Supplemental Material

Supplementary Tables
Table S1

Electrophysiological study data	288 (100)
Number of stimulation sites (n=249) Two sites, n (%)	222 (89.1%)
Number of extra-stimuli (n), median [IQR] Up to 2 Up to 3 Up to 4+	16 (6.5%) 215 (88.1%) 13 (5.3%)
Shortest coupling (ms), median [IQR]	210 [200–230]
Isoproterenol use, n (%)	97 (33.7)
High dose isoproterenol, n (%)	9 (3.1)
PVS+ with isoproterenol, n (%)*	38 (39.2)
Pts experiencing events, n (%)	22/38
PVS- with isoproterenol, n (%)*	59 (60.8)
Pts experiencing events, n (%)	8/59
Inducible sustained monomorphic VT, n (%)	137 (47.6)
Overall number of VTs**, n	218
LBBB, n (%)	158 (72.5)
Inferior Axis, n (%)	48 (22.0)
Superior Axis, n (%)	73 (33.5)
Unknown, n (%)	37 (17.0)
RBBB, n (%)	13 (6.0)
Polymorphic, n (%)	18 (8.3)
Cycle length available, n (%)	137 (62.8)
Median cycle length (ms), median [IQR]	248 [220 – 280]
Cycle length ≥300 ms	7/137 (5.1)
Cycle length 240 - 299 ms, n (%)	79/137 (57.6)
Cycle length 200-239 ms, n (%)	38/137 (27.7)
Cycle length <200 ms, n (%)	13/137 (9.5)
AH interval, median [IQR]	81 [65–100]
HV interval, median [IQR]	45 [40–52]
Contextual VT Ablation, n (%)	26 (9.0)

*Percentage calculated on the total of patients undergoing isoproterenol PVS

**Details of VT morphology were not available in 29 cases

AH: atrial-to-His; HV: His-to-ventricle; LBBB: left bundle branch block; PVS: programmed ventricular stimulation; RBBB: right bundle branch block; VT: ventricular tachycardia;

Table S2

Predictors of sustained VT inducibility at PVS				
	OR [C.I.]	p	aOR [C.I.]	p
Age (per year increase)	0.98 [0.97–1.00]	**0.038**	0.98 [0.97–1.00]	0.073
Male sex	1.36 [0.85–2.17]	0.199		
Caucasian ethnicity	0.68 [0.28–1.62]	0.383		
Proband status	2.11 [1.23–3.65]	**0.007**	1.44 [0.76–2.72]	0.265
Desmosomal variant carrier	1.16 [0.70–1.93]	0.566		
Recent cardiac syncope	1.49 [0.86–2.56]	0.154		
Total number of TWI (per unit increase)	1.19 [1.05–1.34]	**0.005**	1.13 [0.98–1.31]	0.091
NSVT at diagnosis	2.12 [1.32–3.39]	**0.002**	2.10 [1.23–3.56]	**0.006**
24-h PVC count* (per log unit increase)	1.01 [0.96–1.25]	0.166		
RVEF (%) (per % increase)	0.97 [0.95–0.99]	**0.029**	0.98 [0.96–1.01]	0.123
LVEF (%) (per % increase)	1.00 [0.97–1.02]	0.801		
ARVC Risk Score (%) (per % increase)	0.65 [0.41–0.91]	**<0.001**		

aOR: adjusted odds ratio; LVEF: left ventricular ejection fraction; NSVT: non sustained ventricular tachycardia; OR: odds ratio; PVC: premature ventricular contraction; PVS: programmed ventricular stimulation; RVEF: right ventricular ejection fraction; TWI: T wave inversion; VT: ventricular tachycardia.

