TABLE 1. Predictors of obtaining diagnostic samples after TBNA in sarcoidosis

Factors	Diagnostic samples	P value
Sex		
Male	22/31 (71.0%)	.2
Female	15/26 (57.7%)	
Age*		
<40 y	17/27 (62.9%)	.9
≥40 y	19/30 (63.3%)	
Pulmonary lesion (TCT)†		
No	27/41 (65.9%)	.4
Yes	9/16 (56.3%)	
No. of lymph nodes punctured		
One	21/32 (65.6%)	.8
Two	16/25 (64.0%)	
Lymph node station		
Right paratracheal	15/27 (55.6%)	.8
Subcarinal	27/33 (66.7%)	
Other‡	7/12 (58.3%)	
Diameter of the diseased lymph node*		
<20 mm	20/34 (58.8%)	.8
≥20 mm	29/48 (60.4%)	
Indirect signs§		
Yes	13/16 (81.2%)	.08
No	36/66 (54.5%)	

*Cutoff point based in the sample median. †TTC, Thoracic computed tomography. ‡Nine hilar and 3 left paratracheal. §Extrinsic compression, edema, or broadening of the carina in puncture sites.

stage I or II.^{1-3,5,7} Although endobronchial ultrasound techniques can help improve the TBNA diagnosis yield,⁴ they are not always available. In addition, as has been demonstrated, “classic TBNA” is still important in the thoracic sarcoidosis diagnosis.

Supported by Research Intensification Activity from Fondos de Investigación Sanitaria (FIS) and Olympus Company. The authors declare no conflict of interest.

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doi:10.1016/j.jtcvs.2008.07.071

Reply to the Editor:

Supplemental material is available online.

Transbronchial needle aspiration (TBNA) has been increasingly used over the past several years for the pathologic confirmation of sarcoidosis in patients with hilar or mediastinal node enlargement. Early studies, all per-

formed with the standard “blind” method, demonstrated that the diagnosis of sarcoidosis is feasible with TBNA and that acceptable, yet variable, diagnostic yields are obtainable (46%–90%).¹⁻⁷ These studies, however, left questions on the generalizability of the findings inasmuch as they were mostly retrospective,^{2,5-7} included small series,^{2,4,6-8} did not usually accept cytologic TBNA samples as diagnostic,^{1-5,8} used only rigid needles,¹ or lacked computed tomographic guidance to map lymph node areas to be sampled.⁴ More recently, a few studies designed to overcome many of these design limitations showed that a diagnostic yield of more than 75% is reproducible, at least in expert settings.⁹⁻¹¹ Nonetheless, remarkable differences in study populations, needle size used (19-gauge histology versus 22-gauge cytology needle), pathologic examination (cytologic with or without histologic material), availability of a real-time imaging guide (standard, “blind” TBNA versus ultrasound-guided TBNA), and on-site facilities (presence vs absence of rapid on-site cytopathologic examination) make it important to comment on the findings of these recent studies to place TBNA results in sarcoidosis into proper context.

One extremely important aspect of the studies specifically designed to assess the value of TBNA in sarcoidosis is that they were all subject to selection bias. The pre-test probability of sarcoidosis in the study populations was very high, inasmuch as they invariably included patients with highly suggestive clinical and radiologic findings.^{3,4,7-11} As a consequence, the excellent diagnostic yields that the authors obtained are likely to be reproducible in this specific scenario. The success rate of TBNA for sarcoidosis in studies enrolling clinically unselected patients with enlarged mediastinal nodes at imaging studies is somewhat lower and depends mostly on the prevalence of the disease in the population being studied. Satisfactory (>60%) diagnostic rates were reported in study populations with sarcoidosis prevalence of at least 35%,^{12,13} whereas

variable, sometimes disappointing, results were obtained below this threshold, even by using real-time endobronchial ultrasound (EBUS)-guided TBNA.¹⁴⁻¹⁶

