**Supplementary Materials: Marfan Syndrome Versus Bicuspid Aortic Valve Disease: Comparative Analysis Of Obstetric Outcome And Pregnancy-Associated Immediate And Long-Term Aortic Complications**

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Table S1. Baseline characteristics in women with Marfan syndrome (MFS) and with bicuspid aortic valve disease (BAV) according to pregnancy history.

| Variable                                    | MFS (N = 83) | BAV (N = 30) |
|---------------------------------------------|--------------|--------------|
|                                             | Ever-Pregnant | Never-Pregnant | Ever-Pregnant | Never-Pregnant |
| Number of individuals                       | 46           | 37           | 23           | 7             |
| Age at initial contact (years)              | 45 ± 12      | 32 ± 12      | <0.001       | 46 ± 16       | 27 ± 3     | 0.003 |
| Age at diagnosis (years)                    | 35 ± 13      | 20 ± 15      | <0.001       | 36 ± 24       | 19 ± 10   | 0.111 |
| Body height (cm)                            | 179 ± 8      | 180 ± 7      | 0.177        | 166 ± 8       | 171 ± 7   | 0.169 |
| Body weight (kg)                            | 78 ± 18      | 70 ± 12      | 0.024        | 67 ± 14       | 63 ± 9    | 0.712 |
| BMI (kg/m²)                                 | 24 ± 6       | 22 ± 3       | 0.008        | 24 ± 4        | 22 ± 3    | 0.135 |
| BSA (m²)                                    | 2.0 ± 0.2    | 1.9 ± 0.2    | 0.084        | 1.7 ± 0.2     | 1.7 ± 0.1 | 0.941 |
| Total cholesterol (mg/dl)                   | 199 ± 40     | 180 ± 28     | 0.048        | 202 ± 40      | 164 ± 22  | 0.032 |
| HDL cholesterol (mg/dl)                     | 63 ± 17      | 60 ± 15      | 0.453        | 71 ± 21       | 61 ± 13   | 0.130 |
| LDL cholesterol (mg/dl)                     | 109 ± 36     | 95 ± 24      | 0.055        | 107 ± 29      | 86 ± 22   | 0.095 |
| Systolic blood pressure (mm Hg)             | 128 ± 19     | 125 ± 18     | 0.611        | 128 ± 23      | 122 ± 4   | 0.622 |
| Diastolic blood pressure (mm Hg)            | 76 ± 11      | 72 ± 11      | 0.163        | 79 ± 11       | 75 ± 4    | 0.312 |
| BAB medication                              | 25 (54%)     | 19 (51%)     | 0.786        | 12 (52%)      | 1 (14%)   | 0.104 |
| ACEi or ARB medication                       | 24 (52%)     | 14 (38%)     | 0.193        | 5 (22%)       | 0         | 0.304 |
| Anticoagulation                             | 7 (15%)      | 6 (16%)      | 0.901        | 4 (17%)       | 1 (14%)   | 1.000 |
| Aortic root diameter (cm¹)                  | 3.7 ± 0.7    | 3.3 ± 0.4    | 0.060        | 3.3 ± 0.6     | 3.0 ± 0.7 | 0.243 |
| Aortic root Z-score (Devereux)¹             | 1.8 ± 2.8    | 1.1 ± 1.6    | 0.692        | 1.0 ± 2.3     | 0.2 ± 2.6 | 0.289 |
| Diameter of ascending aorta (cm¹)           | 2.9 ± 0.6    | 2.7 ± 1.4    | 0.002        | 3.7 ± 0.9     | 3.2 ± 0.5 | 0.061 |
| Diameter of descending aorta (cm¹)          | 2.6 ± 1.1    | 2.0 ± 0.5    | 0.001        | 2.0 ± 0.5     | 1.8 ± 0.3 | 0.550 |
| Diameter of abdominal aorta (cm¹)           | 2.3 ± 0.9    | 1.7 ± 0.5    | 0.002        | 1.8 ± 0.3     | 1.4 ± 0.2 | 0.074 |
| Ghent-2 systemic score (points)             | 6.7 ± 3.2    | 6.9 ± 3.3    | 0.771        |               |           |       |
| Ectopia lentis                              | 23 (53%)     | 15 (44%)     | 0.414        |               |           |       |
| Family history of disease                   | 33 (72%)     | 19 (51%)     | 0.056        | 2 (9%)        | 0         | 1.000 |
| Family history of sudden death              | 21 (47%)     | 17 (56%)     | 0.948        | 3 (14%)       | 1 (14%)   | 1.000 |
ACEi, angiotensin-converting enzyme inhibitors; ARB, angiotensin receptor blockers; AVR, aortic valve regurgitation; AVS, aortic valve stenosis; BAB, beta-adrenergic blockers; BMI, body mass index; BSA, body surface area; HDL, high-density lipoprotein; LDL, low-density lipoprotein; MV, mitral valve; MVP, mitral valve prolapse; MVR, mitral valve regurgitation; N, number of individuals; TVR, tricuspid valve regurgitation. If less than total, we present the number of individuals with available information behind a slash. 1 Diameters of aortic segments were obtained at initial presentation only in those with native vessels at time of measurement.

