Table 2. Characteristics of included studies – Diagnostiek cardiovasculaire complicaties bij volwassenen met myotone dystrofie type 1

Study	Participants	Data collection	Duration of follow-up	Outcome measures	Results	Risk of bias[1]
Cardona, 2019	52 patients with genetically confirmed MD1, also 12-lead ECG within 6 months of CMR was necessary 38% male 41 ± 14	Association between presence and extent of CMR-LGE myocardial fibrosis and conduction devices **meeting criteria for Permanent pacemaker PPM** **Cohort**	6 months	MIRS for severity and extent of MD1	Overall, 31 (60%) patients had a surface conduction abnormality and 22 (42%) demonstrated midwall myocardial fibrosis by CMR-LGE. After a median of 57 days from CMR exam, 15 patients (29%) underwent PPM implantation. Subjects with vs. without surface conduction abnormality had significantly longer disease length (15.5 vs. 7.8 years, p = 0.015) and higher disease severity on the MIRS scale (p = 0.041)	Prospective cohort study
Creta 2021 UK	154 patients with MD1 58.1% male Mean age: 43.7 ± 13.3	Diagnostic Electrophysiology studies, including 12-lead ECG	53 ± 27 months	Echocardiographic parameters as predictors of prolonged HHV interval	HV ≥70 ms was found on 58 EPSs (28.7%); 9 of 59 patients (15.2%) with PR <200 ms and QRS interval <110 ms on baseline ECG had an HV ≥70 ms on EPS. Among those with PR ≥200 ms and/or QRS interval ≥100 ms, only 33.9% had an HV ≥70 ms on EPS.	High (observational cohort study)
Denicourt, 2015 Canada	127 patients MD1 patients with small CTG expansions (≤200 CTG repeats)	ECG characteristics	11.7 ± 7.6 years	age at entry (relative risk RR, 1.05; (95% CI 1.01–1.08; p = 0.012) and muscular weakness (MIRS) at the entry (RR, 2.03; 95% CI 1.28–3.22; p = 0.003) were significant risk factors for	46 patients out of 82 (56.1%) had a normal ECG and 25 (30.5%) developed severe ECG abnormalities (p < 0.0001) including 6 of them who needed permanent pacemaker insertion. There were also 3 sudden deaths	High (observational cohort study)

				the development of severe ECG abnormality	during the follow-up period.	
Joosten 2023	293 patients undergoing routine cardiac evaluation in the Myotonic Dystrophy Expertise Centre, 235 genetically confirmed patients were included Age 46 ± 14	Holter monitoring abnormalities in which an average of 3 +1 Holter recordings per patient was performed.	64 ± 28 months	Conduction disturbances and arrythmias	Abnormal Holter results were discovered in 126 (54%) patients; mainly consisted of conduction disorders (70%) such as atrioventricular (AV) block. 74 (59%) patients had de novo Holter findings including second-degree AV block, atrial fibrillation/flutter and non-sustained ventricular tachycardia. In 39 out of 133 (29%) patients with normal ECGs upon yearly cardiac screening, abnormalities were found on Holter monitoring during follow-up.	
Joosten 2021	100 MD1-affected individuals who underwent EPS between 2007 and 2018 at one of both centres (Maastricht and Nijmegen).	Electrophysiological study For each individual, the following data were collected: reason for EPS, HV interval, resting ECG parameters prior to EPS, possible PM implantation reason and date, neurological assessment consisting of muscular impairment rating scale (MIRS) score, and MD1 DNA analysis results consisting of the CTG repeat size. Data were compared between patients with a normal HV interval (HV <70 ms) on EPS, and patients with a prolonged HV interval (HV >_70 ms) on EPS	Retrospective study of patients who underwent EPS between 2007 and 2018	ECG criteria predicting abnormal infrahissian conduction	The combination of a prolonged PR interval and widened QRS complex on ECG accurately predicts abnormal infrahissian conduction on EPS in patients with MD1. These ECG parameters could be used as a screening tool to determine the need for referral to a specialized multidisciplinary neuromuscular team with EPS capacity	High (retrospective multicentre cohort study)

