

# Sonography of Lymphangioliomyoma in Lymphangioliomyomatosis: Demonstration of Diurnal Variation in Lesion Size

Nilo A. Avila<sup>1</sup>  
Andrew J. Dwyer<sup>1</sup>  
Diane V. Murphy-Johnson<sup>1</sup>  
Pamela Brooks<sup>2</sup>  
Joel Moss<sup>2</sup>

**OBJECTIVE.** Our aims were to define the sonographic features of abdominal and pelvic lymphangioliomyomas in lymphangioliomyomatosis (LAM) and to evaluate the utility of sonography in visualizing diurnal change in the size of the masses.

**MATERIALS AND METHODS.** Forty-four patients with LAM and abdominal and pelvic lymphangioliomyomas found on screening CT underwent sonography. Twenty-two patients had two studies on the same day, one in the morning and the other late in the afternoon.

**RESULTS.** Forty-nine masses were scanned in the 44 patients. The anatomic distribution of the masses was the following: retroperitoneal (29/44 patients, 66%), pelvic (10/44, 23%), and both retroperitoneal and pelvic (5/44, 11%). Of the 49 masses, 12 (24%) were cystic, 16 (33%) were solid, and 21 (43%) were complex. Twenty-two patients underwent sonography in the morning and afternoon. The masses increased in size between the two studies in all 21 patients in whom the masses were visualized in both studies. In three of 21 patients, the echotexture of the masses changed between the morning and afternoon studies: In two the echotexture changed from solid to complex, and in the other, it changed from hyperechoic to isoechoic relative to the liver.

**CONCLUSION.** The sonographic characteristics of lymphangioliomyomas are similar to some neoplasms such as lymphoma and ovarian cancer (a similarity that sometimes prompts biopsy). After a mass is shown in a patient with LAM, repeat sonography in the morning and afternoon is useful to depict diurnal variation in size and echotexture and to confirm the diagnosis of lymphangioliomyoma and avoid biopsy.

**L**ymphangioliomyomatosis (LAM) is a rare multisystem disorder occurring almost exclusively in women. It is characterized by the proliferation of abnormal smooth-muscle cells—LAM cells—in the lungs (resulting in pulmonary cysts) and in the lymphatics of the thorax and retroperitoneum (resulting in lymphangioliomyomas) [1–4]. Accumulation of LAM cells in the lymphatics may cause mural thickening, obstruction, dilatation, and development of cystic collections of chylous material. The resulting complex lymphatic masses are termed “lymphangioliomyomas” and have CT characteristics similar to those of malignant neoplasms, sometimes prompting biopsy [4].

One feature, which has been shown on CT, helps to differentiate lymphangioliomyomas from malignancy. Lymphangioliomyomas have been shown to increase in size during the day from morning to afternoon—whereas with malignancy, negligible growth is expected in a single day. This diurnal variation

in the size of lymphangioliomyomas also explains the reports of patients of worsening abdominal and pelvic symptoms (e.g., abdominal pain, incontinence, lymphedema, and paresthesias of the lower extremities) at the end of the day [5].

In this report, we illustrate the spectrum and prevalence of the sonographic features of lymphangioliomyomas and assess the utility of sonography in depicting diurnal change in the size of these masses.

## Materials and Methods

The study protocol (95-H-0186) was approved by the National Heart, Lung and Blood Institutional Review Board. Our institution is a referral center currently studying the natural history of LAM. As part of the protocol, all patients have screening CT of the chest, abdomen, and pelvis. Written informed consent was obtained from all study participants. This study includes the initial 255 consecutive patients (all women; age range, 23–77 years; mean, 44 years) with pulmonary LAM evaluated at our institution be-

Received March 29, 2004; accepted after revision June 30, 2004.

<sup>1</sup>Diagnostic Radiology Department, Warren Grant Magnuson Clinical Center, National Institutes of Health, 10 Center Dr., MSC 1182, Bldg. 10, Rm. 1C-658, Bethesda, MD 20892-1182. Address correspondence to N. A. Avila.

<sup>2</sup>Pulmonary-Critical Care Medicine Branch, National Heart, Lung and Blood Institute, National Institutes of Health, Bethesda, MD 20892-1590.

