

VASCULAR PHENOTYPES IN NON-VASCULAR TYPES OF THE EHLERS-DANLOS SYNDROME: A SYSTEMATIC REVIEW

SUPPLEMENTARTY INFORMATION

Sanne D'hondt¹, Tim Van Damme¹, Fransiska Malfait¹

¹Center for Medical Genetics, Ghent University and Ghent University Hospital, Ghent, Belgium

Corresponding author:

Fransiska Malfait, MD PhD

Center for Medical Genetics, Ghent University Hospital, 0K5

De Pintelaan 185, B-9000 Ghent, Belgium

Tel: +3293323601

E-mail: Fransiska.Malfait@UGent.be

Table S1 Overview of search strings used to find relevant references in the electronic databases of PubMed and Web of Science.

| EDS subtype | Search string PubMed | Search string Web of Science |
|--|--|--|
| Classical EDS (COL5A1/2) | ("Ehlers-Danlos syndrome"[Title/Abstract] AND (classic*[Title/Abstract] OR COL5A1[Title/Abstract] OR COL5A2[Title/Abstract])) OR "Ehlers-Danlos syndrome type I"[Title/Abstract] OR "Ehlers-Danlos syndrome type II"[Title/Abstract] | TS=(("Ehlers-Danlos syndrome" AND (classic* OR COL5A1 OR COL5A2)) OR "Ehlers-Danlos syndrome type I" OR "Ehlers-Danlos syndrome type II") |
| Classical-like EDS | "Ehlers-Danlos syndrome"[Title/Abstract] AND (TNXB[Title/Abstract] OR "tenascin-x"[Title/Abstract]) | TS=("Ehlers-Danlos syndrome" AND (TNXB OR "tenascin-x")) |
| Classical EDS (COL1A1) Cardiac-valvular EDS | "Ehlers-Danlos syndrome"[Title/Abstract] AND ((COL1A1[Title/Abstract]) OR COL1A2[Title/Abstract]) | TS=("Ehlers-Danlos syndrome" AND (COL1A1 OR COL1A2)) |
| Arthrochalasia EDS | ("Ehlers-Danlos syndrome"[Title/Abstract] AND arthrochalasia[Title/Abstract]) OR "Ehlers-Danlos syndrome type VIIA"[Title/Abstract] OR "Ehlers-Danlos syndrome type VIIB"[Title/Abstract] | TS=(("Ehlers-Danlos syndrome" AND arthrochalasia) OR "Ehlers-Danlos syndrome type VIIA" OR "Ehlers-Danlos syndrome type VIIB") |
| Dermatosparaxis EDS | ("Ehlers-Danlos syndrome"[Title/Abstract] AND (dermatospara*[Title/Abstract] OR ADAMTS2[Title/Abstract])) OR "Ehlers-Danlos syndrome type VIIC"[Title/Abstract] | TS=(("Ehlers-Danlos syndrome" AND (dermatospara* OR ADAMTS2)) OR "Ehlers-Danlos syndrome type VIIC") |
| Kyphoscoliotic EDS | ("Ehlers-Danlos syndrome"[Title/Abstract] AND (kyphoscolio*[Title/Abstract] OR PLOD1[Title/Abstract])) OR "Ehlers-Danlos syndrome type VIA"[Title/Abstract] ("Ehlers-Danlos syndrome"[Title/Abstract] AND (FKBP14[Title/Abstract])) | TS=(("Ehlers-Danlos syndrome" AND (kyphoscolio* OR PLOD1)) OR "Ehlers-Danlos syndrome type VIA") TS=("Ehlers-Danlos syndrome" AND FKBP14) |
| Brittle Cornea Syndrome | "brittle cornea syndrome"[Title/Abstract] AND (ZNF469[Title/Abstract] OR PRDM5[Title/Abstract]) | TS=("brittle cornea syndrome" AND (ZNF469 OR PRDM5)) |

Table S1 Continued.

