Review Article on Lung Cancer Screening

Managing of screening-detected sub-solid nodules—a European perspective

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Abstract: Since the National Lung Screening Trial in 2011 showed a 20% reduction in lung cancer mortality using annual low-dose computed tomography (LDCT), several randomised controlled trials and studies have been started in Europe. These include the Italian lung study (ITALUNG), the Dutch-Belgian lung cancer screening trial (NELSON), the UK lung cancer screening trial (UKLS), the Detection and screening of early lung cancer with novel imaging technology (DANTE), the Danish lung cancer screening trial (DLCST), the German lung cancer screening intervention trial (LUSI), the Multicentric Italian lung detection trial (MILD) and the CT screening for lung cancer study (COSMOS). As a result of the increasing number of screening trials and the growing utilization of LDCT, the high detection of subsolid nodules is an increasingly important clinical problem. In the last few years, several guidelines have been published and providing guidance on the optimal management of subsolid nodules, but many controversies still exist. Follow-up imaging plays an important role in clinical assessment and subsequent management of this particular type of lung nodules, since they can be transient inflammatory lesions, and if persistent they can be both benign lesions or lung cancers of variable clinical behaviour. However, the vast majority of subsolid nodules retain an indolent course over many years. The aim of this review is to present a European perspective in management of screening detected subsolid nodules.

Keywords: Screening trial; lung cancer; subsolid nodules; ground glass nodules (GGN); guidelines

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Lung cancer mortality accounts for over 267,900 deaths in the European Union in 2018, with an incidence of 312,645 adults all over Europe. Hungary, followed by Serbia, has the highest incidence of lung cancer worldwide with an age-standardised rate per 100,000 of 56.7 and 49.8 respectively (1). Among the newly diagnosed, it has been estimated that <40% are current smokers, >45% are former smokers and 10–15% have never smoked (2).

Without screening, over 70% of symptomatic lung cancers present with locally advanced or metastatic disease. Early diagnosis, using screening for lung cancer with low-dose computed tomography (LDCT) has been recognised

as a key element to increase the survival rate and curability of the most common cause of cancer death worldwide (3).

After several decades of randomised controlled trials utilising chest radiography that failed to demonstrate a mortality reduction, the National Lung Screening Trial (NLST) recruited over 53,000 ever-smokers and confirmed a 20% reduction in lung cancer mortality rate using annual LDCT compared to chest radiography (4).

Using variable thresholds for smoking history and age as risk factors for screening selection, several European randomised controlled trials (RCT) and observational studies have been completed or are ongoing.

These include the Italian lung study (ITALUNG) (5), the Dutch-Belgian lung cancer screening trial (NELSON) (6), the UK lung cancer screening (UKLS) (7), the Detection and screening of early lung cancer with novel imaging technology (DANTE) (8), the Danish lung cancer screening trial (DLCST) (9), the German lung cancer screening intervention trial (LUSI) (10), the Multicentre Italian lung detection (MILD) (11) and the CT screening for lung cancer study (COSMOS) (12) (*Table 1*).

The consequence of multiple European RCT that are small in size, heterogeneous in design, and variable in selection criteria, is a collection of trials that is statistically underpowered. The only European fully powered RCT trial that has provided mortality and cost-effectiveness data is the NELSON trial, another trial that achieved statistical significance is the MILD trial (13).

Even though the impact of LDCT screening in high-risk ever-smokers has been established, its benefit in never-smoker population is still under debate. Currently, in Europe, no screening trial has been conducted in never-smoker population and also the current recommendations in USA state that never-smokers should not be screened. However, this category should not be neglected as the percentage of lung cancer in never-smokers has been growing progressively, particularly in East Asian countries (14).

