

Compressive myelopathy due to thoracic ossified ligamentum flavum, clinic- radiological profile and surgical outcomes

**Submitted for post-doctoral fellowship
Neurosurgery By**

Dr. Sam Scaria

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**SREE CHITRA TIRUNAL INSTITUTE FOR MEDICAL SCIENCES AND
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A THESIS SUBMITTED BY

Dr. Sam Scaria

TO

SREE CHITRA TIRUNAL INSTITUTE FOR MEDICAL SCIENCES AND
TECHNOLOGY, TRIVANDRUM.

IN PARTIAL FULFILMENT OF THE REQUIREMENTS

FOR THE AWARD OF

Programme: Post Doctoral Fellowship

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DECLARATION BY THE STUDENT

CERTIFICATE

I, Sam Scaria hereby certify that I had personally carried out the work depicted in the thesis titled, “Compressive myelopathy due to thoracic ossified ligamentum flavum, clinico radiological profile and surgical outcomes.”

No part of this thesis has been submitted for the award of any other degree or diploma prior to this date.

Signature



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CERTIFICATE BY THE RESEARCH GUIDE

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This is to certify that Sam Scaria, Department of Neurosurgery, of this institute has fulfilled the requirements prescribed for the MCh degree of the Sree Chitra Tirunal Institute for Medical Sciences and Technology, Trivandrum.

The thesis entitled, "Long term outcome of moyamoya angiopathy" was carried out under my direct supervision. No part of the thesis was submitted for the award of any degree or diploma prior to this date.

*Clearance was obtained from the Institutional Ethics Committee for carrying out the study.

Date:31/12/2024

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LIST OF ABBREVIATIONS

S No	Abbreviation	Full Form
1	SSOLF	Short segment ossified ligamentum flavum
2	LSOLF	Long segment ossified ligamentum flavum
3	OLF	Ossified ligamentum flavum
4	DO	Dural ossification

If a large number of abbreviations are used in the thesis, which may be unfamiliar to a reader, a list of abbreviations may be useful

Compressive myelopathy due to thoracic ossified ligamentum flavum comparison of clinical profile and long-term surgical outcome of short vs. long segment disease

SYNOPSIS BY

Dr. Sam Scaria

For post-doctoral fellowship

SREE CHITRA TIRUNAL INSTITUTE FOR MEDICAL SCIENCES AND
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SYNOPSIS

Background:

Compressive myelopathy due to thoracic ossification of the ligamentum flavum (TOLF) is a rare, unique, and perplexing condition among the vast plethora of degenerative diseases of the spine. This study compares the clinical features and surgical outcome of patient's operated for the same.

Material and Methods:

The data of consecutive patients operated exclusively for TOLF in our unit from January 2010 to July 2020 were analyzed retrospectively. A total of 28 patients were included, out of which 20 were males and 8 were females, mean age of 53.2 years and preoperative duration of symptoms ranging from 4 months to 5 years (mean 21 months). They were divided into SSTOLF (n=15), having one or two contiguous levels of involvement, and LSTOLF (n=13), having three or more contiguous levels of involvement. All patients were followed up for a minimum duration of 2 years after surgery (range: 2-12 years, mean

Results:

TOLF commonly affected males above 50 years with a predilection for the lower thoracic spine. There was a significant inverse correlation between the preoperative duration of symptoms and the Hirabayashi Recovery Rate (HRR) ($r = -0.675$, $p = 0.001$). The preoperative Japanese Orthopedic Association (JOA) score strongly correlated with the HRR ($r = 0.715$, $p = 0.001$). The duration of symptoms also correlated moderately negatively with the preoperative JOA score ($r = -0.613$, $p = 0.001$). The mean preoperative JOA scores for SSTOLF and LSTOLF were 6.67 (0.72) and 4.08 (0.76), respectively. The mean JOA scores at the final follow-up for SSTOLF and LSTOLF were 8.93 (1.03) and 5.54 (1.33), respectively. The mean improvement in JOA scores following surgery for SSTOLF and LSTOLF were 2.26 (0.71) and 1.46 (1.13), respectively, which was statistically significant. ($p = 0.03$).

Conclusions:

Longer the duration of symptoms and poor neurological status at presentation are predictors of poor functional outcome following surgery for TOLF with compressive myelopathy. Patients with SSTOLF present relatively early, and even those with poor neurological status

usually improve substantially to attain a reasonably good functional status following timely surgical intervention. In contrast, patients with LSTOLF form a distinct subset, possibly with a different clinicopathological profile a

Key Words: TOLF, OLF, JOA scores, ligamentum flavum

INTRODUCTION

The OLF is considered one of the most significant causes of thoracic myelopathy, particularly in eastern Asia, where its prevalence has been the highest. Multiple factors have been associated with the development of the OLF, including age, gender, genetic variance, high BMI and conditions, such as hypoparathyroidism, diabetes mellitus and bone tuberculosis. However, the definite pathophysiology of the OLF has not been fully understood yet.

up to 51% of patients in need of decompression surgery due to thoracic myelopathy, the presence of the OLF was noted, whereby the prominent clinical feature in these patients was the deficit in vibratory sensation and proprioception on account of the compressed dorsal spinal cord. The numbness was also present in our patient, along with significant pain and acute aggravation of paraplegia. The most prevalent location of OLF is the lower thoracic spine with the highest peak being at Th10-12 (and the second highest at Th3-5, respectively), whereby the ossification of the other spinal ligaments can accompany OLF. Computed tomography (CT) is considered the most useful diagnostic imaging modality in identifying the ossification of the spinal ligaments, including the OLF. In severe cases, the ossification can also

include the dorsal area of the dura, making the surgical treatment of the OLF very challenging, with a high risk of a dural compromise and leakage of the cerebrospinal fluid. Posterior laminectomy is the standard of care for symptomatic, OLF-associated spinal cord compression, despite the considerable perioperative complications.

AIMS AND OBJECTIVES

This study aims to analyse the clinical profile, radiological features of patients with Compressive myelopathy due to thoracic ossified ligamentum flavum operated over a period of 2010 to 2020. And to study the clinical profile, surgical outcome of patients operated for thoracic ossified ligamentum flavum, and to compare the clinical outcome of between subgroups.