| EDS subtype | Search string PubMed | Search string Web of Science |
|--------------------------------|---|---|
| Spondylodysplastic EDS | "Ehlers-Danlos syndrome"[Title/Abstract] AND (progeroid[Title/Abstract] OR B4GALT7[Title/Abstract]) | TS=("Ehlers-Danlos syndrome" AND (progeroid OR B4GALT7)) |
| | "Ehlers-Danlos syndrome"[Title/Abstract] AND (progeroid[Title/Abstract] OR B3GALT6[Title/Abstract]) | TS=("Ehlers-Danlos syndrome" AND (progeroid OR B3GALT6)) |
| | "Ehlers-Danlos syndrome"[Title/Abstract] AND ((spondylocheirodysplas*[Title/Abstract]) OR SLC39A13[Title/Abstract]) | TS=("Ehlers-Danlos syndrome" AND (spondylocheirodysplas* OR SLC39A13)) |
| Musculocontractural EDS | ("Ehlers-Danlos syndrome"[Title/Abstract] AND (musculocontractural[Title/Abstract] OR CHST14[Title/Abstract] OR DSE[Title/Abstract])) OR "Ehlers-Danlos syndrome type VIB"[Title/Abstract] OR "adducted Thumb-clubfoot syndrome"[Title/Abstract] OR "Ehlers-Danlos syndrome Kosho type"[Title/Abstract] OR "D4ST1-deficient Ehlers-Danlos syndrome"[Title/Abstract] | TS=((("Ehlers-Danlos syndrome" AND (musculocontractural OR CHST14 OR DSE)) OR "Ehlers-Danlos syndrome type VIB" OR "adducted thumb-clubfoot syndrome" OR "Ehlers-Danlos syndrome Kosho type" OR "D4ST1-deficient Ehlers-Danlos syndrome") |
| Myopathic EDS | "Ehlers-Danlos syndrome"[Title/Abstract] AND COL12A1[Title/Abstract] | TS=("Ehlers-Danlos syndrome" AND COL12A1) |
| Periodontal EDS | "Ehlers-Danlos syndrome"[Title/Abstract] AND (periodontal[Title/Abstract] OR C1R[Title/Abstract] OR C1S[Title/Abstract]) | TS=("Ehlers-Danlos syndrome" AND (periodontal OR C1R OR C1S)) |

Table S2 List of all references included in the study. References are numbered according to and can be found in the original paper.

| Reference | Type of study | Quality | Race/Ethnicity | EDS subtype (<i>gene</i>) | Families | Gender (#) | Age (y) | Vascular complication |
|-------------------------------|-----------------|---------|----------------|-----------------------------|----------|------------------|--------------|--|
| Watanabe (2016) ²⁷ | case report | fair | ND | cEDS (<i>COL5A1/2</i>) | 1 | M (1) | 9 | GI bleeding |
| Cazzato (2016) ²⁸ | cross-sectional | fair | ND | cEDS (<i>COL5A1/2</i>) | 1 | ND (1) | 45 | / |
| Monroe (2015) ²⁹ | case series | good | ND | cEDS (<i>COL5A1/2</i>) | 1 | M (2) F (1) | 15/43 28 | arterial dissection and aneurysm, intracranial hemorrhage |
| Casey (2014) ³⁰ | case report | fair | ND | cEDS (<i>COL5A1/2</i>) | 1 | M (1) | 55 | / |
| Yasuda (2013) ³¹ | case report | fair | ND | cEDS (<i>COL5A1/2</i>) | 1 | F (1) | 13 | arterial dissection |
| Ritelli (2013) ³² | case series | good | ND | cEDS (<i>COL5A1/2</i>) | 26 | M (15) F (22) | 4-53 6-67 | menometrorrhagia, varicose veins, DVT, small bleeding, arterial hypoplasia |
| | | | | cEDS (<i>COL1A1</i>) | 1 | M (1) | 53 | arterial aneurysm |
| Morais (2013) ³³ | case report | fair | ND | cEDS (<i>COL5A1/2</i>) | 1 | M (1) | 4 | / |
| Mehta (2012) ³⁴ | case report | good | Caucasian | cEDS (<i>COL5A1/2</i>) | 1 | M (1) | 43 | arterial aneurysm with dissection |
| de Leeuw (2012) ³⁵ | case report | fair | ND | cEDS (<i>COL5A1/2</i>) | 1 | M (1) | 9 | arterial aneurysm with dissection |
| Symoens (2011) ³⁶ | case report | poor | ND | cEDS (<i>COL5A1/2</i>) | 1 | F (1) | 12 | / |
| Borck (2010) ³⁷ | case report | good | Caucasian | cEDS (<i>COL5A1/2</i>) | 1 | M (1) | 42 | arterial dissection, varicose veins |
| Symoens (2009) ³⁸ | case series | good | Caucasian | cEDS (<i>COL5A1/2</i>) | 2 | M (1) | 24 | hematoma |
| | | | ND | | | F (1) | 24 | |
| Malfait (2005) ³⁹ | case series | good | ND | cEDS (<i>COL5A1/2</i>) | 25 | M (10) F (15) | 4-40 3-44 | / |
| Pallotta (2004) ⁴⁰ | case series | poor | ND | cEDS (<i>COL5A1/2</i>) | 1 | M (1) F (2) | 5 2/30 | / |
| Takahara (2002) ⁴¹ | case report | poor | ND | cEDS (<i>COL5A1/2</i>) | 1 | M (1) | 5 | / |
| Giunta (2002) ⁴² | case report | fair | Turkish | cEDS (<i>COL5A1/2</i>) | 1 | M (1) | 4 | hematoma |
| Stoler (2001) ⁴³ | case report | poor | Asian | cEDS (<i>COL5A1/2</i>) | 1 | F (1) | 35 | / |
| Bouma (2001) ⁴⁴ | case series | good | ND | cEDS (<i>COL5A1/2</i>) | 1 | M (2) | 18/24 | / |
| | | | | | | F (2) | 46/58 | |

