

## Supplementary Materials

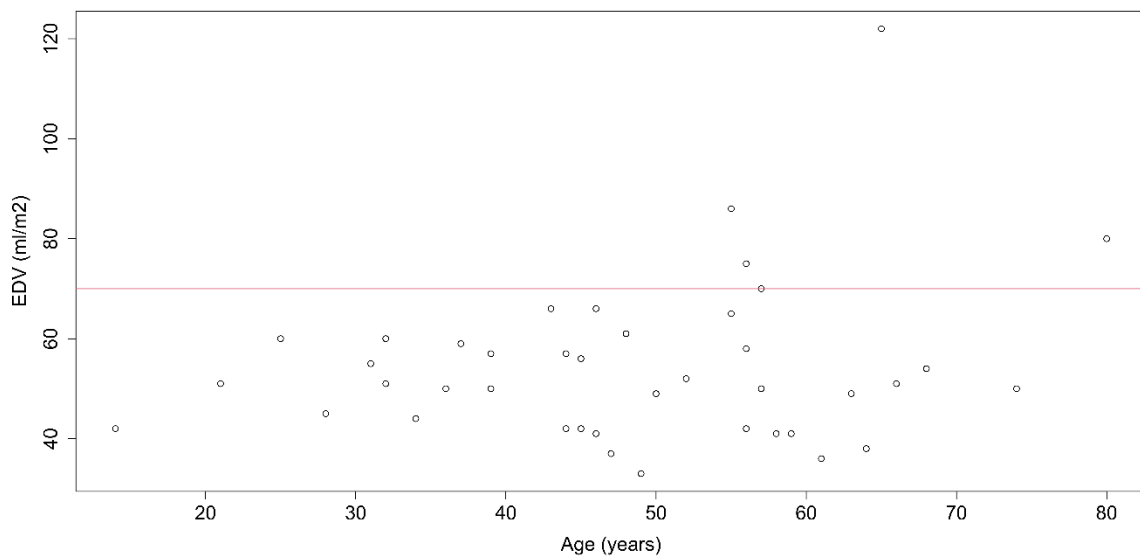


Figure S1. Scatter plot of left ventricular EDVi (ml/m<sup>2</sup>) by age. The pathological threshold is marked by a red line. Spearman's rank test:  $\rho=-0.02$ ,  $p=0.9$ .

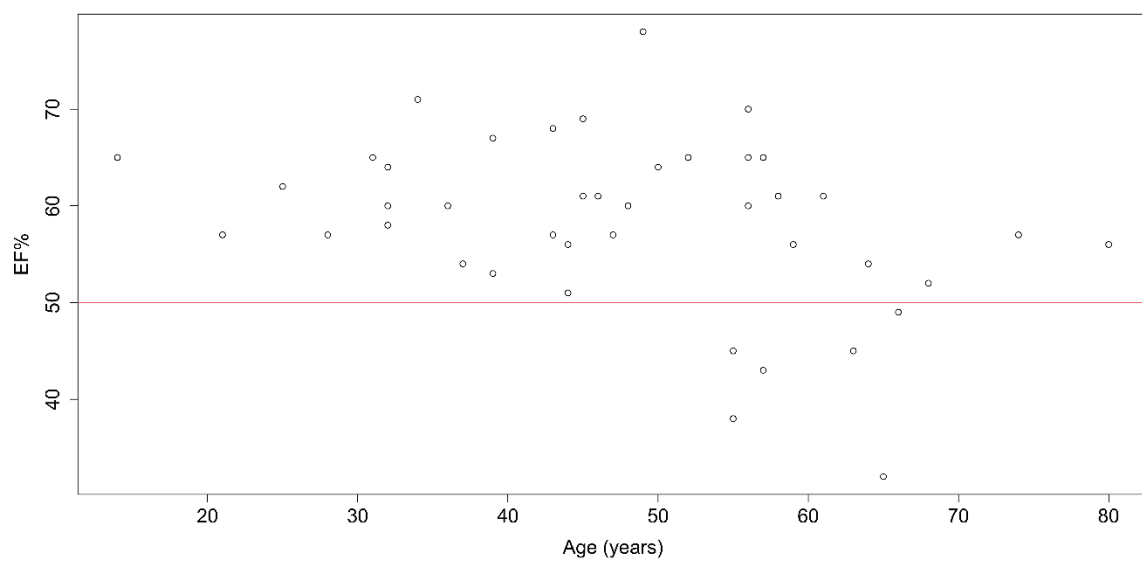


Figure S2. Scatter plot of left ventricular EF (%) by age. The pathological threshold is marked by a red line. Spearman's rank test:  $\rho=-0.35$ ,  $p=0.02$ .

