BioSCIENCE Review Article
DOI: https://doi.org/10.55684/2025.83.e00006

Marfan and Ehlers-Danlos Syndrome: two collagenopathies with similarities and differences

Síndrome de Marfan e Ehlers-Danlos: duas colagenopatias com similaridades e diferenças

Julia Czelusniak[1], Fernanda Ritt de Souza[1], Yasmin de Sá Ortiz[1], Liya Regina Mikami[1], Heloisa Stadler Ribas[1]

ABSTRACT

Introduction: Marfan and Ehler-Danlos syndromes are diseases identified as collagenopathies, that is, they consist of defects in the production of collagen or in its modifying enzymes. Both syndromes present singularities.

Objective: To compare and differentiate Marfan and Ehler-Danlos syndromes regarding their pathophysiology and clinical manifestations.

Method: Literature review using 27 articles published in the last 15 years, in Portuguese and English. The inclusion criteria were to be the subject of collagenopathies, especially Marfan and Ehler-Danlos syndromes.

Result: 27 articles were used.

Conclusion: Among the collagenopathies, they are the most similar in relation to symptoms; however, they differ in treatment, which is specific to each one of them.

KEYWORDS: Marfan syndrome. Ehlers-Danlos syndrome. Collagen diseases. Treatment.

RESUMO

Introdução: Síndromes de Marfan e de Ehler-Danlos são doenças identificadas como colagenopatias, ou seja, são constituídas de defeitos na produção do colágeno ou em suas enzimas modificadoras. As duas síndromes apresentam singularidades.

Objetivo: Comparar e diferenciar as síndromes de Marfan e Ehler-Danlos quanto à sua fisiopatologia e manifestações clínicas.

Método: Revisão de literatura empregando 27 artigos publicados nos últimos 15 anos, nos idiomas português e inglês. Os critérios de inclusão foram ser o tema em colagenopatias, especialmente as síndromes de Marfan e de Ehler-Danlos.

Resultado: Foram utilizados 27 artigos.

Conclusão: Dentre as colagenopatias elas são as mais semelhantes em relação aos sintomas; porém, diferem-se no tratamento, que é específico a cada uma delas.

PALAVRAS-CHAVE: Síndrome de Marfan. Síndrome de Ehlers-Danlos. Doenças do colágeno. Tratamento.

Central message

Marfan and Ehler-Danlos syndromes are diseases identified as collagenopathies, that is, they are made up of defects in the production of collagen or its modifying enzymes. The two syndromes have singularities. The treatment is specific to each type and generally seeks to alleviate and treat complications caused by the absence or reduction of collagen in the body.

Perspective

These syndromes have more similarities than differences in relation to the affected tissue and symptoms. However, their differentiation is fundamental since the drug treatment is different and specific to each of them.

[1]Instituto Presbiteriano Mackenzie, São Paulo, SP, Brazil

Conflict of interest: None | Funding: None | Received: 17/11/2024 | Accepted: 22/01/2025| Publication date: 11/02/2025 | Correspondence: liyamikami@gmail.com | Associate Editor: Ronaldo Mafia Cuenca

How to cite:
Czelusniak J, de Souza FR, Ortiz YS, Mikami LR, Ribas HS. Síndrome de Marfan e Ehlers-Danlos: duas colagenopatias com similaridades e diferenças. BioSCIENCE. 2025;83:e00006

INTRODUCTION

Collagenopathies are genetic diseases that affect the production of various types of collagen in affected individuals. This can occur due to pathogenic variants in the FBN1 gene in Marfan syndrome, and mutations in 47 genes in Ehler-Danlos, which are responsible for the production of collagen or enzymes that modify this protein. Usually, these disorders are usually multisystemic, heterogeneous, and variable, causing damage to various organs, especially those with collagen-rich tissues; therefore, its symptoms are considerably varied.[1-3]

The treatment is specific to each type and generally seeks to alleviate and treat complications caused by the absence or reduction of collagen in the body.[4] Diagnosis is made by evaluation of symptoms and laboratory tests. In Marfan, echocardiograms/MRI, slit-lamp examinations, and genetic tests are performed. Similar methods are used for Ehlers-Danlos syndrome; however, DNA sequencing or sequencing of one/any of the related genes may be considered to confirm the specific type of disease.[5,6] It is noteworthy that because it is a very broad field of study and because collagenosis includes many diseases, there are no general standards for treatment and diagnosis for all of them, as both vary according to the patient's condition.

