Arthroplasty Today 27 (2024) 101390

Contents lists available at ScienceDirect

Arthroplasty Today

journal homepage: http://www.arthroplastytoday.org/

Original Research

Increased Opioid Use in Patients With Ehlers-Danlos Syndrome Before and After Total Hip Arthroplasty

Mackenzie Kelly, MD, Ryland P. Kagan, MD, Jung Yoo, MD*

Department of Orthopaedics and Rehabilitation, Oregon Health & Science University, Portland, OR, USA

ARTICLE INFO

Article history:
Received 18 July 2023
Received in revised form
12 March 2024
Accepted 24 March 2024

Keywords:
Opioid use
Ehlers-Danlos syndrome
Total hip arthroplasty
PearlDiver

ABSTRACT

Background: Ehlers-Danlos syndrome (EDS), a disorder affecting synthesis of collagen, typically presents with chronic pain, hypermobility, and early osteoarthritis. EDS patients undergoing total hip arthroplasty (THA) are at risk of dislocation and revision. Opioid use and impact on outcomes among this population remain unknown.

Methods: A retrospective review was performed with a large national database querying the International Classification of Disease, tenth revision procedure codes identifying 1,244,368 primary THAs from 2015-2020. Two hundred thirty-eight EDS patients underwent THA and were propensity matched with population control based on age, sex, and obesity when comparing opioid prescription. To compare dislocation and revision outcomes, EDS patients were stratified into those receiving opioid prescriptions and those not. Multivariate analysis evaluated the association.

Results: EDS patients were more likely prescribed opioids 90 days before (49.1% vs 34.7.0%, $P < .0001$) and after THA (59.7% vs 41.2%, $P < .0001$), with more preoperatively (1163.6 mme ±1562.8, $P < .0001$) and postoperatively (900.1 mme ±1235.9, $P < .0001$) than controls. In EDS patients prescribed opioids 90 days before THA, dislocation rate was 12.8% vs 7.1% not prescribed (odds ratio 2.08, 95% confidence interval 0.85-5.1). 14.8% of EDS patients who received opioids 90 days after THA dislocated vs 2.1% not prescribed (odds ratio 8.13, 95% confidence interval 1.87-35.7).

Conclusions: EDS patients are more likely prescribed opioids before and after THA. Opioid prescription was associated with risk of dislocation, though we caution interpretation of causation. However, this suggests that the risks of worse outcomes in EDS patients undergoing THA are multifactorial. We should look at strategies to reduce opioid use prior to THA.

Introduction

Ehlers-Danlos syndrome (EDS) is a spectrum of disorders encompassing abnormal collagen synthesis with an incidence of 1 in 5000-20,000 people thought to be underestimated [1,2]. While the syndrome consists of 13 subtypes of varying hereditary patterns, EDS classically includes joint hypermobility, skin hyperextensibility, poor wound healing, as well as other cardiovascular, gastrointestinal, and neurologic manifestations [3–8]. The most common type of EDS, hypermobile type, has been found to have a chronic pain incidence of approximately 90% [9,10]. Patients are often diagnosed at a young age, with 75% of patients presenting with symptoms by 15 years old [11]. Musculoskeletal complaints with EDS include joint pain, swelling, and hyperlaxity postulated to lead to joint microtrauma and osteoarthritis [5,12–14].

Beyond musculoskeletal complaints, EDS typically involves multiple organ system manifestations leading to difficulty with pain control. Opioids use in this population is challenging given their predisposition for decreased gastrointestinal motility, postural orthostatic tachycardia, dysautonomia, and proprioceptive deficits [15,16]. Additionally, similarly to other chronic pain conditions like fibromyalgia, prolonged opioid use has been shown to lead to central pain sensitization in patients with EDS [17–19]. As such, opioids are typically not indicated for EDS-related chronic musculoskeletal pain but are reserved for acute exacerbations or pain refractory to other treatments [11,20].