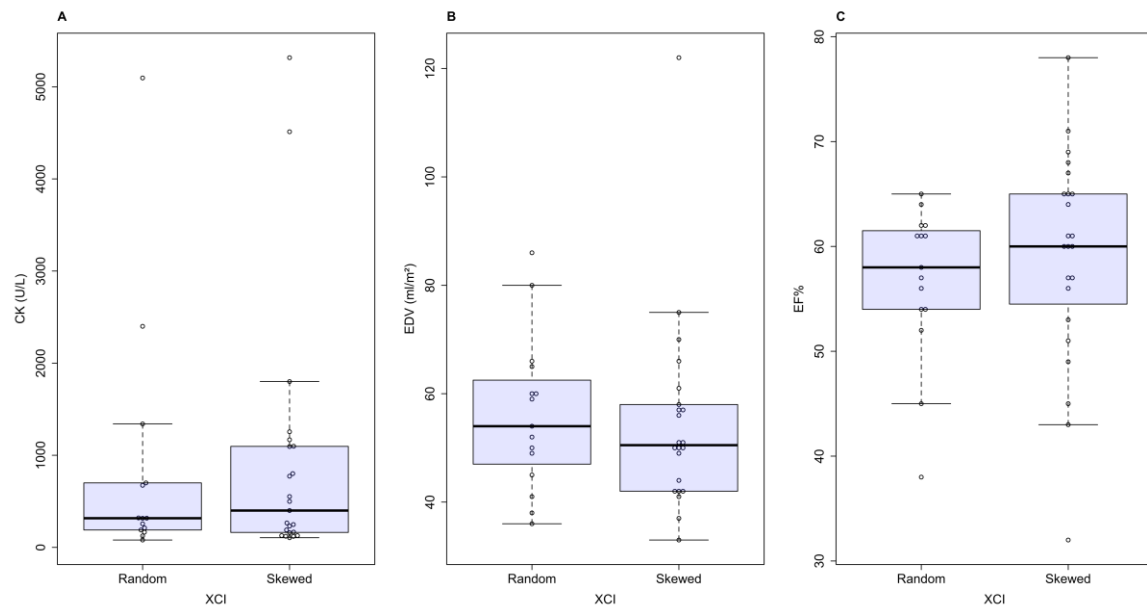


Figure S3. Beeswarm plot of serum CK levels (A), left ventricular EDVi (ml/m<sup>2</sup>) (B) and EF (%) (C) in “skewed” vs. “random” DMD heterozygous females. Wilcoxon rank sum test with continuity correction: A)  $p=0.95$ ; B)  $p=0.55$ , C)  $p=0.37$ .