**Table S2.** Aortic dissection in women with Marfan syndrome (MFS) and with bicuspid aortic valve disease (BAV) according to pregnancy history prior to event.

| Outcome Variable | MFS (N = 81) | BAV (N = 30) |
|------------------|--------------|--------------|
|                  | Ever-Pregnant | Never-Pregnant | p | Ever-Pregnant | Never-Pregnant | p |
| Number of individuals | 43 | 38 | 23 | 7 |
| Age at final contact (years) | 52 ± 12 | 38 ± 12 | <0.001 | 50 ± 16 | 30 ± 4 | 0.002 |
| Number of dissections | 9 (21%) | 7 (18%) | 1.000 | 0 | 0 |
| Dissection by age (years) | 46 ± 9 | 33 ± 8 | 0.011 |
| Type according to Stanford | Type A | 4 (44%) | 3 (43%) | 1.000 | 0 | 0 |
|                     | Type B | 5 (56%) | 4 (57%) | 0 | 0 |

N identifies number of individuals. 1 Two women in the MFS group with aortic dissection during pregnancy were excluded from long-term analysis. 2 One ever-pregnant individual with MFS had no pregnancy prior to event of dissection and was therefore categorized as being never-pregnant.

**Table S3.** Aortic dissection in 81 individuals with Marfan syndrome (MFS)1.

| Aortic Dissection | Absent (N = 65) | Present (N = 16) | Hazard Ratio | Lower 95% CI | Upper 95% CI | p |
|-------------------|-----------------|-----------------|--------------|--------------|--------------|---|
| Age at diagnosis (years) | 28 ± 17 | 31 ± 13 | 0.979 | 0.948 | 1.012 | 0.212 |
| Previous pregnancy | 34 (52%) | 9 (56%) | 0.491 | 0.177 | 1.358 | 0.171 |
| BMI (kg/m²) | 23 ± 4 | 25 ± 7 | 1.035 | 0.951 | 1.127 | 0.429 |
| BSA (m²) | 1.9 ± 0.2 | 2.0 ± 0.2 | 4.279 | 0.446 | 41.046 | 0.208 |
| Total cholesterol (mg/dl) | 190 ± 38 | 193 ± 32 | 0.994 | 0.981 | 1.008 | 0.414 |
| HDL cholesterol (mg/dl) | 62 ± 16 | 59 ± 19 | 0.985 | 0.954 | 1.016 | 0.341 |
| LDL cholesterol (mg/dl) | 104 ± 33 | 100 ± 27 | 0.992 | 0.978 | 1.007 | 0.289 |
|-------------------------|----------|----------|--------|--------|--------|--------|
| Systolic blood pressure (mm Hg) | 123 ± 16 | 144 ± 20 | 1.036 | 1.011 | 1.062 | 0.005 |
| Diastolic blood pressure (mm Hg) | 74 ± 11 | 78 ± 11 | 1.016 | 0.969 | 1.065 | 0.509 |
| BAB medication | 29 (45%) | 14 (88%) | 4.411 | 0.998 | 19.491 | 0.050 |
| ACEi or ARB medication | 24 (37%) | 13 (81%) | 4.805 | 1.367 | 16.889 | 0.014 |
| Ghent-2 systemic score (points) | 6.8 ± 3.2 | 6.5 ± 3.2 | 0.986 | 0.850 | 1.145 | 0.857 |
| Family history of disease | 43 (66%) | 8 (50%) | 0.670 | 0.247 | 1.812 | 0.430 |
| Family history of sudden death | 27 (42%) | 10 (63%) | 1.656 | 0.600 | 4.566 | 0.330 |
| Family history of aortopathy | 27 (42%) | 7 (44%) | 1.404 | 0.519 | 3.800 | 0.504 |
| MV regurgitation | 31/61 (51%) | 11/15 (73%) | 2.219 | 0.700 | 7.033 | 0.176 |
| MV prolapse | 30/63 (48%) | 4/15 (27%) | 0.580 | 0.184 | 1.825 | 0.351 |
| AV regurgitation | 17/61 (28%) | 8/15 (53%) | 1.758 | 0.637 | 4.856 | 0.276 |
| TV regurgitation | 46/61 (75%) | 10/15 (67%) | 1.047 | 0.356 | 3.078 | 0.933 |