REVIEW OF LITERATURE

Introduction

Ossification of the ligamentum flavum (OLF), although a relatively uncommon condition, has been identified as a major contributor to spinal stenosis and the neurologic abnormalities that accompany it, especially in the thoracic portion of the spinal canal. The ossification of other spinal ligaments may overlap with the OLF, which is most common in the thoracic spine, particularly in older male patients in Asia. The etiology of OLF is still unknown, even though several elements are connected to its pathophysiologic development.

Epidemiology

Ossification of ligamentum flavum (OLF) is an infrequent cause of thoracic spinal stenosis, mostly found in Japan and other East Asian countries, and uncommon in other populations. The incidence of dural ossification (DO) ranges from 11–62%. The exact incidence and prevalence of OLF is not known, however, it ranges widely, from 3.8% to 64%, as reported in various series and populations. Most authors opine that OLF mainly affects individuals in 5th-6th decades. It has also been observed that incidence of OLF increases with age. A clear male predominance has been reported in

most of the studies. However, in one study involving volunteers, females had a higher incidence. In yet another study, authors noted a female preponderance in cases of OLF with DO. In this present study, the male: female ratio was 2:1 and the mean age was 51.3 years. Lower thoracic spine is the most affected segment, followed by the mid dorsal spine. The reason for this higher incidence in the lower thoracic spine may be due to the increased mechanical stress, a direct correlation between increased mobility of the spine and repetitive mild trauma or a high tensile force present in the posterior column.

Clinical Presentation

An insidious onset and slow progression of symptoms is common; however, a minor trauma may lead to acute onset of symptoms as seen in one of the cases in the present study. On many occasions, OLF may be asymptomatic and incidentally detected. Gait ataxia is the earliest symptoms to develop due to dorsal column involvement. As the compression progresses, spasticity and weakness develop due to corticospinal involvement. Numbness/hypesthesiae and, bowel and bladder disturbances are not uncommon. Rarely, patients may present with back pain and radiculopathy. It is usually observed that patients often have long-standing symptoms.

Pathology:

The exact causative factors for OLF remain unclear. Both intrinsic and extrinsic factors have been proposed. These include mechanical stress, transformation of elastic fibers into ossified tissue involving genetic cellular properties, inflammation and angiogenesis, TGF-beta, BMP-2, MMPs and interleukins. Skeletal fluorosis has also been reported as an etiological factor. It is generally believed that ossification is a bilateral process. However, the lesion may be asymmetric, wherein ossification on one side is more prominent than the other. A significant proportion may also have concomitant spinal disorders such as OPLL and disc herniations or coexistent cervical/lumbar pathologies. In this series, eight cases had associated spinal pathologies. On many occasions, it was intraoperatively observed that the ossification was not uniform, with areas of non-ossified flavum being interspersed with the ossified one. The author hypothesizes that the hypertrophied and ossified flava are two ends of a spectrum with the interspersing of the two being in the intermediate stage, and if left untreated, there would occur ossification of the remaining hypertrophied flavum in due course of time.

Evaluation and Diagnosis

Imaging

Although, Polgar first discovered OLF on radiographs in 1920, it is obsolete now. MRI is the imaging modality of choice and where MRI is not possible, CT myelogram may be an alternative. However, to further assess the proper morphology and extent of the OLF, bone window CT is essential. The multilevel involvement and the presence of concomitant lesions in the cervical and lumbar spine have made few authors to recommend screening MRI of the entire spine. Hence, in view of increased detection rates of asymptomatic cases by neuroimaging, a thorough clinical examination is paramount to assess exact clinical level for decompression of appropriate levels. Using spinal canal diameter measurements on MRI, Feng et al. suggested that canal grade (paramedian) of <60% can be used as a critical value for determining OLF-induced myelopathy and those requiring subsequent surgical decompression in asymptomatic ones. Intramedullary high T2 signal intensity can often be noted that might indicate cord edema, myelomalacia, demyelination, cavitation or necrosis.

As the disease progresses, there is progression towards the midline creating a characteristic V-shape with anterior concavity. Based on CT imaging, several authors have tried to classify OLF. Sato et al. classified

OLF into five types based on morphology-lateral, extended, enlarged, midline and tuberos. They also observed that the severity of canal stenosis correlated with morphological severity of OLF. Li et al. classified OLF into three types-lateral type, diffuse type and thickened nodular. Kuh et al. simplified this into three types based on axial imaging-unilateral, bilateral and bridged, and two subtypes based on sagittal imaging-round and beak.

Dural ossification (DO) is often observed in OLF, ranging from 11–62%. In this present study, the incidence of DO was 66.6% that is comparable to previous studies. Previous studies have noted that the incidence of DO increases with the morphological severity of OLF. Miyakoshi and associates noted dural adhesions in 21 (62%) of their 34 patients and observed that there is a proportionate increase with the severity of OLF, and all tuberos types in their study had DO. Similarly, Sun et al. reported DO in 86% of the tuberos types. For the detection of DO, CT has been considered as a better imaging technique than MRI. In his series of eight cases of DO confirmed intra-operatively, Muthukumar noted CT evidence of DO in seven out of eight patients while MRI evidence was seen in only four of seven cases. Aizawa et al. considered the absence of contrast medium between the cord and OLF on CT myelogram as evidence of DO. In 2009,

Muthukumar described two radiological signs for preoperative evidence of DO on CT (bone windows), namely the 'tram track sign' (TTS) and the 'comma sign' (CS). However, because of low specificity of TTS, Sun et al. hypothesized that a more effective diagnosis of DO could be achieved by a combination of TTS with other methods. Recently, Zhou et al. proposed a grading system for prediction of DO using unilateral canal occupational rate and other radiological parameters (TTS, CS, TTS + CS) and a score >2 points was highly suspicious of DO. In another recent report, Li et al. described the "bridge sign" (BS) and studied the accuracy rates of TTS, CS and BS in the detection of DO. They noted a combined 94.23% sensitivity and 94.21% specificity for these three imaging signs.

Typically, calcium-containing structures such as calcifications are hypointense on both T1 and T2 sequences. However, the signal void is most apparent on T2 images as calcium has non-mobile protons bound to macromolecules.

