ISSN: 0975-3583, 0976-2833 VOL 12, ISSUE 03, 2021

FREQUENCY OF CARDIAC AFFECTION IN DUCHENNE MUSCULAR DYSTROPHY PATIENTS AND CARRIERS IN AIN SHAMS UNIVERSITY HOSPITALS

Mahmoud Shehta Abdelawad Ahmed, MSc[1], Mona Mostafa Mohamed Rayan, M.D.[2], Nagia Ali Fahmy, M.D.[3], Ahmed Mohamed Onsy, M.D.[4], Islam Mahmoud Bastawy, M.D.[5]

[1] Assistant Lecturer of Cardiology, Cardiology department, Faculty of Medicine, Ain Shams University, Egypt

[2] Professor of Cardiology, Cardiology department, Faculty of Medicine, Ain Shams University, Egypt

[3] Professor of Neurology, Neuropsychiatry department, Faculty of Medicine, Ain Shams University, Egypt

[4] Assistant Professor of Cardiology, Cardiology department, Faculty of Medicine, Ain Shams University, Egypt

[5] Lecturer of Cardiology, Cardiology department, Faculty of Medicine, Ain Shams University, Egypt

Corresponding author: Mahmoud Shehta Abdelawad Ahmed
Cardiology Department, Faculty of Medicine, Ain Shams University, Abbassia square, Abbasia 11566, Cairo, Egypt.
E-mail: dr_mahmoud_shehta@yahoo.com

Abstract

Introduction: Duchenne muscular dystrophy (DMD) is considered the most common inherited neuromuscular disorder that shows an X-linked recessive pattern of inheritance. Cardiac manifestations are the most common causes of death in DMD patients.[1,2] Several studies discussed the effect of the genetic diagnosis on the progression of cardiomyopathy. There is a conflict regarding specific mutations as being either cardioprotective or being risk factor for development of cardiomyopathy.

Methodology: In this study, 30 genetically diagnosed patients and 26 genetically diagnosed carriers were subjected to history taking, clinical examination, ECG and echocardiography.

Results: DMD patients with exon 65 mutation appeared to have a better LV EF compared to patients who don't have this mutation. Female carriers of DMD mutations located 3-6 had larger LV dimensions compared to patients who don't have these mutations.

Conclusion: There is still a conflict regarding relation between different exon mutations and cardiac affection. Exon 65 appeared to have a cardioprotective effect in DMD patients. Female carriers with mutations in exon 3-6 tended to have larger LV internal dimensions.

Key words: Cardiomyopathy, DMD, genetic diagnosis, exon mutations

Background

Duchenne muscular dystrophy (DMD) is considered the most common inherited neuromuscular disorder with X-linked recessive inheritance**.**

The DMD gene is the largest known human gene. The mutation rate is relatively high; in one in three cases, DMD is caused by a de novo mutation. [3,4]

Deletion and duplication of exons represent the most common types of mutations 68%, 11% respectively. The most common affected exons for deletion are between 45-55 and for duplication are between exons 2-10[5]

The normal dystrophin protein acts as a shock absorber during muscle fiber contraction. [6] In DMD, mutations affect dystrophin function by disrupting the reading frame or by generating a premature stop codon. As a result, the muscle fibers are easily damaged during contraction, leading to chronic muscle damage and loss of muscle function and cardiac affection is considered the most common cause of death in DMD patients[7,8].

Some female carriers develop skeletal muscle manifestations and cardiomyopathy. Regular assessment of patients and carriers of DMD is required that includes history taking, clinical examination, electrocardiography (ECG), and non-invasive cardiac imaging technique. Cardiac magnetic resonance (CMR) imaging is important diagnostic tool while transthoracic echocardiography is a simple alternative especially for patients younger than 7 years**.** [1]

ISSN: 0975-3583, 0976-2833 VOL 12, ISSUE 03, 2021

This study aimed to assess the correlation between different types of exon mutations and development of cardiomyopathy in DMD patients and carriers.

Materials and Methods:

This is an observational descriptive cross-sectional study, which was conducted in Ain Shams University hospitals in the period between June 2019 and June 2020.

56 DMD patients and carriers molecularly diagnosed were included in the study. They were subdivided into 2 groups.

Group A included 30 male patients genetically diagnosed as DMD patients.

Group B included 26 female patients genetically diagnosed as DMD carriers.

The study design was approved by the ethical committee of, Ain Shams University faculty of Medicine. All patients or next kin of care signed an informed written consent.

All subjects were subjected to history taking with identification of symptoms of heart failure and physical examination including vital data (Arterial blood pressure and heart rate).

Multiplex ligation dependent probe amplification (MLPA) was used to test for deletion or duplication of the DMD gene.

12 lead surface ECG: was done for all the study participants. The device was calibrated at normal standardization 1mm=0.1 mv and with a speed 25mm per second. Three channel 12 lead ECG was generated followed by an ECG strip of lead II.

Standard ECG-gated trans-thoracic echocardiography was performed for all subjects using a Vivid S5 machine,USA, according to the recommendations of American society of Echocardiography. [9] The following measures were taken; LV diameters (end-diastolic diameter (LVEDD and end-systolic diameter (LVESD), LV volumes end-diastolic volume (LVED vol), LV end-systolic volume (LVES vol), Ejection fraction, Diastolic function (E/A ratio, DT, lateral E', E/E'), LA dimensions, Mitral valve assessment, Aortic valve assessment, Other valvular, endocardial, myocardial or pericardial affection.

