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Original Research

Primary Total Hip Arthroplasty in Patients With Ehlers-Danlos Syndrome: A Retrospective Matched-Cohort Study

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ABSTRACT

Background: Ehlers-Danlos syndromes (EDSs) are connective-tissue disorders resulting in joint laxity. Soft-tissue stability is a concern in these patients when they undergo total hip arthroplasty (THA). Our purpose was to compare THAs in the population with EDS with a matched control undergoing THA for osteoarthritis.

Methods: Thirteen patients with EDS underwent THA from 1997 to 2017. Matching was 1:3 with a control group of patients who underwent THA for osteoarthritis. Matching was based on the gender, age, and length of follow-up.

Results: We found no difference in demographics or postoperative Harris Hip Scores between the cohorts ($P > .05$). Two patients (15.4%) with EDS and 2 patients (5.1%) in the control group suffered a dislocation. We found no difference in the reoperation or revision rate between the groups ($P = .28$).

Conclusion: Patients with EDS have a significant improvement in postoperative Harris Hip Scores after THA. These patients also have a high dislocation rate after surgery, and alternative approaches and technologies such as dual-mobility components should be considered to reduce the rate of dislocation in this population.

Introduction

Ehlers-Danlos syndromes (EDSs) are a collection of connective-tissue disorders caused by genetic mutations that result in aberrant collagen due to disorders in the synthesis or processing. Inherited in an autosomal-dominant fashion, there are 6 types that occur in approximately 1 in 10,000 individuals. Patients commonly present with hypermobility of their tissues, which ultimately may lead to joint pain, instability, and early arthritis [1-4].

The hip joint remains one of the most common joints affected by osteoarthritis. While total hip arthroplasty (THA) is successful in treating pain due to osteoarthritis, there is a paucity of data on technical considerations and outcomes of patients with EDS undergoing such a procedure. There are previous reports of native hip dislocations in patients with EDS due to hypermobility of the surrounding soft tissues [5,6]. Critical to the outcomes of THA are the soft-tissue constraints required for stability; a theoretical concern for increased complications, specifically hip prosthetic dislocations, exists in this population because of their soft-tissue laxity.

The purpose of this study was to evaluate THA performed in the population with EDS. Specifically, the clinical outcomes and complications of patients with EDS undergoing THA were compared with those of a matched cohort of patients undergoing THA for osteoarthritis.

Materials and methods

After institutional review board approval, we retrospectively reviewed our institution's total joint registry to identify patients with EDS [International Classification of Diseases-9 code (756.83) or International Classification of Diseases-10 code (Q79.6)] who underwent primary THA. Each identified patient with EDS had been seen by our genetics team and was verified to have EDS. Thirteen patients were identified who underwent a total hip replacement

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Table 1
Patient baseline and operative characteristics.

Variable	Patients with EDS (N = 13)	Controls (N = 39)	*P*-value
Age at surgery (years)	53.8 (9.4)	53.8 (9.1)	1.00
Sex (male)	3 (23.1%)	9 (23.1%)	1.00
Side of surgery (right)	7 (53.8%)	17 (43.6%)	.54
BMI	28.5 (5.9)	29.7 (6.9)	.52
The number of operations before THA			.45
0	11 (84.6%)	36 (92.3%)	
1	2 (15.4%)	2 (5.1%)	
2	0 (0.0%)	1 (2.6%)	
Approach			1.00
Anterolateral	11 (84.6%)	32 (82.1%)	
Direct anterior	2 (15.4%)	7 (17.9%)	
Posterior	0 (0.0%)	0 (0.0%)	
Constraint			.25
Standard liner	12 (92.3%)	39 (100.0%)	
Dual mobility	1 (7.7%)	0 (0.0%)	
Constrained liner	0 (0.0%)	0 (0.0%)	

The sample mean (standard deviation) is given for continuous variables. *P*-values result from a Wilcoxon rank-sum test or Fisher's exact test. Information was unavailable regarding BMI (N = 17).

between November 1997 and March 2017, all of whom had a minimum follow-up of 24 months. Four of the patients with EDS underwent THA on both their left and right knees (on different dates); for these 4 patients, we included only the first THA to satisfy the statistical assumption of independent measurements. These patients were then matched 1:3 for comparison with a control group consisting of patients who underwent primary THA for a diagnosis of osteoarthritis. Matching was based on the sex, age at the time of surgery (±3 years), and length of follow-up (±90 days). Data were collected regarding baseline characteristics (the age at surgery, sex, side of surgery, body mass index, number of operations before THA, and Harris Hip Scores), operative characteristics (approach and constraint), and postoperative outcomes (Harris hip Scores and occurrence of a complication defined as reoperation, revision, or dislocation). Harris Hip Scores were collected at all routine follow-up visits, and the latest score collected was used for analysis.

