REVIEW ARTICLE

Management of pulmonary nodules according to the 2015 British Thoracic Society guidelines

Key messages for clinical practice

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KEY WORDS

guideline, pulmonary nodules

ABSTRACT

The British Thoracic Society guideline on the investigation and management of pulmonary nodules is based on a comprehensive and systematic review of the literature on pulmonary nodules. Recent evidence has suggested that significant changes to existing guidelines are necessary. The use of 2 malignancy prediction calculators to better characterize the risk of malignancy was firmly supported by evidence, as were the recommendations for a higher nodule size threshold for follow-up (≥5 mm or ≥80 mm^3) and a reduction of the follow-up period to 1 year for solid pulmonary nodules. Although caution is required where there is a history of cancer, both of these recommendations will reduce the number of follow-up computed tomographies, thereby improving cost-effectiveness and pressure on imaging services. Recent evidence has also confirmed the superiority of volumetry as the preferred measurement method and clarified the management of nodules with extended volume-doubling times. Acknowledging the good prognosis of subsolid nodules, there are recommendations for less aggressive options in their management. The guidelines recommend ordinal scale reporting for positron emission tomography–computed tomography to facilitate incorporation into risk models. There are recommendations on when biopsy is most helpful, the threshold for treatment without histological confirmation, and surgical and nonsurgical treatment. The guideline also provides evidence-based recommendations about the information that people need and that should be provided for them. The complexity of managing pulmonary nodules is made more accessible by 4 management algorithms. In the real world, it is surprising how easy these are to follow and how they seem to follow an intuitive approach.

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Received: February 10, 2016.
Accepted: February 11, 2016.
Published online: April 26, 2016.
Conflict of interest: DRB received support for travelling to the World Lung Cancer Conference from Oncimmune Ltd.
Pol Arch Med Wewn. 2016; 126 (4): 262-274
doi:10.20452/pamw.3379

Introduction Originally, pulmonary nodules were defined as well or poorly circumscribed approximately rounded structures of 3 cm or less in diameter, surrounded by an aerated lung and without associated abnormalities in the thorax. This definition is now commonly extended to include nodules in contact with the pleura. The now widespread use of helical multi-detector computed tomography (CT) has made it commonplace to detect, incidentally, solid noncalcified nodules of less than 1 cm in diameter as well as subsolid nodules (SSNs) that are partly or wholly ground-glass opacities. Added to this is the potential introduction of CT screening programs for lung cancer, where a quarter of images detect nodules exceeding 4 mm in diameter, which is the threshold for further workup recommended in previous guidelines. These smaller solid nodules and SSNs have presented a greater clinical challenge than their larger counterparts, although this may not be the case if the British Thoracic Society (BTS) evidence-based guideline recommendations are followed. To avoid confused terminology in the literature, the BTS guideline proposed standardized definitions and terms for SSNs (**TABLE 1** and Supplementary material online, *Figure S1*). It should be noted that ambiguous terms such as "semi-solid nodule" and "ground-glass nodule" (omitting the "pure" qualifier) should be avoided.

This review presents the BTS-recommended approach for the management of adults over the age of 18 years with pulmonary nodules from presentation to definitive treatment or discharge.[1] The topics covered are: 1) the route of detection

TABLE 1 Definition and terms relating to pulmonary nodules (see also Supplementary material online, *Figure S1*)

Nodule definitions	
pulmonary nodule (overall definition)	Focal, rounded opacity ≤3 cm in diameter, mostly surrounded by an aerated lung, including contact with the pleura, but without potentially related abnormalities in the thorax.
subsolid nodule	A part-solid or pure ground glass nodule.
part-solid nodule	A focal opacity that has both solid and ground glass component ≤3 cm in diameter.
pure ground-glass nodule (synonymous with nonsolid nodule)	A focal ground glass opacity ≤3 cm in diameter that does not obscure a vascular pattern.
definition of applicable terms	
solid component	That part of a nodule that obscures the underlying bronchovascular structure.
ground-glass component	Opacification that is greater than that of the background but through which the underlying vascular structure is visible.

of pulmonary nodules; 2) risk assessment for malignancy based on clinical and radiological factors; 3) surveillance of pulmonary nodules; 4) SSNs; 5) biopsy techniques, indications, interpretation, and risks; 6) surgical and nonsurgical treatment; 7) information and support for patients and caregivers; and 8) technical aspects of imaging pulmonary nodules.

Route of detection of pulmonary nodules It is important to understand whether the management of pulmonary nodules should be tailored according to the route of presentation and clinical context because this may impact on the risk of malignancy. The routes of presentation can be broadly divided into: 1) patients with respiratory symptoms referred for chest X-ray or chest CT; 2) incidental finding on chest X-ray, chest CT, or cross-sectional imaging for other purposes; 3) patients participating in lung cancer screening studies or programs; and 4) patients with known cancer undergoing staging investigations or follow-up imaging.

No studies have directly compared the features of pulmonary nodules according to the route of presentation. The prevalence of nodules in 32 larger case series was found to be greater in CT screening studies (mean, 33%; range, 15%–53%) compared with incidental findings (mean, 15%; range, 2%–14%), but this may reflect the radiological techniques employed and the size threshold for reporting. The prevalence of malignancy was similar (around 1.5%).

An important question is whether nodules detected in the context of a previous history of malignancy are more likely to be cancer. There was surprisingly little consensus here, with some studies suggesting there was no difference, while others showing higher rates of malignancy.[2-5] The reported prevalence of malignancy in coexistent nodules of less than 12 mm in diameter in patients selected to undergo curative surgery was 3% to 11%.[6-8] Key recommendations arising from the evidence review were: 1) to consider the presence of previous malignancy when assessing the risk of malignancy, noting that some of the recommended risk calculators included previous malignancy; and 2) to evaluate coexistent lung nodules detected in patients with known lung cancer otherwise suitable for radical treatment in their own right; these nodules should not be assumed to be malignant.

Risk assessment for malignancy based on clinical and radiological factors Assessing the risk of malignancy is regarded as essential to guide management of patients with a pulmonary nodule, with the lowest risk favoring the least invasive approach and vice versa. The BTS guideline identified risk factors consistently associated with malignancy and reviewed the evidence for the accuracy of composite risk models. The initial assessment essentially determines which nodules have a sufficiently low chance of malignancy to recommend imaging follow-up and which should be assessed further. Four clinical and five radiological risk factors were consistently associated with malignancy in solid nodules, with the most dominant factors being age, smoking, and nodule size.

Predictors of a benign etiology included the presence of a diffuse, central, laminated, or popcorn pattern of calcification (odds ratio, 0.07–0.20) and perifissural location. Thus, at the outset of the assessment, these nodules can be excluded from further investigation. Caution is advised with perifissural nodules where there are atypical features or for larger nodules (>10 mm), especially in the presence of known non-lung primary cancer; a radiologist's expert opinion is required here. Perifissural nodules correlate histologically with intrapulmonary lymph nodes and may enlarge despite being benign.[9] The BTS initial assessment algorithm is shown in FIGURE 1. The algorithm shows that nodules with the aforementioned benign features can be discharged. The guideline also recommends discharging nodules of less than 5 mm in the maximum diameter and less than 80 mm^3 in volume. This was supported by CT screening studies.

The Dutch–Belgian CT screening trial, NELSON,[10] showed that subjects with nodules of less than 5 mm in the maximum transverse diameter or less than 100 mm^3 in volume had no greater risk of developing lung cancer after 2 years than those without nodules, thus indicating that the presence of a nodule confers little, if any, additional risk (80 mm^3 was specified by the BTS guideline owing to known variation in measurements produced by different volumetry packages). Undoubtedly, this recommendation will lead to some people with malignant nodules being discharged but this will be very infrequent (<0.5%), and the risk of developing cancer will be mainly determined by background risk. The follow-up of these low-risk nodules is unlikely to be cost-effective. Furthermore, the harm from continued radiation exposure, albeit through low-dose