AJR 2005;184:459–464

0361–803X/05/1842–459

© American Roentgen Ray Society

tween March 1996 and April 2003. The diagnosis of LAM was established by lung biopsy in 186 patients and biopsy of abdominopelvic masses in 10 patients. Fifty-nine patients did not have tissue biopsy but had classic clinical (recurrent spontaneous pneumothorax or pleural effusions or both) and pulmonary CT findings (diffusely scattered thin-walled lung cysts) of LAM. This study comprises 44 patients who had abdominal and pelvic lymphangioliomyomas depicted on screening CT and then had follow-up sonography of the abdomen and pelvis.

**Abdominopelvic Sonography**

Twenty-nine of the 44 patients underwent abdominal sonography, 10 of 44 patients underwent pelvic sonography, and five of 44 patients underwent both abdominal and pelvic sonography. Pelvic masses adjacent to the uterus, bladder, or adnexa were studied with transvaginal sonography (seven patients); those adjacent to the pelvic walls were studied using the transabdominal approach (eight patients). The patients were scanned on ATL 4000 and 5000 (Philips Medical Systems) and Acuson 128XP, Aspen, and Sequoia (Siemens Medical Solutions) scanners. The transducer frequency used

for the abdominal sonograms was between 3.5 and 5 MHz. The endovaginal studies were performed with multifrequency transducers ranging between 5 and 8 MHz. We recorded the maximum transverse, anteroposterior, and longitudinal diameters of the masses and whether the masses were solid, cystic (simple or multiloculated cysts), or complex (contained both cystic and solid components). Other sonographic features recorded were echogenicity relative to the liver in abdominal solid and complex masses, echogenicity relative to the uterus in pelvic solid and complex masses, and wall thickness (for cystic and complex masses). We measured the anteroposterior thickness of the walls on transverse images and used 2 mm as the limit between thin and thick.

**Diurnal Variation**

In 22 patients, sonography was performed in both the morning (8:00–10:00 am) and afternoon (2:30–5:00 pm) of the same day. The patients were scanned by the same technologist using the same machine and the same transducer frequency for both the morning and the afternoon studies. All studies were checked by the same board-certified

radiologist before the patient left the department. The mass sizes were quantified using an estimated volume index that was calculated by multiplying the transverse, anteroposterior, and longitudinal diameters of the masses. The change in volume of the masses during the day was assessed by comparing estimated morning and afternoon volume indexes. The percentage difference in volume between morning and afternoon studies was calculated using the following formula (Table 1):

$$\frac{(\text{Afternoon volume index} - \text{morning volume index})}{\text{morning volume index}} \times 100 \quad (1)$$

**Review of Clinical History**

All patients were interviewed regarding abdominal and pelvic symptoms. Medical records were reviewed to determine whether a patient had a history of abdominopelvic biopsy.

**Results**

Forty-four patients had 49 masses seen on CT that were evaluated on sonography. The anatomic distribution of the masses was retroperitoneal (29/44 patients, 66%), pelvic (10/44, 23%), and both retroperitoneal and pelvic (5/44, 11%). Sixteen (33%) of 49 masses were solid: isoechoic to liver or uterus in 10 (63%) of 16, hypoechoic in five (31%) of 16, and hyperechoic in one (6%) of 16. Twelve (24%) of the 49 masses were cystic: simple cysts in four (33%) of 12 and multiloculated cysts in eight (67%) of 12 (Fig. 1). Twenty-one (43%) of 49 masses were complex (Figs. 2 and 3). Wall thickness in the eight patients with multiloculated masses was thin (three patients) and both thin and thick (five patients). All 21 patients with complex masses had both thin and thick walls.

