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Review article

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Surgical correction of spinal deformities in patients with Ehlers-Danlos syndrome. Non-systematic review

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Abstract

Introduction Ehlers-Danlos Syndrome (EDS) is a group of hereditary pathological conditions caused by various defects in collagen metabolism. EDS can be accompanied by progressive spinal deformities that may require surgical correction. No review papers reporting the results of the interventions were found in the literature. **The objective** was to present and analyze the results of surgical correction of severe progressive spinal deformities in EDS patients. **Material and methods** The review is based on 11 papers published between 1990 and 2014. They report the results of the treatment of 56 patients with half describing individual observations and half reporting clinical cohorts of 7 to 9 cases. **Results and discussion** The results of conservative treatment indicate its low efficiency. Scoliosis ranged between 45° and 143° with low preoperative mobility (20-40 %) at baseline and corresponded to the average surgical correction (30 to 55 %) and insignificant postoperative loss of correction. The average blood loss measured 540 to 1800 ml. A total of 36 complications were noted in 56 patients, with most severe of them being neurological (three cases of paraplegia, without recovery in one of them) and vascular (damage to segmental vessels and major vascular trunks) events developing from ventral access. **Conclusion** Surgical correction of spinal deformities due to EDS is challenging and requires an individual approach in each specific case. Modern technology makes it possible to obtain very good results in the correction of spinal deformities in EDS. There is a paucity of published observations and new studies are needed.

Keywords: Ehlers-Danlos Syndrome, spinal deformity, surgical treatment

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INTRODUCTION

Ehlers-Danlos Syndrome (EDS) is a group of hereditary pathological conditions caused by various defects in collagen metabolism. The disease was first described by J. van Meckeren [1] in 1682 in a 23-year-old Spaniard who was able to pull the skin from the right sternal region to the left ear, from the chin to the scalp and from the knee to the side by 45 cm. The first detailed clinical description (a young man with dislocated elbow and hip joints) belongs to the Russian specialist A. Chernogorov (1891) [2]. Later, dermatologists Dane E. Ehlers [3] and Frenchman H. Danlos [4] published their observations, which made it possible to assign their names to the described syndrome. The incidence of the syndrome is estimated at 1:5000 to 1:25000 births [5]. The conditions are clinically characterized by joint hypermobility and skin hyperextensibility. The skin fissures easily after minor trauma, presenting as thin and wide atrophic scars often referred to as "cigarette paper scars". There is often a bleeding diathesis of variable severity, with ocular, cardiovascular and gastro-intestinal concomitants. Other common stigmata are fleshy swellings known as molluscoid pseudo-tumours, usually in the tissues scarred of the areas, forearms and calcified spheroids, and shins [6]. Molecular identification methods have recognized 13 EDS subtypes [7]. The prevalence of spinal deformity in EDS patients is unknown, and Beighton, Horan [6] reported curvatures of varying severity in 23 patients out of 100 with a verified diagnosis. Severe progressive spinal deformities in EDS patients require surgical treatment with the results presented in a relatively small number of publications. The study of global databases allowed for identification of 11 contributions only [8–18]. There were no review papers found, while the surgical treatment of syndromic scoliosis (including EDS) is known [19] to be accompanied by frequent and severe complications.

The objective was to present and analyze surgical correction of severe progressive spinal deformities in patients with Ehlers-Danlos syndrome.

MATERIAL AND METHODS

The original literature search was conducted on key resources including Scopus, Web of Science and reference lists. The inclusion criterion included results of surgical correction of spinal deformities in EDS patients. The review is based on 11 papers published between 1990 and 2014. They report the results of the treatment of 56 patients with half describing individual observations and half reporting clinical cohorts of 7 to 9 cases.

RESULTS

Results of surgical treatment of 56 EDS patients were reported in the above articles. One- or two-stage intervention performed for all patients but one included deformity correction using metal constructs and dorsal or ventrodorsal fusion. One patient aged 61/2 years was undergoing staged treatment using the VEPTR instrumentation as of this writing [18]. Review of the available papers allowed for presentation of surgical treatment of EDS patients, performed in the second decade of the patient's life in the majority of cases (Table 1).

