

Arrhythmia detection in atrioventricular, single-lead, floating atrial dipole ICD systems compared to conventional single- and dual-chamber defibrillators

Supplementary material

Table S1. Subgroup comparisons of baseline characteristics

| | VVI (N=93) | VDD (N=94) | p-value |
|-----------------------------------|---------------|---------------|---------|
| Dyslipidaemia (n, %) | 79 (85%) | 85 (90%) | 0.254 |
| LVEF (mean±SD) ¹ | 38.5±13.5 | 37.5±13.9 | 0.642 |
| QRS width (mean±SD) ² | 116.9±21.2 | 119±21.6 | 0.909 |
| Heart rate (mean±SD) ³ | 70.7±15.4 | 73.1±14.8 | 0.249 |
| Bradypacing indication (n, %) | 1 (1%) | 3 (3%) | 0.317 |
| Hemoglobin (mean±SD) ⁴ | 130.7±20.6 | 136±16.8 | 0.062 |
| Remote monitoring (n, %) | 6 (7%) | 48 (51%) | <0.001 |
| | VVI (N=93) | DDD (N=69) | p-value |
| Dyslipidaemia (n, %) | 79 (85%) | 48 (71%) | 0.027 |
| LVEF (mean±SD) ¹ | 38.5±13.5 | 47.5±16.3 | <0.001 |
| QRS width (mean±SD) ² | 116.9±21.2 | 136.9±29.2 | <0.001 |
| Heart rate (mean±SD) ³ | 70.7±15.4 | 66.9±18.6 | 0.117 |
| Bradypacing indication (n, %) | 1 (1%) | 36 (55%) | <0.001 |
| Hemoglobin (mean±SD) ⁴ | 130.7±20.6 | 126.2±20.7 | 0.237 |
| Remote monitoring (n, %) | 6 (7%) | 13 (19%) | 0.014 |
| | VDD (N=94) | DDD (N=69) | p-value |
| Dyslipidaemia (n, %) | 85 (90%) | 48 (71%) | 0.001 |
| LVEF (mean±SD) ¹ | 37.5±13.9 | 47.5±16.3 | 0.001 |
| QRS width (mean±SD) ² | 119±21.6 | 136.9±29.2 | 0.001 |
| Heart rate (mean±SD) ³ | 73.1±14.8 | 66.9±18.6 | 0.011 |
| Bradypacing indication (n, %) | 3 (3%) | 36 (55%) | <0.001 |
| Hemoglobin (mean±SD) ⁴ | 136±16.8 | 126.2±20.7 | 0.008 |
| Remote monitoring (n, %) | 48 (51%) | 13 (19%) | <0.001 |

¹ Non-normal distribution, independent samples Mann-Whitney U test.

² Non-normal distribution, independent samples Mann-Whitney U test.

³ Non-normal distribution, independent samples Mann-Whitney U test.

⁴ VVI vs. VDD: Non-normal distribution, independent samples Mann-Whitney U test, VVI vs. DDD: Normal distribution, independent samples t-test, VDD vs. DDD: Non-normal distribution, independent samples Mann-Whitney U test.

VVI: conventional single-chamber ICD; VDD: single-lead ICD device with a floating atrial dipole; DDD: conventional dual-chamber ICD; SD: standard deviation; LVEF: left ventricular ejection fraction

Table S2. Subgroup comparisons of baseline medical therapy

| | VVI (N=93) | VDD (N=94) | p-value |
|---|-----------------------|-----------------------|------------------|
| Beta-blockers (n, %) | 90 (97%) | 90 (96%) | 0.711 |
| Mineralocorticoid receptor antagonists (n, %) | 48 (52%) | 52 (55%) | 0.611 |
| Digitalis glycosides (n, %) | 13 (14%) | 3 (3%) | 0.008 |
| | VVI (N=93) | DDD (N=69) | p-value |
| Beta-blockers (n, %) | 90 (97%) | 53 (83%) | 0.003 |
| Mineralocorticoid receptor antagonists (n, %) | 48 (52%) | 17 (27%) | 0.002 |
| Digitalis glycosides (n, %) | 13 (14%) | 3 (5%) | 0.059 |
| | VDD (N=94) | DDD (N=69) | p-value |
| Beta-blockers (n, %) | 90 (96%) | 53 (83%) | 0.006 |
| Mineralocorticoid receptor antagonists (n, %) | 52 (55%) | 17 (27%) | <0.001 |
| Digitalis glycosides (n, %) | 3 (3%) | 3 (5%) | 0.629 |

Table S3. Multivariate analysis of time to first device detected atrial arrhythmia - VVI vs. VDD

| Risk factor | unadjusted HR (95% CI) | p-value | adjusted HR (95% CI) | p-value |
|--|-----------------------------------|----------------|---------------------------------|------------------|
| ICD type | 6.506 (2.176-19.446) | 0.001 | 7.087 (2.371-21.183) | <0.001 |
| Age | 1.004 (0.969-1.040) | 0.837 | | |
| Male | 0.540 (0.226-1.291) | 0.166 | | |
| Primary prophylaxis | 6.989 (0.940-51.970) | 0.058 | 9.746 (1.301-73.014) | 0.027 |
| Ischemic etiology | 1.561 (0.609-4.002) | 0.354 | | |
| Previously diagnosed atrial fibrillation | 1.916 (0.743-4.942) | 0.179 | | |
| Hypertension | 2.280 (0.303-17.126) | 0.423 | | |
| Dyslipidaemia | 4.127 (0.554-30.776) | 0.167 | | |
| Diabetes mellitus | 1.456 (0.609-3.478) | 0.398 | | |
| Stroke/TIA | 0.043 (0.000-28.860) | 0.343 | | |
| Bradypacing indication | 7.895 (0.994-62.697) | 0.051 | 18.471 (1.973-172.887) | 0.011 |
| LVEF | 0.981 (0.947-1.015) | 0.270 | | |
| QRS width | 1.009 (0.986-1.033) | 0.442 | | |
| Heart rate | 1.033 (1.001-1.066) | 0.042 | 1.038 (1.004-1.074) | 0.028 |
| Creatinine | 1.003 (0.996-1.009) | 0.473 | | |
| Hemoglobin | 1.003 (0.978-1.029) | 0.809 | | |
| Remote monitoring | 2.628 (1.133-6.093) | 0.024 | 0.907 (0.347-2.368) | 0.841 |
| Antiplatelet therapy | 1.013 (0.412-2.489) | 0.977 | | |
| Anticoagulation | 1.609 (0.686-3.770) | 0.274 | | |
| Beta-blockers | 0.682 (0.092-5.075) | 0.709 | | |
| ACEI/ARB/ARNI | 0.550 (0.186-1.627) | 0.280 | | |
| Diuretics | 1.564 (0.668-3.661) | 0.303 | | |
| Calcium channel blockers | 0.884 (0.299-2.616) | 0.824 | | |

| | | |
|--|-----------------------|-------|
| Mineralocorticoid receptor antagonists | 1.020 (0.441-2.358) | 0.963 |
| Statins | 1.057 (0.412-2.709) | 0.909 |
| Amiodarone | 1.285 (0.474-3.483) | 0.623 |
| Digitalis glycosides | 0.045 (0.000-116.944) | 0.440 |

HR: hazard ratio; CI: confidence interval; ICD: implantable cardioverter defibrillator; TIA: transient ischemic attack; ACEI: angiotensin-converting-enzyme inhibitor; ARB: angiotensin II receptor blocker; ARNI: angiotensin receptor-neprilysin inhibitor