In the field of collagenopathies, Marfan and Ehlers-Danlos syndromes stand out for their similarities in symptoms and differences in treatment and in the form of collagen involvement.

Marfan's is caused by mutations in the FBN1 gene that encodes fibrillin-1, a glycoprotein present in the extracellular matrix in the form of microfibrils responsible for the elasticity of connective tissue.[7] One of the major problems arising from this condition is impending aortic aneurysm due to its abnormal dilation. In addition, manifestations in the muscular and skeletal systems are also common, including tall stature due to exaggerated bone growth, deformities related to sternum displacement, scoliosis, flat feet, dural ectasia, and joint laxity.[7] The eyes can also be affected by ectopia lentis and retinal detachment. The phenotypes of the syndrome may manifest in varying degrees and adequate follow-up may provide longer life expectancy.[8]

Ehler-Danlos syndrome, on the other hand, also affects 1 in every 5,000 live births and is caused by failure in the synthesis of some types of collagen (I, III or V). It is classified into 13 types, according to its effects, which vary greatly, reaching from the skin, more elastic than normal and with a greater propensity to bruises, has joints that are more flexible and more sensitive to injuries than normal and thinner blood vessels susceptible to rupture.[9]

Treatment aims to control symptoms and prevent simpler manifestations from evolving into more complex and harmful complications. Medical conduct varies according to the symptom, its intensity, specific clinical picture and involves treatment with beta-blockers, as in Marfan syndrome, pain control medication, physiotherapy to help preserve and prevent injuries, especially in the joints, and even surgical procedures, especially in cases where it is necessary to correct orthopedic problems.[9]

Both Marfan and Ehler-Danlos syndrome are rare genetic entities with the same incidence in live births, but although both are collagenopathies, they have collagen impairment differently.

Symptoms in Ehler-Danlos syndrome include joint hypermobility, abnormal scarring, wound healing, fragile vasculature, and hyperextensible smooth skin. The skin may be stretched several centimeters, but it returns to normal when released. In Marfan syndrome, patients are taller than average for their age, the arm span exceeds height and, in addition, they have arachnodactyly and deformity of the sternum (called "*pectus carinatum*" or "*pectus excavatum*").[5]

Therefore, both Marfan and Ehler-Danlos syndrome have their own singularities that differentiate them from other collagenopathies, and similarities between them, which create a complex connection between the 2 diseases.

Thus, this study aimed to analyze the correlation between the 2 syndromes, focusing on their similarities and differences, in order to assist physicians and other health professionals in their differentiation for accurate diagnosis and, mainly, appropriate pharmacological treatment.

METHOD

This is a narrative review of the literature in which review articles and case reports from 2009 to 2024 were used, in Portuguese and English. In the search, the Scielo, PubMed, Google Scholar and Capes Periódicos databases were consulted, through the application of the following descriptors: Marfan syndrome, Ehlers-Danlos, collagen diseases and treatment. The inclusion criteria were articles and books related to collagenopathies, focusing on the general description or treatment of Marfan and Ehlers-Danlos syndromes, resulting in 25 articles that were included in this study.