The criteria to select who should be screened, within never-smoker population, are yet unknown, but several Asian studies have been published/are ongoing, in order to identify who would benefit the most from LDCT screening and to assess its benefits and harm. An interesting study, recently published by Kang *et al.*, has revealed that most (>80%) of the lung cancers detected in never-smoker population, presented as subsolid nodules and almost all were adenocarcinoma (stage I in 80% of cases) (15).

Nelson and MILD trials

The results of NELSON trial, which recruited 15,792 subjects randomly assigned between screen arm with LDCT (7,900 individuals) and no screen arm (7,892 individuals), have been presented at the 2018 World Conference on Lung Cancer (WCLC), showing that asymptomatic males at high risk for lung cancer have a reduced risk of dying from lung cancer of 26% at 10 years in the screen arm compared to male in the control arm. Moreover, in the subgroup of female participants, the risk reduction is consistently more favourable ranging between 39% and 61% (6).

The 10 years results of MILD trial, that randomized 4,099 participants, to a screening arm [2,376 individuals; additional randomization to annual (1,190) or biennial (1,186) LDCT], or control arm (1,723 individuals), have recently been published. The screen arm has revealed a 39% reduced risk of lung cancer mortality and a 20% decrease of overall mortality compared with control arm (11).

In addition, during the 2019 WCLC, the initial results of the new bioMILD prospective trial, a screening program which combines LDCT and blood microRNA (miRNA) assay in 4,119 volunteers, have been presented. The screening timeline was set according to baseline LDCT and miRNA profile: the double negative LDCT and miRNA repeated LDCT after 3 years, the one positive (positive miRNA or indeterminate/positive LDCT) and the double positive (positive miRNA and indeterminate/positive LDCT) were directed to annual or shorter LDCT. Both the cumulative incidence and mortality for lung cancer were significantly different in the three groups: the risk is significantly higher ($P<0.0001$) in subjects with a single positive (HR =6) and double positive test (HR =36.6); also the mortality is significantly higher ($P<0.0001$) in single positive (HR =4.7) and double positive (HR =32.2). The promising results of bioMILD trial, open a window on the possibility of a personalised detection, based on individual biologic risk assessed by miRNA and LDCT. This strategy may lead to an optimal screening timeline, reducing unnecessary LDCT and may help to refine the management of pulmonary nodules (16).

Notwithstanding these impressive results, several controversies still exist regarding overdiagnosis, false positives and the cost-effectiveness of a screening program. However, targeting those participants at highest risk of lung cancer using validated risk stratification models, helps to reduce the risk of overdiagnosis and false positives, and improves cost effectiveness (17-19).

Table 1 European lung cancer screening trials

Trial	Country of Study	Type of study	Recruitment period	Year of publication	Selection criteria		No. of enrolled subject	Screening methods	Percentage of stage I NSCLC (screening *vs.* control arm)	HR (95% CI) mortality rate screening *vs.* control arm
					Age	Pack-years				
ITALUNG (5)	Italy	RCT	2004–2006	2017	55–69	≥20	3,206	Annual LDCT ×4 years *vs.* no screen	36% *vs.* 11%	0.70 (0.47–1.03), P=0.07
NELSON (6)	Netherlands and Belgium	RCT	2003–2006	2018	50–74	≥15	15,792	LDCT year 1, 2, 4 and 6.5 *vs.* no screen	69%	Male: 0.74 (0.60–0.91), P=0.003; female: 0.61 (0.35–1.04), P=0.0543
UKLS (7)	United Kingdom	RCT	2011–2014	2016	50–75	LLP_{V2} risk model	4,055	Single LDCT *vs.* no screen	67%	–
DANTE (8)	Italy	RCT	2001–2006	2015	60–75	≥20	2,450	Annual LDCT ×5 years *vs.* no screen	71% *vs.* 22%	0.99 (0.69–1.43), no statistically significant
DLCST (9)	Denmark	RCT	2004–2006	2016	50–70	≥20	4,104	Annual LDCT ×5 years *vs.* usual care	50% *vs.* 16%	1.03 (0.66–1.6), P=0.888
LUSI (10)	Germany	RCT	2007–2011	2015	50–69	≥15	4,052	Annual LDCT + smoking cessation ×5 years *vs.* smoking cessation alone	72%	0.74 (0.46–1.19, no statistically significant)
MILD (11)	Italy	RCT	2005–2011	2019	4–75	≥20	4099	No screen *vs.* annual LDCT *vs.* biannual LDCT ×10 years	50% *vs.* 21%	0.61 (0.39–0.95), P=0.02
COSMOS (12)	Italy	Non-randomized	2000–2001	2017	>50	≥20	5203	Annual LDCT ×10 years	–	–

