Diagnostic Accuracy of Contrast-Enhanced Computed Tomography and Positron Emission Tomography With 18-FDG in Identifying Malignant Solitary Pulmonary Nodules

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Abstract: Contrast-enhanced computed tomography (CECT) and positron emission tomography with 18-FDG (FDG-PET/CT) are used to identify malignant solitary pulmonary nodules. The aim of the study was to evaluate the accuracy of CECT and FDG-PET/CT in diagnosing the etiology of solitary pulmonary nodule (SPN).

Eighty patients with newly diagnosed SPN >8 mm were enrolled. The patients were scheduled for either or both, CECT and FDG-PET/CT. The nature of SPN (malignant or benign) was determined either by its pathological examination or radiological criteria.

In 71 patients, the etiology of SPN was established and these patients were included in the final analysis. The median SPN diameter in these patients was 13 mm (range 8–30 mm). Twenty-two nodules (31%) were malignant, whereas 49 nodules were benign.

FDG-PET/CT was performed in 40 patients, and CECT in 39 subjects. Diagnostic accuracy of CECT was 0.58 (95% confidence interval [CI] 0.41–0.74). The optimal cutoff level discriminating between malignant and benign SPN was an enhancement value of 19 Hounsfield units, for which the sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of CECT were 100%, 37%, 32%, and 100%, respectively. Diagnostic accuracy of FDG-PET/CT reached 0.9 (95% CI 0.76–0.9). The optimal cutoff level for FDG-PET/CT was maximal standardized uptake value (SUV max) 2.1. At this point, the sensitivity, specificity, PPV, and NPV were 77%, 92%, 83%, and 89%, respectively.

The diagnostic accuracy of FDG-PET/CT is higher than that of CECT. The advantage of CECT is its high sensitivity and negative predictive value.

INTRODUCTION

Solitary pulmonary nodules (SPNs) are commonly identified by lung imaging studies. They are found in 0.2% to 2% of chest radiographs and in 10% to 40% of computed tomography (CT) scans.1–4 The prevalence of malignancies among SPNs diagnosed in the frame of lung cancer screening programs is about 0.5% to 3.5%. The probability of malignancy is related to both patients’ characteristics and radiological features of the nodule.4 The patient-related risk factors of malignant nature of the lesion are: age, current or past smoking, and previous history of malignancies. Radiological features associated with increased risk of malignancy include large nodule diameter and volume, spiculated margins, and upper lobe location.5,6 Unfortunately, these features are neither sensitive nor specific enough to predict SPN nature. In the context of the large number of patients with SPN detected by CT, there is an urgent need for a high performance diagnostic tool differentiating between malignant nodules, which should be removed without delay and benign lesions where surgery should be avoided. As sensitivity of various sampling techniques is limited and these methods are associated with the substantial risk of complications, novel imaging studies are perceived as a promising solution. In our earlier study, we showed that simplified method of dynamic contrast-enhanced computed tomography (CECT) can be used to predict the benign etiology of SPN.7 Other methods used to differentiate between malignant and benign SPN include nuclear magnetic resonance, single-photon emission CT (SPECT) and positron emission tomography with 18F-fluorodeoxyglucose (FDG-PET).8 Recently updated American College of Chest Physicians’ (ACCP) guidelines strongly point out FDG-PET as the most sensitive and specific imaging technique differentiating between malignant and benign SPN.8 Although FDG-PET is the most accurate test in diagnosing SPN, its costs are substantial and availability is limited. The aim of our study was to evaluate the diagnostic accuracy of CECT and FDG-PET/CT in predicting malignant versus benign SPN etiology.
MATERIALS AND METHODS

The study was approved by the institutional review board of the Medical University of Warsaw. Eighty adult consecutive patients with newly diagnosed SPN referred to the Department of Internal Medicine, Pneumonology and Allergology between 2007 and 2011 were initially enrolled into the prospective study. The inclusion criteria were: age over 18 years and the largest nodule diameter measured in CT scan $\geq 8$ mm. Patients with smaller nodules and those with pulmonary nodules with features strongly suggesting benign etiology (central dense nodule, diffuse solid, or laminar calcification) were excluded. The pre-test probability of malignant SPN etiology was calculated according to Mayo Clinic calculator proposed by Swensen et al.9 In patients with recent history of malignancy, a different model as described by Gould et al.10 was used. The diagnostic approach included medical history, CECT, FDG-PET/CT, bronchoscopy, and video-assisted thoracoscopic surgery with resection of the nodule. However, the ultimate management was individualized according to the probability of malignancy, attending physician recommendations and patient preferences.