Statistical analysis

Continuous variables were summarized with the sample mean and standard deviation. Categorical variables were summarized with the number and percentage of patients. Comparisons of baseline and operative characteristics between patients with EDS and controls were made using a Wilcoxon rank-sum test (continuous variables) or Fisher's exact test (categorical variables).Harris Hip Scores were compared from before to after surgery using a paired Wilcoxon signed-rank test separately for patients with EDS and controls. Postoperative Harris Hip Scores and the change in Harris Hip Scores from before to after surgery were compared between patients with EDS and controls using linear regression models that were adjusted for the length of follow-up.

Occurrence of a postoperative complication (reoperation, revision, or dislocation) was compared between patients with EDS and controls using a log-rank test, where patients who did not experience a postoperative complication were censored on the date of the last follow-up. *P*-values <0.05 were considered as statistically significant, and all statistical tests were two-sided. Statistical analyses were performed using R Statistical Software (version 3.6.2; R Foundation for Statistical Computing, Vienna, Austria).

Results

There were 13 patients with EDS and 39 matched controls included in the study, whose surgeries were performed by 12 arthroplasty surgeons. The average age at the index procedure was 53.8 years (range, 44-72 years) for the patients with EDS and 53.8 years (range, 44-72 years) for the matched controls. The majority of patients were female in both the EDS (10 of 13; 77%) and control populations (30 of 39; 77%). There were no dramatic differences between the 2 groups regarding the age at surgery, sex, side of surgery, body mass index, number of operations before THA, approach, or constraint (all $P \geq .25$) (Table 1).

The mean length of follow-up after surgery was 7.3 years (range: 2.0-20.0 years) for patients with EDS and 7.5 years (range: 2.0-19.8 years) for the controls ($P = .37$). Harris Hip Scores were significantly

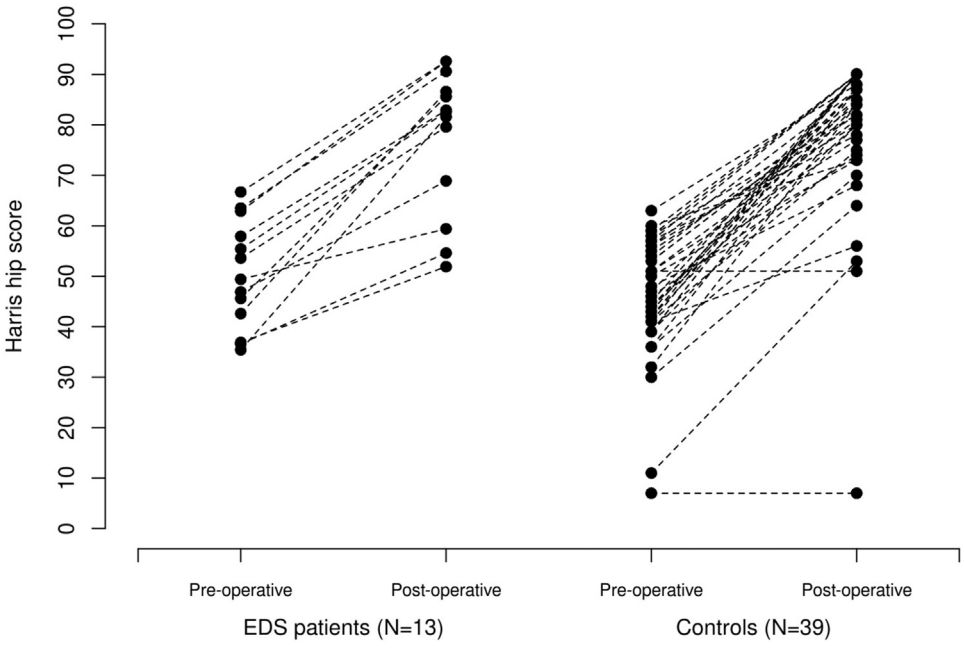

Figure 1. Preoperative and postoperative Harris Hip Scores for patients with EDS and controls.

Table 2
Postoperative information.

