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ORIGINAL REPORT

Randomized Comparison of Power Doppler Ultrasound–Directed Excisional Biopsy With Standard Excisional Biopsy for the Characterization of Lymphadenopathies in Patients With Suspected Lymphoma

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ABSTRACT

Purpose
The sensitivity of lymph node excisional biopsy requires validation. Power Doppler ultrasound (US) helps predict the malignant status of lymphadenopathies. We used power Doppler US to select for biopsy the lymph node most suspected of malignancy.

Patients and Methods
One hundred fifty-two patients having lymphadenopathies with clinical suspicion of lymphoma were divided into two well-matched groups and randomly assigned to undergo either standard or power Doppler US–directed lymph node excisional biopsy.

Results
Histology showed a malignancy in 64% of patients in the standard group (lymphoma, 49 patients; carcinoma, two patients) and in 87% of patients in the US-assisted group (lymphoma, 62 patients; carcinoma, one patient). There were significantly fewer biopsy-related complications in the assisted group than in the standard group. During the follow-up of the patients with lymph nodes reported as being reactive, 14 of 29 patients in the standard group were rebiopsied and were found to have lymphoma (13 patients) or carcinoma at the subsequent lymph node histology, whereas none of the patients in the assisted group (nine patients) required a second biopsy. Thus, biopsy provided false-negative results for malignancy in 21% of patients affected by lymphoma in the standard group and never in the assisted group ($P < .01$).

Conclusion
Power Doppler US is an accurate tool for screening lymphadenopathies to be removed by excisional biopsy in patients with suspected lymphoma.

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INTRODUCTION

In case of clinical suspicion of lymphoma, a lymph node enlargement requires histologic assessment to define a correct diagnosis and to develop a proper treatment plan. Prebiopsy evaluation of enlarged cervical, supraclavicular, axillary, or inguinal lymph nodes is usually left to physical examination alone; a careful and thorough palpation of superficial lymph node regions, performed by a physician experienced in the management of patients with lymphoma, is considered to provide sufficient information to schedule an excisional biopsy.[1] However, the possible presence of enlarged reactive or necrotic

lymph nodes and of nonpalpable but histologically significant malignant lymph nodes may impair the success of an excisional biopsy.[2,3] New approaches to this procedure based on imaging-assisted methods are now available.

Power Doppler ultrasound (US) is a recent imaging technique that is able to accurately define the anatomic site of a lymph node, with its morphologic (including size, shape, and hilar and cortical deformation) and vascular characteristics.[4,5] Compared with the standard color Doppler, the properties of power Doppler US are homogeneous noise appearance, less direction and velocity dependence, less temporal variance, improved vessel contrast, and higher sensitivity. Power Doppler US clearly assesses in vivo intranodal angioarchitecture, mimicking angiography, distinguishing arterial and venous vessels, and calculating velocimetric parameters of the vessel flow.[4-6]

Angiogenesis is recognized as being critical for solid tumor growth, invasion, and metastasis. The various steps of neoplastic angiogenesis, such as basement membrane disruption, endothelial cell migration and proliferation, and tube formation, lead to the development of abnormal vascularization, with stenoses, occlusion, and/or dilation and/or arterovenous shunts.[7] The findings of increased endothelial cell and vessel proliferation in bone marrow or enlarged lymph nodes pointed to a possible role of neoangiogenesis in the pathogenesis of multiple myeloma or B-cell lymphomas.[8,9] With appropriate and standardized methodology,[10] power Doppler US has proven useful to identify malignant lesions because it detects more flow signals than gray-scale and color Doppler US, thus better differentiating between benign and malignant superficial lymphadenopathies.[4-6,11,12] We performed a randomized comparison of power Doppler US–directed excisional biopsy with standard excisional biopsy to characterize superficial lymphadenopathies in patients with clinical suspicion of lymphoma.