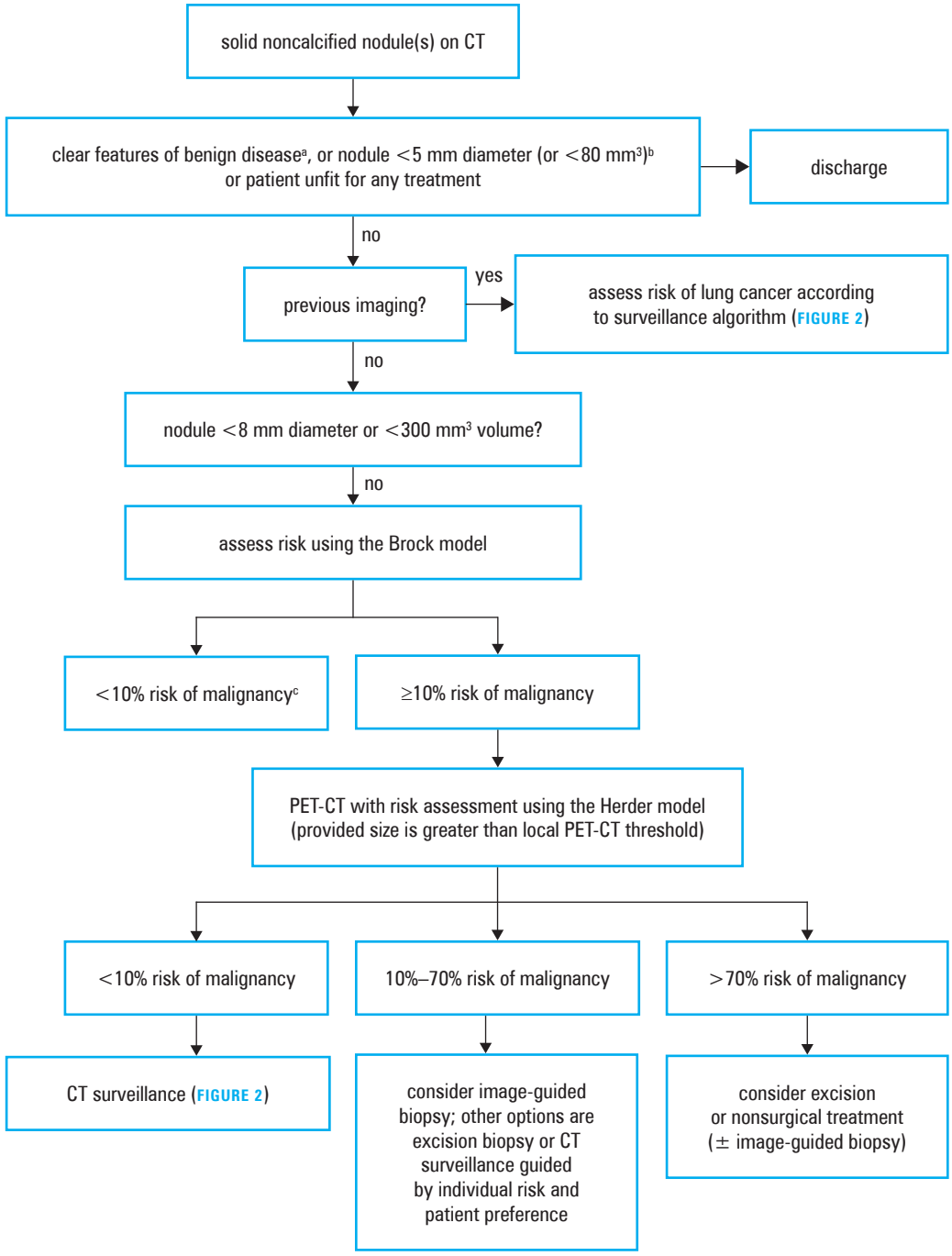

FIGURE 1 British Thoracic Society's algorithm for initial approach to solid pulmonary nodules
a eg, hamartoma, typical perifissural nodule
b consider a lower or no threshold in patients with known or active cancer
c consider positron emission tomography–computed tomography (PET-CT) for larger nodules in young patients with low risk by the Brock score as this score was developed in a screening cohort (50–75 years), so performance in younger patients has not been proved
Abbreviations: CT, computed tomography

CT, as well as investigation of benign or indolent disease, could offset any benefit. Caution is required in patients with a previous history of cancer or active cancer, where the probability of cancer may be higher, and a lower or no threshold for follow-up may be appropriate.

The NELSON study[10] also showed that patients with nodules of 100 to <300 mm³ in volume had a 2-year risk of lung cancer of 2.4%, and for those with a volume of 300 mm³ or higher, the risk was 16.9%. The corresponding chance of lung cancer for a nodule of 5 to <8 mm in diameter was 1.0% and for a nodule of 8 mm or higher in diameter— 9.7%. The algorithm reflects these findings by showing that for nodules of less than 300 mm³ in volume or less than 8 mm in diameter, CT surveillance is recommended.

For nodules of 300 mm³ or higher in volume or 8 mm or higher in diameter, the BTS guideline recommends the use of 2 specific composite risk prediction models, the Brock University model[11] and the Herder model. The Brock model showed the highest accuracy for predicting malignancy without positron emission tomography–computed tomography (PET-CT) and was the most accurate for smaller nodules, reflecting the fact that it was developed in a screening cohort. This has also been confirmed in a validation study in a United Kingdom (UK) population.[12] FIGURE 1 shows that patients with nodules that have a probability of malignancy of less than 10%, join the CT surveillance group and those with a higher risk go on to PET-CT, with the findings used to reassess risk using the Herder model,[13] which has the highest accuracy in the

UK population (area under the curve, 0.92).[14] In the Herder model, ^{18}F-fluorodeoxyglucose (FDG) uptake was classified as absent, faint, moderate, or intense. The authors did not provide objective measures or definitions but others have.[15,16] The latter 2 studies used a 5-point scale that the BTS guideline group adapted to a 4-point scale to facilitate consistency in reporting and use with the Herder model (Supplementary material online, *Table S1*). Further management is then guided by risk (<10% surveillance, 10% to 70% biopsy favored and >70% excision or nonsurgical treatment favored, see below).

The Brock model is the only multivariate model that included an analysis of multiple pulmonary nodules.[11] In this model, the presence of multiple nodules had a small negative effect on the likelihood of malignancy in any one nodule. However, BTS-recommended management is governed by the largest nodule, as this was the approach adopted in the NELSON trial.[17]

The key recommendations (abbreviated) were:

1 Do not offer nodule follow-up or further workup for people with perifissural or subpleural nodules (homogenous, smooth, solid nodules with a lentiform or triangular shape either within 1 cm of a fissure or the pleural surface and <10 mm in diameter).

2 Consider follow-up of larger intrapulmonary lymph nodes, especially in the presence of a known extrapulmonary primary cancer.

3 Do not offer nodule follow-up for people with nodules of less than 5 mm in diameter or less than 80 mm^3 in volume.

4 Offer CT surveillance to people with nodules of 5 mm or more to less than 8 mm in diameter or 80 mm^3 or more to less than 300 mm^3 in volume.

5 Use the Brock model (full, with spiculation) for initial risk assessment of pulmonary nodules of 8 mm or higher in dimater or 300 mm^3 or higher in volume.

6 Offer a PET-CT in patients with a pulmonary nodule with an initial risk of malignancy of more than 10% where the nodule size is greater than the local PET-CT detection threshold.

7 Following reassessment of risk with the Herder model: consider CT surveillance where the chance of malignancy is less than 10%, image-guided biopsy where the risk is 10% and 70% (other options are excision biopsy or CT surveillance guided by individual risk and patient preference), and surgical resection (or nonsurgical treatment for those who are not fit) as the favored option where the risk is >70%.

Further research validating risk prediction models for nodule malignancy in patients with known extrapulmonary cancer was recommended.

Surveillance of solid pulmonary nodules The overall aim of surveillance is to use assessment of nodule growth to discriminate between benign and malignant nodules. Pulmonary nodule size has traditionally been assessed by measuring the largest transverse cross-sectional diameter. The volume-doubling time (VDT) of a nodule can then be estimated from the difference in the nodule diameter between baseline and follow-up CT and the time interval between the 2 scans, using a simple exponential growth model that assumes uniform 3-dimensional tumor growth. Over the last 15 years, a volumetric analysis (calculated either manually or semiautomated/automated) has been increasingly reported as an alternative and better tool to assess nodule growth.[18-21] In addition to growth in the size of a nodule, changes in other parameters have been evaluated. De Hoop et al[22] found that mass measurements showed the least intraobserver and interobserver variation. Xu et al[23] showed that malignant nodules increased in density during CT follow-up compared with benign nodules, although there was significant overlap in density changes between benign and malignant nodules.

Scan interval and growth rate A number of studies have evaluated the scan interval in relation to reliable detection of growth. If automated volumetry is employed, a 3-month interval CT can reliably detect growth, defined as an increase in volume greater than 25%.[20,24-26] However, the accuracy of growth detection diminishes with nodule size so that if diameter measurements are used, the interval for 5- to 6-mm nodules has to be extended to 12 months. The latter may not be an issue except for faster-growing nodules (generally small cell lung cancer and some cases of squamous cell carcinoma).[27-29] A further advantage of a 3-month CT is that the majority of pulmonary nodules that eventually resolve do so after a 3-month interval.[26] The NELSON trial[10] showed that stability at 1 year reliably predicts benign disease, but there are no studies that can confirm this for diameter measurements (in the trial even these were semiautomated). Stability over 2 years of follow-up has traditionally been regarded as indicative of benign disease, having first been proposed on the basis of chest X-ray follow-up of nodules in the 1950s,[30] although the evidence underlying this assumption has been questioned.[31]

FIGURE 2 shows the BTS surveillance algorithm. Reflecting the above evidence, it shows that for nodules of 5 to 6 mm in diameter, a 3-month CT is only indicated if volumetry is performed, and that stability can only be confirmed at 12 months by volumetry. Larger nodules are followed up at 3 months and 12 months with volumetry with a further CT at 24 months if only diameter measurements are available.