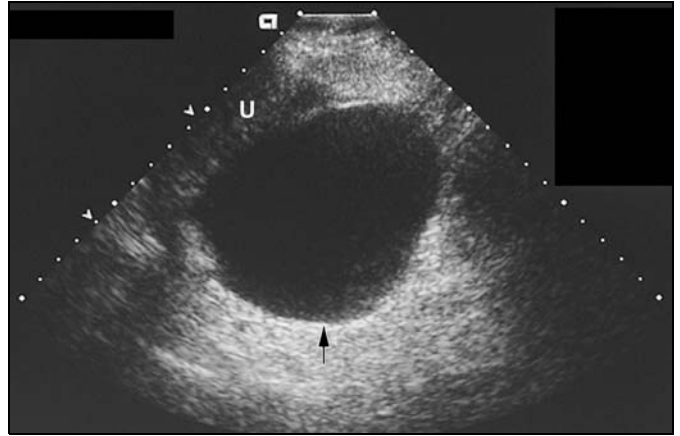
**Diurnal Variation**

Twenty-two patients underwent sonography in the morning and afternoon. In one patient, the mass was not well visualized and therefore not measurable on the afternoon study. The estimated morning volume indexes of the masses ranged from 1 to 521 cm<sup>3</sup> (median, 38 cm<sup>3</sup>). The estimated afternoon volume indexes of the masses ranged from 3 to 647 cm<sup>3</sup> (median, 173 cm<sup>3</sup>). Increase in volume during the day was observed in all 21 patients (Table 1 and Fig. 4). The difference between the afternoon volume and the morning volume indexes ranged from 2 to 237 cm<sup>3</sup> (median, 41 cm<sup>3</sup>). The percentage change in volume ranged from 10% to 484% (median, 38%) (Table 1).

<b>TABLE 1 Change in Volume of Lymphangioliomyomas from the Morning (am) to the Afternoon (pm) Sonogram</b>				
Patient No.	am Volume (cm <sup>3</sup> )	pm Volume (cm <sup>3</sup> )	Difference in Volume (pm–am) (cm <sup>3</sup> )	% Difference in Volume (pm–am)/am × 100
1	12	71	59	484
2	10	43	33	336
3	9	25	16	180
4	166	403	237	143
5	1	3	2	200
6	51	159	108	209
7	36	73	37	99
8	139	153	14	10
9	291	412	121	42
10	33	145	112	340
11	88	204	116	130
12	279	430	151	54
13	19	34	15	79
14	2	9	7	350
15	102	187	85	84
16	157	373	216	138
17	40	72	32	79
18	19	28	9	49
19	13	28	15	116
20	521	647	126	24
21	87	132	45	52

## Sonography of Lymphangioleiomyomatosis

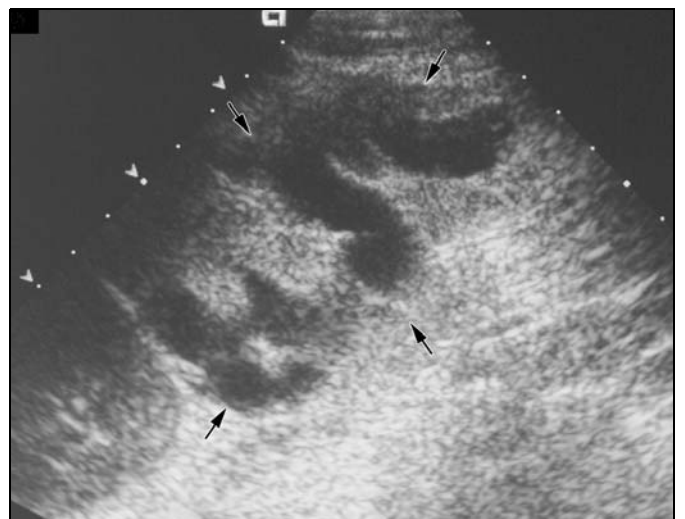
**Fig. 1.**—51-year-old woman with mild lung involvement with lymphangioleiomyomatosis who complained of pelvic discomfort and urinary frequency. Transabdominal longitudinal sonogram of pelvis shows large simple cyst (*arrow*) adjacent to uterus (U).



**Fig. 2.**—33-year-old woman with severe lung involvement with lymphangioleiomyomatosis who complained of increased abdominal girth that worsened during day. Transabdominal longitudinal sonogram of right pelvis shows thick-walled complex mass (*arrows*) with central anechoic space.



**Fig. 3.**—42-year-old woman with mild lung involvement with lymphangioleiomyomatosis diagnosed after biopsy of pelvic mass to exclude ovarian cancer. Abdominal longitudinal sonogram shows large retroperitoneal mass (*arrows*) isoechoic to liver, containing serpiginous central anechoic spaces that had no flow on Doppler interrogation and were thought to represent dilated lymphatic channels.



