# Risk score for the exclusion of arrhythmic events in arrhythmogenic right ventricular cardiomyopathy at first presentation: Appendix

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## Tables

#### Table A.1:

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Year** | **Author** | **Analysed risk** | **Proposed risk factor** | **Quantification** | |
| 2015 | Protonotarios[1] | Arrhythmia | Male gender  Repolarization abnormalities  LV dysfunction | HR 3.26  OR 6.94-9.09  OR 7.07-8.19 | |
| 2015 | Mast[2] | MACE | LVEF<50% | 1year event risk 50% vs 16.7% | |
| 2015 | Ruwald[3] | Arrhythmia or death | Competitive sport | HR 1.99 | |
| 2014 | Saguner[4] | MACE (HF and arrhythmia) | inferior TWI  QRS fragmentation  precordial QRS amplitude ratio ≤0.48 | HR 2.44  HR 2.92  HR 2.65 | |
| 2014 | Liao[5] | Arrhythmia | SAECG fulfilling all 3 Task Force criteria | OR 30.49 | |
| 2014 | Link[6] | ICD treatment | Pre-implantation SMVT or SPVT  T-wave inversions inferiorly | P=0.0029  P=0.0159 | |
| Life-threatening arrhythmias | Younger age | P=0.032 | |
| 2014 | Saguner[7] | MACE | Reduced RVFAC, per 1%  Reduced TAPSE, per unit decrease | HR 1.08  HR 1.01 | |
| 2012 | Peters[8] | Development of RBBB and HF | QRS fragmentation in ≥ 3 leads | r=17.45 | |
| 2013 | James[9] | HF | > average annual exercise | P=0.048 | |
| Arrhythmia | >516h/year sports before presentation  >425h/year sports after presentation | P=0.001  P<0.001 | |
| 2013 | Canpolat[10] | Arrhythmia | Fragmented QRS  RVEF reduction  LV involvement  History of syncope | OR 6.52  OR 3.76  OR 2.88  OR 3.12 | |
| 2013 | Te Riele[11] | Arrhythmia | Arrhythmic events only in patients with both electrical (ECG and/or Holter) and structural (CMR) criteria for ARVC | None given | |
| 2013 | Deac[12] | Arrhythmia | Abnormal CMR | HR 16.1 | |
| 2013 | Bhonsale[13] | Arrhythmia | Proband status  ≥ 3 T-wave inversions  Male sex | HR 7.7  HR 4.2  HR 1.8 | |
| 2013 | Migliore[14] | Arrhythmia | History of cardiac arrest or syncope  Abnormal bipolar endocardial voltage mapping | HR 2.4  HR 1.6 | |
| 2013 | Saguner[15] | MACE | Inducibility of Sustained monomorphic VT | OR 2.87 | |
| 2012 | Santangeli[16] | Appropriate ICD interventions | Fragmented QRS  Abnormal electrograms within scar | HR 21  HR 8.91 | |
| 2012 | Peters[17] | Arrhythmia | QRS fragmentation  Arrhythmia  Left precordial JT prolongation | OR 10.46  OR 5.33  OR 9.67 | |
| 2011 | Bhonsale[18] | Appropriate ICD interventions | Inducibility at electrophysiological study  Non-sustained VT | HR 4.5  HR 10.5 | |
| 2011 | Paul[19] | VT | RV size (moderate vs. no dilatation)  Presence of an ICD  Presence of an abnormal 123I-MIBG SPECT finding | HR 0.135  HR 3.012  HR 4.667 | |
| 2011 | Sarvari[20] | Arrhythmia | Increased RVOT diameter, RVED area, and RVES area and reduced RVFAC | P<0.001 | |
| 2011 | Pinamonti[21] | CV death or HTx | Significant tricuspid regurgitation  Amiodarone  RV dysfunction | HR 7.60  HR 3.40  HR 4.12 | AUC 0.78 |
| Significant tricuspid regurgitation  Amiodarone  Ordinal ventricular dysfunction | HR 5.09  HR 3.72  HR 6.30 | AUC 0.84 |
| 2010 | Corrado[22] | Appropriate ICD interventions | Syncope  NSVT  Age ≤35y  LV dysfunction (EF <55%)  FH of SCD | HR 2.95  HR 1.62  HR 1.22  HR 1.13  HR 0.90 | |
| ICD shocks for VF/Vfl | Syncope  NSVT | HR 3.16  HR 1.28 | |
| 2005 | Piccini[23] | Appropriate ICD interventions | Previous sustained VT/VF | OR 11.44 | |
| 2005 | Lemola[24] | MACE | History of congestive heart failure  LV involvement in echo | P<0.0001  P=0.0003 | |
| 2004 | Roguin[25] | Appropriate ICD interventions | VT induction during electrophysiological study | OR 11.2 | |
| 2004 | Wichter[26] | Apropriate ICD interventions | Extensive RV dysfunction | OR 2.09 | |
| 2003 | Corrado[27] | Appropriate ICD intervention for VF/Vfl | Age/5 y  LVEF  Cardiac arrest  VT with hemodynamic compromise | OR 0.77  OR 0.94  OR 79  OR 14 | |
| 2001 | Turrini[28] | Sudden death | QRS dispersion  History of syncope | OR 1.22  OR 5.9 | |
| 1999 | Peters[29] | Sudden death/malignant ventricular arrhythmias | LV involvement  RV dilatation  Left precordial JT interval prolongation  Precordial QRS dispersion ≥50 ms  Precordial T wave inversions beyond V3 | P<0.00001  P<0.00001  P<0.00001  P<0.005  P<0.0001 | |

