Supplementary

Table S1 DMD mutations present in the patients

Mutation type	Number of patients
14 base pair deletion intron 49	1
Deletion exon 18	1
Deletion exon 18–23	1
Deletion exon 30–43	1
Deletion exon 45	4
Deletion exon 45–50	1
Deletion exon 45–52	1
Deletion exon 46–47	1
Deletion exon 46–49	1
Deletion exon 46–52	1
Deletion exon 46–53	1
Deletion exon 47–48	1
Deletion exon 47–52	1
Deletion exon 47–53	1
Deletion exon 47, 48, 50	1
Deletion exon 49–50	1
Deletion exon 49–55	1
Deletion exon 52	4
Deletion exon 53	1
Deletion exon 54	1
Deletion exon 56–61 (out of frame transcript)	1
Deletion exon 8–9	1
Deletion on chromosome 50	1
Duplication exon 3–7	1
Hemizygous deletion exon 8–44	1
Nonsense mutation exon 52	1
Nonsense mutation exon 69	1
Point mutation exon 24	1
Point mutation exon 55	1
Point mutation exon 6	1
Stop mutation exon 19 (relatively less aggressive phenotype)	1
Total	37

DMD, Duchenne muscular dystrophy.

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Appendix 1

Methods

Short protocol

The patient's EPRs (iSoft V1.6, IBA Health Group Company 2004, Bruxelles, Belgium) and critical care software [CareVue 2012, IntelliSpace Critical Care and Anaesthesia (ICCA) Release F.01.00, PhilipsRespironics, Amsterdam, Netherlands] were used to collect the following parameters:

(I) Demographics, including age (years), gender (male only), BMI (kg/m^2), alive (yes/no), cause of death.

(II) Disease-specific details, including age at diagnosis (years), DMD mutation type, follow up period (months). Age at diagnosis was recorded as the earliest mentioning of the diagnosis.

(III) Comorbidities, classified into "cardiorespiratory" and "other" (including date of diagnosis and time lapse between diagnosis of DMD and comorbidity).

(IV) Medication, including ACE-I (yes/no), beta-blockers (yes/no), Glucocorticoids (yes/no), antidiabetics (yes/no), mineralocorticoid receptor antagonist (yes/no), others (listed). The start date and period of treatment (months) were noted. Patients not taking medication at the time of data collection, even if they had previously, were excluded.

(V) Hospitalisations during follow-up period between 01/1993–06/2021, either classified as hospitalisation secondary to "cardiopulmonary" causes or 'other'; any documented hospitalisation on medical records was included. Cardiopulmonary hospitalisations were further subclassified as (i) respiratory (respiratory review, pneumonia, ventilation wean, HMV initiation, ventilatory failure, elective assessment of sleep-disordered breathing, atelectasis, aspiration, tracheostomy change, intubation, bronchitis, hypoxia, hypercapnia, airway obstruction and bronchoscopy post tracheostomy change), or (ii) cardiovascular [ICD and pacemaker insertion, pulseless electrical activity (PEA) arrest, echocardiography, cardiological review].

(VI) ABG analysis, including the most recent ABG [date, pO_2 (mmHg/kPa), pCO_2 (mmHg/kPa), bicarbonate (HCO_3^-, meq/L), base excess (BE), SpO_2 (%)]. It should be noted that ABGs were not routinely undertaken, they were carried out during acute hospital admissions.

(VII) Sleep study, including the most recent (date), nocturnal pulse oximetry with 4% ODI, heart rate variability (pulse rise index >6 bpm per hour), AHI, average SpO_2 (%), T<90.

(VIII) Ventilation (if applicable), including type (invasive/non-invasive), date of initiation, time elapsed between DMD diagnosis and initiation of ventilation, inspiratory positive airway pressure (IPAP, cmH_2O), expiratory positive airway pressure (EPAP, cmH_2O), pressure support (cmH_2O), back-up rate (BUR, breaths/min), inspiratory time (Ti, s), usage (hours/day).

(IX) Indicators of morbidity, including ambulatory (yes/no), length of time non-ambulatory (years), MIE support (yes/no), feeding assistance [nasogastric tube, PEG, yes/no], length of time on feeding assistance (years), spinal surgery (yes/no). The use of an MIE with/without NIV, the need of feeding assistance, or undergoing spinal surgery was each assigned a score of "0" (not present) or "1" (present) point. The scores were then totalled with a range of 0–3 points to generate a severity score for disease impact on morbidity; more severely affected patients had a higher score.