DISCUSSION

Marfan syndrome

First described in 1896 by French pediatrician Antoine Bernard-Jean Marfan, it affects about 1 in every 5,000 live births, with no predominance of sex or ethnicity. It is a rare autosomal dominant disease with incomplete penetrance that affects the connective tissue, specifically its matrix, due to alterations in collagen synthesis.[4,7,8] The condition is caused by mutations in the FBN1 gene, on chromosome 15q21.1, which alters the amount and structure of collagen.[4,8,10] This gene is responsible for encoding the fibrillin-1 protein, a component of the structure of the microfibrils (10-12 nm in size) of the extracellular matrix, which are essential for the elasticity and tensile strength of the connective tissue.[5,11]

Thus, the main symptoms involve the cardiovascular, musculoskeletal, ocular, pulmonary and central

nervous system systems.[5] Another striking characteristic is that those affected feel a lot of muscle pain, which significantly decreases their quality of life.[12] Therefore, it is important to diagnose early and accurately so that the appropriate medication is prescribed and brings more comfort to the patient. Also, Marfan syndrome is underdiagnosed and therefore the importance of analyzing and knowing its characteristics, in addition to the similarities and differences with other collagenopathies, such as Ehler-Danlos.[4]

Some of the most common manifestations of the syndrome are mitral valve prolapse, which can cause mitral regurgitation, and is often the earliest and most severe symptom of Marfan syndrome, since it can bring more severe insufficiency and lead to death in childhood, and dilation of the descending aorta, usually later, and that it can cause, in addition to mitral regurgitation, aortic regurgitation and rupture. Because it has a higher concentration of elastic fibers, the root of the aorta is more prone to dilation, a typical characteristic of the condition.[13]

As for the musculoskeletal system, the most characteristic and common manifestation is arachnodactyly, which is configured by the presence of long and slender fingers, thoracic deformities, high joint flexibility, scoliosis and hard palate, which causes arching of the teeth.[13] Abnormal TGF-β signaling resulting from changes in the FBN1 gene is responsible for abnormal bone development and osteoporosis development, as it results in irregularities in osteogenesis and osteoclast activity. Exaggerated bone growth causes spinal problems (especially scoliosis) to appear more frequently in patients with Marfan syndrome. However, surgical procedures for its correction are significantly riskier in individuals with the disease.[7]

The diagnosis of Marfan syndrome requires a broad analysis of several factors of the patient, analyzing family history, tests such as complete anthropometry, accurate ophthalmologic examination with a slit lamp, chest X-ray (for visualization of the spine and sternum) and echocardiography.[13] The main form of diagnosis is Ghent nosology, involving the analysis of several factors, including affected family members and manifestations of the disease. This analysis consists of a test with scores up to 20, and it is necessary to evaluate the presence of certain symptoms and family history in determining the reference value, z-score, for the diagnosis (Table). These criteria were improved in 2010 so that the diagnosis would be more accurate.[4,8]

Early diagnosis is essential for a better prognosis, since its manifestations are progressive and irreversible. When the disease is detected early, many complications can be avoided, increasing the life expectancy of the carrier.[4,8] This diagnosis tends to be more difficult in childhood, as certain symptoms only manifest in adulthood. Therefore, children with suspected Marfan syndrome should be followed up regularly to monitor symptoms.[4,8]

Other factors that may make diagnosis difficult are highly variable inter- and intrafamilial expressiveness; certain clinical manifestations being age-dependent; large number of *de novo* mutations; and clinical overlap with several other connective tissue diseases.[8]

TABLE— Ghent nosology simplified, with the main clinical characteristics and respective scores

No family history	With a family history
Aortic root ≥, +2 z-score, and ectopy of the crystalline	Lens ectopy
Aortic root ≥, +2 z-score, and aortic mutation Fibrillin-1 (BNF-1)	Systematic score ≥ 7
Aortic root ≥, +2 z-score and score systemic ≥ 7.	Aortic root ≥, +3 z-score if < 20 years old. Or ≥ aortic root, +2 z-score if > 20 years.
Lens ectopia and mutation of the Fibrillin-1	