Variable	Patients with EDS (N = 13)	Controls (N = 39)	*P*-value
Length of follow-up (years)	7.3 (6.5)	7.5 (5.5)	.37
Harris Hip Score			
Preoperative	50.3 (10.7)	45.6 (11.9)	.34
Postoperative	77.7 (14.2)	78.4 (15.7)	.89
Postoperative minus preoperative	27.4 (10.7)	32.7 (12.9)	.19
Complication[a]	2 (15.4%)	3 (7.7%)	.31
Reoperation	0 (0.0%)	1 (2.6%)	.58
Revision	0 (0.0%)	1 (2.6%)	.58
Dislocation	2 (15.4%)	2 (5.1%)	.46

The sample mean (standard deviation) is given for continuous variables. Comparisons of the length of follow-up and preoperative Harris Hip Score between patients with EDS and controls were made using Wilcoxon rank sum tests. Comparisons of postoperative Harris Hip Score and postoperative minus preoperative Harris Hip Score were made using linear regression models that were adjusted for length of follow-up. Comparisons of complications between patients with EDS and control were made using log-rank tests.

[a] One control experienced more than one type of complication.

higher at postoperative follow-up than the preoperative assessment for both patients with EDS and controls (both $P < .001$); there was not a significant difference between the 2 groups regarding the degree of improvement from the preoperative to postoperative period (mean change: 27.4 vs 32.7, $P = .19$, Fig. 1).

Postoperative complications (defined as reoperation, revision, or dislocation) occurred relatively rarely and at a similar rate between patients with EDS and controls ($P = .28$) (Table 2). There were 2 patients with postoperative complications in the EDS cohort (15.4%) and 3 patients in the matched controls (7.7%). No patients in the EDS cohort underwent a reoperation or revision procedure for any cause. One patient in the matched cohort underwent a reoperation to remove a heterotopic bone.

There were 2 patients with dislocations in the EDS cohort (15.4%) and 2 patients with dislocations in the matched controls (5.1%) ($P = .46$). Both patients who suffered dislocations in the EDS cohort underwent an anterolateral approach, and both had 28-mm femoral heads with flat liners. The first reported a total of 3 dislocations, beginning 6 years after the index procedure (Fig. 2). The second patient had 2 dislocations, first occurring approximately 8 months after THA. In contrast, both patients in the control cohort had only a single dislocation each. One underwent an anterolateral approach with placement of a 28-mm femoral head and suffered a dislocation 2 years after the index procedure. The second patient underwent a direct anterior approach with placement of a 32-mm head and suffered dislocation 1 month after surgery. Finally, there were no patients in either cohort who complained of a leg-length discrepancy after surgery.

Discussion

Chronic pain has been estimated to occur in up to 85%-90% of patients with EDS, with several studies reporting lower health-related quality-of-life measures not only in healthy controls but also in patients with rheumatoid arthritis [7-12]. These findings are thought to be in part due to hypermobility and laxity around the joints, leading to instability and early arthritis [11,13-16]. The characteristics of hypermobility and laxity in patients with EDS must be accounted for when planning to perform THA, which relies on the soft tissues for stability. Presently, there is no literature specifically evaluating outcomes and complications after THA in this patient population. The purpose of this study was to evaluate and compare characteristics, clinical outcomes, and complications after THA in this unique patient population with those of a matched cohort of patients undergoing THA for osteoarthritis.

To the author's knowledge, the report by Larson et al represents the only comparison of outcome scores in the EDS population specifically after surgery of the hip. Those authors found significantly improved scores postoperatively compared with preoperative values in patients with EDS undergoing hip arthroscopy for femoroacetabular impingement pain and capsular laxity [17]. This result is in contrast to a more dated study by Ainsworth et al, who generally recommended against reconstructive procedures in this population because of high complication rates [18].

In the present study, both the EDS and matched cohorts demonstrated a significant improvement in their Harris Hip Scores postoperatively compared with the preoperative values. We did not find a statistical difference in the final Harris Hip Scores between the 2 groups, suggesting that the patients with EDS can expect to obtain significant improvement after surgery.