RCT, randomized controlled trial; LLP_{v2}, Liverpool Lung Project risk model, version 2; LDCT, low-dose computed tomography; NSCLC, non-small cell lung cancer; HR, hazard ratio; CI, confidence interval.

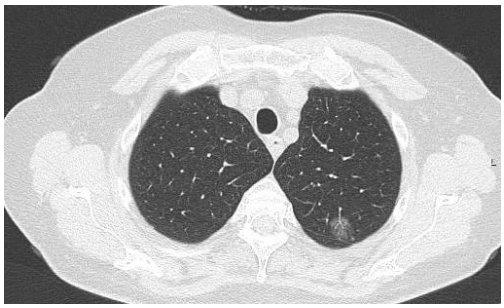

Figure 1 Computed Tomography image of pure ground-glass opacity (GGO).

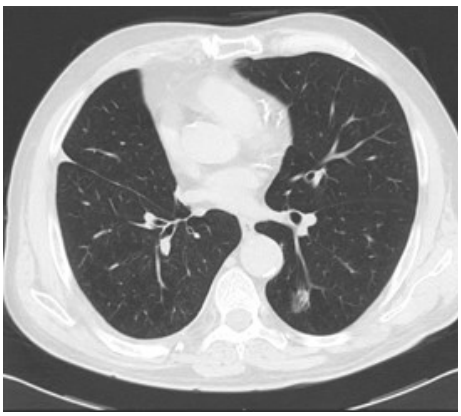

Figure 2 Computed tomography image of part solid ground-glass opacity (GGO).

The lung nodule is the main target of LDCT during a screening trial: its size, location, multiplicity, density and imaging features at first diagnosis are the parameters that inform the diagnostic algorithm. Pulmonary nodules can be categorised as solid or subsolid, and the subsolid category can be further separated into pure ground glass nodules (pGGN) and part-solid nodules (PSN) (*Figures 1*,*2*). The risk of each nodule being malignant differs between prevalence and incidence rounds, with incident nodules typically less frequent but more likely to progress to lung cancer (20). For each nodule category, risk of malignancy varies with CT morphology, nodule size and size of solid component: these features largely determine whether a LDCT is regarded as negative, positive or indeterminate. Nodules less than 5 mm can be ignored (a negative scan), irrespective of morphology, but the frequent detection of small lung nodules at baseline (solid nodules, typically 5–7 mm in size, or equivalent volume of sub solid nodes) creates an "indeterminate" category, neither positive or negative, where an additional LDCT is required to assess short-term behaviour. In the European trials (among 18,931 screenees) the prevalence of indeterminate nodules may be as high as 17%. Consequently, more than one in six patients required supplementary LDCT but an indeterminate result may be psychologically less harmful and limit the potential for physical harm by favouring surveillance over invasive biopsies or even surgical resection (21).

Sub-solid nodules, defined as a focal area of hazy increased attenuation on CT through preservation of bronchial and vascular structures, show a higher risk of malignancy compared to solid nodules (22). These particular nodules are radiologically distinguished into 2 types: pure GGNs which do not present any solid component, and part-solid or mixed GGNs that have both a pGGN and a consolidated part (23).

