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Fat infiltration of the posterior paraspinal muscles is inversely associated with the fat infiltration of the psoas muscle: a potential compensatory mechanism in the lumbar spine

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Abstract

Background The function of the paraspinal muscles and especially the psoas muscle in maintaining an upright posture is not fully understood. While usually considered solely as a hip flexor, the psoas muscle and its complex anatomy suggest that the muscle has other functions involved in stabilizing the lumbar spine. The aim of this study is to determine how the psoas muscle and the posterior paraspinal muscles (PPM; *erector spinae and multifidus*) interact with each other.

Methods A retrospective review including patients undergoing posterior lumbar fusion surgery between 2014 and 2021 at a tertiary care center was conducted. Patients with a preoperative lumbar magnetic resonance imaging (MRI) scan performed within 12 months prior to surgery were considered eligible. Exclusion criteria included previous spinal surgery at any level, lumbar scoliosis with a Cobb Angle > 20° and patients with incompatible MRIs. MRI-based quantitative assessments of the cross-sectional area (CSA), the functional cross-sectional area (fCSA) and the fat area (FAT) at L4 was conducted. The degree of fat infiltration (FI) was further calculated. FI thresholds for FI_{PPM} were defined according to literature and patients were divided into two groups (< or ≥ 50% FI_{PPM}).

Results One hundred ninetypatients (57.9% female) with a median age of 64.7 years and median BMI of 28.3 kg/m² met the inclusion criteria and were analyzed. Patients with a $FI_{PPM} \ge 50\%$ had a significantly lower FI in the psoas muscle in both sexes. Furthermore, a significant inverse correlation was evident between FI_{PPM} and FI_{Psoas} for both sexes. A significant positive correlation between FAT_{PPM} and $fCSA_{Psoas}$ was also found for both sexes. No significant differences were found for both sexes in both FI_{PPM} groups.

Conclusion As the FI_{PPM} increases, the FI_{Psoas} decreases. Increased FI is a surrogate marker for a decrease in muscular strength. Since the psoas and the PPM both segmentally stabilize the lumbar spine, these results may be indicative of a potential compensatory mechanism. Due to the weakened PPM, the psoas may compensate for a loss in strength in order to stabilize the spine segmentally.

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Keywords Connective tissue, Muscle quality, Spinal fusion, Spine, Lumbar Iordosis, Spinal stability, Posterior paraspinal muscles, Psoas muscle

Background

Upright human posture and bipedalism are distinguishing characteristics of humans from other primates [1-3]. The standing stance is balanced, consumes little energy, and can be maintained for a long time. A number of factors contribute to the standing posture, including the spine that connects the upper extremities to the lower extremities and enables a stable, low-energy upright posture [3].

The stabilization of the spine is based on several factors such as an active and passive stabilization system in addition to a neural control system [4, 5]. The interaction of these three systems allows movement, distribution of forces acting on the bony spine, and protection of the spinal cord [4, 5]. The musculoskeletal portion of the spine is part of both the active and passive systems. The passive system consists of the vertebral bodies, the intervertebral discs, ligaments of the spine, the facet joints and the associated joint capsules [4, 5]. The active stabilization system includes the paravertebral muscles, superficial multi-segmental acting muscles including the deeper mono-segmental muscles, and the tendons of these muscles. Thus, the musculature involvement is complex given the required interactions to stabilize the entire spine stable and the individual vertebral segments [4-6]. The neural system has control and feedback functions and thus interacts with the active and passive systems [4, 5].

Imbalances in the stabilization systems can lead to the development of segmental instabilities [7]. In the physiological aging process of striated musculature, there is an increase in fat infiltration (FI) and a decrease in lean musculature (functional cross-sectional area=fCSA) [8, 9]. These two parameters can be determined with MRI muscle measurements. Increased FI and reduced fCSA are taken as surrogate markers for degraded, weaker muscle [10]. The literature highlights that FI is probably the more important parameter in determining muscle functional status. A higher FI is indicative of worse muscle function [11].