Management

There is no role of conservative treatment for symptomatic OLF. Early diagnosis and adequate decompression are important factors for better outcomes,. Several techniques have been described such as enbloc laminectomy, open door laminectomy, hemilaminectomy, laminoplasty, fenestration and laminectomy with fusion. Among them, laminectomy is considered to be the gold standard. Based on the type of OLF, few authors have suggested different surgical techniques. Li et al. advocated en bloc laminectomy for lateral type and diffuse type lesions, and separating laminectomy for thickened, nodular type ossifications. For the first three types, Sato et al. suggested fenestration or French-door laminectomy while for the latter two types, they advocated en bloc laminectomy. In their multicentric study, Ando et al. described three different techniques for various types of OLF, however, no significant differences were observed between them. Addition of fusion to decompression procedure is controversial, with few authors advocating fusion to prevent late instability and kyphotic deformity. However, majority of the authors do not recommend fusion procedures for isolated OLF, but they may be performed in cases of associated OPLL. The present author is also of the opinion that laminectomy alone remains sufficient in majority of cases of OLF. Fusion may be required in only a few cases where complete facet removal is warranted for adequate

decompression of the cord. Few authors have reported minimally invasive techniques for excision of thoracic OLF.

Improvement rates after surgery range from 46–100%, as quoted in various series, Spasticity and weakness show the best improvement followed by bowel/bladder problems. However, dysesthesia may remain even after surgery, requiring neuropathic medications. Till date, various factors have been studied to look for correlation with postoperative outcomes. These parameters included age, number of levels of OLF (single/multilevel), preoperative duration of symptoms, neurologic function, bowel/bladder incontinence, intramedullary high T2 signal, DO, type of OLF morphology and presence of concomitant spinal pathologies such as OPLL, etc. Of all these variables, preoperative neurologic score has been considered the most consistent factor in most of the studies. Sanghvi et al. concluded that the most important predictors of surgical outcome were preoperative duration of symptoms and intramedullary signal changes on MRI, with early surgery benefiting and signal changes >15mm having a delayed recovery. In the study by Ando et al., the authors concluded that disease duration (>6 months), DO and type D ossification of anterior longitudinal ligament (OALL) were risk factors related to poor outcomes. Kuh et al. considered beak type OLF and intramedullary cord signal changes as poor prognostic factors. Miyakoshi et al. noted that dural adhesions were considered to be a deleterious factor for

preoperative and short-term postoperative neurological status, but not for long-term prognosis. However, Sun et al. observed no correlation between DO and postoperative neurological recovery. The results of this present paper are in accordance with the previous reports that presence of DO or other factors do not significantly affect the final outcome.

Complications

CSF leakage is one of the most common complications and occurs predominantly in cases with DO. In such cases, duroplasty with artificial dura may be performed. Few authors have advocated preservation of the arachnoid to avoid iatrogenic cord damage. But this is more often easily said than done, as echoed by a few authors as well. As the dural lacerations are ragged, achieving a watertight dural closure with duraplasty or primary repair remains very difficult. In one series, a very high proportion of patients with DO (94%) developed post-operative CSF leak. Smaller dural defects were repaired primarily while muscle or artificial dura were used for larger defects. In their series of 16 cases, Mohindra and associates observed dural tears in eight cases (two minor tears and arachnoid layer intact in six cases) and all patients underwent prophylactic lumbar drainage to prevent surgical wound problems. Sun et al. found significant differences in dural tears between short-segment (2–3) versus long-segment surgeries (4–12). On the contrary, none of the

dural defects were repaired in the study by Yang et al. and nonexperienced wound-related or neurological complications. In this present study, despite utmost precautions, all 10 patients with DO developed irregular dural tears with arachnoid layer exposure during removal of OLF. However, none underwent primary repair or duraplasty. Only one patient developed minor wound leak postoperatively that was managed by resuturing. This is probably because, as previously mentioned, despite all measures, achieving a watertight dural closure is practically impossible in cases of irregular dural tears during removal of OLF. In such circumstances, achieving good closure of the fascia and overlying layers remains paramount. Other possible complications that have been reported include epidural hematoma and infection, ranging from 0.8–4.2%. Neurological deterioration is also one of the complications reported in various series that might be transient in few cases. This particular complication might occur for two main reasons. Firstly, it may be because of inadvertent cord damage during drilling and secondly, due to inadequate laminectomy or sometimes a wrong level procedure. In this present series, after bony exposure (usually one level above and below the affected segment), the lamina was initially drilled using a 5mm cutting burr at around 50000-60000rpm. It has to be noted that drilling should always be from a lateral to medial direction. Later on, when the lamina was thinned to the level of inner cortical bone, a smaller cutting burr at around 30000-40000 rpm was used to

drill off the remaining lamina and the ossified flavum. It is well known that the ligamentum flavum is deficient in the mid lamina as it traverses from the undersurface of the inferior lamina to the middle of the superior lamina. Using this anatomical knowledge, it is imperative that removal of OLF should start from the mid lamina downwards. The presence of epidural fat acts as a protective guard against dural tear/injury during drilling. Finally, when only a thin shell of cortical bone was left behind, micro ronguers or occasionally, a knife was used with utmost precaution to remove the OLF and DO, in a piecemeal fashion. After the lateral gutters are decompressed with undercutting of the facets, the central canal part is to be decompressed in a similar fashion. This might help prevent or reduce iatrogenic cord damage. It is advisable to perform the entire decompression procedure with utmost care under microscopic magnification. Other late-onset complications that may occur include post-laminectomy kyphotic deformity with resultant deterioration or local backache

MATERIALS AND METHODOLOGY

Patient population and clinic- radiological data

After obtaining approval from the Institutional Review Board, the electronic medical records and imaging data of consecutive patients who underwent surgery exclusively for TOLF-related myelopathy between January 2010 and July 2020 were analyzed retrospectively. Besides overall analysis, subgroup analysis was done after dividing these patients into those with one or two contiguous levels of involvement (SSTOLF) and those with three or more contiguous levels of involvement (LSTOLF), with particular emphasis on direct comparison of clinicopathological profile and surgical outcome between these two groups. Three of the 33 patients had also undergone surgery for symptomatic simultaneous tandem lesions at cervical and lumbar levels. In two other patients, imaging data were unavailable and lost to follow-up early after discharge. Therefore, all of them were excluded from this study.

