ABSTRACT

OBJECTIVE: To determine the value of whole-body [18F] fluorodeoxyglucose positron emission tomography/computed tomography (FDG-PET/CT) for diagnosing occult malignant disease in patients with myositis compared with broad conventional cancer screening.

METHODS: We prospectively studied 55 consecutive patients with a recent diagnosis of myositis in 3 teaching hospitals over a 3-year period by whole-body FDG-PET/CT and compared the results with those of conventional cancer screening, which included thoracoabdominal CT, mammography, gynecologic examination, ultrasonography, and tumor marker analysis. Comparisons were made using predictive values and their 95% confidence intervals.

RESULTS: A total of 9 of 55 patients were diagnosed with paraneoplastic myositis. FDG uptake was positive in 7 patients (1 false-positive), negative in 44 patients (3 false-negative), and inconclusive in 4 patients. Positive and negative predictive values of FDG-PET/CT for the diagnosis of cancer were 85.7% and 93.8%, respectively. Conventional screening was cancer-positive in 9 patients (2 false-positive) and negative in the remaining 46 patients (2 false-negative). Positive and negative predictive values were 77.8% and 95.7%, respectively. The overall predictive value of broad conventional screening was the same as that of FDG-PET/CT (92.7 vs 92.7).

CONCLUSION: The performance of FDG-PET/CT, a single imaging study, for diagnosing occult malignant disease in patients with myositis was comparable to that of broad conventional screening, which includes multiple tests.

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Authorship: All authors had access to the data and played a role in writing this manuscript.

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Idiopathic inflammatory myopathies are systemic diseases that include dermatomyositis, polymyositis, and sporadic inclusion body myositis.1 An association between cancer and inflammatory myopathies, mainly dermatomyositis and to a lesser extent polymyositis, has been reported in various studies.2,3 Cancer screening is usually recommended in these patients, but there is no consensus regarding how, and how often, they should be tested.4-7 Positron emission tomography (PET) using [18F] fluorodeoxyglucose (FDG), and more recently, combined FDG-PET/computed tomography (FDG-PET/CT), is one of the most sensitive imaging
techniques to detect malignant lesions and has been used in paraneoplastic conditions with variable success.\(^8\)-\(^{13}\) To our knowledge, it has not been applied systematically to the diagnosis of occult tumors in patients with dermatomyositis/polymyositis. Our aim was to assess the performance of FDG-PET/CT in the detection of occult malignant disease in patients with dermatomyositis/polymyositis and compare it with broad, conventional cancer screening.

**PATIENTS AND METHODS**

**Patients**
The study included 55 consecutive adult white patients who were recently diagnosed with dermatomyositis/polymyositis, consulting at 3 tertiary teaching hospitals in Barcelona (Vall d’Hebron General Hospital, Bellvitge Hospital, and Hospital Clinic) between February 2006 and January 2009. Altogether, these referral hospitals have 2500 beds for a catchment population of approximately 2.5 million inhabitants. Patients included in the study gave informed written consent to undergo FDG-PET/CT. The study was approved by the institutional review boards of all the participating hospitals. The data for all patients were prospectively obtained.

The diagnosis of dermatomyositis/polymyositis was based on the criteria of Bohan and Peter,\(^ {14,15}\) and only patients with definite or probable disease were included in the study. Cancer-associated myositis was defined according to the modified Bohan and Peter classification\(^6\) as cancer within 3 years of the myositis diagnosis and the fact that if cancer is cured, myositis also is cured.

Patients were excluded if they had previous cancer, an active infection that could produce misleading FDG-PET uptake (eg, tuberculosis), or a critical clinical situation making additional examinations dangerous (eg, severe respiratory failure).

After the diagnosis of dermatomyositis/polymyositis had been reached and immunosuppressive therapy was established, patients were asked to participate in the study. All the patients included underwent conventional cancer screening and FDG-PET/CT to investigate the presence of an occult malignancy. Most examinations were carried out within the first 6 months after the diagnosis.

Conventional cancer screening (standard test) included a complete physical examination, laboratory tests (complete blood count and serum chemistry panel), thoracoabdominal CT study, tumor markers (CA125, CA19.9, carcinoembryonic antigen, prostate-specific antigen), and gynecologic examination in women, including ultrasonography and mammography.

Two categories, positive and negative, were established on the basis of conventional cancer screening. Abnormal findings in any of the various tests included in the conventional screening were confirmed by an appropriate procedure.

**CLINICAL SIGNIFICANCE**

- Inflammatory myopathies, particularly dermatomyositis, are associated with an increased risk of malignant disease. Cancer screening is usually recommended.
- The yield of FDG-PET/CT scanning is similar to that of conventional cancer screening to detect occult malignant disease in patients with dermatomyositis/polymyositis.
- Performing only 1 test (FDG-PET/CT) would be better for the patient and provide equal accuracy.

