

## リンパ脈管筋腫症における全肺外科的胸膜被覆術後のシロリムス投与による 気胸再発リスクの低下に関する研究

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### 研究要旨

リンパ脈管筋腫症（LAM）患者は気胸を頻繁に合併しそのコントロールは重要である。シロリムス治療はLAMの標準的治療であるが、気胸に対する効果は議論が必要とされている。近年LAM患者の気胸治療の外科的オプションとして、全胸膜被覆（Total pleural covering: TPC）療法、修正TPC（Modified TPC: mTPC）が報告されているが、術後の気胸再発に対するシロリムスの効果は明らかではない。シロリムス治療を含む何らの要因が術後の気胸再発の予測因子をあきらかにするため、NHO近畿中央呼吸器センターにて外科的胸膜被覆（Surgical pleural covering: SPC）を受けたLAM気胸症例について術後再発予測因子を検討した。その結果、SPCを受けたLAM患者の気胸再発をシロリムス投与で抑制する可能性がある。

### A. 研究目的

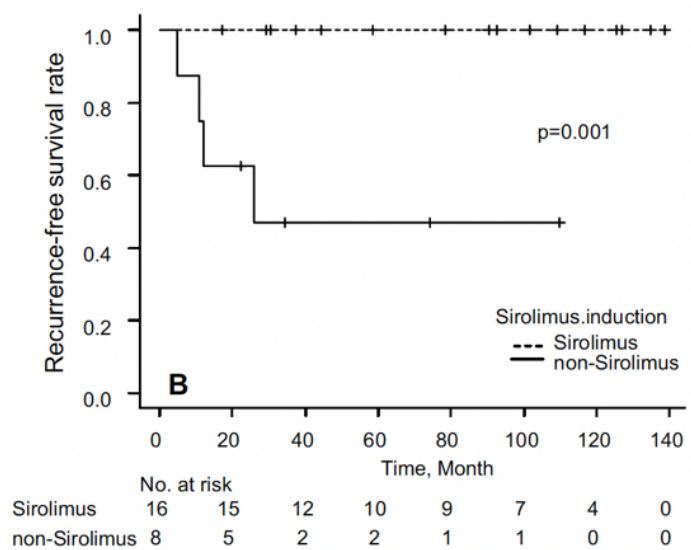
外科的胸膜被覆（Surgical pleural covering: SPC）としてTPC療法、mTPCを行ったLAMの気胸患者について、気胸再発に対するシロリムスの効果をあきらかにする。

### B. 研究方法

2005年1月から2019年1月の間にNHO近畿中央呼吸器センター外科データベースに登録され、SPCを受けたLAM気胸症例{18例; 24手術（TPC17手術、mTPC7手術、合計24手術）について術後再発予測因子を検討した。

### C. 研究結果

SPC24手術のうち、14手術（58.3%）は2回以上の同側気胸の病歴があり、11手術（45.8%）はSPCの前に同側の胸膜手術の病歴があった。12人の患者の16手術（66.6%）は、SPCの後シロリムス投与を受けた（シロリムス群）。追跡期間中央値はSPC後69.0か月、患者3人で術後再発があり4回の手術（16.6%）を実施した。SPC後5年間の無再発生存率（RFS）は82.9%であった。術後再発例は血管内皮増殖因子Dの血清レベルが非再発例よりも有意に高く（3260.5対892.7 pg / mL、 $p=0.02$ ）、再発群のシロリムス治療率は、再発なし群よりも有意に低かった（0対80%、 $p=0.006$ ）。ログランク検定ではシロリムス群（SPC後のシロリムス使用）のRFSは非シロリムス群のRFSよりも有意に優れていた（ $p=0.001$ ）。他の要因については有意差はなし（図）。



#### **D. 考察**

症例数は少ないが SPC を受けた LAM 患者の気胸再発をシロリムス投与で抑制する可能性があることを報告した。SPC (TPC または mTPC) 後のシロリムス導入は、繰り返す難治性頻発気胸を認める LAM 患者における有口で実行可能な選択肢であろう。

#### **E. 結論**

Airway-centered Fibroelastosis に伴う肺高血圧症は肺病変の進行にともなう 3 群と思われたが今後症例数の蓄積が必要である。

#### **F. 研究発表**

##### 1. 論文

Sakurai T, Arai T, Hirose M, Kojima K, Sakamoto T, Matsuda Y, Sugimoto C, Yoon HE, Inoue Y. Reduced risk of recurrent pneumothorax for sirolimus therapy after surgical pleural covering of entire lung in lymphangiomyomatosis. *Orphanet J Rare Dis.* 2021 Nov 3;16(1):466.

RESEARCH

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# Reduced risk of recurrent pneumothorax for sirolimus therapy after surgical pleural covering of entire lung in lymphangiomyomatosis

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## Abstract

**Background:** Patients with lymphangiomyomatosis (LAM) frequently experience pneumothorax. Although sirolimus is the standard therapy for LAM, its effect on pneumothorax is controversial. Recently, total pleural covering (TPC) and modified TPC (mTPC) were introduced as surgical treatment options for pneumothorax for patients with LAM. However, the effect of sirolimus on the recurrence of pneumothorax in patients who underwent the treatments is still uncertain. We hypothesized that some clinical factors including sirolimus treatment could predict postoperative recurrence of pneumothorax. In order to clarify this hypothesis, we retrospectively analyzed the clinical data from 18 consecutive patients with LAM who underwent 24 surgical pleural covering of entire lung (SPC) as 17 TPC and 7 mTPC against pneumothoraces from surgical database between January 2005 and January 2019, and we determined the predictors of postoperative recurrence.

**Results:** Of the 24 surgeries of SPC, 14 surgeries (58.3%) had a history of two or more ipsilateral pneumothoraces, and 11 surgeries (45.8%) had a history of ipsilateral pleural procedures before SPC. Sixteen surgeries (66.6%) in 12 patients received treatment of sirolimus after SPC (sirolimus group). With a median follow-up time of 69.0 months after SPC, four surgeries (16.6%) in three patients had a postoperative recurrence, and the 5-year recurrence-free survival (RFS) after SPC was 82.9%. In patients with postoperative recurrence, serum level of vascular endothelial growth factor D was significantly higher than that in those with non-recurrence (3260.5 vs. 892.7 pg/mL,  $p=0.02$ ), and the rate of sirolimus treatment in the recurrence group was significantly lower than that in the no-recurrence group (0 vs. 80%,  $p=0.006$ ). The log-rank test showed that the RFS of the sirolimus group (sirolimus use after SPC) was significantly better than that of the non-sirolimus group ( $p=0.001$ ), and no significant difference was observed for other factors.

**Conclusion:** We first reported sirolimus might effectively suppress the recurrence of pneumothoraces in LAM patients who received SPC. Sirolimus induction after SPC (TPC or mTPC) might be a feasible option for frequent pneumothorax in LAM.

**Keywords:** Lymphangiomyomatosis, Pneumothorax, Sirolimus, Vascular endothelial growth factor D, Total pleural covering, Surgical pleural covering

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## Background

Lymphangiomyomatosis (LAM) is a rare multi-organ disease that predominantly affects women [1].

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