*logarithmic relationship

Table S3

| ICD programming available (n = 148 pts)			
	Overall Cohort (n = 148)	PVS+ (n = 88)	PVS- (n = 60)	p
Monitor zone (ms), median [IQR]	350 [330–375]	333 [324–400]	351 [333–375]	0.419
VT Therapy zone (ms), median [IQR]	307 [293–329]	300 [292–330]	310 [300–322]	0.986

Abbreviations as per table S1

Supplementary figures

Figure S1: Distribution of predicted risks according to the ARVC risk calculator
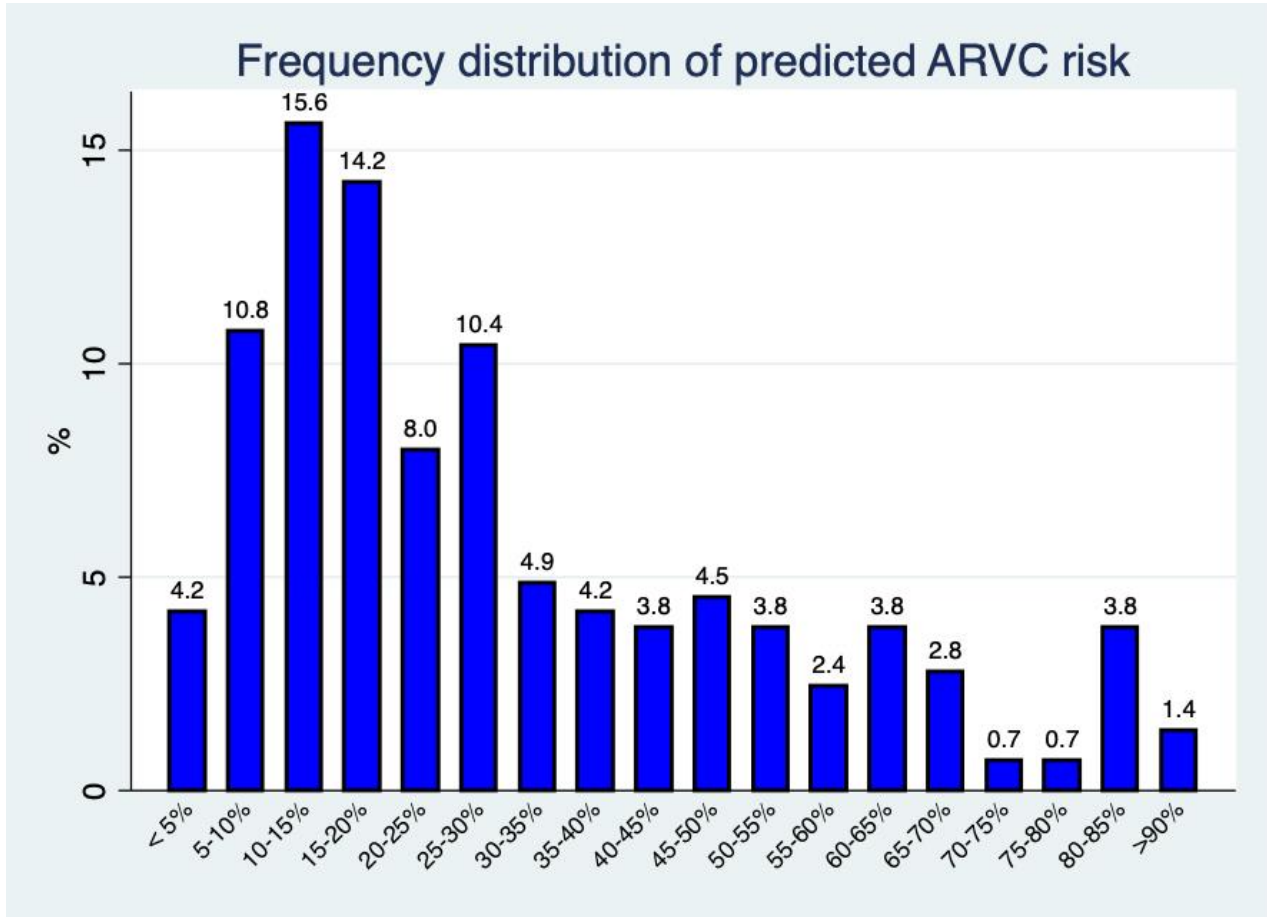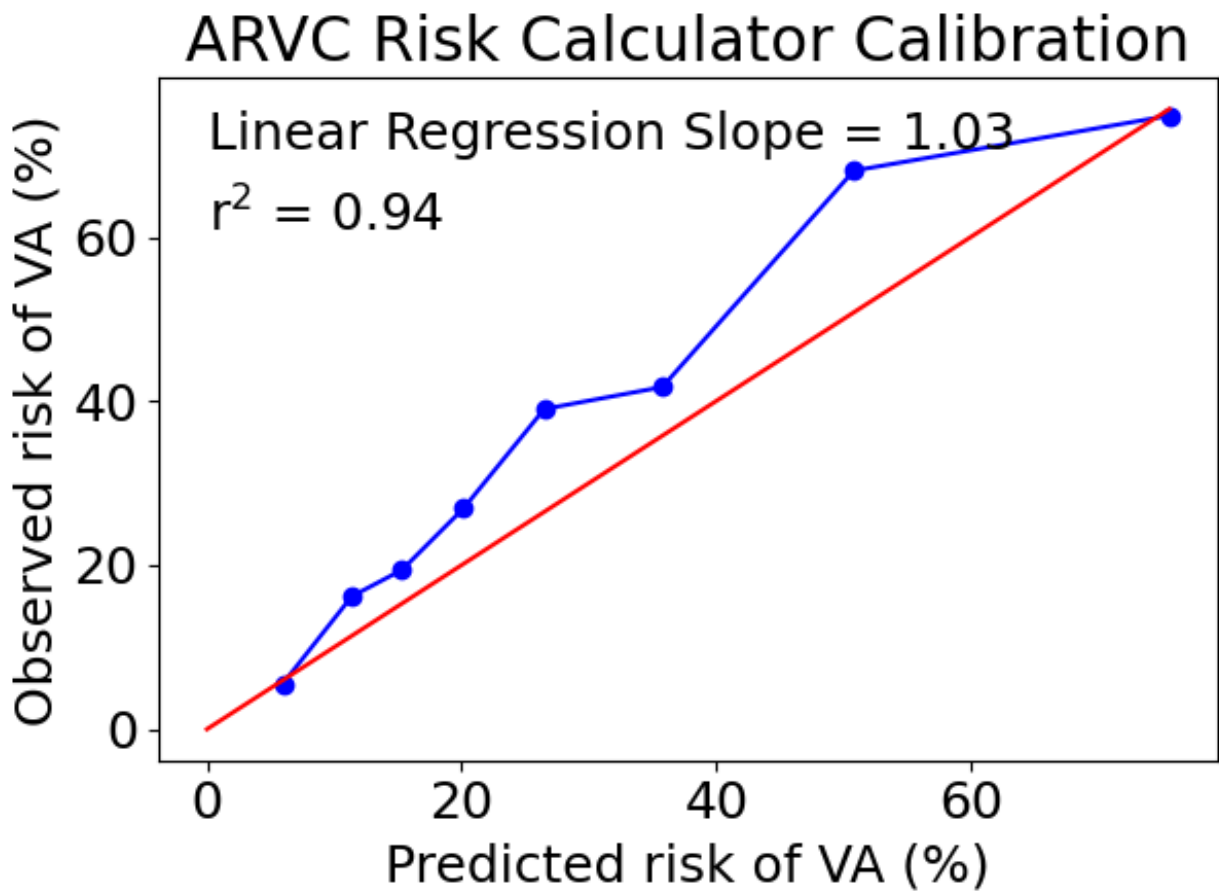
Figure S2: ICD implantation flowchart
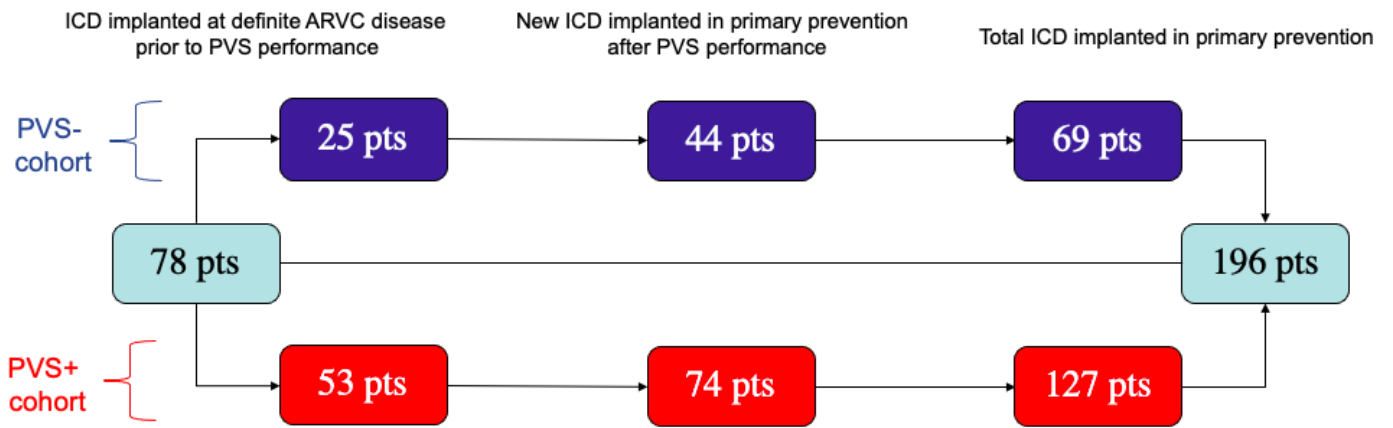
ICD: implantable cardioverter defibrillator, ARVC: arrhythmogenic right ventricular cardiomyopathy, PVS: programmed ventricular stimulation