**Multivariate Cox Regression Analysis**

| Hazard Ratio | Lower 95% CI | Upper 95% CI | p |
|--------------|--------------|--------------|---|
| Systolic blood pressure (mm Hg) | 1.037 | 1.010 | 1.064 | 0.006 |
| ACEi or ARB medication | 5.211 | 1.151 | 23.588 | 0.032 |

ACEi, angiotensin-converting enzyme inhibitors; ARB, angiotensin receptor blockers; AV, aortic valve; BAB, beta-adrenergic blockers; BMI, body mass index; BSA, body surface area; CI, confidence interval; HDL, high-density lipoprotein; LDL, low-density lipoprotein; MV, mitral valve; N, number of events; TV, tricuspid valve.

If less than total, we present the number of individuals with available information behind a slash. The two women in the MFS cohort with aortic dissection during pregnancy were excluded from long-term analysis.

**Table S4.** Proximal aortic surgery in women with Marfan syndrome (MFS) and with bicuspid aortic valve disease (BAV) according to pregnancy history prior to event.

| Outcome Variable | MFS (N = 81) | BAV (N = 30) |
|------------------|--------------|--------------|
|                  | Ever-Pregnant | Never-Pregnant | p  | Ever-Pregnant | Never-Pregnant | p  |
| Number of individuals | 41 | 40 | 23 | 7 | 0.002 |
| Age at final contact (years) | 53 ± 12 | 38 ± 12 | <0.001 | 50 ± 16 | 30 ± 4 | 0.548 |
| Number of proximal surgeries | 13 (32%) | 20 (50%) | 0.116 | 4 (17%) | 0 | 0 |
| Proximal surgery by age (years) | 44 ± 9 | 32 ± 9 | 0.001 | 59 ± 7 |  |  |
| **Proximal surgery by indication** |  |  |  |  |  |  |
| Prophylactic surgery | 9 (69%) | 17 (85%) | 0.393 | 4 (100%) | 0 | 0.548 |
| Urgent surgery | 4 (31%) | 3 (15%) | 0 | 0 | 0 | 0 |
| **Proximal surgery by technique** |  |  |  |  |  |  |
| Valve-sparing procedures | 8 (62%) | 16 (80%) | 1 (25%) | 0 |
Table S5. Proximal aortic surgery in 81 individuals with Marfan syndrome (MFS)1.