PATIENTS AND METHODS

Study Design and Patient Characteristics

During the past 4 years, 152 consecutive subjects (82 men and 70 women; median age, 44 years; range, 15 to 82 years) who were referred for superficial lymph node enlargement of unknown origin entered onto the study. Of these patients, 40, 60, and 52 had palpable lymph nodes in a one, two, or three anatomic regions, respectively. Clinical indication to perform an excisional biopsy was the only inclusion criterion. Patients affected by Epstein-Barr virus, cytomegalovirus, herpes simplex virus, rubella, toxoplasma, or tuberculosis infection were excluded. A minority of patients had already had computed tomography scans, and the findings of deep-seated lymph nodes had strengthened the suspicion of a malignant systemic disease. The study was a single-center trial involving two study groups and was approved by the local ethics committee. Patients were randomly assigned to receive lymph node biopsy using one of two methods, standard excisional biopsy (nonassisted group) or excisional biopsy under power Doppler US direction (assisted group). The primary aim of the study was to evaluate the capacity to predict the lymph node status, which was measured in terms of the percentage of cases of malignant involvement detected by power Doppler US–directed excisional biopsy versus standard excisional biopsy. Additional aims were the evaluation of biopsy-related complications and the discovery of a malignant disease during the follow-up of patients who had had the first biopsy negative for malignancy. The overall diagnostic accuracy was defined as the rate of correct patient classification, on the basis of having or not having lymph nodes positive for malignancy during the follow-up. Patients were informed of the aims of the study, the potential results of the procedures, and the meaning of the randomization, and signed a consent form before the operation. All biopsy procedures were performed by one of three surgeons experienced in lymph node resection, according to standard methods.[13] To avoid imbalance in infectious risk, patients in both groups received a short course of antibiotic prophylaxis (amoxicillin plus clavulanic acid, 2 g/d orally for 4 days) starting the day of biopsy.

Biopsy Procedure in the Nonassisted Group

In a day-hospital regimen or as in-patients and under local or general anesthesia (at surgeon's discretion), biopsy was directed to the region containing the most superficial and/or largest lymph node, as suggested by the physical examination. The lymph nodes were harvested through skin-crease incision obtained by free-hand methods.

Biopsy Procedure in the Assisted Group

Patients underwent US exploration of all superficial lymph node areas, including those apparently not involved in the disease, 24 hours before biopsy, and any abnormal (for size, shape, or hilus conformation) lymph node underwent power Doppler US. The information yielded was used to select the site of biopsy. Examinations were carried out by the same operator (M.P., a hematologist trained in diagnostic US),[14,15] using a high-resolution US Hitachi instrument equipped with power Doppler (EUB 6500; Hitachi, Tokyo, Japan) and a 13-6 MHz broad-band linear array transducer (EUB 54 M probe; Hitachi). Lymph nodes were assessed by gray scale to define their anatomic site, depth, size, shape, and hilus and by power Doppler to investigate the intranodal vascular pattern. Shape was studied with the long-to-short axis ratio (L/S) and defined as round for L/S values between 1 and 1.5 and oval for L/S values between 1.5 and 2, as described by other authors.[5] Settings for power Doppler were standardized for the highest sensitivity in the absence of apparent noise, using high-pass filter at 50 Hz, pulsed repetition frequency at 650 to 800 Hz, moderate-to-long persistence, and a slow-sweep technique. Under these conditions, the lowest possible measurable blood velocity was defined below 5 cm/sec. The method for appropriate gain optimization was in accordance with the criteria described by Bude and Rubin.[12] Intranodal vascular mapping was categorized as central/hilar type, peripheral type, mixed type (central/hilar and peripheral vessel signal), and chaotic type (vessel signal chaotically distributed within the node), in accordance with other authors.[5,11] As for Doppler spectral analysis, the resistive index (RI) value of arterial vessels (peak systolic velocity-end diastolic velocity/peak systolic velocity, as defined by Pourcelot)[16] was calculated by sampling at least three different intranodal sites (periphery, interior, and center/hilus); each RI measurement was determined after at least three stable consecutive cycles of waveform.

For each enlarged lymph node, the mean value of three measurements was calculated.

The main criterion used for selecting the node to be biopsied was the RI value; for each patient, the lymph node with the highest RI mean value was labeled and selected as target for biopsy. When more nodes had similar RI values, additional selection criteria were round shape, hilus absent, and intranodal hypervascularization.

In 12 patients, the selected lymph node was studied by repeated power Doppler US assessments on two occasions at a 1-hour interval by the same operator (intraobserver reproducibility) and by another operator unaware of the previous result, always using the same US machine (interobserver reproducibility).[17,18] The target area for biopsy was marked on the skin with indelible ink surrounding the probe contour, and the size and deepness of the lymph node were recorded. In the day-hospital regimen or as in-patients and under local or general anesthesia (at surgeon's discretion), the lymph nodes were harvested through skin-crease incision guided by the skin markings indicating the power Doppler US–selected lymph node.