A total of 28 patients were included, out of which 20 were males and 8 were females, mean age of 53.2 years and preoperative duration of symptoms ranging from 4 months to 5 years (mean 21 months). Thirteen patients had three or more contiguous levels of involvement (of which additional contiguous dual insignificant skip levels of involvement was seen in 1), eight

had contiguous double level (of which additional skip levels were seen in 2, was significant in one of them who underwent surgery at these levels also) and seven had a single level of involvement, i.e., 15 patients had SSTOLF and 13 patients had LSTOLF. In addition, five patients had associated mild cervical and lumbar degenerative disease, which were not significant enough to cause symptoms.

Surgical management

All patients underwent adequate laminectomy and decompression of the ossified ligamentum flavum using a combination of high-speed drill and Kerrison's ronguers. Most patients had unilateral facet joint involvement at the affected level(s), requiring unilateral partial facetectomy for complete decompression of OLF at the corresponding level. After adequate laminectomy, the ossified mass was thinned out using a diamond-tipped burr and detached from the dura using fine dissectors. Laminectomy was adequately performed at all involved levels when symptomatic OLF presented at skip levels. Dense dural adhesions were seen in 9 patients in whom the ossification was thinned out and left floating; dural injury occurred in 2 of these patients. Instrumented fusion was done in 2 patients with LS-TOLF extending to the thoracolumbar junction (D12-L1 intervertebral level) and

mandating D12 with partial L1 laminectomy. After meticulous hemostasis, the wound was closed in layers over a sub-fascial suction drainage system.

Assessment of neurologic status and outcome

Neurological status at presentation, post-surgery, and last follow-up was interpreted using the JOA scoring system for thoracic myelopathy¹⁰. The postoperative Hirabayashi Recovery Rate (HRR) was calculated using the following formula:¹⁰

$$\text{HRR (\%)} = (\text{postoperative JOA score} - \text{preoperative JOA score}) / (11 - \text{preoperative JOA score}) \times 100$$

The majority of available articles have classified the recovery rate based on this formula as good (50%–100%), fair (25%–49%), unchanged (0%–24%), or deteriorated (< 0). However, due to some fallacies of this classification (described in detail below), we used the absolute percentage values of the HRR for analysis.

Follow-up

All patients were followed up for a minimum of 2 years after surgery (range: 2-12 years, mean: 6.14 years). In general, the JOA score of any patient two years after surgery did not improve further on long-term follow-up. Three patients with LSTOLF were lost to follow-up at 4, 6, and 7 years following surgery. None of the patients developed symptomatic recurrent lesions at the operated levels. Five years after surgery, one patient with SSTOLF underwent re-operation at a different non-contiguous level, with good neurological improvement and functional outcome. Two patients with single-level lesions and good postoperative functional outcome died at 5 and 7 years of follow-up due to unrelated causes.

Statistical Analysis

After entering the data in Microsoft Excel, the Statistical Package for Social Sciences software for Windows (Ver. 26.0, SPSS Inc, Chicago, IL, USA) was used for analysis. The quantitative variables were expressed as means and standard deviations. The categorical variables were expressed as proportions and percentages. The groups for comparison were SSTOLF and LSTOLF. The HRR expressed as a percentage was the outcome variable. When analyzing continuous data, normally distributed variables were subjected to parametric tests (student's t-tests, ANOVA), and non-parametric variables were subjected to Mann-Whitney U tests. Pearson's correlation coefficients were used to test the correlations between various quantitative factors and the recovery rate. Scatter plots and the correlation coefficient were present for all correlations. The chi-square test was used to compare the categorical variables between two and three groups. Clustered bar graphs were used wherever the Chi-square test was done. A p-value less than 0.05 was considered statistically significant.

RESULTS

Preoperative parameters affecting outcome

The overall preoperative duration of symptoms was 21.29 (17.52) months, which for SSTOLF was lower compared to LSTOLF (11.33 (7.19), 32.77 (19.07), $p = 0.001$). There was a significant inverse correlation between the preoperative duration of symptoms and the HRR ($r = -0.675$, $p = 0.001$). The preoperative JOA score strongly correlated with the recovery rate ($r = 0.715$, $p = 0.001$). The duration of symptoms also correlated moderately negatively with the preoperative JOA score ($r = -0.613$, $p = 0.001$).

		Short				Long			
Factors	Classification	N	Mean +- SD	t/F	p	N	Mean +- SD	t	p
Sex	Male	9	50.0 (22.0)	1.52	0.15	11	19.7 (22.9)	-0.17	0.87
	Female	6	30.8 (26.5)			2	22.5 (3.5)		
Age at surgery	<60	12	38.2 (26.2)	0.80	0.47	9	24.5 (11.6)	0.64	0.55
	60-70	2	58.3 (11.8)			3	8.3 (42.5)		
	>70	1	60.0			1	16.6		
Pre-operative duration of symptoms	<6 months	7	49.0 (24.8)	2.20	0.15	1	33.3	0.25	0.78
	6-12 m	3	55.6 (9.6)			2	24.3 (6.1)		
	>12 months	5	25.0 (25.0)			10	18.0 (23.6)		
Pre-operative severity of myelopathy (JOA Score)	<=6	0				3	26.2 (8.6)	0.55	0.59
	>=7	15	42.3 (24.9)			10	18.3 (23.6)		
Immediate Post-Op JOA Score	<=6	0				6	13.1 (29.6)	-1.134	0.28
	>=7	15	42.3 (24.9)			7	26.2 (7.7)		

Table 1: Correlations of post-operative RR and various factors by means of univariate analysis

Recovery following surgery in SSTOLF vs. LSTOLF

All patients (n=15, 100%) in the SSTOLF group showed an improvement in the JOA score, whereas 11 out of 13 patients (84.6%) in LSTOLF group showed improvement in the JOA score. The mean preoperative JOA scores for SSTOLF and LSTOLF were 6.67 (0.72) and 4.08 (0.76), respectively. The mean JOA scores at the final follow-up for SSTOLF and LSTOLF were 8.93 (1.03) and 5.54 (1.33), respectively. The mean difference in JOA scores for SSTOLF and LSTOLF were 2.26 (0.71) and 1.46 (1.13) ($p = 0.03$). Most of the recoveries were partial (just one patient in the short segment had a 100% recovery), with LSTOLF having a lower recovery rate than SSTOLF. The overall recovery rate ($n = 28$) was 38.8%; that for SSTOLF was 54.1%, and for LSTOLF was 21.2% ($p = 0.001$).

When a post-surgery JOA score cut-off of 8 or more was adopted, 13/15 patients (87%) with SSTOLF and only 1/13 (7.7%) with LSTOLF met this criterion.