* Corresponding author. 3181 SW Sam Jackson Road, Portland, OR 97239, USA. Tel. : +1 503 494 6400.
E-mail address: yooj@ohsu.edu

https://doi.org/10.1016/j.artd.2024.101390

Retrospective studies have demonstrated patients with EDS who undergo total hip arthroplasty (THA) are at increased risk for dislocation and revision [21,22]. A small retrospective study of HT-EDS patients undergoing hip arthroscopy for hip pain and sensation of instability showed pervasive femoroacetabular impingement as well as extreme capsular laxity, possibly leading to earlier indications for THA [12]. Opioid use in patients who have EDS undergoing THA remains unclear both preoperatively and postoperatively. Furthermore, the effect of opioid use on THA outcomes in the EDS population remains unknown. The primary aim of this investigation was to investigate opioid use for patients with EDS who undergo THA. The secondary aim is to investigate the associated risk of opioid use at the time of THA in patients with EDS comparing dislocation and revision risk to a population control without EDS.

Material and methods

A retrospective review was performed using the all-claims data files from the PearlDiver database (PearlDiver Technologies, Inc., Fort Wayne, IN) comprised of 151 million deidentified patients based on national all-claims data including Medicare, Medicaid, government, and private. We queried the International Classification of Disease, tenth revision diagnostic codes for EDS from the PearlDiver database from 2015-2020 (Appendix 1). The queried cohort was filtered for age between 45 and 75. To create a control population, we created a random adult population without EDS using a random patient generator within the PearlDiver software.

Patients with EDS who underwent primary THA for osteoarthritis were identified and propensity-matched with a population control to determine the incidence of THA and compare opioid prescription. A population control was matched using a propensity ratio based on age, sex, and obesity. The propensity-matched control population of 1,244,368 control patients were compared to 25,688 patients who carried a diagnosis of EDS. Both prematched and postmatched patient demographics of the EDS group undergoing THA and propensity-matched controls are shown in Table 1.

Opioid prescription rate and quantity 90 days before and after THA was calculated for both propensity matched control and EDS. Opioid prescription rate was determined by patients receiving a prescription for opioids within the prescribed time, and quantity was compared after conversion of opioid to morphine milliequivalent dose (mme), which is similar methodology to prior arthroplasty opioid studies [23,24]. In comparing the duration of opioids, we classified patients into 2 categories, those who did not receive opioid prescriptions within 90 days after the operation, and those who were prescribed opioids at 365 days.

Statistical analysis was performed using R (R Core Team, 2021). Descriptive statistics were calculated for demographic variables. Opioid prescription rates were described as a proportion of the entire cohort. Differences in opioid prescriptions based on continuous variables (age) and categorical variables (sex and obesity diagnosis) were analyzed using t-tests and chi-square tests, respectively. A *P*-value of less than .05 was considered a statistically significant outcome. Because of the large number present in the cohorts, statistically significant differences can be found without relevant clinical importance. Cohen's d calculation was done for continuous variables, and the effect size was calculated. We used the commonly used convention of Cohen's d of 0.2 as a small effect, 0.5 as a medium effect, and 0.8 or greater as a large effect. Effect sizes for discrete variables are presented as odds ratios (ORs).

Results

Frequency of complications within the propensity-matched controls and EDS group are demonstrated in Tables 2 and 3, respectively. Of the EDS group, 238 EDS patients underwent THA for osteoarthritis. Of those with EDS, 117 (49.2%) were recorded to receive opioid prescriptions 90 days preoperatively, 142 (59.7%) at 90 days postoperatively, and 93 (39.1%) at 365 days postoperatively. Dislocation occurred in 23 (9.7%) patients with EDS. Of those who experienced dislocation, 21 were prescribed opioids within 90 days postoperatively, and 5 were prescribed opioids 365 days postoperatively. Of those with EDS, 7 (2.9%) became infected, 9 (3.8%) experienced medical complications, and 6 (2.5%) underwent revision. As the PearlDiver database does not report outcomes with fewer than 10 patients to maintain patient anonymity, the distribution of infection, medical complications, and revision were stratified as <10 for those prescribed opioids at 90 days preoperatively, 90 days postoperatively, and 365 days postoperatively.