Although most sub-solid nodules are transient (with a disappearance rate of 38% in pGGN and 49% in PSN) (24), persistent sub-solid nodules, especially part-solid, have a high probability of malignancy when compared to solid nodules: 34% for pGGN, 63% for PSN, and only 7% for solid nodules (22). However, these estimates predate the latest version of the lung cancer staging manual (TNM VIII) and most recent WHO classification of lung tumours. Here, 'bronchoalveolar cell carcinoma' is replaced by 'adenocarcinoma in situ', and a new entity of minimally invasive adenocarcinoma is recognised, both with indolent courses and long-term survival without intervention. Consequently, as the majority of subsolid lesions reflect a preinvasive and minimally invasive histology (25,26) they have a better prognosis and typically possess a slow rate of progression to invasion, itself heralded by the development of a solid component (>5 mm, or volume equivalent) and detectable by serial CT imaging.

Subsolid nodules detected in European screening trials

Three subset analyses based on MILD and NELSON trials populations have been conducted to clarify the frequency of subsolid nodules and how many invasive lung cancers develop from subsolid nodules during the screening program (27-29).

In the study conducted by Scholten *et al.* (27), all individuals who had a subsolid nodule ≥5 mm in NELSON trial database on any LDCT round, have been analysed. The median follow-up was 95 months (range, 20–110 months). Among 7,135 volunteers, 264 subsolid nodules in 234 individuals (3.3%) were detected. The majority (63%, 147/264 in 126 participants) disappeared at

follow-up, favouring a surveillance approach. Among 117 persistent subsolid nodules in 108 volunteers, 11 nodules in 8 participants were resected and 5 nodules in 5 participants could not be evaluated due to missing data. Therefore, a growth-rate analysis has been conducted on 101 subsolid nodules in 98 individuals. Eighty-one persistent subsolid nodules were prevalent nodules and 36 were incident. Forty-eight nodules were PSN at detection; 69 nodules were pGGN at the time of detection and 20 nodules developed a solid component during follow-up. Since an approach based on close follow-up of persistent nodules was chosen during the trial, only 33 GGNs (28.2%) were resected. Among them 5 nodules were benign (1 pure GGN, 4 part-solid GGN), 9 were adenocarcinoma *in situ* (6 pure GGNs, 1 part-solid, 2 pure GGNs which developed a solid component) and 19 were invasive carcinoma (4 pure GGNs, 10 part-solid, 5 pure GGNs which developed a solid component). The authors concluded that long-term follow-up could be a safe choice in management of persistent subsolid nodules and only suggest an intervention (stereotactic radiotherapy or percutaneous interventions or surgery) where subsolid nodule demonstrates ≥30% growth or develops a new solid component (27).

Silva *et al.* (28) have analysed patients who had subsolid nodule at baseline LDCT in MILD trial database. The follow-up time was 50.26±7.3 months. Among a total of 1866 subjects, 76 subsolid nodules were identified in 56 individuals (3%) (48 pGGN and 28 PSN). At follow-up fifteen pGGN (31.3%) disappeared, four (8.3%) reduced in size, 21 (43.8%) remained unchanged, and 8 (16.7%) increased in size. For PSN with a solid component <5 mm [26/28], 3 disappeared at follow up (11.5%), 11 (42.3%) remained stable, and 12 (46.2%) progressed. Only two PSN with a solid component >5 mm were identified, one reducing in size and one remaining stable. In this cohort only one lung cancer occurred from a PSN, and was resected at stage IA. The authors conclude that in the absence of clinical disease progression of subsolid nodules, a conservative management approach with active surveillance should be recommended (28).