Characteristic	Quantity points
Fist and thumb sign	3
Pectus carinatum	2
Protrusion of the acetabulum	2
Pneumothorax	2
Dilatation of the dura mater	2
Retrope deformity	1
Wrist or thumb sign	1
Low elbow joint extension movement	1
Flat feet	1
Stretch marks on the skin	1
Scoliosis or problems related to the position of the spine vertebral	1
Increased length of the upper limbs and height	1
Myopia	1
Oblique palpebral clefts	1
Mitral valve prolapse	1

Regarding treatment, those affected are advised not to smoke, pay attention to their blood pressure and avoid high-intensity sports.[8] Musculoskeletal symptoms are usually treated with occupational therapies or physical therapy, without the need for medication, and for aortic complications, beta-blockers are used, which are prescribed to all those affected by Marfan syndrome, including children. Such drugs reduce the heart rate and reduce hemodynamic stress on the aortic wall, preventing its dilation and dissection, and reducing the risk of the appearance of other cardiovascular complications, as well as the need for surgical intervention in the myocardium.[8] The most significant risk of Marfan syndrome is associated with aortic dilation with the eventual development of an aneurysm.[7] Consequently, its treatment is more urgent and, in most cases, indispensable. Losartan is an angiotensin II type I receptor antagonist that has been shown to prevent progressive dilation of the aortic wall. In addition to its antihypertensive action, the drug induces a reduction in plasma levels of TGF β. In addition, losartan does not interfere with the angiotensin II type II receptor, which is responsible for anti-inflammatory and antiproliferative effects, maintaining the homeostasis of the aortic wall and helping to prevent aneurysms.[8]

When aortic dilation becomes a risk factor, the Bentall procedure is recommended, which consists of replacing the aortic valve with a mechanical valve, also called a composite valved graft, and which subsequently requires the continuous use of anticoagulants such as warfarin.[7,14]

In addition, the nature of Marfan syndrome makes conditions such as myopia and astigmatism common among affected individuals. Its treatment is simple,

and it is possible to resort to correction lenses.[7] During childhood, it is recommended to visit medical geneticists and cardiologists. In addition, periodic visits to pediatric cardiologists and annual examination of the aorta should occur, in cases where the size of the aortic root exceeds 4 cm or with high growth of 0.5 cm per year, it is recommended that these examinations be performed every six months.[7] In adulthood, monitoring should remain constant to avoid complications and, if they arise, treat them as soon as possible. Pressure should be controlled and preferably kept below 130/80 mmHg in order to avoid hypertensive conditions and certain medications such as hydralazine, calcium channel blockers and fluoroquinolones, which are associated with increased aortic dissection and increase the risk of aneurysm. Also, sports such as diving and those related to extreme heights are not recommended due to the risk of spontaneous pneumothorax.[7] The prognosis of carriers is relatively good, if diagnosis and treatment are early. With the use of beta-blockers, the life expectancy of patients can reach more than 72 years.[8] In addition, although it is a possible way to relieve problems related to the spine (such as scoliosis, common in Marfan), surgical repair of the spine poses great risks to those with Marfan syndrome, which can interfere with their quality of life.[7] In general, those affected will have their way of life affected by the multisystem complications resulting from the disease. Despite this, it is possible for the individual to have a long survival, if appropriate treatment is given.

Ehler-Danlos syndrome

This syndrome is a set of diseases with predominantly autosomal dominant inheritance, with great genetic heterogeneity[15] caused by mutations in about 47 genes that encode proteins that act in the formation of connective tissue. They are: ADAMTS2, AEBP1, ALDH18A1, ATP6V0A2, ATP6V1A, ATP7A, B3GALT6, B4GALT7, BGN, C1R, C1S, CBS, CHST14, COL12A1, COL1A1, COL1A2, COL3A1, COL5A1, COL5A2, COL6A1, COL6A2, COL6A3, DSE, EFEMP2, ELN, FBLN5, FBN1, FBN2, FKBP14, GORAB, LOX, LTBP4, PLOD1, PRDM5, PYCR1, RIN2, ROBO3, SKI, SLC39A13, SMAD2, SMAD3, TGFB2, TGFB3, TGFBR1, TGFBR2, TNXB, ZNF469.[3] Its incidence ranges from 1 in 2,500 to 1 in 5,000 individuals.[16]