Table S4. Multivariate analysis of time to first device detected atrial arrhythmia - VDD vs. DDD

| Risk factor | unadjusted HR (95% CI) | p-value | adjusted HR (95% CI) | p-value |
|--|---------------------------|------------------|-------------------------|--------------|
| ICD type | 2.011 (1.110-3.642) | 0.021 | 1.781 (0.737-4.301) | 0.200 |
| Age | 1.038 (1.012-1.066) | 0.004 | 0.992 (0.959-1.026) | 0.645 |
| Male | 0.731 (0.384-1.390) | 0.339 | | |
| Primary prophylaxis | 1.951 (0.941-4.044) | 0.072 | 1.001 (0.379-2.643) | 0.998 |
| Ischemic etiology | 1.522 (0.816-2.838) | 0.187 | | |
| Previously diagnosed atrial fibrillation | 3.822 (2.085-7.005) | <0.001 | 4.300 (1.687-10.959) | 0.002 |
| Hypertension | 3.185 (0.765-13.260) | 0.111 | | |
| Dyslipidaemia | 1.334 (0.617-2.881) | 0.464 | | |
| Diabetes mellitus | 1.344 (0.735-2.458) | 0.337 | | |
| Stroke/TIA | 0.451 (0.109-1.867) | 0.272 | | |
| Bradypacing indication | 2.195 (1.207-3.992) | 0.010 | 0.749 (0.216-2.601) | 0.649 |
| LVEF | 0.999 (0.981-1.018) | 0.950 | | |
| QRS width | 1.013 (0.999-1.026) | 0.065 | 0.998 (0.979-1.017) | 0.833 |
| Heart rate | 1.019 (0.998-1.041) | 0.075 | 1.008 (0.974-1.043) | 0.668 |
| Creatinine | 1.002 (0.997-1.007) | 0.470 | | |
| Hemoglobin | 0.995 (0.977-1.013) | 0.582 | | |
| Remote monitoring | 0.388 (0.200-0.751) | 0.005 | 0.323 (0.123-0.852) | 0.022 |
| Antiplatelet therapy | 1.139 (0.609-2.131) | 0.684 | | |
| Anticoagulation | 2.723 (1.506-4.924) | 0.001 | 0.746 (0.295-1.883) | 0.535 |
| Beta-blockers | 1.685 (0.520-5.456) | 0.384 | | |
| ACEI/ARB/ARNI | 1.043 (0.482-2.255) | 0.915 | | |
| Diuretics | 1.731 (0.953-3.147) | 0.072 | 4.105 (1.610-10.462) | 0.003 |
| Calcium channel blockers | 1.043 (0.527-2.066) | 0.903 | | |
| Mineralocorticoid receptor antagonists | 0.752 (0.403-1.405) | 0.371 | | |
| Statins | 1.245 (0.638-2.431) | 0.520 | | |
| Amiodarone | 1.901 (0.930-3.886) | 0.078 | 1.178 (0.403-3.447) | 0.765 |
| Digitalis glycosides | 3.043 (0.731-12.672) | 0.126 | | |

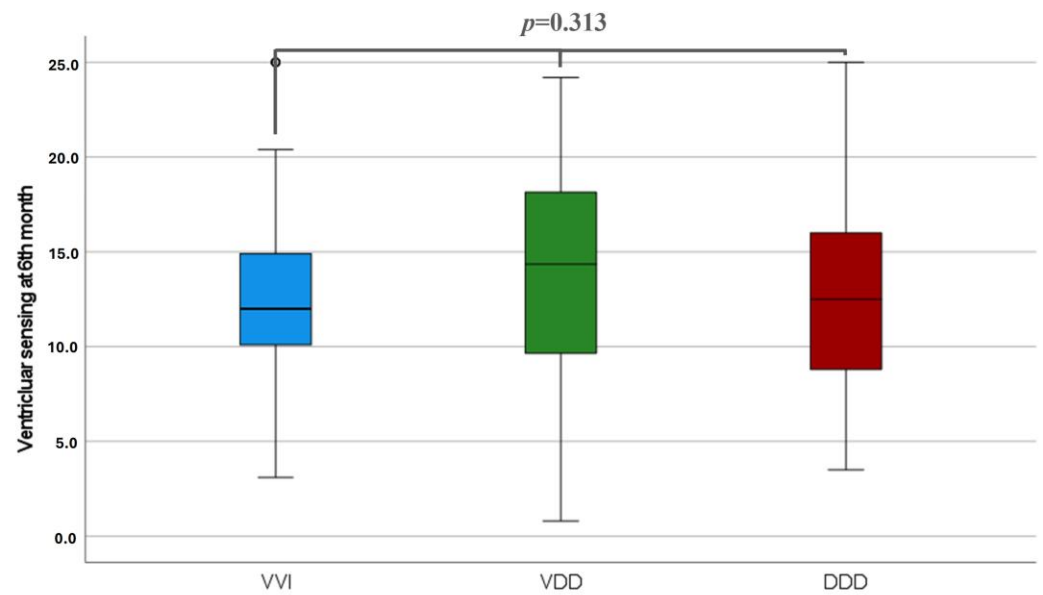


Figure S1 Ventricular sensing in VVI vs. VDD vs. DDD ICDs at 6th month

Table S5. Detailed distribution of device detected atrial arrhythmias

| | VVI (N=93) | VDD (N=94) | DDD (N=69) | p-value |
|--|---------------|---------------|---------------|---------|
| Total number of first device detected atrial arrhythmias | 4 | 18 | 28 | |
| Paroxysmal atrial fibrillation (n, %) | 4 (100%) | 15 (83%) | 23 (82%) | |
| Persistent atrial fibrillation (n, %) | 0 (0%) | 2 (11%) | 1 (4%) | 0.609 |
| Regular atrial arrhythmias (n, %) | 0 (0%) | 1 (6%) | 4 (14%) | |

Table S6. Subgroup analysis of complication rates

| | VVI (N=93) | VDD (N=94) | p-value |
|----------------------|---------------|---------------|---------|
| Complications (n, %) | 7 (8%) | 12 (13%) | 0.236 |
| | VVI (N=93) | DDD (N=69) | p-value |
| Complications (n, %) | 7 (8%) | 14 (20%) | 0.017 |
| | VDD (N=94) | DDD (N=69) | p-value |
| Complications (n, %) | 12 (13%) | 14 (20%) | 0.195 |

Table S7. Distribution of complications between all groups

| | VVI (N=93) | VDD (N=94) | DDD (N=69) |
|---------------------------------|-----------------------|-----------------------|-----------------------|
| Superficial infection (n,%) | 2 (2%) | 5 (5%) | 3 (4%) |
| Pocket infection (n,%) | 1 (1%) | 0 (0%) | 2 (3%) |
| Systemic infection (n,%) | 2 (2%) | 0 (0%) | 1 (1%) |
| Hematoma (n,%) | 1 (1%) | 2 (2%) | 2 (3%) |
| Deep venous thrombosis (n,%) | 0 (0%) | 0 (0%) | 1 (1%) |
| Lead-related complication (n,%) | 1 (1%) | 5 (5%) | 5 (7%) |

