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Soluble EMMPRIN levels discriminate aortic ectasia in Marfan syndrome patients

Erica Rurali et al.

Supplementary Materials

Table S1: Comparison of the clinical profile of eligible vs enrolled patients

Patients' profile		Eligible cohort	Enrolled cohort	*p value*
Sex	Male	16	16	0.828
	Female	29	26	
Age (yr)		36 [28-48]	35 [29-48]	0.882
Height (cm)		177.9±10.3	178.3±10.4	0.858
Weight (kg)		71.7±16.0	71.6±16.4	0.978
BSA (m^2)		1.88±0.22	1.88±0.22	0.977
Systemic score		9.3±3.3	9.3±3.3	0.996
MFS familial history	Yes	31	29	1.000
	No	14	13	
Skeletal manifestation	Yes	45	42	1.000
	No	0	0	
Ectopia lentis	Yes	19	16	0.827
	No	26	26	
Dural ectasia	Yes	25	24	1.000
	No	9	9	
Mitral valve prolapse	Yes	35	33	1.000
	No	8	7	
Aortic valve regurgitation	Yes	7	6	1.000
	No	38	36	
Aortic ectasia (Z-score≥2)	Yes	24	21	0.831
	No	21	21	
Antihypertensive treatment	BB	1	1	0.997
	ARB	13	12	
	BB+ARB	18	16	
	None	13	13	

Table S2: FBN1 mutations found in MFS patients

Patients' code	FBN1 mutation	Relatives
MFS#1	c.3509G>A, p.Arg1170His c.4190G>A, p.Gly1397Ala	/
MFS#2	IVS64+1G>A, splicing defect	/
MFS#3	c.3632_3634delTCT, p.Phe1211del	/
MFS#4	c.7754T>C, p.Ile2585Thr	MFS#5
MFS#5	c.7754T>C, p.Ile2585Thr	MFS#4
MFS#6	c.5060G>A, p.Cys1687Tyr	/
MFS#7	IVS37+1G>A, splicing defect	/
MFS#8	IVS41-2A>G, splicing defect	MFS#26
MFS#9	c.6988G>T, p.Glu2330Stop	/
MFS#10	c.7540G>A, p.Gly2514Arg	MFS#11
MFS#11	c.7540G>A, p.Gly2514Arg	MFS#10
MFS#12	c.1679G>A, p.Gly560Asp	/
MFS#13	c.7506C>G, p.Asn2502Lys	MFS#15
MFS#14	c.4400insC, frameshift	/
MFS#15	c.7506C>G, p.Asn2502Lys	MFS#13
MFS#16	c.2953G>A, p.Gly985Arg	/
MFS#17	c.4050_4051delinsAG, p.Cys1350Stop	/
MFS#18	IVS58+1G>C, splicing defect	/
MFS#19	c.5518C>T, p.Arg1840Cys	/
MFS#20	c.7240C>T, p.Arg2414Stop	/
MFS#21	IVS41-2A>G, splicing defect	/
MFS#22	c.670T>C, p.Cys224Arg	/
MFS#23	c.3973G>T, p.Glu1325Stop	/
MFS#24	c.7240C>T, p.Arg2414Stop	/
MFS#25	c.2941T>C, p.Cys981Arg	/
MFS#26	IVS41-2A>G, splicing defect	MFS#8
MFS#27	IVS40-1G>T, splicing defect	/
MFS#28	IVS21-1G>A, splicing defect	/
MFS#29	IVS41-2A>G, splicing defect	/
MFS#30	c.3058A>G, p.Thr1020Ala	/
MFS#31	IVS20+2T>G, splicing defect	MFS#32
MFS#32	IVS20+2T>G, splicing defect	MFS#31
MFS#33	c.1904A>G, p.Tyr635Cys	/
MFS#34	c.1665C>A, p.Cys555Stop	/
MFS#35	c.3373C>T, p.Arg1125Stop	/
MFS#36	c.7916A>G, p.Tyr2639Cys	/
MFS#37	c.7754T>C, p.Ile2585Thr	/
MFS#38	c.6169C>T, p.Arg2057Stop	/

MFS#39	IVS21-2A>G, splicing defect	/
MFS#40	c.8071C>A, p.Gly2691Ser	/
MFS#41	c.3506G>T, p.Gly1169Val	MFS#42
MFS#42	c.3506G>T, p.Gly1169Val	MFS#41