Statistical analysis

Version 22 of Statistical Package for Social Science (IBM SPSS) was used for data analysis. The setting for the confidence interval was 95% and the margin of error accepted was set to 5%, so the p-value was considered significant if $P < 0.05$

Results:

DMD patients (Group A)

The most common exons mutations in group A were exons 49-50 in 37.9% of the patients followed by exon 48 in 27.6% of the patients followed by exon 45-47 in 24.1% of the patients.

There was no significant statistical relation between different sites of exon mutations and IVSd, PWd, LVEDD, LVESD, LVED vol or LVES vol.

On comparing different sites of exon mutation and EF by modified simpson's method, there was a statistically significant difference between patients with exon 65 mutation with a mean of (70.00 ± 3.46) % and patients who don't have the mutation (61.27 ± 5.23) %. P= 0.009 ***(Table 1)***

There was no significant statistical difference between different sites of exon mutation and diastolic function by E/E'. ***(Table 2)***

There was no significant statistical difference between different sites of exon mutation and PR interval. ***(Table 3)***

On comparing different sites of exon mutation and QRS duration, there was a statistically significant difference between patients with exon 45 mutation with a mean of (95.00 ± 4.08) msec and patients who don't have the mutation (88.86 ± 5.96) msec. P= 0.018 (Table 5)

ISSN: 0975-3583, 0976-2833 VOL 12, ISSUE 03, 2021

There was also a statistically significant difference between patients with exon 55 mutation with a mean of (83.33 ± 2.89) msec and patients who don't have the mutation (91.15 ± 5.88) msec. P= 0.033 ***(Table 4)***

DMD Carriers (Group B)

The most common exons mutations in group B were exons 49-50 in 40% of the patients followed by exon 48 in 28% of the patients followed by exon 45-47 in 24% of the patients.

There was no significant statistical relation between different sites of exon mutations and IVSd, or PWd.

Patients with exon mutation in exons 3-6 were found to have larger LVEDD, LVESD, LVEDV and LVESV when compared to patients who don't have these mutations.

Patients with exon 65 mutations had a smaller LVESDD compared to patients who didn't have this mutation.

There was no significant statistical difference between different sites of exon mutation and EF by modified Simpson's method in Group B. ***(Table 5)***

There was no significant statistical difference between different sites of exon mutation and diastolic function E/E' method in Group B. ***(Table 6)***

There was no significant statistical difference between different sites of exon mutation and PR interval in Group B***. (Table 7)***

On comparing different sites of exon mutations and QRS duration, there was a significant statistical difference between patients with exon 2 mutation with mean (100.00 ± 0.00) msec. and patient who don't have the mutation with mean (88.00 ± 6.55) msec. P=0.018 ***(Table 8)***

There was a significant statistical difference between patients with exon 49 mutation with mean (85.40 ± 6.00) msec. and patient who don't have the mutation with mean (91.33 ± 6.94) msec. P=0.038 ***(Table 8)***

There was a significant statistical difference between patients with exon 50 mutation with mean (85.40 ± 6.00) msec. and patient who don't have the mutation with mean (91.33 ± 6.94) msec. P=0.038 ***(Table 8)***

Discussion

Duchenne muscular dystrophy (DMD) is considered the most common inherited neuromuscular disorder with X-linked recessive pattern inheritance. Cardiac manifestations are the most common causes of death in DMD patients. This study is a trial to establish a relation between genetic diagnosis and cardiac affection in DMD patients and carriers.

In this study, there was no significant relation between different exon mutations and LV dimensions, volumes nor diastolic function by E/E'. Only DMD patients with exon 65 mutation appeared to have a higher EF with a mean of (70.00 ± 3.46) % and patients who do not have the mutation (61.27 ± 5.23) % which may suggest it had a cardioprotective role.

Jefferies and his colleagues found that exon 12, 14, 15, 16 and 17 mutations are associated with development of cardiomyopathy. Also, they found that exon 51 and 52 mutations tend to be protective against cardiomyopathy which didn't agree with this study[10].

ISSN: 0975-3583, 0976-2833 VOL 12, ISSUE 03, 2021

Ashwath and her colleagues conducted a study on 75 DMD patients. They divided the patient into 4 groups according to presence and severity of cardiomyopathy. Also, they divided the patients into 4 groups regarding the site of the genetic mutations. They found that distribution of the mutations appeared similar in the 4 severity groups[11].

In this study, there was no significant relation between site of exon mutations and LV systolic function nor diastolic function using E/E'. Although, female carriers with exon mutation in exons 3-6 had larger LVEDD, LVESD, LVEDV and LVESV when compared to patients who don't have these mutations. Also, Patients with exon 65 mutations had a smaller LVESDD compared to patients who didn't have this mutation.

Thomas Mccaffrey and his colleagues conducted a study on 130 female patients diagnosed as carriers of DMD and BMD; 88 carriers of DMD and 42 carriers of BMD. They defined 63 different genetic mutations and they didn't find any relation between specific type or location of mutation and development of cardiomyopathy which agreed with this study.[12]

Conclusion:

Cardiac affection is the most common cause of death in DMD patients. Different studies were done trying to establish a relation between different sites of genetic mutations and cardiac affection. In this study, exon 65 mutation was noticed to have a cardioprotective effect. Female carriers with exon mutations 3-6 appeared to have larger LV dimensions and volumes.

