Overview of the medical and research literature of Marfan Syndrome in 2016-2017

This is a short overview of what has been going on in the research field during the past year. This list is not exhaustive and does not include case reports (report concerning one single patient). If you want a more detailed summary and access to the article please visit Pubmed (https://www.ncbi.nlm.nih.gov/pubmed). If you have questions you can contact me at l.janssen@marfan.be and I'll do my best to help you.

Cardiology

- "***Valve-Sparing Root Replacement Compared With Composite Valve Graft Procedures in Patients With Aortic Root Dilation***. " *Ouzounian M, Rao V, Manlhiot C, Abraham N, David C, Feindel CM, David TE.* J Am Coll Cardiol. *2016 Oct 25;68(17):1838-1847.*
- ***"Abnormal heart rate recovery and deficient chronotropic response after submaximal exercise in young Marfan syndrome patients."*** *Peres P, Carvalho AC, Perez AB, Medeiros WM.* Cardiol Young. 2016 Oct;26(7):1274-81
- ***"Chronobiology of Acute Aortic Dissection in the Marfan Syndrome (from the National Registry of Genetically Triggered Thoracic Aortic Aneurysms and Cardiovascular Conditions and the International Registry of Acute Aortic Dissection)."*** *Siddiqi HK, Luminais SN, Montgomery D, Bossone E, Dietz H, Evangelista A, Isselbacher E, LeMaire S, Manfredini R, Milewicz D, Nienaber CA, Roman M, Sechtem U, Silberbach M, Eagle KA, Pyeritz RE; GenTAC and IRAD investigators.* Am J Cardiol. 2016 Dec 2. → Statistical analysis of 257 aortic dissection cases in Marfans between 1980 et 2012, showing an increased dissection rate in winter/spring (57%) and during the day (mean: 65 % ; men 74 % ; women 51 %).
- ***"Abdominal Aortic Aneurysm in Marfan Syndrome."*** *Hagerty T, Geraghty P, Braverman AC.* Ann Vasc Surg. 2016 Nov 25
- ***"Modelling and numerical simulation of the in vivo mechanical response of the ascending aortic aneurysm in Marfan syndrome".*** *García-Herrera CM, Celentano DJ, Herrera EA.* Med Biol Eng Comput. 2016 Jun 1 → this work aims at creating a mathematical model to evaluate various treatment methods.
- ***"Ambulatory (24 h) blood pressure and arterial stiffness measurement in Marfan syndrome patients: a case control feasibility and pilot study".*** *Hillebrand M, Nouri G, Hametner B, Parragh S, Köster J, Mortensen K, Schwarz A, von Kodolitsch Y, Wassertheurer S.* BMC Cardiovasc Disord. 2016 May 6;16:81.
- ***"Mild aerobic exercise blocks elastin fiber fragmentation and aortic dilatation in a mouse model of Marfan syndrome associated aortic aneurysm."*** *Gibson CP, Nielsen C, Alex R, Cooper K, Farney M, Gaufin D, Cui JZ, van Breemen C, Broderick TL, Vallejo-Elias J, Esfandiarei M.* J Appl Physiol (1985). 2017 Apr 6
- ***"A Novel Murine Model of Marfan Syndrome Accelerates Aortopathy and Cardiomyopathy."*** *Cavanaugh NB, Qian L, Westergaard NM, Kutschke WJ, Born EJ, Turek JW.* Ann Thorac Surg. 2017 Mar 24.

- ***"Longitudinal Evaluation of Aortic Hemodynamics in Marfan Syndrome: New Insights from a 4D Flow Cardiovascular Magnetic Resonance Multi-Year Follow-Up Study."*** *Geiger J, Hirtler D, Gottfried K, Rahman O, Bollache E, Barker AJ, Markl M, Stiller B.* J Cardiovasc Magn Reson. 2017 Mar 22;19(1):33
- ***"Altered aortic 3D hemodynamics and geometry in pediatric Marfan syndrome patients."*** *van der Palen RL, Barker AJ, Bollache E, Garcia J, Rose MJ, van Ooij P, Young LT, Roest AA, Markl M, Robinson JD, Rigsby CK.* J Cardiovasc Magn Reson. 2017 Mar 17;19(1):30
- ***"Aortopathy in a Mouse Model of Marfan Syndrome Is Not Mediated by Altered Transforming Growth Factor β Signaling".*** *Wei H, Hu JH, Angelov SN, Fox K, Yan J, Enstrom R, Smith A, Dichek DA.* J Am Heart Assoc. 2017 Jan 24;6(1).
- ***"NT-proBNP and diastolic left ventricular function in patients with Marfan syndrome."*** *Gehle P, Robinson PN, Heinzel F, Edelmann F, Yigitbasi M, Berger F, Falk V, Pieske B, Wellnhofer E.* Int J Cardiol Heart Vasc. 2016 May 18;12:15-20. → Study showing increased NT-proBNP levels and diastolic anomalies in Marfan patients with a normal ejection fraction.
- ***"Efficacy of losartan as add-on therapy to prevent aortic growth and ventricular dysfunction in patients with Marfan syndrome: a randomized, double-blind clinical trial."*** *Muiño-Mosquera L, De Nobele S, Devos D, Campens L, De Paepe A, De Backer* J. Acta Cardiol. 2017 Jun 28:1-9. → Study showing that Losartan on top of betablockers does NOT increase the efficacy of the beta blockers regarding aortic dilatation and cardiac function in Marfans.
- ***"Mitral valve prolapse and Marfan syndrome."*** *Thacoor A.* Congenit Heart Dis. 2017 Jun 5. Review