Table 1

Main clinical and radiological characteristics of patients included in the review

Authors, year, reference No.	Total number of patients	Age at the time of surgery (years)	M:F	Number of patients by syndrome type	Cobb angle,°			Follow-up period (years)
					pre-op	post-op	At the end of follow-up period	
Pozdnikin et al., 1990 [8]	8	14-16	1:7	5 (type VI)	68.2 (67-90) scoliosis	33.7	3-5 (loss of correction)	1.5-2
				3 (type VII)	-80.5 (50-100) kyphosis	50.5		
El-Shaker M., Watts H., 1991 [9]	1	14	0:1	–	125	67	–	–
McMaster et al., 1994 [10]	5	11.8 (10.5-13.7)	0:5	–	95	41	–	–
					115	75	–	–
					100	73	74	4
					75	15	16	1.5
					68	22	38	1
Vogel et al., 1996 [11]	4	9.6 (7-13)	1:3	–	115	53 endocorrector removed, neurology	86	–
					90	neurology	–	–
Akpinar et al., 2003 [12]	5	14 (8-20)	0:5	5 (type VI)	90		35	6
					45	18	min	2.5
					106	70	min	2
					70 (thoracic lordosis)	26 (thoracic kyphosis)	–	–
					45	10	min	–
Debnath, 2007 [13]	1	20	1:0	1 (type VI)	95	95	–	died
Yang et al., 2009 [14]	3	9.6 (7-13)	2:1	1 (type I)	105	–	28	5
				1 (type II)	84	–	40	3
				1 (type III)	82	32	32	2
Jasiewicz et al., 2010 [15]	11	13.8 (7-18)	6:5	11 (type IV)	109.5 (83-142)	79.3 (56-105)	5.9	5.5
Yang Liu et al., 2011 [16]	3	13.3 (13-14)	0:3	3 (type VI)	78	15	16	5.8
					36	8	10	6
					50	10	12	4.5
Rabenhorst et al., 2012 [17]	6	13.1 (3.2-18.5)	3:3	2 (type III)	50	9	12	2
					117	37	37	–
				2 (type VI)	98	77	76	8.5
					61	34	41	–
				2 (type VII)	63	29	38	9
					63	4	8	0.5
Mikhailovsky et al., 2014 [18]	9	12.5 (6.6-17.3)	5:4		95.2 (30-143)	50.9 (13-79)	8.2	3
Total number of patients	56		19:37					

(-), no information; min, minimal loss of correction.

Twenty-seven out of 56 patients [8, 10, 12, 15-17] received conservative treatment using corsets, massage, exercise therapy, etc. in early stages of the pathology with no noticeable effect. The results of surgical treatment of 56 patients were presented in 11 papers published between 1990 and 2014. It was difficult to analyze this unique material because the average results of relatively large groups of patients (range, 8-11) were reported in three papers [8,15,18] and more detailed case reports (from one to six) were provided in the rest papers. The age of patients at the time of surgery ranged from 3 to 20 years with the intervention performed in most cases when the progression of the deformity accelerated. There were twice as many girls among the patients as boys, 37 versus 19. EDS type was identified in 37 patients out of 56: types I and II (one case each), type III (n = 2), type IV (n = 12), type VI (n = 16), type VII (n = 5). The scoliotic deformity was greater than 60-70° in the majority of cases, reaching 120-140° in some cases. Preoperative mobility of scoliotic deformity (traction, bending-test) was explored in six cases [9, 11, 14, 16]. The curvature decreased from 80.3° to 49.0°, on average, that is, by 31.3° (24-40°) or 39 %. B. Jasiewicz et al. (2010) reported preoperative flexibility of scoliotic curve in thoracic and lumbar regions being equaled 22 % and 27.2 % respectively, Yu.I. Pozdnikina et al. (1990) indicated 15-20 % and M.V. Mikhailovsky et al. (2014) mentioned 28.2 %.