**Statistical Analysis**

A descriptive analysis was made of the demographic data and some clinical features. Qualitative data are expressed as percentages, and quantitative data are expressed as the median with the interquartile range. The Fisher exact or chi-square test, as appropriate, was used to assess the relationships between qualitative variables. Concordance between the FDG-PET/CT findings of 2 blinded experienced readers (1 nuclear medicine physician and 1 radiologist) was measured using the kappa coefficient. The positive and negative predictive values, sensitivity, specificity, and overall predictive value with 95% confidence intervals were calculated for both FDG-PET/CT and conventional screening.
Statistical significance was set at $P$ less than .05, and all analyses were performed with the Statistical Package for the Social Sciences version 15.0 (SPSS Inc, Chicago, Ill). Statistical significance of the difference in the overall predictive value was assessed by the 95% CI. We followed the STARD$^{17}$ statement to improve the quality of reporting of observational and diagnostic studies.

RESULTS
Between February 2006 and January 2009, 55 consecutive patients, 37 women and 18 men, with a median (interquartile range) age of 57.5 (46.1-68.9) years, were diagnosed with inflammatory myopathy (6 polymyositis/49 dermatomyositis). The median (interquartile range) duration of follow-up of patients with a negative or inconclusive FDG-PET/CT report was 14 (8-30) months. Nine patients were diagnosed with paraneoplastic myositis (16%). The tumor was located in the breast in 5 patients and in the lung, pancreas, vagina, and colon in 1 patient each. Three of the patients (affected in pancreas [1], lung [1], and colon [1]) developed an aggressive form of cancer that resulted in death. In 4 of the 6 remaining cases (1 patient with vaginal cancer and 3 patients with breast cancer), myositis clearly improved after cancer treatment, although small dosages of corticoids (5 mg/d) were needed. The remaining 2 patients (both with breast cancer) improved with cancer therapy, but adjuvant immunosuppressive therapy also was required. No new incidental cancers were observed in any of the 9 patients with cancer. Six patients were excluded (4 dermatomyositis), 4 because of administrative difficulties in performing FDG-PET/CT and 2 because of severe disease and progression to death. Only 4 patients underwent FDG-PET/CT and broad conventional cancer screening more than 6 months after the diagnosis; none of them were paraneoplastic. The time between conventional screening and FDG-PET/CT was less than 4 weeks in all patients. No adverse events occurred after standard screening or FDG-PET/CT.

Concordance between the participating radiologists in the interpretation of FDG-PET/CT findings was high (kappa = 0.9; there were only 2 discrepancies; in both cases consisting of a negative result by 1 reader and inconclusive result by 1 reader). FDG-PET/CT was positive in 7 patients. In 6 of these patients, cancer was confirmed, and in 1 patient with suspected colon cancer, colonoscopy ruled out the disease. Three of 44 patients with a negative FDG-PET/CT were diagnosed with cancer: A breast cancer was found at 6 months in 1 patient and at 2 years of follow-up in 1 patient, and a vaginal carcinoma that had been missed by FDG-PET/CT was detected by gynecologic examination in 1 patient. Infracentimetric lung nodules were present in 6 patients, and proper follow-up did not disclose evolution to cancer.

The FDG-PET/CT imaging study was considered inconclusive in 4 patients. In 1 of these patients (patient 9), FDG-PET/CT findings of a right axillary lymph adenopathy and cervical spine uptake were inconclusive, and 2 additional examinations were performed (cervical CT and axillary ultrasound), with negative findings. Conventional cancer screening results were normal. Cancer of the left breast developed in the patient 2 years later, which apparently was unrelated to the previous inconclusive PET/CT findings (as reevaluated by other professionals, cancer was not visible in the initial imaging studies).

The diagnostic performance of FDG-PET/CT to detect cancer yielded a positive predictive value of 85.7%, negative predictive value of 93.8%, sensitivity of 66.7%, and specificity of 97.8%. The overall predictive value of the test was 92.7% (Table 1).

Conventional cancer screening detected abnormalities in 9 patients (Table 2). A diagnosis of neoplasma was established in 7 of them, and in the remaining 2 patients, a high carcinoembryonic antigen value required confirmatory colonoscopy, which was normal. Results obtained in the remaining 46 cases were negative for cancer, but 2 of these patients developed breast cancer 6 months and 2 years after screening. No malignant disease manifested over follow-up of the other patients. The positive and negative predictive values were 77.8% and 97.8%, respectively, and the overall predictive value was 92.7%. No statistically significant differences in diagnostic accuracy were found when FDG-PET/CT was compared with conventional cancer screening (Figure 1). The number of additional tests to rule out cancer was similar with the 2 approaches (2 vs 2; $P$ = not significant). A flow chart depicting the diagnostic accuracy of FDG-PET/CT and conventional cancer screening is shown in Figure 2.