Recent studies have shown that increased FI of the posterior paraspinal musculature is associated with spinal pathologies such as degenerative spondylolisthesis, lumbar intervertebral disc degeneration and degenerative lumbar kyphosis [12–15]. It has also been demonstrated that the muscular area (CSA) of the posterior paraspinal muscles (PPM) is associated with the degree of lumbar lordosis. In the case of muscle atrophy or prolonged bed rest that results in weakened muscles, there could be

alterations in lumbar lordosis [16–19]. Due to the weakening of the paraspinal muscles from age or degenerative pathologies, the stabilization capacity of the active system might be limited. This can cause segmental instabilities in the sagittal plane and lead to a loss of lumbar lordosis (LL) due to reduced extension capacity. The function of the psoas muscle on the lumbar spine has not been fully elucidated. Whether the psoas muscle has a compensatory function to maintain the stability and lordosis of the lumbar spine is still unknown. The aim of this study was to investigate the interaction between psoas and PPM muscle composition to elucidate if the fat infiltration (FI) of the psoas muscle is associated with the posterior paraspinal morphology.

Methods

Subjects

A retrospective review of patients undergoing posterior lumbar fusion between 2014 to 2021 due to degenerative spinal conditions at a single academic institution was conducted. The investigation was approved by the institutional review board and was in compliance with the Helsinki Declaration. The institutional review board at Hospital for Special Surgery waived the requirement for written informed consent due to the retrospective study design. Inclusion criteria included patients > 18 years old, a preoperative magnetic resonance imagining (MRI) of the lumbar spine within 12 months prior to surgery, and availability of a preoperative lumbar radiograph. Exclusion criteria included any previous lumbar spine surgery, a Cobb angle > 20°, missing radiographs and non-measurable MR images due to technical incompatibility (Fig. 1). Patients' records were reviewed for demographic data, diagnoses, treated segments, American Society of Anesthesiology (ASA) score, and common comorbidities.

Muscle measurements

Prior to performing the muscle measurements, the upper endplate of L4 was set as the measurement level because it was previously shown that L4 is predictive for FI of the lumbar paraspinal musculature [20, 21]. The muscles assessed were the psoas muscle and the posterior paraspinal musculature consisting of the erector spinae and multifidus. Using axial T2-weighted MR images, the muscles were segmented utilizing a dedicated software (ITK SNAP version 3.8.0; www.itksnap.org [22];) (Fig. 2A and B). After the segmentation, a custom written software (Matlab version R2019a, The MathWorks, Inc.,



Fig. 1 Flowchart of patient inclusion and exclusion

Natick, MA, USA) was applied to calculate the cross-sectional area (CSA), the functional cross-sectional area (fCSA) and the fat area (FAT) of each muscle (Fig. 2C and D). The calculation is based on pixel intensity thresholds of the segmented muscles and identifies pixels either as fat or muscle by selecting an automatic threshold signal with intensity bias correction by quadratic fitting. Pixels above the threshold are considered as fat and pixels below as muscle. The results of the calculations include the CSA (=fCSA+FAT), fCSA and FAT. Fat infiltration (FI, %) was further calculated for the segmented muscles using the following equation: $FI = \left(\frac{FAT}{CSA}\right) * 100$. The right and left sides of the muscles were summarized and normalized by patient height (cm^2/m^2) . It has recently been demonstrated that the muscle measurement method we used has an excellent intra- and inter-rater reliability [23].

Lumbar lordosis measurement

Lumbar lordosis (LL) was measured on preoperative lateral lumbar spine radiographs by one orthopaedic resident. LL was determined using the Cobb angle from the superior endplate of L1 and S1.

Statistical analysis

First, the data were tested for normal distribution using the Shapiro wilk test. Depending on the distribution, mean and standard deviation (SD) or median and interquartile range [IQR] are reported in the manuscript. According to Kjaer et al., patients can be divided into three groups with low (<10%), medium (10-50%) and high FI (\geq 50%). Since none of our patients had < 10% FI_{PPM}, we divided patients into high fat infiltration (>50%) and low to moderate fat infiltration (<50%)of the PPM [24, 25]. All analyses were stratified by sex. For group comparisons of continuous variables, either the t-test or the Mann-Whitney-U test was conducted depending on the distribution of the data. A multiple linear regression analysis was conducted with FI_{Psoas} as the dependent variable. Age, body mass index, sex, race and FI_{PPM} were the independent variables for the regression model. Spearman rank correlation testing was conducted to determine the associations between the muscular parameters. Statistical significance was set to p < 0.05. All analysis were conducted using SPSS Version 28.0 (IBM Corporation, New York, United States).