Leali, 2023	34 MD1 patients referred from neurology unit to CMR laboratory 62% male Age: 45 ± 12 Compared to 68 age-matched and gender-matched controls Age: 48 ± 15	CMR findings and prognostic significance in MD1	Mean follow-up 3.7 years [range 2.0 to 5.0]	All available ECG, Holter recordings and device interrogations performed after CMR examination were searched for evidence of atrioventricular blocks (AVB), intraventricular conduction disturbances (IVCD), atrial fibrillation or flutter (AF/Fl), and repetitive (Lown class 4)40 ventricular ectopic beats (VEBs). Furthermore, all echocardiographic and CMR reports were checked for the presence of LVSD. Overall, AVB, IVCD, AF/Fl, evidence of Lown class 4 VEBs at Holter monitoring and LVSD were considered as separate surrogate end points. When available, CMR examinations after the first one were analyzed.	At CMR, biventricular and biatrial volumes were significantly smaller (all P<0.05), as was left ventricular mass (P<0.001); left ventricular ejection fraction (LVEF) and right ventricular ejection fraction (RVEF) were significantly lower (all P<0.01). Five (15%) patients had a LVEF less than 50% and four (12%) a RVEF less than 50%. Nine patients (26%) showed mid-wall late gadolinium enhancement (LGE; 5W2% of LVM), and 14 (41%) fatty infiltration.	High (case control study)
Petri, 2024	195 patients with genetically confirmed MD1 52% men Mean age at baseline: 42 years (Range 14-79)	Patient characteristics, 12-lead ECG, Holter and echocardiography from retrospective charts	Median follow-up 01.5 years	Overall prevalence increased from 42% to 66% end of follow-up, especially in men: 74% vs 44%. most common types of cardiac involvement were conduction abnormalities (48%), arrhythmias (35%), and left ventricular systolic dysfunction (21%). Only 17% of patients reported cardiac symptoms.	standard 12-lead ECG was the most sensitive diagnostic modality and documented cardiac involvement in 24% at baseline and in 49% at latest follow-up. However, addition of Holter monitoring and echocardiography significantly increased the diagnostic yield with 18 and 13% points at baseline and latest follow-up, respectively. Despite surveillance 35	High (retrospective cohort study)

					patients (18%) died during follow-up; seven due to SCD.	
Petri 2024 Myocardial fibrosis	30 unrelated MD1 patients: 18 (10 men, mean age 51 years) with and 12 (7 men, mean age 41 years) without abnormal findings on ECG, Holter and echocardiography	prevalence of myocardial fibrosis in patients with MD1 assessed by CMR, and the association between myocardial fibrosis and abnormal findings on ECG, Holter-monitoring and echocardiography	Cross-sectional	prevalence of myocardial fibrosis in patients with MD1 assessed by CMR, and the association between myocardial fibrosis and abnormal findings on ECG, Holter-monitoring and echocardiography	There was no association between the presence of myocardial fibrosis and the following ECG parameters: AVB grade I, LBBB and prolonged QTc	High: observational cohort study
Valaperta, 2016 Case-control study	59 MD patients and 22 healthy controls, an additional group of 62 control with similar cardiac defects MD cases Median age 47.1 (35.5–59.0) 63% men Healthy controls Median age: 40.2 (34.3–48.9) 58% men	Serum cardiac biomarkers and clinical parameters; complete clinical cardiac evaluation including physical examination, standard 12-lead ECG, 24- hour Holter monitoring and 2D-echocardiography		NT-pro BNP, hs-cTnT and CK levels were significantly increased in MD patients compared to healthy subjects (p=0.0008, p b 0.0001, p b 0.0001). Also, hs-cTnT levels were significantly higher in MD compared to control Group with cardiac defects (p=0.0003). Positive correlation was found between hs-cTnT and hs-cTnI in both MD patients and controls (p= 0.019, p = 0.002). Independently from the age, the risk of MD disease was positively related to an increase in hs-cTnT (p=0.03). On the contrary, the risk of MD was not related to hs-cTnI, but		High (observational cohort study)

				was evidenced a role of PR interval (p= 0.03) and CK (p= 0.08).		

Studies in pediatric MD1 patients

Brunet-Garcia 2022	67 **pediatric** MD1patients (clinically diagnosed and genetically confirmed); 56 c MD1 and 11 non-c MD1	Retrospective observational cohort of patients referred to center between December 2000 and November 2020	Median 8.0 [3.25–11.0] years	Clinical and cardiac evaluation with 12-lead ECG, transthoracic echo and Holter	43 (87.8%) presented ECG abnormalities; asymptomatic conduction disease (n = 23, 46.9%), of which 21 (42.9%) had 1st AVB. Mortality: 4 (7.1%) patients died at a median age of 8.5 [6.25- 16.75] years. 1 explained due to disease and 3 sudden, 1 patient had pacemaker implantation	High (retrospective observational cohort study)