**Table 2**. Literature review of the reported *DES* gene variants associated with Arrhythmogenic Cardiomyopathy and reported clinical and pathological abnormalities

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| --- | --- | --- | --- | --- | --- | --- | --- |
| **Publications** | **Variant** | **Cases (n)** | **ECG abnormalities** | **Ventricular involvement** | **Ventricular Arrhythmia** | **Heart failure** | **Histology and IHC** |
| ﻿van Tintelen et al.6 and van Spaendonck-Zwarts et al.42 | ﻿c.38C>T, p.Ser13Phe | 2 | Low-voltage, precordial TWI (n=1) | RV predominance (n=2) | None | Yes (n=2) | NA |
| Vernengo L et al.38 | c.340\_342del, p.Glu114del | 3 | RBBB, LAFB | RV or LV predominance | VE | Yes | Desmin aggregates in peripheral muscle biopsy |
| ﻿Klauke et al.39 | ﻿c.347A>G, p.Asn116Ser | 1 | Precordial TWI | RV predominance | None | Yes | Myocardial fibrofatty replacement |
| Lorenzon et al. | ﻿﻿c.721A>G, p.Lys241Glu\* | 1 | Precordial TWI | RV predominance | VT | None | NA |
| ﻿van Spaendonck-Zwarts et al.42 and Otten et al.29 | ﻿c.1024A>G, p.Asn342Asp | 3 | Precordial TWI (n=1), First degree AVB (n=2) | RV or LV predominance | VE and VT (n=1), SCD (n=1) | None | Desmin aggregates in peripheral muscle biopsy |
| Bermudez-Jimenez et al.25 | ﻿ ﻿c.1203G>C , p.Glu401Asp | 23 | Low voltage (n=12), Precordial TWI (n=14), Inferior TWI (n=11) | LV predominance (n=15) | VE (n=17), VT (n=6), SCD (n=4) | Yes (n=9) | Myocardial degeneration, adipose tissue infiltration. Reduced ID DSP and PG. No desmin aggregates. |
| Ripol-Vera et al.43 | ﻿p.R415E† | 1 | None | LV predominance | VT, SCD | None | NA |
| Oomen et al.28 and Otten et al.29 | c.1360C>T. p.Arg454Trp | 5 | Complete AVB (n=3) | LV predominance (n=3) | VE and VF (n=1) and VT (n=1) | Yes (n=3) | Myocardial fibrosis (n=2) and inflammation (n=1). Reduced ID DSP, PKP2, CX43 (n=2). Desmin aggregates (n=2). |

AVB=Atrio-ventricular block; CX43=Connexin 43; DSP=Desmoplakin; EW=Epsilon wave; ID=Intercalated disc; IHC=Immunohistochemistry; LAFB=Left anterior fascicular block; LV=Left ventricular; NA=Not available; PKP2=Plakophilin-2; PG=Plakoglobin; RBBB=Right bundle branch block; RV=Right ventricular; SCD=Sudden cardiac death; TWI=T-wave inversion; VE=ventricular ectopy; VF=Ventricular fibrillation; VT=Ventricular tachycardia. (\*) A plakophilin-2 gene variant was also present. (†) cDNA change not available and variant likely erroneously reported, as, assuming the presence of a single nucleotide substitution, Arginine cannot mutate to Glutamic acid based on the human genetic code.