Patients with EDS were more likely to have undergone THA compared to controls, with an OR of 1.82 ($P < .0001$). Patients with EDS were more likely to receive opioid prescriptions 90 days before (49.1% vs 34.7%, OR = 1.78, $P < .0001$) and after the operation (59.7% vs 41.2%, OR = 2.08, $P < .0001$) compared to the non-EDS control group. Additionally, the study found that EDS patients were prescribed more opioids than the matched control group at 90 days preoperatively (1163.6 mme ±1562.8 vs 731.9 mme ±1230.7, $P < .0001$, Cohen's d = 0.31) and 90 days postoperatively (900.1 mme ±1235.9 vs 651.7 mme ±1150.9, $P < .0001$, Cohen's d = 0.21). The proportion of patients who did not receive an opioid prescription at 90 days postoperatively was 39.1% for EDS patients compared to 60.5% for non-EDS patients (OR = 0.45, $P < .0001$). The proportion of patients receiving opioid prescriptions at 365 days postoperatively was 50.8% for EDS patients and 31.0% for non-EDS patients (OR = 2.17, $P < .0001$). The remaining 10.1% of patients with EDS and 8.5% of controls were presumably not prescribed opioids postoperatively.

Those who were using opioids within 90 days preoperatively were significantly more likely to be using opioids 90 days postoperatively (OR 8.19, CI 4.47-15.02), as well as more likely to continue to receive opioid prescriptions at 1 year postoperatively (OR 4.93, CI 2.84-8.53). EDS patients who were prescribed opioids 90 days postoperatively were more likely to experience dislocation (OR 8.16, CI 1.87-35.66). However, there were no statistically significant differences between dislocation rates with opioid

Table 1
Demographics of patients with Ehlers-Danlos syndrome and matched population cohorts without Ehlers-Danlos syndrome demonstrating a difference in age, as well as postpropensity matching demographics demonstrating no difference in age, sex, and obesity postmatch cohort.

	Prepropensity matching				Postpropensity matching		
	EDS	Control	Standard deviation	Variation ratio	Propensity matched control	Standard deviation	Variation ratio
Age (years)	54.31	50.78	0.43	0.26	54.31	0.00	1.00
Sex F	0.84	0.59	0.69	N/A	0.84	0.00	N/A
Sex M	0.16	0.41	−0.69	N/A	0.16	0.00	N/A
Obesity	0.30	0.24	0.13	N/A	0.31	0.00	N/A

Table 2
Frequency of complications recorded within population control undergoing total hip arthroplasty stratified by opioid use timeframe.

Complication	Opioid use		
	90-day preoperative	90-day postoperative	365-day postoperative
Dislocation (n = 12,390)	6045	6764	7929
Infection (n = 13,623)	7076	7652	8933
Medical (n = 13,437)	5335	5639	6805
Revision (n = 6069)	3217	3729	4409
Total control (n = 405,013)	140,344	166,730	198,755

prescription preoperatively or with opioid prescription at 365 days compared to those who were not prescribed opioids. Similarly, there was no difference in revision, infection, or medical complications between subjects with EDS who had an opioid prescription and those without an opioid prescription preoperatively or postoperatively at either 90 or 365 days.

Discussion

This study is the first to demonstrate higher levels of opioid prescription among patients with EDS in arthroplasty. Our findings confirm our hypothesis that EDS patients are prescribed greater amounts of opioids before and after THA and continue to receive prescriptions for opioids for an extended period up to 1 year following surgery compared to non-EDS patients. The percentage of patients who are prescribed opioids after surgery, including up to 1 year after the procedure, is significantly higher in EDS patients, with an OR greater than 2. Additionally, the percentage of EDS patients who no longer received opioid prescriptions at 90 days was significantly lower. Although Cohen's d for the difference in opioid dose was low to moderate, this modulation in the effect was due to large variability in opioid dose in both groups. In fact, the standard deviation was greater than the mean mme for all time points and for both groups. On average, EDS patients were prescribed 58.9% more opioids within 90 days preoperatively and 38.2% more opioids in the first 90 days postoperatively than non-EDS patients.