Histopathologic Evaluation

Histopathologic examination was performed in a single pathology unit by three expert hematopathologists who were blinded to the patient's clinical condition, to the excision method, and to the histologic results of the other operators. Lymph node samples were routinely fixed in formalin and embedded in paraffin. The histologic sections were stained according to standard methods (hematoxylin and eosin and Giemsa). All cases of lymphoma were diagnosed by a combination of morphologic and immunohistochemical (using a large panel of monoclonal antibodies) assessment and were classified according to the current Revised European-American Lymphoma and WHO criteria.[19,20] Distinction between lymphomas with indolent or aggressive clinical behavior was made as reported by other authors.[21,22] Epithelial metastatic tumors were identified by monoclonal antibodies to cytokeratin. Overall, biopsies were categorized as either positive for malignancy (samples containing adequate number of cells with morphologic atypia and immunohistochemical evidence of monoclonality) or negative for malignancy (samples containing adequate number of cells with no evidence of malignancy). Patients classified as having a histologic result negative for malignancy underwent strict follow-up by clinicians blinded to the excision method used for biopsy.

Statistical Analysis

Statistical evaluations, including χ^2 (P was expressed as Yates corrected) and Student's t test, analysis of variance with Bonferroni correction, Pearson correlation, and log-rank test (to compare curves representing event-free survival), were performed with SPSS for Windows software (version 9.0; SPSS, Chicago, IL).

RESULTS

Of the 152 patients randomly assigned to a study group, 80 (53%) received standard excisional biopsy, and 72 (47%) received power Doppler US–directed excisional biopsy (a few patients were lost to follow-up after randomization and before biopsy, and this occurred by chance more frequently in the assisted group). Both groups were well matched at entry with respect to age and sex (Table 1). A total of 116 lymph nodes were removed and examined from the 80 patients in the nonassisted group, whereas only one lymph node was removed from each of the 72 patients in the assisted group. There was no significant difference between the two groups regarding the size of the lymph nodes removed. Patients in the nonassisted group had slightly more cervical and inguinal biopsies, whereas patients in the assisted group had slightly more supraclavicular and axillary biopsies.

Table 1. Patient Characteristics in the Two Study Groups

Characteristic	Nonassisted Group (No.)	US-Assisted Group (No.)	*P*
Total patients	80	72	
Sex			
Male	42	40	NS
Female	38	32	
Age, years			
Median	45	43	NS
Range	17-82	15-78	
Biopsy site			
Cervical	48	34	.01
Supraclavicular	6	13	.05
Axillary	6	16	.02
Inguinal	20	9	.01
No. of lymph nodes removed	116	72	< .001
Diameter of examined lymph nodes,* cm			
Median	1.8	2.0	NS
Range	0.4-6.0	0.4-7.0	

Abbreviation: NS, not significant.
*Long axis.

Histology

Of the 80 patients in the nonassisted group, 51 (64%) had lymph nodes positive for malignancy (B-cell non-Hodgkin's lymphoma [NHL], 26 patients; Hodgkin's disease [HD], 23 patients; and metastatic carcinoma, two patients), and 29 (36%) had lymph nodes negative for malignancy (described as benign lymphoid hyperplasia in all patients, with steato-fibrotic and/or necrotic changes in 18 of the patients). Of the 72 patients in the assisted group, 63 (87.5%) had lymph nodes positive for malignancy (B-cell NHL, 29 patients; T-cell NHL, four patients; HD, 29 patients, and metastatic carcinoma, one patient), and nine (12.5%) had lymph nodes negative for malignancy (benign lymphoid hyperplasia). There was complete agreement among the three pathologists on the histologic diagnosis (Table 2).