Ophtalmology

- "***The Structural Role of Elastic Fibers in the Cornea Investigated Using a Mouse Model for Marfan Syndrome.***" *White TL, Lewis P, Hayes S, Fergusson J, Bell J, Farinha L, White NS, Pereira LV, Meek KM.* Invest Ophthalmol Vis Sci. 2017 Apr 1;58(4):2106-2116.
- *"**Biometry Characteristics in Adults and Children With Marfan Syndrome: From the Marfan Eye Consortium of Chicago.**" Kinori M, Wehrli S, Kassem IS, Azar NF, Maumenee IH, Mets MB.* Am J Ophthalmol. 2017 May;177:144-149 → Study showing a link between flat cornea and ectopia lentis.
- *"**Comparative data on SD-OCT for the retinal nerve fiber layer and retinal macular thickness in a large cohort with Marfan syndrome.**" Xu W, Kurup SP, Fawzi AA, Durbin MK, Maumenee IH, Mets MB.* Ophthalmic Genet. 2017 Jan-Feb;38(1):34-38. → Study showing a reduced thickness of the fibrous layer of the optic nerve in Marfan patients.
- ***"NGS panel analysis in 24 ectopia lentis patients; a clinically relevant test with a high diagnostic yield"*** *E. Overwater, K. Floor, van Beek, K. de Boer, T. van Dijk, Y. Hilhorst-Hofstee, A.J.M. Hoogeboom, K.J. van Kaam, J.M. van de Kamp, M. Kempers, I.P.C. Krapels, H.Y. Kroes, B. Loeys, S. Salemink, C.T.R.M. Stumpel, V.J.M. Verhoeven, E. Wijnands-van den Berg, J.M. Cobben, J.P. van Tintelen, M.M. Weiss, A.C. Houweling, A. Maugeri.* Eur J Med Genet. 2017 Sep;60(9):465-473

Orthopedics

- ***"Orthopaedic Aspects of Marfan Syndrome : The Experience of a Referral Center for Diagnosis of Rare Diseases."*** *De Maio F, Fichera A, De Luna V, Mancini F, Caterini R.* Adv Orthop. 2016;2016:8275391. → Italian study on 146 patients

Dermatology

- ***"Raman microspectroscopy as a diagnostic tool for the non-invasive analysis of fibrillin-1 deficiency in the skin and in the in vitro skin models."*** *Brauchle E, Bauer H, Fernes P, Zuk A, Schenke-Layland K, Sengle G.* Acta Biomater. 2016 Dec 9 → Study evaluating the use of Raman spectrometry to observe elastic fibers in the skin and use this as diagnostic tool.

Endocrinology and Metabolism

- "***Characterization of metabolic health in mouse models of fibrillin-1 perturbation***." *Walji TA, Turecamo SE, DeMarsilis AJ, Sakai LY, Mecham RP, Craft CS.* Matrix Biol. 2016 Sep;55:63-76 → Study of the metabolism of adipose tissue in marfan mice
- ***« MANAGEMENT OF ENDOCRINE DISEASE: Diagnostic and therapeutic approach of tall stature."*** *Albuquerque EV, Scalco RC, Jorge AA.* Eur J Endocrinol. 2017 Jun;176(6):R339-R353.