Results

A total of 190 patients (57.9% female) with a median age of 64.7 [56.7;71.4] years and median BMI of 28.3 [25.7;32.7] kg/m² were analyzed. The majority of patients were Caucasian (90%) and the most common surgical diagnosis was degenerative spondylolisthesis (81.1%) followed by spinal stenosis (78.9%). 59.4% of patients received a monosegmental posterior fusion and had an ASA score of II (71.6%). A detailed description of patients' demographics can be found in Table 1 stratified by sex.



Fig. 2 Muscle measurement technique. Images A and B demonstrate the segmentation process utilizing ITK Snap. Images C and D highlight the use of the custom written software program and the pixel intensity thresholds

Associations between the posterior paraspinal muscles and the psoas muscle

In females, 65 (59.5%) were found to have FI_{PPM} less than < 50%. In this group of low to medium FI, both FAT_{Psoas} and FI_{Psoas} were significantly lower than in high FI patients with $\text{FI}_{\text{PPM}} \ge 50\%$. The majority of males, 82.5% (*n*=66), had a $\text{FI}_{\text{PPM}} < 50\%$ compared to the 17.5% (*n*=14) with a $\text{FI}_{\text{PPM}} \ge 50\%$. However, A similar picture as in females is seen in males. Men with $\text{FI}_{\text{PPM}} \ge 50\%$ had a significantly lower FI_{Psoas} . Group comparison showed that both FAT_{PPM} and FI_{PPM} were significantly greater in the $\text{FI}_{\text{PPM}} \ge 50\%$ group. fCSA_{PPM} was significantly lower in the $\ge 50\%$ FI_{PPM} (Table 2).

The correlation analysis revealed several significant associations between the posterior paraspinal muscles and the psoas for both men and women. An increase in FI_{PPM} is associated with a significant lower FI_{Psoas} in both men and women (f: ρ =-0.403, p<0.001; m: ρ =-0.452, p<0.001). Similarly, an increase in FAT_{PPM} leads to a significant decrease in $\text{FAT}_{\text{Psoas}}$ and FI_{Psoas} in both men and women. However, there was a positive association

between $fCSA_{PPM}$ and FI_{Psoas} found only in women. (Table 3).

The overall multiple linear regression model (Table 4) was significant (p < 0.001) and represented 17.1% (Corrected R²=0.171) of the variation of the dependent variable, FI_{Psoas}. FI_{PPM} (β =-0.520; p < 0.001) and sex (β =0.151; p=0.032) could predict FI_{Psoas}.

Lumbar lordosis and paraspinal muscle measurements.

There was no significant difference in lumbar lordosis between the groups with < 50% FI_{PPM} and \geq 50% FI_{PPM} in both males and females (Table 5).

Discussion

To the authors' knowledge, this is the first time that a reciprocal relationship between qualitatively assessed FI of the PPM and psoas has been described in males and females. Since FI of the musculature is an important surrogate parameter for muscular function, these results suggest a possible compensatory mechanism of the psoas muscle resulting from increased muscular

Table 1 Patient demographics

	Patient demographics				
	All	Female	Male		
N	190	110	80		
Age [years]	64.7 [56.7;71.4]	65.6 [58.3;71.7]	63.1 [54.5;69.9]		
BMI [kg/m ²]	28.3 [25.7;32.7]	27.8 [24.8;32.2]	29.0 [26.9;33.8]		
Race N (%)					
Caucasian	171 (90)	101 (91.8)	70 (87.5)		
African American	12 (6.3)	6 (5.5)	6 (7.5)		
Asian	4 (2.1)	1 (0.9)	3 (3.8)		
other	3 (1.6)	2 (1.8)	1 (1.2)		
Diagnosis* N (%)					
Spinal Stenosis	150 (78.9)	86 (78.2)	64 (80)		
Foraminal Stenosis	6 (3.2)	2 (1.8)	4 (5)		
DDD	123 (64.7)	62 (56.4)	61 (76.3)		
Spondylolisthesis	154 (81.1)	87 (79.1)	67 (83.8)		
Neurogenic Claudication	57 (30)	33 (30)	24 (30)		
Herniated Nucleus Pulposus	21 (11.1)	13 (11.1)	8 (10)		
Treated Segments N (%)					
I	113 (59.4)	66 (60)	47 (58.8)		
II	63 (33.2)	37 (33.6)	26 (32.5)		
III	11 (5.8)	6 (5.5)	5 (6.3)		
IV	2 (1.1)	1 (0.9)	1 (1.2)		
V	1 (0.5)	0 (0)	1 (1.2)		
ASA-Score N (%)					
I	8 (4.2)	5 (4.6)	3 (3.8)		
II	136 (71.6)	79 (71.8)	57 (71.2)		
III	46 (24.2)	26 (23.6)	20 (25.0)		
Comorbidities N (%)					
Diabetes Mellitus N (%)	17 (8.9)	11 (10.0)	6 (7.5)		
COPD N (%)	7 (3.7)	5 (4.6)	2 (2.5)		
Hypertension N (%)	77 (40.5)	43 (39.1)	34 (42.5)		
Congestive Heart Failure N (%)	0 (0)	0 (0)	0 (0)		
Ever Smoker N (%)	78 (41.1)	40 (36.4)	38 (47.5)		