Limitation:

Small number of patients as the disease is relatively uncommon.

Conflicts of interest:

The authors certify that there is no conflict of interest with any financial organization regarding the material discussed in the manuscript.

Funding:

The authors report no involvement in the research by the sponsor that could have influenced the outcome of this work.

ISSN: 0975-3583, 0976-2833 VOL 12, ISSUE 03, 2021

Tables

Table (1) Comparison between different sites of exon mutation and EF by modified simpson's method in group (A)

	EF% Modified Simpson's (%)		P-value
	No mutation	Mutation	
	Mean ± SD	Mean ± SD	
1	62.19 ± 5.90	62.00 ± 2.83	0.966
2	62.52 ± 5.95	60.00 ± 3.74	0.422
3	62.27 ± 6.00	61.33 ± 2.31	0.793
4	62.27 ± 6.00	61.33 ± 2.31	0.793
5	62.27 ± 6.00	61.33 ± 2.31	0.793
6	62.27 ± 6.00	61.33 ± 2.31	0.793
7	62.25 ± 5.80	60.00 ± 0.00	0.706
8	62.15 ± 5.92	62.50 ± 0.71	0.935
9	62.15 ± 5.92	62.50 ± 0.71	0.935
10	62.15 ± 5.92	62.50 ± 0.71	0.935
11	62.15 ± 5.92	62.50 ± 0.71	0.935
12	62.15 ± 5.92	62.50 ± 0.71	0.935
13	62.15 ± 5.92	62.50 ± 0.71	0.935
14	62.15 ± 5.92	62.50 ± 0.71	0.935
15	62.15 ± 5.92	62.50 ± 0.71	0.935
16	62.15 ± 5.92	62.50 ± 0.71	0.935
17	62.15 ± 5.92	62.50 ± 0.71	0.935
18	62.15 ± 5.92	62.50 ± 0.71	0.935
19	62.15 ± 5.92	62.50 ± 0.71	0.935
20	62.15 ± 5.92	62.50 ± 0.71	0.935
21	62.15 ± 5.92	62.50 ± 0.71	0.935
41	62.37 ± 5.87	59.50 ± 0.71	0.503
43	62.25 ± 5.80	60.00 ± 0.00	0.706
45	62.91 ± 5.22	59.86 ± 6.96	0.224
46	62.86 ± 5.78	60.00 ± 5.26	0.255
47	62.86 ± 5.78	60.00 ± 5.26	0.255
48	62.38 ± 5.45	61.63 ± 6.70	0.756
49	62.72 ± 5.83	61.27 ± 5.66	0.517
50	62.72 ± 5.83	61.27 ± 5.66	0.517
51	62.72 ± 5.95	58.75 ± 1.71	0.202
52	62.72 ± 5.95	58.75 ± 1.71	0.202
53	62.72 ± 5.95	58.75 ± 1.71	0.202
54	62.72 ± 5.95	58.75 ± 1.71	0.202
55	62.50 ± 5.93	59.33 ± 1.53	0.372
56	62.29 ± 5.78	59.00 ± 0.00	0.581
57	62.29 ± 5.78	59.00 ± 0.00	0.581
58	62.29 ± 5.78	59.00 ± 0.00	0.581
59	62.29 ± 5.78	59.00 ± 0.00	0.581
60	62.29 ± 5.78	59.00 ± 0.00	0.581
61	62.29 ± 5.78	59.00 ± 0.00	0.581
62	62.29 ± 5.78	59.00 ± 0.00	0.581
65	61.27 ± 5.23	70.00 ± 3.46	0.009

P-value >0.05: Non significant (NS); P-value <0.05: Significant (S)

•: Independent t-test

ISSN: 0975-3583, 0976-2833 VOL 12, ISSUE 03, 2021

Table (2) Comparison between different sites of exon mutation and diastolic function (E/E') in group (A)