Overall, the 38 patients with lymph nodes negative for malignancy (defined as reactive or inflammatory) were observed for a median of 11 months (range, 1 to 40 months). During the follow-up, for 14 of 29 patients in the nonassisted group, the clinicians required a second lymph node biopsy, and a malignancy was finally detected. The second

Table 2. Histologic Characterization of Removed Lymph Nodes in the Two Study Groups

Histology	No. of Patients	
	Nonassisted Group	US-Assisted Group
Aggressive non-Hodgkin's lymphoma		
Diffuse large B-cell lymphoma	12	9
Follicular (grade 3) lymphoma	0	3
Mantle-cell lymphoma	4	7
Other B-cell lymphomas	1	4
T-cell lymphoma	0	4
Indolent non-Hodgkin's lymphoma		
Follicular (grade 1 to 2) lymphoma	6	5
Small lymphocytic lymphoma	3	1
Hodgkin's disease	23	29
Metastatic carcinoma	2	1
Nonmalignant findings		
Benign lymphoid hyperplasia	29	9

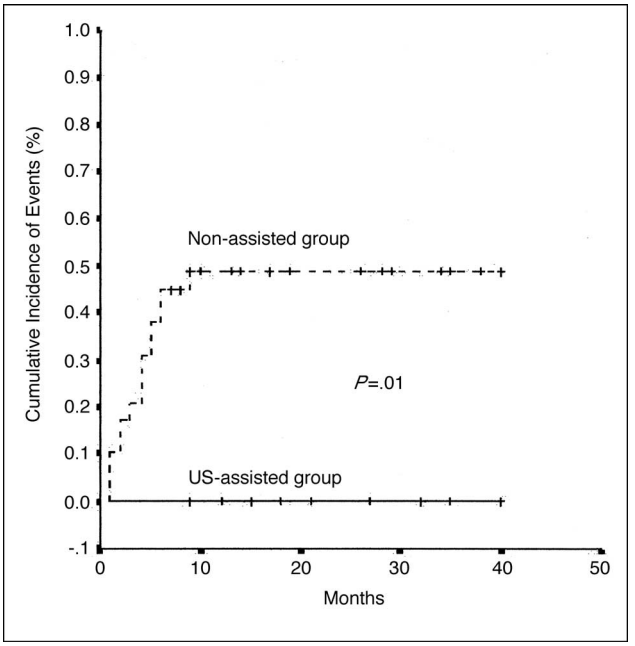

Fig 1. Probability of developing overt malignancy in patients with nonmalignant findings at the first lymph node biopsy in the nonassisted group (n = 29) and in the ultrasound (US)-assisted group (n = 9). Months = months from the first biopsy.

biopsy, which was performed after a median of 4 months (range, 1 to 9 months) from the first biopsy, demonstrated HD in seven patients, NHL in five patients, melanoma in one patient, and Rosai-Dorfman disease in one patient (with a severe clinical course requiring cytotoxic treatment as a lymphoma; Table 3). In contrast, none of the nine patients who had had diagnosis of a benign lesion at the first biopsy in the assisted group required a second biopsy or developed a malignancy, with a median follow-up of 21 months (range, 9 to 40 months; $P = .01$; Fig 1).

Therefore, the overall diagnostic accuracy of lymph node status in the nonassisted group was 82% (ie, results accurate in 66 of 80 patients), with a sensitivity of 78% (51 of 65 patients with lymph nodes positive for malignancy were identified) and a false-negative rate of 22% (14 of 65 patients with lymph nodes positive for malignancy were not identified). By contrast, the overall diagnostic accuracy and the sensitivity of the lymph node status in the assisted group

Table 3. Findings in 14 Patients in the Nonassisted Group Who Underwent a Second Biopsy

Patient No.	No. of Months Between the Two Biopsies	Biopsy Site		Size of the Removed Nodes (cm)*		Histologic Diagnosis	
		First	Second	First	Second	First	Second
1	1	Cervical	Cervical	1.0	2.0	Reactive†	Grade 1 follicular NHL
2	1	Inguinal	Supraclavicular	2.0	2.5	Reactive	Nodal small lymphocytic NHL
3	1	Axillary	Cervical	1.5	3.0	Reactive†	Anaplastic large cell NHL
4	2	Inguinal	Axillary	2.0	4.0	Reactive	Grade 1 follicular NHL
5	2	Cervical	Supraclavicular	1.5	2.8	Reactive†	Nodular sclerosis HD
6	3	Cervical	Supraclavicular	2.0	4.0	Reactive†	Nodular sclerosis HD
7	4	Inguinal	Axillary	1.8	3.8	Reactive	Grade 1 follicular NHL
8	4	Cervical	Supraclavicular	1.5	4.0	Reactive†	Melanoma
9	4	Inguinal	Cervical	1.0	4.2	Reactive†	Mixed cellularity HD
10	5	Cervical	Cervical	2.0	2.0	Reactive	Mixed cellularity HD
11	5	Cervical	Cervical	2.5	5.0	Reactive†	Mixed cellularity HD
12	6	Cervical	Supraclavicular	2.0	4.7	Reactive†	Nodular sclerosis HD
13	6	Inguinal	Axillary	3.0	4.8	Reactive	Nodular sclerosis HD
14	9	Inguinal	Axillary	3.3	4.5	Reactive†	Rosai-Dorfman disease