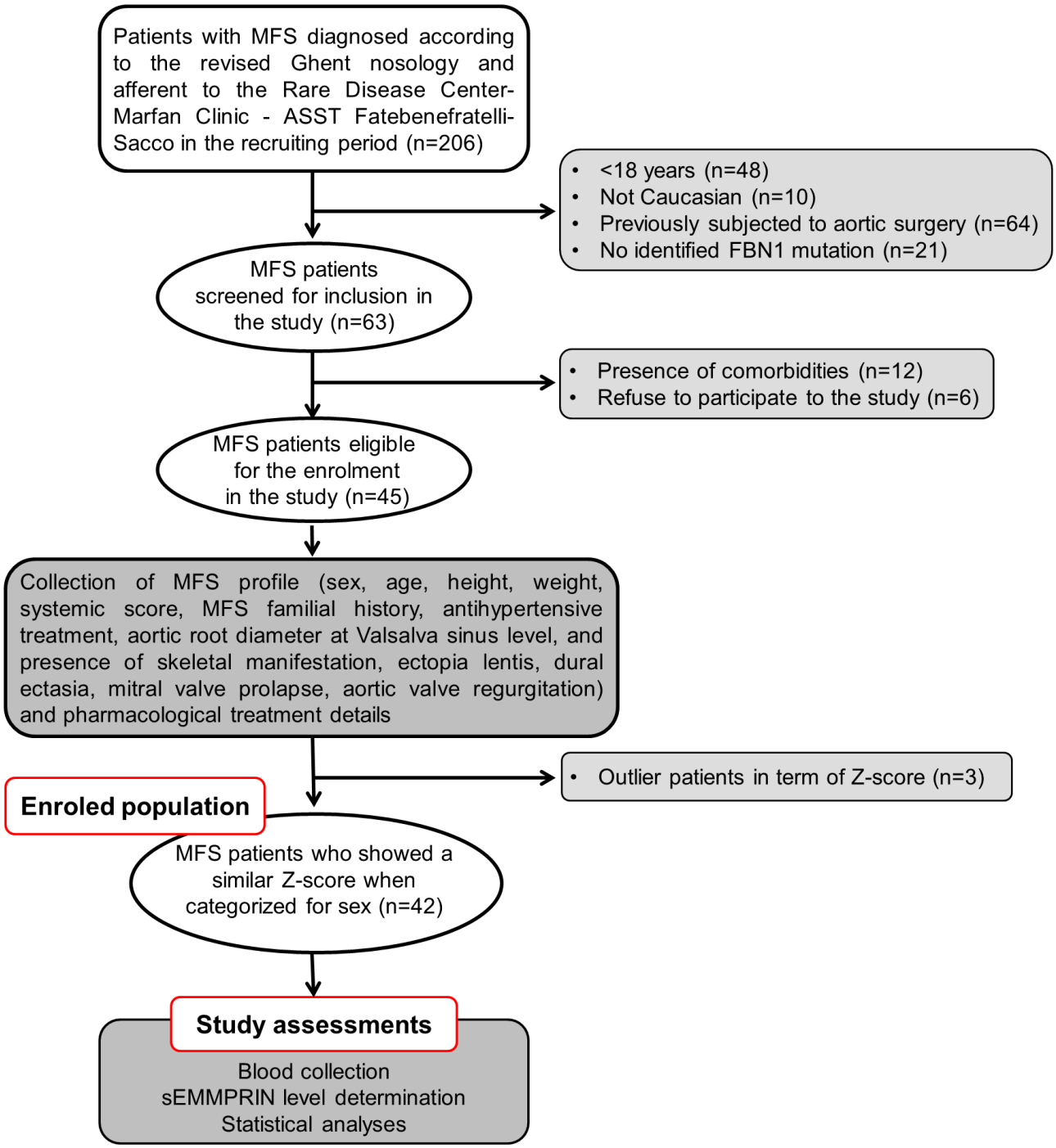


Figure S1: Patient recruitment and study flow-chart. MFS: Marfan Syndrome, FBN1: fibrillin 1.