	Diastolic function E/E'		P-value
	No mutation	Mutation	
	Mean ± SD	Mean ± SD	
1	4.67 ± 1.30	3.50 ± 0.71	0.226
2	4.76 ± 1.30	3.50 ± 0.58	0.070
3	4.69 ± 1.32	3.67 ± 0.58	0.200
4	4.69 ± 1.32	3.67 ± 0.58	0.200
5	4.69 ± 1.32	3.67 ± 0.58	0.200
6	4.69 ± 1.32	3.67 ± 0.58	0.200
7	4.61 ± 1.31	4.00 ± 0.00	0.654
8	4.48 ± 1.25	6.00 ± 1.41	0.111
9	4.48 ± 1.25	6.00 ± 1.41	0.111
10	4.48 ± 1.25	6.00 ± 1.41	0.111
11	4.48 ± 1.25	6.00 ± 1.41	0.111
12	4.48 ± 1.25	6.00 ± 1.41	0.111
13	4.48 ± 1.25	6.00 ± 1.41	0.111
14	4.48 ± 1.25	6.00 ± 1.41	0.111
15	4.48 ± 1.25	6.00 ± 1.41	0.111
16	4.48 ± 1.25	6.00 ± 1.41	0.111
17	4.48 ± 1.25	6.00 ± 1.41	0.111
18	4.48 ± 1.25	6.00 ± 1.41	0.111
19	4.48 ± 1.25	6.00 ± 1.41	0.111
20	4.48 ± 1.25	6.00 ± 1.41	0.111
21	4.48 ± 1.25	6.00 ± 1.41	0.111
41	4.67 ± 1.30	3.50 ± 0.71	0.226
43	4.57 ± 1.32	5.00 ± 0.00	0.752
45	4.45 ± 1.34	5.00 ± 1.15	0.341
46	4.55 ± 1.44	4.71 ± 0.76	0.770
47	4.55 ± 1.44	4.71 ± 0.76	0.770
48	4.48 ± 1.44	4.88 ± 0.83	0.469
49	4.50 ± 1.50	4.73 ± 0.90	0.655
50	4.50 ± 1.50	4.73 ± 0.90	0.655
51	4.48 ± 1.36	5.25 ± 0.50	0.278
52	4.48 ± 1.36	5.25 ± 0.50	0.278
53	4.48 ± 1.36	5.25 ± 0.50	0.278
54	4.48 ± 1.36	5.25 ± 0.50	0.278
55	4.50 ± 1.33	5.33 ± 0.58	0.300
56	4.57 ± 1.32	5.00 ± 0.00	0.752
57	4.57 ± 1.32	5.00 ± 0.00	0.752
58	4.57 ± 1.32	5.00 ± 0.00	0.752
59	4.57 ± 1.32	5.00 ± 0.00	0.752
60	4.57 ± 1.32	5.00 ± 0.00	0.752
61	4.57 ± 1.32	5.00 ± 0.00	0.752
62	4.57 ± 1.32	5.00 ± 0.00	0.752
65	4.73 ± 1.28	3.33 ± 0.58	0.076

P-value >0.05: Non significant (NS); P-value <0.05: Significant (S)

•: Independent t-test

ISSN: 0975-3583, 0976-2833 VOL 12, ISSUE 03, 2021

Table (3) Comparison between different sites of exon mutation and PR interval in group (A)

	PR interval (msec)		P-value
	No mutation	mutation	
	Mean ± SD	Mean ± SD	
1	153.52 ± 16.28	142.50 ± 24.75	0.375
2	153.00 ± 16.83	151.25 ± 17.50	0.849
3	154.42 ± 15.90	138.33 ± 18.93	0.114
4	154.42 ± 15.90	138.33 ± 18.93	0.114
5	154.42 ± 15.90	138.33 ± 18.93	0.114
6	154.42 ± 15.90	138.33 ± 18.93	0.114
7	153.57 ± 16.32	130.00 ± 0.00	0.167
8	153.33 ± 17.04	145.00 ± 7.07	0.504
9	153.33 ± 17.04	145.00 ± 7.07	0.504
10	153.33 ± 17.04	145.00 ± 7.07	0.504
11	153.33 ± 17.04	145.00 ± 7.07	0.504
12	153.33 ± 17.04	145.00 ± 7.07	0.504
13	153.33 ± 17.04	145.00 ± 7.07	0.504
14	153.33 ± 17.04	145.00 ± 7.07	0.504
15	153.33 ± 17.04	145.00 ± 7.07	0.504
16	153.33 ± 17.04	145.00 ± 7.07	0.504
17	153.33 ± 17.04	145.00 ± 7.07	0.504
18	153.33 ± 17.04	145.00 ± 7.07	0.504
19	153.33 ± 17.04	145.00 ± 7.07	0.504
20	153.33 ± 17.04	145.00 ± 7.07	0.504
21	153.33 ± 17.04	145.00 ± 7.07	0.504
41	153.33 ± 17.04	145.00 ± 7.07	0.504
43	152.86 ± 16.91	150.00 ± 0.00	0.869
45	152.50 ± 16.46	153.57 ± 18.42	0.885
46	150.68 ± 16.06	159.29 ± 17.90	0.239
47	150.68 ± 16.06	159.29 ± 17.90	0.239
48	149.29 ± 15.02	161.88 ± 18.11	0.067
49	151.39 ± 13.48	155.00 ± 21.33	0.579
50	151.39 ± 13.48	155.00 ± 21.33	0.579
51	151.60 ± 17.42	160.00 ± 8.16	0.357
52	151.60 ± 17.42	160.00 ± 8.16	0.357
53	151.60 ± 17.42	160.00 ± 8.16	0.357
54	151.60 ± 17.42	160.00 ± 8.16	0.357
55	151.54 ± 17.07	163.33 ± 5.77	0.251
56	152.50 ± 16.86	160.00 ± 0.00	0.666
57	152.50 ± 16.86	160.00 ± 0.00	0.666
58	152.50 ± 16.86	160.00 ± 0.00	0.666
59	152.50 ± 16.86	160.00 ± 0.00	0.666
60	152.50 ± 16.86	160.00 ± 0.00	0.666
61	152.50 ± 16.86	160.00 ± 0.00	0.666
62	152.50 ± 16.86	160.00 ± 0.00	0.666
65	151.54 ± 17.07	163.33 ± 5.77	0.251

P-value >0.05: Non significant (NS); P-value <0.05: Significant (S)

•: Independent t-test

ISSN: 0975-3583, 0976-2833 VOL 12, ISSUE 03, 2021

Table (4) Comparison between different sites of exon mutation and QRS duration in group (A)