Reported risk factors for adverse outcomes in patients with ARVC. LV: left ventricular/ventricle, HR: hazard ratio, OR odds ratio, MACE: major adverse cardiac events, LVEF: left ventricular ejection fraction, HF: heart failure, TWI: T wave inversions, SAECG: signal averaged ECG, ICD: implantable cardioverter-defibrillator, SMVT: sustained monomorphic ventricular tachycardia (VT), SPVT: sustained polymorphic VT, RVFAC: fractional area of change, TAPSE: tricuspid annular plane systolic excursion, RBBB: right bundle branch block, RVEF: right ventricular ejection fraction, CMR: cardiac magnetic resonance, RV: right ventricular, 123I-MIBG SPECT: I-123-metaiodobenzylguanidine–single photon emission [computed tomography](http://www.sciencedirect.com/science/article/pii/S0022510X00002793#200005257), RVOT: right ventricular outflow tract, RVED: right ventricular end-diastolic, RVES: right ventricular end-systolic, NSVT: nonsustained VT, FH: family history, SCD: sudden cardiac death, VFl: ventricular flutter

#### Table A.2:

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|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **Recurrent arrhythmia**  **n = 35** | **Favourable outcome**  **n = 100** | **p-value** | **p-value adapted** |
| Age at diagnosis | 38.5 ± 13.0 | 41.8 ± 15.1 | 0.254 | 0.649 |
| Time of follow up (months) | 109.5 ± 57.4 | 111.1 ± 67.160 | 0.899 | 1.000 |
| Male sex | 25 (71.4%) | 57 (57.0%) | 0.161 | 0.495 |
| Caucasians | 32 (94.1%) | 95 (96.0%) | 0.645 | 0.835 |
| Family history SCD | 12 (37.5%) | 46 (50.0%) | 0.304 | 0.691 |
| Multiple family history SCD | 5 (11.6%) | 21 (9.1%) | 0.575 | 0.802 |
| Single desmosomal pathogenic mutation | 14 (40.0%) | 42 (42.0%) | 1.000 | 1.000 |
| Desmoplakin pathogenic mutation | 3 (8.6%) | 15 (15.0%) | 0.402 | 0.727 |
| Plakophilin-2 pathogenic mutation | 11 (31.4%) | 32 (32.0%) | 1.000 | 1.000 |
| Desmoglein-2 pathogenic mutation | 5 (14.3%) | 11 (11.0%) | 0.560 | 0.802 |
| Desmocollin-2 pathogenic mutation | 2 (5.7%) | 2 (2.0%) | 0.276 | 0.657 |
| Plakoglobin pathogenic mutation | 1 (2.9%) | 1 (1.0%) | 0.453 | 0.789 |
| 2 desmosomal mutations, same gene | 1 (2.9%) | 10 (10.0%) | 0.288 | 0.671 |
| 2 desmosomal mutations, different genes | 8 (8.0%) | 5 (14.3%) | 0.321 | 0.706 |
| Structural major criterion | 21 (60.0%) | 50 (50.5%) | 0.431 | 0.761 |
| Structural minor criterion | 2 (5.7%) | 15 (15.2%) | 0.237 | 0.615 |
| Tissue major criterion | 2 (5.7%) | 3 (3.1%) | 0.607 | 0.813 |
| Tissue minor criterion | 0 (0.0%) | 0 (0.0%) | NA | NA |
| Repolarisation major criterion | 16 (45.7%) | 49 (49.5%) | 0.844 | 0.994 |
| Repolarisation minor criterion | 5 (14.3%) | 12 (12.1%) | 0.771 | 0.927 |
| Depolarisation major criterion | 4 (11.4%) | 3 (3.0%) | 0.076 | 0.320 |
| Depolarisation minor criterion | 4 (11.4%) | 16 (16.2%) | 0.591 | 0.813 |
| Arrhythmias major criterion | 24 (68.6%) | 47 (48.0%) | **0.048** | 0.252 |
| Arrhythmias minor criterion | 10 (27.8%) | 10 (28.6%) | 1.000 | 1.000 |
| Family history major criterion | 24 (68.6%) | 74 (75.5%) | 0.503 | 0.802 |
| Family history minor criterion | 1 (2.9%) | 3 (3.1%) | 1.000 | 1.000 |