The surgical technique was described in 51 patients, of which 29 were operated on in one stage (correction with a dorsal implant, dorsal fusion) and 22 underwent two stage treatment with correction preceding an anterior approach with discectomy and interbody fusion. The authors used Harrington distractors, Luque instrumentation, CDI and its analogues as endocorrectors; halo-traction was applied first in some cases to be followed by major procedure.

The magnitude of the scoliosis correction achieved is difficult to identify with different authors who presented individual observations with no indications to pre- and/or postoperative Cobb angle, while others reported the average measurements in 8-11 patients. Scoliosis reported in 20 patients [9-12, 14, 16, 17] was corrected on average from 79.3° (36-125°) to 34.9° (4-77°) or by 44.4° (55.9 %).

Cohort studies reported by Yu.I. Pozdnikina et al. (1990) showed correction 34.5° (50.6 %) in 8 patients, B. Jasiewicz et al. (2010) described correction of 30.2° (27.6 %) in 11 patients, M.V. Mikhailovsky et al. (2014) indicated 44.3° (47.4 %) correction in 9 patients. The table presented shows a range in the correction achieved. Postoperative loss of correction reported in 14 patients [10-12,14,16,17] was 5.6° (0-33°) or 12.5 % of the correction achieved. Approximately the same loss of correction was reported by Yu.I. Pozdnikin et al. (1990): 3-5°, B. Jasiewicz et al. (2010): 5.9° and M.V. Mikhailovsky et al. (2014): 8.2°.

Spinal deformity in the sagittal plane was noted in most patients with the nature being confusing. Kyphoscoliosis was described as the leading component in some cases, and others referred to kyphosis forming at the junction of two opposite scoliotic curves and termed as hyperrotation by Y. Cotrel and J. Dubousset [20]. The circumstance reduces the possibility of analyzing the degree of correction of the kyphotic component of the deformity. Yu.I. Pozdnikina et al. (1990) reported kyphosis measuring 80.5° (50-100°) preoperatively and 50.5° postoperatively. B. Jasiewicz et al. (2010) reported minimal correction of kyphosis ranging from 89.1° (32-150°) to 79.5° (21-170°), and increased later to 94.5°. M.V. Mikhailovsky et al. (2014) reported kyphosis correction from 93.7 to 53.9° (37.7 %) with progression of 5.7°. Kyphosis correction reported in five individually presented observations measured from 95 to 41° and from 55 to 24° [10], from 70 to 38° and from 40 to 5° [12] and from 95 to 24.5° [13].

Given the condition of the vascular wall characteristic of this pathology and increased tissue bleeding intraoperative blood loss was particularly important for EDS patients. The average blood loss reported in six publications (n = 37) was: 1243 ml (M. McMaster et al., 1994), 1050 ml (J. Yang et al., 2009), 818 ml (B. Jasiewicz et al., 2010), 1833 ml (Yang Liu et al., 2011), 1730 ml (B. Rabenhorst et al., 2012), 542 ml (M.V. Mikhailovsky et al., 2014).

The global coronal imbalance was reported by two groups of authors. B. Jasiewicz et al. (2010) reported the mean trunk shift measuring 17 mm preoperatively, 8.8 mm postoperatively and 19.3 mm after follow up. The measurements reported by M.V. Mikhailovsky et al. (2014) were 28.3, 39.4 and 22 mm, respectively. A total of 36 complications of varying severity were reported in 56 patients described in 11 publications.

Neurological complications. Mild adverse events included intraoperative injury to the durae mater and neuropathy of the brachial plexus because of preoperative halo traction, and both were arrested unevetfully. Three patients developed severe neurological complications [11]: paraplegia and transient neurogenic bladder. Another patient experienced avulsion of segmental arteries during anterior spinal surgery. Metal constructs were removed with partial recovery of spinal cord function seen in two patients.

Vascular complications were varied: avulsion of segmental vessels, injury to the common iliac vein and artery (during anterior spinal surgery), injury to segmental arteries, abdominal aorta and external iliac artery (during anterior spinal surgery), avulsion of

segmental arteries, injury to the iliac artery and vein, injury to the superior gluteal artery during iliac crest bone graft harvesting. The complications were arrested uneventfully. B. Rabenhorst et al. (2012) reported a case of fatal postoperative intra-abdominal hemorrhage in a 14-year-old girl treated with posterior spinal fusion using Luque-Galveston fixation. Three weeks later, her hemoperitoneum evolved to massive intra-abdominal bleeding from a myriad of peritoneal micro-aneurysms.

