Comparative Analysis of Spondylolisthesis and Spinal Fusion Incidence in Adult Patients with Ehlers-Danlos Syndrome and Age-Gender Matched Control Group

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INTRODUCTION: Spinal fusion serves as a treatment approach for various conditions involving spinal instability or deformity, including injuries such as spondylolisthesis. The decision to proceed with surgery for spondylolisthesis depends on several factors, including the extent of displacement, presence of pain and neurogenic symptoms, as well as perceived instability from imaging and exam interpretation. This injury and subsequent surgical fixation may disproportionately impact individuals with joint hypermobility and tissue fragility, increasing the need for orthopedic care in patients with connective tissue diseases. Ehlers-Danlos Syndrome (EDS) is one such condition. EDS is a group of inherited disorders that impacts collagen synthesis, leading to hypermobility, early osteoarthritis, and often chronic pain. Treating spondylolisthesis in EDS patients requires a more comprehensive understanding of the complex issues related to spinal instability. Due to their lack of musculoskeletal stability and weak supporting tissues, individuals with EDS may be more prone to developing spondylolisthesis. Additionally, the presence of chronic pain and hypermobility in affected segments may further increase the need for spinal fusion. The purpose of this study was to gain a deeper insight into the impact of hypermobility in EDS patients on spinal pathology. Specifically, we aimed to determine the incidence of spondylolisthesis and the necessity for spinal fusion in these patients compared to the general adult population.

METHODS: This retrospective review was conducted by querying diagnostic codes from the International Classification of Disease (ICD) system, including both ICD-9 and ICD-10, from the PearlDiver database covering the period from 2010 to 2020. Additionally, we queried the Current Procedural Terminology (CPT) code for posterior spinal instrumentation. The initial query focused on patients aged 45 to 75. To establish a control population, a group of 3.5 million patients was created from the database who were further refined based on age and the absence of an Ehlers-Danlos Syndrome (EDS) diagnosis. The two groups, EDS and control, were compared in terms of the incidence of spondylolisthesis and posterior spinal fusion. To analyze the data, a t-test was performed to compare the means of age, while a chi-squared analysis was used to compare the rates of spondylolisthesis and spinal fusion. To ensure comparability between the EDS group and the control group, propensity matching was employed, matching age and gender at a ratio of 3 control patients to 1 EDS patient. From this propensity-matched group, the rates of spondylolisthesis and spinal fusion were compared using chi-squared analysis. Significance was determined if the p-value was less than 0.05, and the results are reported with risk ratio (RR) and a 95% confidence interval (CI).

RESULTS: In our query of the database, we identified a total of 25,688 EDS patients aged between 45 and 75. The control group consisted of 1,231,960 patients. The incidence of spondylolisthesis was found to be 8.4% among EDS patients, while it was 4.6% in the control group (RR = 1.82, CI = 1.74-1.90, $p < 0.0001$). The rate of spinal fusion was 1.2% for EDS patients and 0.5% for the control group (RR = 2.50, CI = 2.23-2.80, $p < 0.0001$).

Furthermore, we observed that the average age of patients with spondylolisthesis requiring fusion was younger in the EDS group (54.8 ± 9.3) compared to the control group (60.5 ± 8.1, $p < 0.001$). Additionally, a higher proportion of females underwent fusion in the EDS group compared to the control group (84.5% vs. 63.0%, $p < 0.0001$). Both male and female EDS patients had a higher risk of requiring posterior fusion for spondylolisthesis compared to the control group (RR = 2.81 and 2.29, respectively).After propensity matching the groups based on age and gender, the analysis showed that the risk of spondylolisthesis (RR = In1.39, $p < 0.0001$) and spinal fusion (RR = 1.62, $p < 0.0001$) remained increased in the EDS group compared to the control group, as observed in the univariate analysis.

DISCUSSION: The results of this study suggest that adults with Ehlers-Danlos syndrome have a higher prevalence of spondylolisthesis and a greater need for posterior spinal fusion. The elevated rate of spinal fusion surpasses the increased incidence rate of spondylolisthesis, indicating that EDS patients may experience a more appreciable degree of pain associated with this injury compared to the general population. These findings emphasize the importance of considering the implications of EDS for spinal injury risk, and suggest that guideline development for management of spondylolisthesis and other spinal pathologies in this patient population may be necessary.

SIGNIFICANCE/CLINICAL RELEVANCE: Individuals with connective tissue disorders like Ehlers-Danlos syndrome often face a higher burden of injury and associated pain, which may contribute to surgical fixation incidence in spinal pathology. Awareness of the impact EDS on spinal injury risk and relative need for surgery can contribute to developing better clinical and surgical decision-making guidelines for this population.

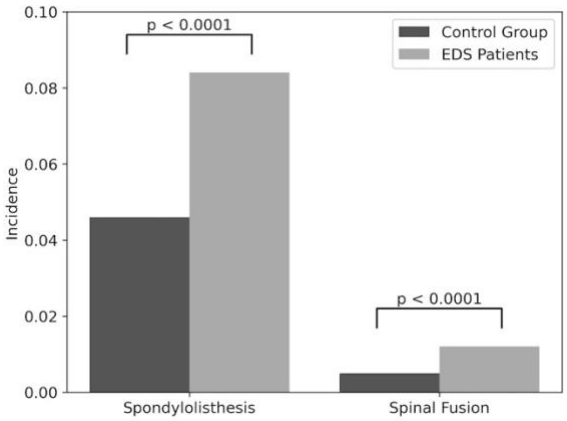

Figure 1: Incidence of spondylolisthesis and spinal fusion rates in EDS patients vs control group.