	QRS duration (msec)		P-value
	No mutation	Mutation	
	Mean ± SD	Mean ± SD	
1	90.74 ± 6.16	85.00 ± 0.00	0.206
2	90.60 ± 6.34	88.75 ± 4.79	0.584
3	90.58 ± 6.22	88.33 ± 5.77	0.557
4	90.58 ± 6.22	88.33 ± 5.77	0.557
5	90.58 ± 6.22	88.33 ± 5.77	0.557
6	90.58 ± 6.22	88.33 ± 5.77	0.557
7	90.18 ± 6.16	95.00 ± 0.00	0.448
8	90.00 ± 6.04	95.00 ± 7.07	0.272
9	90.00 ± 6.04	95.00 ± 7.07	0.272
10	90.00 ± 6.04	95.00 ± 7.07	0.272
11	90.00 ± 6.04	95.00 ± 7.07	0.272
12	90.00 ± 6.04	95.00 ± 7.07	0.272
13	90.00 ± 6.04	95.00 ± 7.07	0.272
14	90.00 ± 6.04	95.00 ± 7.07	0.272
15	90.00 ± 6.04	95.00 ± 7.07	0.272
16	90.00 ± 6.04	95.00 ± 7.07	0.272
17	90.00 ± 6.04	95.00 ± 7.07	0.272
18	90.00 ± 6.04	95.00 ± 7.07	0.272
19	90.00 ± 6.04	95.00 ± 7.07	0.272
20	90.00 ± 6.04	95.00 ± 7.07	0.272
21	90.00 ± 6.04	95.00 ± 7.07	0.272
41	90.93 ± 5.89	82.50 ± 3.54	0.058
43	90.36 ± 6.23	90.00 ± 0.00	0.955
45	88.86 ± 5.96	95.00 ± 4.08	0.018
46	90.23 ± 6.07	90.71 ± 6.73	0.858
47	90.23 ± 6.07	90.71 ± 6.73	0.858
48	90.24 ± 6.22	90.63 ± 6.23	0.882
49	90.83 ± 6.47	89.55 ± 5.68	0.591
50	90.83 ± 6.47	89.55 ± 5.68	0.591
51	91.00 ± 5.95	86.25 ± 6.29	0.152
52	91.00 ± 5.95	86.25 ± 6.29	0.152
53	91.00 ± 5.95	86.25 ± 6.29	0.152
54	91.00 ± 5.95	86.25 ± 6.29	0.152
55	91.15 ± 5.88	83.33 ± 2.89	0.033
56	90.54 ± 6.14	85.00 ± 0.00	0.383
57	90.54 ± 6.14	85.00 ± 0.00	0.383
58	90.54 ± 6.14	85.00 ± 0.00	0.383
59	90.54 ± 6.14	85.00 ± 0.00	0.383
60	90.54 ± 6.14	85.00 ± 0.00	0.383
61	90.54 ± 6.14	85.00 ± 0.00	0.383
62	90.54 ± 6.14	85.00 ± 0.00	0.383
65	90.58 ± 5.71	88.33 ± 10.41	0.557

P-value >0.05: Non significant (NS); P-value <0.05: Significant (S)

•: Independent t-test

ISSN: 0975-3583, 0976-2833 VOL 12, ISSUE 03, 2021

Table (5) Comparison between different sites of exon mutation and EF by modified Simpson's method in group (B)

	EF% Modified Simpson's (%)		P-value
	No mutation	Mutation	
	Mean ± SD	Mean ± SD	
1	63.96 ± 5.32	61.00 ± 0.00	0.591
2	63.39 ± 4.64	69.00 ± 11.31	0.150
3	64.09 ± 5.40	61.00 ± 0.00	0.436
4	64.09 ± 5.40	61.00 ± 0.00	0.436
5	64.09 ± 5.40	61.00 ± 0.00	0.436
6	64.09 ± 5.40	61.00 ± 0.00	0.436
7	63.96 ± 5.32	61.00 ± 0.00	0.591
8	63.67 ± 5.28	68.00 ± 0.00	0.430
9	63.67 ± 5.28	68.00 ± 0.00	0.430
10	63.67 ± 5.28	68.00 ± 0.00	0.430
11	63.67 ± 5.28	68.00 ± 0.00	0.430
12	63.67 ± 5.28	68.00 ± 0.00	0.430
13	63.67 ± 5.28	68.00 ± 0.00	0.430
14	63.67 ± 5.28	68.00 ± 0.00	0.430
15	63.67 ± 5.28	68.00 ± 0.00	0.430
16	63.67 ± 5.28	68.00 ± 0.00	0.430
17	63.67 ± 5.28	68.00 ± 0.00	0.430
18	63.67 ± 5.28	68.00 ± 0.00	0.430
19	63.67 ± 5.28	68.00 ± 0.00	0.430
20	63.67 ± 5.28	68.00 ± 0.00	0.430
21	63.67 ± 5.28	68.00 ± 0.00	0.430
41	63.96 ± 5.41	62.50 ± 3.54	0.715
43	63.79 ± 5.35	65.00 ± 0.00	0.827
45	63.32 ± 4.92	65.50 ± 6.35	0.385
46	63.63 ± 4.89	64.50 ± 6.72	0.732
47	63.63 ± 4.89	64.50 ± 6.72	0.732
48	63.56 ± 5.02	64.57 ± 6.13	0.673
49	63.20 ± 4.84	64.80 ± 5.92	0.466
50	63.20 ± 4.84	64.80 ± 5.92	0.466
51	63.25 ± 5.01	66.20 ± 6.06	0.269
52	63.25 ± 5.01	66.20 ± 6.06	0.269
53	63.25 ± 5.01	66.20 ± 6.06	0.269
54	63.25 ± 5.01	66.20 ± 6.06	0.269
55	64.13 ± 5.37	60.50 ± 0.71	0.358
56	63.96 ± 5.32	61.00 ± 0.00	0.591
57	63.96 ± 5.32	61.00 ± 0.00	0.591
58	63.96 ± 5.32	61.00 ± 0.00	0.591
59	63.96 ± 5.32	61.00 ± 0.00	0.591
60	63.96 ± 5.32	61.00 ± 0.00	0.591
61	63.96 ± 5.32	61.00 ± 0.00	0.591
62	63.96 ± 5.32	61.00 ± 0.00	0.591
65	64.52 ± 5.35	60.25 ± 2.87	0.138

