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# OSSIFICATION OF THE LIGAMENTUM FLAVUM OF THE LUMBOSACRAL SPINE IN THE POLISH HOSPITALIZED POPULATION — A PROSPECTIVE COHORT STUDY

**Abstract:** Aim: The aim of this study was to assess the prevalence, clinical features and distribution of lumbosacral ossifications of the ligamentum flavum (OLF), using MRI, CT and microCT, in hospitalized Polish patients.
Methods: Patients were recruited prospectively between January 2011 and January 2013. Patients were further qualified to the study group only if CT or MRI of the lumbosacral region detected OLF. Level of OLF excision was determined by the localization of spinal stenosis. After excision the LF fragments containing OLF were stored in a 4% solution of formaldehyde until microCT assessment.
Results: A total of 184 agreed to take part in the study. In 50 patients (27.2%) OLF were found. Thus, the study group consisted of 17 women (34%) and 33 men, with a mean age of 55.4 ± 17.2 years. OLF occurred more often in men (66%) than in women (34%) ($p = 0.0014$). The most common site for the localization of OLF in women, as well as in men was the L5/S1 level (60% and 53.3% respectively). The mean volume of OLF was 3.87 ± 5.27 $mm^3$ (4.66 ± 5.71 $mm^3$ vs. 1.27 ± 2.19 $mm^3$, in men and women respectively; $p = 0.023$).
The LF were thickened in 21 (42%) patients. The mean volume of OLF in patients with normal LF was 4.78 ± 5.95 $mm^3$ and in patients with thickened LF 5.33 ± 6.10 $mm^3$ ($p = 0.75$).
Conclusions: The prevalence of lumbosacral OLF in the Polish hospitalized population is very high. The most common site of their localization is the L5/S1 level. LF thickening is not associated with OLF formation.

**Key words:** ligamentum flavum, lumbosacral, microCT, OLF, yellow ligament.

## INTRODUCTION

The first report concerning myeloradiculopathy caused by ossfication of the ligamnetum flavum (OLF) was published in 1920 by Polgar [1]. OLF is relatively common in East Asia countries [2–4], though the majority of reports originate from Japan [5]. There also exist individual reports, on the subject of OLF, among Caucasians [6], Africans [7] and Arabs [8, 9]. However all of the above mentioned studies are limited either by the size of the sample, diagnostic method used or region of the spine that was investigated.

Most cases of OLF remain asymptomatic and can involve any vertebral segment of the spinal column [1].

The imaging method of choice for OLF detection is a T2-weighted sagittal MRI [2]. The diagnostic accuracy can be further enhanced by combining MRI with CT [10, 11].

Most of the studies focusing on the subject of OLF analyse the thoracic spine [3–5, 10], and base on MRI as the diagnostic method of choice [2, 9]. Studies analyzing OLF in the lumbar region are scarce [12, 13]. To the authors best knowledge, there are no studies regarding the subject of OLF prevalence in the Polish population.

The aim of this study was to assess the prevalence, clinical features and distribution of lumbosacral OLF, using MRI, CT and microCT, in hospitalized Polish patients.

## MATERIALS AND METHODS

### PATIENTS

The patients were recruited prospectively between January 2011 and January 2013 in the Department of Traumatology and Neuroorthopaedics (Rydygier Specialistic Hospital, Krakow, Poland). Patients were eligible if they were above 18 years of age and had been qualified for spine surgery (during which the ligamentum flavum — LF is routinely excised) of the lumbar region due to either trauma, discopathy or spinal stenosis. Exclusion criteria included lack of consent to participate in the study and spinal stenosis due to a malignant process.

### PREOPERATIVE DATA COLLECTION

Medical data regarding comorbidities, medications taken and duration of symptoms, was registered for each patient from patient files. Next, a full physical examination was conducted by an experienced orthopaedic surgeon.

Each patient qualified for the study had either a CT or MRI (Fig. 1) of the lumbosacral region performed. MRI was the imaging method of choice, and CT was only performed in the case of patients after trauma or having metal implants preventing MRI. Patients were further qualified to the study group only if CT or MRI of the lumbosacral region detected OLF. Imaging allowed to assess the morphology of the LF, the presence, localization and type of OFL and the level of spinal stenosis. This level was always treated as the site from which the OLF was excised.

Ligamentum flavum thickening and spinal stenosis were defined as per the definitions given by Sakamaki *et al.* [14].

Fig. 1. A T2 lumbosacral spine saggital MRI image. OLF can be seen at the L2–L3, L3–L4, L4–L5 and L5–S1 levels.