Higher rates of postoperative complications, including wound infections, have been noted after surgery in the patient population with EDS [13,19]. Such an increased risk has resulted in some authors recommending against arthroplasty for these patients [18]. In our series, we were unable to find a significant difference in the postoperative complication rates between the patients with EDS

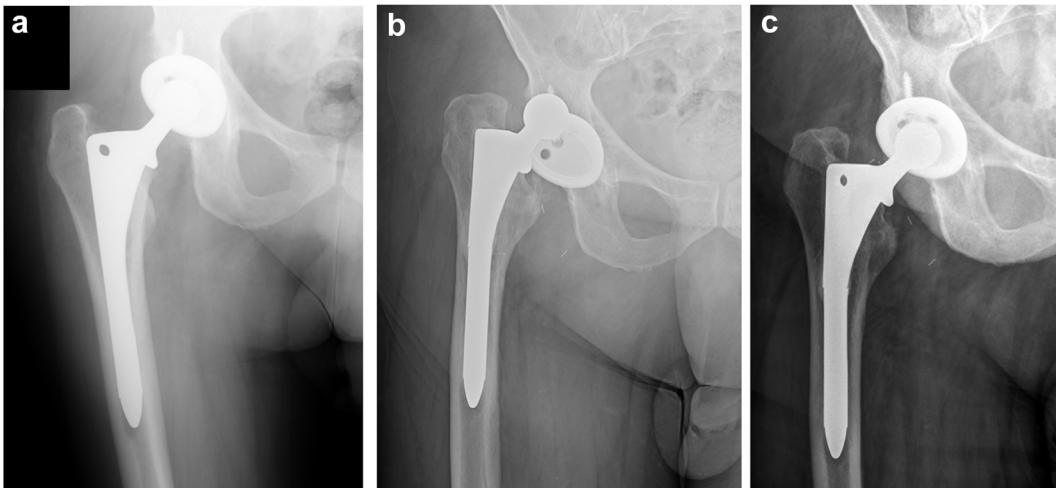

Figure 2. Postoperative radiographs after THA in a patient with EDS (a). The patient suffered 3 dislocations postoperatively, along with a fracture in the femoral stem (b). The patient was treated nonoperatively and underwent a functioning THA 20 years after the index procedure (c).

and the matched controls. Of interest, no patients in the EDS cohort developed postoperative wound complications or infections in our small series. We did however observe a relatively higher dislocation rate in the patients with EDS (15.4%) than in the controls (5.1%), although this was not statistically significant.

Given the relatively high dislocation rate observed in the patients with EDS, it may be worthwhile for the surgeon to consider alternate approaches and newer technology. In the present study, all patients with EDS underwent either an anterolateral or direct anterior approach as these are thought to confer less cumulative risk of dislocation than a posterior approach [20-22]. Additional technologies such as dual-mobility components have been found to lessen the risk of dislocation after THA [23]. As only one patient in the EDS cohort received dual-mobility implants, it remains currently unknown if these same benefits would translate to these patients.

Leg-length discrepancy is a concern after THA, especially in patients with lax soft tissues. Although we did not observe postoperative leg-length discrepancies in our cohort of patients with EDS, this concern exists and surgeons should be especially mindful of overlengthening in these patients during the procedure.

Several limitations of this study are apparent, including the inherent weaknesses of a small, retrospective design. In addition, the sample size is relatively small, introducing the possibility of a type II error (false-negative finding). Thus, in our small series, we cannot conclude that a difference does not exist between the groups, simply because of the presence of a nonsignificant *P*-value.

In conclusion, patients with EDS have significant improvements in Harris Hip Scores after hip arthroplasty, similar to a matched cohort of patients undergoing THA for osteoarthritis. Patients with EDS, however, may have a higher rate of dislocations after surgery. Surgeons should consider the use of alternate approaches and technology, such as dual-mobility components, to possibly reduce the rate of dislocations postoperatively.

Conflict of interest

M.J. Taunton receives royalties from DJO Global, is a paid consultant for DJO Global, receives research support as a principal investigator from Stryker and DePuy, receives royalties or financial or material support from and is a member of the editorial board of the *Journal of Arthroplasty* and is a board member of the AAHKS and AAOS. B.K. Wilke receives research support as a principal investigator from Summit Medical. The other authors declare no potential conflicts of interest.