EDS patients have a complex relationship with pain and analgesia. A retrospective single-center study by Song et al. reviewing the treatment efficacy of 98 EDS patients presenting to a physical medicine and rehabilitation clinic found that the most common type of treatment modality pursued by EDS patients was complimentary/alternative medicine (89.7%) closely followed by opioid and opioid-like pain medications (88.8%) [25]. Despite this high prescription rate for opioids, only 40% of patients reported improvement in pain with opiates and opiate-like medications, with 22% reporting adverse symptoms. This study also found that the most effective treatment was bracing of joints, with 70% reporting improvement in their symptoms. This study concluded that practitioners may want to consider a multidisciplinary approach to patients with EDS, involving pain medicine physicians who may be better equipped with specialized training in therapeutic options for EDS beyond opioids. Our findings further support this given the larger opioid prescriptions appreciated preoperatively and postoperatively, with continued prescriptions at 1 year following surgery. In our study population, 39.1% of EDS patients were no longer receiving an opioid prescription 90 days postoperatively, whereas 60.5% of non-EDS patients were no longer prescribed opioids. Furthermore, over half of EDS patients continued to receive opioid prescriptions at 1 year postoperatively. EDS patients with opioid prescriptions preoperatively were far more likely to continue to be prescribed opioids at 90 days and 1 year postoperatively. With such a high likelihood of persistent opioid prescription 1 year postoperatively, orthopaedic surgeons may want to consider engaging pain specialist for additional recommendations for long-term pain control options, given that THA as well as opioids may not be improving pain and may conversely be causing adverse symptoms.

Table 3
Frequency of complications of patients with Ehlers-Danlos syndrome undergoing total hip arthroplasty stratified by opioid use timeframe.

Complication	Opioid use		
	90-d preoperative	90-d postoperative	365-d postoperative
Dislocation (n = 23)	23	21	5
Infection (n = 7)	[a]	[a]	[a]
Medical (n = 9)	[a]	[a]	[a]
Revision (n = 66)	[a]	[a]	[a]
Total EDS (n = 238)	117	142	93

[a] Less than 10 cases recorded within the PearlDiver database.

Patients with EDS have been shown to have an increased risk of adverse perioperative and postoperative events following THA; however, no studies to date have evaluated opioids in this population or assessed postoperative complications with their use. One recent retrospective database study of patients undergoing primary THA demonstrated an increased risk of complications with preoperative opioid use in a dose-dependent manner, although this study does not specifically address patients with connective tissue disorders [24]. In a general study of connective tissue disorders from 1999 surveying 214 joint-related procedures of the shoulder, elbow, knee, and ankle, postoperative complications occurred more often in patients with connective tissue disorders compared to those without [26]. Additionally, a recent PearlDiver database study performed by Moore et al. of 365 patients with EDS undergoing THA demonstrated that patients with EDS experienced significantly higher rates of periprosthetic dislocation (4.2% vs 1.7%, $P = .001$) [21]. At 5 years postoperatively, 10.3% of patients with EDS experienced dislocations compared with 3.3% of matched control group. Patients with EDS had a significantly lower revision-free survivorship, where 92.7% had revision-free implant survival at 5 years and 96.1% for matched group ($P = .004$). In our study, patients with EDS who were prescribed opioids 90 days postoperatively were more likely to experience dislocation, which suggests that opioids may exacerbate this complication in a population already at heightened risk. However, further study regarding causation is warranted as increased opioid use may be a result of pain from dislocation rather than opioid use leading to the dislocation event itself.