The NELSON study[10] also showed that patients with nodules with a VDT of less than 400 days and 400 to 600 days measured after a 3- or 12-month interval, had 2-year cancer probabilities of 9.7% and 4.1%, respectively, significantly greater than the cancer risk of subjects without nodules (0.4%) and the screened population as a whole (1.3%).[10] The 2-year risk of lung cancer

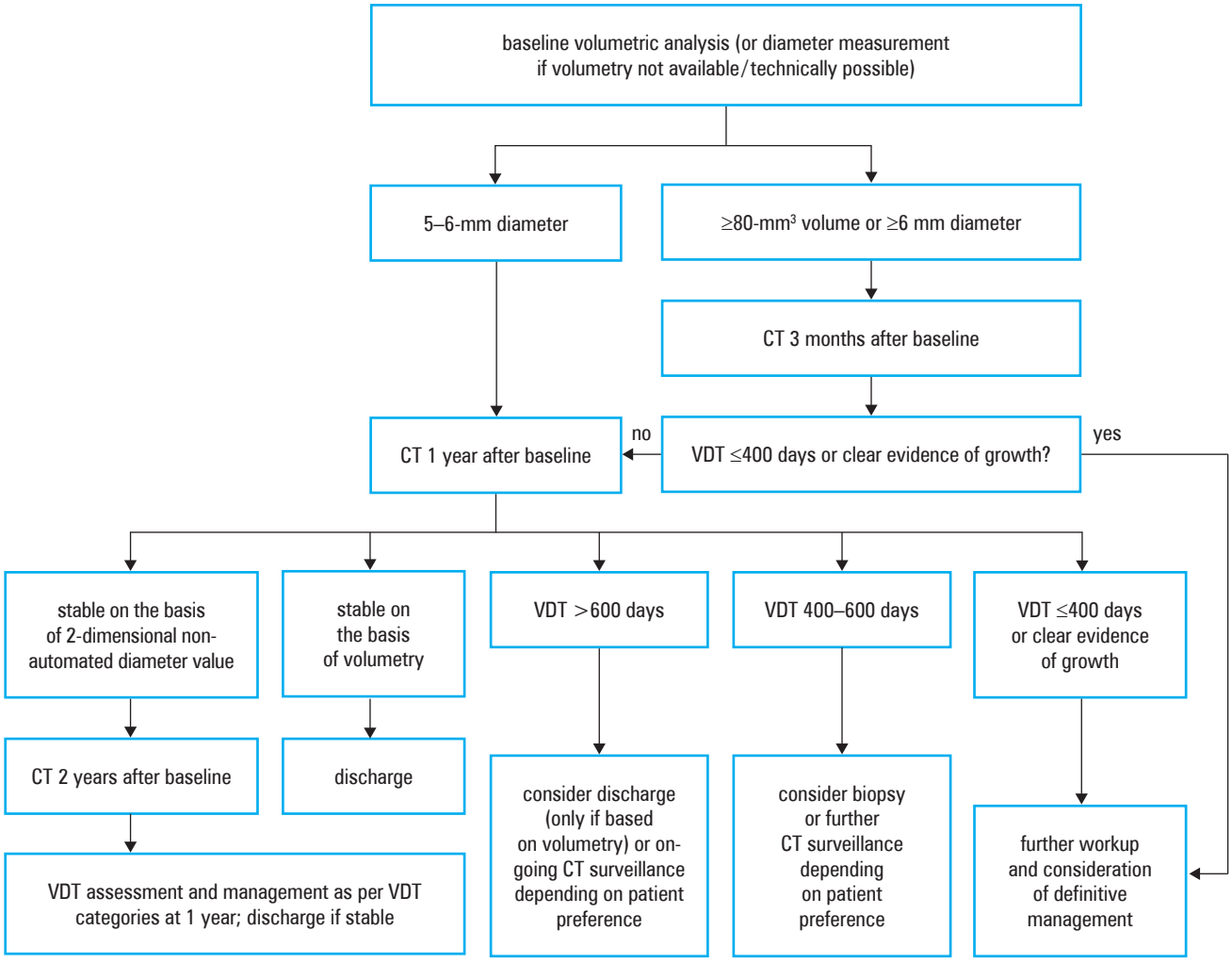

FIGURE 2 British Thoracic Society's algorithm for solid pulmonary nodule surveillance
Abbreviations: VDT, volume-doubling time; others, see **FIGURE 1**

was 0.8% when the VDT was longer than 600 days, not achieving significance compared with subjects without nodules (P = 0.06). This is reflected in **FIGURE 2**, where nodules that have a VDT of more than 400 days are referred for workup, nodules with a VDT of 400 to 600 days are either biopsied or followed further, and those with a VDT of longer than 600 days can be discharged or followed further, depending on the patient's preference and considering their indolent nature.

There is little evidence regarding the management of new nodules that appear in follow-up CTs, although evidence published since the BTS guideline in an abstract form suggests that new nodules detected in a screening study (NELSON[10]) have an approximate 4% risk of malignancy and hence should be followed closely. Here, the risk of malignancy will depend on the growth rate, and it should be noted that rapid growth may imply an inflammatory process rather than malignancy.

Thus, the BTS recommendations on surveillance of solid nodules differ from those of previous guidelines by recommending volumetry as the preferred method of measurement, reducing the number of follow-up CTs needed and stratifying management on the basis of VDT.

The key recommendations were:

1 Where initial risk stratification assigns a nodule a chance of malignancy of less than 10%, assess growth rate using interval CT with capability for automated volumetric analysis.
2 Assess growth for nodules of 80 mm³ or higher in volume or 6 mm or more in the maximum diameter by calculating VDT on the basis of repeat CT at 3 months and 1 year.
3 Use a 25% or higher change in volume to define significant growth.
4 Offer further diagnostic workup (biopsy, imaging, or resection) for patients with nodules showing clear growth or a VDT of less than 400 days (assessed after 3 months and 1 year).
5 Discharge patients with solid nodules that show stability (less than 25% change in volume) on CT after 1 year.
6 If 2-dimensional diameter measurements are used to assess growth, follow up with CT for a total of 2 years.
7 Consider ongoing annual surveillance or biopsy for people with nodules that have a VDT of 400 to 600 days, according to the patient's preference.
8 Where nodules are detected in the context of an extrapulmonary primary cancer, consider the growth rate in the context of the primary and any treatment thereof.

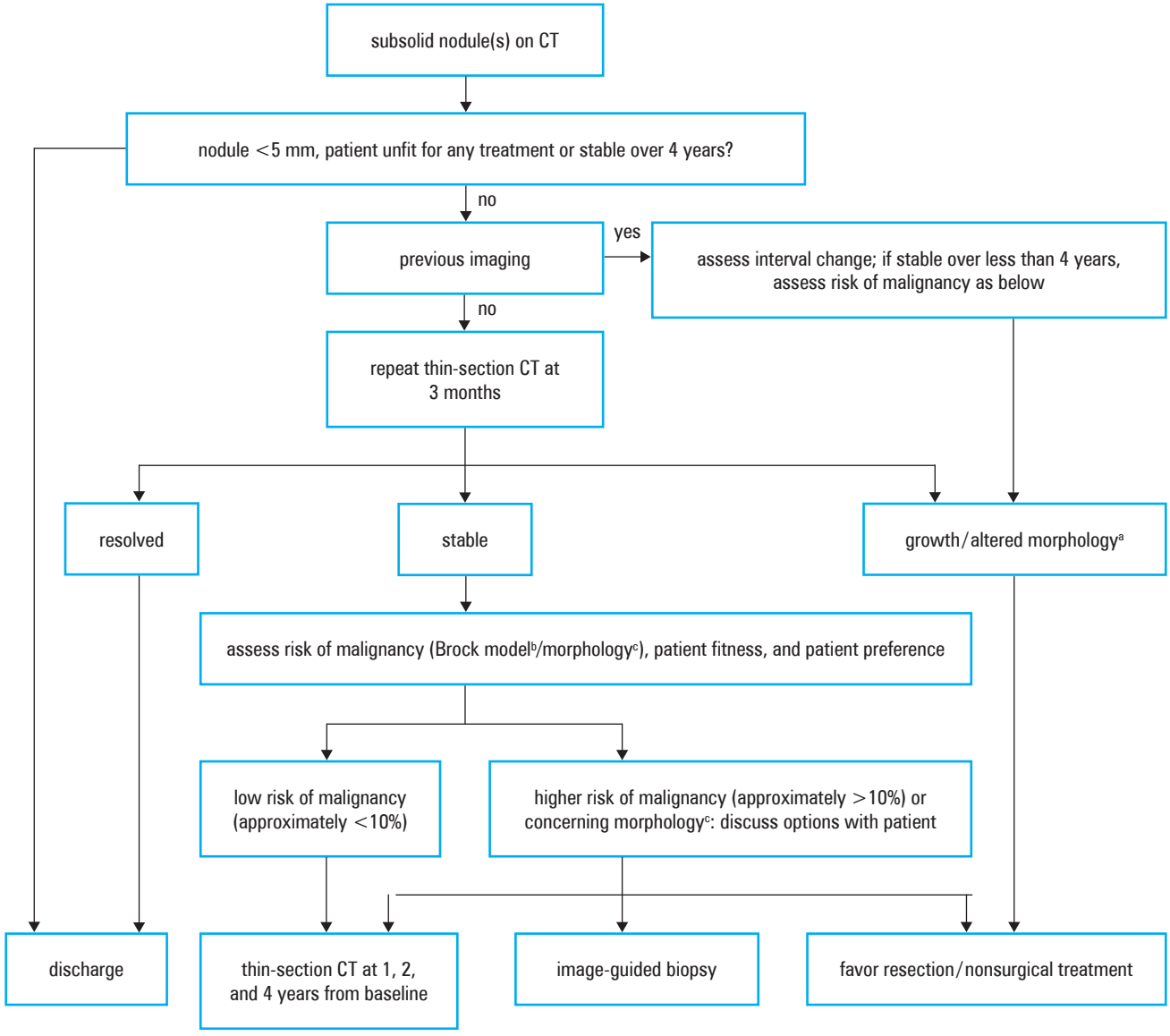

FIGURE 3 British Thoracic Society's algorithm for a subsolid pulmonary nodule
a change in mass / new solid component
b the Brock model may underestimate risk of malignancy in a subsolid nodule that persist at 3 months
c size of the solid component in a part-solid nodule, pleural indentation, and bubble-like appearance
Abbreviations: see **FIGURE 1**

Management of subsolid nodules SSNs require a different management approach than solid nodules because they often represent more indolent disease with a better prognosis. The pathological correlates are atypical adenomatous hyperplasia (usually smaller pure ground-glass nodule [pGGN]), adenocarcinoma in situ (often larger pGGN), minimally invasive adenocarcinoma (part-solid nodule [PSN] with a smaller solid component), and invasive adenocarcinoma (larger PSN).[32-34] Thus, SSNs may represent preinvasive and invasive lesions, and there are imaging predictors of progression to invasive disease, especially the development of a solid component (which is usually small in relation to the ground-glass component).[35] However, there is some debate about how these lesions should be managed because surgical series have reported a 100% cure rate in nodules that are ground glass in more than 50%.[36-38] The prevalence of SSNs is difficult to extract from most studies as it is not directly reported, but falls in the range of 2.2% to 3.8% of CTs for pGGN and 0.2% to 1% for PSNs.[11,34,39,40] Most series employed thin-section CT, necessary to accurately characterize the nodules.