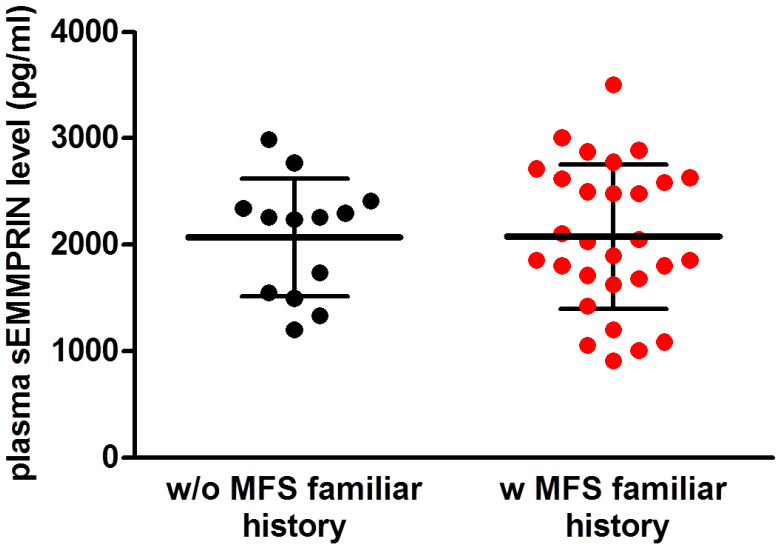


Figure S2: Differences in plasma sEMMPRIN levels in patients presenting or not a familial history of the disease. w/o: without, w: with.