(X) Echocardiogram (ECHO), including dates of first and most recent ECHO, initial and most recent LVEF (%), proportionate change in the LVEF over time [(first measured LVEF – last LVEF)/first LVEF × 100], left ventricular (LV) systolic and diastolic diameter (cm), right ventricular (RV) systolic and diastolic area (cm^2), RV fractional area change (%), RV systolic and diastolic pressure (mmHg), acceleration time (ms), regional wall motion abnormalities (RWMA, yes/no), and examiners comments. If a range was reported for the LVEF, the mid-range point (half-way between min and max) was quoted.

(XI) ECG, including date of initial and most recent ECG, initial and most recent comments. Reports from cardiologists were used to group abnormalities into the following pathologies: arrhythmia (tachycardia, bradycardia, general arrhythmia), bundle branch block (left, right, incomplete), T-wave flattening/inversion, dominant R-wave V1/2, pathological Q-waves (lateral, high lateral, inferior, and anterior leads), axis deviation

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(left, right, extreme), and normal.

Rules were created to identify the date of diagnosis, the length of time elapsed between diagnosis and other conditions/severity measures/ventilation, and period established on each medication.

(I) For the initial date of the DMD diagnosis:
Take the first mention of DMD OR loss of ambulation OR osteoporosis/scoliosis OR ventilation OR DMD related hospitalisations [spinal surgery, tenotomy/respiratory review/cardiac assessment/respiratory arrest/tracheostomy/lower respiratory tract infection (LRTI)] OR DMD related medication (ACE-I/clinical trial participant) OR age of diagnosis.

(II) For any condition or medication: take the start date as the date of first mention.

(III) For any condition or medication start date where only the year is recorded: take the start date as January of that year.

(IV) Data for passed patients was collected from the first records available, and any final dates used to measure the length of time were taken as the date of passing.

(V) The age of the patients (alive) was calculated for 15th June 2021.

Additional results

Hospitalisations

Each patient experienced 3 (2–5.8) hospitalisations during the follow up period. 66% of hospitalisations were secondary to cardiopulmonary causes {2 [1–3] hospitalisations/patient}, and a further hospitalisation period {1 [0–2] hospitalisation/patient} was due to other causes. The median of the total hospitalisations of survivors was 3 (1–5.8) hospitalisations, with 2 [0–3] due to cardiopulmonary and 1 [0–2] due to other causes. Deceased patients experienced 3.5 (2.3–5.8) hospitalisations, with 2 (1.3–3.8) hospitalisations as a result of cardiopulmonary causes, and 2 [1–2] for other causes. There was no significant difference in total hospitalisations between survivors and deceased patients (P=0.39).

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Table S2 Comorbidities

Condition	Number of patients
Cardiomyopathy	58
Respiratory failure	49
Chest wall deformity (scoliosis/kyphoscoliosis)	37
Type 2 diabetes mellitus	13
Sleep disordered breathing/OSA	10
Anxiety	7
Delayed puberty	5
Fracture	5
Bulbar dysfunction/poor swallow	5
ICD/CRT	4
Total	189
Total other conditions	118

OSA, obstructive sleep apnoea; ICD, implantable cardiac defibrillator; CRT, cardiac resynchronisation therapy.

Table S3 Ventilator device

Type of ventilator	Number of patients
NIPPY III+	55
A40	1
NIPPY III+ → BIPAP	1
NIPPY III+ → CPAP	1
NIPPY junior support	1
Trilogy ventilator	1
Not stated	1
Total	61

NIPPY, non-invasive positive pressure ventilation; BIPAP, bilevel positive airway pressure; CPAP, continuous positive airway pressure.

Table S4 ECG abnormalities

ECG finding	Initially presenting, n	Presenting at final follow up, n
Arrhythmia	9	10
Bundle branch block	13	13
T wave flattening/inversion	5	8
Dominant R-wave V1/2	5	22
Pathological Q-waves	29	30
Axis deviation	10	13
Total	71	96

ECG, electrocardiogram.

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