Our study found no increase in medical complications or infections for those with EDS who were prescribed opioids preoperatively or postoperatively. Opioid use in the EDS population is theoretically at higher risk given multi-organ EDS manifestations including decreased gastrointestinal motility, orthostatic hypotension, dysautonomia, postural orthostatic tachycardia syndrome, and psychiatric side effects [16]. However, increased medical complications have not been supported in prior literature, where no difference in adverse events including cardiovascular complications, surgical site infection, or periprosthetic infection has been appreciated in the EDS population [21]. Our study supports this finding, with EDS patients using opioids were no more likely to experience medical complications or infection. As such, while our study highlights the increased usage of opioids surrounding THA, further study regarding the medical impact of opioids following THA is warranted.

This study is not without limitations, particularly given its retrospective nature and potential coding bias given its reliance on

the International Classification of Disease and Current Procedural Terminology codes. Furthermore, EDS encompasses a variety of phenotypes with varying degrees of orthopaedic and multiorgan system involvement that cannot be accounted for given database limitations. We are unable to control for varying degrees of hip disease, which may act as a confounder within this study. This study was also unable to assess concurrent or alternative analgesic use as well as other analgesic strategies like physical and occupational therapy, which may impact opioid use. Presumptive opioid use and amount are based on records of opioid prescriptions, and as such, may not accurately represent true patient opioid use. Additionally, this study was unable to determine the etiology of pain leading to opioid prescription, and as such, opioid use may be attributed to pain from other sources beyond the hip.

Conclusions

Elevated risk of opioid use and amount both preoperatively and postoperatively should be considered when advising patients with EDS who are considering THA. Patients who persistently use opioids postoperatively may be at heightened risk for dislocation; however, causation remains unclear as opioids may be prescribed for pain resulting from dislocation events. We recommend counseling patients regarding opioid use and considering a multidisciplinary approach with involvement of pain specialists to discuss alternative analgesic modalities to best treat pain associated with EDS.

Conflicts of interest

R. Kagan is a paid consultant for OrthAlign Corporation and Smith and Nephew, receives research support from OrthoDevelopment Corporation, Smith and Nephew, and 3M KCI Acelity, is an editorial board member of the Journal of Arthroplasty, and is a board/committee member of AAOS AJRR research committee and AAHKS Evidence Based Medicine Committee. All other authors declare no potential conflicts of interest.

For full disclosure statements refer to https://doi.org/10.1016/j.artd.2024.101390.

CRediT authorship contribution statement

Mackenzie Kelly: Conceptualization, Data curation, Formal analysis, Methodology, Writing – original draft, Writing – review & editing. **Ryland P. Kagan:** Conceptualization, Formal analysis, Methodology, Supervision, Writing – original draft, Writing – review & editing. **Jung Yoo:** Writing – review & editing, Writing – original draft, Software, Methodology, Conceptualization, Data curation, Formal analysis.

References

[1] Malfait F, Francomano C, Byers P, Belmont J, Berglund B, Black J, et al. The 2017 international classification of the Ehlers-Danlos syndromes. Am J Med Genet C Semin Med Genet 2017;175:8–26. https://doi.org/10.1002/ajmg.c.31552.

[2] Demmler JC, Atkinson MD, Reinhold EJ, Choy E, Lyons RA, Brophy ST. Diagnosed prevalence of Ehlers-Danlos syndrome and hypermobility spectrum disorder in Wales, UK: a national electronic cohort study and case–control comparison. BMJ Open 2019;9:e031365. https://doi.org/10.1136/bmjopen-2019-031365.

[3] Germain DP. Clinical and genetic features of vascular Ehlers-Danlos syndrome. Ann Vasc Surg 2002;16:391–7. https://doi.org/10.1007/s10016-001-0229-y.

[4] Beighton P. Ehlers-Danlos syndrome. Ann Rheum Dis 1970;29:332–3. https://doi.org/10.1136/ard.29.3.332.

[5] Beighton P, Horan F. Orthopaedic aspects of the Ehlers-Danlos syndrome. J Bone Joint Surg Br 1969;51:444–53.