Abbreviations: NHL, non-Hodgkin's lymphoma; HD, Hodgkin's disease.
*Long axis.
†With intranodal steato-fibrotic and necrotic changes.

were 100% (ie, no false-negative cases; Fig 2). There was a statistically significant difference between the two groups regarding diagnostic accuracy and sensitivity ($P < .001$).

Power Doppler US Results

The average time required for power Doppler US examination was 30 minutes (range, 20 to 50 minutes). Intraobserver and interobserver reproducibility of intranodal vascular mapping and RI measurements were excellent. Of the 12 lymph nodes tested for reproducibility, 11 (91%) were classified identically by the same observer at two power Doppler US examinations 1 hour apart ($r = 0.9$), and 10 (83%) were classified identically by observers A and B ($r = 0.88$).

For each lymph node removed, shape and size were classified identically by the US operator and the pathologist. This finding consistently demonstrated that the surgeon had removed the indicated lymph node. Depth of the selected lymph nodes was between 1 and 4 cm. As for morphologic characteristics, malignant lymph nodes had a median of the long axis of 2 cm (range, 0.4 to 7.0 cm), were round in 50 cases and oval in 13 cases, and had hilus absent in 42 cases and present in 21 cases. Vascular mapping of malignant lymph nodes was mixed in 30 cases, chaotic in 24 cases, peripheral in six cases, and central/hilar in three cases (Fig 3). There were nine lymph nodes (12.5%) classified as suspected of malignancy by power Doppler US, which were shown to be reactive at histology. Of these nodes, the median of the long axis was 1.9 cm (range, 0.8 to 3.0 cm), six were oval, three were round, five were hilus present, and four were hilus absent; vascular mapping was of the hilar type in four, mixed in three, and peripheral in two. The median RI value of aggressive NHL (0.85; range, 0.7 to 0.98) was significantly ($P < .01$) higher than the median values of HD (0.74; range, 0.6 to 0.96), indolent NHL (0.71; range, 0.68 to 0.87), and benign lymphoid hyperplasia (0.68; range, 0.6 to 0.77; Fig 4). The metastatic carcinoma RI value was 0.8. Overall, the positive predictive value for malignancy of the parameters studied was as follows: for gray-scale US: round shape, 79%; hilus absent, 67%; and size ≥ 2 cm, 48%; and for vascular mapping by power Doppler US: mixed type, 48%; chaotic type, 38%; peripheral type, 10%; and central/hilar type, 5%. As for RI, considering a cutoff value ≥ 0.8, the predictive value for malignancy was 48%.

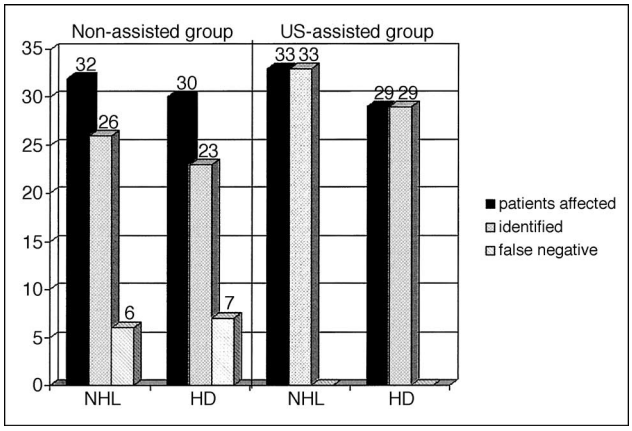

Fig 2. Diagnostic accuracy in detecting lymph nodes involved by lymphoma in the two study groups. US, ultrasound; NHL, non-Hodgkin's lymphoma; HD, Hodgkin's disease.