General characteristics. MACE: major adverse cardiac events, AUC: area under the curve, CI: confidence interval, OR: odds ratio. SCD: sudden cardiac death.

#### Table A.3:

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Symptoms at initial presentation** | **Recurrent arrhythmia**  **n = 35** | **Favourable outcome**  **n = 97** | **p-value** | **p-value adapted** |
| Family history as reason for screening | 2 (5.7%) | 40 (40.0%) | **0.000** | 0.017 |
| VT/VF as reason for screening | 20 (57.1%) | 22 (22.0%) | **0.000** | 0.017 |
| Cardiovascular symptoms as reason for screening | 13 (37.1%) | 31 (31.0%) | 0.534 | 0.802 |
| Incidental findings as reason for screening | 0 (0.0%) | 4 (4.0%) | 0.572 | 0.802 |
| Dyspnea | 6 (18.8%) | 17 (17.7%) | 1.000 | 1.000 |
| Chest pain | 2 (6.3%) | 14 (14.6%) | 0.355 | 0.727 |
| Palpitations | 13 (40.6%) | 39 (40.6%) | 1.000 | 1.000 |
| Presyncope | 7 (21.9%) | 26 (27.1%) | 0.646 | 0.835 |
| Syncope | 9 (28.1%) | 35 (36.5%) | 0.520 | 0.802 |

Clinical symptoms at baseline. MACE: major adverse cardiac events, AUC: area under the curve, CI: confidence interval, OR: odds ratio, VT: ventricular tachycardia, VF: ventricular fibrillation