P-value >0.05: Non significant (NS); P-value <0.05: Significant (S)

•: Independent t-test

ISSN: 0975-3583, 0976-2833 VOL 12, ISSUE 03, 2021

Table (6) Comparison between different sites of exon mutation and Diastolic function E/E' in group (B)

	Diastolic function E/E'		P-value
	No mutation	Mutation	
	Mean ± SD	Mean ± SD	
1	5.71 ± 1.00	4.00 ± 0.00	0.107
2	5.70 ± 1.02	5.00 ± 1.41	0.374
3	5.74 ± 1.01	4.50 ± 0.71	0.106
4	5.74 ± 1.01	4.50 ± 0.71	0.106
5	5.74 ± 1.01	4.50 ± 0.71	0.106
6	5.74 ± 1.01	4.50 ± 0.71	0.106
7	5.67 ± 1.05	5.00 ± 0.00	0.540
8	5.63 ± 1.06	6.00 ± 0.00	0.731
9	5.63 ± 1.06	6.00 ± 0.00	0.731
10	5.63 ± 1.06	6.00 ± 0.00	0.731
11	5.63 ± 1.06	6.00 ± 0.00	0.731
12	5.63 ± 1.06	6.00 ± 0.00	0.731
13	5.63 ± 1.06	6.00 ± 0.00	0.731
14	5.63 ± 1.06	6.00 ± 0.00	0.731
15	5.63 ± 1.06	6.00 ± 0.00	0.731
16	5.63 ± 1.06	6.00 ± 0.00	0.731
17	5.63 ± 1.06	6.00 ± 0.00	0.731
18	5.63 ± 1.06	6.00 ± 0.00	0.731
19	5.63 ± 1.06	6.00 ± 0.00	0.731
20	5.63 ± 1.06	6.00 ± 0.00	0.731
21	5.63 ± 1.06	6.00 ± 0.00	0.731
41	5.61 ± 1.08	6.00 ± 0.00	0.619
43	5.71 ± 1.00	4.00 ± 0.00	0.107
45	5.58 ± 1.02	5.83 ± 1.17	0.611
46	5.68 ± 1.06	5.50 ± 1.05	0.713
47	5.68 ± 1.06	5.50 ± 1.05	0.713
48	5.72 ± 1.07	5.43 ± 0.98	0.536
49	5.80 ± 1.01	5.40 ± 1.07	0.355
50	5.80 ± 1.01	5.40 ± 1.07	0.355
51	5.65 ± 0.99	5.60 ± 1.34	0.926
52	5.65 ± 0.99	5.601.34	0.926
53	5.65 ± 0.99	5.60 ± 1.34	0.926
54	5.65 ± 0.99	5.60 ± 1.34	0.926
55	5.61 ± 1.03	6.00 ± 1.41	0.619
56	5.58 ± 1.02	7.00 ± 0.00	0.186
57	5.58 ± 1.02	7.00 ± 0.00	0.186
58	5.58 ± 1.02	7.00 ± 0.00	0.186
59	5.58 ± 1.02	7.00 ± 0.00	0.186
60	5.58 ± 1.02	7.00 ± 0.00	0.186
61	5.58 ± 1.02	7.00 ± 0.00	0.186
62	5.58 ± 1.02	7.00 ± 0.00	0.186
65	5.48 ± 1.03	6.50 ± 0.58	0.069

P-value >0.05: Non significant (NS); P-value <0.05: Significant (S)

•: Independent t-test

ISSN: 0975-3583, 0976-2833 VOL 12, ISSUE 03, 2021

Table (7) Comparison between different sites of exon mutation and PR interval in group (B)