Table S8. Multivariate analysis of time to first appropriate therapy - VVI vs. VDD

| Risk factor | unadjusted HR (95% CI) | p-value | adjusted HR (95% CI) | p-value |
|--|-----------------------------------|----------------|---------------------------------|----------------|
| ICD type | 0.874 (0.574-1.332) | 0.532 | 0.983 (0.641-1.508) | 0.937 |
| Age | 1.023 (1.004-1.043) | 0.019 | 1.019 (0.999-1.039) | 0.057 |
| Male | 1.127 (0.691-1.838) | 0.631 | | |
| Primary prophylaxis | 2.760 (1.533-4.972) | 0.001 | 2.204 (1.192-4.074) | 0.012 |
| Ischemic etiology | 0.893 (0.586-1.359) | 0.597 | | |
| Previously diagnosed atrial fibrillation | 0.920 (0.577-1.469) | 0.728 | | |
| Hypertension | 1.050 (0.483-2.281) | 0.902 | | |
| Dyslipidaemia | 1.275 (0.678-2.398) | 0.450 | | |
| Diabetes mellitus | 0.812 (0.512-1.287) | 0.375 | | |
| Stroke/TIA | 0.942 (0.455-1.950) | 0.873 | | |
| Bradypacing indication | 0.634 (0.088-4.562) | 0.651 | | |
| LVEF | 1.000 (0.985-1.014) | 0.949 | | |
| QRS width | 1.003 (0.991-1.014) | 0.655 | | |
| Heart rate | 0.993 (0.978-1.009) | 0.376 | | |
| Creatinine | 1.003 (0.998-1.008) | 0.194 | | |
| Hemoglobin | 1.000 (0.987-1.014) | 0.950 | | |
| Remote monitoring | 0.895 (0.565-1.419) | 0.637 | | |
| Antiplatelet therapy | 0.882 (0.577-1.349) | 0.563 | | |
| Anticoagulation | 0.827 (0.540-1.266) | 0.381 | | |
| Beta-blockers | 0.255 (0.103-0.636) | 0.003 | 0.256 (0.101-0.648) | 0.004 |
| ACEI/ARB/ARNI | 1.140 (0.572-2.271) | 0.710 | | |
| Diuretics | 1.172 (0.775-1.772) | 0.452 | | |
| Calcium channel blockers | 1.736 (1.088-2.770) | 0.021 | 1.352 (0.837-2.184) | 0.218 |
| Mineralocorticoid receptor antagonists | 0.975 (0.646-1.473) | 0.906 | | |
| Statins | 0.719 (0.464-1.114) | 0.139 | | |
| Amiodarone | 1.691 (1.051-2.721) | 0.030 | 1.521 (0.926-2.498) | 0.098 |
| Digitalis glycosides | 0.618 (0.270-1.416) | 0.255 | | |

Table S9. Multivariate analysis of time to first appropriate therapy - VDD vs. DDD

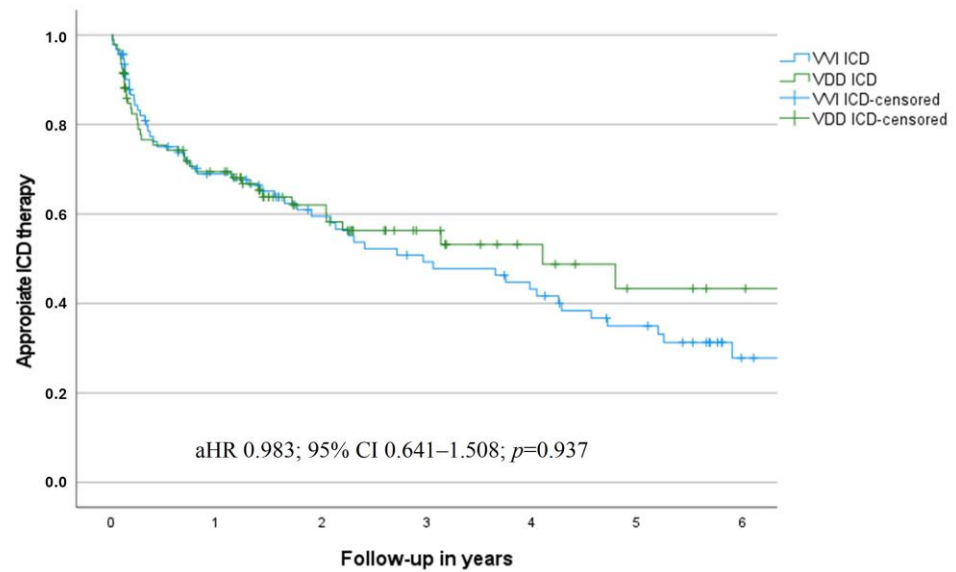
| Risk factor | unadjusted HR (95% CI) | p-value | adjusted HR (95% CI) | p-value |
|---|-----------------------------------|------------------|---------------------------------|----------------|
| ICD type | 0.611 (0.359-1.040) | 0.069 | 0.651 (0.371-1.142) | 0.135 |
| Age | 1.012 (0.991-1.033) | 0.240 | | |
| Male | 1.088 (0.597-1.983) | 0.784 | | |
| Primary prophylaxis | 3.488 (1.714-7.097) | <0.001 | 3.341 (1.564-7.138) | 0.002 |
| Ischemic etiology | 1.330 (0.782-2.262) | 0.293 | | |
| Previously diagnosed atrial fibrillation | 0.954 (0.548-1.663) | 0.869 | | |
| Hypertension | 1.353 (0.489-3.745) | 0.560 | | |
| Dyslipidaemia | 1.645 (0.779-3.473) | 0.192 | | |
| Diabetes mellitus | 0.785 (0.446-1.382) | 0.401 | | |
| Stroke/TIA | 0.641 (0.232-1.771) | 0.391 | | |
| Bradypacing indication | 0.523 (0.265-1.035) | 0.063 | 0.721 (0.315-1.650) | 0.439 |
| LVEF | 0.992 (0.976-1.008) | 0.336 | | |
| QRS width | 0.999 (0.987-1.011) | 0.883 | | |
| Heart rate | 0.993 (0.974-1.011) | 0.438 | | |
| Creatinine | 1.002 (0.996-1.008) | 0.560 | | |
| Hemoglobin | 1.002 (0.986-1.018) | 0.822 | | |
| Remote monitoring | 1.420 (0.850-2.371) | 0.181 | | |
| Antiplatelet therapy | 0.898 (0.529-1.526) | 0.691 | | |
| Anticoagulation | 1.269 (0.752-2.141) | 0.371 | | |
| Beta-blockers | 1.301 (0.470-3.603) | 0.612 | | |
| ACEI/ARB/ARNI | 0.971 (0.476-1.983) | 0.936 | | |
| Diuretics | 1.146 (0.681-1.927) | 0.608 | | |
| Calcium channel blockers | 1.483 (0.840-2.617) | 0.174 | | |
| Mineralocorticoid receptor antagonists | 0.962 (0.562-1.647) | 0.888 | | |
| Statins | 0.912 (0.521-1.594) | 0.745 | | |
| Amiodarone | 2.480 (1.374-4.479) | 0.003 | 1.949 (1.073-3.540) | 0.028 |
| Digitalis glycosides | 0.046 (0.000-11.224) | 0.272 | | |