Table S2 Continued.

| Reference | Type of study | Quality | Race/Ethnicity | EDS subtype (<i>gene</i>) | Families | Gender (#) | Age (y) | Vascular complication |
|-----------------------------------|---------------|---------|----------------|-----------------------------|----------|----------------|----------------|--|
| Schwarze (2000) ⁴⁵ | case series | fair | ND | cEDS (<i>COL5A1/2</i>) | 5 | M (3) F (2) | 14-25 4/32 | / |
| Giunta (2000) ⁴⁶ | case series | fair | ND | cEDS (<i>COL5A1/2</i>) | 1 | M (1) F (1) | 57 6 | varicose veins |
| Michalickova (1998) ⁴⁷ | case series | fair | ND | cEDS (<i>COL5A1/2</i>) | 2 | ND (2) | 3/13 | / |
| De Paepe (1997) ⁴⁸ | case series | fair | ND | cEDS (<i>COL5A1/2</i>) | 3 | M (4) F (5) | 17-40 13-60 | varicose veins |
| Wenstrup (1996) ⁴⁹ | case series | fair | White | cEDS (<i>COL5A1/2</i>) | 2 | M (1) F (3) | 38 18-46 | / |
| Nicholls (1996) ⁵⁰ | case report | poor | ND | cEDS (<i>COL5A1/2</i>) | 1 | F (1) | 24 | / |
| Toriello (1996) ⁵¹ | case report | good | Black | cEDS (<i>COL5A1/2</i>) | 1 | F (1) | 12 | / |
| Colombi (2017) ⁵² | case series | good | Caucasian | cEDS (<i>COL1A1</i>) | 1 | M (2) F (4) | 28/52 17-69 | varicose veins |
| Gaines (2015) ⁵³ | case report | good | Hispanic | cEDS (<i>COL1A1</i>) | 1 | M (1) | 39 | arterial dissection |
| Malfait (2007) ⁵⁴ | case series | good | ND | cEDS (<i>COL1A1</i>) | 1 | M (1) F (1) | 16 43 | arterial dissection |
| Nuytinck (2000) ⁵⁵ | case series | fair | ND | cEDS (<i>COL1A1</i>) | 2 | M (1) F (1) | 7 5 | / |
| Kaufman (2017) ⁵⁶ | case report | fair | ND | clEDS (<i>TNXB</i>) | 1 | F (1) | 28 | / |
| Demirdas (2016) ⁵⁷ | case series | good | Dutch | clEDS (<i>TNXB</i>) | 6 | M (3) F (5) | 6-16 12-48 | hematoma, postpartum hemorrhage, GI bleeding, varicose veins |
| Chen (2016) ⁵⁸ | case series | good | ND | clEDS (<i>TNXB</i>) | 3 | M (3) | 19-29 | / |
| Sakiyama (2015) ⁵⁹ | case report | poor | ND | clEDS (<i>TNXB</i>) | 1 | F (1) | 45 | hematoma |