## OLF EXCISION, MICROCT SCANNING AND SAMPLE VIRTUAL RECONSTRUCION

Surgery was performed using the posterior approach. The LF were always excised in the same way, starting at the lamina of the vertebral arch. The internal, external, cranial and caudal edges of the excised LF fragment were marked using different surgical sutures.

The excised fragments were stored in a 4% solution of formaldehyde and transported to the Jagiellonian University Institute of Physics for microCT (SkyScan 1172, Bruker, Belgium) assessment. The spatial resolution was set to 13.68 μm per pixel [15]. The shadow images were obtained with X-ray source energy of 80 keV using the 0.5 mm Al filter. The angular step between image acquisitions was 0.4° and the image was averaged from 5 frames. The samples were mounted on a custom plasticine attachment which allowed for precise repositioning of the specimen in the scanning system along the Z-axis (error <1 voxel) with minimal rotational error (<1 degree).

Virtual reconstructions were prepared using NRecon software (SkyScan). CTvox software (SkyScan) was used for primary volume rendering of every sample. The

transfer function was appropriately set to visualize OLF inside the sample. The obtained microCT images (Fig. 2) were analyzed using ImageJ software [16]. The analysis allowed to precisely assess the volume and shape of the OLF.

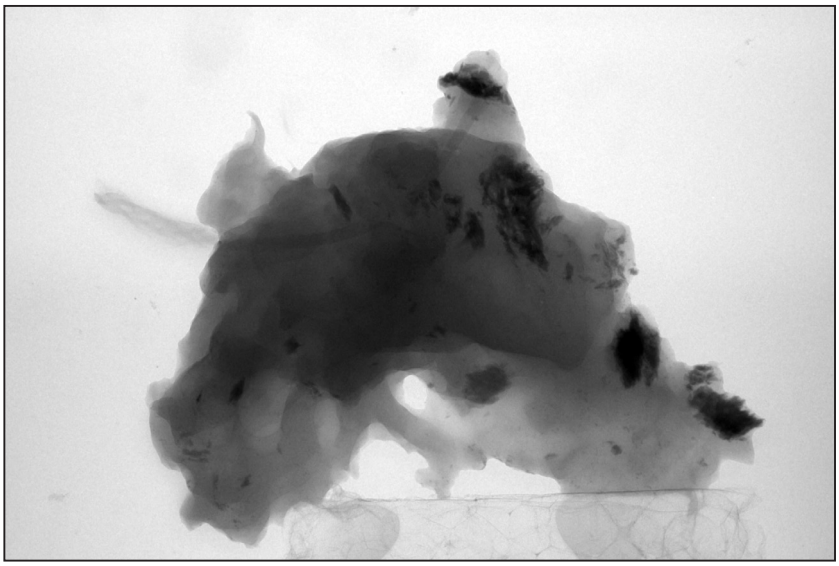

Fig. 2. A microCT image of a yellow ligament fragment. The darker shapes represent ossifications.

## STATISTICAL EVALUATION

Statistical analysis was conducted using computer software Statistica 10.0 PL by StatSoft Poland (licensed to the Jagiellonian University Medical College, Krakow, Poland). Descriptive statistics (mean, standard deviation, percentage distribution) were used. The Mann-Whitney U-test was used when comparing quantitative variables. The chi-square test was used when comparing qualitative variables. Correlations were assessed using Spearman correlation coefficient. The significance level was set at $p < 0.05$.

## ETHICAL APPROVAL

The protocol of this study has been approved by the Jagiellonian University Medical College Bioethical Committee (registry number KBET/176/B/2011). Each patient gave their informed consent to participate in this study. The study has been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments.

## RESULTS

### PATIENT CHARACTERISTICS

During the 24 month recruitment period a total of 184 (67 women — 36.4%) agreed to take part in the study. In 50 patients (27.2%), using either MRI or CT, OLF were found. Thus, the study group consisted of 17 women (34%) and 33 men, with a mean age of 55.4 ± 17.2 years.

The OLF occurred more often in men (66%) than i women (34%) ($p = 0.0014$).

There was no correlation between the existence of OLF and patient comorbidities such as hypertension, ischaemic heart disease, diabetes and thyroid diseases, as well as with the patients blood type ($p>0.05$). There was also no correlation between a patient's age and the volume of the OLF ($r = 0.3$, $p > 0.05$).

The most common site for the localization of OLF in women, as well as in men was the L5/S1 level (60% and 53.3% respectively).

The mean volume of the OLF was 3.87 ± 5.27 $mm^3$ (4.66 ± 5.71 $mm^3$ vs. 1.27 ± 2.19 $mm^3$, in men and women respectively; $p = 0.023$).