#### Table A.4:

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **ECG at baseline** | **Recurrent arrhythmia**  **n = 35** | **Favourable outcome**  **n = 95** | **p-value** | **p-value adapted** |
| QRS duration V1 | 100.28 ± 18.54 | 94.02 ± 18.86 | 0.107 | 0.386 |
| QRS duration V6 | 79.06 ± 20.12 | 80.22 ± 18.65 | 0.768 | 0.927 |
| S upstroke duration V1 | 45.00 ± 13.74 | 38.09 ± 13.24 | **0.014** | 0.106 |
| S upstroke duration V2 | 48.59 ± 16.81 | 42.70 ± 14.81 | 0.065 | 0.308 |
| Abnormal axis | 9 (26.5%) | 19 (20.2%) | 0.473 | 0.789 |
| Epsilon wave V1 | 0 (0.0%) | 3 (3.2%) | 0.563 | 0.802 |
| Epsilon wave V2 | 0 (0.0%) | 3 (3.2%) | 0.563 | 0.802 |
| Epsilon wave V3 | 1 (2.9%) | 2 (2.1%) | 1.000 | 1.000 |
| Epsilon wave II | 0 (0.0%) | 3 (3.2%) | 0.563 | 0.802 |
| Epsilon wave III | 0 (0.0%) | 6 (6.3%) | 0.190 | 0.543 |
| Epsilon wave aVF | 0 (0.0%) | 6 (6.3%) | 0.190 | 0.543 |
| Negative T wave V1 | 28 (80.0%) | 65 (68.4%) | 0.273 | 0.657 |
| Negative T wave V2 | 25 (71.4%) | 51 (53.7%) | 0.075 | 0.320 |
| Negative T wave V3 | 22 (62.9%) | 44 (46.3%) | 0.115 | 0.390 |
| Negative T wave V4 | 18 (51.4%) | 35 (36.8%) | 0.161 | 0.495 |
| Negative T wave V5 | 12 (34.3%) | 22 (23.2%) | 0.260 | 0.654 |
| Negative T wave V6 | 6 (17.1%) | 17 (17.9%) | 1.000 | 1.000 |
| Negative T wave I | 3 (8.6%) | 4 (4.2%) | 0.386 | 0.727 |
| Positive T wave I | 21 (60.0%) | 72 (75.8%) | 0.084 | 0.324 |
| Negative T wave II | 6 (17.1%) | 11 (11.6%) | 0.394 | 0.727 |
| Positive T wave II | 17 (48.6%) | 53 (55.8%) | 0.553 | 0.802 |
| Negative T wave III | 14 (40.0%) | 31 (32.6%) | 0.533 | 0.802 |
| Positive T wave III | 7 (20.0%) | 30 (31.6%) | 0.273 | 0.657 |
| Negative T wave aVR | 15 (42.9%) | 69 (72.6%) | **0.003** | 0.038 |
| Positive T wave aVR | 5 (14.3%) | 8 (8.4%) | 0.334 | 0.719 |
| Negative T wave aVL | 5 (14.3%) | 9 (9.5%) | 0.524 | 0.802 |
| Positive T wave aVL | 17 (48.6%) | 56 (58.9%) | 0.323 | 0.706 |
| Negative T wave aVF | 9 (25.7%) | 18 (18.9%) | 0.466 | 0.789 |
| Positive T wave aVF | 11 (31.4%) | 47 (49.5%) | 0.076 | 0.320 |
| Q wave V1 | 0 (0.0%) | 3 (3.2%) | 0.566 | 0.802 |
| Q wave V2 | 0 (0.0%) | 2 (2.1%) | 1.000 | 1.000 |
| Q wave V3 | 0 (0.0%) | 2 (2.1%) | 1.000 | 1.000 |
| Q wave V4 | 2 (5.9%) | 4 (4.2%) | 0.654 | 0.835 |
| Q wave V5 | 8 (23.5%) | 15 (15.8%) | 0.309 | 0.693 |
| Q wave V6 | 8 (23.5%) | 21 (22.1%) | 1.000 | 1.000 |
| Q wave I | 7 (20.6%) | 15 (15.8%) | 0.597 | 0.813 |
| Q wave II | 6 (17.6%) | 18 (18.9%) | 1.000 | 1.000 |
| Q wave III | 5 (14.7%) | 22 (23.2%) | 0.338 | 0.719 |
| Q wave aVR | 3 (8.8%) | 12 (12.6%) | 0.758 | 0.927 |
| Q wave aVL | 6 (17.6%) | 17 (17.9%) | 1.000 | 1.000 |
| Q wave aVF | 7 (20.6%) | 18 (18.9%) | 0.805 | 0.961 |
| Left bundle branch block (complete +incomplete) | 3 (8.6%) | 4 (4.2%) | 0.386 | 0.727 |
| Complete LBBB | 1 (2.9%) | 2 (2.1%) | 1.000 | 1.000 |
| Right bundle branch block (complete +incomplete) | 2 (5.7%) | 12 (12.6%) | 0.350 | 0.727 |
| Complete RBBB | 0 (0.0%) | 4 (4.2%) | 0.574 | 0.802 |
| Low voltage | 10 (28.6%) | 22 (23.2%) | 0.647 | 0.835 |
| Poor R wave progression | 12 (35.3%) | 32 (34.8%) | 1.000 | 1.000 |

ECG characteristics at baseline. MACE: major adverse cardiac events, AUC: area under the curve, CI: confidence interval, OR: odds ratio, LBBB: left bundle branch block, RBBB: right bundle branch block