| Variable                          | Absent (N = 48) | Present (N = 33) | Hazard Ratio | Lower 95% CI | Upper 95% CI | p       |
|-----------------------------------|-----------------|-----------------|--------------|--------------|--------------|---------|
| Age at diagnosis (years)          | 28 ± 17         | 30 ± 15         | 1.007        | 0.985        | 1.029        | 0.555   |
| Previous pregnancy                | 28 (58%)        | 13 (39%)        | 0.203        | 0.096        | 0.431        | <0.001  |
| BMI (kg/m²)                       | 23 ± 4          | 24 ± 5          | 1.028        | 0.971        | 1.088        | 0.341   |
| BSA (m²)                          | 1.9 ± 0.2       | 1.9 ± 0.2       | 1.736        | 0.348        | 8.654        | 0.501   |
| Total cholesterol (mg/dl)         | 194 ± 37        | 185 ± 36        | 0.996        | 0.986        | 1.006        | 0.394   |
| HDL cholesterol (mg/dl)           | 61 ± 16         | 61 ± 14         | 1.002        | 0.980        | 1.024        | 0.876   |
| LDL cholesterol (mg/dl)           | 107 ± 33        | 98 ± 28         | 0.995        | 0.983        | 1.006        | 0.352   |
| Systolic blood pressure (mm Hg)   | 127 ± 16        | 127 ± 21        | 1.003        | 0.985        | 1.021        | 0.767   |
| Diastolic blood pressure (mm Hg)  | 74 ± 10         | 75 ± 12         | 1.011        | 0.978        | 1.046        | 0.508   |
| BAB medication                    | 26 (54%)        | 17 (52%)        | 0.993        | 0.501        | 1.970        | 0.984   |
| ACEi or ARB medication            | 23 (48%)        | 14 (42%)        | 0.855        | 0.428        | 1.706        | 0.657   |
| Aortic root diameter (cm)         | 3.4 ± 0.6       | 4.1 ± 0.5       | 2.544        | 1.072        | 6.035        | 0.034   |
| Aortic root Z-score               | 1.0 ± 2.1       | 4.3 ± 1.6       | 1.355        | 1.087        | 1.690        | 0.007   |
| Diameter of ascending aorta (cm)  | 2.8 ± 1.1       | 3.1 ± 0.9       | 1.274        | 0.477        | 3.403        | 0.629   |
| Diameter of descending aorta (cm) | 2.2 ± 1.1       | 2.6 ± 0.6       | 1.065        | 0.779        | 1.455        | 0.694   |
| Diameter of abdominal aorta (cm)  | 2.0 ± 0.8       | 2.2 ± 0.7       | 0.968        | 0.586        | 1.597        | 0.898   |
| Ghent-2 systemic score (points)   | 6.8 ± 3.3       | 6.7 ± 3.1       | 1.000        | 0.896        | 1.116        | 0.998   |
| Family history of disease         | 27 (56%)        | 24 (73%)        | 1.488        | 0.690        | 3.211        | 0.311   |
| Family history of sudden death    | 20 (43%)        | 17 (52%)        | 1.281        | 0.645        | 2.544        | 0.479   |
| Family history of aortopathy      | 21 (44%)        | 12 (36%)        | 0.713        | 0.350        | 1.451        | 0.350   |
| MV regurgitation                  | 28 (60%)        | 13 (45%)        | 0.624        | 0.300        | 1.300        | 0.208   |
| MV prolapse                       | 23 (49%)        | 11 (36%)        | 0.642        | 0.307        | 1.343        | 0.239   |
| AV regurgitation                  | 19 (40%)        | 7 (24%)         | 0.632        | 0.270        | 1.481        | 0.291   |
| TV regurgitation                  | 38 (81%)        | 18 (62%)        | 0.631        | 0.298        | 1.339        | 0.230   |

N identifies number of individuals. 1Two women in the MFS cohort with aortic dissection during pregnancy were excluded from long-term analysis. 2Three women with MFS had their first pregnancies after proximal aortic surgery had been performed and were therefore categorized as being never-pregnant.
ACEi, angiotensin-converting enzyme inhibitors; ARB, angiotensin receptor blockers; AV, aortic valve; BAB, beta-adrenergic blockers; BMI, body mass index; BSA, body surface area; CI, confidence interval; HDL, high-density lipoprotein; LDL, low-density lipoprotein; MV, mitral valve; N, number of events; TV, tricuspid valve.

If less than total, we present the number of individuals with available information behind a slash. ¹ Two women in the MFS cohort with aortic dissection during pregnancy were excluded from long-term analysis.