Age and body mass index (BMI) is presented as median and interquartile range. Categorical variables are presented as frequencies (=N) and percentage (%). DDD Degenerative disc disease, ASA Score American Society of Anesthesiology Score

activity and reduced FI to stabilize the lumbar spine when the PPM are deteriorated.

The stabilization of the lumbar spine is based on three subsystems [4, 5] In addition to the passive and neural systems, the active system is essential for adequate spinal stability. In the absence of the paraspinal muscles, the spine would be highly unstable even under minimal loads [5] It is known that with increasing age, but also with spinal pathologies, the PPM degenerates. Radiologically, this can be measured using surrogate markers such as fCSA and FI where a higher FI implies weaker muscle [10, 11, 26] However, definitive cut off values for the paraspinal muscles have not been established to date to understand when FI is considered pathological. Özcan-Ekşi et al. have already described a reciprocal relationship between multifidus and psoas in their study for women. Our study confirms the results for women and shows that there is a similar phenomenon for men. In the work presented here, we have the advantage of having qualitative measurements of the musculature, which is particularly advantageous for the psoas muscle, which is known to have little fat infiltration [27].

The function of the PPM on the lumbar spine is of interest to researchers. Due to the high prevalence of back pain and the close functional relationship between the paraspinal musculature and the spine, it is assumed that the paraspinal muscular morphology, especially a higher FI and lower fCSA, is associated with the Table 2 Comparison of the female and male groups classified based on fat infiltration of the posterior paraspinal muscles (PPM)

	Muscle Measu	Muscle Measurements						
			< 50% FI _{PPM}	\geq 50% FI _{PPM}	<i>p</i> -value			
Females	Psoas	CSA [cm ² /m ²]	6.6 [5.6;8.1]	6.7 [6.1;7.8]	0.801			
		fCSA [cm ² /m ²]	6.0 [5.2;7.3]	6.3 [5.7;7.7]	0.348			
		FAT [cm ² /m ²]	0.36 [0.16;0.71]	0.23 [0.10;0.43]	0.016			
		FI [%]	5.6 [2.6;9.7]	3.2 [1.3;6.4]	0.009			
	PPM	CSA [cm ² /m ²]	18.2 [16.2;20.2]	19.9 [17.8;23.6]	0.002			
		fCSA [cm ² /m ²]	11.0 [9.2;12.3]	8.6 [7.4;10.2]	< 0.001			
		FAT [cm ² /m ²]	7.5 [6.2;8.6]	11.4 [9.9;13.5]	< 0.001			
		FI [%]	40.9 [35.1;46.9]	55.5 [53.4;59.2]	< 0.001			
Males	Psoas	CSA [cm ² /m ²]	9.4 [7.8;11.3]	10.0 [8.1;11.2]	0.685			
		fCSA [cm ² /m ²]	8.6 [7.4:10.2]	9.6 [8.0;11.0]	0.311			
		FAT [cm ² /m ²]	0.37 [0.21;0.65]	0.33 [0.10;0.38]	0.068			
		FI [%]	3.7 [2.2;7.8]	3.0 [1.0;3.8]	0.034			
	PPM	CSA [cm ² /m ²]	19.5 [17.2;23.0]	17.7 [16.9;19.2]	0.083			
		fCSA [cm ² /m ²]	12.0 [10.8;14.1]	8.1 [7.1;8.8]	< 0.001			
		FAT [cm ² /m ²]	7.4 [5.8;9.3]	10.3 [9.3;11.0]	< 0.001			
		FI [%]	38.9 [32.7;44.0]	54.6 [53.1;60.0]	< 0.001			