[6] Atzinger CL, Meyer RA, Khoury PR, Gao Z, Tinkle BT. Cross-sectional and longitudinal assessment of aortic root dilation and valvular anomalies in hypermobile and classic Ehlers-Danlos syndrome. J Pediatr 2011;158:826–830.e1. https://doi.org/10.1016/j.jpeds.2010.11.023.

[7] Fikree A, Chelimsky G, Collins H, Kovacic K, Aziz Q. Gastrointestinal involvement in the Ehlers-Danlos syndromes. Am J Med Genet C Semin Med Genet 2017;175:181–7. https://doi.org/10.1002/ajmg.c.31546.

[8] Gensemer C, Burks R, Kautz S, Judge DP, Lavallee M, Norris RA. Hypermobile Ehlers-Danlos syndromes: complex phenotypes, challenging diagnoses, and poorly understood causes. Dev Dyn 2021;250:318–44. https://doi.org/10.1002/dvdy.220.

[9] Rombaut L, Scheper M, De Wandele I, De Vries J, Meeus M, Malfait F, et al. Chronic pain in patients with the hypermobility type of Ehlers-Danlos syndrome: evidence for generalized hyperalgesia. Clin Rheumatol 2015;34:1121–9. https://doi.org/10.1007/s10067-014-2499-0.

[10] 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;40:370–8. https://doi.org/10.1016/j.jpainsymman.2009.12.026.

[11] Gazit Y, Jacob G, Grahame R. Ehlers-Danlos syndrome-hypermobility type: a much neglected multisystemic disorder. Rambam Maimonides Med J 2016;7:e0034. https://doi.org/10.5041/RMMJ.10261.

[12] Larson CM, Stone RM, Grossi EF, Giveans MR, Cornelsen GD. Ehlers-Danlos syndrome: arthroscopic management for extreme soft-tissue hip instability. Arthroscopy 2015;31:2287–94. https://doi.org/10.1016/j.arthro.2015.06.005.

[13] Stanitski DF, Nadjarian R, Stanitski CL, Bawle E, Tsipouras P. Orthopaedic manifestations of Ehlers-Danlos syndrome. Clin Orthop Relat Res 2000:213–21. https://doi.org/10.1097/00003086-200007000-00029.

[14] Castori M, Tinkle B, Levy H, Grahame R, Malfait F, Hakim A. A framework for the classification of joint hypermobility and related conditions. Am J Med Genet C Semin Med Genet 2017;175:148–57. https://doi.org/10.1002/ajmg.c.31539.

[15] De Wandele I, Rombaut L, Malfait F, De Backer T, De Paepe A, Calders P. Clinical heterogeneity in patients with the hypermobility type of Ehlers-Danlos syndrome. Res Dev Disabil 2013;34:873–81. https://doi.org/10.1016/j.ridd.2012.11.018.

[16] Scheper MC, de Vries JE, Verbunt J, Engelbert RH. Chronic pain in hypermobility syndrome and Ehlers-Danlos syndrome (hypermobility type): it is a challenge. J Pain Res 2015;8:591–601. https://doi.org/10.2147/JPR.S64251.

[17] Zhou Z, Rewari A, Shanthanna H. Management of chronic pain in Ehlers-Danlos syndrome: two case reports and a review of literature. Medicine (Baltimore) 2018;97:e13115. https://doi.org/10.1097/MD.0000000000013115.

[18] Chopra P, Tinkle B, Hamonet C, Brock I, Gompel A, Bulbena A, et al. Pain management in the Ehlers-Danlos syndromes. Am J Med Genet C Semin Med Genet 2017;175:212–9. https://doi.org/10.1002/ajmg.c.31554.

[19] Ericson WB, Wolman R. Orthopaedic management of the Ehlers-Danlos syndromes. Am J Med Genet C Semin Med Genet 2017;175:188–94. https://doi.org/10.1002/ajmg.c.31551.