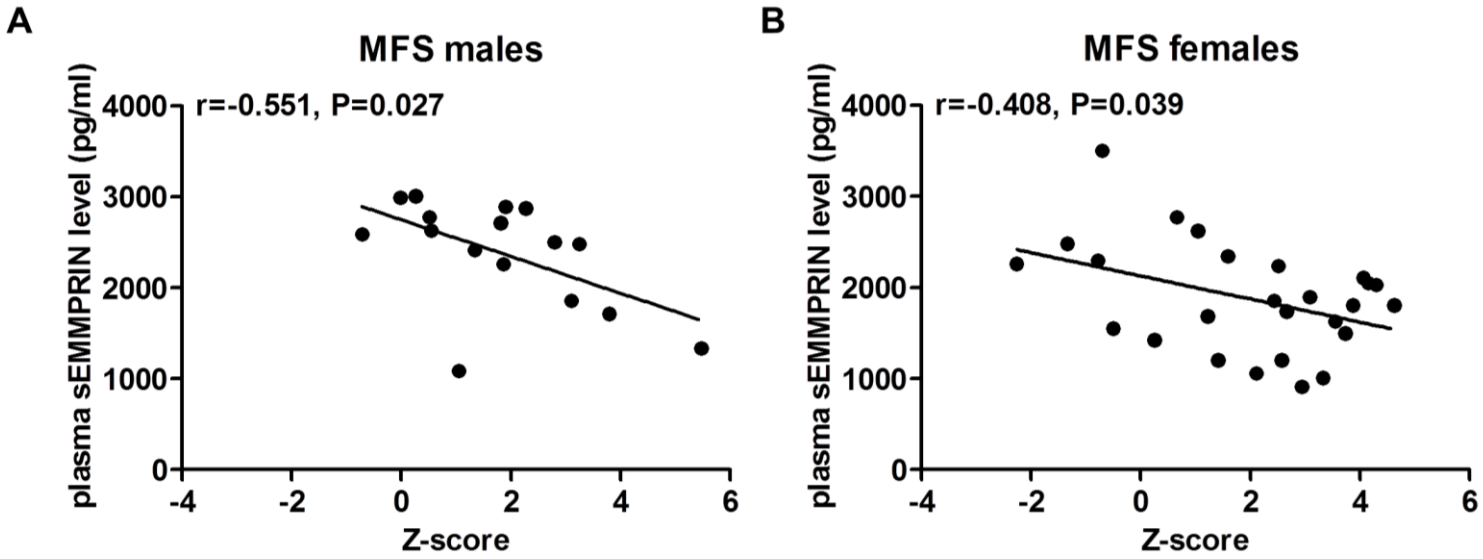
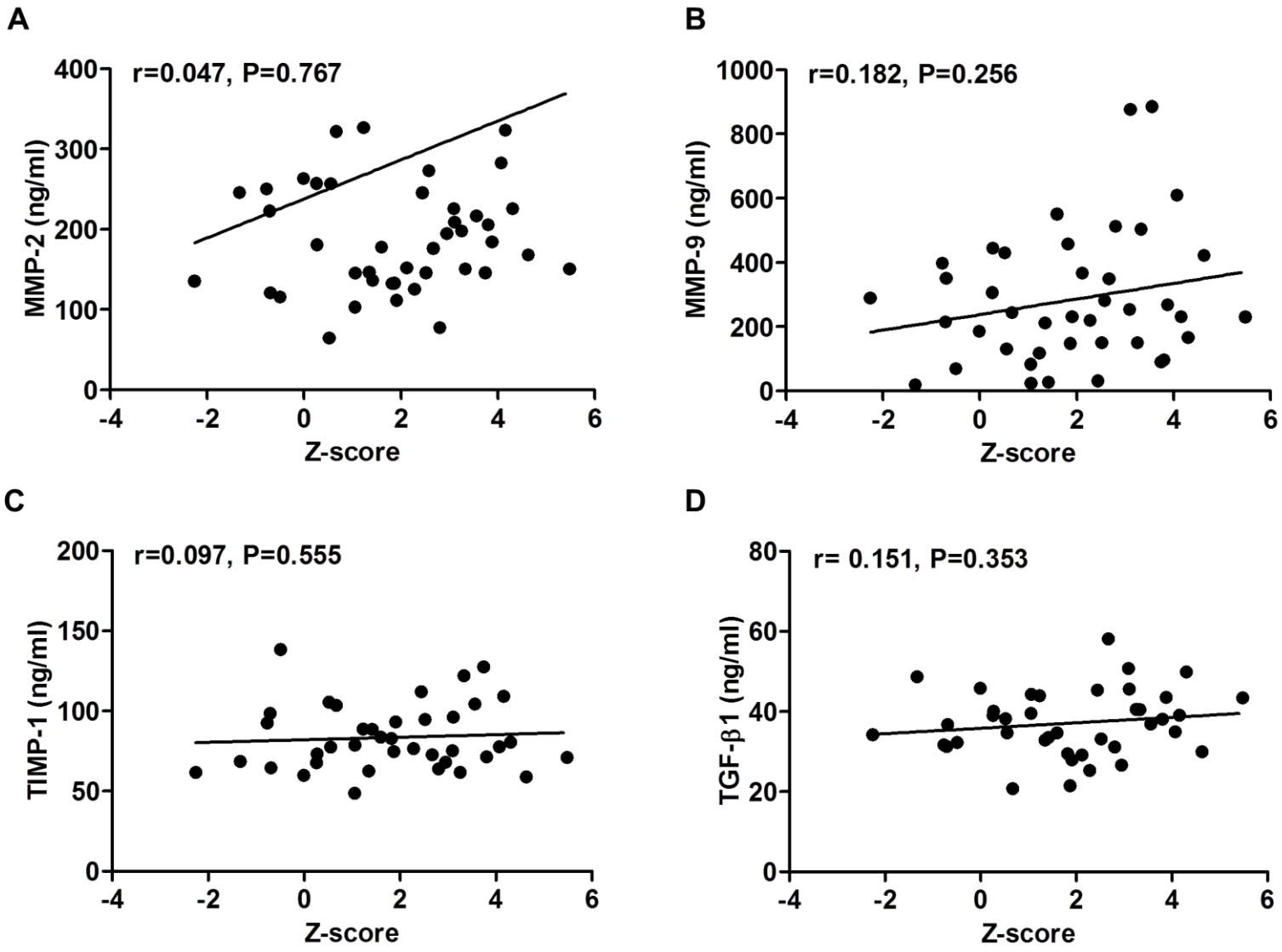
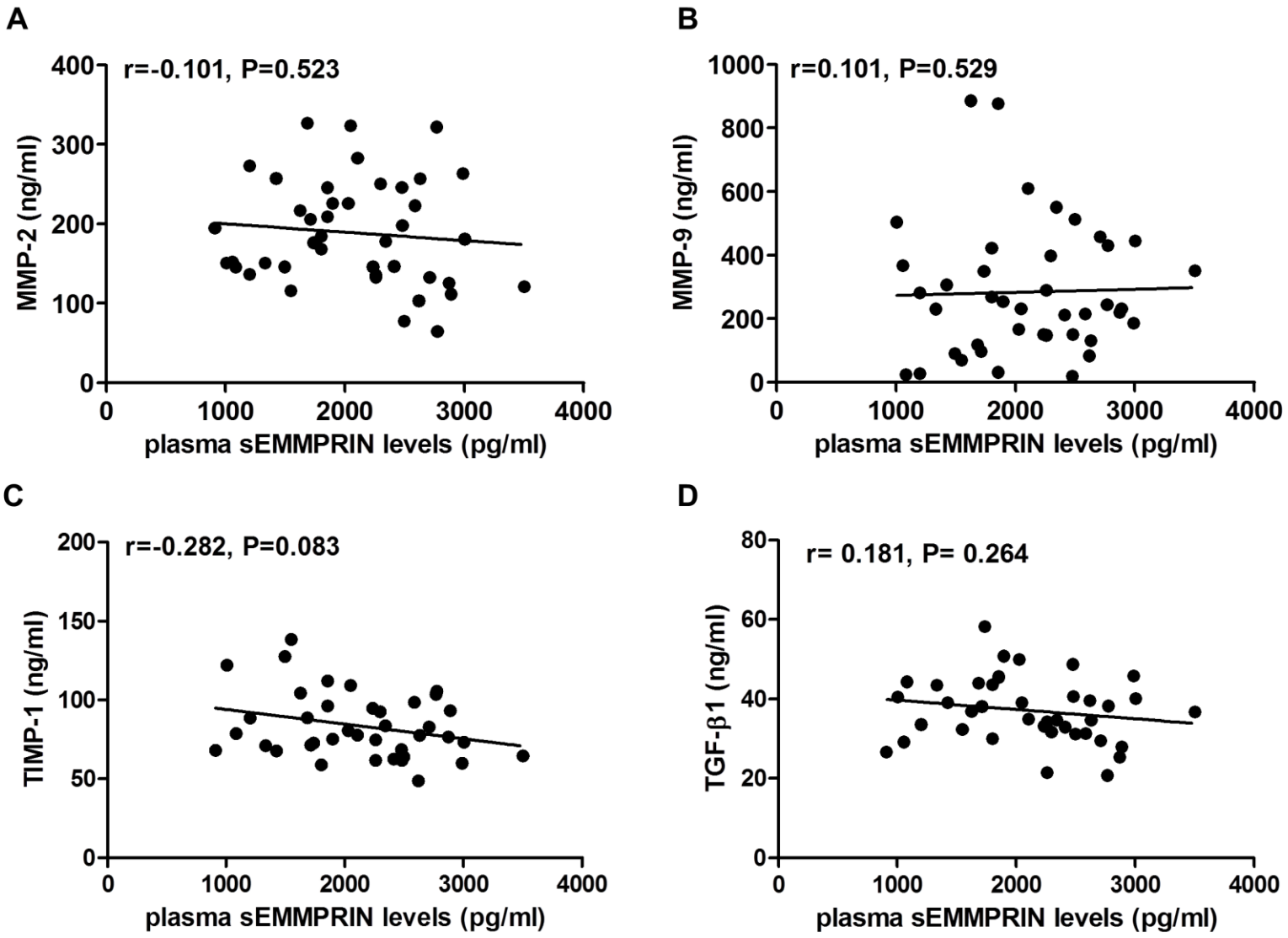