Significant values are written in bold. Statistical significance was set at a *p*-value < 0.05. *FI* Fat infiltration; *CSA* Cross sectional area, *fCSA* Functional cross-sectional area, *FAT* Total fat area

 Table 3
 Correlation analysis for the muscular parameters stratified for sex

			Posterior Paraspinal Muscles (PPM)							
			Female			Male				
			CSA [cm ² /m ²]	fCSA [cm ² /m ²]	FAT [cm ² /m ²]	FI [%]	CSA [cm ² /m ²]	fCSA [cm ² /m ²]	FAT [cm ² /m ²]	FI [%]
Psoas	Female	CSA [cm ² /m ²]	,337**	,366**	,136	-,076				
		fCSA [cm ² /m ²]	,380**	,307**	,230 [*]	,022				
		FAT [cm ² /m ²]	-,076	,299**	-,316**	-,392**				
		FI [%]	-,177	,222*	-,383**	-,403**				
	Male	CSA [cm ² /m ²]					,370**	,350**	,239 [*]	-,043
		fCSA [cm ² /m ²]					,434**	,325**	,380**	,091
		FAT [cm ² /m ²]					-,117	,160	-,444**	-,427**
		FI [%]					-,255*	,058	-,558**	-,452**

Significant values are marked with * or **. ρ -values marked with * are significant at the 0.05 level. ρ -values marked with ** are significant at the 0.01 level. CSA Cross sectional area, *FCSA* Functional cross-sectional area, *FAT* Total fat area, *FI* fat infiltration

development of back pain [28–31]. However, the literature is still inconclusive. Further studies investigated the relationship between degenerative spinal diseases and the paraspinal musculature [32–34]. A biomechanical study showed that weakened PPM are associated with the development and worsening of degenerative spondylolisthesis [35]. Clinical studies have shown that the fCSA was smaller and the ratio of fCSA to CSA was higher in patients without degenerative spondylolisthesis [13]. Another study demonstrated that degenerative lumbar kyphosis was associated with a significantly lower fCSA and higher FI of the PPM [15]. In recent years, research has indicated the importance of the musculature is for upright posture [36, 37]. However, the relationship between LL and PPM has not been fully elucidated. Biomechanical studies assume that the PPM generates a follower load in the lumbar spine [38]. The concept of a follower load is based on the fact that the resulting force of the PPM is tangential to the sagittal spinal curve to support the lumbar spine in carrying the weight of the upper body [6, 39]. Increased LL requires a higher follower load and thus stronger PPM [40]. Studies have shown that there is a relationship between CSA_{PPM} and LL, but it has not been shown if this relationship is causative or correlative [38].

Predictor	b [95%-Cl]	SE	Beta	t	p	VIF
(Constant)	11.463 [4.659,18.266]	3.449		3.324	0.001	
FI _{PPM} [%]	-0.297 [-0.391,-0.203]	0.048	-0.520	-6.235	< 0.001	1.158
Age [years]	0.070 [-0.012,0.160]	0.041	0.135	1.683	0.094	1.474
BMI [kg/m ²]	0.024 [-0.112,0.160]	0.069	0.024	0.350	0.727	1.036
Sex	1.870 [0.165,3.576]	0.864	0.151	2.164	0.032	1.106
Race	-0.315 [-1.881,1.251]	0.794	-0.027	-0.397	0.692	1.019

Table 4 Multiple linear regression model with fat infiltration of the psoas (FI_{Psoasr} %) as the dependent variable

Note. R²=.171 (p<0.001) Durbin-Watson Statistics: 1.982

Independent variables were age, body mass index (BMI), sex, race and fat infiltration of the posterior paraspinal muscles (FI_{PPM}, %). Significant values are marked in bold. Statistical significance was defined as p < 0.05

Table 5 Lumbar lordosis (LL) in the posterior paraspinal muscle (PPM) groups stratified by sex

	< 50% FI _{PPM}	\geq 50% FI _{PPM}	<i>p</i> -value
Female LL [°]	51.9±13.4	52.3±11.1	0.852
Male LL [°]	49.6 ± 14.8	46.0 ± 9.9	0.392