The best evidence for the proportion of SSNs detected that are malignant comes from the Canadian screening trials: in the PanCan dataset,[11] 1.9% (21 of 1105) of pGGNs and 6.6% (20 of 303) of PSNs were malignant, and in the British Columbia Cancer Agency, the numbers were lower but the rates were 1.3% (6 of 467) and 22.2% (10 of 45), respectively. Baseline factors consistently associated with malignancy in SSNs are older age, previous history of lung cancer, size of the nodule, and part-solid nature.[11,22,33,34,41-51] The Brock university prediction model also included SSNs and found that although pGGNs are more often malignant than solid nodules, they conferred a lower chance of being malignant when adjusted for other factors in the risk prediction model. However, PSNs were independent predictors of malignancy. Morphological features predictive of malignancy other than initial size were pleural retraction or indentation and a bubble-like appearance in a pGGN. Studies have also shown that around 25% of SSNs resolve after 3 months.

FIGURE 3 shows the subsolid nodule algorithm of the BTS. After an initial 3-month interval thin-section CT to check whether the SSN is persistent, the Brock model is used to classify nodules into those with a risk of malignancy above or below 10%. It can be seen that imaging follow-up is for a total of 4 years which reflects the slow and intermittent growing nature of these nodules, with VDTs exceeding 1000 days.[44,45,48] For nodules with a higher chance of malignancy, a less aggressive approach than for solid nodules is recommended. This is because studies have confirmed the excellent prognosis of these lesions whether first observed or resected immediately.[43-45] Indeed, a small study showed an excellent prognosis without surgery even when cytology was suspicious of malignancy.[52] However, the BTS algorithm does favor resection for larger nodules, for pGGN that enlarge more than 2 mm and those with a new or enlarging solid component. This is also supported by the observation that the size of the solid component is an independent predictor of lymph node metastases,[33] although in 1 large study,[53] no pGGN or PSN with a solid component of 10 mm or less had nodal metastases. PET-CT is not recommended for the routine characterization of SSNs although the sensitivity, specificity, and accuracy of FDG PET-CT is higher for PSN.[54]

The key recommendations were:

1 Reassess all SSNs with a repeat thin-section CT at 3 months.

2 Use the Brock risk prediction tool to calculate risk of malignancy in SSNs of 5 mm or higher in diameter that are unchanged at 3 months.

3 Consider using other factors to further refine the estimate of risk of malignancy including smoking status, peripheral eosinophilia, history of lung cancer, size of solid component, bubble-like appearance, and pleural indentation.

4 Consider resection / nonsurgical treatment or observation for pGGN that enlarge 2 mm or more in the maximum diameter; if observed, repeat CT after a maximum of 6 months. Take into account the patient's choice, age, comorbidities, and risk of surgery.

5 Favor resection / nonsurgical treatment over observation for PSN that show enlargement of the solid component or for pGGN that develop a solid component. Take into account the patient's choice, age, comorbidities, and risk of surgery.

Biopsy techniques, indications, interpretation, and risks

Nonsurgical biopsy Nonsurgical biopsy or further nonimaging tests are used where there is sufficient uncertainty about the diagnosis to allow definitive management. The choice of test may depend on the preferences of the patient; therefore, it is especially important to ensure that the balance of accuracy and safety has been explained and that this is acceptable to the patient. The BTS guideline group evaluated a variety of biomarkers and techniques. Some biomarkers showed interesting early results but further studies were recommended to validate their performance.[55,56] Standard bronchoscopy has a very low yield but this can be increased with the image-guidance techniques described (fluoroscopy, radial endobronchial ultrasound [EBUS], and electromagnetic navigation bronchoscopy [ENB],[57] especially in the presence of a CT bronchus sign). The reported yields were 65% to 84%[58-61] for ENB and 46% to 77% for radial EBUS[62-64]; lower for lesions of less than 2 cm in diameter in the peripheral third of the lung. This is considerably less than those for CT-guided percutaneous transthoracic biopsy (pooled 91%), although the latter has a much higher pneumothorax rate (6.6% requiring chest drain in the largest series).[65-68] The latter may be important for some patients, although ENB and, to a lesser extent, radial EBUS may be very time-consuming and are not as widely available as percutaneous biopsy.

CT-guided biopsy was thus identified as the preferred minimally invasive biopsy technique with an average negative likelihood ratio of 0.1. *Figure S2* in Supplementary material online shows how the pretest probability of malignancy prior to percutaneous biopsy is altered by a negative biopsy result. This influenced the range of pretest probability of malignancy that appears in the initial assessment algorithm by showing that a biopsy has most influence in the intermediate probability range. There was also evidence that repeat biopsies usually achieved a diagnosis when the first was indeterminate.[68]

Variables associated with better CT-guided biopsy performance were nodule size,[69] nodule morphology,[70] needle path length, use of C-arm cone beam system,[71] multiplanar reconstruction,[72] and immediate cytological assessment.[73]

The BTS guideline provides greater clarity about the utility of biopsy in indeterminate lesions and specifically recommends repeating the procedure when the first is indeterminate.

Surgical excision biopsy Excision biopsy of pulmonary nodules is performed in 2 situations: first, where clinical suspicion of malignancy remains high despite a benign or indeterminate preoperative biopsy, and second, where a nodule is considered of sufficiently high risk for malignancy to merit the option of excision without an attempt at preoperative biopsy. All of the BTS nodule management algorithms show a place for excision biopsy. This was based on case series that showed this could be done safely and efficiently[74,75] with some suggestion that waiting times were reduced. The relative performance of thoracoscopic excision wedge biopsy and CT-guided percutaneous lung biopsy were compared in a case series by Mitruka et al.[76] Of 312 patients undergoing CT-guided biopsy, 64% (n = 205) had a malignant diagnosis, 6% (n = 19) had a specific benign diagnosis, and 29% (n = 91) had a nonspecific benign diagnosis. Of the latter group, 47 went on to the excision biopsy group, of which 32 (68%) were malignant. Percutaneous biopsy

had an accuracy of 86% for malignant disease and 71% for benign disease, whereas specific diagnoses were achieved for 97% of patients undergoing excision biopsy.

The benign resection rate is critically dependent on the prevalence of malignancy in the population and the quality of preoperative assessment of the probability of malignancy. Benign resection rates in case series of indeterminate pulmonary nodules undergoing surgical excision vary widely from 12%[77] to 86%.[78] Surgical series may not reflect the contemporary world of pulmonary nodules but the recently published UK lung cancer screening study, which adopted a similar protocol to that of the BTS guideline, showed a benign resection rate of only 10%.[79] No studies have specifically addressed the issue of what constitutes an optimal or acceptable benign resection rate. Factors that influence the threshold for surgical resection include the risk of morbidity and mortality for excision (particularly if the nodule turns out to be benign) compared to the possibility of stage progression during a period of radiological surveillance. Inpatient mortality for wedge resection / segmentectomy was reported to be 0.4% by the UK and Ireland Society of Cardio-Thoracic Surgeons (2010; personal communication). The English National Lung Cancer Audit reported a 30-day mortality of 2.1% and a 90-day mortality of 4.2% (35 deaths and 70 deaths, respectively) from 1671 patients undergoing wedge resection or segmentectomy.[80] No accurate estimate of the risk of stage progression during surveillance is available, although the recently published International Association for the Study of Lung Cancer did show survival differences between tumors of less than 1 cm and 1 to 2 cm in diameter.[81]

The key recommendations were:

1 Offer percutaneous lung biopsy where the result will alter the management plan.

2 Consider the use of other imaging techniques such as C-arm cone beam CT and multiplanar reconstruction to improve diagnostic accuracy.

3 Interpret negative lung biopsies in the context of the pretest probability of malignancy.

4 Consider repeating percutaneous lung biopsies where the probability of malignancy is high.

Surgical and nonsurgical treatment

Optimal surgical treatment Once a decision is made to proceed with surgical excision of a pulmonary nodule, 2 subsequent issues to consider are the surgical approach (video-assisted thoracic surgery [VATS] / thoracotomy) and the extent of the initial lung resection (wedge resection / segmentectomy / lobectomy). The extent of lung resection will also depend on the location of the nodule and the need for lung sparing, but there is also the question of whether sublobar or lobar resection is best. The only prospective randomized controlled trial of lobectomy versus sublobar resection for early stage lung cancer showed more loco-regional recurrence in the sublobar group, the latter grouped segmentectomy with wedge resection.[82,83] There is some nonrandomized low-quality evidence to suggest that segmentectomy is superior to wedge resection in terms of loco-regional recurrence and cancer-related deaths.[82,84,85]

Whether segmentectomy is equivalent or inferior to lobectomy is a subject open to debate. In a meta-analysis of 22 studies comparing lobectomy or segmentectomy for stage I lung cancer, segmentectomy was associated with significantly worse survival for stage I tumors (hazard ratio [HR], 1.2; 95% confidence interval [CI], 1.04–1.38) and stage IA tumors (HR, 1.24; 95% CI, 1.08–1.42).[86] However, no difference in survival was seen between these surgical techniques for tumors of 2 cm or smaller in diameter (HR, 1.05; 95% CI, 0.89–1.24). The evidence comparing a lobar versus sublobar resection in SSNs was limited to case series but the excellent survival rate and low rates of recurrence from sublobar resections in these series suggest that there may be little to be gained by extending to a lobectomy. Unfortunately, there was inconsistency in the inclusion criteria reported relating to the cut-off for inclusion of PSNs (eg, >50% ground glass component versus consolidation / tumor ratio of <0.25). Therefore, the recommendation for sublobar resection can only be confidently made for pGGNs.