Figure S3: **Calibration plot illustrating the performance of the ARVC risk score for 5-year sustained VA prediction.**
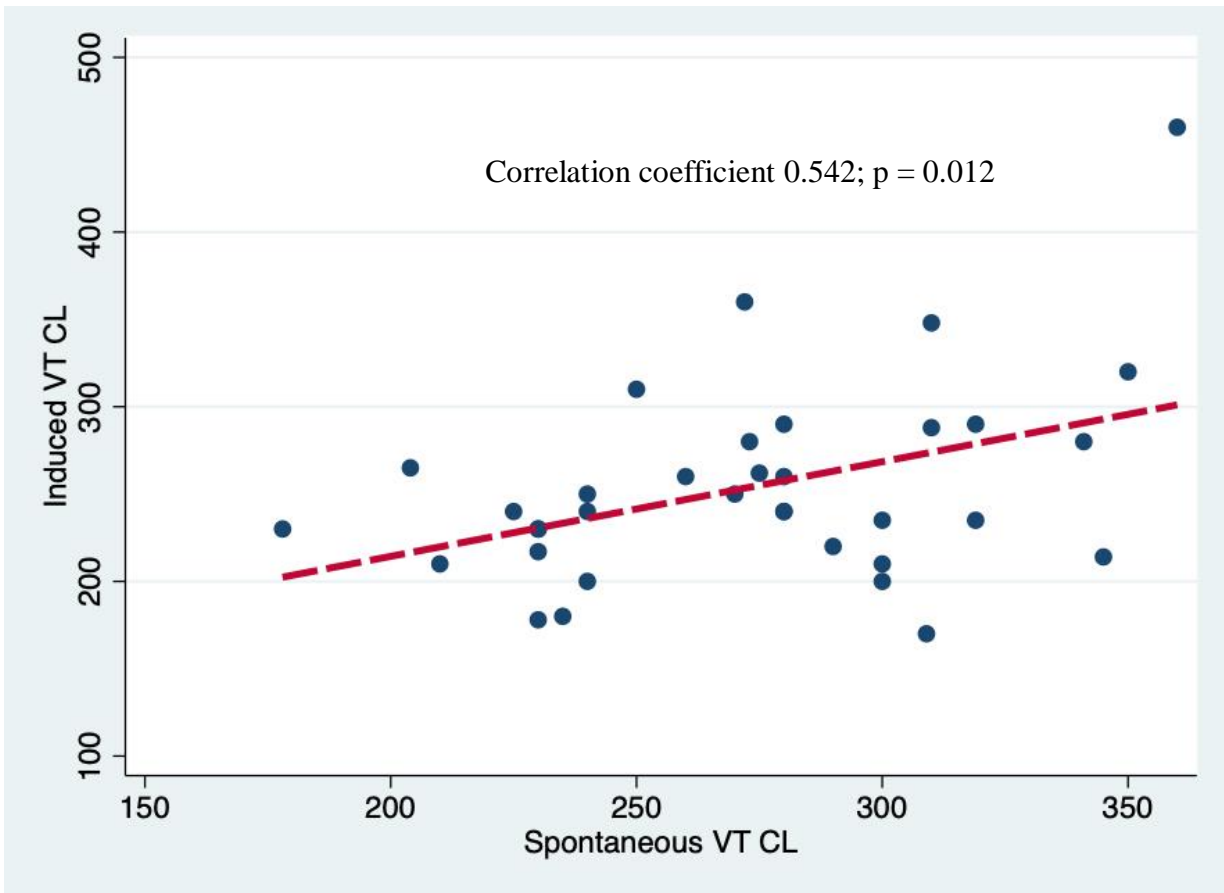

