

# Canadian respirologists' experience with lymphangioleiomyomatosis

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**BACKGROUND:** Lymphangioleiomyomatosis (LAM) is a rare pulmonary disease occurring primarily in women. A literature review of LAM in Canada found sporadic mention of LAM in case reports or within lung transplant studies. The LAM Foundation, a patient support and research funding organization, lists 23 Canadian patients in its database. The present study was designed to assess the scope of LAM across Canada and to identify potential patients for further evaluation.

**OBJECTIVES:** To ascertain Canadian respirologists' experience with patients with LAM (current and historical), lung transplantation (single or bilateral) and deaths due to LAM, and awareness of the LAM Foundation.

**METHODS:** Four hundred twelve brief surveys were sent anonymously to members of the Canadian Lung Association (inserted in their newsletters) to ascertain the experience of Canadian respirologists with LAM.

**RESULTS:** One hundred twelve surveys were returned (27%). Fifty-one respondents had 'ever' been involved in the care of at least one patient with LAM; eight had cared for three or more

patients. At the time of the study, 26 respondents were following a total of 46 patients with LAM; 22 of the 51 respirologists (43%) who had ever cared for a patient with LAM reported the death of a patient. Thirty-three patients had been put on wait lists for transplantation; six died while on the wait list. Nineteen patients underwent lung transplantation – six single-lung recipients and 13 bilateral lung recipients. Of the 51 respirologists who had ever cared for a patient with LAM, only 30 (61%) were aware of the LAM Foundation's services. Of the 112 respondents, only 47 (43%) were aware of the LAM Foundation.

**CONCLUSIONS:** This study identified a moderate level of awareness of a significant existing patient support and research service (the LAM Foundation). There were many patients with LAM who were unknown to the LAM Foundation and could benefit from its resources. Results suggest that there may be more patients with LAM in Canada than are reported in the existing literature.

**Key Words:** *Canadian experience; Lung transplantation; Lymphangioleiomyomatosis; Lymphangioleiomyomatosis Foundation*

*Résumé à la page suivante*

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## L'expérience des pneumologues canadiens avec le lymphangioliéiomyosarcome

**HISTORIQUE :** Le lymphangioliéiomyosarcome (LAM) est une maladie pulmonaire rare qui se manifeste surtout chez les femmes. Une analyse bibliographique du LAM au Canada permet de repérer des mentions sporadiques du LAM dans des rapports de cas ou des études de greffes pulmonaires. La fondation LAM, un organisme de soutien des patients et de financement de la recherche, compte 23 patients canadiens dans sa base de données. La présente étude a été conçue pour évaluer la portée du LAM au Canada et pour dépister des patients potentiels en vue d'une évaluation plus approfondie.

**OBJECTIFS :** Notre but consistait à vérifier l'expérience des pneumologues canadiens avec les patients atteints de LAM (actuelle et passée), la greffe pulmonaire (unilatérale ou bilatérale) et les décès causés par le LAM, ainsi que la sensibilisation à la fondation LAM.

**MÉTHODOLOGIE :** Quatre cent douze brefs sondages ont été postés de manière anonyme aux membres de l'Association pulmonaire du Canada (insérés dans le bulletin) afin de vérifier l'expérience des pneumologues canadiens avec le LAM.

**RÉSULTATS :** Cent douze sondages ont été renvoyés (27 %). Cinquante et un répondants n'avaient jamais participé aux soins d'au moins un patient atteint de LAM, tandis que huit en avaient soigné au moins trois. Au moment de l'étude, 26 répondants suivaient un total de 46 patients atteints de LAM. Vingt-deux des 51 pneumologues (43 %) qui avaient soigné des patients atteints de LAM ont déclaré qu'un patient était décédé. Trente-trois patients avaient été mis sur la liste d'attente des greffes. Six étaient morts pendant cette période d'attente. Dix-neuf patients avaient subi une greffe pulmonaire, soit six une greffe unilatérale et 13 une greffe bilatérale. Des 51 pneumologues qui avaient déjà soigné un patient atteint de LAM, seulement 30 (61 %) connaissaient les services de la fondation LAM, tandis que sur les 112 répondants, seulement 47 (43 %) connaissaient cette fondation.