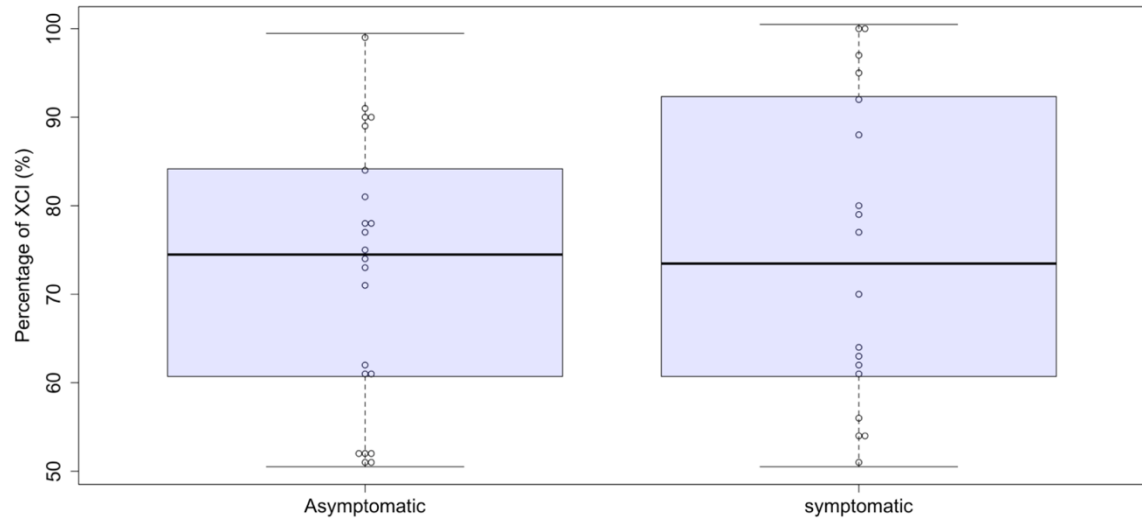


Figure S4. Beeswarm plot of XCI pattern (%) in Asymptomatic and Symptomatic patients.

Wilcoxon rank-sum test,  $p=0.6$ .

Table S1. Clinical and genetic features of DMD heterozygous females.

| ID | FAMILY | DMD MUTATION(S)      | FAMILY HISTORY | CLINICAL SEVERITY | AGE AT ONSET | AGE AT LOA | AGE AT LAST VISIT | CARDIO-MYOPATHY | CK (U/L) |
|----|--------|----------------------|----------------|-------------------|--------------|------------|-------------------|-----------------|----------|
| 1  | 1      | del Dp427c-45        | Yes            | Asymptomatic      | -            | Ambulant   | 43                | No              | 801      |
| 2  | 2      | dup 3-43             | Yes            | Mild              | 57           | Ambulant   | 58                | No              | 128      |
| 3  | 3      | del 51               | Yes            | Severe            | 8            | 43         | 57                | No              | 128      |
| 4  | 4      | del 44               | No             | Intermediate      | 58           | Ambulant   | 59                | No              | 322      |
| 5  | 5      | dup 28-43            | No             | Severe            | 35           | Ambulant   | 66                | Yes             | 773      |
| 6  | 6      | c.2548G>T            | Yes            | Asymptomatic      | -            | Ambulant   | 45                | No              | 105      |
| 7  | 7      | c.2302C>T            | Yes            | Severe            | 50           | Ambulant   | 74                | No              | 1162     |
| 8  | 8      | c.2656C>T            | Yes            | Asymptomatic      | -            | Ambulant   | 34                | No              | 1168     |
| 9  | 9      | del 10-21            | Yes            | Intermediate      | 8            | Ambulant   | 32                | No              | 499      |
| 10 | 10     | c.7222_7223del       | Yes            | Intermediate      | 69           | Ambulant   | 80                | Yes             | 674      |
| 11 | 11     | c.2548G>T            | Yes            | Intermediate      | 45           | Ambulant   | 68                | Yes             | 256      |
| 12 | 12     | del 8-43             | Yes            | Asymptomatic      | -            | Ambulant   | 32                | No              | 125      |
| 13 | 13     | c.2555-2556delG      | Yes            | Asymptomatic      | -            | Ambulant   | 44                | No              | 231      |
| 14 | 14     | c.2285A>C; c.4495C>T | Yes            | Asymptomatic      | -            | Ambulant   | 34                | NA              | 265      |
| 15 | 15     | c.8879G>A            | Yes            | Mild              | 46           | Ambulant   | 46                | No              | 316      |
| 16 | 16     | c.6805C>T            | Yes            | Asymptomatic      | -            | Ambulant   | 55                | Yes             | 700      |