Dural Ectasia

- ***"Epidural analgesia complicated by dural ectasia in the Marfan syndrome."*** *Vacula BB, Gray C, Hofkamp MP, Noonan PT Jr, McAllister RK, Pilkinton KA, Diao Z.* Proc (Bayl Univ Med Cent). *2016 Oct;29(4):385-386.*

Obstetrics

- ***"Aortic disease and pregnancy."*** *Bons LR, Roos-Hesselink JW.* Curr Opin Cardiol. *2016 Nov;31(6):611-617.*
- ***"Management of Marfan Syndrome during pregnancy: A real world experience from a Joint Cardiac Obstetric Service."*** *Lim JCE, Cauldwell M, Patel RR, Uebing A, Curry RA, Johnson MR, Gatzoulis MA, Swan L.* Int J Cardiol. 2017 May 22.
- ***"Birth characteristics of women with Marfan syndrome, obstetric and neonatal outcomes of their pregnancies-A nationwide cohort and case-control study."*** *Kernell K, Sydsjö G, Bladh M, Josefsson A.* Eur J Obstet Gynecol Reprod Biol. 2017 Aug;215:106-111. → Swedish study showing that Marfan woman are more likely to have prematured or small compared to age babies and delivery by c-section.
- ***"Sex, pregnancy and aortic disease in Marfan syndrome."*** *Renard M, Muiño-Mosquera L, Manalo EC, Tufa S, Carlson EJ, Keene DR, De Backer J, Sakai LY.* PLoS One. 2017 Jul 14;12(7):e0181166. → Preliminary study comparing the aortic root diameters of a man group, a pregnant group, and non-pregnant woman group, showing an increased dilatation in the man and pregnant group, possibly showing a protective effect of estrogen in women (as 17β-estradiol is known to activate the production of fibrillin-1 in vascular smooth muscle cells in the aorta)

Genetic-phenotype

- ***"Homozygous and compound heterozygous mutations in the FBN1 gene: unexpected findings in molecular diagnosis of Marfan syndrome. "*** *Arnaud P, Hanna N, Aubart M, Leheup B, Dupuis-Girod S, Naudion S, Lacombe D, Milleron O, Odent S, Faivre L, Bal L, Edouard T, Collod-Beroud G, Langeois M, Spentchian M, Gouya L, Jondeau G, Boileau C.* J Med Genet. 2016 *Aug 31.* →Study evaluating the severity of Marfan syndrome based on the mutation type.

- ***"Relationship between fibrillin-1 genotype and severity of cardiovascular involvement in Marfan syndrome."*** *Franken R, Teixido-Tura G, Brion M, Forteza A, Rodriguez-Palomares J, Gutierrez L, Garcia Dorado D, Pals G, Mulder BJ, Evangelista A.* Heart. 2017 May 3.
- Éditorial concernant le même sujet que l'article précédent. ***"Genotype-phenotype correlations in Marfan syndrome."*** *Landis BJ, Veldtman GR, Ware SM.* Heart. 2017 Jun 8.
- "***FBN1: The disease-causing gene for Marfan syndrome and other genetic disorders.***" *Sakai LY, Keene DR, Renard M, De Backer J.* Gene. *2016 Oct 10;591(1):279-91 Review.*
- ***"Associations of Age and Sex With Marfan Phenotype: The National Heart, Lung, and Blood Institute GenTAC (Genetically Triggered Thoracic Aortic Aneurysms and Cardiovascular Conditions) Registry."*** *Roman MJ, Devereux RB, Preiss LR, Asch FM, Eagle KA, Holmes KW, LeMaire SA, Maslen CL, Milewicz DM, Morris SA, Prakash SK, Pyeritz RE, Ravekes WJ, Shohet RV, Song HK, Weinsaft JW; GenTAC Investigators.* Circ Cardiovasc Genet. 2017 Jun;10(3). → Study showing that pulmonary, squeletal and aortic signs are more present in adult Marfan patients then in children, but not the other signs.