The relation of the percentage change in size of the masses during the day to the size of the masses in the morning was graphed (Fig. 5). As expected, greater percentage changes in volume were more common in smaller masses. All three masses with changes in volume of less than 10 cm<sup>3</sup> (2, 7, and 9 cm<sup>3</sup>) clearly showed increase in the percentage change in size (200%, 350%, and 49%, respectively).

The echotexture of the masses changed between the morning and afternoon studies in three patients. In two patients, solid masses on the morning studies became complex

(with both cystic and solid elements) on the afternoon study (Fig. 6). In one patient, a hyperechoic mass in the morning study became isoechoic to the liver on the afternoon study.

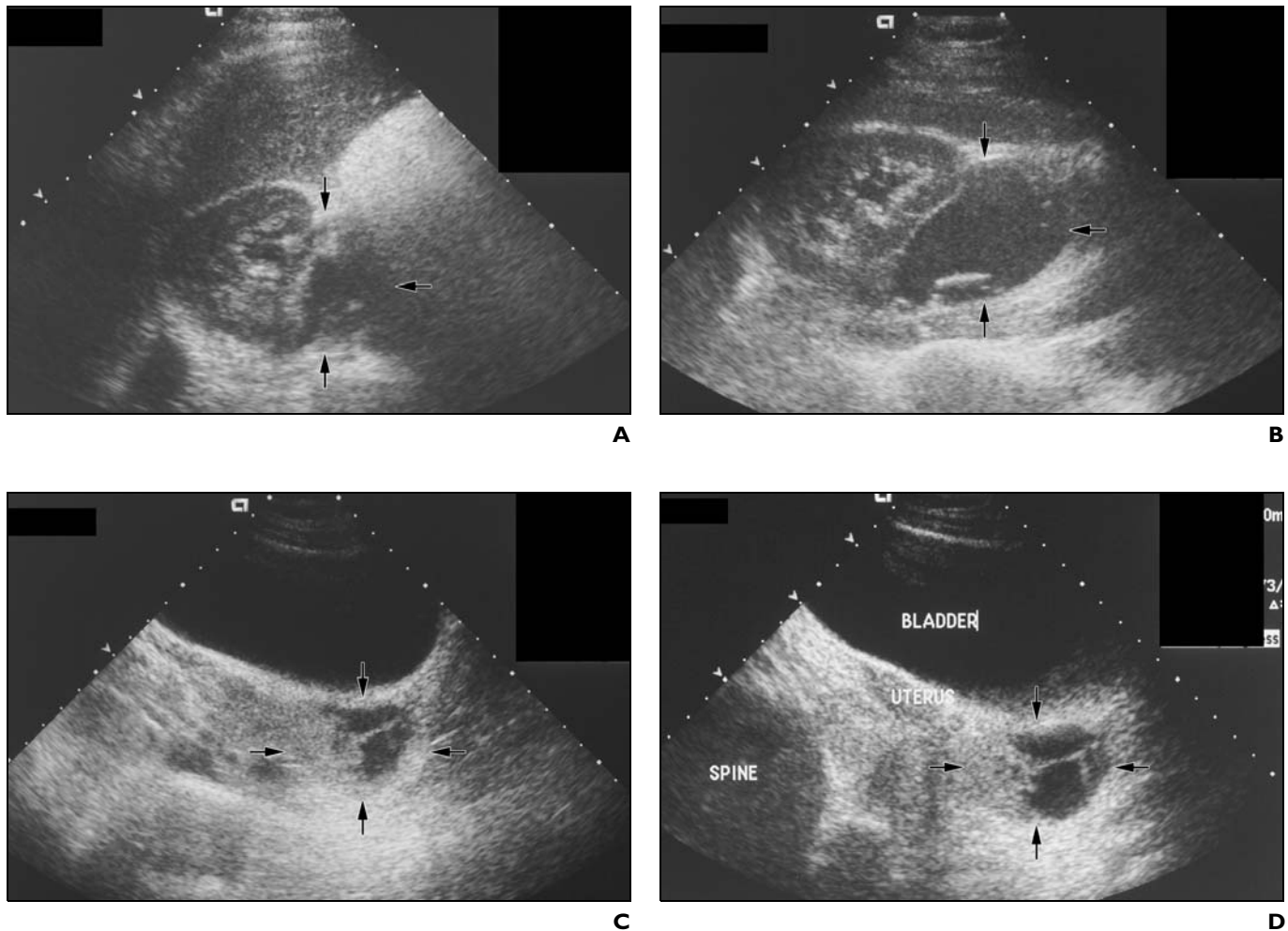
**Review of Clinical History**

Patients described the following symptoms, which worsened during the course of the day and were most pronounced in the evening: abdominal bloating (*n* = 23), abdominal pain (*n* = 3), back pain (*n* = 1), urinary frequency (*n* = 1), pelvic pain (*n* = 1), constipation (*n* = 1), lower extremity edema (*n* = 4), and lower extremity paresthesia (*n* = 2). Ten patients who had under-

gone abdominal and pelvic CT or sonography before the diagnosis of LAM had been misdiagnosed with cancer because of masses found on the imaging studies: Six patients were told they had ovarian cancer and four were told they had lymphoma. Subsequent biopsies on these patients revealed no evidence of cancer and established the diagnosis of LAM.