	PR interval (msec)		P-value
	No	Yes	
	Mean ± SD	Mean ± SD	
1	155.42 ± 18.23	140.00 ± 0.00	0.416
2	155.22 ± 18.62	150.00 ± 14.14	0.705
3	156.09 ± 18.34	140.00 ± 0.00	0.236
4	156.09 ± 18.34	140.00 ± 0.00	0.236
5	156.09 ± 18.34	140.00 ± 0.00	0.236
6	156.09 ± 18.34	140.00 ± 0.00	0.236
7	155.42 ± 18.23	140.00 ± 0.00	0.416
8	156.04 ± 17.38	125.00 ± 0.00	0.093
9	156.04 ± 17.38	125.00 ± 0.00	0.093
10	156.04 ± 17.38	125.00 ± 0.00	0.093
11	156.04 ± 17.38	125.00 ± 0.00	0.093
12	156.04 ± 17.38	125.00 ± 0.00	0.093
13	156.04 ± 17.38	125.00 ± 0.00	0.093
14	156.04 ± 17.38	125.00 ± 0.00	0.093
15	156.04 ± 17.38	125.00 ± 0.00	0.093
16	156.04 ± 17.38	125.00 ± 0.00	0.093
17	156.04 ± 17.38	125.00 ± 0.00	0.093
18	156.04 ± 17.38	125.00 ± 0.00	0.093
19	156.04 ± 17.38	125.00 ± 0.00	0.093
20	156.04 ± 17.38	125.00 ± 0.00	0.093
21	156.04 ± 17.38	125.00 ± 0.00	0.093
41	155.65 ± 18.61	145.00 ± 7.07	0.437
43	154.58 ± 18.47	160.00 ± 0.00	0.776
45	153.68 ± 16.82	158.33 ± 23.17	0.594
46	151.58 ± 17.16	165.00 ± 18.71	0.115
47	151.58 ± 17.16	165.00 ± 18.71	0.115
48	149.44 ± 14.84	168.57 ± 19.52	0.014
49	151.00 ± 15.61	160.50 ± 20.88	0.205
50	151.00 ± 15.61	160.50 ± 20.88	0.205
51	152.75 ± 18.17	163.00 ± 17.18	0.267
52	152.75 ± 18.17	163.00 ± 17.18	0.267
53	152.75 ± 18.17	163.00 ± 17.18	0.267
54	152.75 ± 18.17	163.00 ± 17.18	0.267
55	155.00 ± 18.15	152.50 ± 24.75	0.856
56	155.63 ± 18.02	135.00 ± 0.00	0.274
57	155.63 ± 18.02	135.00 ± 0.00	0.274
58	155.63 ± 18.02	135.000.00	0.274
59	155.63 ± 18.02	135.00 ± 0.00	0.274
60	155.63 ± 18.02	135.00 ± 0.00	0.274
61	155.63 ± 18.02	135.00 ± 0.00	0.274
62	155.63 ± 18.02	135.00 ± 0.00	0.274
65	154.76 ± 19.20	155.00 ± 12.91	0.981

P-value >0.05: Non significant (NS); P-value <0.05: Significant (S)

•: Independent t-test

ISSN: 0975-3583, 0976-2833 VOL 12, ISSUE 03, 2021

Table (8) Comparison between different sites of exon mutation and QRS duration in group (B)

	QRS duration (msec)		P-value
	No mutation	Mutation	
	Mean ± SD	Mean ± SD	
1	88.50 ± 6.86	100.00 ± 0.00	0.114
2	88.00 ± 6.55	100.00 ± 0.00	0.018
3	88.43 ± 7.01	95.00 ± 7.07	0.217
4	88.43 ± 7.01	95.00 ± 7.07	0.217
5	88.43 ± 7.01	95.00 ± 7.07	0.217
6	88.43 ± 7.01	95.00 ± 7.07	0.217
7	88.92 ± 7.25	90.00 ± 0.00	0.885
8	89.13 ± 7.20	85.00 ± 0.00	0.580
9	89.13 ± 7.20	85.00 ± 0.00	0.580
10	89.13 ± 7.20	85.00 ± 0.00	0.580
11	89.13 ± 7.20	85.00 ± 0.00	0.580
12	89.13 ± 7.20	85.00 ± 0.00	0.580
13	89.13 ± 7.20	85.00 ± 0.00	0.580
14	89.13 ± 7.20	85.00 ± 0.00	0.580
15	89.13 ± 7.20	85.00 ± 0.00	0.580
16	89.13 ± 7.20	85.00 ± 0.00	0.580
17	89.13 ± 7.20	85.00 ± 0.00	0.580
18	89.13 ± 7.20	85.00 ± 0.00	0.580
19	89.13 ± 7.20	85.00 ± 0.00	0.580
20	89.13 ± 7.20	85.00 ± 0.00	0.580
21	89.13 ± 7.20	85.00 ± 0.00	0.580
41	88.43 ± 7.17	95.00 ± 0.00	0.217
43	88.71 ± 7.14	95.00 ± 0.00	0.397
45	90.26 ± 7.35	84.83 ± 4.49	0.103
46	90.00 ± 7.26	85.67 ± 5.89	0.198
47	90.00 ± 7.26	85.67 ± 5.89	0.198
48	90.56 ± 7.05	84.86 ± 5.79	0.070
49	91.33 ± 6.94	85.40 ± 6.00	0.038
50	91.33 ± 6.94	85.40 ± 6.00	0.038
51	89.257.30	87.80 ± 6.83	0.692
52	89.25 ± 7.30	87.80 ± 6.83	0.692
53	89.25 ± 7.30	87.80 ± 6.83	0.692
54	89.25 ± 7.30	87.80 ± 6.83	0.692
55	88.43 ± 7.17	95.00 ± 0.00	0.217
56	88.71 ± 7.14	95.00 ± 0.00	0.397
57	88.71 ± 7.14	95.00 ± 0.00	0.397
58	88.71 ± 7.14	95.00 ± 0.00	0.397
59	88.71 ± 7.14	95.00 ± 0.00	0.397
60	88.71 ± 7.14	95.00 ± 0.00	0.397
61	88.71 ± 7.14	95.00 ± 0.00	0.397
62	88.71 ± 7.14	95.00 ± 0.00	0.397
65	88.05 ± 7.00	93.75 ± 6.29	0.144