DISCUSSION
In this prospective multicenter study including 55 consecutive patients with dermatomyositis/polymyositis, whole-body FDG-PET/CT scanning was comparable to conventional cancer screening for detecting occult malignant disease. The study included all patients diagnosed with dermatomyositis and polymyositis in our area over a 3-year period. The number of cases that occurred in that time is in keeping with our previously reported epidemiologic data,$^{18}$ and therefore a population selection bias seems unlikely.

### Table 1 Diagnostic Performance of the Two Cancer Detection Approaches

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<th>FDG-PET/CT</th>
<th>Conventional Screening</th>
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<td><strong>PPV</strong></td>
<td>85.7 (42.1-99.6)</td>
<td>77.8 (40.0-97.2)</td>
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<td><strong>NPV</strong></td>
<td>93.8 (82.8-98.7)</td>
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<td><strong>OPV</strong></td>
<td>92.7 (82.4-98.0)</td>
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<td><strong>Sensitivity</strong></td>
<td>66.7 (29.9-92.5)</td>
<td>77.8 (40.9-97.2)</td>
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<td><strong>Specificity</strong></td>
<td>97.8 (88.5-99.4)</td>
<td>95.7 (85.2-99.5)</td>
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FDG-PET/CT = [18F] fluorodeoxyglucose positron emission tomography/computed tomography; NPV = negative predictive value; OPV = overall predictive value; PPV = positive predictive value. Results are expressed as percentages with 95% confidence interval.
Various studies performed in neurologic paraneoplastic syndromes have shown that FDG-PET/CT provides improved tumor detection. To our knowledge, there are no prospective studies investigating the diagnostic value of FDG-PET/CT for detecting cancer in patients with dermatomyositis/polymyositis. The individual cases reported seem to demonstrate that the method is useful for diagnosing occult malignancy, but it is likely that a positive result bias exists in these studies. In the single study including 13 patients diagnosed with dermatomyositis, which was retrospective in nature, 4 patients presented cancer and 1 additional patient had false-positive results. In view of the detection rates found in the present study, we suggest that FDG-PET/CT is a good alternative to broad conventional cancer screening for these patients, with the added advantage that a single imaging test is more convenient for both the patient and the physician. The sensitivity and specificity of FDG-PET/CT and conventional cancer screening for excluding occult malignancy were similar. False-positive and false-negative results occur with both approaches, and a combination of the 2 methods does not significantly increase the predictive value.

It should be taken into account that the predictive value of FDG-PET/CT also depends on the number of cases with inconclusive results. Thus, the use of a score to classify the

<table>
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<th>Table 2 Patients with Paraneoplastic Myositis</th>
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CEA = carcinoembryonic antigen; CT = computed tomography; DM = dermatomyositis; FDG PET/CT = [18F] fluorodeoxyglucose-positron emission tomography/computed tomography; FNAC = fine-needle aspiration cytology; ND = not done; PM = polymyositis.

Patient 9, with inconclusive uptake on PET/CT, developed breast cancer 2 years later, unrelated with the equivocal uptake.

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Figure 1 Overall predictive values of FDG-PET/CT* detection versus conventional cancer screening. *Inconclusive uptake was considered negative. Results are expressed as percentages with 95% confidence interval.

*Figure 2 Flow chart showing the diagnostic accuracy of FDG-PET/CT and conventional cancer screening. DM = dermatomyositis; FDG-PET/CT = [18F] fluorodeoxyglucose-positron emission tomography/computed tomography; IIM = idiopathic inflammatory myopathy; PM = polymyositis. *One patient with inconclusive uptake on PET/CT developed breast cancer 2 years later, unrelated with the equivocal uptake.
imaging findings and minimize the number of inconclusive cases is critical to analyze the results. Because inconclusive uptake does not indicate negative status, additional examinations are occasionally needed to clarify the findings. Nonetheless, in the present study, the number of additional tests required to rule out cancer was similar with both conventional screening and FDG-PET/CT.

The clinical entity known as cancer-associated myositis is based on the idea that myositis is a paraneoplastic phenomenon. A 3-year limit around the myositis diagnosis has been established by general consensus, but this cutoff cannot guarantee a true association between the 2 processes. Some studies have shown an increased risk of cancer even 4 or 5 years after myositis onset; therefore, the incidence of cancer-associated myositis may be underestimated in the present study because the median follow-up was less than 3 years. This could be a source of bias in the analysis of the true value of FDG-PET/CT and broad cancer screening in paraneoplastic myositis and must be considered a limitation of the study. Nevertheless, it is likely that this factor would not have an influence on the conclusions because both cancer-screening approaches would be affected.

Determination of a newly described autoantibody against a 155-kD protein that seems to be related to paraneoplastic dermatomyositis may help to increase the accuracy of FDG-PET/CT. Whether this method would be more useful in patients who are positive to this autoantibody remains to be determined.

References