**Discussion**

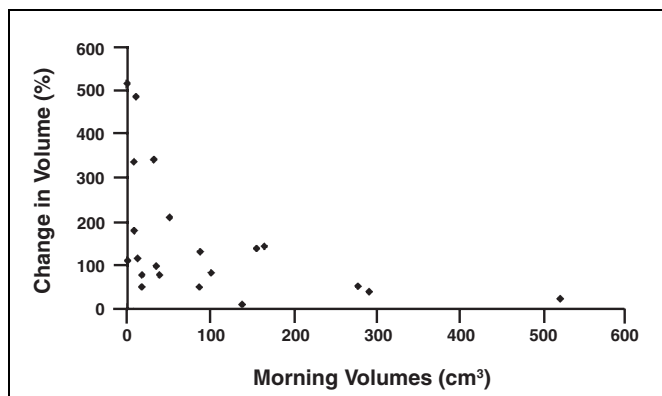
The most common clinical characteristics of LAM that lead to the correct diagnosis include exertional dyspnea (46%) and pneumothorax (43%). Patients may undergo



**Fig. 4.**—25-year-old woman having severe lung involvement with lymphangioleiomyomatosis, diagnosed after biopsy of pelvic mass to exclude ovarian cancer. Patient complained of chronic back pain and urinary frequency that worsened during day.  
**A,** Transverse sonogram obtained at 8:30 am at level of right kidney shows complex mass (arrows) that measures 3.3 × 4.8 × 5.5 cm in anteroposterior, transverse, and longitudinal diameters.  
**B,** Follow-up sonogram obtained at 2:45 pm shows interval increase in size of cystic portion of mass (arrows) that then measured 4.8 × 5.0 × 7.0 cm in anteroposterior, transverse, and longitudinal diameters.  
**C,** Transabdominal longitudinal sonogram of left adnexa obtained at 8:15 am shows complex left pelvic mass (arrows) that measures 2.5 × 2.6 × 3.1 cm in anteroposterior, transverse, and longitudinal diameters.  
**D,** Follow-up transabdominal sonogram obtained at 3:00 pm shows interval increase in size of left adnexal mass (arrows) that then measured 3.7 × 3.8 × 3.8 cm in anteroposterior, transverse, and longitudinal diameters.