Another matter of debate in the medical community is the reliability of a diagnosis of sarcoidosis based solely on cytologic material obtained with TBNA.⁶⁻¹¹ This topic is of particular importance inasmuch as real-time EBUS-guided TBNA, whose spread is predictable in the near future owing to its excellent performance characteristics, yields cytologic material inasmuch as only 22-gauge needles can be used with these devices, for the time being. When dealing with this topic, however, we must first recognize that the pathologist can identify a noncaseating granuloma but cannot diagnose sarcoidosis, because sarcoidal granulomas have no unique pathologic features to differentiate them from other granulomas, not even at histologic examination. It is, therefore, the clinician's task to rate the likelihood of a diagnosis of sarcoidosis after careful examination of clinical, radiologic, and pathologic findings. This said, data from a growing body of literature suggest that the demonstration of nonnecrotizing epithelioid granulomas on cytologic material is feasible, and more and more authors did recently rely on the cytologic findings observed in TBNA samples to strengthen a suspicion of sarcoidosis raised on clinical and radiologic grounds.^{6,7,9-16}

No studies directly compared standard versus ultrasound-guided TBNA in patients with suspected sarcoidosis up to now. However, if we analyze the characteristics and results of the only 3 prospective studies with a study population of more than 50 patients that were specifically designed to assess the value of either standard or EBUS-guided TBNA in sarcoidosis,⁹⁻¹¹ we realize that the diagnostic yield is very high (79%–91%) for both methods, yet slightly higher for the ultrasound-guided technique. If we take a closer look (Table E1), the study populations are very similar in terms of disease prevalence, average lymph

node size, lymph node stations most commonly punctured, and percentage of patients in whom TBNA retrieved adequate lymph node material. It seems likely, therefore, that rapid on-site cytopathologic examination, which was available in studies assessing ultrasound-guided TBNA, but not in the one evaluating standard TBNA, contributed to the extra diagnostic value achieved with ultrasound-guided aspiration. A possible explanation to the surprisingly high yield of a "blind" method, such as standard TBNA, is that right paratracheal and subcarinal stations are enlarged in many patients with stage I and II sarcoidosis and that the average lymph node size is quite relevant, making sarcoidosis a good diagnostic setting also for standard TBNA.⁶⁻¹¹ It is widely known, in fact, that unlike EBUS-guided TBNA, which has an excellent diagnostic yield regardless of size and location of lymph nodes, standard TBNA performs better in specific lymph node stations (right paratracheal, subcarinal) and for increasingly large nodes.

So, where do we stand with TBNA in sarcoidosis? It is now clear that the vast majority of patients with a likely diagnosis of sarcoidosis based on clinical and radiologic grounds can safely receive a pathologic confirmation with either EBUS-guided or standard TBNA. This subset of patients can be offered TBNA as the first-step diagnostic technique, in the absence of sites more easily accessible for biopsy (eg, skin, conjunctiva, peripheral nodes). It remains to be seen in future studies whether real-time EBUS-guided TBNA will be able to preclude the need for surgical diagnostic procedures (mediastinoscopy, video-assisted thoracic surgery) also in a substantial percentage of patients with sarcoidosis who have discrete node enlargement and no clear-cut clinical picture.

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doi:10.1016/j.jtcvs.2008.12.016

TABLE E1. Comparative analysis of prospective studies with a study population of more than 50 patients designed to assess the yield of either standard or ultrasound-guided TBNA in sarcoidosis

	Wong, ¹⁰ 2007 (EBUS)	Garwood, ¹¹ 2007 (EBUS)	Trisolini, ⁹ 2008 (TBNA)
Patients (No.)	65	50	61
Sarcoidosis prevalence (% study population)	94–98*	96–98†	86
Successful LN sampling (% patients)	95	92	94
Average size of sampled LNs (mm)	20	16‡	18.5
Sampling in 4R and/or 7 LN areas (% total sampled LNs)	58	63	89
TBNA: diagnostic yield (%)	87–92*	84–85†	79
ROSE availability (y/n)	Yes	Yes	No

TBNA, Transbronchial needle aspiration; EBUS, endobronchial ultrasound; ROSE, rapid on-site cytopathologic evaluation; LN, lymph node; 4R, right paratracheal; 7, subcarinal.

*Three patients with indefinite final diagnosis; prevalence and yield are provided as a range of values encompassing the worst (all patient with indefinite diagnosis did have sarcoidosis) and best (all patient with indefinite diagnosis did not have sarcoidosis) case scenario. †One patient with indefinite final diagnosis; prevalence and yield are provided as a range of values encompassing the worst (all patient with indefinite diagnosis did have sarcoidosis) and best (all patient with indefinite diagnosis did not have sarcoidosis) case scenario. ‡Lymph node size available for 55% of the study population, and expressed as median.