#### Table A.5:

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **SAECG at baseline** | **Recurrent arrhythmia**  **n = 22** | **Favourable outcome**  **n = 71** | **p-value** | **p-value adapted** |
| Filtered QRS duration | 124.7 ± 22.5 | 114.2 ± 21.2 | **0.050** | 0.252 |
| Filtered QRS duration ≥ 114 ms | 16 (72.7%) | 29 (42.0%) | **0.012** | 0.095 |
| Filtered QRS duration ≥ 117 ms | 16 (72.7%) | 21 (30.4%) | **<0.001** | 0.017 |
| Filtered QRS duration ≥ 106 ms | 18 (81.8%) | 41 (59.4%) | 0.055 | 0.269 |
| Filtered QRS duration ≥ 108 ms (BL) | 17 (77.3%) | 39 (56.5%) | 0.081 | 0.320 |
| RMS 40 | 20.9 ± 22.6 | 24.8 ± 18.0 | 0.402 | 0.727 |
| RMS 40 ≤ 20 | 14 (63.6%) | 37 (53.6%) | 0.410 | 0.732 |
| RMS 40 ≤ 23.6 | 16 (72.7%) | 37 (53.6%) | 0.114 | 0.390 |
| RMS 40 ≤ 30 | 17 (77.3%) | 45 (65.2%) | 0.291 | 0.671 |
| LAS | 51.1 ± 22.2 | 40.1 ± 19.6 | **0.028** | 0.172 |
| LAS ≥ 36 | 17 (77.3%) | 37 (53.6%) | **0.049** | 0.252 |
| LAS ≥ 38 | 15 (68.2%) | 33 (47.8%) | 0.096 | 0.354 |
| LAS ≥ 42 | 15 (68.2%) | 26 (38.0%) | **0.012** | 0.095 |
| All 3 parameters positive | 13 (59.1%) | 23 (33.3%) | **0.031** | 0.183 |
| Z QRS duration | 116.3 ± 27.3 | 108.2 ± 15.5 | 0.115 | 0.390 |
| Z RMS 40 | 22.1 ± 26.9 | 17.2 ± 12.1 | 0.277 | 0.657 |
| Z LAS | 50.4 ± 25.8 | 44.4 ± 15.5 | 0.235 | 0.615 |
| Number of beats | 326 ± 138 | 342 ± 189 | 0.724 | 0.904 |
| Filtered noise | 0.376 ± 0.073 | 0.385 ± 0.062 | 0.605 | 0.813 |

Signal averaged ECG (SAECG) measurements at baseline. MACE: major adverse cardiac events, AUC: area under the curve, CI: confidence interval, OR: odds ratio, RMS: Root-mean-square voltage of the terminal 40 ms, LAS: low amplitude signal < 40 µV duration, Z: Z-vector

#### Table A.6:

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **24h-ECG at baseline** | **Recurrent arrhythmia**  **n = 20** | **Favourable outcome**  **n = 66** | **p-value** | **p-value adapted** |
| Number of VPB | 3509 ± 3892 | 2140 ± 4672 | 0.237 | 0.615 |
| VPB present | 20 (100%) | 62 (93.9%) | 0.569 | 0.802 |
| ≥ 440 VPB | 17 (85%) | 33 (50.0%) | 0.009 | 0.083 |
| ≥ 800 VPB | 16 (80.0%) | 26 (39.4%) | 0.002 | 0.028 |
| Number of couplets | 308 ± 450 | 136 ± 356 | 0.091 | 0.343 |
| Couplets present | 17 (94.4%) | 37 (56.1%) | 0.002 | 0.028 |
| ≥ 8 couplets | 16 (88.9%) | 25 (37.9%) | 0.000 | 0.000 |
| Number of triplets | 27 ± 51 | 9 ± 34 | 0.081 | 0.320 |
| Triplets present | 15 (83.3%) | 19 (29.2%) | 0.000 | 0.000 |
| Polymorphic VPBs | 12 (70.6%) | 32 (57.1%) | 0.403 | 0.727 |
| VT present | 7 (41.2%) | 15 (22.1%) | 0.128 | 0.425 |
| Number of VT | 1 ± 3 | 3 ± 15 | 0.754 | 0.927 |
| Max beats VT | 5 ± 4 | 3 ± 5 | 0.184 | 0.544 |
| Max HR VT | 148 ± 34 | 149 ± 53 | 0.954 | 1.000 |
| Number SVE | 561 ± 1343 | 309 ± 1499 | 0.541 | 0.802 |
| AF present | 0 (0.0%) | 2 (3.0%) | 1.000 | 1.000 |
| SVT present | 2 (11.1%) | 4 (6.0%) | 0.604 | 0.813 |

Holter results at baseline. MACE: major adverse cardiac events, AUC: area under the curve, CI: confidence interval, OR: odds ratio, VPB: ventricular premature beats, VT: ventricular tachycardia, SVE: supraventricular ectopics, AF: atrial fibrillation, SVT: supraventricular tachycardia