Parameters not affecting outcome

Age, sex, sphincter involvement, CT classification of the type of OLF,¹¹ MRI T2 hyperintensity of the cord at the affected level, and dural injury at surgery

did not correlate with postoperative HRR or JOA score. In 21 patients who had preoperative erect lateral radiographs, the change in the kyphotic angle at the last follow-up was 0.50° ($-2.0 - 2.0$) and 1.00° ($-2.0 - 3.0$) ($p = 0.602$) for SSTOLF and LSTOLF respectively. The change in kyphotic angle following surgery was not significantly correlated with postoperative HRR or JOA score.

Overall					
Factors	Classification	N	Mean +- SD	t/F	p
Sex	Male	20	33.3 (26.8)	0.425	0.67
	Female	8	28.7 (22.8)		
Age at surgery	<60	21	32.3 (21.9)	0.108	0.90
	60-70	5	28.3 (41.1)		
	>70	2	38.3 (30.6)		
Pre-operative duration of symptoms	<6 months	8	47.1 (23.7)	4.31	0.025
	6-12 months	5	43.0 (18.7)		
	>12 months	15	20.3 (23.4)		
Pre-operative severity of myelopathy (JOA Score)	<=6	3	26.2 (8.6)	-0.41	0.68
	>=7	25	32.7 (26.7)		
Immediate Post-Op JOA Score	<=6	6	13.1 (29.6)	-2.2	0.037
	>=7	22	37.2 (22.2)		

Table 2: Overall demographic characteristics

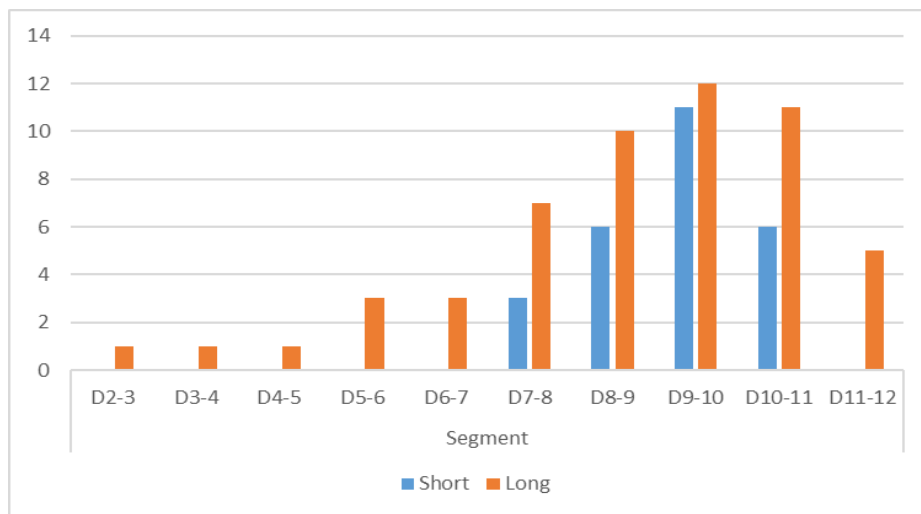


Fig 1 Graphical representation of thoracic OLF and numbers

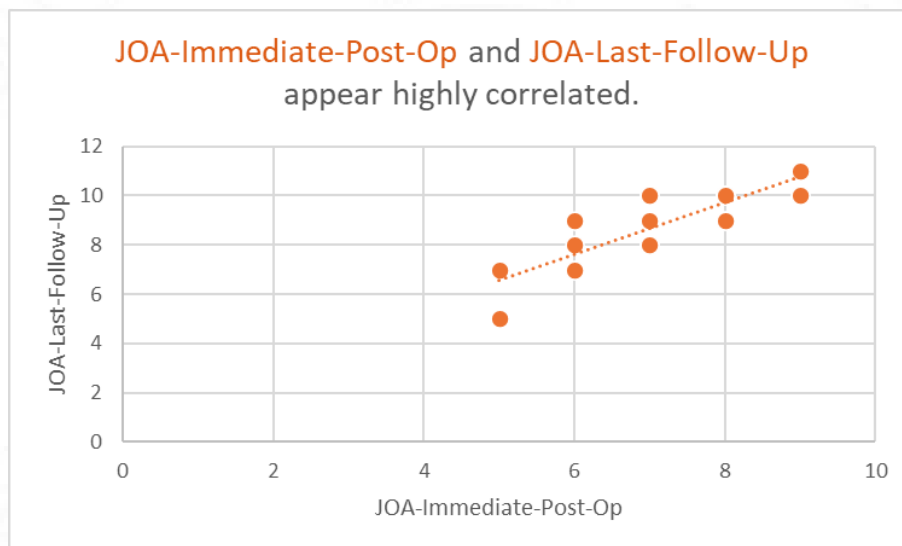
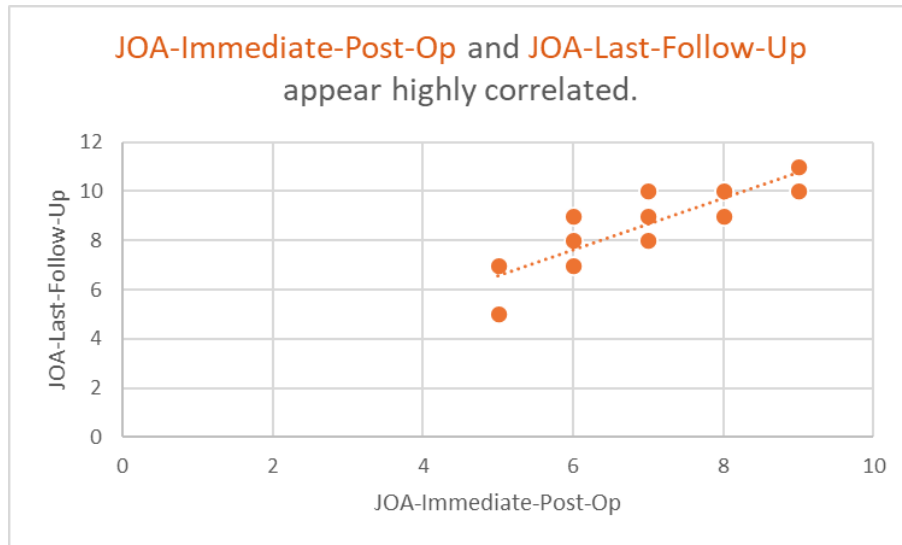