 $\mathsf{FI}=\mathsf{fat}$ infiltration. Significant values are marked in bold. Statistical significance was defined as p<0.05

Some studies assume that the strength of the muscles is proportional to their CSA [38, 41, 42]. However, this concept is questionable in the PPM since longitudinal studies have shown that there is no change in the CSA at L3/4 of the PPM with age, but a shift to higher FI in patients at the age of 50 years at baseline [43]. Whether age-related loss of LL is due to weakened PPM muscles or due to degenerative changes has not been determined. It is also possible that LL changes only as an adaptation mechanism to changes in pelvic tilt [44]. This concept has recently been proposed but has not been validated by longitudinal studies. The currently accepted concept is that the loss of LL is due to degenerative changes in the intervertebral disc [1]. However, our data reveals no significant differences for both sexes regarding the LL between < 50% FI_{PPM} and \geq 50% FI_{PPM} , which may indicate that LL may be more tightly regulated by other factors than the PPM such as intervertebral disc degenerations, increased pelvic tilt or anterior wedging of the vertebrae.

The function of the psoas muscle on the lumbar spinal column remains unclear. Three main theories about psoas muscle function have been proposed: 1) reduction of lumbar lordosis by bending the trunk forward, 2) increase in LL, and 3) stabilization of the lordotic curve by adaptation of the contraction of the individual fascicles [45–54]. Our data suggest that the psoas may help maintain LL even if the PPM has a higher FI, which, is in line with the third proposed theory. The significantly lower FI_{Psoas} in both men and women with \geq 50% FI_{PPM}

indicates there may be increased psoas muscular activity resulting in a lower FI of the muscle. The potential higher activity in the psoas muscle may be necessary to maintain LL to allow optimal force distribution across the lumbar spine.

Arbanas et al. demonstrated in their study that patients with low back pain (LBP) have a significantly larger CSA_{Psoas} than patients without LBP [55]. However, the FI in the work of Arbanas et al. was only measured quantitatively based on a four grade visual scale. Due to the relatively low FI of the psoas, they were probably unable to demonstrate any significant differences for the FI_{Psoas}. Arbans et al. hypothesized that the psoas may compensate by increasing activity to maintain the stability of the lumbar spine as the CSA_{Psoas} was larger in the group with LBP [55].

Our study is not free of limitations. First, causality cannot be established due to our retrospective cross-sectional study design. Additionally due to the retrospective design, we were unable to include other factors influencing muscle composition such as physical activity in our study. Well-designed prospective longitudinal studies are necessary to control for co-factors such as physical activity and to establish causality. Furthermore, it must be noted that only 14 males with a $FI_{PPM} \ge 50\%$ were in our patient population and therefore the results for males must be interpreted with caution. Another point that needs to be addressed is that only patients undergoing lumbar fusion surgery due to degenerative spinal pathologies were included, which limits the generalizability of our results. However, our study population represents a cohort that is frequently seen in orthopedic practice and therefore of high clinical relevance. Another limitation of our study is the uncertainty and variation in posture affecting the LL, and the possibility of changes of the LL throughout the day. However, due to the cross-sectional study design, it is not possible to observe this exactly. We think that due to the relatively large number of patients, the statement of the LL in our study is valid.

Conclusion

In conclusion, our work provides indications that the psoas might have a compensatory function in stabilizing the lumbar spine and maintaining lumbar lordosis when the posterior paraspinal muscles are degenerated. However, further studies are needed to verify our findings and hypothesis that the psoas muscle is more active when the posterior paraspinal muscles are deteriorated.

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Authors' contributions

Conception and design: Muellner, Haffer. Acquisition of data: Muellner, Haffer, Chiapparelli, Analysis and interpretation of data: Muellner, Hughes. Drafting the article: Muellner. Critically revising the article: all authors. Reviewed submitted version of manuscript: all authors. Approved the final version of the manuscript on behalf of all authors: Hughes. Statistical analysis: Dodo, Zhu. Administrative/ technical/material support: Tan, Shue. Study supervision: Hughes.

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Availability of data and materials

The datasets generated and analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

All experimental protocols were approved by the institutional review board of the Hospital for Special Surgery (NYC, NY, USA) (2014–084) and all methods were carried out in accordance with the Helsinki Declaration. The institutional review board at Hospital for Special Surgery waived the requirement for written informed consent due to the retrospective study design.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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