The definite nature of the nodule was determined on the basis of cyto-histopathological findings and/or radiological follow-up. The criteria of nodule benignity were as follows: absence of malignant cells/tissue in the resected nodule or stable nodule dimensions in CT scan followed-up for at least 24 months from the initial diagnosis. Time intervals between subsequent CT scans were consistent with ACCP recommendations.7

Thorax CT scans were performed with 16-row CT scanner (LightSpeed 16 General Electric Medical Systems, Milwaukee, WI) using 1.25-mm collimation, pitch 1.375, 120–140 kV (peak), 200 mA current, matrix size 512 x 512 and 0.5 second scanning time. In general, the CECT procedure was based on the protocol proposed by Swensen et al.,11 but the number of post-contrast measurements was reduced to 2, as described elsewhere.7 Thus, 3 CT scans were performed in each patient: before contrast administration, 30 sec and 4 min after intravenous contrast injection (Iomeron, Bracco; 2 mL/sec; 300 mg/mL). Insignificant nodule administration, 30 sec and 4 min after intravenous contrast injection (Iomeron, Bracco; 2 mL/sec; 300 mg/mL). Insignificant nodule enhancement (<=15 Hounsfield units, HU) after contrast injection has been suggested to be strongly predictive of its benignity.11 The measurements were performed by an experienced chest radiologist with 20 years of experience in chest radiology, who was unaware of the final diagnosis of the nodule.

FDG-PET/CT was done according to the protocol proposed by Gould et al.12 Half-body PET/CT examinations from vertex to upper thighs were performed on a Biograph 64 TruePoint PET/CT scanner (Siemens Medical Solutions, Knoxville, TN) using 3-dimensional mode. Patients were injected 300 to 370 MBq 18F-FDG and imaged after a 60-min uptake period. CT was acquired continuously in spiral mode using a pitch of 0.8, 120 kV (peak), 170 mA current, and 2-mm post-processing slice thickness. PET study was acquired covering an area identical to that covered by CT at 2 min per bed position (6–7 bed positions depending on the size of the patient). Emission data were reconstructed on a 168 x 168 matrix using ordered subsets expectation maximization algorithm (2 iterations, 14 subsets) and corrected for attenuation using CT. The PET/CT images were transferred to a Multi-Modality Work Station, Syngo (TrueD) (Siemens Medical Solutions) for analysis. The malignant etiology of the nodule was suspected if the nodule was visible in PET examination and maximal standardized uptake value (SUV max) was $>2.5.13,14$ The results of FDG-PET/CT were analyzed by 1 radiologist and 1 nuclear medicine specialist with 10 years of experience in nuclear medicine, both of them were unaware of the final diagnosis of the nodule.

Statistical analysis was performed using STATISTICA 10.0 (StatSoft, Inc. Tulsa, OK) and MedCalc 9.5.2.0 (MedCalc Software bvba, Ostend, Belgium) software packages. Quantitative variables are presented as median, interquartile range (IQR), and/or ranges, whereas qualitative variables are presented as number and percentage. Nonparametric Mann–Whitney U test or Chi-square test was used to assess the difference between variables in different groups. Receiver-operating characteristic (ROC) curve was analyzed to evaluate the diagnostic accuracy of CECT and FDG-PET/CT. Diagnostic performance of an earlier proposed algorithm that included CECT as the first diagnostic step (if CECT is negative no further tests are performed, if positive, then FDG-PET/CT is conclusive) and FDG-PET/CT as the second,15,16 was also analyzed. Diagnostic accuracy of imaging tests was expressed in 2 ways, as area under the ROC curve (AUC-ROC) and as the proportion of true-positive and true-negative results to all results. The Spearman rank correlation coefficient was applied to test correlations between quantitative variables. A P value $<0.05$ was regarded as significant.