It is characterized by hypermobility of the joints, hyperelastic skin, slow healing, fragility of tissues, and frequent dislocations or subluxations after minor traumas.[12,17] Due to these changes, those affected feel a lot of muscle pain and the arterial fragility of the organs can cause premature death.[12,18] There are also cardiac, neurological and psychological complications.[12]

In 2017, the international classification of diseases that make up Ehlers-Danlos syndrome (EDS) was created, which were divided into 13 subtypes, some of which stand out for having characteristics, similar to Marfan syndrome. Such subtypes are: classic EDS, cardiac-valvular EDS, vascular EDS, arthrolasia EDS, kyphoscoliotic EDS, fragile corneal syndrome, and musculocontractural EDS. In these subtypes, some characteristics and symptoms present in patients are very similar and should be carefully analyzed, such as complications of joint hypermobility, severe progressive heart valve problems (aortic valve, mitral valve), arterial rupture, pneumothorax, kyphoscoliosis, rupture/aneurysm of a medium-caliber artery, chest deformity, refractive errors (myopia, hyperopia), retinal detachment, scoliosis, and arachnodactyly.[5,19]

Regarding its treatment, multidisciplinary conduct is indicated, including physical and occupational therapy and preventive care for the complications generated by the disease.[12] Regarding arterial fragility, celiprolol is used. The studies by Franck et al.[18] demonstrated that patients treated with celiprolol had a higher survival rate, which depended on the dose received of the drug, compared to those who did not use this medication ($p = 0.0004$).

Marfan syndrome vs Ehler-Danlos syndrome

The syndromes chosen for this review were Marfan and Ehler-Danlos syndromes due to their symptomatic similarities, but distinct in treatments in certain aspects. Both affect the body's connective tissues, generating several complications in common systems, such as cardiac and ocular systems. Despite this, the treatment for these collagenoses, although it coincides with certain complications, is different, since the genes affected by each one is particular, as well as the way in which these genetic alterations affect each part of the organism.

When compared to other collagenopathies, there is a variety in manifestations within the group, with several diseases with the most varied symptoms, such as rheumatoid arthritis (joint pain, small peripheral joints, edema, general stiffness and weakness, subcutaneous rheumatoid nodules, bronchiolitis and interstitial lung disease)[20,21], progressive systemic sclerosis (inflammation, vasculopathy, and cutaneous and visceral fibrosis, with collagen deposits in the dermis and thickening of collagen fibers)[21], and dermatopolymyositis (interstitial inflammatory infiltrate, non-specific interstitial pneumonia, organizing pneumonia, deep alveolar damage, and muscle necrosis).[22,23]

One of the similarities between Marfan and Ehler-Danlos is in their classification, since both are collagenopathies, as they affect collagen synthesis.[7,9] Treatment involves the management of beta-blockers to avoid complications related to dilation and possible rupture of the arteries.[7,24] In EDS, the commonly prescribed medication is celiprolol - reducing heart rate and blood pressure, and consequently, also reducing the mechanical stress applied to the arterial walls. In Marfan syndrome the most commonly used drug is losartan, which decreases plasma levels of TGF-β. However, in experimental studies, it did not present significant effects in rats induced for Ehler-Danlos syndrome, configuring one of the differences between the 2 syndromes.[25]

Ocular involvement can also occur in both diseases. However, this symptom is different for each of them. In Marfan syndrome, there is an alteration in the lens (subluxated or displaced upwards) and in EDS, there is involvement and fragility of the sclera, resulting in

perforation of the eyeball in severe cases.[5]

Symptoms affecting the musculoskeletal system are also similar in the 2 syndromes, especially spinal deformities (scoliosis, congenital or early-onset kyphoscoliosis, which can be progressive or non-progressive), chest deformity, arachnodactyly, complications of joint hypermobility (e.g., sprains, dislocation/subluxation, pain, and flexible flat foot).[7,19] Lifestyle is also shaped in a similar way between individuals with both diseases. Cardiac and musculoskeletal frailty implies that those affected avoid playing very intense sports.[8] In addition, the treatment of Marfan syndrome and Ehler-Danlos syndrome involves a multidisciplinary scope, with an approach that mainly aims to help reverse and avoid possible complications in the systems compromised by the diseases, with the cardiac system being the system that requires the most attention because it has more severe complications.