Localization techniques for pulmonary nodules If limited resection is planned, nodules that are either of small size, located deep to the visceral pleura, or of ground-glass morphology may be difficult to locate at thoracoscopic surgery. A number of preoperative marking techniques have been developed to facilitate localization of these nodules including CT-guided hookwire[87] / needle[88] / microcoil[89] insertion, lipiodal injection[90] (lipid-soluble contrast medium with subsequent intraoperative fluoroscopy), methylene blue injection[91] (to identify the overlying visceral pleura to guide resection) or radiotracer injection[92] (using technetium-99m macroaggregated albumin with subsequent use of intraoperative gamma probe).

FIGURE 4 shows the BTS treatment algorithm that reflects the key recommendations for optimal surgery for pulmonary nodules listed below:

1 Surgical resection of pulmonary nodules should preferentially be by VATS rather than an open approach.

2 Offer lobectomy as definitive management of a pulmonary nodule confirmed as lung cancer preoperatively or following wedge resection and intraoperative frozen section analysis at the same anesthetic.

3 Consider anatomical segmentectomy where preservation of functioning lung tissue may reduce the operative risk and improve physiological outcome.

4 Consider a diagnostic anatomical segmentectomy for nodules less than 2 cm in diameter without nodal disease when there has been no pathological confirmation and frozen section is not possible.

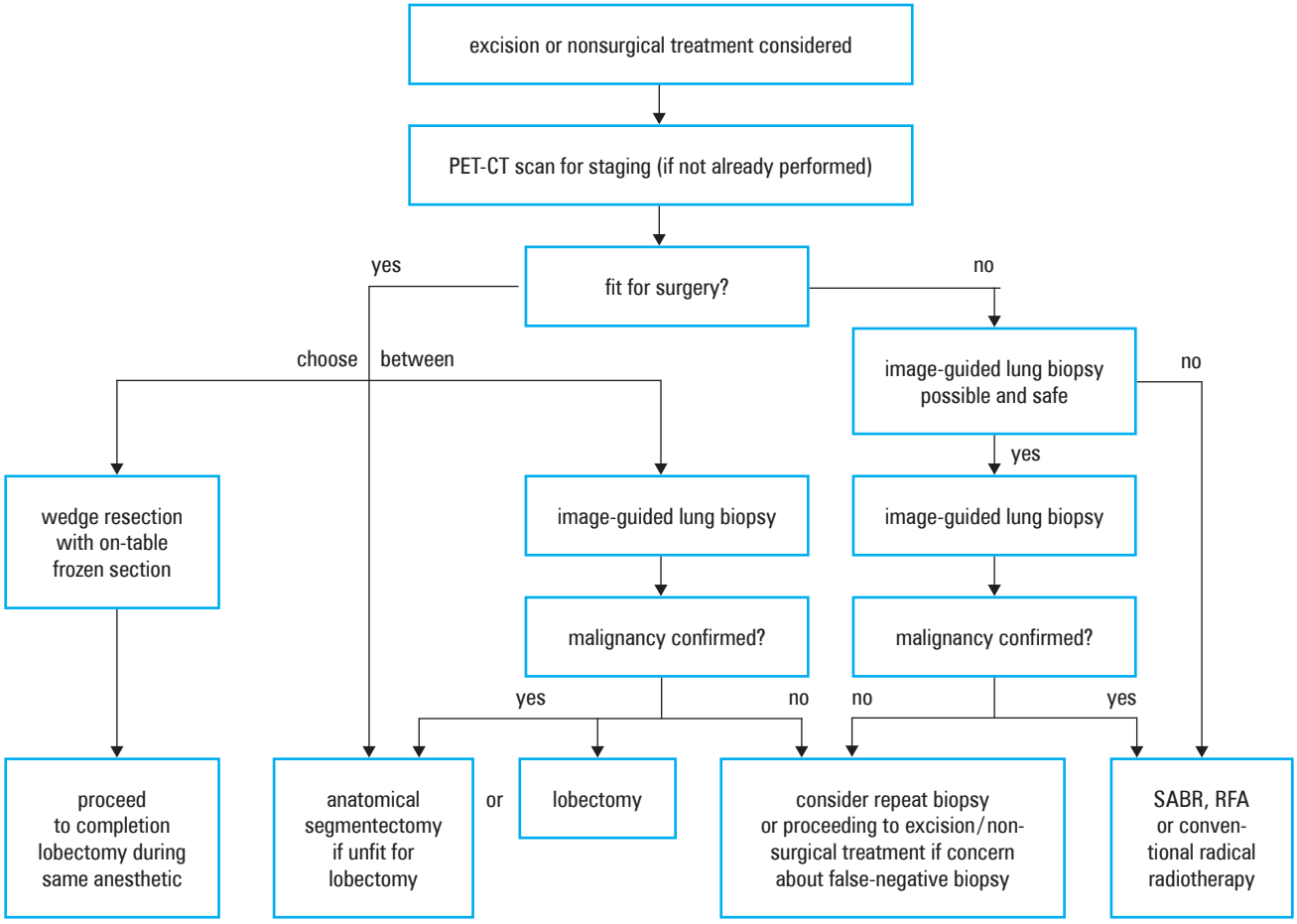

FIGURE 4 British Thoracic Society's algorithm for pulmonary nodule treatment
Abbreviations: RFA, radiofrequency ablation; SABR, stereotactic body radiotherapy

5 Use localization techniques depending on local availability and expertise to facilitate limited resection of pulmonary nodules.

Nonsurgical treatment without pathological confirmation FIGURE 4 shows the approach to patients with pulmonary nodules who are judged to be unfit for surgical treatment. This also includes those patients who choose nonsurgical treatment. Where possible, histological confirmation should be attempted but where this is not safe, treatment may proceed without, provided the risk of malignancy is higher than 70%.

Four retrospective cohort studies compared outcomes in patients treated with stereotactic body radiotherapy (SABR) with clinically diagnosed lung cancer versus patients with pathologically proven non-small cell lung cancer.[93-95] They found similar survival rates although only 3 studies were explicit about potential confounding variables.

The BTS guideline reviewed evidence for several nonsurgical treatments. The majority of evidence found was for SABR and radiofrequency ablation (RFA), although the variability in case definition, pathological confirmation, proportion of primary and secondary cancer, selection criteria, and concomitant treatment made comparison inappropriate. One study used propensity score matching in a comparison of SABR and VATS for stage I–II lung cancer and showed similar 3-year outcomes.[96] Nonsurgical treatments show marked variation in the frequency of harms, something that is likely to be strongly influenced by case selection and technique employed.

FIGURE 4 reflects the key recommendations about nonsurgical treatment as follows:

1 Consider people that are unfit for surgery who have pulmonary nodule(s) with high probability of malignancy, where biopsy is nondiagnostic or not possible, for treatment with SABR or RFA if technically suitable.

2 Consider people that are unfit for surgery who have pulmonary nodule(s) with high probability of malignancy, where biopsy is nondiagnostic or not possible, for treatment with conventional radical radiotherapy if not suitable for SABR or RFA.

Information and support Patients who have pulmonary nodules detected by whatever method may be concerned or anxious about the implications for their health. A clear understanding is essential for patients and their caregivers to make informed choices about the options for management. They may need professional support when interpreting information, provided, for example, by a lung cancer specialist nurse.

The BTS evidence review found 3 papers of sufficient quality on psychological consequences of the finding of pulmonary nodules.[97-99] The key findings were that: the finding of a pulmonary nodule has an adverse impact on the quality

of life; patients commonly assume that the finding of a nodule means that they have cancer; patients may be frustrated if health care providers fail to address concerns about cancer or potential adverse effects of surveillance; and effective communication by the health care team can reduce the impact on the quality of life after diagnosis of a pulmonary nodule.

The key recommendations were:

1 Offer accurate and understandable information to patients and caregivers about the probability of malignancy of the pulmonary nodule.

2 Ensure patients have the opportunity to discuss concerns about lung cancer and surveillance regimes.

3 Offer patients the choice of seeing a lung cancer nurse specialist where the probability of malignancy is high or when patients are anxious about the possibility of having lung cancer.

4 Ensure that clear written and verbal information is available on follow-up schedules and the number of repeat CT scans required.

5 Explain the risks and benefits of investigations and treatment. Where appropriate, offer a choice of management.

Technical aspects of the imaging of pulmonary nodules The BTS guideline reviewed evidence for the method of detection, measurement and growth estimation, and factor influencing accuracy. Detection is improved if the maximum section thickness is 1.25 mm[100-102] and reconstruction algorithms such as multiplanar reconstruction, maximum intensity projection, and volume rendering are used.[103-108] Technical factors that can influence measurement include section thickness, reconstruction algorithm, lung volume, intravenous contrast, and make of software. Patient-related factors include nodule shape, juxta pleural or juxta vascular position, smaller nodule size, and cardiac motion. Low-radiation-dose CT has been shown to produce reliable measurements.[109,110]

The key recommendations were:

1 Where CT scans are performed that include the chest where nodule detection is of potential importance, use a maximum section thickness of 1.25 mm.