P-value >0.05: Non significant (NS); P-value <0.05: Significant (S)
•: Independent t-test

List of abbreviations
2D: 2-dimensional

ISSN: 0975-3583, 0976-2833 VOL 12, ISSUE 03, 2021

cm: centimeter
CMR: cardiac magnetic resonance
DMD: Duchenne muscular dystrophy
ECG: electrocardiogram
EF: ejection fraction
IVSd: Interventricular septum diameter at the end-diastole
LA: left atrium diameter
LV: left ventricle
LVEDD: LV end-diastolic diameter
LVEDV: LV end-diastolic volume
LVESD: LV end-systolic diameter
LVESV: LV end-systolic volume
MLPA: multiplex ligation-dependent probe amplification
mm: millimeter
M-mode: motion mode
msec: millisecond
Pwd: posterior wall diameter at the end-diastole
SPSS: Statistical Package for Social Science

ISSN: 0975-3583, 0976-2833 VOL 12, ISSUE 03, 2021

References:

[1] Birnkrant DJ, Bushby K, Bann CM, Alman BA, Apkon SD, Blackwell A, et al. Diagnosis and management of Duchenne muscular dystrophy, part 2: respiratory, cardiac, bone health, and orthopaedic management. Lancet Neurol 2018;17:347–61. https://doi.org/10.1016/S1474-4422(18)30025-5.

[2] Birnkrant DJ, Bushby K, Bann CM, Apkon SD, Blackwell A, Brumbaugh D, et al. Diagnosis and management of Duchenne muscular dystrophy, part 1: diagnosis, and neuromuscular, rehabilitation, endocrine, and gastrointestinal and nutritional management. Lancet Neurol 2018;17:251–67. https://doi.org/10.1016/S1474-4422(18)30024-3.

[3] Bladen CL, Salgado D, Monges S, Foncuberta ME, Kekou K, Kosma K, et al. The TREAT-NMD DMD Global Database : Analysis of More than 7 , 000 Duchenne Muscular Dystrophy Mutations 2015. https://doi.org/10.1002/humu.22758.

[4] Aartsma-rus A, Deutekom JCTVAN, Fokkema IVOF. ENTRIES IN THE LEIDEN DUCHENNE MUSCULAR DYSTROPHY MUTATION DATABASE : AN OVERVIEW OF MUTATION TYPES AND PARADOXICAL CASES THAT CONFIRM THE READING-FRAME RULE n.d. https://doi.org/10.1002/mus.20586.

[5] Ankala A, Kohn JN, Hegde A, Meka A, Lip C, Ephrem H, et al. Aberrant firing of replication origins potentially explains intragenic nonrecurrent rearrangements within genes , including the human DMD gene 2012:25–34. https://doi.org/10.1101/gr.123463.111.mal.

[6] Aartsma-rus A, Ginjaar IB, Bushby K. The importance of genetic diagnosis for Duchenne muscular dystrophy 2016:145–51. https://doi.org/10.1136/jmedgenet-2015-103387.

[7] Bushby K, Finkel R, Birnkrant DJ, Case LE, Clemens PR, Cripe L, et al. Diagnosis and management of Duchenne muscular dystrophy, part 2: implementation of multidisciplinary care. Lancet Neurol 2010;9:177–89. https://doi.org/10.1016/S1474-4422(09)70272-8.

[8] Bushby K, Finkel R, Birnkrant DJ, Case LE, Clemens PR, Cripe L, et al. Diagnosis and management of Duchenne muscular dystrophy, part 1: diagnosis, and pharmacological and psychosocial management. Lancet Neurol 2010;9:77–93. https://doi.org/10.1016/S1474-4422(09)70271-6.

[9] Mitchell C, Rahko PS, Blauwet LA, Canaday B, Finstuen JA, Foster MC, et al. Guidelines for Performing a Comprehensive Transthoracic Echocardiographic Examination in Adults: Recommendations from the American Society of Echocardiography. J Am Soc Echocardiogr 2019;32:1–64. https://doi.org/10.1016/j.echo.2018.06.004.

[10] Jefferies JL, Eidem BW, Belmont JW, Craigen WJ, Ware SM, Fernbach SD, et al. Genetic Predictors and Remodeling of Dilated Cardiomyopathy in Muscular Dystrophy 2005. https://doi.org/10.1161/CIRCULATIONAHA.104.528281.

[11] Ashwath ML, Jacobs IB, Crowe CA, Ashwath RC, Super DM, Bahler RC. Left Ventricular Dysfunction in Duchenne Muscular Dystrophy and Genotype. Am J Cardiol 2014;114:284–9. https://doi.org/10.1016/j.amjcard.2014.04.038.

[12] Mccaffrey T, Guglieri M, Murphy AP, Bushby K, Johnson A BJ. CARDIAC INVOLVEMENT IN FEMALE CARRIERS OF DUCHENNE OR BECKER MUSCULAR DYSTROPHY n.d. https://doi.org/10.1002/mus.25445.