A severe complication that can be equally attributed to vascular and neurological adverse events was reported [13]. A 20-year-old patient with 95° scoliosis underwent a two-stage intervention in a span of two weeks including ventral release and dorsal deformity correction with a metal construct. The first stage was uneventful. The patient developed signs of abdominal organs after 54 hours of the second stage, and celiac artery thrombosis was diagnosed at the aortic root. An emergency laparotomy revealed diffuse peritonitis, perforation of the stomach wall, ischemia and necrosis of the gallbladder, partial ischemia of the liver, lack of blood flow in the hepatic, left gastric and splenic arteries. Gastric perforation was repaired, the gallbladder resected and the celiac artery embolus removed. CT scan showed necrosis of the liver and spleen. A second laparotomy was performed the same day with hemihepatectomy, splenectomy. Three weeks after weaning from mechanical ventilation, he developed quadriparesis possibly due to anterior spinal artery ischemia at the C5-C6 level. Minimal regression of neurological symptoms was noted at 6 months and bronchopneumonia caused respiratory failure at 10 months. Another fatal outcome was described by M. McMaster et al. death was caused by cardiopulmonary failure that developed five years after the operation.

Implant-related complications were noted in 10 cases with six requiring reoperation.

Other complications were respiratory distress syndrome, hemopneumothorax, hematoma (n = 5), PJK (n = 2), superficial infection (n = 2), wound dehiscence (n = 2).

Self-evaluation of quality of life results of self-assessment of the quality of life was reported in one paper [18]. Patients were requested to complete the SRS-24 questionnaire at 6, 12 and 24 months. Four domains out of 7 including (pain, postoperative self-image, postoperative function, general activity) showed improvement and three domains including general self-image, professional activity, satisfaction with surgery demonstrated no improvement in the patients.

DISCUSSION

Ehlers-Danlos syndrome often leads to progressive deformities of the spine, that do not respond to conservative treatment. There is a paucity of literature reporting correction of the deformities and the following can be concluded:

1. A high rate of curvature progression is noted in most cases and spinal deformities can develop into severe curves.

2. The deformity retains sufficient mobility regardless of the magnitude of curvature.

3. The use of modern methods of surgical correction during the second decade of life allows for a completely satisfactory and stable result, comparable to that achieved in the treatment of adolescent idiopathic scoliosis [21, 22]. It is noteworthy that patients in our review underwent surgical correction before the age of 20, and the results obtained confirmed the adequate approach.

4. Specific features of the underlying pathological process including vulnerable vascular wall were the cause of a significant number of severe complications. A number of extremely severe cases were reported with the development of massive bleeding, paraplegia and death, and vascular damage was associated with ventral accesses aimed at prevention of the "crankshaft phenomena" [23]. The rate of implant-related complications and pathology of adjacent levels in EDS was that of the frequency in the treatment of idiopathic scoliosis.

The authors reported PJK developed in two cases, which is difficult to explain, given the fact that EDS is based on severe connective tissue pathology.

5. Intraoperative blood loss significantly exceeded that measured during surgical correction of idiopathic scoliosis in adolescents, even in the absence of complications.

The circumstances bring in additional difficulties into the problem of correction of spinal deformities in EDS patients and must be considered in preoperative planning. The available literature material is very limited and predetermines the need for new research.

CONCLUSION

Ehlers-Danlos syndrome is relatively rare and well known to clinicians. Spinal deformities associated with the syndrome are difficult to treat conservatively, can developed into severe condition and require surgical intervention. Case reports presented in the literature indicate that surgical correction is effective, and the results achieved are stable. The number of observations is very limited with a high rate of complications. Systematic analysis can be performed with new data accumulated emphasizing the role of multicenter efforts in evaluation of long-term results and integral analysis.

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