#### Table A.7:

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **CPEX at baseline** | **Recurrent arrhythmia**  **n = 31** | **Favourable outcome**  **n = 88** | **p-value** | **p-value adapted** |
| Beta blockers | 22 (71.0%) | 41 (46.6%) | 0.022 | 0.146 |
| Calcium channel blockers | 0 (0.0%) | 1 (1.1%) | 1.000 | 1.000 |
| Sotalol | 4 (12.9%) | 7 (8.0%) | 0.476 | 0.789 |
| Amiodarone | 3 (9.7%) | 4 (4.6%) | 0.377 | 0.727 |
| Antiarrhythmics | 2 (6.5%) | 7 (8.0%) | 1.000 | 1.000 |
| Arrhythmias at rest | 16 (51.6%) | 33 (37.95) | 0.207 | 0.582 |
| Arrhythmias during exercise | 24 (77.4%) | 47 (54.0%) | 0.025 | 0.160 |
| NSVT during exercise | 4 (12.9%) | 3 (3.4%) | 0.077 | 0.320 |
| Arrhythmias during recovery | 17 (54.8%) | 36 (41.3%) | 0.214 | 0.592 |
| NSVT during recovery | 1 (3.2%) | 1 (1.1%) | 0.458 | 0.789 |
| %VO2max | 76.7 ± 29.8 | 80.4 ± 22.4 | 0.475 | 0.789 |
| VO2 max (ml/min/1.73m2) | 23.4 ± 7.6 | 23.9 ± 7.7 | 0.760 | 0.927 |
| RQ | 1.09 ± 0.11 | 1.10 ± 0.10 | 0.680 | 0.862 |
| Minutes | 8.3 ± 2.7 | 8.6 ± 2.4 | 0.647 | 0.835 |
| Watts | 148.8 ± 55.5 | 149.0 ± 61.0 | 0.985 | 1.000 |
| Max HR | 129 ± 23.7 | 145.7 ± 29.0 | 0.005 | 0.049 |
| Predicted max HR | 159.6 ± 43.6 | 154.2 ± 44.4 | 0.573 | 0.802 |

Results from cardiopulmonary exercise test (CPEX) at baseline. MACE: major adverse cardiac events, AUC: area under the curve, CI: confidence interval, OR: odds ratio, NSVT: nonsustained VT, VO2max: maximal oxygen uptake, %VO2max: VO2max, % of predicted, RQ: respiratory quotient, HR: heart rate

#### Table A.8:

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Echocardiogram at baseline** | **Recurrent arrhythmia**  **n = 35** | **Favourable outcome**  **n = 97** | **p-value** | **p-value adapted** |
| Reduced RV function (incl. borderline) | 22 (62.9%) | 40 (41.2%) | 0.032 | 0.183 |
| Reduced RV function (excl. borderline) | 21 (60.0%) | 40 (41.2%) | 0.075 | 0.320 |
| RV dilatation (incl. upper normal) | 31 (88.6%) | 62 (63.9%) | 0.005 | 0.049 |
| RV dilatation (excl. upper normal) | 29 (82.9%) | 52 (53.6%) | 0.002 | 0.028 |
| RVOT PLAX (cm) | 3.8 ± 0.4 | 3.5 ± 0.8 | 0.144 | 0.469 |
| RVOT PLAX ≥ 3.6 cm | 17 (70.8%) | 30 (42.3%) | 0.019 | 0.131 |
| RVOT PLAX ≥ 3.4 cm | 22 (91.7%) | 41 (57.7%) | 0.002 | 0.028 |
| RVOT PLAX/BSA | 1.9 ± 0.2 | 1.8 ± 0.4 | 0.367 | 0.727 |
| RVOT PLAX/BSA ≥ 1.85 | 11 (64.7%) | 20 (35.7%) | 0.050 | 0.252 |
| RVOT PLAX/BSA ≥ 1.68 | 15 (88.2%) | 30 (53.6%) | 0.011 | 0.095 |
| RVOT PSAX (cm) | 3.5 ± 0.6 | 3.2 ± 0.6 | 0.190 | 0.544 |
| RVOT PSAX/BSA | 1.7 ± 0.3 | 1.6 ± 0.4 | 0.686 | 0.863 |
| RVIT (cm) | 4.3 ± 0.8 | 3.6 ± 0.8 | 0.001 | 0.021 |
| RVIT ≥ 3.7 cm | 18 (81.8%) | 27 (46.6%) | 0.005 | 0.049 |
| RV/LV | 1.3 ± 0.7 | 0.9 ± 0.5 | 0.005 | 0.049 |
| RV/LV ≥ 0.81 | 16 (80.0%) | 15 (34.1%) | 0.001 | 0.021 |
| RV/LV ≥ 0.79 | 18 (90.0%) | 20 (45.5%) | 0.001 | 0.021 |
| RV regional wall motion abnormalities | 23 (67.6%) | 51 (52.6%) | 0.160 | 0.495 |
| Akinesia or dyskinesia RV | 9 (27.3%) | 23 (23.7%) | 0.815 | 0.966 |
| Dyskinesia RV | 6 (18.2%) | 12 (12.4%) | 0.395 | 0.727 |
| Bulge RV | 4 (12.1%) | 12 (12.6%) | 1.000 | 1.000 |
| RV aneurysm | 4 (12.1%) | 11 (11.6%) | 1.000 | 1.000 |
| LVEDD | 5.0 ± 0.5 | 5.2 ± 0.6 | 0.363 | 0.727 |
| LVESD | 3.5 ± 0.6 | 3.6 ± 0.7 | 0.368 | 0.727 |
| IVS | 0.9 ± 0.2 | 0.8 ± 0.2 | 0.363 | 0.727 |
| Posterior LV wall | 0.8 ± 0.2 | 0.8 ± 0.2 | 0.526 | 0.802 |
| Left atrium | 3.5 ± 0.7 | 3.7 ± 0.5 | 0.017 | 0.122 |
| EF | 57.8 ± 12.3 | 57.8 ± 12.2 | 0.988 | 1.000 |
| LV regional wall motion abnormalities | 9 (26.5%) | 20 (20.6%) | 0.480 | 0.789 |
| LV akinesia or dyskinesia | 4 (11.8%) | 5 (5.2%) | 0.237 | 0.615 |
| LV dyskinesia | 2 (5.9%) | 4 (4.1%) | 0.649 | 0.835 |
| LV aneurysm | 1 (3.0%) | 2 (2.1%) | 1.000 | 1.000 |