|    |    |             |     |              |    |          |     |     |      |
|----|----|-------------|-----|--------------|----|----------|-----|-----|------|
| 17 | 17 | del 52      | Yes | Asymptomatic | -  | Ambulant | 39  | No  | 248  |
| 18 | 18 | c.1990C>T   | Yes | Asymptomatic | -  | Ambulant | 39  | No  | 189  |
| 19 | 19 | del 49-52   | No  | Asymptomatic | -  | Ambulant | 43  | No  | 1098 |
| 20 | 20 | del 8-9     | Yes | Asymptomatic | -  | Ambulant | 50  | No  | 189  |
| 21 | 21 | dup 6-7     | Yes | Mild         | 55 | Ambulant | 55  | Yes | 320  |
| 22 | 22 | del 44-47   | Yes | Asymptomatic | -  | Ambulant | 44  | No  | 159  |
| 23 | 23 | c.9685delT  | Yes | Asymptomatic | -  | Ambulant | 52  | No  | NA   |
| 24 | 24 | dup 3-7     | No  | Asymptomatic | -  | Ambulant | 31  | No  | 3740 |
| 25 | 25 | c.3151C>T   | Yes | Asymptomatic | -  | Ambulant | 48  | No  | 166  |
| 26 | 26 | del 61-63   | Yes | Asymptomatic | -  | Ambulant | 53  | NA  | NA   |
| 27 | 27 | del 49-54   | Yes | Severe       | 38 | Ambulant | 65# | Yes | 552  |
| 28 | 28 | del 49-50   | Yes | Mild         | 59 | Ambulant | 64  | No  | 80   |
| 29 | 28 | del 49-50   | Yes | Severe       | 27 | Ambulant | 57  | Yes | 1095 |
| 30 | 28 | del 49-50   | Yes | Asymptomatic | -  | Ambulant | 37  | No  | 211  |
| 31 | 29 | del 45-52   | Yes | Mild         | 48 | Ambulant | 56  | Yes | 121  |
| 32 | 30 | c.1150-1G>T | Yes | Asymptomatic | -  | Ambulant | 41  | No  | NA   |
| 33 | 31 | c.2168+1G>A | Yes | Asymptomatic | -  | Ambulant | 49  | No  | 120  |
| 34 | 32 | c.6591delA  | No  | Mild         | 20 | Ambulant | 28  | No  | 5096 |
| 35 | 33 | c.1507G>T   | No  | Severe       | 32 | Ambulant | 56  | No  | 1800 |
| 36 | 34 | del 46-55   | Yes | Severe       | 40 | Ambulant | 61  | No  | 1340 |

|           |    |                                |     |              |    |          |    |     |      |
|-----------|----|--------------------------------|-----|--------------|----|----------|----|-----|------|
| <b>37</b> | 35 | del 10-11                      | No  | Asymptomatic | -  | Ambulant | 21 | No  | 657  |
| <b>38</b> | 36 | 15 Mb inversion in g<br>Xp21.1 | Yes | Asymptomatic | -  | Ambulant | 47 | No  | 400  |
| <b>39</b> | 37 | dup 51-67                      | Yes | Mild         | 23 | Ambulant | 25 | No  | 317  |
| <b>40</b> | 27 | del 49-54                      | Yes | Asymptomatic | -  | Ambulant | 46 | No  | 165  |
| <b>41</b> | 38 | c.7310-19A>G                   | No  | Asymptomatic | -  | Ambulant | 14 | No  | 5316 |
| <b>42</b> | 39 | del Dp427m-47                  | Yes | Asymptomatic | -  | Ambulant | 45 | NA  | 132  |
| <b>43</b> | 33 | c.1507G>T                      | Yes | Asymptomatic | -  | Ambulant | 23 | NA  | 2400 |
| <b>44</b> | 40 | c.358-2A>G                     | Yes | Asymptomatic | -  | Ambulant | 56 | No  | 704  |
| <b>45</b> | 41 | del 45-50                      | No  | Intermediate | 35 | Ambulant | 45 | No  | 4512 |
| <b>46</b> | 42 | c.2950-2A>C                    | Yes | Asymptomatic | -  | Ambulant | 32 | No  | 210  |
| <b>47</b> | 37 | dup 51-67                      | Yes | Intermediate | 43 | Ambulant | 63 | Yes | 1255 |

LoA: loss of ambulation; NA: not available; del: deletion; dup: duplication.

Table S2. Clinical features in females with dystrophinopathy (manifesting DMD carriers).