Table S10. Multivariate analysis of time to first inappropriate therapy - VVI vs. VDD

| Risk factor | unadjusted HR (95% CI) | p-value | adjusted HR (95% CI) | p-value |
|---|-----------------------------------|----------------|---------------------------------|----------------|
| ICD type | 0.782 (0.338-1.811) | 0.566 | 0.742 (0.313-1.757) | 0.497 |
| Age | 0.994 (0.960-1.029) | 0.729 | | |
| Male | 0.613 (0.262-1.434) | 0.259 | | |
| Primary prophylaxis | 0.938 (0.372-2.365) | 0.892 | | |
| Ischemic etiology | 0.527 (0.236-1.178) | 0.119 | | |
| Previously diagnosed atrial fibrillation | 1.111 (0.459-2.689) | 0.816 | | |
| Hypertension | 0.588 (0.173-1.996) | 0.395 | | |
| Dyslipidaemia | 0.332 (0.142-0.777) | 0.011 | 0.533 (0.213-1.332) | 0.178 |
| Diabetes mellitus | 0.592 (0.221-1.586) | 0.297 | | |
| Stroke/TIA | 0.043 (0.000-24.731) | 0.332 | | |
| Bradypacing indication | 0.048 (0.000- 132902.528) | 0.689 | | |
| LVEF | 0.984 (0.952-1.016) | 0.322 | | |
| QRS width | 1.006 (0.982-1.031) | 0.637 | | |
| Heart rate | 1.007 (0.980-1.034) | 0.628 | | |
| Creatinine | 1.002 (0.996-1.009) | 0.482 | | |
| Hemoglobin | 1.011 (0.984-1.039) | 0.430 | | |
| Remote monitoring | 0.717 (0.284-1.808) | 0.480 | | |
| Antiplatelet therapy | 0.365 (0.161-0.824) | 0.015 | 0.327 (0.142-0.753) | 0.009 |
| Anticoagulation | 1.519 (0.677-3.410) | 0.311 | | |
| Beta-blockers | 0.240 (0.056-1.026) | 0.054 | 0.167 (0.037-0.742) | 0.019 |
| ACEI/ARB/ARNI | 0.406 (0.151-1.088) | 0.073 | 0.667 (0.214-2.078) | 0.485 |
| Diuretics | 1.419 (0.630-3.197) | 0.398 | | |
| Calcium channel blockers | 0.525 (0.156-1.761) | 0.297 | | |
| Mineralocorticoid receptor antagonists | 1.131 (0.506-2.530) | 0.764 | | |
| Statins | 0.464 (0.207-1.036) | 0.061 | 1.158 (0.339-3.955) | 0.815 |
| Amiodarone | 0.938 (0.321-2.747) | 0.908 | | |
| Digitalis glycosides | 1.602 (0.477-5.377) | 0.446 | | |

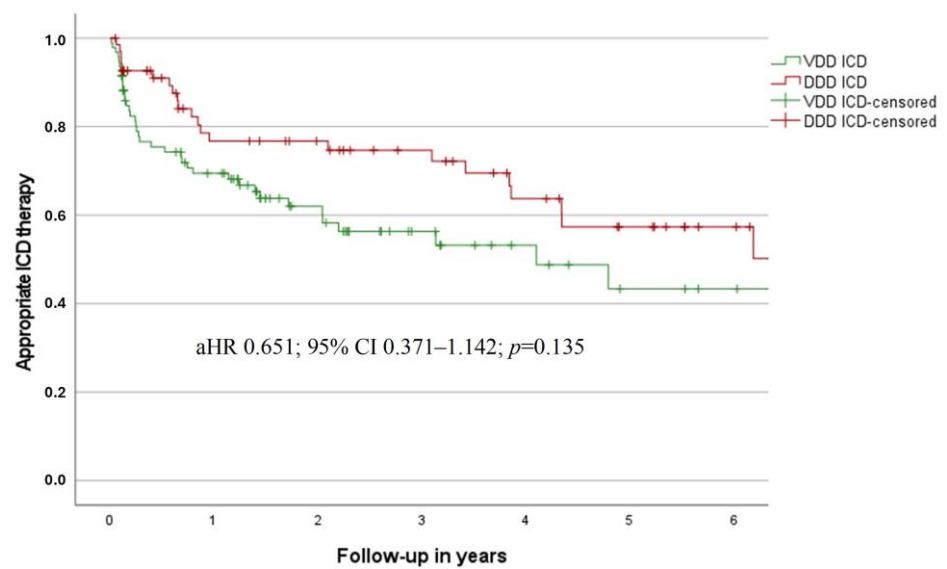
Table S11. Multivariate analysis of time to first inappropriate therapy - VDD vs. DDD

| Risk factor | unadjusted HR (95% CI) | p-value | adjusted HR (95% CI) | p-value |
|---|-----------------------------------|----------------|---------------------------------|----------------|
| ICD type | 0.710 (0.249-2.024) | 0.522 | 0.618 (0.203-1.878) | 0.396 |
| Age | 0.986 (0.955-1.019) | 0.399 | | |
| Male | 1.396 (0.397-4.907) | 0.603 | | |
| Primary prophylaxis | 1.927 (0.548-6.774) | 0.307 | | |
| Ischemic etiology | 0.483 (0.179-1.306) | 0.152 | | |
| Previously diagnosed atrial fibrillation | 1.703 (0.599-4.839) | 0.318 | | |
| Hypertension | 1.753 (0.229-13.404) | 0.589 | | |
| Dyslipidaemia | 1.090 (0.309-3.847) | 0.893 | | |
| Diabetes mellitus | 0.624 (0.199-1.957) | 0.418 | | |
| Stroke/TIA | 0.042 (0.000-58.362) | 0.390 | | |
| Bradypacing indication | 0.383 (0.086-1.705) | 0.208 | | |
| LVEF | 0.988 (0.956-1.022) | 0.491 | | |
| QRS width | 1.000 (0.974-1.025) | 0.971 | | |
| Heart rate | 0.974 (0.936-1.014) | 0.197 | | |
| Creatinine | 1.002 (0.994-1.011) | 0.558 | | |
| Hemoglobin | 1.030 (0.988-1.074) | 0.158 | | |
| Remote monitoring | 0.783 (0.284-2.159) | 0.636 | | |
| Antiplatelet therapy | 0.484 (0.175-1.340) | 0.162 | | |
| Anticoagulation | 2.314 (0.796-6.723) | 0.123 | | |
| Beta-blockers | 0.751 (0.168-3.366) | 0.708 | | |
| ACEI/ARB/ARNI | 0.843 (0.237-3.001) | 0.792 | | |
| Diuretics | 1.754 (0.623-4.937) | 0.287 | | |
| Calcium channel blockers | 1.018 (0.323-3.212) | 0.976 | | |
| Mineralocorticoid receptor antagonists | 2.211 (0.761-6.424) | 0.145 | | |
| Statins | 0.606 (0.215-1.708) | 0.344 | | |
| Amiodarone | 1.457 (0.404-5.249) | 0.565 | | |
| Digitalis glycosides | 5.246 (1.169-23.545) | 0.030 | 5.246 (1.169-23.545) | 0.030 |



| Patients at risk | 1 year | 2 years | 3 years | 4 years | 5 years | 6 years | 7 years |
|------------------|--------|---------|---------|---------|---------|---------|---------|
| VVI | 93 | 55 | 41 | 33 | 28 | 20 | 7 |
| VDD | 94 | 56 | 33 | 19 | 12 | 7 | 5 |

Figure S2A Time to first appropriate therapy – VVI vs. VDD



| Patients at risk | 1 year | 2 years | 3 years | 4 years | 5 years | 6 years | 7 years |
|------------------|--------|---------|---------|---------|---------|---------|---------|
| VDD | 94 | 56 | 33 | 19 | 12 | 7 | 5 |
| DDD | 69 | 42 | 37 | 30 | 22 | 16 | 10 |