## Sonography of Lymphangioliomyomatosis

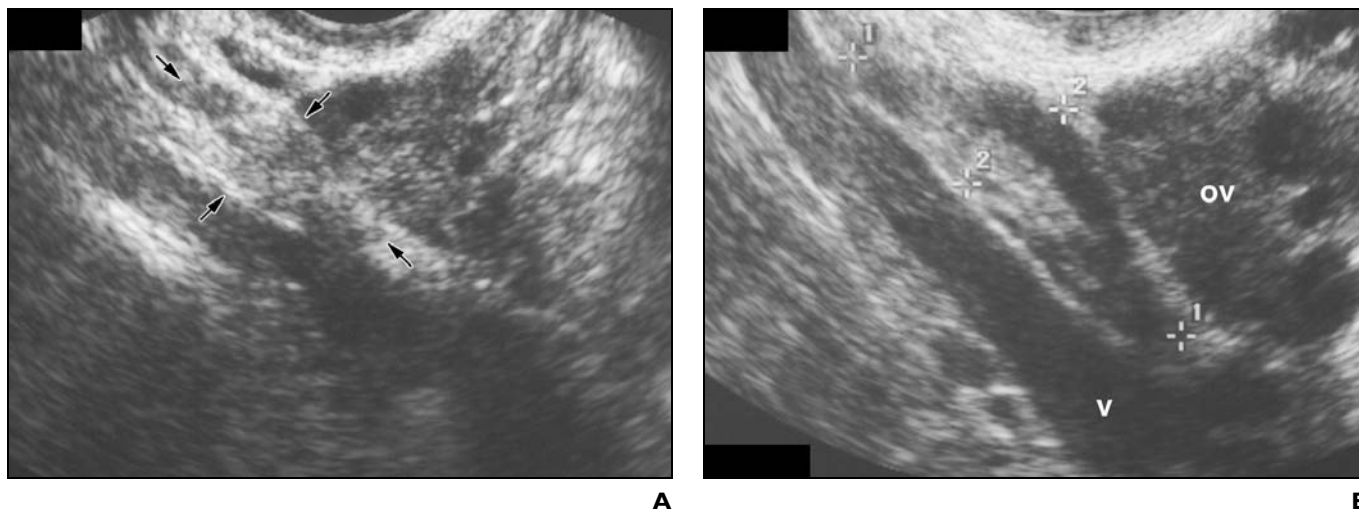
**Fig. 5.**—Scatterplot of percentage change in volume as function of morning volume indexes of lymphangioliomyomas in 21 patients. Morning volume indexes (antero-posterior × transverse × longitudinal measurements) ranged from 1 to 521 cm<sup>3</sup> (median, 38 cm<sup>3</sup>). Percentage change in volume ranged from 10% to 484% (median, 38%). Greater percentage changes in volume were more common in smaller masses.