| ID | Clinical severity | Age at onset | Symptoms at onset                                         | Age at LoA | Age at last visit | Muscle hypotrophy or hypertrophy                   | Gowers' manoeuvre | Macroglossia | Muscle weakness pattern              | Right iliopsoas | Left iliopsoas | Right gluteus maximus | Left gluteus maximus | Right quadriceps | Left quadriceps | Right deltoid | Left deltoid |
|----|-------------------|--------------|-----------------------------------------------------------|------------|-------------------|----------------------------------------------------|-------------------|--------------|--------------------------------------|-----------------|----------------|-----------------------|----------------------|------------------|-----------------|---------------|--------------|
| 2  | Mild              | 57           | Myalgia, mild proximal muscle weakness in the lower limbs | Ambulant   | 58                | No                                                 | No                | No           | Proximal; axial                      | 5/5             | 5/5            | 4+/5                  | 4+/5                 | 5/5              | 5/5             | 5/5           | 5/5          |
| 3  | Severe            | 8            | Difficulty in running                                     | 43         | 57                | Global muscle hypotrophy but mild calf hypertrophy | Unable to rise    | No           | Proximal> distal; axial              | 2/5             | 2/5            | 2/5                   | 2/5                  | 2/5              | 2/5             | 2/5           | 2/5          |
| 4  | Intermediate      | 58           | Myalgia, fatigue                                          | Ambulant   | 59                | Mild left calf hypertrophy                         | No                | No           | Proximal; Axial                      | 4/5             | 4/5            | 4/5                   | 4/5                  | 4/5              | 4/5             | 5/5           | 5/5          |
| 5  | Severe            | 35           | Proximal muscle weakness                                  | Ambulant   | 66                | No                                                 | Unable to rise    | No           | Asymmetric; Proximal > distal; axial | 5-/5            | 5/5            | 3-/5                  | 3-/5                 | 5/5              | 5-/5            | 4/5           | 5-/5         |
| 7  | Severe            | 50           | Difficulty in running                                     | Ambulant   | 74                | No                                                 | Yes               | No           | Proximal > distal; axial             | 4-/5            | 4-/5           | 2/5                   | 2/5                  | 3-/5             | 3-/5            | 5/5           | 5/5          |
| 9  | Intermediate      | 8            | Difficulty in running                                     | Ambulant   | 32                | Calf hypertrophy                                   | Yes               | No           | Proximal                             | 4/5             | 4/5            | 3/5                   | 3/5                  | 5-/5             | 5-/5            | 5-/5          | 5-/5         |
| 10 | Intermediate      | 69           | Difficulty in climbing stairs, myalgia                    | Ambulant   | 80                | Calf hypertrophy                                   | Unable to rise    | Yes          | Proximal > distal; axial             | 4+/5            | 4+/5           | 4-/5                  | 4-/5                 | 5/5              | 5/5             | 5/5           | 5/5          |
| 11 | Intermediate      | 45           | Proximal muscle weakness                                  | Ambulant   | 68                | Lower limb hypertrophy                             | Yes               | No           | Proximal>distal; axial               | 4-/5            | 4-/5           | 4-/5                  | 4-/5                 | 3/5              | 3/5             | 5/5           | 5/5          |
| 15 | Mild              | 46           | Myalgia, mild proximal muscle weakness in the lower limbs | Ambulant   | 46                | No                                                 | No                | No           | Axial; proximal                      | 5/5             | 5/5            | 5-/5                  | 5-/5                 | 5/5              | 5/5             | 5/5           | 5/5          |