CONCLUSION

Marfan and Ehler-Danlos syndromes are collagenopathies caused by mutations in genes involved in collagen synthesis or in the enzymes responsible for its structure. These syndromes have more similarities than differences in relation to the affected tissue and symptoms. However, their differentiation is fundamental since the drug treatment is different and specific to each of them.

Authors' contributions

Julia Czelusniak: Conceptualization, Writing (review and editing)
Fernanda Ritt de Souza: Methodology, Writing (review and editing)
Yasmin de Sá Ortiz: Supervision, Writing (review and editing)
Liya Regina Mikami: Writing (original draft), Writing (review and editing)
Heloisa Stadler Ribas: Writing (review and editing)

REFERENCES

1. Carrera LG, Hernan GB. Pulmonary manifestations of collagen diseases. Arch Bronconeumol. 2013;49(6):249–60. https://doi.org/10.1016/j.arbr.2012.11.017
2. Carter EM, Raggio CL. Genetic and orthopedic aspects of collagen disorders. Curr Opin Pediatr. 2009;21(1):46–54. https://doi.org/10.1097/mop.0b013e32832185c5
3. Genoma. Genoma. Available from: https://genoma.ib.usp.br/labteg/exame/14
4. Costa FDC, da Silva CFN, da Silva NMJ, Leite AM da S, Da Cunha MRPA. Síndrome de Marfan em Idade Pediátrica: Um Diagnóstico Raro nos Cuidados de Saúde Primários. Gaz médica. 2020. https://doi.org/10.29315/gm.v7i4.327
5. Pessler F. Síndrome de Marfan. Manuais MSD edição para profissionais. 2022. Available from: https://www.msdmanuals.com/pt-br/profissional/pediatria/dist%C3%BArbios-do-tecido-conjuntivo-em-crian%C3%A7as/s%C3%ADndrome-de-marfan#Sinais-e-sintomas_v1093924_pt
6. Neto C. EDS Síndrome de Ehler Danlos: Causas e tratamento. 2020. Available from: https://www.dasagenomica.com/blog/eds-sindrome-de-ehler-danlos/#:~:text=M%C3%A9todo%20de%20an%C3%A1lise%20da%20EDS,autoss%C3%B4mico%20recessivo%20e%20autoss%C3%B4mico%20dominante
7. Zeigler S, Sloan B, Jones JA. The Pathophysiology and Pathogenesis of Marfan Syndrome. Adv Exp Med Biol. 2021;1348:185–206. https://doi.org/10.1007/978-3-030-80614-9_8
8. Coelho SG, Almeida AG. Marfan syndrome revisited: From genetics to clinical practice. Rev Port Cardiol (Engl Ed). 2020;39(4):215-226. https://doi.org/10.1016/j.repce.2020.04.004
9. Espósito ACC, Coneglian LB, Jorge MFS, Jorge Júnior LA, Miot HÁ. Síndrome de Ehlers-Danlos, variante clássica: apresentação de um caso e revisão da literatura. 2016;21(3):118-21. Available from: https://www.apm.org.br/wp-content/uploads/Diagnostico-Tratamento-v21-n3_2016.pdf#page=24
10. OMIM Entry - # 154700 - MARFAN SYNDROME; MFS. Available from: https://www.omim.org/entry/154700?search=fbn1&highlight=fbn1
11. UniProt. Available from: https://www.uniprot.org/uniprotkb/P35555/entry
12. Riley B. The many facets of hypermobile Ehlers-danlos syndrome. J Am Osteopath Assoc. 2020;120(1):30–2. https://doi.org/10.7556/jaoa.2020.012