Table S2 Continued.

| Reference | Type of study | Quality | Race/Ethnicity | EDS subtype (<i>gene</i>) | Families | Gender (#) | Age (y) | Vascular complication |
|---------------------------------------|---------------|---------|----------------|-----------------------------|----------|----------------|----------------|---|
| Penisson-Besnier (2013) ⁶⁰ | case report | fair | ND | clEDS (<i>TNXB</i>) | 1 | M (1) | 42 | hematoma |
| Schalkwijk (2001) ⁶¹ | case series | good | ND | clEDS (<i>TNXB</i>) | 4 | M (1) F (4) | 44 32-53 | hematoma, GI bleeding |
| Melis (2012) ⁶² | case report | fair | ND | cvEDS (<i>COL1A2</i>) | 1 | F (1) | 1m | / |
| Malfait (2006) ⁶³ | case report | good | Portuguese | cvEDS (<i>COL1A2</i>) | 1 | M (1) | 6 | / |
| Schwarze (2004) ⁶⁴ | case series | fair | ND | cvEDS (<i>COL1A2</i>) | 3 | M (2) F (1) | 30/45 38 | arterial dissection, perioperative hemorrhage |
| Hatamochi (2014) ⁶⁵ | case report | fair | Japanese | aEDS (<i>COL1A1/2</i>) | 1 | F (1) | 46 | / |
| Giunta (1999) ⁶⁶ | case series | good | German | aEDS (<i>COL1A1/2</i>) | 2 | M (2) | birth/13 | / |
| Byers (1997) ⁶⁷ | case series | good | ND | aEDS (<i>COL1A1/2</i>) | 7 | M (2) F (5) | birth birth | perioperative hemorrhage |
| Ho (1994) ⁶⁸ | case report | poor | Chinese | aEDS (<i>COL1A1/2</i>) | 1 | ND (1) | ND | / |
| Carr (1994) ⁶⁹ | case report | fair | ND | aEDS (<i>COL1A1/2</i>) | 1 | F (1) | 32 | postpartum hemorrhage |
| Chiodo (1992) ⁷⁰ | case report | poor | ND | aEDS (<i>COL1A1/2</i>) | 1 | F (1) | 30 | / |
| Watson (1992) ⁷¹ | case report | good | South-African | aEDS (<i>COL1A1/2</i>) | 1 | F (1) | 28 | / |
| Vasan (1991) ⁷² | case report | fair | ND | aEDS (<i>COL1A1/2</i>) | 1 | F (1) | 10 | / |
| D'Allesio (1991) ⁷³ | case report | fair | ND | aEDS (<i>COL1A1/2</i>) | 1 | F (1) | 4 | / |
| Wirtz (1987) ⁷⁴ | case report | good | Libyan | aEDS (<i>COL1A1/2</i>) | 1 | F (1) | 1 | / |

Table S2 Continued.