Echo characteristics at baseline. AUC: area under the curve, CI: confidence interval, MACE: major adverse cardiac events, OR: odds ratio, PLAX: parasternal long axis view, RV: right ventricle/ventricular, RVOT: right ventricular outflow tract, BSA: body surface area, PSAX: parasternal short axis view, RVIT: right ventricular inflow tract, LV: left ventricle/ventricular, LVEDD: left ventricular end-diastolic diameter, LVESD: left ventricular end-systolic diameter, IVS: interventricular septum thickness, EF: ejection fraction

#### Table A.9: Risk Score Proposals

|  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **SAECG** | **24h-ECG** | **ECG** | **CPEX** | **P value** | **Nagelkerke**  **R2** | **PAC (%)** | **Sensitivity (%)** | **Specificity (%)** | **AUC** | **OR** |
| Test 1 | fQRSd≥106ms | ≥800 VPB |  | Arrhythmias exercise | 0.001 | 0.365 | 83.9 | 54.5 | 90.2 | 0.83 (0.71-0.94) | 7.82 (2.16-28.32) |
| Test 2 | fQRSd≥108ms | ≥800 VPB |  | Arrhythmias exercise | 0.001 | 0.320 | 82.0 | 45.5 | 90.0 | 0.81 (0.69-0.93) | 6.18 (1.87-20.40) |
| Test 3 | LAS≥38ms | ≥800 VPB |  | Arrhythmias exercise | 0.001 | 0.341 | 82.3 | 45.5 | 90.2 | 0.82 (0.71-0.93) | 6.06 (1.90-19.37) |
| Test 4 | LAS≥42ms | ≥440 VPB |  | Arrhythmias exercise | 0.000 | 0.419 | 85.5 | 54.5 | 92.2 | 0.85 (0.74-0.96) | 8.76 (2.27-33.71) |
| Test 5 | LAS≥42ms | ≥800 VPB |  | Arrhythmias exercise | 0.000 | 0.416 | 85.5 | 45.5 | 94.1 | 0.85 (0.74-0.95) | 8.93 (2.25-35.48) |
| Test 6 | fQRSd≥117ms | Triplets | Absence neg T aVR |  | 0.000 | 0.557 | 86.9 | 36.4 | 100.0 | 0.90 (0.80-0.99) | 12.14 (2.84-51.80) |
| Test 7 | RMS≤23.6mV | Triplets | Absence neg T aVR |  | 0.000 | 0.522 | 88.5 | 45.5 | 98.0 | 0.89 (0.80-0.99) | 10.58 (2.57-43.54) |
| Test 8 | LAS≥36ms | ≥8 couplets | Absence neg T aVR |  | 0.000 | 0.468 | 88.7 | 54.5 | 96.1 | 0.87 (0.76-0.98) | 8.52 (2.36-30.78) |
| Test 9 | LAS≥36ms | Triplets | Absence neg T aVR |  | 0.000 | 0.537 | 90.2 | 54.5 | 98.0 | 0.89 (0.79-0.99) | 11.72 (2.69-51.09) |
| Test 10 | fQRSd≥117ms | NSVT ≥3 beats | Absence neg T aVR |  | 0.000 | 0.556 | 88.9 | 36.4 | 100.0 | 0.90 (0.80-0.99) | 13.03 (2.99-56.87) |