**CONCLUSION :** L'étude a dépisté une sensibilisation moyenne à un service important de soutien aux patients et de recherche (la fondation LAM). De nombreux patients atteints de LAM n'étaient pas connus de la fondation LAM et pourraient bénéficier des ressources de l'organisme. Les résultats laissent supposer qu'il pourrait y avoir plus de patients atteints de LAM au Canada que le nombre déclaré dans la documentation scientifique existante.

Pulmonary lymphangioliomyomatosis (LAM) is a rare, systemic disease that affects lung function in young women. It is a progressive, debilitating disorder with extreme variability in its rate of progression. The pathophysiology of LAM involves smooth muscle proliferation that increasingly invades lung tissue (1-3). Treatments have focused on estrogen reduction (eg, progesterone, oophorectomy, tamoxifen), based on the observation that LAM tends to present only in women of childbearing age, suggesting hormonal involvement (1,2). Unfortunately, there is no consensus on the efficacy of hormonal manipulations, and recent results from the National Institutes of Health (NIH) study on patients with LAM presented by Dr J Moss at the annual LAM Research Conference (March 2002) suggest that progesterone is only minimally effective. No curative remedy is available, although lung transplantation is used with some success as a therapeutic approach for advanced disease (4).

Recent advances have linked the genetic mutation on the *TSC1* and *TSC2* genes to LAM, the same genetic mutation related to tuberous sclerosis (TS) (3,5,6). It is thought that approximately 5% of women with TS also have pulmonary LAM, but LAM can also occur as an isolated disorder (sporadic LAM) (6). Population estimates propose that 1% of the populace has TS, suggesting that the true incidence of LAM is much higher than is currently known. Under-reporting and underdetection of LAM is likely due to the difficulty inherent in diagnosing LAM. Plain chest radiographs are unable to detect early, and sometimes even advanced, changes related to smooth muscle proliferation; therefore, computed tomography scan and/or biopsy are required for diagnosis (7). LAM is commonly misdiagnosed as asthma, emphysema or chronic obstructive pulmonary disease (8).

As reported by SM Pollock-BarZiv at the American Transplant Congress (April 2002), patients waiting for lung transplants and patients with LAM who have undergone transplantation have indicated that there is an extremely

poor understanding of LAM by health professionals other than their primary respirologists or pulmonologists. Moreover, sufferers of rare diseases may be isolated and may lack outlets for support from others suffering from the same diseases. Comparatively, consider other conditions such as cancer, in which peer support is common and has been shown to improve health (9). Thus, it is important to identify patients with LAM so that connections with other patients may be facilitated to enhance social support (10). The LAM Foundation, a research funding and support organization located in the United States, was created to gather information and to create a network of patients with LAM around the world (<http://lam.uc.edu>). Currently, there are 690 women registered with the LAM Foundation, including 23 Canadian women. A literature search of LAM in Canada using PubMed (National Center for Biotechnology Information, USA) found only sporadic mention of cases of LAM, often in case reports or embedded within lung transplant studies.

The present study was designed to assess the scope of patients with LAM across Canada and to identify potential patients for further research studies. Our goal was to ascertain Canadian respirologists' experience with patients with LAM (current and historical), lung transplantation (single and bilateral) for LAM, deaths due to LAM, and awareness of the LAM Foundation and its services to patients.

### METHODS

The sampling frame was respirologists who were members of the Canadian Lung Association (CLA); this was likely the best database to use to reach Canadian respirologists. The Association would not provide the researchers with the names of its members but was willing to include a brief questionnaire with its regular CLA newsletter.

At the time of mailing, there were 412 physicians listed with the CLA. A brief, two-page survey was inserted into the CLA newsletter, and recipients were asked to fax back their

**TABLE 1**  
**Sample of survey questions**

1. Have you ever been involved in the care of or in treating any patients with LAM?
2. Have you ever had a patient with LAM who died? If yes, how many?
3. Do you currently follow any patients with LAM? If yes, how many?
4. Have any of your LAM patients ever been wait-listed for lung transplantation? How many?
5. Did any patient die while wait-listed? If yes, how many?
6. Have any of your LAM patients undergone lung transplantation?
7. How many were single-lung transplants?
8. How many were double-lung transplants?
9. How many are currently alive post-transplant?
10. What was the average time on the transplant wait list? \_\_\_\_\_ months
11. What was the range of waiting times your LAM patients encountered? \_\_\_\_\_ months to \_\_\_\_\_ months
12. We are currently undertaking a psychosocial study of living with LAM. Would you be willing to provide us with the names of any LAM patients that you are currently seeing (with their permission)?
13. Are you aware of the LAM Foundation and its services to LAM patients?