|    |                  |    |                                                           |          |    |                                             |                |     |                                      |      |      |      |      |      |      |     |     |
|----|------------------|----|-----------------------------------------------------------|----------|----|---------------------------------------------|----------------|-----|--------------------------------------|------|------|------|------|------|------|-----|-----|
| 21 | Mild             | 55 | Proximal muscle weakness                                  | Ambulant | 55 | No                                          | No             | No  | Proximal                             | 5/5  | 5/5  | 4+/5 | 4+/5 | 5/5  | 5/5  | 5/5 | 5/5 |
| 27 | Severe           | 38 | Proximal muscle weakness                                  | Ambulant | 65 | Calf hypertrophy                            | Unable to rise | Yes | Asymmetric; proximal> distal; axial  | 3-/5 | 4-/5 | NA   | NA   | 3-/5 | 3-/5 | 2/5 | 2/5 |
| 28 | Mild             | 59 | Myalgia, mild proximal muscle weakness in the lower limbs | Ambulant | 64 | No                                          | Yes            | No  | Proximal                             | 5/5  | 5/5  | 4+/5 | 4+/5 | 5/5  | 5/5  | 5/5 | 5/5 |
| 29 | Severe           | 27 | Proximal muscle weakness                                  | Ambulant | 57 | No                                          | Unable to rise | Yes | Asymmetric; proximal=distal          | 4/5  | 3-/5 | 4+/5 | 3-/5 | 4+/5 | 2/5  | 4/5 | 4/5 |
| 31 | Mild             | 48 | Proximal muscle weakness                                  | Ambulant | 56 | No                                          | Yes            | No  | Proximal                             | 5/5  | 5/5  | 4+/5 | 4+/5 | 5/5  | 5/5  | 5/5 | 5/5 |
| 34 | Mild             | 20 | Difficulty in climbing stairs; frequent falls             | Ambulant | 28 | No                                          | No             | No  | Proximal                             | 5-/5 | 5-/5 | 5/5  | 5/5  | 5/5  | 5/5  | 5/5 | 5/5 |
| 35 | Severe           | 32 | Difficulty in climbing stairs                             | Ambulant | 56 | Calf hypertrophy                            | Unable to rise | Yes | Asymmetric; Proximal>distal          | 3/5  | 3/5  | 2/5  | 2/5  | 3-/5 | 4/5  | 4/5 | 4/5 |
| 36 | Severe           | 40 | Proximal muscle weakness                                  | Ambulant | 61 | Calf hypertrophy                            | Yes            | No  | Asymmetric; proximal                 | 4+/5 | 3+/5 | 3+/5 | 2/5  | 5/5  | 3-/5 | 5/5 | 5/5 |
| 39 | Mild             | 23 | Myalgia, mild proximal muscle weakness in the lower limbs | Ambulant | 25 | Calf hypertrophy                            | No             | No  | Proximal; axial                      | 4+/5 | 4+/5 | 4+/5 | 4+/5 | 5/5  | 5/5  | 5/5 | 5/5 |
| 45 | Intermedi<br>ate | 35 | Proximal muscle weakness                                  | Ambulant | 45 | Left arm hypotrophy, right calf hypertrophy | Yes            | No  | Asymmetric; distal > proximal; axial | 4/5  | 4+/5 | NA   | NA   | 5-/5 | 5-/5 | 4/5 | 4/5 |
| 47 | Intermedi<br>ate | 43 | Difficulty in jumping and running                         | Ambulant | 63 | Lower limb hypertrophy                      | Yes            | No  | Proximal lower limbs and axial       | 5/5  | 5/5  | 4-/5 | 4-/5 | 5/5  | 5/5  | 5/5 | 5/5 |

Table S3. Cardiac status in DMD heterozygous women.