The LF were thickened in 21 (42%) patients. The mean volume of the OLF in patients with normal LF was 4.78 ± 5.95 $mm^3$ and in patients with thickened LF 5.33 ± 6.10 $mm^3$ ($p = 0.75$).

## DISCUSSION

The aim of this study was to assess the prevalence, clinical features and distribution of lumbosacral OLF in hospitalized Polish patients. To the authors best knowledge, this is the first study to employ microCT in the analysis of OLF. No studies as of yet have tried to determine OLF volumes.

The epidemiology of OLF varies depending on race and geographic area. There is an abundance of studies reporting on the subject of thoracic OLF frequency [2–5]. On the other hand, the prevalence of lumbar OLF is rarely described. In our study, the prevalence of lumbosacral OLF was found to be 27.2%. This frequency is considerably higher than the one reported by Guo *et al.* [2] who found the lumbar OLF frequency to be 0.1% out of the 1736 Chinese patients who had undergone MRI. A roentgenogram based study by Kurihara *et al.* [17] reported the prevalence of lumbar OLF in Japanese individuals to be 8.6% (out of the 2403 analyzed cases). However, as classic roentgenography is not the imaging method of choice for OLF, this study might severely underscore the population frequency of lumbar OLF. A study by Ergun and Lakadamyali [13], basing on CT imaging, reports the frequency of lumbar OLF, in the Turkish population, to be 35% (out of the 114 analyzed patients). A Belgian CT study estimated the prevalence of lumbar OLF to be 5.44% (out of the 1021 analyzed cases) [18]. As one can see

the current literature displays no agreement can be reached as to the prevalence of lumbar OLF. Further MRI studies regarding the prevalence of OLF, basing on larger patient samples, need to be performed.

Regarding OLF gender distribution, our study reports a male predominance. This stands in line with some of the other studies [2, 11]. However some studies report a higher rate of OLF in females [8, 15], or report no gender difference at all [9]. AS mentioned above, this warrants further studies on this matter.

A study by Guo *et al.* [2] has shown that the presence of OLF is age dependent, with older patients being more prone to developing OLF. This is not too surprising and is in accordance with clinical experience. However symptomatic OLF tend to be present among those patients being over 50 years of age.

The most common site for lumbosacral OLF localization was the L5/S1 level, with no gender differences. What is interesting, in our study the volume of OLF was significantly larger in men than in women. This might suggest that women tend to go to the doctor earlier than men, not waiting for their radiculopathy symptoms to worsen. Consequently, women undergo surgery on an earlier stage. This allows less time for large OLF to form. On the other hand, men tend to have wider spinal canals (when assessed on the sagittal plane) [19], thus allowing more time before the OLF grows to the point when it becomes symptomatic.

Another interesting observation is that OLF volume seems not to impact LF thickness. Patients with thickened LF and patients with normal LF do not differ in OLF volume. This shows that LF thickening is not associated with OLF formation, but rather with LF hypertrophy caused by fibrosis [20].

A number of authors have suggested that a whole spine T2-weighted sagittal MRI should be performed in all OLF patients [10, 11, 21] as there is a risk of multiple level lesion and combined pathologies such as hidden cervical and lumbar stenoses. This is backed-up by the data obtained by Guo *et al.* [2] which shows that almost 1/3 of patients with OLF has more than one level of the spine involved.

Concluding, the prevalence of lumbosacral OLF in the Polish hospitalized population is very high. The most common site of their localization is the L5/S1 level. Ligamentum flavum thickening is not associated with OLF formation. OLF should be kept in mind as a possible cause of radiculopathy.

## AUTHOR CONTRIBUTION

Michał Kłosiński was involved in study design, material acquisition, specimen preparation, analysis and interpretation of data and revision of the manuscript.

Krzysztof A. Tomaszewski was involved in study design, analysis and interpretation of data, drafting and revision of the manuscript.

Andrzej Wróbel was involved in specimen preparation and analysis and interpretation of data.

Krzysztof Piech was involved in searching bibliographic databases, analysis and interpretation of data and revision of the manuscript.

Janusz Skrzat was involved in study design, analysis and interpretation of data and obtaining funding.

Piotr Kłosiński was involved in material acquisition and specimen preparation.

Jerzy A. Walocha was involved in study design, analysis and interpretation of data and critical revision of the manuscript.

All authors approved the final version of the manuscript.

## CONFLICT OF INTEREST STATEMENT

The authors declare that they have no conflict of interest or financial relationship to disclose.

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