RESULTS

Of 80 patients enrolled into the study, 9 were lost to follow-up and had to be excluded from analysis. Thus, the final analysis included 71 patients (45 females, 26 males), median age 69 years (range 45–88 years). Six patients had a history of malignancy in the last 10 years preceding the diagnosis of SPN. The median nodule diameter was 13 mm, range 8–30 mm. There were 43 and 28 patients with SPN located in the right and the left lung, respectively. The distribution of nodule size was as follows: 8–10 mm in 23 patients; 11–20 mm in 34 patients, and 21–30 mm in 14 patients. In 61 patients, CT showed a solid nodule, 6 patients were diagnosed with ground glass opacity, and 4 had a subsolid nodule (both solid and ground glass areas). In 49 of 71 (69%) patients, benign SPN was diagnosed. Of these, 9 patients underwent nodule resection with pathological examination which revealed: hamartoma (n = 4), nonspecific inflammation (n = 2), tuberculosis (n = 2), and neurinoma (n = 1). All resections were performed within 4 to 14 weeks from CECT and FDG-PET/CT imaging. In 10 patients, a significant decrease of nodule size or even complete resolution was documented in follow-up CT scans. In the remaining 30 patients, the benign nature of SPN was defined based on stable nodule dimensions in CT scan performed at least 24 months after the initial diagnosis.

There were 22 of 71 (31%) patients with malignant pulmonary nodules. The most common tumor was primary lung adenocarcinoma (n = 12), followed by squamous cell carcinoma (n = 5), typical carcinoid (n = 1), and small cell lung carcinoma (n = 1). In 3 patients, metastases from extrapulmonary tumors were diagnosed (colon adenocarcinoma in 2 cases and 1 pheochromocytoma). The median time between CECT and FDG-PET/CT scanning and tumor resection was 5 weeks (range 12 weeks).

Comparison of selected demographic data and nodule characteristics in patients with benign versus malignant nodules is presented in Table 1 and Table 2. There were no significant differences between these 2 groups in terms of age and sex. Although the proportion of active smokers, ex-, and never smokers was not different in benign and malignant SPN groups, the total exposure to tobacco smoke was significantly higher in
TABLE 1. Characteristics of the Patients

|                | Benign (n = 49) | Malignant (n = 22) |
|----------------|-----------------|-------------------|
| Age (years)    | 66 (45–88)      | 71 (57–82)        |
| Sex (male/female) | 14/35          | 12/10             |
| Smoking history |                 |                   |
| Smokers        | 7               | 10                |
| Ex-smokers     | 19              | 9                 |
| Never smokers  | 21              | 3                 |
| Pack years¹    | 12.5 (0–58)     | 43.5 (0–90)       |

Values are presented as number or as median and range.

¹ 1 pack year—20 cigarettes/day/year.

¹ Statistically significant (P < 0.05).

TABLE 2. Characteristics of the Nodules

| Nodule Characteristics | Nodule Etiology | Benign (n = 49) | Malignant (n = 22) |
|------------------------|-----------------|-----------------|-------------------|
| Size (mm)              |                 | 12 (8–30)       | 20.5 (8–30)       |
| Location               | Right/left      | 29/20           | 14/8              |
|                        | Upper/middle/lower lobe | 23/6/20       | 12/2/8            |
| Margins                | Smooth/lobulated/spiculated | 24/20/5       | 5/10/7           |
| Structure              | Solid or subsolid/ground glass opacity | 45/4        | 20/2              |
| Pre-test probability of malignant etiology | 16 (3–86)       | 50 (15–85)      |

Values are presented as number or as median and range.

² Statistically significant (P < 0.05).
differentiate between benign and malignant lesions. The predictive role of different diagnostic methods used to relatively low. The prevalence of malignancy in the population respectively, Surprisingly enough, a meta-analysis of 4 imaging modalities (CEPT, FDG-PET, SPECT, and magnetic resonance imaging) did not reveal significant differences in the ability to discriminate benign and malignant SPNs. The positive result of the test with known high PPV in a population with a relatively high prevalence of malignant nodules identifies nodules with a very high probability of malignancy that require surgical resection. However, diagnostic methods characterized by high NPV may be more useful in populations with low prevalence of malignancy. Under these circumstances, negative test result makes malignant nodule etiology highly unlikely and thus justifies a "watchful waiting" strategy.