References

[1] Rose PS, Johnson CA, Hungerford DS, McFarland EG. Total knee arthroplasty in Ehlers-Danlos syndrome. J Arthroplasty 2004;19(2):190.
[2] Pepin M, Schwarze U, Superti-Furga A, Byers PH. Clinical and genetic features of Ehlers-Danlos syndrome type IV, the vascular type. N Engl J Med 2000;342(10):673.
[3] Beighton P, De Paepe A, Steinmann B, Tsipouras P, Wenstrup RJ. Ehlers-Danlos syndromes: revised nosology, Villefranche, 1997. Ehlers-Danlos National Foundation (USA) and ehlers-danlos support group (UK). Am J Med Genet 1998;77(1):31.
[4] Tibbo ME, Wyles CC, Houdek MT, Wilke BK. Outcomes of primary total knee arthroplasty in patients with ehlers-danlos syndromes. J Arthroplasty 2019;34(2):315.
[5] Chang JD, Yoo JH, Umarani GS, Kim YS. Obturator hip dislocation with intrapelvic migration of the femoral head in Ehlers-Danlos syndrome. J Orthop Sci 2012;17(1):87.
[6] Harris WH. Traumatic arthritis of the hip after dislocation and acetabular fractures: treatment by mold arthroplasty. An end-result study using a new method of result evaluation. J Bone Joint Surg Am 1969;51(4):737.
[7] Shirley ED, Demaio M, Bodurtha J. Ehlers-danlos syndrome in orthopaedics: etiology, diagnosis, and treatment implications. Sports Health 2012;4(5):394.
[8] Stanitski DF, Nadjarian R, Stanitski CL, Bawle E, Tsipouras P. Orthopaedic manifestations of Ehlers-Danlos syndrome. Clin Orthop Relat Res 2000;376:213.
[9] Voermans NC, Knoop H, Bleijenberg G, van Engelen BG. Pain in ehlers-danlos syndrome is common, severe, and associated with functional impairment. J Pain Symptom Manage 2010;40(3):370.
[10] Berglund B, Pettersson C, Pigg M, Kristiansson P. Self-reported quality of life, anxiety and depression in individuals with Ehlers-Danlos syndrome (EDS): a questionnaire study. BMC Musculoskelet Disord 2015;16:89.
[11] Rombaut L, Malfait F, De Paepe A, et al. Impairment and impact of pain in female patients with Ehlers-Danlos syndrome: a comparative study with fibromyalgia and rheumatoid arthritis. Arthritis Rheum 2011;63(7):1979.
[12] Rombaut L, Malfait F, De Wandele I, et al. Muscle mass, muscle strength, functional performance, and physical impairment in women with the hypermobility type of Ehlers-Danlos syndrome. Arthritis Care Res (Hoboken) 2012;64(10):1584.
[13] Weinberg J, Doering C, McFarland EG. Joint surgery in Ehlers-Danlos patients: results of a survey. Am J Orthop (Belle Mead NJ) 1999;28(7):406.
[14] Ericson Jr WB, Wolman R. Orthopaedic management of the Ehlers-Danlos syndromes. Am J Med Genet C Semin Med Genet 2017;175(1):188.
[15] Castori M, Camerota F, Celletti C, et al. Natural history and manifestations of the hypermobility type Ehlers-Danlos syndrome: a pilot study on 21 patients. Am J Med Genet A 2010;152A(3):556.
[16] Steer G, Jayson MI, Dixon AS, Beighton P. Joint capsule collagen. Analysis by the study of intra-articular pressure during joint distension. Measurements in the knees of control subjects and patients with rheumatoid arthritis and Ehlers-Danlos syndrome. Ann Rheum Dis 1971;30(5):481.
[17] Larson CM, Stone RM, Grossi EF, Giveans MR, Cornelsen GD. Ehlers-Danlos syndrome: arthroscopic management for extreme soft-tissue hip instability. Arthroscopy 2015;31(12):2287.
[18] Ainsworth SR, Aulicino PL. A survey of patients with Ehlers-Danlos syndrome. Clin Orthop Relat Res 1993;(286):250.
[19] Beighton P, Horan FT. Surgical aspects of the Ehlers-Danlos syndrome. A survey of 100 cases. Br J Surg 1969;56(4):255.
[20] Berry DJ, von Knoch M, Schleck CD, Harmsen WS. Effect of femoral head diameter and operative approach on risk of dislocation after primary total hip arthroplasty. J Bone Joint Surg Am 2005;87(11):2456.
[21] Tamaki T, Oinuma K, Miura Y, Higashi H, Kaneyama R, Shiratsuchi H. Epidemiology of dislocation following direct anterior total hip arthroplasty: a minimum 5-year follow-up study. J Arthroplasty 2016;31(12):2886.
[22] Tsukada S, Wakui M. Lower dislocation rate following total hip arthroplasty via direct anterior approach than via posterior approach: five-year-average follow-up results. Open Orthop J 2015;9:157.
[23] Reina N, Pareek A, Krych AJ, Pagnano MW, Berry DJ, Abdel MP. Dual-mobility constructs in primary and revision total hip arthroplasty: a systematic review of comparative studies. J Arthroplasty 2019;34(3):594.