Figure S2B Time to first appropriate therapy – VDD vs. DDD

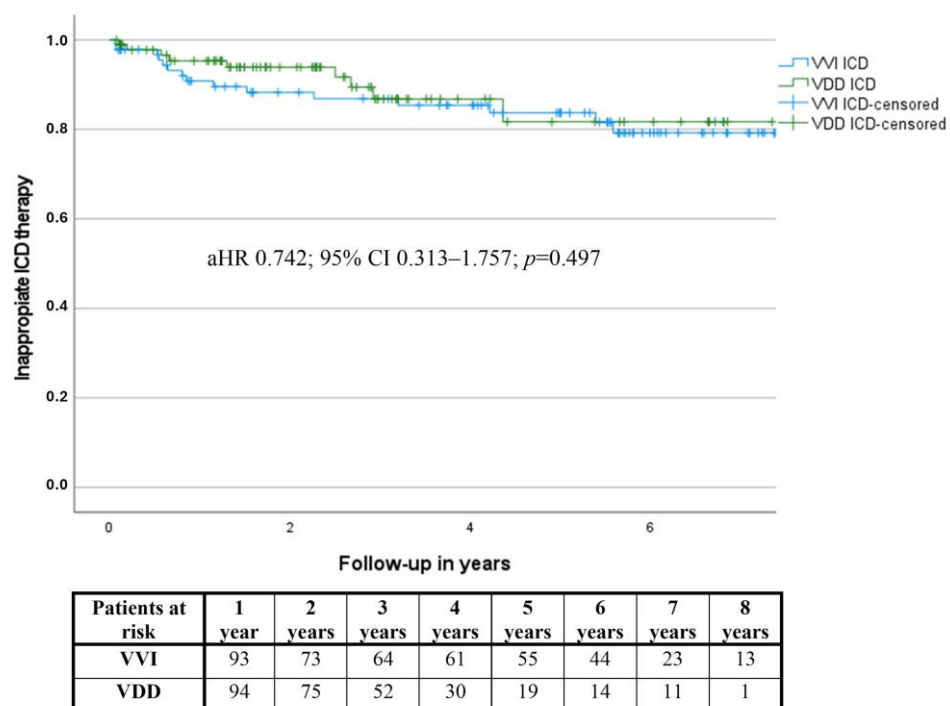


Figure S2C Time to first inappropriate therapy – VVI vs. VDD

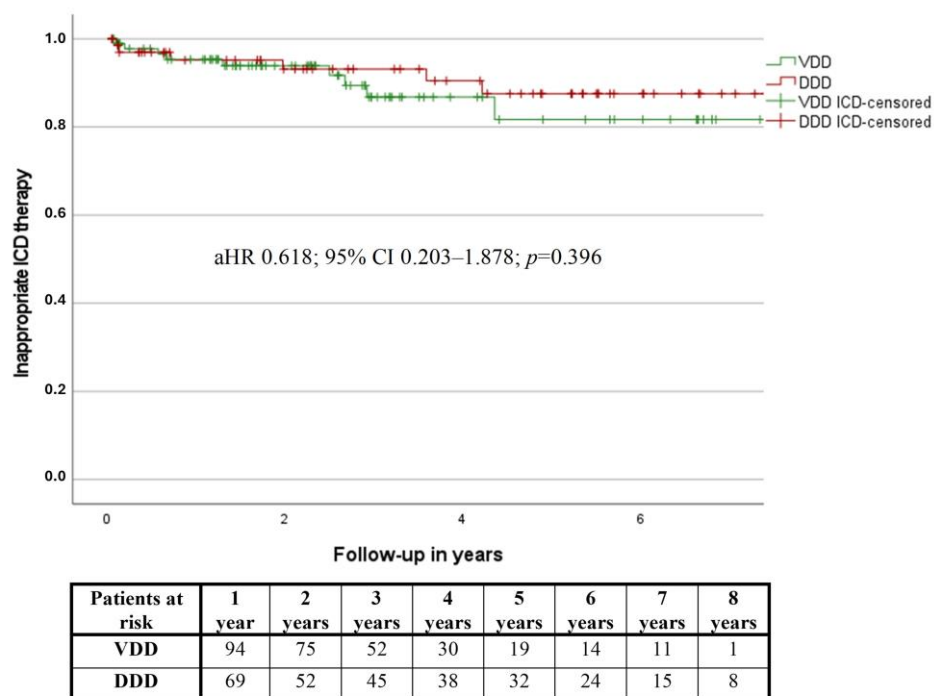


Figure S2D Time to first inappropriate therapy – VDD vs. DDD

Table S12. Multivariate analysis of time to first hospitalization due to arrhythmic cause - VVI vs. VDD

| Risk factor | unadjusted HR (95% CI) | p-value | adjusted HR (95% CI) | p-value |
|---|-----------------------------------|----------------|---------------------------------|----------------|
| ICD type | 1.463 (0.899-2.379) | 0.125 | 1.706 (1.043-2.792) | 0.033 |
| Age | 1.009 (0.988-1.031) | 0.390 | | |
| Male | 0.733 (0.430-1.248) | 0.253 | | |
| Primary prophylaxis | 2.804 (1.339-5.869) | 0.006 | 3.041 (1.443-6.411) | 0.003 |
| Ischemic etiology | 0.770 (0.475-1.248) | 0.289 | | |
| Previously diagnosed atrial fibrillation | 0.981 (0.576-1.671) | 0.943 | | |
| Hypertension | 0.939 (0.376-2.348) | 0.893 | | |
| Dyslipidaemia | 1.410 (0.672-2.957) | 0.363 | | |
| Diabetes mellitus | 1.380 (0.840-2.267) | 0.203 | | |
| Stroke/TIA | 0.881 (0.353-2.198) | 0.786 | | |
| Bradypacing indication | 1.258 (0.174-9.096) | 0.820 | | |
| LVEF | 0.995 (0.977-1.013) | 0.555 | | |
| QRS width | 0.995 (0.981-1.009) | 0.491 | | |
| Heart rate | 0.991 (0.973-1.009) | 0.328 | | |
| Creatinine | 1.004 (0.999-1.008) | 0.104 | | |
| Hemoglobin | 0.996 (0.982-1.011) | 0.620 | | |
| Remote monitoring | 1.394 (0.848-2.289) | 0.190 | | |
| Antiplatelet therapy | 1.054 (0.639-1.737) | 0.838 | | |
| Anticoagulation | 0.760 (0.459-1.260) | 0.288 | | |
| Beta-blockers | 0.806 (0.197-3.300) | 0.764 | | |
| ACEI/ARB/ARNI | 0.415 (0.226-0.761) | 0.004 | 0.404 (0.219-0.745) | 0.004 |
| Diuretics | 0.939 (0.581-1.518) | 0.797 | | |
| Calcium channel blockers | 1.555 (0.905-2.672) | 0.110 | | |
| Mineralocorticoid receptor antagonists | 0.803 (0.495-1.302) | 0.374 | | |
| Statins | 0.867 (0.520-1.444) | 0.583 | | |
| Amiodarone | 1.618 (0.942-2.778) | 0.081 | 1.277 (0.734-2.220) | 0.387 |
| Digitalis glycosides | 0.619 (0.225-1.703) | 0.353 | | |