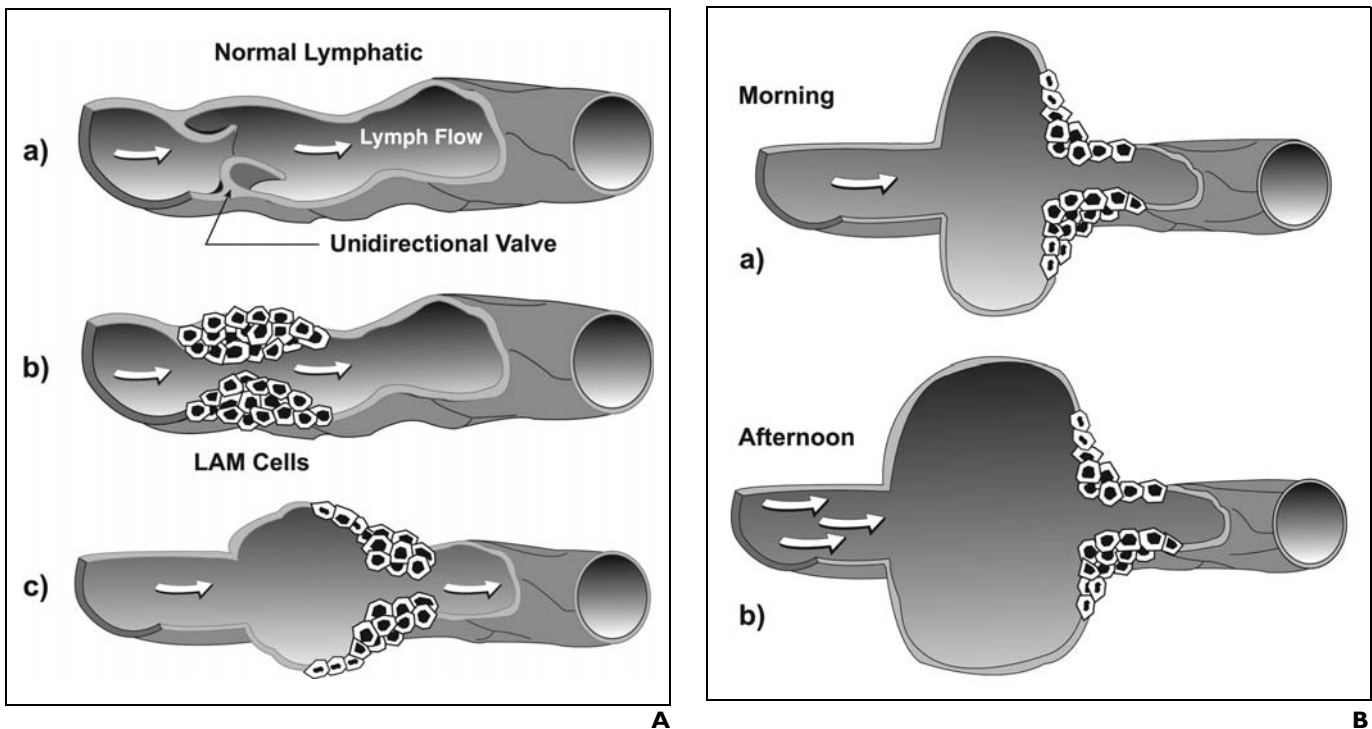
transbronchial biopsy that shows proliferation of immature smooth-muscle cells (LAM cells) in the lungs and the bronchial wall lymphatics [3]. Twenty-one percent of patients with LAM develop complex lymphatic masses that may cause symptoms (urinary frequency and lower extremity edema) by compressing adjacent organs [5]. Usually when an abdominal or pelvic mass due to LAM is discovered, the diagnosis of pulmonary LAM is already known. However, in some cases, the diagnosis of LAM follows discovery of the mass. In our series, this occurred in 10 of 44 patients with LAM with masses; in these patients, the diagnosis of LAM was established by biopsy of masses discovered on CT or sonography. Hence, the awareness of the thoracic and abdominal imaging features of LAM in expediting diagnosis and precluding unnecessary biopsy is important.

The sonographic characteristics of lymphangioliomyomas are not specific and are similar to those of malignant abdominal and pelvic masses such as lymphoma and ovarian cancer (a similarity that sometimes prompts biopsy). One distinctive feature of lymphangioliomyomas is an increase in size during the day. This phenomenon (which we have termed “diurnal variation”) is caused by accumulation of lymph within the mass (Fig. 7). Because malignant neoplasms commonly exhibit negligible change in size in a day, reliable evidence of diurnal variation can differentiate a lymphangioliomyoma from a malignant mass. Also, diurnal variation explains the worsening of symptoms (bloating, abdominal discomfort, lymphedema, and lower extremity paresthesias) toward the end of the day reported by patients with lymphangioliomyomas [5].

Diurnal variation in the size of lymphangioliomyomas is likely the result of several factors: first, greater lymph flow through the pelvis and abdomen during the day (resulting from increased chyle production after meals and increased lymphatic return from the lower extremities due to walking and other daytime muscular activities) and second, the effect of gravity on intraluminal pressure and its dependence on patient position. During the day—when the patient is predominantly upright—intraluminal pressure is increased within the abdominal and pelvic lymph collections and draining lymphatics (which are working “up-hill” against gravity to return lymph to the thoracic duct). The increased intraluminal pressure induces dilatation of the lymph collections and lymphatics. At night, when the patient is recumbent, this effect of gravity on intraluminal pressure is nullified [5] (Fig. 7B).



**Fig. 6.**—43-year-old woman having moderate involvement of lungs with lymphangioliomyomatosis. **A**, Endovaginal longitudinal sonogram of right adnexa obtained at 10:00 am shows solid mass (arrows) isoechoic to uterus and situated between right iliac vessels and right ovary. **B**, Follow-up sonogram obtained at 2:50 pm shows increase in size of mass (calipers), which now contains anechoic spaces in addition to solid component. ov = ovary, v = pelvic vessel.