Biopsy Procedures and Complications

Sixteen patients underwent biopsy (axillary, n = 6; supraclavicular, n = 6; and cervical, n = 4) under general anesthesia, with an average hospitalization of 2.5 days (all in the nonassisted group). All other patients underwent biopsy in a day-hospital regimen under local anesthesia. The procedures were equally distributed among the three surgeons; no surgeon had more complications compared with the others. Patients who received non-US–directed biopsy had significantly more pain, numbness, or paresthesia and larger scars than patients who underwent US-directed biopsy. Moreover, 11 patients in the nonassisted group and no patient in the assisted group developed lymphorrhea; all patients recovered from the complication after one or more liquid aspirations (between 20 and 50 mL for each patient; Table 4).

DISCUSSION

The aim of this study was to determine the ability of power Doppler US to predict the presence of intranodal malignancy, thus improving the diagnostic accuracy of excisional biopsy in patients who have enlarged lymph nodes with clinical suspicion of lymphoma. The enlargement may often involve more than one lymph node; because the biopsy procedure has only a diagnostic purpose, the surgeon will select the easiest to reach lymph nodes (usually those seated superficially in a cervical or inguinal region). However, not all lymph nodes may be involved by the main disease entity; there is a risk of removing satellite reactive lymph nodes, thus missing the primary diagnosis of a malignant disease present in another node, which is sometimes deeper seated or even seated in a different anatomic area.[23] An affected lymph node may also undergo necrosis and/or steatofibrotic changes, which could avert the pathologist from the correct diagnosis.[3] These are all potential sources of inaccuracy in standard excisional biopsy. Preliminary reports indicating that power Doppler US might predict the presence of malignancy in superficial or deep-seated lesions have recently appeared.[4-6,11,24] In the present randomized study, we used power Doppler US to identify as biopsy target the most suspected area of malignancy. The selected lymph node was fully characterized as far as anatomic location, depth, size, shape, hilus alterations, and intranodal angioarchitecture were concerned. Intranodal hypervascularization and arterial vessels with relatively high RI value fulfilled