Figure S3: Correlation between plasma sEMMPRIN levels and Z-score in MFS patients categorised for sex. Graphic representation of the correlation between plasma sEMMPRIN levels and Z-score of MFS males (A) and females (B).


A
r=0.047, P=0.767
MMP-2 (ng/ml)
400
300
200
100
0
-4
-2
0
2
4
6
Z-score
B
r=0.182, P=0.256
MMP-9 (ng/ml)
1000
800
600
400
200
0
-4
-2
0
2
4
6
Z-score
C
r=0.097, P=0.555
TIMP-1 (ng/ml)
200
150
100
50
0
-4
-2
0
2
4
6
Z-score
D
r= 0.151, P=0.353
TGF-β1 (ng/ml)
80
60
40
20
0
-4
-2
0
2
4
6
Z-score

16

Figure S4: Correlation between Z-score and circulating biomarkers in MFS patients. Graphic representation of the correlation between Z-score and MMP-2 (A), MMP-9 (B), TIMP-1 (C) or TGF-β1 (D) in our MFS cohort. MMP: matrix metalloproteases; TGF-β1: transforming growth factor beta 1; TIMP: tissue inhibitor of metalloproteases.


A
r=-0.101, P=0.523
MMP-2 (ng/ml)
400
300
200
100
0
0
1000
2000
3000
4000
plasma sEMMPRIN levels (pg/ml)
B
r=0.101, P=0.529
MMP-9 (ng/ml)
1000
800
600
400
200
0
0
1000
2000
3000
4000
plasma sEMMPRIN levels (pg/ml)
C
r=-0.282, P=0.083
TIMP-1 (ng/ml)
200
150
100
50
0
0
1000
2000
3000
4000
plasma sEMMPRIN levels (pg/ml)
D
r= 0.181, P= 0.264
TGF-β1 (ng/ml)
80
60
40
20
0
0
1000
2000
3000
4000
plasma sEMMPRIN levels (pg/ml)

20

Figure S5: Correlation between plasma sEMMPRIN levels and circulating biomarkers in MFS patients. Graphic representation of the correlation between plasma sEMMPRIN levels and MMP-2 (A), MMP-9 (B), TIMP-1 (C) or TGF-β1 (D) in our MFS cohort. . MMP: matrix metalloproteases; TGFβ-1: transforming growth factor beta 1; TIMP: tissue inhibitor of metalloproteases.