The reliability of various functional imaging techniques in differentiating between malignant and benign pulmonary nodules is still a matter of discussion. Both CECT and FDG-PET have been used for >25 years, but FDG-PET/CT became more available in the last 15 years. Previous ACCP guidelines recommended both FDG-PET/CT and CECT in the evaluation of SPN in patients with low to moderate (5–65%) pre-test probability of malignancy. Recent guidelines also mention both methods, but highlight higher specificity and accuracy of FDG-PET/CT. The superiority of FDG-PET/CT over CECT in terms of diagnostic accuracy was clearly shown in our present study (AUC-ROC for FDG-PET/CT was 0.9 as compared with 0.58 for CECT). Similar results were earlier reported by Christensen et al., who compared the utility of CECT and FDG-PET in diagnosing the etiology of SPN in 42 patients with pulmonary nodules >7 mm. In that study, the sensitivity and specificity for CECT were 100% and 29% and for FDG-PET 88% and 76%, respectively. Although FDG-PET/CT is considered the most precise imaging tool differentiating malignant and benign pulmonary nodules, the optimal cutoff value of SUV is still discussed. SUV max >2.5 was commonly used as a diagnostic threshold strongly suggesting malignancy. In our study, the value of SUV >2.1 was associated with the highest area under ROC curve and the highest diagnostic accuracy. However, recent studies indicate that a higher cutoff level (SUV max >4) may be more even accurate. Our results do not confirm this observation. Increasing the cutoff level of SUV to 2.9 resulted in only a modest increase in specificity and PPV at the cost of a significant decrease in sensitivity and NPV. The use of a low

| Age (years) | Patients with CECT or FDG-PET/CT (n = 57) | Patients without CECT or FDG-PET/CT (n = 14) |
|------------|----------------------------------------|---------------------------------------------|
|            | 67 (45–88) | 71 (48–81) |
| Smoking history, S/ES/NS | 14/22/21 | 3/6/5 |
| Diameter of nodule (mm) | 14 (8–30) | 12 (8–30) |
| Pre-test probability of malignant etiology | 19 (3–86) | 19.5 (3–85) |
| Benign nodules | 39 (68%) | 10 (72%) |
| Malignant nodules | 18 (32%) | 4 (28%) |
| Number of surgery procedures | 24 (42%) | 4 (29%) |
| Number of surgery procedures in benign nodules | 6 (15%) | 0 |

Values are presented as median and range or number and percentage. No statistical differences between the parameters were found.

CEPT = contrast-enhanced computed tomography, CT = computed tomography, ES = ex-smoker, FDG-PET = positron emission tomography with 18-FDG, NS = never smoker, S = smoker.

| Cutoff Value | >10 HU | >15 HU | >19 HU | >23 HU |
|--------------|--------|--------|--------|--------|
| Sensitivity  | 100% (66–100) | 100% (66–100) | 100% (66–100) | 78% (40–96) |
| Specificity  | 7% (1–22) | 33% (17–53) | 37% (20–56) | 43% (25–63) |
| Diagnostic accuracy | 28% | 49% | 51% | 51% |
| Positive predictive value | 24% | 31% | 32% | 29% |
| Negative predictive value | 100% | 100% | 100% | 87% |
| LR+ | 1.1 | 1.5 | 1.6 | 1.4 |
| LR− | 0 | 0 | 0 | 0.5 |

95% confidence interval is given in the brackets. CECT = contrast-enhanced computed tomography, LR = likelihood ratio.
The cutoff value <1.4 enables the most reliable selection of patients with benign nodules (the highest NPV). In CECT, 15 HU was proposed as the most accurate post-contrast enhancement threshold discriminating between malignant and benign nodules. Some authors suggested the threshold value of 20 HU or even higher. In our study, the cutoff level of post-contrast enhancement between 10 and 19 HU resulted in 100% NPV; its increase >19 HU gave a notable decrease in NPV.

The relationship between the enhancement value in CECT and SUV max measured in FDG-PET/CT is an interesting issue. We expected a significant correlation between these 2 indices; however, this was not the case in our study. Nonetheless, we are aware that such a correlation had earlier been reported. Tateishi et al demonstrated a significant correlation between CECT enhancement and SUV max in malignant pulmonary tumors ($r = 0.665$; $P < 0.0001$), but not in benign lesions. There was also a significant correlation between microvessel density in malignant tumors and the enhancement measured in CECT as well as SUV max found in FDG-PET/CT. In our study, we could not reliably evaluate this relation because only 4 patients with a malignant nodule underwent both CECT and FDG-PET/CT. The direct comparison of CECT and FDG-PET/CT results may carry a certain risk, as these functional imaging methods reflect slightly different aspects of SPN characteristics. The result of FDG-PET/CT depends on glucose metabolism, whereas the result of CECT is closely related to angiogenesis, blood vessel network, and blood flow.