| Reference | Type of study | Quality | Race/Ethnicity | EDS subtype (<i>gene</i>) | Families | Gender (#) | Age (y) | Vascular complication |
|----------------------------------|---------------|---------|--|-----------------------------|----------|----------------|----------------|--|
| Van Damme (2016) ⁷⁵ | case series | good | Caucasian, Turkish | dEDS (<i>ADAMTS2</i>) | 5 | M (4) F (1) | 2-7 2 | small bleeding |
| Solomons (2013) ⁷⁶ | case report | good | Pakistani | dEDS (<i>ADAMTS2</i>) | 1 | F (1) | birth | hematoma |
| Bar-Yosef (2008) ⁷⁷ | case report | fair | Ashkenazi | dEDS (<i>ADAMTS2</i>) | 1 | M (1) | birth | intracranial hemorrhage |
| Malfait (2004) ⁷⁸ | case series | fair | Caucasian | dEDS (<i>ADAMTS2</i>) | 1 | F (1) | 3 | hematoma, hemothorax |
| Colige (2004) ⁷⁹ | case series | fair | Caucasian | dEDS (<i>ADAMTS2</i>) | 2 | M (2) | 5/7 | / |
| Colige (1999) ⁸⁰ | case series | poor | Ashkenazi, Caucasian | dEDS (<i>ADAMTS2</i>) | 4 | M (2) F (3) | birth-2 | intracranial hemorrhage |
| Abdalla (2015) ⁸¹ | case series | fair | Egyptian | kEDS (<i>PLOD1</i>) | 4 | M (3) F (3) | 6m-4 4-6 | / |
| Tosun (2014) ⁸² | case report | fair | ND | kEDS (<i>PLOD1</i>) | 1 | F (1) | 3 | intracranial hemorrhage |
| Gok (2012) ⁸³ | case report | good | Turkish | kEDS (<i>PLOD1</i>) | 1 | M (1) | 12 | arterial dissection |
| Rohrbach (2011) ⁸⁴ | case series | good | Macedonian, Serbian, Iranian, Turkish, Dutch, Somali, Spanish, Iraqi | kEDS (<i>PLOD1</i>) | 10 | M (7) F (6) | 6m-6 5m-6 | arterial dissection, intracranial hemorrhage |
| Kariminejad (2009) ⁸⁵ | case report | fair | ND | kEDS (<i>PLOD1</i>) | 1 | M (1) | 17 | / |
| Voermans (2009) ⁸⁶ | case report | fair | Dutch | kEDS (<i>PLOD1</i>) | 1 | M (1) | 15 | arterial aneurysm with dissection |
| Yis (2008) ⁸⁷ | case report | good | Turkish | kEDS (<i>PLOD1</i>) | 1 | M (1) | 1 | / |
| Salavoura (2006) ⁸⁸ | case report | fair | ND | kEDS (<i>PLOD1</i>) | 1 | F (1) | 4 | / |
| Giunta (2005) ⁸⁹ | case series | poor | Arabian | kEDS (<i>PLOD1</i>) | 6 | M (2) F (4) | 7/10 3m-18m | / |

Table S2 Continued.

| Reference | Type of study | Quality | Race/Ethnicity | EDS subtype (<i>gene</i>) | Families | Gender (#) | Age (y) | Vascular complication |
|--------------------------------|---------------|---------|---|-----------------------------|----------|----------------|---------------|-------------------------|
| Giunta (2005) ⁹⁰ | case series | good | Turkish, German, Albanian, Bosnian, Arabian, Greek, Italian, French | kEDS (<i>PLOD1</i>) | 9 | M (4) F (5) | 5-14 3-30 | intracranial hemorrhage |
| Brunk (2004) ⁹¹ | case report | fair | Turkish | kEDS (<i>PLOD1</i>) | 1 | F (1) | 7 | intracranial hemorrhage |
| Eyre (2002) ⁹² | case report | fair | ND | kEDS (<i>PLOD1</i>) | 1 | F (1) | 17 | / |
| Yeowell (2000) ⁹³ | case series | poor | ND | kEDS (<i>PLOD1</i>) | 2 | ND (2) | ND | arterial dissection |
| Yeowell (2000) ⁹⁴ | case series | poor | North-America | kEDS (<i>PLOD1</i>) | 7 | ND (7) | ND | / |
| Walker (1999) ⁹⁵ | case report | fair | White | kEDS (<i>PLOD1</i>) | 1 | M (1) | 5m | / |
| Pousi (1994) ⁹⁶ | case report | good | Caucasian | kEDS (<i>PLOD1</i>) | 1 | F (1) | 49 | / |
| Dembure (1987) ⁹⁷ | cohort | poor | Mexican-American | kEDS (<i>PLOD1</i>) | 1 | M (1) | 15 | DVT |
| Bursztejn (2017) ⁹⁸ | case report | good | French | kEDS (<i>FKBP14</i>) | 1 | F (1) | 16 | / |
| Dordoni (2016) ⁹⁹ | case report | good | Italian | kEDS (<i>FKBP14</i>) | 1 | M (1) | 6 | arterial dissection |
| Aldeeri (2014) ¹⁰⁰ | case series | poor | ND | kEDS (<i>FKBP14</i>) | 1 | M (1) | 2 | / |
| Murray (2014) ¹⁰¹ | case report | good | Caucasian | kEDS (<i>FKBP14</i>) | 1 | M (1) | 42 | arterial dissection |
| Baumann (2014) ⁴ | case series | poor | Austrian, Italian, German, French, Turkish | kEDS (<i>FKBP14</i>) | 5 | M (2) F (4) | 11/16 3-48 | / |