Figure 2 ; JOA immediate postop and JOA last followup



Fig; 3: JOA immediate Postop and JOA last followup

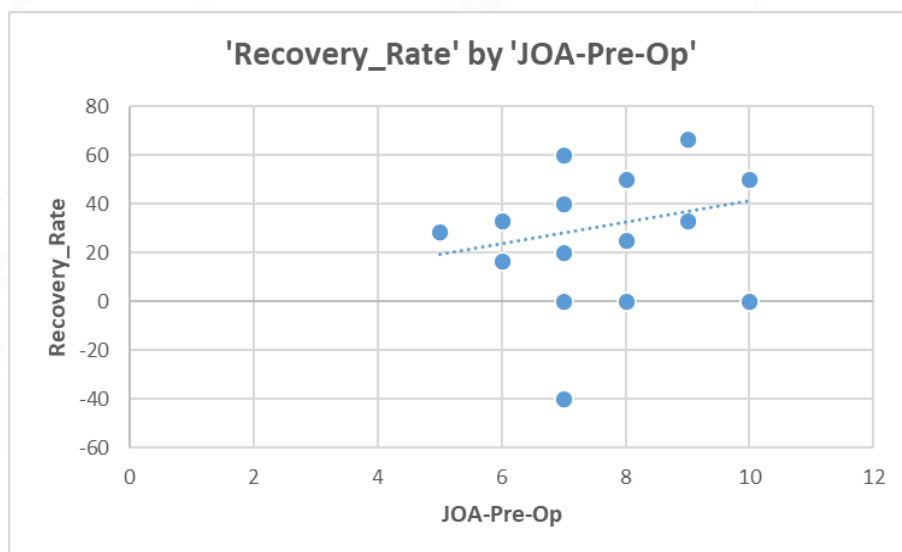


Figure 4. Recovery rate and Preop JOA

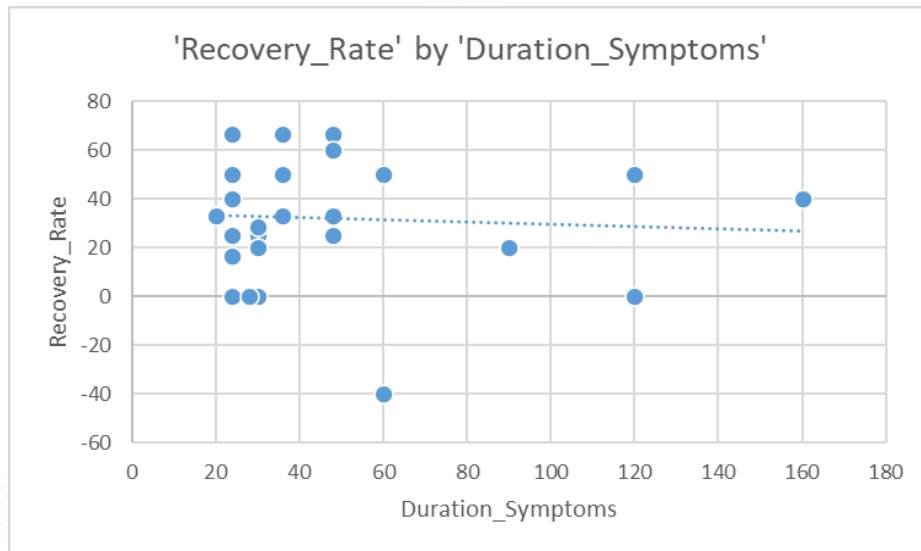


Figure 5: Recovery rate and duration of symptoms

DISCUSSION

Although ossified ligamentum flavum as a cause of myeloradiculopathy was first described by Polgar¹² based on a lateral X-ray film more than a century back, its epidemiology and etiology remain obscure even now. Despite being rare, it ranks as the primary cause of thoracic compressive myelopathy, followed by ossified posterior longitudinal ligament and herniated nucleus pulposus.¹³ Several intrinsic factors like genetic, chronic degenerative, hereditary and metabolic alterations and extrinsic factors like biomechanical stress, environmental conditions, and trauma are said to be involved in the development and progression of this disease¹ where hypertrophied fibrous tissues in the LF undergo endochondral ossification.² Recent research has implicated crucial roles of various growth factors, including bone morphogenetic proteins and transforming growth factor- β in the longitudinal (intervertebral) and axial expansion of TOLF.³ Several other diseases like diffuse idiopathic skeletal hyperostosis, ankylosing spondylitis, adenocarcinomatous metastasis, metabolic disorders like Paget's disease, fluorosis, hypophosphatemic vitamin D resistant rickets, X-linked hypophosphatemia and hypoparathyroidism can also be associated with TOLF.^{4,5} Although classically described to be a disease of Asians, especially Japanese, it is being increasingly reported in North America, the Middle East, and the Caribbean as well.⁶⁻⁹

The data on epidemiology and natural history of TOLF is scarce. It has been postulated that TOLF usually begins in the lateral capsular part of the LF, encroaches onto the medial laminar aspect, enlarges anteriorly, and eventually fuses with the contralateral ossification forming a central mass compressing the cord.¹⁴ In addition to this axial growth pattern, we feel that TOLF has a longitudinal (intervertebral) growth pattern differing in clinical profile, pathobiology, and prognosis. Those with a relatively subacute presentation of short-segment disease limited to one or two intervertebral levels usually have an axially expansive growth pattern and seek early surgery before the spinal cord parenchyma is irreversibly damaged; hence they bear an excellent prognosis. It seems plausible that short-segment disease may also remain quiescent with subtle symptoms for a considerable duration before it becomes significant enough to seek medical attention. A subset of these patients develops gradually progressive neurological decline as they transform to LSTOLF, leading to disabling symptoms due to chronic irreversible cord changes and hence carry a poor prognosis even with surgical decompression. It was noted that even in the three patients having discontinuous lesions, the prognosis varied based on the number of contiguous levels involved rather than the actual number of levels of TOLF.