A further analysis has recently been conducted by Silva *et al.* (29), using the MILD trial database (2,303 participants) and a median follow-up time of 9.3±1.2 years. Out of a total of 6,541 detected nodules in 1,227 subjects, the number of subsolid nodules was 389 (16.9%), 284 detected at baseline LDCT (12.3%). Another 105 nodules were observed during follow-up (2.3% during 2-year follow-up and 2.8% at 4 years). During observation, only 30 lung cancers were detected in 389 volunteers with subsolid nodules (7.7%), and only 26.7% [8/30] of these developed invasive carcinomas. Lung cancers resulting from subsolid nodules were all adenocarcinomas, four at stage IA, three at stage IB and one at stage IIIA (multifocal adenocarcinoma). During the follow-up period no volunteers died for lung cancer arising from a subsolid nodule. The authors concluded that a conservative management approach for screening detected subsolid nodules does not increase the mortality and does avoid unnecessary surgeries. A more aggressive approach may cause pulmonary function loss in subjects at risk for developing a cancer in different sites as the authors postulate that subsolid nodules are a phenotypic expression of a lung cancer predisposition, and should be considered as a prognostic indicator rather than diagnostic marker (29).

Open controversies on subsolid nodules

The relatively high proportion of GGNs detected in the MILD trial (16.9%) increases the question on the correct management of subsolid nodules detected during screening trial.

During a screening program, an appropriate balance is required between the benefits of early resection of an eventually invasive lung cancer, and the possible harms inherent in all screening programmes. One of the more likely worries is the unnecessary treatment of benign lesions or indolent tumours, as the majority of sub solid nodules are. For this reason, subsolid nodules are one of the leading causes of overdiagnosis, over management, and overtreatment in lung cancer screening (19).

Three important parameters of GGNs can predict the malignancy potential of the nodule and guide its management: the size, the proportion of solid component and the growth. Additional parameters such as participant age and comorbidity may also influence the clinical decision-making process.

According to size and proportion of solid component, several guidelines have been written and are summarized in *Table 2* (30-34). BTS and ACCP guidelines recommend to use the same diagnostic approach for incidentally found and screen-detected subsolid nodules, Lung-RADS and NCCN guidelines refer specifically to screen-detected nodules and Fleischner Society criteria are intended for incidentally found nodules only.

A recent systematic review on slow-growing tumours that arose from subsolid nodules, has showed that the

Table 2 Guidelines for screening detected GGN

Guideline	No Follow-up	3-month follow-up	6-month follow-up	12-month follow-up	Further diagnostic procedure
ACCP (30)	pGGN ≤5 mm	psGGN ≤15 mm	–	pGGN >5 mm	psGGN >15 mm
LungRADS (31)	–	psGGN ≥6 mm, SC 6–8 mm	pGGN ≥20 mm; psGGN ≥6 mm, SC <6 mm	pGGN <20 mm, psGGN <6 mm	psGGN, SC ≥8 mm
Fleischner (32)	pGGN <6 mm, psGGN <6 mm	pGGN ≥6 mm, psGGN ≥6 mm	–	–	psGGN≥6 mm
NCCN (33)	–	pGGN >10 mm, psGGN 6–8 mm	pGGN 5–10 mm	pGGN <5 mm, psGGN <6 mm	psGGN ≥8 mm, SC ≥6 mm
BTS (34)	GGN <5 mm	GGN≥5 mm	–	–	–

NCCN, National Comprehensive Cancer Network; ACCP, American College of Chest Physicians; BTS, British Thoracic Society; pGGN, pure ground glass nodule; psGGN, part solid ground glass nodule; SC, solid component.

proportion of the solid component, but not their total size, is associated with long term outcome (35).

Alternatively, volume and volume doubling time (VDT) using a semi-automated segmentation software can be used to evaluate and monitor nodule dimension over time. This approach allows an accurate estimation of nodule size for solid nodules, but it is less accurate for subsolid ones. The volume alone is not specific enough for growth evaluation of GGN since the variation can be displayed by increasing density of the nodule, where the volume itself may be unchanging or even reduced. Therefore, the growth rate of subsolid nodules should be defined by nodule mass, a combination of volume and density (36,37).