2 Use low-radiation-dose CT with a maximum section thickness of 1.25 mm in follow-up imaging.

3 Use maximum intensity projection or volume rendering to improve nodule detection and characterization.

4 When reporting on growth, take into account factors that may reduce accuracy, such as nodule shape and position and interval between scans.

5 Ensure a radiologist or radiographer checks that the nodule has been accurately segmented.

Conclusions The BTS guideline is primarily aimed to guide clinical practice in the UK but will be applicable in other countries, especially those with similar populations. The significant changes to recommendations should promote a more cost-effective approach to the management of pulmonary nodules while encouraging a safe and consistent approach. Although much of the evidence reviewed was recent (a third of the references are from 2012 onwards), it is recognized that ongoing trials may suggest updated guidance is required. For this reason, it is recommended that a record of people with nodules is kept in case a longer-term follow-up is recommended.

Supplementary material online Supplementary material online is available with the online version of the article at www.pamw.pl.

REFERENCES

1 Callister ME, Baldwin DR, Akram AR, et al. British Thoracic Society guidelines for the investigation and management of pulmonary nodules. Thorax. 2015; 70: 794-798.

2 Quint LE, Park CH, Iannettoni MD. Solitary pulmonary nodules in patients with extrapulmonary neoplasms. Radiology. 2000; 217: 257-261.

3 Khokhar S, Vickers A, Moore MS, et al. Significance of non-calcified pulmonary nodules in patients with extrapulmonary cancers. Thorax. 2006; 61: 331-336.

4 Hanamiya M, Aoki T, Yamashita Y, et al. Frequency and significance of pulmonary nodules on thin-section CT in patients with extrapulmonary malignant neoplasms. Eur J Radiol. 2012; 81: 152-157.

5 Mery CM, Pappas AN, Bueno R, et al. Relationship between a history of antecedent cancer and the probability of malignancy for a solitary pulmonary nodule. Chest. 2004; 125: 2175-2181.

6 Yuan Y, Matsumoto T, Hiyama A, et al. The probability of malignancy in small pulmonary nodules coexisting with potentially operable lung cancer detected by CT. Eur Radiol. 2003; 13: 2447-2453.

7 Kim YH, Lee KS, Primack SL, et al. Small pulmonary nodules on CT accompanying surgically resectable lung cancer: likelihood of malignancy. J Thorac Imaging. 2002; 17: 40-46.

8 Keogan MT, Tung KT, Kaplan DK, et al. The significance of pulmonary nodules detected on CT staging for lung cancer. Clinical Radiology. 1993; 48: 94-96.

9 de Hoop B, van Ginneken B, Gietema H, et al. Pulmonary perifissural nodules on CT scans: rapid growth is not a predictor of malignancy. Radiology. 2012; 265: 611-616.

10 Horeweg N, van Rosmalen J, Heuvelmans MA, et al. Lung cancer probability in patients with CT-detected pulmonary nodules: a prespecified analysis of data from the NELSON trial of low-dose CT screening. Lancet Oncol. 2014; 15: 1332-1341.

11 McWilliams A, Tammemagi MC, Mayo JR, et al. Probability of cancer in pulmonary nodules detected on first screening CT. N Engl J Med. 2013; 369: 910-919.

12 Al-Ameri A, Malhotra P, Thygesen H, et al. Risk of malignancy in pulmonary nodules: A validation study of four prediction models. Lung Cancer. 2015; 89: 27-30.

13 Herder GJ, van Tinteren H, Golding RP, et al. Clinical prediction model to characterize pulmonary nodules: validation and added value of 18F-fluorodeoxyglucose positron emission tomography. Chest. 2005; 128: 2490-2496.

14 Al Ameri MN, Mohamed W, Makramalla E, et al. Renal patients' views on generic prescribing and substitution: example from the United Arab Emirates. East Mediterr Health J. 2013; 19: 373-381.

15 Fletcher JW, Kymes SM, Gould M, et al. A comparison of the diagnostic accuracy of 18F-FDG PET and CT in the characterization of solitary pulmonary nodules. J Nuclear Med. 2008; 49: 179-185.

16 Vansteenkiste JF, Stroobants SG, Dupont PJ, et al. FDG-PET scan in potentially operable non-small cell lung cancer: do anatometabolic PET-CT fusion images improve the localisation of regional lymph node metastases? The Leuven Lung Cancer Group. Eur J Nucl Med. 1998; 25: 1495-1501.

17 van Klaveren RJ, Oudkerk M, Prokop M, et al. Management of lung nodules detected by volume CT scanning. New Eng J Med. 2009; 361: 2221-2229.

18 Revel MP, Bissery A, Bienvenu M, et al. Are Two-dimensional CT Measurements of Small Noncalcified Pulmonary Nodules Reliable? Radiology. 2004; 231: 453-458.

19 Korst RJ, Lee BE, Krinsky GA, et al. The utility of automated volumetric growth analysis in a dedicated pulmonary nodule clinic. J Thorac Cardiovasc Surg. 2011; 142: 372-377.

20 Ko JP, Berman EJ, Kaur M, et al. Pulmonary Nodules: growth rate assessment in patients by using serial CT and three-dimensional volumetry. Radiology. 2012; 262: 662-671.

21 Revel MP, Merlin A, Peyrard S, et al. Software volumetric evaluation of doubling times for differentiating benign versus malignant pulmonary nodules. AJR Am J Roentgenol. 2006; 187: 135-142.

22 de Hoop B, Gietema H, van de Vorst S, et al. Pulmonary ground-glass nodules: increase in mass as an early indicator of growth. Radiology. 2010; 255: 199-206.

23 Xu DM, van Klaveren RJ, de Bock GH, et al. Role of baseline nodule density and changes in density and nodule features in the discrimination between benign and malignant solid indeterminate pulmonary nodules. Eur J Radiol. 2009; 70: 492-498.

24 Kostis WJ, Yankelevitz DF, Reeves AP, et al. Small pulmonary nodules, reproducibility of three-dimensional volumetric measurement and estimation of time to follow-up CT. Radiology. 2004; 231: 446-452.

25 Xu DM, van der Zaag-Loonen HJ, Oudkerk M, et al. Smooth or attached solid indeterminate nodules detected at baseline CT screening in the NELSON study: cancer risk during 1 year of follow-up. Radiology. 2009; 250: 264-272.

26 Zhao YR, Heuvelmans MA, Dorrius MD, et al. Features of resolving and nonresolving indeterminate pulmonary nodules at follow-up CT: the NELSON study. Radiology. 2014; 270: 872-879.

27 Hasegawa M, Sone S, Takashima S, et al. Growth rate of small lung cancers detected on mass CT screening. Br J Radiol. 2000; 73: 1252-1259.

28 Winer-Muram HT, Jennings SG, Tarver RD, et al. Volumetric growth rate of stage I lung cancer prior to treatment: serial CT scanning. Radiology. 2002; 223: 798-805.

29 Henschke CI, Yankelevitz DF, Yip R, et al. Lung cancers diagnosed at annual CT screening: volume doubling times. Radiology. 2012; 263: 578-583.

30 Good CA, Wilson TW. The solitary circumscribed pulmonary nodule; study of seven hundred five cases encountered roentgenologically in a period of three and one-half years. J Am Med Assoc. 1958; 166: 210-215.

31 Yankelevitz DF, Henschke CI. Does 2-year stability imply that pulmonary nodules are benign? AJR American Journal of Roentgenology. 1997; 168: 325-328.

32 Travis WD, Brambilla E, Noguchi M, et al. International association for the study of lung cancer/american thoracic society/european respiratory society international multidisciplinary classification of lung adenocarcinoma. J Thorac Oncol. 2011; 6: 244-285.

33 Ichinose J, Kohno T, Fujimori S, et al. Invasiveness and malignant potential of pulmonary lesions presenting as pure ground-glass opacities. Ann Thorac Cardiovasc Surg. 2014; 20: 347-352.

34 Matsuguma H, Mori K, Nakahara R, et al. Characteristics of subsolid pulmonary nodules showing growth during follow-up with CT scanning. Chest. 2013; 143: 436-443.

35 Matsuguma H, Yokoi K, Anraku M, et al. Proportion of ground-glass opacity on high-resolution computed tomography in clinical T1 N0 M0 adenocarcinoma of the lung: A predictor of lymph node metastasis. J Thorac Cardiovasc Surg. 2002; 124: 278-284.

36 Hung JJ, Jeng WJ, Chou TY, et al. Prognostic value of the new International Association for the Study of Lung Cancer/American Thoracic Society/European Respiratory Society lung adenocarcinoma classification on death and recurrence in completely resected stage I lung adenocarcinoma. Ann Surg. 2013; 258: 1079-1086.

37 Hung JJ, Yeh YC, Jeng WJ, et al. Predictive Value of the International Association for the Study of Lung Cancer/American Thoracic Society/European Respiratory Society Classification of Lung Adenocarcinoma in Tumor Recurrence and Patient Survival. J Clin Oncol. 2014; 32: 2357-2364.

38 Russell PA, Wainer Z, Wright GM, et al. Does lung adenocarcinoma subtype predict patient survival?: A clinicopathologic study based on the new International Association for the Study of Lung Cancer/American Thoracic Society/European Respiratory Society international multidisciplinary lung adenocarcinoma classification. J Thorac Oncol. 2011; 6: 1496-1504.

39 National Lung Screening Trial Research Team, Aberle DR, Adams AM, et al. Reduced lung-cancer mortality with low-dose computed tomographic screening. N Engl J Med. 2011; 365: 395-409.