Clinico-pathological and imaging characteristics

Like our series, most studies affirm that TOLF generally affects men aged 50-60 years and has a predilection for the lower third of the thoracic spine, bearing the maximum load with significant mobility.^{1,2,15} Co-existing ossification of the posterior longitudinal ligament leading to ventral compression and symptomatic tandem lesions in the cervical and lumbar spine are common confounding factors in many studies. Hence, we have included only cases limited to the thoracic spine without a ventral compressive element. The ossified LF was confirmed by histopathological examination in all patients. Though there is much data on the prognostic indicators predictive of surgical outcome in TOLF, the results among available studies are grossly inconsistent to draw any significant conclusions or guidelines because most of the published articles are either case reports or case series with a limited number of subjects and hence ineffective in attaining statistical significance.¹⁶ But there is reasonable agreement that patients with longer duration of symptoms and lower JOA score at presentation carry a poor prognosis for recovery following surgery,^{11,17-22} as was seen in our series too (p-value 0.001) (Fig. 3).

Although it is logical to assume that a longer duration of symptoms leads to

poorer neurological status, our data revealed that even in patients with relatively poor JOA scores, those with short duration of symptoms lasting less than six months and presenting with subacute neurological worsening had a good surgical outcome. These patients harbored SSTOLF in contrast to the slow, gradually progressive myelopathy leading to chronic irreversible cord changes in LSTOLF. Many authors have also confirmed the irreversible nature of worsening of preoperative neurological status over a long period in contrast to acute deteriorations, which are mostly reversible^{21,23}. Sphincter involvement was seen in patients irrespective of the number of levels involved and was not found to have a bearing on the outcome.

On CT imaging, there was no significant difference in the distribution of the three axial types (unilateral, bilateral, and bridged) or two longitudinal types (beak and round) of ossification¹¹ (Fig 4) between LS and SS-TOLF. Likewise, intrinsic cord hyperintensity, seen in most patients on T2 weighted MRI, was not significantly associated with the neurological status, the number of involved levels, or recovery rates. Because of these clinical and radiological observations, it seems prudent to infer that many of the indolent SSTOLF patients, over a while, evolve to LSTOLF with longitudinal involvement of adjacent intervertebral segments; the clinical evolution being masked by this slowly progressive compression leading to neuronal

compensation and plasticity until there is significant neuronal loss heralding major disability and irreversibility with decompression. Therefore, although better outcomes are generally related to early surgical intervention, it is in this setting that we emphasize the need for early decompressive surgery in SSTOLF with myelopathy and brief duration of symptoms at presentation. The natural history of TOLF from a recent large-scale longitudinal population-based cohort study adds credence to these observations.²⁴

Surgery, recovery rate and complications

Due to its progressive nature and poor outcome with conservative management, surgical decompression is undoubtedly the treatment of choice for TOLF-associated compressive myelopathy.^{25–28} Although there exists considerable variability in the ideal surgical procedure, laminectomy with adequate decompression of the cord at all levels of compression is the widely accepted technique; foraminotomy and partial resection of up to half of the involved facet(s) may be done based on the extent of involvement. With irregular ossification inside the spinal canal, laminoplasty carries potential risks of spinal cord injury. Besides the possibility of re-closure, the chances of leaving a residual leading to recurrent compression are also high with laminoplasty.²¹ Considering the mechanical stress on ligamentum flavum as a

cause for OLF, few authors have also described laminectomy combined with instrumented fusion as the treatment of choice.²⁹ However, it is generally reserved for extensive TOLF crossing the cervicothoracic or thoracolumbar junctions,³⁰ as was done in two of our patients.

Our mean HRR following surgery was 54.11 and 21.20 % in SSTOLF and LSTOLF groups, respectively, thus indicating a poorer recovery rate when there is contiguous involvement of three or more levels (p-value 0.001). However, our overall HRR of 38.8% is in the lower range when considering the mean recovery rates of 33% to 63% documented in the literature,^{19,21,22,29–33} as close to half of our patients presented with long segment involvement in contrast to fewer than 10% of patients with long segment involvement in the majority of these studies, which adds to the value of our observations. The recovery was partial in 96% of our patients, with most of them complaining of residual paraesthesia in the lower extremities at the last follow-up, which is in concordance with literature where the vast majority of recoveries following surgery surgery complete.^{21,22,34}

Irrespective of the surgical technique, persistent neurological deficits, and transient or permanent neurological decline are common, rendering the surgical risks unpredictable for a relatively simple procedure.^{30,31} Early post-

operative deterioration is usually reversible and occurs due to epidural hematoma which requires urgent evacuation, cord edema usually responsive to corticosteroids and diuretics, or cord contusion and ischemia resulting from poor operative technique or intraoperative hypotension. In our series, four patients each from SSTOLF and LSTOLF groups with severe cord compression, developed transient deterioration in lower limb motor function, which improved in four to six weeks with conservative treatment and physiotherapy. Microvascular causes leading to ischemia-reperfusion injury and sudden perfusion changes due to quick re-expansion of the spinal cord following decompression seems to be the main factors for late deterioration. Presumably, for this reason, we had one patient of LSTOLF with neurological worsening following surgery and remained bed bound at the last follow-up after two years.

Although neurological decline following surgery is not directly related to the number of levels involved, we assume that these microvascular factors play a pivotal role in hindering the neurological recovery of the chronically compressed, decompensated cord seen in LSTOLF compared to the relatively acute compression seen in SSTOLF. Inadvertent intra-operative dural injury was seen in two patients with LSTOLF; this number was too small for statistical analysis to look for a causal relation with outcome. Despite the risk

of late kyphosis following multilevel laminectomy, there was no significant change in kyphotic angles at long-term follow-up in our series. Most large clinical series have documented this and inferred that post-operative kyphosis does not affect the outcome significantly.^{6,23,35,36}

SSTOLF vs. LSTOLF: Limitations of available studies

As mentioned previously, no clinical studies have directly compared the surgical outcome of short vs. long-segment TOLF. Most studies have concluded that the number of involved levels does not affect the outcome following surgery by just analyzing for a correlation between the HRR-based outcome category and the number of involved levels.^{14,20,29,35–39} The conclusions drawn from most of these studies are misleading and create false hope of good recovery when operating on LSTOLF involving three or more levels. Firstly all these studies attempt to find a linear relation between the number of levels involved and outcome rather than dividing these patients into single/dual levels and three or more contiguous levels. But in reality, this division is significant as the pathophysiology and prognosis following surgery show a distinct difference between these groups. Still, it is not that significant even if the number of involved levels rises beyond the three-level mark. Therefore a direct linear relation of the number of levels vs. outcome is hard

to obtain in any study unless there are a large number of patients with ultra-long segment involvement.