| ID | Muscle weakness severity | EDV (ml/m <sup>2</sup> ) | EF % | WMA | Strain % | Age at cardiomyopathy onset | Cardiomyopathy | ECG                            | Conduction/Rhythm abnormalities                  | Heart failure symptoms | Cardiac therapy   |
|----|--------------------------|--------------------------|------|-----|----------|-----------------------------|----------------|--------------------------------|--------------------------------------------------|------------------------|-------------------|
| 1  | Asymptomatic             | 66                       | 57   | 0   | -16      | -                           | No             | Normal                         | No                                               | No                     | No                |
| 2  | Mild                     | 41                       | 61   | 0   | -19      | -                           | No             | Normal                         | No                                               | No                     | ACEi              |
| 3  | Severe                   | 50                       | 65   | NA  | NA       | -                           | No             | Normal                         | No                                               | No                     | No                |
| 4  | Intermediate             | 41                       | 56   | 0   | NA       | -                           | No             | Normal                         | No                                               | No                     | No                |
| 5  | Severe                   | 51                       | 49   | 1   | NA       | NA                          | Yes            | Left anterior fascicular block | Left anterior fascicular block                   | No                     | BB, ARB, diuretic |
| 6  | Asymptomatic             | 56                       | 61   | 0   | -20      | -                           | No             | Normal                         | Incomplete right bundle branch block             | No                     | No                |
| 7  | Severe                   | 50                       | 57   | 0   | NA       | -                           | No             | Normal                         | No                                               | No                     | ACEi              |
| 8  | Asymptomatic             | 50                       | 60   | 0   | NA       | -                           | No             | Normal                         | No                                               | No                     | No                |
| 9  | Intermediate             | 51                       | 64   | 0   | -19      | -                           | No             | Normal                         | No                                               | No                     | No                |
| 10 | Intermediate             | 80                       | 56   | 1   | NA       | 74                          | Yes            | Normal                         | Supraventricular and ventricular ectopic beats   | No                     | ACEi, diuretic    |
| 11 | Intermediate             | 54                       | 52   | 1   | -16      | NA                          | Yes            | Normal                         | No                                               | No                     | ACEi              |
| 12 | Asymptomatic             | 60                       | 58   | 0   | -20      | -                           | No             | Normal                         | No                                               | No                     | No                |
| 13 | Asymptomatic             | 57                       | 56   | 0   | -17.4    | -                           | No             | Normal                         | No                                               | No                     | No                |
| 14 | Asymptomatic             | 44                       | 71   | 0   | NA       | -                           | No             | Normal                         | No                                               | No                     | No                |
| 15 | Mild                     | 41                       | 61   | 0   | NA       | -                           | No             | Normal                         | No                                               | No                     | No                |
| 16 | Asymptomatic             | 86                       | 45   | 1   | NA       | 32                          | Yes            | Normal                         | Episode of VT                                    | No                     | BB, ACEi, ASA     |
| 17 | Asymptomatic             | 50                       | 67   | 0   | -20      | -                           | No             | Normal                         | No                                               | No                     | No                |
| 18 | Asymptomatic             | 57                       | 53   | 0   | -18      | -                           | No             | Normal                         | No                                               | No                     | No                |
| 19 | Asymptomatic             | NA                       | 68   | NA  | NA       | -                           | No             | NA                             | NA                                               | No                     | No                |
| 20 | Asymptomatic             | 49                       | 64   | 0   | -20      | -                           | No             | Normal                         | No                                               | No                     | No                |
| 21 | Mild                     | 65                       | 38   | 1   | NA       | 40                          | Yes            | Normal                         | Implantable cardiac defibrillator at 52 years of | Yes                    | BB, ACEi          |

[illegible]

|    |              |    |    |    |    |    |     |        |                                       |    |          |
|----|--------------|----|----|----|----|----|-----|--------|---------------------------------------|----|----------|
| 44 | Asymptomatic | 42 | 70 | 0  | NA | -  | No  | Normal | No                                    | No | No       |
| 45 | Intermediate | 42 | 69 | 0  | NA | .  | No  | Normal | No                                    | No | No       |
| 46 | Asymptomatic | 60 | 60 | NA | NA | -  | No  | Normal | Ventricular<br>ectopic beats          | No | No       |
| 47 | Intermediate | 49 | 45 | 1  | NA | 54 | Yes | Normal | Supraventricu<br>lar ectopic<br>beats | No | BB, ACEi |

*ACEi: ACE inhibitors; AFB: anterior fascicular block; ARB: angiotensin receptor blockers; ASA: acetylsalicylic acid; BB: beta blockers; CCB: calcium channel blockers; ECG: electrocardiogram; NA: not available. sVT: sustained ventricular tachycardia. WMA: wall motion alterations (0 no, 1 yes).*

*Table S4. Dystrophin protein expression and XCI pattern in DMD heterozygous women; age at muscle biopsy (years) and age at blood collection for XCI assessment (years) are reported. NA: patients with unknown percentage of dystrophin negative fibers, dystrophin amount. Homozygote refers to the inability to establish XCI phase due to equal number of CAG repeats in the first exon of the AR gene.*