40 Henschke CI, Yankelevitz DF, Mirtcheva R, et al. CT screening for lung cancer: frequency and significance of part-solid and nonsolid nodules. AJR Am J Roentgenol. 2002; 178: 1053-1057.

41 Fan L, Liu SY, Li QC, et al. Multidetector CT features of pulmonary focal ground-glass opacity: differences between benign and malignant. Br J Radiol. 2012; 85: 897-904.

42 Kim TJ, Park CM, Goo JM, Lee KW. Is there a role for FDG PET in the management of lung cancer manifesting predominantly as ground-glass opacity? AJR Am J Roentgenol. 2012; 198: 83-88.

43 Kobayashi Y, Sakao Y, Deshpande GA, et al. The association between baseline clinical-radiological characteristics and growth of pulmonary nodules with ground-glass opacity. Lung Cancer. 2014; 83: 61-66.

44 Lee SW, Leem CS, Kim TJ, et al. The long-term course of ground-glass opacities detected on thin-section computed tomography. Respir Med. 2013; 107: 904-910.

45 Takahashi S, Ueda K, Kido S, et al. Long term follow-up for small pure ground-glass nodules: Implications of determining an optimum follow-up period and high-resolution CT findings to predict the growth of nodules. Jpn J Radiol. 2012; 30: 206-217.

46 Tamura M, Shimizu Y, Yamamoto T, et al. Predictive value of one-dimensional mean computed tomography value of ground-glass opacity on high-resolution images for the possibility of future change. J Thorac Oncol. 2014; 9: 469-472.

47 Attina D, Niro F, Stellino M, et al. Evolution of the subsolid pulmonary nodule: a retrospective study in patients with different neoplastic diseases in a nonscreening clinical context. Radiol Med. 2013; 118: 1269-1280.

48 Chang B, Hwang JH, Choi YH, et al. Natural history of pure ground-glass opacity lung nodules detected by low-dose CT scan. Chest. 2013; 143: 172-178.

49 Choi WS, Park CM, Song YS, et al. Transient subsolid nodules in patients with extrapulmonary malignancies: their frequency and differential features. Acta Radiol. 2014; 56: 428-437.

50 Lee KH, Goo JM, Park SJ, et al. Correlation between the size of the solid component on thin-section CT and the invasive component on pathology in small lung adenocarcinomas manifesting as ground-glass nodules. J Thorac Oncol. 2014; 9: 74-82.

51 Nakamura S, Fukui T, Taniguchi T, et al. Prognostic impact of tumor size eliminating the ground glass opacity component: modified clinical T descriptors of the tumor, node, metastasis classification of lung cancer. J Thorac Oncol. 2013; 8: 1551-1557.

52 Gulati CM, Schreiner AM, Libby DM, et al. Outcomes of unresected ground-glass nodules with cytology suspicious for adenocarcinoma. J Thorac Oncol. 2014; 9: 685-691.

53 Maeyashiki T, Suzuki K, Hattori A, et al. The size of consolidation on thin-section computed tomography is a better predictor of survival than the maximum tumour dimension in resectable lung cancer. Eur J Cardiothorac Surg. 2013; 43: 915-918.

54 Veronesi G, Bellomi M, Veronesi U, et al. Role of positron emission tomography scanning in the management of lung nodules detected at baseline computed tomography screening. Ann Thorac Surg. 2007; 84: 959-966.

55 Shen J, Liu Z, Todd NW, et al. Diagnosis of lung cancer in individuals with solitary pulmonary nodules by plasma microRNA biomarkers. BMC Cancer. 2011; 11: 374.

56 Higgins G, Roper KM, Watson IJ, et al. Variant Ciz1 is a circulating biomarker for early-stage lung cancer. Proc Natl Acad Sci USA. 2012; 109: E3128-E3135.

57 Baaklini WA, Reinoso MA, Gorin AB, et al. Diagnostic yield of fiberoptic bronchoscopy in evaluating solitary pulmonary nodules. Chest. 2000; 117: 1049-1054.

58 Eberhardt R, Morgan RK, Ernst A, et al. Comparison of suction catheter versus forceps biopsy for sampling of solitary pulmonary nodules guided by electromagnetic navigational bronchoscopy. Respiration. 2010; 79: 54-60.

59 Gildea TR, Mazzone PJ, Karnak D, et al. Electromagnetic navigation diagnostic bronchoscopy: a prospective study. Am J Respir Crit Care Med. 2006; 174: 982-989.

60 Jensen KW, Hsia DW, Seijo LM, et al. Multicenter experience with electromagnetic navigation bronchoscopy for the diagnosis of pulmonary nodules. J Bronchology Interv Pulmonol. 2012; 19: 195-199.

61 Lamprecht B, Porsch P, Wegleitner B, et al. Electromagnetic navigation bronchoscopy (ENB): Increasing diagnostic yield. Respir Med. 2012; 106: 710-715.

62 Herth FJ, Eberhardt R, Becker HD, et al. Endobronchial ultrasound-guided transbronchial lung biopsy in fluoroscopically invisible solitary pulmonary nodules: a prospective trial. Chest. 2006; 129: 147-150.

63 Eberhardt R, Ernst A, Herth FJ. Ultrasound-guided transbronchial biopsy of solitary pulmonary nodules less than 20 mm. Eur Respir J. 2009; 34: 1284-1287.

64 Kurimoto N, Miyazawa T, Okimasa S, et al. Endobronchial ultrasonography using a guide sheath increases the ability to diagnose peripheral pulmonary lesions endoscopically. Chest. 2004; 126: 959-965.

65 Baldwin DR, Eaton T, Kolbe J, et al. Management of solitary pulmonary nodules: how do thoracic computed tomography and guided fine needle biopsy influence clinical decisions? Thorax. 2002; 57: 817-822.

66 Gupta S, Krishnamurthy S, Broemeling LD, et al. Small (≤2-cm) subpleural pulmonary lesions: Short-versus long-needle-path CT-guided biopsy: comparison of diagnostic yields and complications. Radiology. 2005; 234: 631-637.

67 Wagnetz U, Menezes RJ, Boerner S, et al. CT screening for lung cancer: implication of lung biopsy recommendations. AJR Am J Roentgenol. 2012; 198: 351-358.

68 Fontaine-Delaruelle C, Souquet PJ, Gamondes D, et al. Negative predictive value of transthoracic core needle biopsy: a multicenter study. Chest. 2015; 148: 472-480.

69 Wallace MJ, Krishnamurthy S, Broemeling LD, et al. CT-guided percutaneous fine-needle aspiration biopsy of small (< or =1-cm) pulmonary lesions. Radiology. 2002; 225: 823-828.

70 De Filippo M, Saba L, Concari G, et al. Predictive factors of diagnostic accuracy of CT-guided transthoracic fine-needle aspiration for solid noncalcified, subsolid and mixed pulmonary nodules. Radiol Med. 2013; 118: 1071-1081.

71 Choi JW, Park CM, Goo JM, et al. C-arm cone-beam CT-guided percutaneous transthoracic needle biopsy of small (</= 20 mm) lung

nodules: diagnostic accuracy and complications in 161 patients. AJR Am J Roentgenol. 2012; 199: W322-W330.

72 Ohno Y, Hatabu H, Takenaka D, et al. Transthoracic CT-guided biopsy with multiplanar reconstruction image improves diagnostic accuracy of solitary pulmonary nodules. Eur J Radiol. 2004; 51: 160-168.

73 Santambrogio L, Nosotti M, Bellaviti N, et al. CT-guided fine-needle aspiration cytology of solitary pulmonary nodules: a prospective, randomized study of immediate cytologic evaluation. Chest. 1997; 112: 423-425.

74 Heo EY, Lee KW, Jheon S, et al. Surgical resection of highly suspicious pulmonary nodules without a tissue diagnosis. Jpn J Clin Oncol. 2011; 41: 1017-1022.

75 Sihoe AD, Hiranandani R, Wong H, et al. Operating on a suspicious lung mass without a preoperative tissue diagnosis: pros and cons. Eur J Cardiothorac Surg. 2013; 44: 231-237.

76 Mitruka S, Landreneau RJ, Mack MJ, et al. Diagnosing the indeterminate pulmonary nodule: percutaneous biopsy versus thoracoscopy. Surgery. 1995; 118: 676-684.

77 Petersen RH, Hansen HJ, Dirksen A, et al. Lung cancer screening and video-assisted thoracic surgery. J Thorac Oncol. 2012; 7: 1026-1031.

78 Cardillo G, Regal M, Sera F, et al. Videothoracoscopic management of the solitary pulmonary nodule: a single-institution study on 429 cases. Ann Thorac Surg. 2003; 75: 1607-1611.

79 Field JK, Duffy SW, Baldwin DR, et al. UK Lung Cancer RCT Pilot Screening Trial: baseline findings from the screening arm provide evidence for the potential implementation of lung cancer screening. Thorax. 2016; 71: 161-170.

80 Powell HA, Tata LJ, Baldwin DR, et al. Early mortality after surgical resection for lung cancer: an analysis of the English National Lung cancer audit. Thorax. 2013; 68: 826-834.

81 Goldstraw P, Chansky K, Crowley J, et al. The IASLC Lung Cancer Staging Project: Proposals for Revision of the TNM Stage Groupings in the Forthcoming (Eighth) Edition of the TNM Classification for Lung Cancer. J Thorac Oncol. 2016; 11: 39-51.

82 Ginsberg RJ, Rubinstein LV. Randomized trial of lobectomy versus limited resection for T1 N0 non-small cell lung cancer. Lung Cancer Study Group. Ann Thorac Surg. 1995; 60: 615-622.

