arrest due to VT, ≥16 years, able to comprehend Dutch Exclusion: n.r.	Oth. (antiarrhythmic drugs, angioplasty, or surgical revascularization)	168 (133, 35) E: n.r. FU: 12 months	✓			2b–
				"In general, OT (other treatment) patients achieved a better quality of life than ICD patients"			
Probst et al. (32) 2011 France Cross-sectional study	Prevention: n.r. Inclusion: Brugada Syndrome (Type 1 ECG before or after a sodium channel blocker challenge) Exclusion: <18 years, no valid mailing address	Oth. (asymptomatic patients without an ICD)	190 (138, 52) E: n.r. FU: n.a.		✓		4–
				"BrS (Brugada Syndrome) patients have a good quality of life with no difference between implanted and non-implanted patients"			
Opic et al. (33) 2012 The Netherlands, Belgium Multicenter cross-sectional study	Prevention: n.r. Inclusion: young adults with ToF Exclusion: n.r.	Oth. (ToF patients without an ICD)	54 (26, 28) E: n.r. FU: n.a.		✓		4–
				"ToF patients with an ICD show less favorable psychosocial functioning compared to ToF patients without ICD"			
Cross et al. (24) 2010 USA Observational study	Prevention: n.r. Inclusion: ICD therapy and/or diagnosis of CAD Exclusion: obstructive sleep apnea, restless legs syndrome	Oth. (patients with CAD)	60 (30, 30) E: n.r. FU: 14 days			✓	4–
				"The purpose of this study was to compare sleep patterns between CAD and ICD patients […]. The primary and surprising finding was that CAD patients had poorer sleep compared with ICD patients in terms of sleep efficiency and total sleep time"			

Recent Meta-analysis:
Lower QoL was apparent among patients with an ICD who experienced several device discharges.

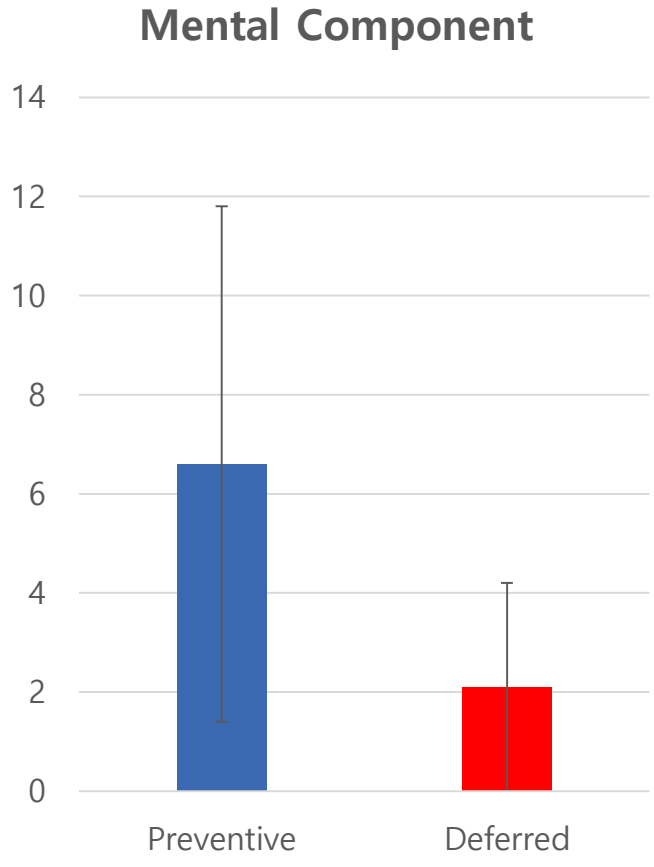
KHRS 2023

RESUTS & DISCUSSION

Quality of life improvement (SF-36)