VA: ventricular arrhythmia

Figure S4: Correlation between cycle length of PVS induced VT and spontaneous observed VT in the study cohort

CL: cycle length, VT: ventricular tachycardia

Section B – Complete Case Analysis

Population: n=227 pts; n=98 pts with PVS+

- Total cohort:
  - Sensitivity   76.6 [66.6 – 85.5];
  - Specificity   70.3 [63.2 – 77.5];
  - Positive predictive value   54.5 [44.6 – 64.3];
  - Negative predictive value   85.8 [79.8 – 91.8];
  - Positive likelihood ratio   2.58;
  - Negative likelihood ratio   0.33.
- A priori risk <25%:
  - Positive predictive value   45.8 [31.4 – 60.2];
  - Negative predictive value   92.9 [87.6 – 98.3];
  - Positive likelihood ratio   3.35;
  - Negative likelihood ratio   0.25.
- A priori risk >=25%:
  - Positive predictive value   62.4 [49.3 – 75.6];
  - Negative predictive value   70.6 [56.5 – 84.7];
  - Positive likelihood ratio   1.79;
  - Negative likelihood ratio   0.44.
- Association between ARVC calculator / PVS and outcomes
  - Concordance for ARVC calculator alone: 0.688
  - Concordance for PVS alone: 0.674
    - HR of PVS alone: 4.71 [2.69 – 8.25]; $p < 0.001$
  - Concordance for ARVC + PVS: 0.738
    - HR of PVS: 2.70 [1.54 – 4.73]; $p < 0.001$
  - LLR test for superiority of combined model: Test Statistic 7.369; $p = 0.007$

No significant differences in the overall results were observed between the complete-case and the complete cohort using multiple imputation by chained equation analyses.

Section C –Patient characteristics by registry

Johns Hopkins Registry (n=108)	
Age, mean±s.d.	35.2±12.8
Male sex, n (%)	50 (46.3)
Caucasian, n (%)	106 (98.1)
Proband Status, n (%)	74 (68.5)
Recent cardiac syncope, n (%)	26 (24.1)
Leads with TWI on ECG	
TWI in ≥3 precordial leads, n (%)	73 (67.6)
TWI in ≥2 inferior leads, n (%)	25 (23.1)
NSVT at diagnosis, n (%)	57 (52.8)
24-h PVC count, median [IQR]	1647 [357–5160]
Imaging at baseline	
RVEF (%), mean±s.d.	40.6±11.6
LVEF (%), mean±s.d.	58.0±7.3
Beta-blockers at baseline, n (%)	44 (40.7)
Events at follow up, n (%)	52 (48.1)

LVEF: Left ventricular ejection fraction, NSVT: non-sustained ventricular tachycardia, PVC: premature ventricular complex, RVEF: right ventricular ejection fraction, TWI: T-wave inversion.