[20] Tinkle B, Castori M, Berglund B, Cohen H, Grahame R, Kazkaz H, et al. Hypermobile Ehlers-Danlos syndrome (a.k.a. Ehlers-Danlos syndrome Type III and Ehlers-Danlos syndrome hypermobility type): clinical description and natural history. Am J Med Genet C Semin Med Genet 2017;175:48–69. https://doi.org/10.1002/ajmg.c.31538.

[21] Moore HG, Burroughs PJ, Rubin LE, Frumberg DB, Sculco PK, Grauer JN. Patients with Ehlers-Danlos syndromes experience higher rates of prosthetic dislocation after total hip arthroplasty and worse implant survival at 5 years. J Am Acad Orthop Surg 2022;30:177–83. https://doi.org/10.5435/JAAOS-D-21-00347.

[22] Guier C, Shi G, Ledford C, Taunton M, Heckman M, Wilke B. Primary total hip arthroplasty in patients with Ehlers-Danlos syndrome: a retrospective matched-cohort study. Arthroplast Today 2020;6:386–9. https://doi.org/10.1016/j.artd.2020.05.006.

[23] Kagan R, Welling S, Mildren ME, Smith S, Philipp T, Yoo J. It is the opioids not the spine surgeon; dislocation after total hip arthroplasty is associated with opioid use in patients who have prior lumbar spine fusion. J Arthroplasty 2023;38:S336–9. https://doi.org/10.1016/j.arth.2023.02.080.

[24] Terhune EB, Hannon CP, Burnett RA, Della Valle CJ. Preoperative opioids and the dose-dependent effect on outcomes after total hip arthroplasty. J Arthroplasty 2022;37:S864–70. https://doi.org/10.1016/j.arth.2021.12.017.

[25] Song B, Yeh P, Nguyen D, Ikpeama U, Epstein M, Harrell J. Ehlers-Danlos syndrome: an analysis of the current treatment options. Pain Physician 2020;23:429–38.

[26] Weinberg J, Doering C, McFarland EG. Joint surgery in Ehlers-Danlos patients: results of a survey. Am J Orthop (Belle Mead NJ) 1999;28:406–9.

Appendix 1
ICD-10 procedure and diagnosis codes used for inclusion.

Procedure	Procedure codes
Primary THA	ICD-10-P-0SR9019, ICD-10-P-0SR901A, ICD-10-P-0SR901Z, ICD-10-P-0SR9029, ICD-10-P-0SR902A, ICD-10-P-0SR902Z, ICD-10-P-0SR9039, ICD-10-P-0SR903A, ICD-10-P-0SR903Z, ICD-10-P-0SR9049, ICD-10-P-0SR904A, ICD-10-P-0SR904Z, ICD-10-P-0SR9069, ICD-10-P-0SR906A, ICD-10-P-0SR906Z, ICD-10-P-0SRB019, ICD-10-P-0SRB01A, ICD-10-P-0SRB01Z, ICD-10-P-0SRB029, ICD-10-P-0SRB02A, ICD-10-P-0SRB02Z, ICD-10-P-0SRB039, ICD-10-P-0SRB03A, ICD-10-P-0SRB03Z, ICD-10-P-0SRB049, ICD-10-P-0SRB04A, ICD-10-P-0SRB04Z, ICD-10-P-0SRB069, ICD-10-P-0SRB06A, ICD-10-P-0SRB06Z
Hip arthroscopy	CPT-29860, CPT-29861, CPT-29862, CPT-29863, CPT-29914, CPT-29915, CPT-29916
Diagnosis	Diagnosis codes
Ehlers-Danlos	ICD-9-D-75683, ICD-10-D-Q796, ICD-10-D-Q7960, ICD-10-D-Q7961, ICD-10-D-Q7962, ICD-10-D-Q7963, ICD-10-D-Q7969
Obesity	ICD-10-D-E6601, ICD-10-D-E6609, ICD-10-D-E661, ICD-10-D-E662, ICD-10-D-E668, ICD-10-D-E669

ICD-10, International Classification of Disease, tenth revision.