MD 2.73 [0.13 – 5.33]
p = 0.04; I^2 = 0%

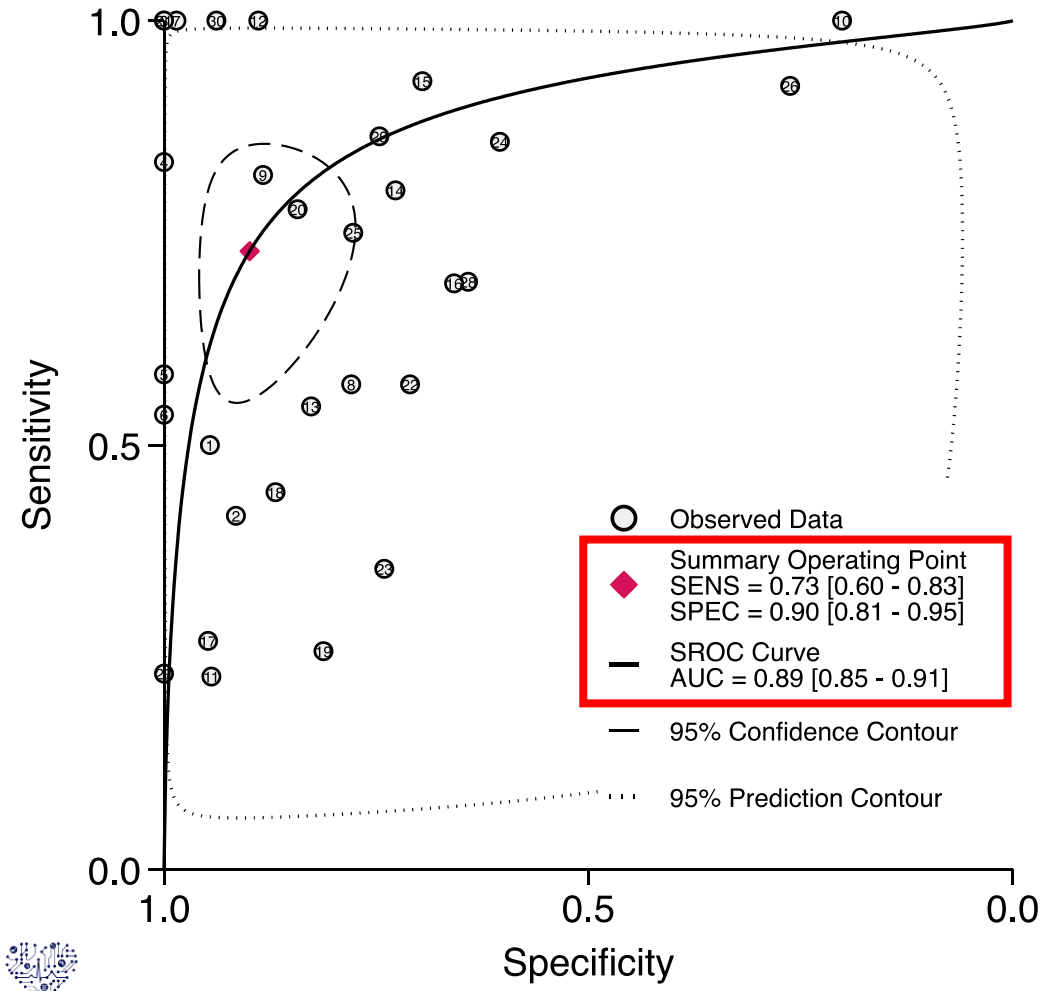


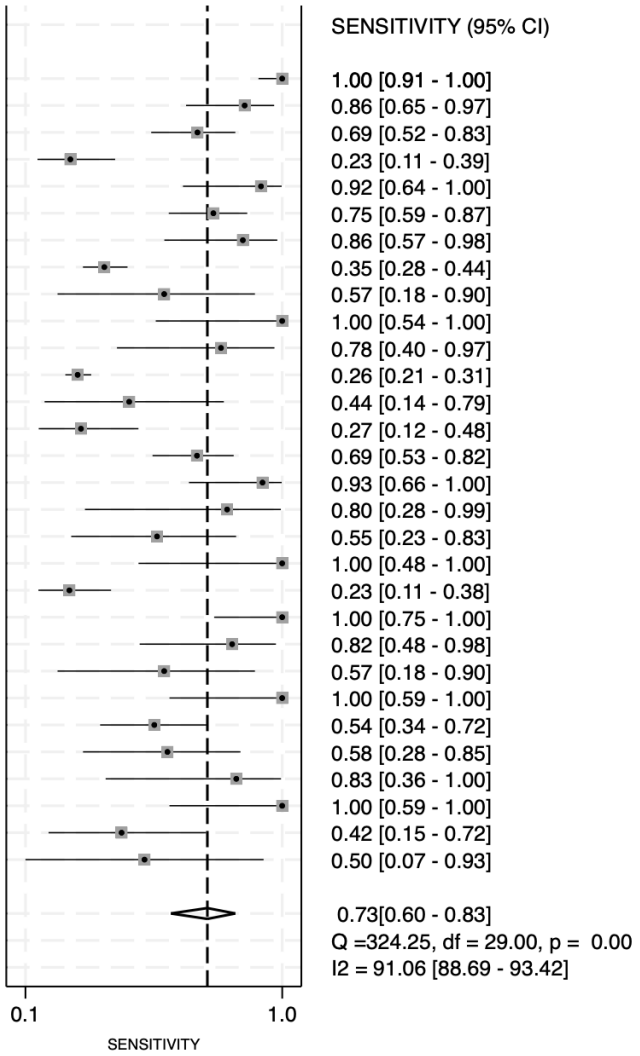
MD 3.70 [0.14 – 7.27]
p = 0.04; I^2 = 30%