Interestingly, an increased glucose metabolism measured as SUV might have a prognostic value in terms of tumor progression, recurrence, and hazard of death. However, Cappabianca et al reported no correlation between SUV and grading of malignant SPN. Although FDG-PET/CT seems to be a more accurate method in evaluating the nature of SPN, it is not flawless. The availability of FDG-PET/CT, although increasing, is still

### TABLE 5. Diagnostic Performance of FDG-PET/CT in the Evaluation of Pulmonary Nodules (Cutoff Levels Indicated by ROC)

| Cutoff Value | SUV ≥1.4 | SUV >1.6 | SUV>2.1 | SUV >2.5 | SUV >2.9 |
|--------------|----------|----------|---------|----------|----------|
| Sensitivity  | 85% (65–95) | 77% (46–95) | 77% (46–95) | 69% (39–91) | 54% (25–81) |
| Specificity  | 85% (54–98) | 85% (65–95) | 92% (75–99) | 92% (75–99) | 96% (80–99) |
| Diagnostic accuracy | 85% | 82.5% | 87.5% | 85% | 82.5% |
| Positive predictive value | 73% | 71% | 83% | 82% | 87% |
| Negative predictive value | 92% | 88% | 89% | 86% | 81% |
| LR+          | 5.5 | 5.0 | 10.0 | 9.0 | 14.0 |
| LR−          | 0.18 | 0.27 | 0.25 | 0.33 | 0.48 |

95% confidence interval is given in the brackets. CT = computed tomography, FDG-PET = positron emission tomography with 18-FDG, LR = likelihood ratio, ROC = receiver-operating characteristic curve, SUV = standardized uptake value.

### TABLE 6. Comparison of Results of CECT and FDG-PET/CT

| Initials | Probability of Malignancy, % | Diameter of Nodule (HU) | CECT (SUV) | PET/CT (SUV) | Nodules’ Etiology |
|----------|-------------------------------|--------------------------|------------|-------------|------------------|
| 1 ZC     | 23                            | 15                       | 10         | 1           | Benign           |
| 2 JG     | 82                            | 20                       | 83         | 2.1         | Benign           |
| 3 TG     | 17                            | 13                       | <15        | <1          | Benign           |
| 4 SG     | 26                            | 16                       | 24         | <1          | Benign (hamartoma) |
| 5 JJ     | 10                            | 13                       | 22         | 1.3         | Benign (hamartoma) |
| 6 SJ     | 21                            | 8                        | 111        | 1           | Benign (inflammation) |
| 7 LJ     | 18                            | 18                       | 52         | <1          | Benign           |
| 8 EK     | 75                            | 22                       | 43         | 4.7         | Benign (tuberculoma) |
| 9 JK     | 8                             | 17                       | 22         | 1.4         | Benign           |
| 10 HK    | 41                            | 20                       | 15         | 1.8         | Benign (granuloma) |
| 11 JK    | 3                             | 9                        | 67         | <1          | Benign           |
| 12 HK    | 14                            | 13                       | 19         | <1          | Benign           |
| 13 JL    | 11                            | 9                        | 77         | <1          | Benign           |
| 14 AO    | 8                             | 12                       | 11         | <1          | Benign           |
| 15 MP    | 5                             | 9                        | <15        | <1          | Benign           |
| 16 EP    | 16                            | 9                        | 11         | <1          | Benign           |
| 17 AS    | 4                             | 8                        | 47         | <1          | Benign           |
| 18 MW    | 16                            | 11                       | 43         | <1          | Benign           |
| 19 AI    | 87                            | 24                       | 35         | 2.9         | Adenocarcinoma   |
| 20 EJ    | 26                            | 12                       | 77         | 1.6         | Adenocarcinoma   |
| 21 SM    | 82                            | 25                       | 22         | 12.6        | Squamous cell carcinoma |
| 22 JP    | 44                            | 25                       | 23         | 9.9         | Adenocarcinoma   |