Table S13. Multivariate analysis of time to first hospitalization due to arrhythmic cause - VDD vs. DDD

| Risk factor | unadjusted HR (95% CI) | p-value | adjusted HR (95% CI) | p-value |
|---|-----------------------------------|----------------|---------------------------------|----------------|
| ICD type | 0.638 (0.366-1.113) | 0.114 | 0.700 (0.365-1.341) | 0.282 |
| Age | 1.009 (0.987-1.030) | 0.429 | | |
| Male | 0.960 (0.523-1.761) | 0.895 | | |
| Primary prophylaxis | 1.523 (0.830-2.796) | 0.175 | | |
| Ischemic etiology | 0.936 (0.548-1.601) | 0.810 | | |
| Previously diagnosed atrial fibrillation | 1.106 (0.628-1.949) | 0.727 | | |
| Hypertension | 1.694 (0.527-5.439) | 0.376 | | |
| Dyslipidaemia | 1.117 (0.561-2.221) | 0.753 | | |
| Diabetes mellitus | 1.221 (0.709-2.103) | 0.472 | | |
| Stroke/TIA | 0.643 (0.231-1.785) | 0.396 | | |
| Bradypacing indication | 0.647 (0.332-1.261) | 0.201 | | |
| LVEF | 0.986 (0.969-1.004) | 0.117 | | |
| QRS width | 1.002 (0.990-1.014) | 0.786 | | |
| Heart rate | 0.983 (0.962-1.003) | 0.101 | | |
| Creatinine | 1.005 (1.000-1.009) | 0.041 | 1.005 (1.000-1.009) | 0.049 |
| Hemoglobin | 1.005 (0.988-1.022) | 0.594 | | |
| Remote monitoring | 1.466 (0.862-2.492) | 0.158 | | |
| Antiplatelet therapy | 1.012 (0.586-1.746) | 0.967 | | |
| Anticoagulation | 1.118 (0.651-1.920) | 0.686 | | |
| Beta-blockers | 1.464 (0.525-4.086) | 0.466 | | |
| ACEI/ARB/ARNI | 0.764 (0.384-1.519) | 0.442 | | |
| Diuretics | 1.199 (0.706-2.037) | 0.501 | | |
| Calcium channel blockers | 1.748 (1.001-3.051) | 0.050 | 1.412 (0.770-2.589) | 0.265 |
| Mineralocorticoid receptor antagonists | 0.710 (0.398-1.265) | 0.245 | | |
| Statins | 0.788 (0.451-1.379) | 0.404 | | |
| Amiodarone | 2.744 (1.513-4.976) | 0.001 | 2.761 (1.461-5.218) | 0.002 |
| Digitalis glycosides | 0.885 (0.215-3.640) | 0.865 | | |

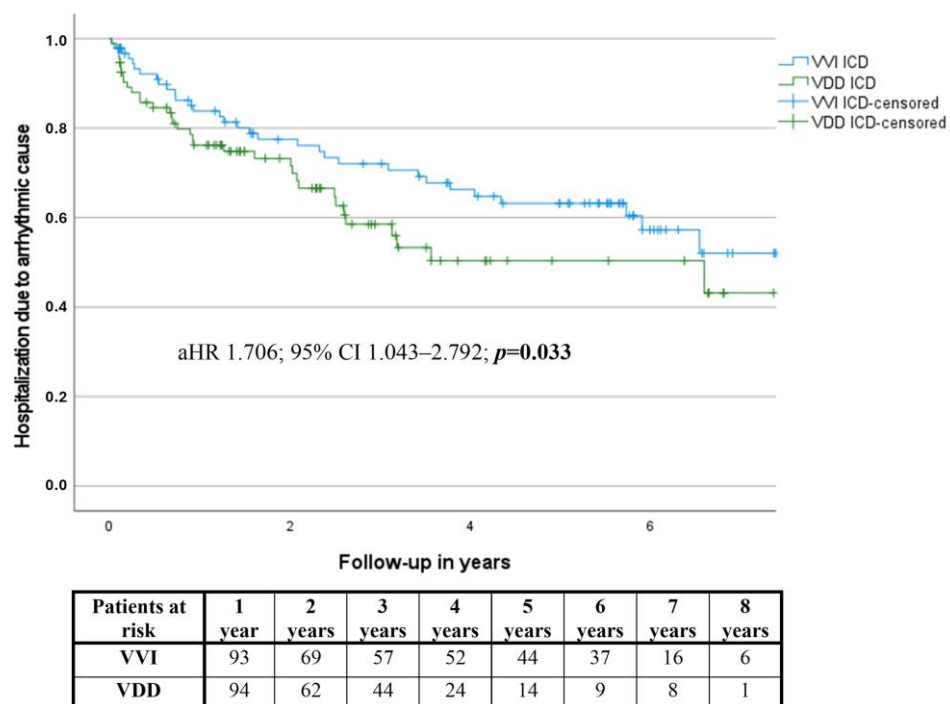


Figure S3A Time to first hospitalization due to arrhythmic cause – VVI vs. VDD

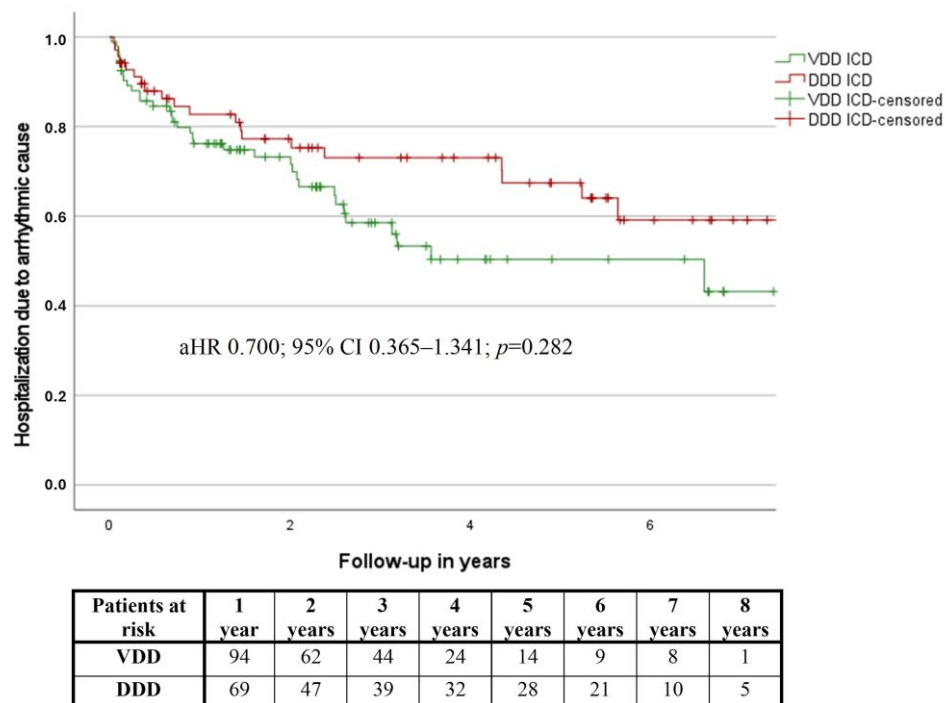


Figure S3B Time to first hospitalization due to arrhythmic cause – VDD vs. DDD

Table S14. Arrhythmia-related hospitalization events in the different groups

| | VVI (N=93) | VDD (N=94) | DDD (N=69) |
|--|---------------|---------------|---------------|
| Total number of first arrhythmia-related hospitalization events | 32 | 35 | 21 |
| <i>Admission due to ventricular tachycardia or electric storm (n, %)</i> | 27 (84%) | 23 (66%) | 10 (48%) |
| <i>Admission due to management of supraventricular tachycardia (including elective admission due to ECV or catheter ablation) (n, %)</i> | 3 (10%) | 8 (23%) | 5 (24%) |
| <i>Admission due to other causes (electrode malfunction, BIV-upgrade, syncope, etc.)</i> | 2 (6%) | 4 (11%) | 6 (28%) |

