

Outcomes of primary total hip arthroplasty in patients with Ehlers Danlos Syndromes

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Background: The Ehlers Danlos Syndromes (EDS) are inherited in an autosomal dominant pattern and patients classically present with hypermobility, skin hyper-elasticity, blood vessel fragility and atrophic scarring. Due to hypermobility, disorders such as joint pain and early arthritis are common. The aim of this study was to assess clinical and radiological outcomes of total hip arthroplasty (THA) in patients with EDS treated in a high volume orthopaedic centre.

Methods: A search was performed of the electronic patient record system at our institution from 1998 - 2019 using the search terms 'EDS' or 'Danlos' and 'arthroplasty'. Over the 22-year study period, there were approximately 32,000 primary THAs performed at our institution. We collated demographic information including age, gender, BMI, smoking history and medical comorbidities. Implant type, bearing surfaces and size was also documented, with clinical and radiological assessment at last known follow up.

Results: A total of n=5 primary THAs were identified in n=4 patients at a median follow-up of 3 years. All patients were female with a median age of 68 (SD 18.9) years and a median BMI of 30.7 (SD 4.5). The majority of patients were smokers, and had a chronic history of low back pain (n=3, 75%). Uncemented implants were used on n=3 occasions with the remainder being hybrid (n=2). Femoral head size ranged from 28mm to 44mm. One patient had a post-operative surgical wound erythema that resolved within 48 hours of onset, otherwise there were no significant wound complications. To date, there have been no documented dislocations, with all patients having satisfactory clinical and radiological outcome at last known follow up.

Conclusions: This study demonstrates that total hip arthroplasty can be safely performed in patients with a diagnosis of EDS, with no significant complications in the intermediate term.

Keywords: osteosarcoma, tumor metastasis, differentially expressed genes, prognosis prediction model.

INTRODUCTION

Ehlers-Danlos Syndromes (EDS) represent a constellation of connective tissue disorders with much clinical variability and genetic heterogeneity that has been described to affect almost all of the joints in the human body. These disorders share a common phenotype manifesting as skin hyperelasticity, joint hypermobility¹, blood vessel fragility and atrophic scarring². Classification of EDS began in the late 1960s before arriving at the Villefranche classification, which broke it down into six subtypes; i) classical, ii) hypermobility, iii) vascular, iv) kyphoscoliosis, v) arthrochalasia and vi) dermatosparaxis³. Types i, ii and iii are thought to be the most common and demonstrate an autosomal dominant inheritance pattern with complete penetrance³. Clinical severity has been reported to vary amongst family members and women are reported

to be more severely affected than men³. The overall prevalence is unknown but estimated to be approximately 1/10,000⁸. This six-subtype classification has been superseded in 2017 by an international consortium led by Malfait et al, which has recognized 13 major subtypes¹.

EDS and its effects on the native hip joint have been sparsely researched. It is thought that instability of the hip in those with a diagnosis of EDS is related to capsular and ligamentous laxity⁵. The resultant repetitive microtrauma is thought to be a potent source of pain as well as an instigator for articular injury, which could be a risk factor in the development of osteoarthritis⁵.

Skin involvement in EDS can be most severe in the classical type with tissue fragility resulting in skin splitting after relatively minor trauma⁶. Surgical wounds are known to heal slowly and can result in a

thin and atrophic scar⁶. There is also an increased risk of bleeding which is thought to be related to vascular fragility as opposed to platelet defect or coagulation dysfunction, given that laboratory coagulation investigations are usually normal⁷.

There is a lack of literature assessing the relationship between total hip arthroplasty and EDS. In total knee arthroplasty (TKA) however, two studies of 1⁸, and 16⁹ patients, have been published, with the former reporting an overall improvement in tibiofemoral stability in all but one patient, but a lower overall satisfaction rate in comparison to those undergoing TKA for conventional indications. The latter study reported that patients with EDS were not at increased risk of reoperation, revision surgery or decreased survivorship when compared to a control group who underwent TKA for osteoarthritis.

The aim of this study is to evaluate the clinical and radiological outcome of patients with a confirmed diagnosis of EDS who underwent primary total hip arthroplasty for osteoarthritis in an orthopaedic tertiary referral centre. Our hypothesis is that those patients undergoing a primary THA with a diagnosis of EDS would be more likely to develop complications such as delayed wound healing, infection and dislocation.

METHODS

The electronic patient record (EPR) system at our institution was interrogated using Structured Query Language (SQL) queries via an "R" script. Every clinic note from 1998-2019 was searched for the terms 'EDS', 'Danlos' and/or 'Arthroplasty'. The term 'Ehlers' was not searched for as this would have been more likely to be subject to mis-spellings. The results of this search were then matched against every operation note. Over the 22-year study period approximately 32,000 primary total hip arthroplasties were performed at our institution. Demographic information including age, sex, BMI, smoking history and medical comorbidities was documented on a secure database compliant with information governance guidelines. Implant type, bearing surfaces and sizes were also collated as well as both clinical and radiological assessment at follow up.

Our search string initially revealed 8 patients with a total of 9 operations (n=9). A total of four patients were excluded from the final analysis as one had EDS incorrectly entered (instead of EDC (end of distal clavicle)). The remaining three patients were excluded as it was documented that they did *not* have a diagnosis of EDS and thus were falsely picked up in the search. The final number of patients was n=4 with 5 total hip arthroplasties.