Discordant results are marked as shading. CECT = contrast-enhanced computed tomography, CT = computed tomography, FDG-PET = positron emission tomography with 18-FDG.
limited; the procedure is expensive, and is associated with quite high effective dose of radiation. In contrast, CECT is widely available and its costs are significantly lower. When an appropriate cutoff level is applied, CECT can reliably select SPNs with very low probability of malignancy (high NPV). Thus, combination of both methods, with sequential use of CECT as the first diagnostic step and FDG-PET/CT as the second, may decrease the number of FDG-PET/CT procedures and reduce the costs of diagnostics. Such approach has already been proposed by Christensen et al. The authors assumed that with a negative result of CECT, a malignant SPN is highly unlikely and, if so, further diagnostics could be avoided. If CECT enhancement was >15HU, the patient was referred to FDG-PET/CT. The authors concluded that their diagnostic algorithm allowed a more accurate characterization of indeterminate SPN. The cost-effectiveness of this approach had been documented in another study.

It might be calculated that application of the above diagnostic algorithm in our study group would result in a 27% reduction of FDG-PET/CT procedures without a negative impact the diagnostic performance. In our hospital, the cost of CECT was calculated as 700 PLN (167 EUR) and of FDG-PET/CT as 4100 PLN (976 EUR). Therefore, implementing this diagnostic approach would save the sum of 267 EUR per patient. These numbers clearly show the advantages of the combined CECT and FDG-PET/CT diagnostic algorithm and justify the use of both methods in a patient with SPN.

There are some limitations of our study. First, its results refer exclusively to patients with SPN ≥8 mm in diameter. Patients with smaller nodules could not have been included, as the diagnostic accuracy of CECT and FDG-PET/CT in nodules <8 mm is not satisfactory. Nonetheless, the criterion of the nodule diameter ≥8 mm used in our study seems to be consistent with recent suggestion that only nodules larger than 7 to 8 mm should be considered as positive results in lung cancer screening programs. This approach is intended to reduce the large number of false-positive results. Second, the number of patients in whom both CECT and FDG-PET/CT were performed is relatively small. Therefore, direct comparison of the results of both methods was possible in only one-third of our study group. Finally, our study included a small subgroup of patients (n = 14) in whom neither CECT nor FDG-PET/CT was performed. The diagnostic performance of advanced functional imaging techniques could not have been assessed in these patients. However, it seems striking that in this group of patients, a high accuracy of referral to surgery had been achieved. This group included 4 patients with a malignant nodule and all these patients underwent resection without delay (Table 3). Moreover, none of the 10 patients with a benign nodule was referred for unnecessary surgery. Thus, although no functional imaging had been used in this group, the prediction of the nature of the lesion was highly effective. This may call into question the usefulness of the advanced functional imaging of SPN, especially since 4 unnecessary surgical resections were performed in the CECT/FDG-PET/CT group (Table 3). Thus, in terms of proper patient selection for surgical resection, the results in non-CECT, non-FDG-PET/CT group were superior to those found in CECT/FDG-PET/CT group. We believe this might be an incidental finding resulting from the small number of patients and related to a selection bias. The small group of 14 patients included 4 patients with very high probability of malignancy and 7 patients with low probability of malignancy who a priori gave no consent to advanced imaging procedures and surgical treatment and in whom the benign character of SPN was proved in radiological follow-up. Thus, in our opinion, no reliable conclusion can be drawn from this observation. To study the above phenomenon, the patients should have been randomly assigned to 2 study arms with different diagnostic algorithms—including versus not including functional imaging techniques.

CONCLUSIONS

The diagnostic accuracy of FDG-PET/CT is higher than that of CECT. Nevertheless, both functional imaging methods may be useful in differentiating between a malignant and benign pulmonary nodule. As the advantage of CECT is very high sensitivity and NPV, the method might be preferred in populations with low prevalence of pulmonary malignancies with its major clinical application to exclude the malignant nature of the nodule. Conversely, the high specificity and high PPV of FDG-PET/CT may be effectively applied to confirm malignant nodule in patients with high prevalence of malignant pulmonary lesions. Diagnostic algorithm that includes CECT as the first diagnostic step may significantly decrease the number of patients that require FDG-PET/CT imaging and reduce the cost of the diagnostic work-up.

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