Cell and molecular research

- ***"Vascular smooth muscle cells in Marfan syndrome aneurysm: the broken bricks in the aortic wall".*** *Perrucci GL, Rurali E, Gowran A, Pini A, Antona C, Chiesa R, Pompilio G, Nigro P.* Cell Mol Life Sci. *2016 Aug 17. Review. → Cellular and Molecular Mechanism of aortic dissection*
- **"The TGF-β Signalling Network in Muscle Development, Adaptation and Disease."** *Chen JL, Colgan TD, Walton KL, Gregorevic P, Harrison CA.* Adv Exp Med Biol. *2016;900:97-131. Review.*
- **"TGF-β signalopathies as a paradigm for translational medicine."** *Cannaerts E, van de Beek G, Verstraeten A, Van Laer L, Loeys B.* Eur J Med Genet. *2015 Dec;58(12):695-703 Review.*
- ***"Loss of Axin2 results in impaired heart valve maturation and subsequent myxomatous valve disease."*** *Hulin A, Moore V, James JM, Yutzey KE* Cardiovasc Res. 2017 Jan;113(1):40-51. → Observation of a decrease of axn2 and an increased Wnt/ β-catenin in myxomatous mitral valve in marfan mice.
- ***"Nitric oxide mediates aortic disease in mice deficient in the metalloprotease Adamts1 and in a mouse model of Marfan syndrome."*** *Oller J, Méndez-Barbero N, Ruiz EJ, Villahoz S, Renard M, Canelas LI, Briones AM, Alberca R, Lozano-Vidal N1, Hurlé MA, Milewicz D, Evangelista A, Salaices M, Nistal JF, Jiménez-Borreguero LJ, De Backer J, Campanero MR, Redondo JM.* Nat Med. 2017 Jan 9. → Observation of increased nitric oxid levels in aortic dilatations, and protection of aortic dilatation by inhibition of nitric oxid in Marfan mice.
- ***"An iPSC-derived vascular model of Marfan syndrome identifies key mediators of smooth muscle cell death."*** *Granata A, Serrano F, Bernard WG, McNamara M, Low L, Sastry P, Sinha S.* Nat Genet. 2017 Jan;49(1):97-109. → Study showing that TGF-β inhibition rescues abnormalities in fibrillin-1 accumulation and matrix metalloproteinase expression but only the noncanonical p38 pathway regulated SMC apoptosis, suggesting p38 and KLF4 should be considered as potential drug targets for Marfan Syndrome.
- ***"Long-term miR-29b suppression reduces aneurysm formation in a Marfan mouse model."*** *Okamura H, Emrich F, Trojan J, Chiu P, Dalal AR, Arakawa M, Sato T, Penov K, Koyano T, Pedroza A, Connolly AJ, Rabinovitch M, Alvira C, Fischbein MP*. Physiol Rep. 2017 Apr;5(8).

- ***"Aortic microcalcification associates with elastin fragmentation in Marfan syndrome."*** *Wanga SA, Hibender S, Ridwan Y, van Roomen C, Vos M, van der Made I, van Vliet N, Franken R, van Riel LA, Groenink M, Zwinderman AH, Mulder BJ, de Vries CJ, Essers J, de Waard V.* J Pathol. 2017 Jul 20. → Study suggesting studying aortic microcalcification as prediction method for aortic dissection.

Pain and quality of life

- ***"Satisfaction with life in adults with Marfan syndrome (MFS): associations with health-related consequences of MFS, pain, fatigue, and demographic factors. "*** *Velvin G, Bathen T, Rand-Hendriksen S, Geirdal AØ.* Qual Life Res. *2016 Jul;25(7):1779-90* –> Study showing that severe fatigue, aortic dissection, and psychological aspects are associated with lower satisfaction with life
- ***"Systematic review of chronic pain in persons with Marfan syndrome."*** *Velvin G, Bathen T, Rand-Hendriksen S, Geirdal AØ.* Clin Genet. *2016 Jun;89(6):647-58. Review.*
- ***"Characterization of pain, disability, and psychological burden in Marfan syndrome."*** *Speed TJ, Mathur VA, Hand M, Christensen B, Sponseller PD, Williams KA, Campbell CM.* Am J Med Genet A. 2016 Nov 14 → Study on 245 Marfan patients, showing that 89 % of the patients complain of pain, from which 28 % are Marfan related pains, resulting in a psychological burden.
- ***"Marfan Syndrome and Quality of Life in the GenTAC Registry."*** *Goldfinger JZ, Preiss LR, Devereux RB, Roman MJ, Hendershot TP, Kroner BL, Eagle KA; GenTAC Registry Consortium.* J Am Coll Cardiol. 2017 Jun 13;69(23):2821-2830. → American study showing that Marfan patients have a lower quality of life then a control group, but the perception of the quality of life is linked to socioeconomical factors and not to general health or severity of MFS.
- ***"Inpatient rehabilitation for adult patients with Marfan syndrome: an observational pilot study."*** *Benninghoven D, Hamann D, von Kodolitsch Y, Rybczynski M, Lechinger J, Schroeder F, Vogler M, Hoberg E.* Orphanet J Rare Dis. 2017 Jul 12;12(1):127. → Pilot study showing an improvement in mental health, fatigue, vitality and reduced pain perception after a rehabilitation training for adult marfan patients.

General research

- ***"The role of the multidisciplinary health care team in the management of patients with Marfan syndrome."*** von Kodolitsch Y, Rybczynski M, Vogler M, Mir TS, Schüler H, Kutsche K, Rosenberger G, Detter C, Bernhardt AM, Larena-Avellaneda A, Kölbel T, Debus ES, Schroeder M, Linke SJ, Fuisting B, Napp B, Kammal AL, Püschel K, Bannas P, Hoffmann BA, Gessler N, Vahle-Hinz E, Kahl-Nieke B, Thomalla G, Weiler-Normann C, Ohm G, Neumann S, Benninghoven D, Blankenberg S, Pyeritz RE. J Multidiscip Healthc. 2016 Nov 3;9:587-614.