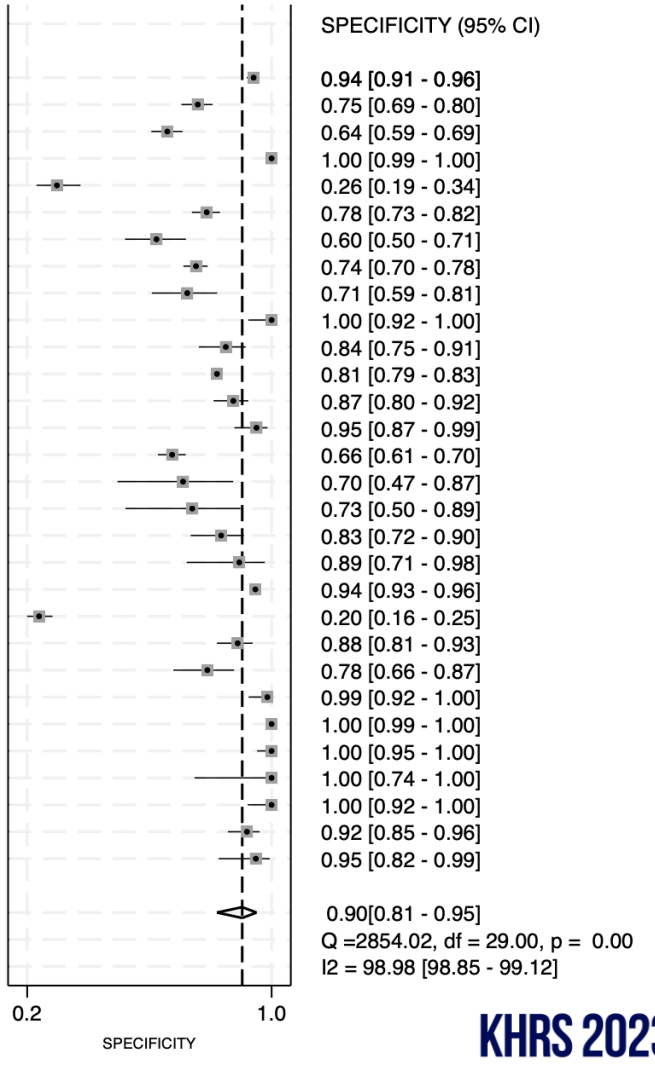
Which patients are really at risk of experiencing VT?