13. Cantarino CWL, Rittershaussen VPT, Mocelin MM, Lorena PDD da E, Azevedo PDNL de. Síndrome de Marfan. ACTA MSM - Periódico da EMSM. 2021;8(3):145–5. Available from: https://revista.souzamarques.br/index.php/ACTA_MSM/article/view/492/593
14. Al-Mudhaffar SS, Alwan A, Ouj R, Mowaffaq A, Kakamad FH, Ahmad OF, et al. Bentall procedure as a lifesaving surgery: A single center experience. Medicine International. 2023;3(1):8. https://doi.org/10.3892/mi.2023.68
15. Caramalac SM, Caramalac SM, Barbosa CF, Ferreira JF, Oliveira-Filho JP de, Borges AS, et al. Ehlers-Danlos syndrome in a crossbreed cat. Cienc Rural. 2022;52(11):e20210160. https://doi.org/10.1590/0103-8478cr20210160
16. Camelia ȘA, Ionela C. The importance of physical therapy intervention in improving the quality of life in a patient with Ehlers-Danlos Syndrome. GYMNASIUM. 2023;24(2):145–60. https://doi.org/10.29081/gsjesh.2023.24.2.10
17. Bedeschi MF, Bonarrigop F, Manzoni F, Milani D, Piemontese MR, Guez S, et al. Ehlers-Danlos syndrome versus cleidocranial dysplasia. Ital J Pediatr. 2014;40(1):49. http://doi.org/10.1186/1824-7288-40-49
18. Frank M, Adham S, Seigle S, Legrand A, Mirault T, Henneton P, et al. Vascular Ehlers-Danlos Syndrome. J Am Coll Cardiol. 2019 Apr;73(15):1948–57. https://doi.org/10.1016/j.jacc.2019.01.058
19. Ghali N, Sobey G, Burrows N. Ehlers-Danlos syndromes. BMJ. 2019;366:l4966. https://doi.org/10.1136/bmj.l4966
20. Yaseen K. Artrite reumatoide. Manuais MSD edição para profissionais; 2022. Available from: https://www.msdmanuals.com/pt-br/profissional/dist%C3%BArbios-dos-tecidos-conjuntivo-e-musculoesquel%C3%A9tico/doen%C3%A7as-articulares/artrite-reumatoide?query=artrite%20reumatoide#Etiologia_v29657170_pt
21. Chauhan K, Jandu JS, Brent LH, Al-Dhahir MA. Rheumatoid arthritis. PubMed. Treasure Island (FL): StatPearls Publishing; 2023. Available from: https://www.ncbi.nlm.nih.gov/books/NBK441999/
22. Marchiori PE, Hirata MTA, Scaff M, de Oliveira RM, Cossermelli W, Levy JA, et al. Dermatopolimiosite: avaliação de 63 pacientes. Arq Neuro-Psiquiatr. 1987;45:137–42. https://doi.org/10.1590/S0004-282X1987000200006
23. Isabela C, Silva S, Müller N. Open-access Manifestações intratorácicas das doenças do colágeno na tomografia computadorizada de alta resolução do tórax. Radiol Bras. 2008;41(3):189–97. https://doi.org/10.1590/S0100-39842008000300012
24. Giunta C, Rohrbach M, Fauth C, Baumann M. FKBP14 Kyphoscoliotic Ehlers-Danlos Syndrome. GeneReviews. 2019. Available from: https://www.ncbi.nlm.nih.gov/books/NBK541503/
25. Dubacher N, Münger J, Gorosabel MC, Crabb J, Ksiazek AA, Caspar SM, et al. Celiprolol but not losartan improves the biomechanical integrity of the aorta in a mouse model of vascular Ehlers-Danlos syndrome. Cardiovasc Res. 2020;116(2):457–65. https://doi.org/10.1093/cvr/cvz095