**Fig. 7.**—Proposal models for effects of lymphangioliomyomatosis (LAM) on lymphatics.

**A.** Models of effect of LAM on lymphatics show normal lymphatic vessel with unidirectional valve and normal direction of lymph flow (arrows) (a), proliferation of abnormal smooth-muscle cells (LAM cells) on walls of lymphatic that causes mural thickening and luminal narrowing (b), and obstruction of lymph flow by LAM cells that results in dilatation of lymphatic proximal to obstruction, creating lymphangioliomyoma (c).

**B.** Models show diurnal variation in size of lymphangioliomyomas between morning and afternoon. Normal lymphatic flow (arrows) is shown in morning (a). By late afternoon, lymphangioliomyoma has increased in size (b). Phenomenon results from combination of factors: increased lymph flow during day caused by increased lymph production after meals and increased return of chyle from extremities after normal daily exercise.

Along with the measurable increase in size between the morning and afternoon studies, the dynamic nature of lymphangioliomyomas is further revealed by the fact that some of the masses changed in echotexture between the morning and afternoon studies (i.e., masses that were solid in the morning study appeared complex or hypoechoic on the afternoon examination). We attribute this change in sonographic appearance to the accumulation of lymph within the lymphatic channels in the masses that have been described histologically but are too small to be resolved as discrete structures sonographically [6].

Patients with LAM are usually screened with CT. We propose that when an abdominal or pelvic mass is found on CT, a repeat examination be performed to evaluate changes in size of the mass. Visualization of diurnal variation, on either sonography or CT, should exclude a diagnosis of malignancy and avoid the need for biopsy. For this evaluation, we suggest that sonography, rather than CT, be used initially. Because patients newly diagnosed with LAM are usually premenopausal women and because lymphangioliomyomas arise most commonly from the abdomen and pelvis, performing sonography will

avoid radiation to the pelvic organs. If the mass is not satisfactorily visualized on sonography or if evidence of diurnal variation is not certain, then a repeat limited CT study should be performed at the level of the mass for better characterization.

There are technical limitations of sonography as a diagnostic tool to evaluate diurnal variation. Most masses arise in the abdomen and pelvis, thus bowel artifact may obscure or preclude unequivocal identification of the masses. Further, diurnal variation in size may be difficult to document if a mass is small or if the change in size is small. Given the dependency of sonographic findings on technique, the initial and follow-up sonography should be performed by the same sonographer who can be certain that the same anatomic area is scanned in the same cross-section on both studies. Another limitation of the study is the absence of assessment of intraobserver variability; unfortunately, time constraints caused by patient scheduling precluded us from rescanning the patients multiple times to obtain this data.

The sonographic characteristics of lymphangioliomyomas are similar to those of malignant abdominal and pelvic masses such as lymphoma and ovarian cancer. Sonography, repeated in the

morning and afternoon, is useful in documenting diurnal variation in size and differentiating lymphangioliomyomas from neoplastic masses.

## References

1. Kitaichi M, Nishimura K, Itoh H, Izumi T. Pulmonary lymphangioliomyomatosis: a report of 46 patients including a clinicopathologic study of prognostic factors. *Am J Respir Crit Care Med* 1995;151:527-533
2. Taylor JR, Ryu J, Colby T, Raffin T. Lymphangioliomyomatosis: clinical course in 32 patients. *N Engl J Med* 1990;323:1254-1260
3. Chu SC, Horiba K, Usuki J, et al. Comprehensive evaluation of 35 patients with lymphangioliomyomatosis. *Chest* 1999;115:1041-1052
4. Carrington CB, Cugell DW, Gaensler EA, et al. Lymphangiomyomatosis: physiologic-pathologic-radiologic correlations. *Am Rev Respir Dis* 1977;116:977-995
5. Avila NA, Bechtel J, Dwyer AJ, Ferrans VJ, Moss J. Lymphangioliomyomatosis: CT of diurnal variation of lymphangioliomyomas. *Radiology* 2001;221:415-421
6. Matsui K, Tatsuguchi A, Valencia J, et al. Extrapulmonary lymphangioliomyomatosis (LAM): clinicopathologic features in 22 cases. *Hum Pathol* 2000;31:1242-1248