*LAM Lymphangioleiomyomatosis*

responses to the investigators. The survey included a cover letter providing information about the study objectives, as well as contact information, including phone, e-mail and Web site information for the LAM Foundation. This brief survey was designed to determine how many Canadian respirologists had ever been involved in the care of a patient with LAM. If members had been involved in such care, they were asked to report on the number of patients with LAM seen at that time or in the past, any patient deaths from LAM, any patients that were on wait lists for transplants and any patients that had received a lung transplant for LAM. All of the survey recipients were asked about their awareness of the LAM Foundation and its services. Recipients who were involved in the care of patients with LAM were also asked whether they would be willing to release their names, phone numbers and e-mail addresses to the researchers (Table 1).

### RESULTS

One hundred twelve surveys were returned (27%); three were excluded because the respondents were not clinicians (eg, pathologist) or had received more than one survey. Of the respondents, 51 indicated that they had 'ever' been involved in the care of at least one patient with LAM; eight of these respirologists had cared for three or more patients with LAM. At the time of the study, twenty-six respondents were following a total of 46 patients with LAM; 18 were following one patient, three were following two patients, and five were following three or more patients. Twenty-two of the respirologists (43%) who had ever cared for a patient with LAM reported the death of a patient with LAM.

Respondents reported that 33 patients had been put on wait lists for transplantation; six patients had died while waiting for a transplant. A total of 19 patients had undergone lung transplantation – six were single-lung transplants and 13 were bilateral lung transplants.

Of the 51 respirologists who had ever cared for a patient with LAM, only 30 (61%) were aware of the services

(research and support) offered by the LAM Foundation. Of the 26 respondents who were following a patient with LAM at the time of the study, only 19 (73%) were aware of the LAM Foundation. Of the 112 respondents, 47 (42%) indicated that they were aware of the LAM Foundation. Of note is that three respondents indicated that their patients were enrolled in a study of LAM at the NIH, Bethesda, Maryland, USA, and two physicians asked for additional information on LAM.

Of the respondents who had 'ever' cared for a patient with LAM, 38 of 51 (74.5%) provided their names and contact information to participate in further study of patients with LAM. Of those who were following patients with LAM at the time of the study, 17 of 26 (65.4%) provided their names and contact information.

### DISCUSSION

Because the survey was anonymous, we cannot ascertain if respondents had experience with the same patients. Therefore, we cannot determine the true prevalence of LAM in Canada from this survey. Given the relatively low response rate, it may have been that respirologists who had experience with patients with LAM were more eager to respond to the survey. Given the anonymous nature of the survey methodology, we were unable to perform additional mailings. Based on the locations of respirologists who gave permission for us to contact them, it appeared that surveys were returned from most geographical regions in Canada.

This study identified a low to moderate level of awareness of a significant existing patient support and research service (ie, the LAM Foundation), and more effort is needed to increase this awareness. Increasing the awareness of such organizations facilitates patient support and the recruitment of patients into research protocols offered in a centralized manner to enhance the understanding of rare diseases such as LAM.

Results of the present study suggest that there are more patients with LAM in Canada than are reported in the existing literature, and than are known to the LAM Foundation or the NIH LAM study. Rare diseases such as LAM necessitate combining data on patients in areas such as transplant outcomes, treatment course and outcomes, and quality of life. Furthermore, this study helped to identify many patients with LAM unknown to the LAM Foundation who could benefit from its resources. Many Canadian respirologists are aware of and/or have had some experience with patients with LAM. With enhanced imaging techniques and the knowledge that LAM is associated with TS, Canadian respirologists may be increasingly exposed to patients with LAM.

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