Significant models in multivariable logistic regression. AUC: area under the curve, CPEX: cardiopulmonary exercise test, fQRSd: filtered QRS duration, LAS: low amplitude signal duration, neg: negative, OR: odds ratio, PAC: percentage accuracy in classification, RMS: root-mean-square of the last 40 ms, SAECG signal averaged ECG, VPB: ventricular premature beats.

#### Table A.10:

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Risk Score** | **Parameter** | **Sensitivity (%)** | **Specificity (%)** | **PPV (%)** | **NPV (%)** | **OR** | **AUC** |
| Protonotarios[1] | 1 of male sex, repolarisation abnormalities, LV RWMA | 85.7 | 9.0 | 24.8 | 64.3 | 0.59 (0.18-1.91) | 0.53 (0.41-0.64) |
| Protonotarios[1] | 2 of male sex, repolarisation abnormalities, LV RWMA | 64.7 | 58.3 | 35.5 | 82.4 | 2.57 (1.14-5.78) | 0.62 (0.51-0.73) |
| Protonotarios[1] | 3 of male sex, repolarisation abnormalities, LV RWMA | 8.6 | 93.0 | 30.0 | 74.4 | 1.25 (0.30-5.11) | 0.51 (0.40-0.62) |
| Mast[2] | LVEF < 50% | 25.7 | 80.4 | 32.1 | 75.0 | 1.42 (0.57-3.53) | 0.53 (0.42-0.64) |
| Liao[5] | All 3 SAECG parameters positive | 59.1 | 66.2 | 35.1 | 83.0 | 2.83 (1.06-7.55) | 0.63 (0.049-0.76) |
| Bhonsale 2013[13] | Proband, Male and 3 or more TWI | 31.4 | 77.1 | 33.3 | 75.5 | 1.54 (0.65-3.64) | 0.54 (0.43-0.66) |
| Corrado 2010[22] | Syncope and NSVT | 7.4 | 90.8 | 20.0 | 76.0 | 0.79 (0.16-3.97) | 0.49 (0.37-0.62) |
| Piccini[23] | VT or VF | 57.1 | 78.0 | 47.6 | 83.9 | 4.73 (2.08-10.73) | 0.68 (0.57-0.78) |
| Wichter[26] | RV dysfunction | 60.0 | 58.8 | 34.4 | 80.3 | 2.14 (0.97-4.70) | 0.59 (0.48-0.70) |
| 2015 Task Force[30] | LV/RV dysfunction, syncope or NSVT | 100 | 20.2 | 30.4 | 100 | 1.44 (1.26-1.63) | 0.60 (0.50-0.71) |

Previously reported risk factors for arrhythmias, sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), odds ratio (OR) and area under the curve (AUC) calculated in our population. LV: left ventricular, RWMA: regional wall motion abnormalities, LVEF: left ventricular ejection fraction, SAECG: signal averaged ECG, TWI: T wave inversions, NSVT: nonsustained ventricular tachycardia (VT), VF: ventricular fibrillation, RV: right ventricular

## Figures

#### Figure A.1

*H:\Annina\ARVC Studien\Risk Score\Figure1ARVCriskscore.tif*

Flow-chart of patients included. ARVC: arrhythmogenic right ventricular cardiomyopathy, ICD: implantable cardioverter-defibrillator

#### Figure A.2

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Receiver operating characteristic curves for risk score based on filtered QRS duration ≥117 ms, NSVT ≥3 beats on 24h-ECG, absence of negative T wave in lead aVR

#### Figure A.3

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Clustered Bar Chart for risk score based on filtered QRS duration ≥117 ms, NSVT ≥3 beats on 24h-ECG, absence of negative T wave in lead aVR in patients with definite ARVC with and without VT/VF before initial investigation. Green bars: recurrent arrhythmia, blue bars: favourable outcome.

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