Table S2 Continued.

| Reference | Type of study | Quality | Race/Ethnicity | EDS subtype (<i>gene</i>) | Families | Gender (#) | Age (y) | Vascular complication |
|-----------------------------------|---------------|---------|--|-----------------------------|----------|------------------|----------------|-----------------------|
| Rohrbach (2013) ¹⁰² | case series | poor | British, Indian, Pakistani, Saudi Arabian, Syrian, Yemeni | BCS (<i>ZNF469</i>) | 18 | M (6) F (12) | 6-21 5-28 | / |
| Al-Owain (2012) ² | case series | good | ND | BCS (<i>ZNF469</i>) | 1 | M (3) F (2) | 16-25 14/23 | / |
| Khan (2010) ¹⁰³ | case series | poor | Syrian | BCS (<i>ZNF469</i>) | 2 | M (1) F (1) | 13 8 | / |
| Christensen (2010) ¹⁰⁴ | case series | fair | ND | BCS (<i>ZNF469</i>) | 1 | M (1) F (1) | birth 2 | / |
| Abu (2008) ¹⁰⁵ | case series | fair | Palestinian, Tunisian | BCS (<i>ZNF469</i>) | 3 | M (2) F (6) | ND | / |
| Porter (2015) ¹⁰⁶ | case series | poor | ND | BCS (<i>PRDM5</i>) | 1 | F (1) | 9 | / |
| Porter (2015) ¹⁰⁷ | case report | poor | ND | BCS (<i>PRDM5</i>) | 1 | F (1) | 26 | / |
| Avgitidou (2015) ¹⁰⁸ | case report | fair | ND | BCS (<i>PRDM5</i>) | 1 | M (1) | 3 | / |
| Aldahmesh (2012) ¹⁰⁹ | case report | poor | Saudi Arabian | BCS (<i>PRDM5</i>) | 1 | F (1) | 2 | / |
| Wright (2011) ¹¹⁰ | case series | fair | Pakistani, Yemeni, Syrian | BCS (<i>PRDM5</i>) | 7 | M (3) F (9) | ND | / |
| Salter (2016) ¹¹¹ | case series | good | ND | spEDS (<i>B4GALT7</i>) | 2 | M (1) F (1) | 6m 5 | / |
| Cartault (2015) ¹¹² | case series | good | ND | spEDS (<i>B4GALT7</i>) | 20 | M (11) F (11) | 11-32 4-46 | / |
| Guo (2013) ¹¹³ | case report | fair | ND | spEDS (<i>B4GALT7</i>) | 1 | M (1) | 10 | / |

Table S2 Continued.