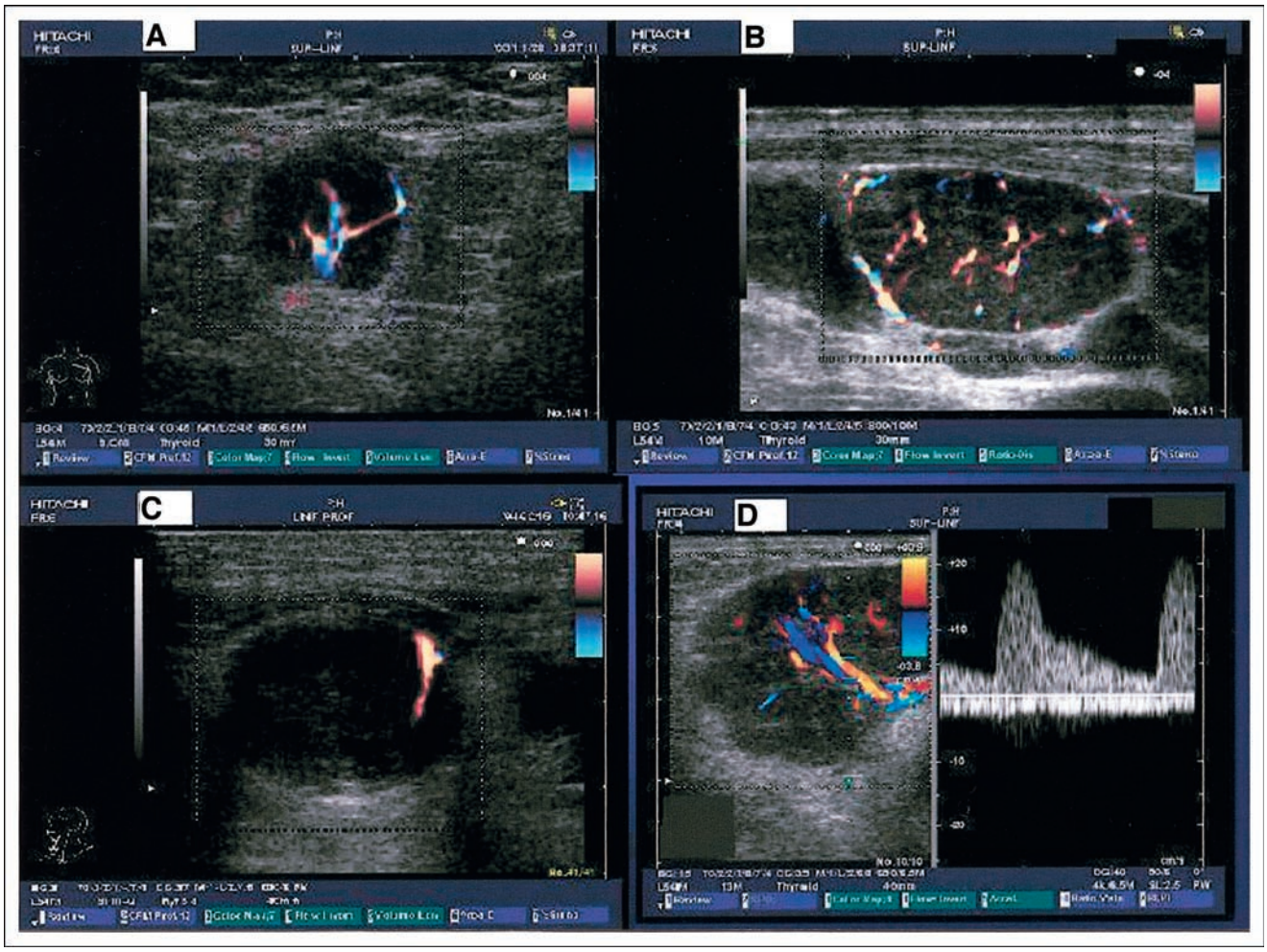

Fig 3. Angioarchitecture of lymph nodes affected by an aggressive lymphoma as revealed by power Doppler ultrasound in four patients. Mixed type (A), chaotic type (B), peripheral type (C), and hilar type with aberrant resistive index value (D).

the selection requirements. Lymph nodes showing no perfusion or low vascularization (tiny flow signals), likely caused by steato-fibrotic and/or necrotic changes of intranodal tissue, were avoided. The US examination was carried out by members of the hematology staff trained in diagnostic ultrasonography; the low intraobserver and interobserver variability of power Doppler assessments proved the high reliability of the examination. The result of this study shows that power Doppler US–directed excisional biopsy is significantly more effective in identifying lymph nodes positive for malignancy than standard excisional biopsy. We would like to underline the excellent tissue samples obtained in the US-directed group, which were informative and successful (tissue adequate for a correct histologic diagnosis), establishing the specific etiology of the enlargement, in all instances. Event-free survival of patients with negative biopsy for malignancy was significantly better in the assisted group than in the nonassisted group. Fourteen patients, in whom a few months earlier a non-US–directed biopsy had provided results of a benign adenopathy, were found to have a malignant disease involving other lymph nodes. Of them, 11 patients underwent rebiopsy in an anatomic area different from that biopsied the first time. It is reasonable to assert that the malignancy was already present at the time of the first biopsy and could have been detected by selecting a more significant lymph node had a power Doppler US study been performed. The higher prevalence of biopsy in inguinal areas in the nonassisted group may not be incidental. Supraclavicular and axillary nodes are often deep seated and less detectable by physical examination and, thus, are less frequently selected by the clinician or the surgeon as target for the biopsy; in contrast, these nodes can be more specific for the basic malignant disease and, thus, more frequently selected for the biopsy by the US operator.

By summing the number of patients who received diagnosis of malignancy at the first or second biopsy in the nonassisted group (51 + 14 = 65 of 80 patients), we found a percentage of malignancy similar to that observed in the

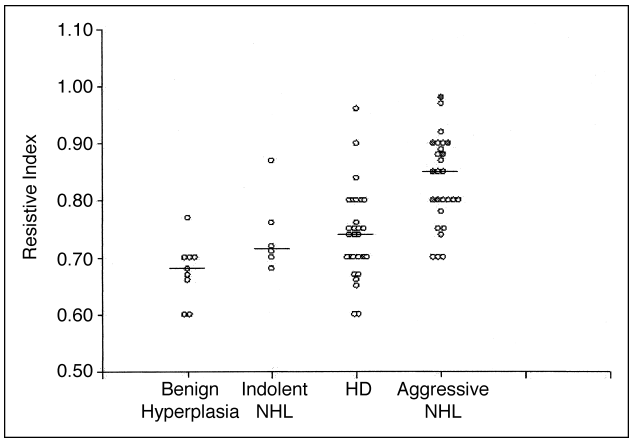

Fig 4. Power Doppler ultrasound measured resistive index (RI) in various patient categories. A correlation between RI and clinical aggressiveness emerges. Mantle-cell lymphoma (shaded circles) behaves as an aggressive lymphoma. NHL, non-Hodgkin's lymphoma; HD, Hodgkin's disease.