Table S15. Multivariate analysis of time to first hospitalization due to heart failure - VVI vs. VDD

| Risk factor | unadjusted HR (95% CI) | p-value | adjusted HR (95% CI) | p-value |
|--|---------------------------|--------------|-------------------------|------------------|
| ICD type | 0.949 (0.449-2.006) | 0.891 | 1.628 (0.619-4.279) | 0.323 |
| Age | 0.989 (0.959-1.020) | 0.477 | | |
| Male | 0.670 (0.305-1.474) | 0.320 | | |
| Primary prophylaxis | 0.330 (0.159-0.685) | 0.003 | 0.399 (0.136-1.170) | 0.094 |
| Ischemic etiology | 0.809 (0.389-1.681) | 0.570 | | |
| Previously diagnosed atrial fibrillation | 2.329 (1.114-4.867) | 0.025 | 2.160 (0.670-6.967) | 0.197 |
| Hypertension | 0.660 (0.198-2.197) | 0.499 | | |
| Dyslipidaemia | 1.584 (0.478-5.252) | 0.452 | | |
| Diabetes mellitus | 1.712 (0.816-3.590) | 0.155 | | |
| Stroke/TIA | 2.544 (0.959-6.745) | 0.061 | 1.980 (0.628-6.240) | 0.243 |
| Bradypacing indication | 0.048 (0.000-52297.115) | 0.669 | | |
| LVEF | 0.957 (0.925-0.990) | 0.011 | 1.002 (0.961-1.045) | 0.917 |
| QRS width | 1.005 (0.985-1.025) | 0.645 | | |
| Heart rate | 1.021 (1.000-1.042) | 0.046 | 1.023 (0.997-1.051) | 0.087 |
| Creatinine | 1.010 (1.003-1.017) | 0.005 | 1.012 (1.004-1.020) | 0.003 |
| Hemoglobin | 0.973 (0.954-0.993) | 0.009 | 0.958 (0.937-0.980) | <0.001 |
| Remote monitoring | 0.697 (0.297-1.635) | 0.407 | | |
| Antiplatelet therapy | 0.692 (0.333-1.439) | 0.324 | | |
| Anticoagulation | 1.875 (0.900-3.908) | 0.093 | 0.649 (0.239-1.764) | 0.397 |
| Beta-blockers | 21.124 (0.002-267352.000) | 0.527 | | |
| ACEI/ARB/ARNI | 0.501 (0.191-1.314) | 0.160 | | |
| Diuretics | 2.801 (1.237-6.339) | 0.013 | 1.378 (0.460-4.130) | 0.567 |
| Calcium channel blockers | 0.414 (0.125-1.368) | 0.414 | | |
| Mineralocorticoid receptor antagonists | 3.849 (1.561-9.489) | 0.003 | 2.827 (0.934-8.560) | 0.066 |
| Statins | 0.566 (0.270-1.186) | 0.132 | | |

| | | | | |
|----------------------|----------------------|--------|----------------------|-------|
| Amiodarone | 0.719 (0.250-2.067) | 0.719 | | |
| Digitalis glycosides | 4.770 (2.097-10.848) | <0.001 | 3.521 (1.224-10.132) | 0.020 |

Table S16. Multivariate analysis of time to first hospitalization due to heart failure - VDD vs. DDD

| Risk factor | unadjusted HR (95% CI) | p-value | adjusted HR (95% CI) | p-value |
|---|------------------------------|--------------|-------------------------|--------------|
| ICD type | 0.586 (0.219-1.570) | 0.287 | 0.949 (0.301-2.991) | 0.928 |
| Age | 0.987 (0.957-1.019) | 0.436 | | |
| Male | 0.633 (0.237-1.689) | 0.362 | | |
| Primary prophylaxis | 0.379 (0.150-0.962) | 0.041 | 0.413 (0.151-1.126) | 0.084 |
| Ischemic etiology | 0.870 (0.343-2.206) | 0.769 | | |
| Previously diagnosed atrial fibrillation | 1.556 (0.596-4.060) | 0.366 | | |
| Hypertension | 0.757 (0.172-3.326) | 0.712 | | |
| Dyslipidaemia | 0.858 (0.280-2.627) | 0.789 | | |
| Diabetes mellitus | 1.042 (0.391-2.781) | 0.934 | | |
| Stroke/TIA | 1.141 (0.262-4.971) | 0.860 | | |
| Bradypacing indication | 0.817 (0.268-2.487) | 0.722 | | |
| LVEF | 0.941 (0.903-0.980) | 0.003 | 0.957 (0.922-0.993) | 0.019 |
| QRS width | 0.999 (0.977-1.021) | 0.895 | | |
| Heart rate | 1.002 (0.972-1.033) | 0.887 | | |
| Creatinine | 1.010 (1.003-1.018) | 0.003 | 1.011 (1.003-1.018) | 0.005 |
| Hemoglobin | 0.984 (0.958-1.011) | 0.244 | | |
| Remote monitoring | 0.812 (0.314-2.101) | 0.668 | | |
| Antiplatelet therapy | 0.736 (0.290-1.867) | 0.519 | | |
| Anticoagulation | 1.010 (0.389-2.622) | 0.983 | | |
| Beta-blockers | 23.676 (0.024- 23075.647) | 0.367 | | |
| ACEI/ARB/ARNI | 0.635 (0.208-1.933) | 0.423 | | |
| Diuretics | 1.744 (0.676-4.501) | 0.250 | | |
| Calcium channel blockers | 0.364 (0.084-1.584) | 0.178 | | |
| Mineralocorticoid receptor antagonists | 1.901 (0.746-4.840) | 0.178 | | |
| Statins | 0.666 (0.258-1.719) | 0.401 | | |
| Amiodarone | 1.079 (0.310-3.762) | 0.904 | | |
| Digitalis glycosides | 1.572 (0.209-11.839) | 0.661 | | |