Consequently, mass doubling time (MDT) could be considered a preferable measure of subsolid nodule progression. de Hoop and colleagues reinforce the indolent nature of invasive carcinomas derived from subsolid nodules with an MDT >400 days (35). Long-term follow-up, rather than immediate investigation, seems to be the most clinically effective approach for subsolid nodules, where features of aggressive biological behaviour are absent.

Further controversies regarding diagnostic approach in subsolid nodules, are the role of positron emission tomography (PET) and of transthoracic biopsy.

It is well known that false-negative results during an ^{18}F-FDG PET-CT may arise in small nodules, in tumours with low growth and metabolic activity (e.g., AIS or MIA). The greatest limit of PET-CT is represented by small pGGN (especially <10 mm) that are usually PET negative. Moreover, due to the low probability of nodal involvement or distant metastases associated with pGGN (consequent upon a lack of invasion), the role of PET-CT is limited (38-40).

Several studies confirm the low sensitivity of PET-CT in adenocarcinoma presenting as pGGN that is reported to be less than 40% (41-43).

In contrast, there is a clear role for the use of ^{18}FDG PET-CT in the diagnostic assessment of subsolid nodules where PSN with a solid component >10 mm, and may be indicated in those with a solid component between 5 and 10 mm, but a higher rate of false negative results can be expected (44).

The use of transthoracic biopsy in subsolid nodules requires careful consideration, particularly within the context of screening. It should be reserved for those subsolid nodules that persist, declare significant growth, develop a new solid component (>5 mm) or other concerning features for invasive malignancy (45,46). Its diagnostic performance is lower than that for solid nodules (45) and complication rates are higher: subsolid nodules are an independent risk factor for percutaneous biopsy-related haemoptysis (47). However, it is preferable to gain cytological or histological confirmation prior to surgery to minimise benign resection rates, facilitate consent and reduce operating costs.

Several investigators have commented on an appropriate management strategy for subsolid nodules. Zhan and colleagues suggest careful consideration of subsolid nodule features favouring a watchful approach in case of very low probability of relevant cancer. Where risk of malignancy is intermediate, PET-CT and/or transthoracic biopsy are advised, and finally, in case of high probability of cancer, surgical excision should be considered (48).

In the MILD protocol, both pGGNs and PSN with a solid component <5 mm, have been followed up (with LDCT) without taking into consideration their size and number. PSN larger than 8 mm with a solid component >5 mm has been addressed to PET-CT and/or diagnostic

Table 3 Management of solid and part solid nodules in NELSON and MILD screening trials

Screening trial	Positive	Indeterminate
NELSON	• Prevalent nodule >500 mm^3; • VDT <400 days	• Prevalent nodule 50–500 mm^3/incident 15–50 mm^3: LDCT after 3 months; • Incident nodule 50–500 mm^3: LDCT after 6–8 weeks; • VDT between 400 and 600 days: annual LDCT
MILD	• Prevalent/incident nodule >250 mm^3	• Prevalent nodule 60–250 mm^3/incident 1–250 mm^3: LDCT after 3 months

VDT, volume doubling time, refer to the solid component of part-solid nodule or to the entire volume of solid nodules. Positive, detection in LDCT which requires diagnostic work-up; Indeterminate, LDCT findings requiring additional LDCT.

percutaneous biopsy (11,28).

Within the NELSON protocol, only PSN with a solid component >500 mm^3 at baseline have been referred for further investigations. All other subsolid nodules have been followed over time and evaluated in case of growth or density change. Considering mass as a parameter, the authors have concluded that a total increase in mass <30% is consistent with non-malignancy. Change in mass ≥30% demonstrates an increased likelihood of malignancy but non-malignant change remains very possible. Where there is a change in mass ≥30%, the increase of a solid component or the appearance of a new solid component, suggests that a minimally invasive intervention should be considered (6,27). *Table 3* summarises the management strategy of solid and part-solid nodules in NELSON and MILD screening trials.