| ID | MUTATION(S)          | PERCENT OF DYSTROPHIN NEGATIVE FIBRES | DYSTROPHIN AMOUNT (% OF NORMAL) | X-INACTIVATION | AGE AT MUSCLE BIOPSY | AGE AT BLOOD COLLECTION FOR XCI ASSESSMENT |
|----|----------------------|---------------------------------------|---------------------------------|----------------|----------------------|--------------------------------------------|
| 1  | del Dp427c-45        | NA                                    | NA                              | 78             | -                    | 44                                         |
| 2  | dup 3-43             | NA                                    | NA                              | 79             | -                    | 57                                         |
| 3  | del 51               | NA                                    | NA                              | 77             | -                    | 57                                         |
| 4  | del 44               | NA                                    | NA                              | Homozygote     | -                    | -                                          |
| 5  | dup 28-43            | NA                                    | NA                              | 80             | -                    | 67                                         |
| 6  | c.2548G>T            | NA                                    | NA                              | 91             | -                    | 45                                         |
| 7  | c.2302C>T            | 10                                    | 49                              | Homozygote     | 55                   | -                                          |
| 8  | c.2656C>T            | 11                                    | 62                              | 89             | 36                   | 35                                         |
| 9  | del 10-21            | 18                                    | 27                              | 92             | 2                    | 32                                         |
| 10 | c.7222_7223del       | 5                                     | 50                              | 63             | 69                   | 74                                         |
| 11 | c.2548G>T            | NA                                    | NA                              | 61             | -                    | 66                                         |
| 12 | del 8-43             | NA                                    | NA                              | 52             | -                    | 32                                         |
| 13 | c.2555-2556delG      | NA                                    | NA                              | 90             | -                    | 44                                         |
| 14 | c.2285A>C; c.4495C>T | NA                                    | NA                              | 75             | -                    | 34                                         |
| 15 | c.8879G>A            | NA                                    | NA                              | 54             | -                    | 45                                         |
| 16 | c.6805C>T            | NA                                    | NA                              | 52             | -                    | 45                                         |
| 17 | del 52               | NA                                    | NA                              | 71             | -                    | 39                                         |
| 18 | c.1990C>T            | NA                                    | NA                              | 74             | -                    | 40                                         |
| 19 | del 49-52            | NA                                    | NA                              | 99             | -                    | 40                                         |
| 20 | del 8-9              | NA                                    | NA                              | 61             | -                    | 50                                         |
| 21 | dup 6-7              | 2                                     | 45                              | 64             | 28                   | 55                                         |
| 22 | del 44-47            | NA                                    | NA                              | 78             | -                    | 44                                         |
| 23 | c.9685delT           | NA                                    | NA                              | 61             | -                    | 51                                         |
| 24 | dup 3-7              | NA                                    | 39                              | Homozygote     | 3                    | -                                          |
| 25 | c.3151C>T            | NA                                    | NA                              | 81             | -                    | 44                                         |
| 26 | del 61-63            | NA                                    | NA                              | 73             | -                    | 49                                         |
| 27 | del 49-54            | 10                                    | 91                              | 100            | 38                   | 55                                         |
| 28 | del 49-50            | NA                                    | NA                              | 62             | -                    | 64                                         |
| 29 | del 49-50            | NA                                    | 6                               | 100            | 30                   | 56                                         |
| 30 | del 49-50            | NA                                    | NA                              | 51             | -                    | 37                                         |
| 31 | del 45-52            | NA                                    | NA                              | 70             | -                    | 56                                         |
| 32 | c.1150-1G>T          | NA                                    | NA                              | 52             | -                    | 35                                         |
| 33 | c.2168+1G>A          | NA                                    | NA                              | 84             | -                    | 49                                         |

|           |                             |    |    |            |    |    |
|-----------|-----------------------------|----|----|------------|----|----|
| <b>34</b> | c.6591delA                  | NA | NA | 51         | -  | 20 |
| <b>35</b> | c.1507G>T                   | 14 | 40 | 95         | 36 | 53 |
| <b>36</b> | del 46-55                   | NA | NA | 56         | -  | 59 |
| <b>37</b> | del 10-11                   | 8  | 50 | Homozygote | 8  | -  |
| <b>38</b> | 15 Mb inversion in g Xp21.1 | 15 | 49 | 77         | 47 | 47 |
| <b>39</b> | dup 51-67                   | NA | NA | 54         | -  | 22 |
| <b>40</b> | del 49-54                   | NA | NA | 51         | -  | 46 |
| <b>41</b> | c.7310-19A>G                | NA | 27 | 90         | 4  | 5  |
| <b>42</b> | del Dp427m-47               | NA | NA | Homozygote | -  | -  |
| <b>43</b> | c.1507G>T                   | 12 | 68 | 62         | 4  | 21 |
| <b>44</b> | c.358-2A>G                  | NA | NA | Homozygote | -  | -  |
| <b>45</b> | del 45-50                   | 99 | 0  | 97         | 16 | 50 |
| <b>46</b> | c.2950-2A>C                 | NA | NA | Homozygote | -  | -  |
| <b>47</b> | dup 51-67                   | 98 | 8  | 88         | 43 | 59 |