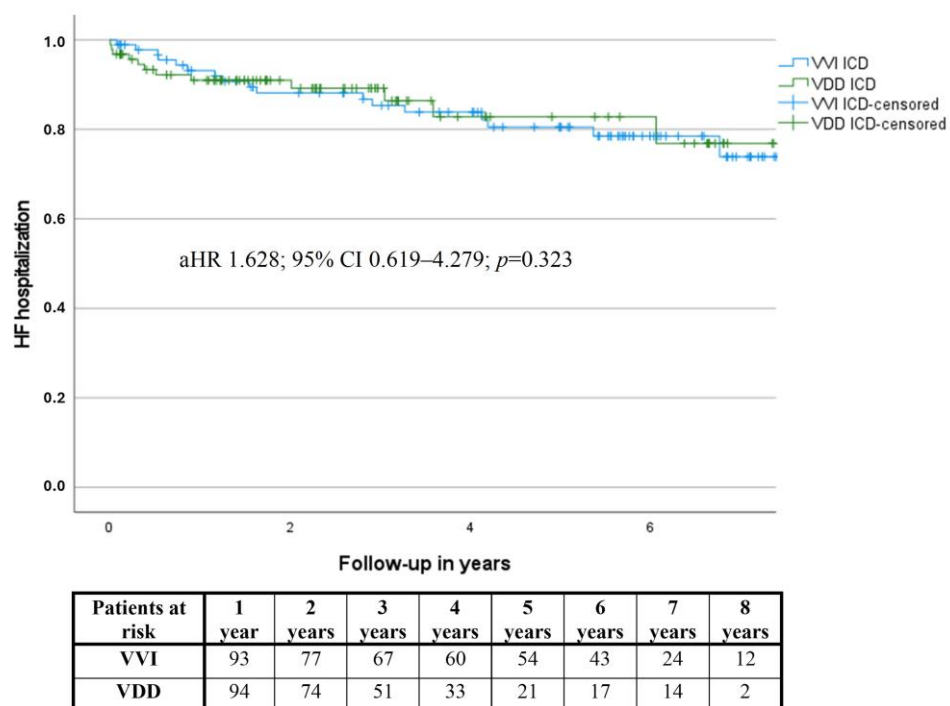


Figure S4A Time to first heart failure (HF) hospitalization – VVI vs. VDD

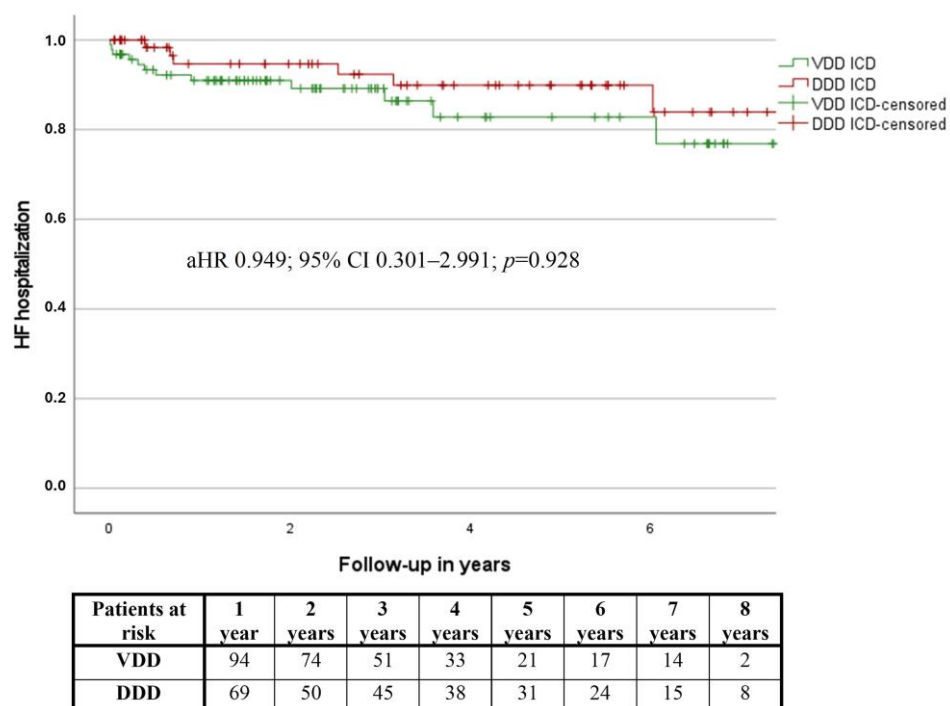


Figure S4B Time to first HF hospitalization – VDD vs. DDD

Table S17. Multivariate analysis of all-cause mortality - all groups

| Risk factor | unadjusted HR (95% CI) | p-value | adjusted HR (95% CI) | p-value |
|---|---------------------------|------------------|-------------------------|------------------|
| ICD type | 0.906 (0.696-1.179) | 0.463 | 0.960 (0.711-1.295) | 0.787 |
| Age | 1.060 (1.037-1.084) | <0.001 | 1.060 (1.031-1.089) | <0.001 |
| Male | 0.883 (0.546-1.426) | 0.611 | | |
| Primary prophylaxis | 0.849 (0.534-1.349) | 0.488 | | |
| Ischemic etiology | 1.297 (0.830-2.028) | 0.253 | | |
| Previously diagnosed atrial fibrillation | 1.958 (1.268-3.023) | 0.002 | 1.536 (0.936-2.521) | 0.089 |
| Hypertension | 4.969 (1.220-20.233) | 0.025 | 1.177 (0.272-5.094) | 0.828 |
| Dyslipidaemia | 1.645 (0.872-3.105) | 0.125 | | |
| Diabetes mellitus | 1.968 (1.277-3.033) | 0.002 | 2.215 (1.361-3.607) | 0.001 |
| Stroke/TIA | 1.409 (0.726-2.733) | 0.311 | | |
| Bradypacing indication | 1.035 (0.575-1.864) | 0.908 | | |
| LVEF | 0.975 (0.959-0.991) | 0.002 | 0.967 (0.948-0.986) | 0.001 |
| QRS width | 1.008 (0.997-1.018) | 0.146 | | |
| Heart rate | 1.017 (1.003-1.030) | 0.013 | 1.005 (0.992-1.018) | 0.460 |
| Creatinine | 1.002 (0.997-1.006) | 0.486 | | |
| Hemoglobin | 0.990 (0.977-1.004) | 0.163 | | |
| Remote monitoring | 0.248 (0.114-0.538) | <0.001 | 0.320 (0.145-0.709) | 0.005 |
| Antiplatelet therapy | 0.948 (0.603-1.489) | 0.816 | | |
| Anticoagulation | 1.840 (1.190-2.843) | 0.006 | 1.172 (0.637-2.158) | 0.609 |
| Beta-blockers | 0.935 (0.407-2.152) | 0.875 | | |
| ACEI/ARB/ARNI | 1.023 (0.554-1.889) | 0.942 | | |
| Diuretics | 1.740 (1.111-2.725) | 0.015 | 1.451 (0.855-2.463) | 0.167 |
| Calcium channel blockers | 0.888 (0.519-1.519) | 0.666 | | |
| Mineralocorticoid receptor antagonists | 1.347 (0.870-2.085) | 0.182 | | |
| Statins | 1.114 (0.686-1.808) | 0.662 | | |
| Amiodarone | 1.244 (0.729-2.125) | 0.423 | | |
| Digitalis glycosides | 1.021 (0.470-2.220) | 0.958 | | |

Table S18. Distribution of structural heart diseases between all groups

| | VVI (N=93) | VDD (N=94) | DDD (N=69) |
|--|---------------|---------------|---------------|
| Ischemic cardiomyopathy (n,%) | 56 (60%) | 58 (62%) | 39 (57%) |
| Dilatative cardiomyopathy (n,%) | 30 (32%) | 26 (28%) | 9 (13%) |
| Hypertrophic cardiomyopathy (n,%) | 0 (0%) | 4 (4%) | 9 (13%) |
| Arrhythmogenic right ventricular cardiomyopathy (n,%) | 0 (0%) | 0 (0%) | 1 (2%) |
| Long QT syndrome (n,%) | 1 (1%) | 0 (0%) | 4 (6%) |
| Ischemic cardiomyopathy (n,%) | 56 (60%) | 58 (62%) | 39 (57%) |
| Dilatative cardiomyopathy (n,%) | 30 (32%) | 26 (28%) | 9 (13%) |

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