RESULTS

Patient demographics are displayed in Table I. All four patients reviewed were female with a median age of 68 (standard deviation, SD 18.9) and had a median body mass index (BMI) of 30.7 (SD 4.5). One patient had confirmed hypermobile EDS (Type III) the rest are all assumed to have either classic EDS (Type I and II) or hypermobile (Type III). Minimum follow up was 1 year with a median of 3 years. One patient was an active smoker and the majority (n=3, 75%) had a history of chronic low back pain.

THA Implant type and results of follow up are displayed in Table II. Three joint replacements were performed using uncemented implants with the remainder being hybrid (n=2). Femoral head size ranged between 28-44mm with bearing surfaces varying between metal on polyethylene (n=3), ceramic on ceramic (n=1) and ceramic on polyethylene (n=1). Only one patient had another joint replacement (total knee arthroplasty, TKA) with the exception of the single patient who underwent two total hip arthroplasties included in this review (Table 1). No patient sustained a significant intra- or post-operative complication. One patient reported a 48-hour history of wound erythema during the initial inpatient stay, which settled without antimicrobial or surgical intervention. Minimum follow up was 1 year with a range of 1-3 years. There have been no dislocations to date and no revisions of the primary implant. Patient radiographs at their most recent follow up appointment did not show any evidence of implant failure such as bony sclerosis, lucency, or fracture. Each patient stated that they were happy with the outcome of their surgery at the most recent clinic review.

DISCUSSION

At the time of conception this was the first case series of its kind in evaluating total hip arthroplasty for those with a diagnosis EDS. It is based on the cohort of a single large volume tertiary referral orthopaedic hospital (with an in-house rheumatology department) performing approximately 32,000 total hip arthroplasties over the last 22 years.

Our working hypothesis, with the cohort of patients with a diagnosis of EDS having undergone a primary THA, was that we would notice an increase in wound complications such as delayed healing and infection, as well as dislocations given the presence of soft tissue laxity. These complications were, however, not seen in our study.

Table I. — Demographic information for patients identified with Ehlers Danlos Syndromes undergoing total hip arthroplasty

Patient Demographics									
Patient	Sex	Time Since Surgery (Years)	Age at Time of Surgery	BMI	EDS Type	Smoker	Previous Joint Replacements	Comorbidities	Family History
Patient 1	F	3	68	30.7	III	NO	Yes - TKR	OA, Chronic Pain, Raynauds, Back pain, AF, HTN, CKD3	Son
Patient 2	F	2	40	33.4	III	YES	NO	LBP, previous dislocations of shoulders	Half Sister
Patient 3	F	13	77	27.7	III	NO	Bilateral THR	OA, Wrist Pain, Localised back pain, (Previous Hx Hep A)	Daughter & Granddaughter
Patient 3 (Contralateral Hip)	F	10	80	27.7	III	NO	Bilateral THR	OA, Wrist Pain, Localised back pain, (Previous Hx Hep A)	Daughter & Granddaughter
Patient 4	F	1	43	40	III	NO	No	Depression, recurrent shoulder dislocations, gastric bypass, low vit D, Hx poor wound healing.	N/A

Table II. — Implant Type and Follow Up Information for patients with Ehlers Danlos Syndromes undergoing total hip arthroplasty

Implant Type & Follow Up							
Patient	Implant & Bearing Surfaces	Head Size	Time - surgery to last follow up	Patient Satisfied ?	Time - surgery to latest x-ray	X-ray Outcome	Implant Revised ?
Patient 1	Uncemented - Metal on Polyethylene	28mm	1 year	Yes -	1 year	Satisfactory	No
Patient 2	Uncemented - Ceramic on Ceramic	32mm	1 year	Yes	1 year	Satisfactory	No
Patient 3	Uncemented - Metal on Polyethylene	40mm	3 years	Yes	3 years	Satisfactory	No
Patient 3 (Contralateral Hip)	Hybrid - Metal on Polyethylene	44mm	1 year	Yes	1 year	Satisfactory	No
Patient 4	Hybrid - Ceramic on Polyethylene	36mm	1 year	Yes	1	Satisfactory	No

Arthroplasty on other joints such as the shoulder and knee have been reported in EDS patients in the literature. Rose et al⁸ presented a case series of ten patients having undergone a total of twelve primary total knee arthroplasties for either arthritis or tibiofemoral instability. They report that outcomes were poorer in those with EDS undergoing total knee arthroplasty with only 70% of patients willing to undergo surgery again. Most recently in 2020, Guier et al¹¹ published a matched retrospective cohort study of 13 patients

who had a diagnosis of EDS and underwent a primary total hip arthroplasty. Two patients from each group sustained a dislocation although this represented a higher proportion in the EDS group. The frequency for dislocation in the EDS patients was also higher.

One of the limitations of this study is the absence of functional outcome measures. Our evaluation of patients is also limited to a review of the case notes on our electronic system. We are also unable to differentiate between the EDS types in the patient cohort. We may

not necessarily have picked up other complications given our relatively short follow up period. We take note of Guier et al¹¹ as above with their two patients dislocating at 8 months and 6 years from the primary surgery.

This study is also limited by our ability to interrogate our electronic patient record system given that we could only look for specific words and not for specifically coded procedures or conditions. We therefore may have unintentionally excluded patients if spelling mistakes had been made.

Our case series of 5 total hip arthroplasties in 4 patients did not demonstrate any wound complications, dislocation, revision or implant failure with a median follow up of three years. In summary, whilst caution should be exercised given the small series and retrospective design, we put forward an argument that total hip arthroplasty is a safe and viable treatment modality for those with chronic hip pain, degenerative changes and a diagnosis of EDS.

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