Italian Registry (n=87)	
Age, mean±s.d.	47.8±13.3
Male sex, n (%)	66 (75.9)
Caucasian, n (%)	87 (100)
Proband Status, n (%)	76 (87.4)
Recent cardiac syncope, n (%)	25 (28.7)
Leads with TWI on ECG	
TWI in ≥3 precordial leads, n (%)	54 (62.1)
TWI in ≥2 inferior leads, n (%)	25 (28.7)
NSVT at diagnosis, n (%)	26 (29.9)
24-h PVC count, median [IQR]	1100 [500–2341]
Imaging at baseline	
RVEF (%), mean±s.d.	46.2±8.9
LVEF (%), mean±s.d.	52.2±10.1
Beta-blockers, n (%)	43 (49.4)
Events at follow up, n (%)	36 (41.4)

Montreal site from the Canadian HIRO registry (n=8)	
Age, mean±s.d.	43.3±14.4
Male sex, n (%)	4 (50.0)
Caucasian, n (%)	2 (25.0)
Proband Status, n (%)	6 (75.0)
Recent cardiac syncope, n (%)	6 (75.0)
Leads with TWI on ECG	
TWI in ≥3 precordial leads, n (%)	5 (62.5)
TWI in ≥2 inferior leads, n (%)	2 (25.0)
NSVT at diagnosis, n (%)	5 (62.5)
24-h PVC count, median [IQR]	1623 [1445–3343]
Imaging at baseline	
RVEF (%), mean±s.d.	35.0±17.7
LVEF (%), mean±s.d.	52.6±8.0
Beta-blockers, n (%)	2 (25.0)
Events at follow up, n (%)	6 (75.0)

Dutch Registry (n=43)	
Age, mean±s.d.	42.7±13.9
Male sex, n (%)	20 (46.5)
Caucasian, n (%)	42 (97.7)
Proband Status, n (%)	22 (51.2)
Recent cardiac syncope, n (%)	13 (30.2)
Leads with TWI on ECG	
TWI in ≥3 precordial leads, n (%)	27 (62.8)
TWI in ≥2 inferior leads, n (%)	14 (32.6)
NSVT at diagnosis, n (%)	26 (60.5)
24-h PVC count, median [IQR]	2057 [975–4008]
Imaging at baseline	
RVEF (%), mean±s.d.	43.3±10.2
LVEF (%), mean±s.d.	56.6±7.5
Beta-blockers, n (%)	14 (32.6)
Events at follow up, n (%)	15 (34.9)

Swiss Registry (n=27)	
Age, mean±s.d.	39.7±14.5
Male sex, n (%)	14 (51.9)
Caucasian, n (%)	27 (100)
Proband Status, n (%)	23 (85.2)
Recent cardiac syncope, n (%)	8 (29.6)
Leads with TWI on ECG	
TWI in ≥3 precordial leads, n (%)	21 (87.5)
TWI in ≥2 inferior leads, n (%)	2 (7.4)
NSVT at diagnosis, n (%)	14 (51.9)
24-h PVC count, median [IQR]	1005 [500–3386]
Imaging at baseline	
RVEF (%), mean±s.d.	37.7±14.5
LVEF (%), mean±s.d.	57.2±10.0
Beta-blockers, n (%)	13 (48.1)
Events at follow up, n (%)	7 (25.9)

Nordic Registry (Norway and Sweden) (n=15)	
Age, mean±s.d.	41.8±18.8
Male sex, n (%)	7 (46.7)
Caucasian, n (%)	14 (93.3)
Proband Status, n (%)	11 (73.3)
Recent cardiac syncope, n (%)	7 (46.7)
Leads with TWI on ECG	
TWI in ≥3 precordial leads, n (%)	9 (60.0)
TWI in ≥2 inferior leads, n (%)	3 (20.0)
NSVT at diagnosis, n (%)	7 (46.7)
24-h PVC count, median [IQR]	1735 [109–10000]
Imaging at baseline	
RVEF (%), mean±s.d.	40.3±13.9
LVEF (%), mean±s.d.	53.9±10.2
Beta-blockers, n (%)	7 (46.7)
Events at follow up, n (%)	4 (26.7)