RESUTS & DISCUSSION

Role of Programmed Ventricular Stimulation



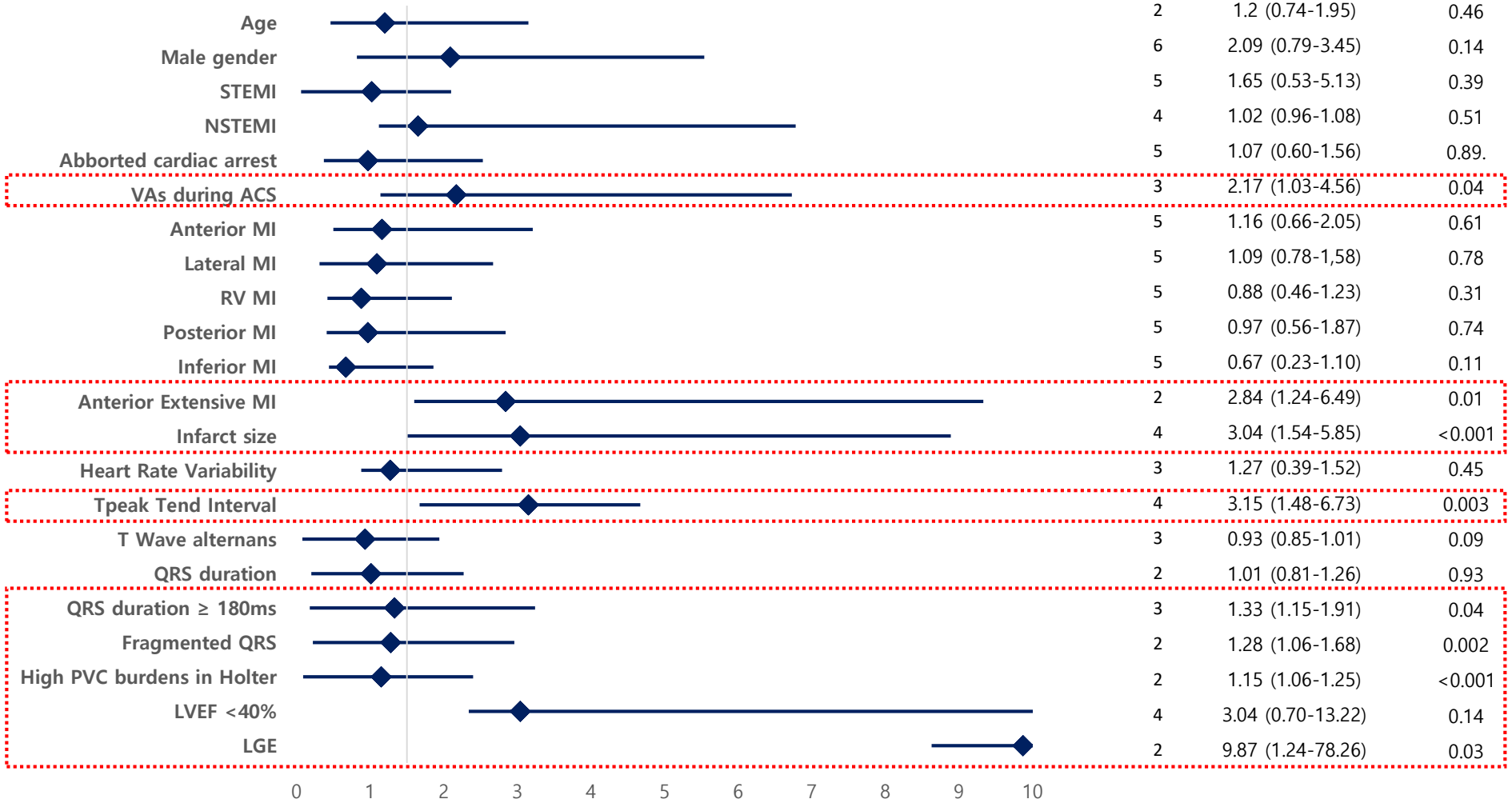




KHRS 2023

RESUTS & DISCUSSION

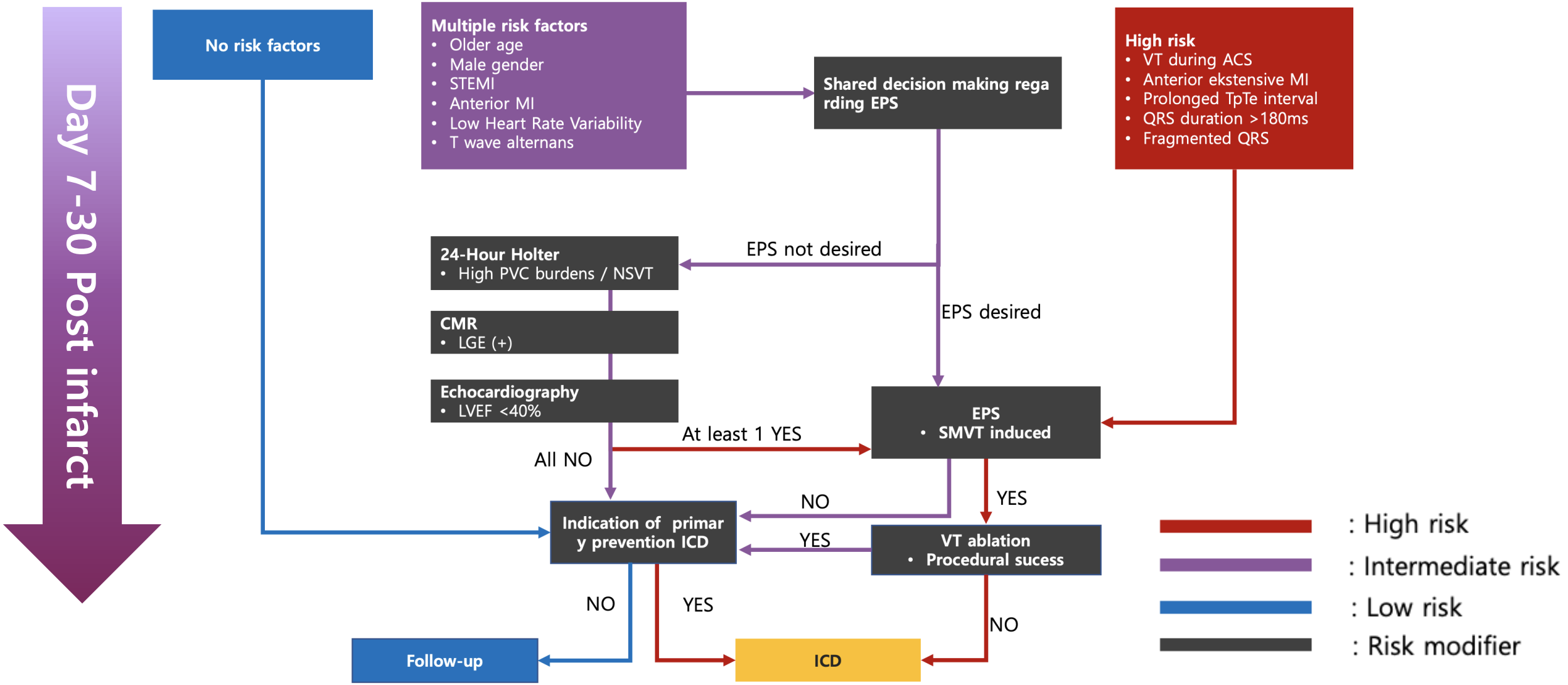
Other non-invasive risk factors of VT after MI



	Studies	RR (95% CI)	P value
Age	2	1.2 (0.74-1.95)	0.46
Male gender	6	2.09 (0.79-3.45)	0.14
STEMI	5	1.65 (0.53-5.13)	0.39
NSTEMI	4	1.02 (0.96-1.08)	0.51
Abborted cardiac arrest	5	1.07 (0.60-1.56)	0.89.
VAs during ACS	3	2.17 (1.03-4.56)	0.04
Anterior MI	5	1.16 (0.66-2.05)	0.61
Lateral MI	5	1.09 (0.78-1,58)	0.78
RV MI	5	0.88 (0.46-1.23)	0.31
Posterior MI	5	0.97 (0.56-1.87)	0.74
Inferior MI	5	0.67 (0.23-1.10)	0.11
Anterior Extensive MI	2	2.84 (1.24-6.49)	0.01
Infarct size	4	3.04 (1.54-5.85)	<0.001
Heart Rate Variability	3	1.27 (0.39-1.52)	0.45
Tpeak Tend Interval	4	3.15 (1.48-6.73)	0.003
T Wave alternans	3	0.93 (0.85-1.01)	0.09
QRS duration	2	1.01 (0.81-1.26)	0.93
QRS duration ≥ 180ms	3	1.33 (1.15-1.91)	0.04
Fragmented QRS	2	1.28 (1.06-1.68)	0.002
High PVC burdens in Holter	2	1.15 (1.06-1.25)	<0.001
LVEF <40%	4	3.04 (0.70-13.22)	0.14
LGE	2	9.87 (1.24-78.26)	0.03

RESUTS & DISCUSSION

Proposed algorhythm of VT risk stratification to ablation post MI



CONCLUSION

- Although there is no significant difference in terms of reducing mortality, **preventive VT ablation has been shown to reduce VT burdens and improve quality of life.**
- Noninvasive to invasive risk stratification has the potential to pro vide benefits in determining which patients require **routine PVS,** especially in **intermediate phase post MI**

Thank You

Prana Jagannatha, MD

Udayana University Hospital, Bali, Indonesia