Secondly, the number of contiguous levels of involvement causing severe irreversible chronic spinal cord damage is the determinant of prognosis in LSTOLF. None of the existing studies have considered this while classifying the number of levels. Multiple skip levels of short-segment involvement may not portend a poor prognosis even if the total number of levels is three or more, thus creating a bias. Thirdly a direct comparison of short vs. long segment disease has not been made in these articles mainly because the number of LSTOLF patients had been too small to attain statistical significance. However, in the very few studies that specifically included a sizeable number of patients with long segment involvement, a clear negative correlation was seen between the number of levels involved and the outcome.^{6,18}

Finally, while comparing the outcome of LSTOLF vs. SSTOLF, the HRR indicates a relative improvement from the preoperative status and hence is not a sensitive index of the true reflection of the actual functional status of these patients following surgery.²¹ Further, in most studies, the HRR-based outcome is broadly divided into four groups based on the difference in JOA scores

before and after surgery¹⁰. For instance, if two patients improve by 3 points each from JOA scores 4 to 7 and from 6 to 9 following surgery, they shall have recovery rates of 50% and 75%, respectively. Still, both shall be grouped in the "good outcome" category for statistical analysis. In real life scenario, a patient with a JOA score of 9 with minor sensory disturbance of trunk and legs is functionally independent in contrast to a JOA score of 7, who is likely to be bed-bound and dependent for activities of daily living. Also, as LSTOLF patients present with a poorer JOA score, even if the recovery grades following surgery are similar in these groups, the JOA score improvement following surgery in LSTOLF is not to the extent of them becoming functionally independent, as is usually seen in SSTOLF. Hence we have also compared the absolute values of the HRR between the groups, which showed a statistically significant difference between LSTOLF and SSTOLF, thereby underscoring the prognostic importance of this division.

SSTOLF vs. LSTOLF: Long-term surgical outcome

As seen in our study, since LSTOLF usually presents with a poor functional status than SSTOLF, the prognosis regarding functional outcome can be unraveled only by directly comparing the mean JOA scores before and after surgery in both these groups. As evident from Fig. 2, the mean preoperative and postoperative JOA scores in SSTOLF vs. LSTOLF were 6.67 and 8.93 vs. 4.08 and 5.54, respectively, which re-iterates the consistently poor functional outcome in LSTOLF patients. Based on this data and the limitations in literature as mentioned above, we feel that even though there is no direct statistical correlation between the number of levels involved and the recovery rates in most of the available studies, there is a definite prognostic cut-off as regards TOLF involving three or more contiguous levels vs. single or dual levels. When viewed in the background of available scientific evidence, these findings portend a uniformly grim prognosis for functional outcomes in patients with LSTOLF with disabling myelopathy. On the other hand, prompt surgical decompression entails excellent results in almost all patients with SSTOLF, most of whom present early and with a good JOA score.

Very few authors have specifically included the surgical outcome details of LSTOLF in their studies (Table 3). Gao et al., in their analysis of 75 LSTOLF patients, found that patients with long duration of symptoms, longer levels of involvement, and low preoperative JOA scores were significantly prone to

have poor surgical outcomes.¹⁸ Kawaguchi et al. opined that OLF affecting more than two segments was predictive of poor outcome.⁴⁰ In a later study, they concluded that a higher number of affected levels negatively co-related with post-surgical recovery rates, implicating severe cord damage due to prolonged spinal cord compression.⁶ Li et al. noted that there was no prognostic importance for the number of levels when they compared patients with a single involved level, with those having two or more involved levels rather than three.³⁰ In contrast, Kuh et al. found that single-level disease had a favorable prognosis compared to multilevel involvement.¹¹ An illustrative summary of the anatomy, evolution, progression and prognostic factors of TOLF based on the number of involved levels is depicted in Figure 5. Further studies directly comparing the clinical profile and long-term surgical outcome of a large number of SSTOLF and LSTOLF patients are necessary to demystify the natural history and prognosis of this rare entity based on the number of contiguous levels involved.

Limitation of the study:

This study was a retrospective analysis of patients operated in a single centre, There were different procedures done over the period of one decade by different surgeons, and the sample size was not large enough to extrapolate.

Conclusion

Despite the inherent drawbacks of a retrospective study with a limited number of patients, ours is by far the first series comparing the clinicopathological features and surgical outcome in patients with short and long-segment TOLF, a rare, multifactorial entity causing thoracic compressive myelopathy. Decompressive laminectomy, though simple, safe, and highly effective in SSTOLF, carries significant morbidity in patients with LSTOLF who usually present late into the illness with poor functional status. Furthermore, it is likely that a proportion of SSTOLF remains indolent and gradually progresses into LSTOLF. Therefore, it is imperative that the surgeon be aware of the stark, contrasting clinicopathological and prognostic features between these two entities to detect and offer early surgery to those symptomatic patients with SSTOLF vis a vis intervene at a stage when the disease has relentlessly advanced to LSTOLF leading to chronic disabling symptoms non-responsive to surgery.

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ANNEXURES

Curriculum Vitae

APPENDIX A – ETHICS COMMITTEE APPROVAL



Curriculum Vitae

SCARIA	SAM	
Last Name	First Name	Middle Name
Date of Birth (dd/mm/yy) 22/04/1989		Sex: male
Study Site Affiliaton-Co-Investigator		
Professional Mailing Address (Include Institution name)		Study Site Address (Include Institution name)
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Academic Qualifications (Most recent qualification first)		
Degree/Certificate	Year	Institution, Country
MBBS	2015	Government Medical College, Thrissur, India
Details of professional registration : (MCI/State Registration/Bar Council/DCL/etc including Registration Number and Vear of Registration:TCMC-56277		
Current and previous positions (most recent position first)		
Month and Vear	Title	Institution/Company, Country
January 2019	Resident Neurosurgery	SCTIMST
May 2017-18	Resident General Surgery	GMC Palakkad
March 2016-17	Lecturer General Surgery	GMC Thrissur
Brief summary of relevant research experience: Synchronous Papillary Carcinoma of Thyroglossal Duct Cyst and Thyroid managed by a Single Transverse Neck Incision - A Case Report		

Current project/s at

Signature: _____



Date: 05/08/2019

Place: Trivandru