83 Detterbeck FC. Lobectomy versus limited resection in T1N0 lung cancer. Ann Thorac Surg. 2013; 96: 742-744.

84 Billmeier SE, Ayanian JZ, Zaslavsky AM, et al. Predictors and outcomes of limited resection for early-stage non-small cell lung cancer. J Natl Cancer Inst. 2011; 103: 1621-1629.

85 Okami J, Ito Y, Higashiyama M, et al. Sublobar resection provides an equivalent survival after lobectomy in elderly patients with early lung cancer. Ann Thorac Surg. 2010; 90: 1651-1656.

86 Bao F, Ye P, Yang Y, et al. Segmentectomy or lobectomy for early stage lung cancer: a meta-analysis. Eur J Cardiothorac Surg. 2014; 46: 1-7.

87 Miyoshi K, Toyooka S, Gobara H, et al. Clinical outcomes of short hook wire and suture marking system in thoracoscopic resection for pulmonary nodules. Eur J Cardiothorac Surg. 2009; 36: 378-382.

88 Koyama H, Noma S, Tamaki Y, et al. CT localisation of small pulmonary nodules prior to thorascopic resection: Evaluation of a point marker system. Eur J Radiol. 2008; 65: 468-472.

89 Mayo JR, Clifton JC, Powell TI, et al. Lung nodules: CT-guided placement of microcoils to direct video-assisted thoracoscopic surgical resection. Radiology. 2009; 250: 576-585.

90 Watanabe K, Nomori H, Ohtsuka T, et al. Usefulness and complications of computed tomography-guided lipiodol marking for fluoroscopy-assisted thoracoscopic resection of small pulmonary nodules: experience with 174 nodules. J Thorac Cardiovasc Surg. 2006; 132: 320-324.

91 Vandoni RE, Cuttat JF, Wicky S, et al. CT-guided methylene-blue labelling before thoracoscopic resection of pulmonary nodules. Eur J Cardiothorac Sur. 1998; 14: 265-270.

92 Ambrogi MC, Melfi F, Zirafa C, et al. Radio-guided thoracoscopic surgery (RGTS) of small pulmonary nodules. Surg Endosc. 2012; 26: 914-919.

93 Takeda A, Kunieda E, Sanuki N, et al. Stereotactic body radiotherapy (SBRT) for solitary pulmonary nodules clinically diagnosed as lung cancer with no pathological confirmation: Comparison with non-small-cell lung cancer. Lung Cancer. 2012; 77: 77-82.

94 Verstegen NE, Lagerwaard FJ, Haasbeek CJ, et al. Outcomes of stereotactic ablative radiotherapy following a clinical diagnosis of stage I NSCLC: comparison with a contemporaneous cohort with pathologically proven disease. Radiother Oncol. 2011; 101: 250-254.

95 Haidar YM, Rahn DA 3rd, Nath S, et al. Comparison of outcomes following stereotactic body radiotherapy for non-small cell lung cancer in patients with and without pathological confirmation. Ther Adv Respir Dis. 2014; 8: 3-12.

96 Verstegen NE, Oosterhuis JW, Palma DA, et al. Stage I-II non-small-cell lung cancer treated using either stereotactic ablative radiotherapy (SABR) or lobectomy by video-assisted thoracoscopic surgery (VATS): outcomes of a propensity score-matched analysis. Ann Oncol. 2013; 24:1543-1548.

97 Lemonnier I, Baumann C, Jolly D, et al. Solitary pulmonary nodules: consequences for patient quality of life. Qual Life Res. 2011; 20: 101-109.

98 van den Bergh KAM, Essink-Bot ML, Borsboom GJJM, et al. Short-term health-related quality of life consequences in a lung cancer CT screening trial (NELSON). Br J Cancer. 2010; 102: 27-34.

99 Wiener RS, Gould MK, Woloshin S, et al. What do you mean, a spot?: A qualitative analysis of patients' reactions to discussions with their physicians about pulmonary nodules. Chest. 2013; 143: 672-677.

100 Fischbach F, Knollmann F, Griesshaber V, et al. Detection of pulmonary nodules by multislice computed tomography: improved detection rate with reduced slice thickness. Eur Radiol. 2003; 13: 2378-2383.

101 Lee HY, Goo JM, Lee HJ, et al. Usefulness of concurrent reading using thin-section and thick-section CT images in subcentimetre solitary pulmonary nodules. Clin Radiol. 2009; 64: 127-132.

102 Sinsuat M, Saita S, Kawata Y, et al. Influence of slice thickness on diagnoses of pulmonary nodules using low-dose CT: potential dependence of detection and diagnostic agreement on features and location of nodule. Acad Radiol. 2011; 18: 594-604.

103 Cui Y, Ma DQ, Liu WH. Value of multiplanar reconstruction in MSCT in demonstrating the relationship between solitary pulmonary nodule and bronchus. Clin Imaging. 2009; 33: 15-21.

104 Jankowski A, Martinelli T, Timsit JF, et al. Pulmonary nodule detection on MDCT images: evaluation of diagnostic performance using thin axial images, maximum intensity projections, and computer-assisted detection. Eur Radiol. 2007; 17: 3148-3156.

105 Kawel N, Seifert B, Luetolf M, et al. Effect of slab thickness on the CT detection of pulmonary nodules: use of sliding thin-slab maximum intensity projection and volume rendering. AJR Am J Roentgenol. 2009; 192: 1324-1329.

106 Matsumoto S, Ohno Y, Yamagata H, et al. Potential contribution of multiplanar reconstruction (MPR) to computer-aided detection of lung nodules on MDCT. Eur J Radiol. 2012; 81: 366-370.

107 Park EA, Goo JM, Lee JW, et al. Efficacy of computer-aided detection system and thin-slab maximum intensity porojection technique in the detection of pulmonary nodules in patients with resected metastases. Invest Radiol. 2009; 44: 105-113.

108 Yoneda K, Ueno J, Nishihara S, et al. Postprocessing technique with MDCT data improves the accuracy of the detection of lung nodules. Radiat Med. 2007; 25: 511-515.

109 Hein PA, Romano VC, Rogalla P, et al. Variability of semiautomated lung nodule volumetry on ultralow-dose CT: comparison with nodule volumetry on standard-dose CT. J Digit Imaging. 2010; 23: 8-17.

110 Christe A, Torrente JC, Lin M, et al. CT screening and follow-up of lung nodules: effects of tube current-time setting and nodule size and density on detectability and of tube current-time setting on apparent size. AJR Am J Roentgenol. 2011; 197: 623-630.

ARTYKUŁ POGLĄDOWY

Postępowanie u chorych z guzkami płuc według wytycznych British Thoracic Society 2015

Najważniejsze informacje praktyczne

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SŁOWA KLUCZOWE

guzki płuc, wytyczne

STRESZCZENIE

Wytyczne British Thoracic Society dotyczące badań oraz postępowania w przypadku wykrycia guzków płuc oparto na wynikach obszernego przeglądu systematycznego piśmiennictwa na ten temat. Najnowsze dane naukowe wskazały na konieczność wprowadzenia istotnych zmian do istniejących wytycznych. Wyniki badań zdecydowanie popierają stosowanie dwóch skal oceny ryzyka obecności nowotworu złośliwego, a także zalecenia dotyczące zwiększenia rozmiaru guzków, które należy obserwować (≥5 mm lub ≥80 mm^3) oraz skrócenie czasu monitorowania do roku w przypadku guzków całkowicie litych. Zawsze, gdy mamy do czynienia z obecnością nowotworu złośliwego w wywiadzie konieczna jest ostrożność, niemniej jednak oba te zalecenia zmniejszą liczbę kontrolnych tomografii komputerowych, poprawiając skuteczność w stosunku do ponoszonych kosztów oraz zmniejszając obciążenie placówek wykonujących te badania. Najnowsze dane naukowe potwierdziły również wyższość analizy wolumetrycznej jako preferowanej metody pomiaru i pozwoliły na ustalenie postępowania u chorych z guzkami o wydłużonym czasie podwojenia objętości. Zalecenia dotyczące chorych z guzkami częściowo litymi obejmują również wykorzystanie mniej agresywnych opcji postępowania, ponieważ ustalono, że rokowanie u tych pacjentów jest dobre. W wytycznych zaleca się podawanie wyników pozytonowej tomografii emisyjnej skojarzonej z tomografią komputerową za pomocą skali porządkowej w celu ułatwienia ich wykorzystania w modelach ryzyka. Sformułowano zalecenia precyzujące sytuacje, w których biopsja jest najbardziej przydatna, a także kryteria kwalifikacji do leczenia chorych bez potwierdzenia histopatologicznego oraz leczenia chirurgicznego i zachowawczego. Wytyczne zawierają również oparte na danych naukowych zalecenia dotyczące informacji, których chorzy potrzebują i które należy im przekazać. Opracowanie czterech algorytmów ułatwia zrozumienie złożonego postępowania u chorych z guzkami płuc. Stosowanie zaleceń wytycznych w codziennej praktyce jest zaskakująco proste i zgodne z intuicyjnym podejściem lekarza.

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Praca wpłynęła: 10.02.2016.
Przyjęta do druku: 11.02.2016.
Publikacja *online*: 26.04.2016.
Zgłoszono sprzeczność interesów: DRB otrzymał finansowanie kosztów podróży na konferencję World Lung Cancer Conference od firmy Oncimmune Ltd.
Pol Arch Med Wewn. 2016; 126 (4): 262-274
doi:10.20452/pamw.3379
Tłumaczył lek. Marcin Pustkowski