Both the MILD and NELSON trials demonstrated the characteristic slow growth and indolent behaviour of subsolid nodules. Scholten *et al.*, in their analysis with a median follow-up of 95 months, also demonstrated, using a cut-off of 30% growth in mass and/or volume of the solid component, that no clinically relevant tumours were missed (27).

In accordance with the European trials finding, a recent ESR/ERS statement paper on lung cancer screening, suggests a conservative management of subsolid nodules (49).

The authors state that a possible strategy to decrease overdiagnosis and overtreatment is based on:

- The use of risk models for a comprehensive stratification of individuals and nodules;
- Conservative management of GGNs;
- Assessment of the VDT;
- A lengthened screening interval.

Role of surgery

Since guidelines on subsolid nodule management are still lacking, surgical indications are frequently based on surgeons' behaviour and understanding of the natural history, and the patient's wishes, also influenced by their understanding of the problem. Every patient should be discussed within a multidisciplinary team to determine optimal diagnostic and therapeutic strategy.

After an appropriate follow-up period, in case of persistent PSN with solid component greater than 10 mm, particularly with a solid component >5 mm and/or ^{18}F-FDG PET positive, surgical resection may be appropriate (preferably following histologic confirmation by CT biopsy or navigational bronchoscopy) (50).

If surgical resection is considered to be necessary, a minimally invasive approach is advised. Although minimally invasive lobectomy is considered the gold standard treatment for early stage NSCLC, anatomical segmentectomy or wide wedge resection and lymph node sampling may offer promising results for small tumours <2 cm in size and affords an opportunity for lung sparing resection where metachronous second primary lung cancers may be more common (51).

Two recent reviews and one meta-analysis state that sublobar resection for pure adenocarcinoma *in situ* ≤2 cm, produce similar long-term outcomes as lobar resection (52-55).

The JCOG0804/WJOG4507L trial, analysing the impact on long term survival of wide wedge resection in ground-glass opacity (GGO) dominant peripheral lung cancer (with maximum tumour diameter ≤2.0 cm and with consolidation tumour ratio ≤0.25), has shown a 5-year relapse-free survival (RFS) of 99.7%, with no local recurrences. This study concludes that sublobar resection (primarily wedge resection) offers adequate local control and RFS for peripheral GGO-dominant lung cancer (56).

These publications collectively demonstrate good long-term outcomes when surgically resecting *in-situ* or minimally invasive disease, which it may be argued would have occurred in any event. Surveillance imaging remains the optimal management for these entities until imaging suggests the possibility of invasion. Whether sublobar resection is the optimal treatment strategy for small screen

detected invasive carcinomas remains a subject of debate.

If sublobar resection as a parenchymal sparing surgery is considered, percutaneous or bronchoscopic ablation therapies (microwave or radiofrequency) or stereotactic radiotherapy may also play a role and have the advantage in presence of multiple lesions that may be treated with preservation of lung function (57). The main question remains, as to whether such lesions are relevant and require treatment.

Conclusions

Modern screening strategies are detecting an increasing number of subsolid nodules, that remain one of the leading causes of overdiagnosis and overtreatment during lung cancer screening.

Data from MILD and NELSON confirm an indolent behaviour of lung cancer originated from subsolid nodules and confirms that careful surveillance of subsolid nodules should be performed in the first instance, to identify biologically relevant nodules (especially PSN with a solid component >5 mm, a new solid component and a short mass doubling time) justifying the risks of further investigation, biopsy and treatment.

Although several guidelines are available to guide physicians in nodule management, many controversies remain regarding timing and extent of surgical resection. Ultimately, decision making will require appropriate patient counselling and an understanding of the risk of malignancy, risk of treatment and expected benefit. Designated screening centres should have a clear management strategy for the evaluation and treatment of subsolid nodules to minimise harms.

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