Table S6. Distal aortic repair in women with Marfan syndrome (MFS) and with bicuspid aortic valve disease (BAV) according to pregnancy history prior to event.

| Outcome Variable | MFS (N = 81)¹ | BAV (N = 30) | p   |
|------------------|--------------|--------------|-----|
|                  | Ever-Pregnant| Never-Pregnant|     |
|                  |             |              |     |
| Number of individuals | 44 | 37 | <0.001 |
| Number of distal repairs | 52 ± 12 | 38 ± 12 | 0.359 |
| Distal repair by age (years) | 52 ± 5 | 27 | |
| Distal repair by indication | | | |
| Elective procedure (true or false lumen expansion) | 2 (50%) | 0 | 1.000 |
| Urgent procedure (rupture/dissection) | 2 (50%) | 1 (100%) | 0 |
| Distal repair by technique | | | |
| Surgical | 2 (50%) | 0 | 1.000 |
| Endovascular | 2 (50%) | 1 (100%) | 0 |

N identifies number of events. ¹ Two women in the MFS group with aortic dissection during pregnancy were excluded from long-term analysis.

Table S7. Distal aortic repair in 81 individuals with Marfan syndrome (MFS)¹.

| Variable | Distal Aortic Repair | Univariate Cox Regression Analysis |
|----------|-----------------------|-----------------------------------|
|          | Absent (N = 76) | Present (N = 5) | Hazard Ratio | Lower 95% CI | Upper 95% CI | p     |
| Age at diagnosis (years) | 28 ± 16 | 36 ± 15 | 1.025 | 0.968 | 1.086 | 0.401 |
| Previous pregnancy | 37 (49%) | 4 (80%) | 1.269 | 0.134 | 12.016 | 0.835 |
| BMI (kg/m²) | 23 ± 5 | 24 ± 3 | 1.030 | 0.895 | 1.185 | 0.678 |
| BSA (m²) | 1.9 ± 0.2 | 2.0 ± 0.1 | 3.517 | 0.059 | 210.481 | 0.547 |
| Total cholesterol (mg/dl) | 189 ± 37 | 219 ± 22 | 1.021 | 0.997 | 1.045 | 0.091 |
| HDL cholesterol (mg/dl) | 60 ± 15 | 67 ± 20 | 1.031 | 0.972 | 1.094 | 0.310 |
| LDL cholesterol (mg/dl) | 102 ± 31 | 125 ± 30 | 1.019 | 0.994 | 1.044 | 0.131 |
| Systolic blood pressure (mm Hg) | 127 ± 19 | 131 ± 6 | 1.009 | 0.966 | 1.054 | 0.684 |
| Diastolic blood pressure (mm Hg) | 74 ± 11 | 74 ± 7 | 0.997 | 0.908 | 1.095 | 0.951 |
### Table S8. Long-term aortic growth in individuals with Marfan syndrome (MFS) and with bicuspid aortic valve disease (BAV).

#### Multiple regression analysis

| Aortic Segment | Variable                   | Estimate (mm) | Standard Error | p     |
|----------------|----------------------------|---------------|----------------|-------|
| Aortic root    | Baseline diameter (mm)     | -1.77         | 0.90           | 0.300 |
| (N = 51)       | Follow-up time (years)     | 0.64          | 0.19           | 0.002 |
|                | Presence of MFS            | 1.91          | 1.33           | 0.156 |
|                | Previous pregnancy         | -0.20         | 0.93           | 0.835 |
| Ascending aorta| Baseline diameter (mm)     | -2.13         | 1.01           | 0.040 |
| (N = 50)       | Follow-up time (years)     | 0.16          | 0.18           | 0.367 |
|                | Presence of MFS            | -3.72         | 1.41           | 0.012 |
|                | Previous pregnancy         | 0.57          | 0.86           | 0.514 |
|                      | Baseline diameter (mm) | Follow-up time (years) | Presence of MFS | Previous pregnancy |
|----------------------|------------------------|------------------------|-----------------|-------------------|
| **Descending aorta** |                        |                        |                 |                   |
| (N = 64)             | 0.56                   | 0.83                   | 0.01            | 0.75              |
|                      | (N = 64)               |                        |                 |                   |
| **Abdominal aorta**  | 1.74                   | 0.86                   | 0.74            | 1.26              |
| (N = 47)             |                        | 0.30                   | 3.02            | 0.832             |

N, number of individuals with available diameters.