| Reference | Type of study | Quality | Race/Ethnicity | EDS subtype (<i>gene</i>) | Families | Gender (#) | Age (y) | Vascular complication |
|-------------------------------------|---------------|---------|---|-----------------------------|----------|----------------|----------------|---|
| Faiyaz-UI-Haque (2004) ⁸ | case series | good | Arabian | spEDS (<i>B4GALT7</i>) | 1 | M (1) F (1) | 33 2 | / |
| Okajima (1999) ¹¹⁴ | case report | good | Danish | spEDS (<i>B4GALT7</i>) | 1 | M (1) | 4 | / |
| Vorster (2015) ¹¹⁵ | case series | poor | South-African | spEDS (<i>B3GALT6</i>) | 8 | ND (8) | ND | / |
| Sellars (2014) ¹¹⁶ | case report | fair | ND | spEDS (<i>B3GALT6</i>) | 1 | M (1) | birth | / |
| Nakajima (2013) ¹¹⁷ | case series | poor | Japanese, Singaporean, Vietnamese, Italian, Canadian, Brazilian | spEDS (<i>B3GALT6</i>) | 9 | M (5) F (6) | 8m-34 1m-13 | / |
| Malfait (2013) ⁹ | case series | poor | Iranian | spEDS (<i>B3GALT6</i>) | 5 | M (2) F (3) | 9/26 2-7 | intracranial hemorrhage |
| Giunta (2008) ¹¹⁸ | case series | poor | ND | spEDS (<i>SLC39A13</i>) | 2 | M (3) F (3) | 2-10 5-12 | / |
| Fukada (2008) ⁵ | case series | fair | Caucasian | spEDS (<i>SLC39A13</i>) | 1 | M (1) F (1) | 22 ND | intracranial hemorrhage, varicose veins |
| Mizumoto (2017) ¹¹⁹ | case series | fair | ND | mcEDS (<i>CHST14</i>) | 5 | M (2) F (5) | 10/32 4-41 | hematoma, GI |
| Janecke (2016) ¹²⁰ | case series | poor | Pakistani, Hispanic | mcEDS (<i>CHST14</i>) | 4 | M (4) F (3) | 2-3 7-59 | hematoma, intracranial hemorrhage |
| Mochida (2016) ¹²¹ | case report | poor | Japanese | mcEDS (<i>CHST14</i>) | 1 | M (1) | 13 | hematoma |

Table S2 Continued.

| Reference | Type of study | Quality | Race/Ethnicity | EDS subtype (<i>gene</i>) | Families | Gender (#) | Age (y) | Vascular complication |
|--|---------------|---------|--------------------------------|-----------------------------|----------|------------------|------------|--|
| Syx (2015) ¹²² | case series | poor | Asian, Curacao, Moroccan | mcEDS (<i>CHST14</i>) | 4 | M (5) F (1) | 6-23 36 | hematoma, intracranial hemorrhage, perioperative hemorrhage, small bleeding |
| | | | Spanish | mcEDS (<i>DSE</i>) | 1 | F (2) | 39/48 | hematoma |
| Winters (2012) ¹²³ | case report | good | Miccosukee | mcEDS (<i>CHST14</i>) | 1 | F (1) | 16 | hematoma |
| Mendoza-Londono (2012) ¹²⁴ | case series | poor | Afghani | mcEDS (<i>CHST14</i>) | 1 | F (2) | birth/11 | intracranial hemorrhage, hematoma |
| Voermans (2012) ¹²⁵ | case report | good | Dutch | mcEDS (<i>CHST14</i>) | 1 | F (1) | 20 | hematoma |
| Shimizu (2011) ¹²⁶ | case series | fair | Japanese | mcEDS (<i>CHST14</i>) | 2 | M (2) | 2/6 | hematoma |
| Malfait (2010) ¹²⁷ | case series | good | Turkish, Indian | mcEDS (<i>CHST14</i>) | 2 | F (3) | 12-22 | small bleeding, perioperative hemorrhage |
| Miyake (2010) ⁶ | case series | poor | Japanese | mcEDS (<i>CHST14</i>) | 6 | M (2) F (4) | ND | hematoma |
| Dundar (2009) ¹²⁸ | case series | poor | Austrian, Turkish, Japanese | mcEDS (<i>CHST14</i>) | 4 | ND (7) | ND | / |
| Müller (2013) ⁷ | case report | poor | Indian | mcEDS (<i>DSE</i>) | 1 | M (1) | 2 | / |
| Zou (2014) ¹²⁹ | case series | good | Turkish | mEDS (<i>COL12A1</i>) | 2 | M (3) | 1-2 | / |
| Hicks (2014) ¹³⁰ | case series | fair | ND | mEDS (<i>COL12A1</i>) | 2 | M (3) | 22-48 | / |
| | | | | | | F (2) | 6/42 | |
| Kapferer-Seebacher (2016) ¹³¹ | case series | fair | ND | pEDS (<i>C1R/S</i>) | 17 | M (25) F (30) | ND | intracranial hemorrhage, GI bleeding, perioperative hemorrhage |

ND: not defined, M: male, F: female, m: month(s), GI: gastro-intestinal, DVT: deep venous thrombosis