assisted group (63 of 72 patients), in whom all diagnoses were made by a single biopsy. These data confirm that standard excisional biopsy may carry a significant number of false-negative results. The false-negative rate was slightly higher in HD than in NHL patients; it was also higher for inguinal nodes (30%) compared with other sites (axillary, 17%; cervical, 8%; and supraclavicular, 0%).

Quantitative assessment of intranodal vascularization provided relevant information. High RI values (rapid systolic flow and poor telediastolic component) were predictive of an aggressive malignant disease (aggressive NHL or metastatic carcinoma), whereas lower RI values were found in HD, indolent NHL, and benign lymphoid hyperplasia. Interestingly, mantle-cell lymphoma, a small-cleaved lymphocytic lesion with a severe clinical course, which was considered as a low-grade lymphoma until a few years ago,[22] showed RI values in the range of aggressive diseases (median RI, 0.88) that were even higher than the RI values of diffuse large B-cell lymphoma (median RI, 0.8), grade 3 follicular lymphoma (median RI, 0.8), and other B- or T-cell aggressive lymphomas (median RI, 0.85; Fig 4). The mechanism by which lymphoma lesions have such diversified angiopatterns is still unclear. In aggressive NHLs, the magnitude of neoangiogenesis is probably the most relevant factor. In situ data obtained by transmission electron microscopy in B-cell NHL showed that angiogenesis, defined as formation of new vessels and remodeling of existing vessels, increases with tumor progression (in terms of increasing malignancy grading); the network of new vessels with irregular diameter and defective wall structure leads to abnormal flow and, hence, to the aberrant Doppler spectral patterns.[9] Similar findings were reported in bone marrow during progression from monoclonal gammopathy of undetermined significance to multiple myeloma.[8] In indolent NHL and in HD, this mechanism could be less operative, making the differentiation from reactive or inflammatory lesions less clear cut. In such instances, power Doppler US findings of round shape, hilus absent, and intranodal hypervascularization with chaotic feature may be additional selection criteria, as described by other authors.[5,11] In a small fraction of patients in the assisted group (12.5%), power Doppler US examination suggested malignancy that was neither confirmed subsequently at histology nor occurred during the follow-up. This means that power Doppler US study is highly sensitive but not absolutely specific.

Table 4. Compliance to Biopsy in the Two Study Groups

Complication	Non-Assisted Group (%)	US-Assisted Group (%)	*P*
Pain on operated site*			
No	30	78	< .001
Yes, mild and transient	33	11	
Yes, continuous	37	11	
Numbness on operated site			
No	20	88	< .001
Yes	80	12	
Swelling on operated site			
No	86	100	.003
Yes	14	0	
Aesthetic appearance of biopsy scar†			
Acceptable	30	83	< .001
Unpleasant	70	17	

*Postoperative pain was evaluated as absent, mild (not requiring analgesia), or continuous (requiring analgesia).
†As judged by the patients themselves 1 month after biopsy.

Power Doppler US–directed excisional biopsies were carried out always in a day-hospital regimen and under local anesthesia, whereas some patients in the nonassisted group needed general anesthesia and ward admission. The better tolerance of US-directed biopsies (less pain, less swelling, and more acceptable aesthetic scars) can be attributed to the perfect knowledge by the surgeon of the site and depth of the node to be removed, which lead to a precise incision and to the removal of a single node, thus avoiding larger cuts and intraoperative maneuvers.

In conclusion, our study provides evidence justifying the use of power Doppler US assistance as part of the work-up before performing a biopsy of superficial lesions suspected of lymphoma. This method improves the diagnostic accuracy and safety of excisional biopsy for the characterization of lymphadenopathies. It reliably provides adequate tissue for a correct histologic diagnosis, obviating the risk of underdiagnosis, which may cause a harmful diagnostic delay, and reducing postbiopsy morbidity and hospitalization costs.

Authors' Disclosures of Potential Conflicts of Interest

The authors indicated no potential conflicts of interest.

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