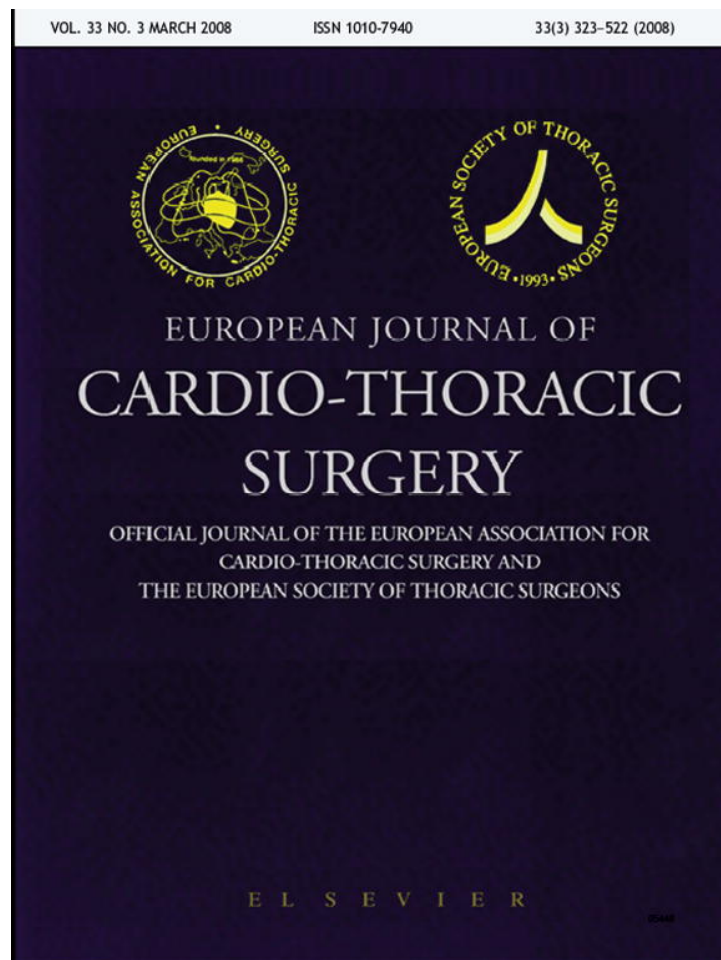


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Management of solitary pulmonary nodule

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Abstract

Objectives: The pulmonary nodule is an important diagnostic and therapeutic problem. Diagnostic certainty is only obtained by histological examination. Mini-invasive surgery allows removal of the nodule with minimal sequelae for the patient. **Methods:** From October 1991 to December 2006, 370 resections for a pulmonary nodule were performed at our Department of General Surgery of the University of Milan: 276 wedge resections and 94 lobectomies. **Results:** Frozen section was performed in all the wedge resections, and in the presence of cancer (77 cases), whenever possible (61 cases), the intervention was converted to lobectomy in the same session. In the other 94 cases, the nodule was removed by lobectomy due to the impossibility of performing a wedge resection. **Conclusions:** Despite the refinement of diagnostic techniques, only exeresis of a pulmonary nodule ensures a definitive diagnosis, thus resolving the problem of benign pathologies and initiating the correct therapy for malignant lesions in the same session.

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Keywords: Coin lesion; Pulmonary nodule; Videothoracoscopy; Non-small cell lung cancer; VATS surgery

1. Introduction

The pulmonary nodule is a neof ormation of unknown origin that appears at chest X-ray as a well-defined opacity of 1–3 cm in diameter, surrounded by normal pulmonary parenchyma and not associated to atelectasis or adenopathy [1]. There are more than 80 aetiologic possibilities, and they vary from benign to primary or metastatic pulmonary cancer [2].

In the last 20 years, the introduction of modern imaging techniques, fine-needle aspiration (FNA) [3] and positron emission tomography (PET) [4] has improved the diagnostic possibilities without, however, definitively resolving the problem. Surgical resection obtains a sure diagnosis and removal of the nodule. However, in the past, there were objections to surgery because of invasiveness of thoracotomy in the presence of a lesion that is often benign, observed in young patients, and usually asymptomatic. Refinement of videoendoscopic techniques at the beginning of the nineties made it possible to perform such interventions with a minimally invasive access [5,6].

We report our experience with videothoracoscopic (VTS) surgery in the treatment of solitary pulmonary nodules and

analyse the evolution of the diagnostic–therapeutic techniques developed in the last 20 years.

2. Material and methods

2.1. Patients

During the period October 1991–December 2006, 2921 VTS procedures were performed at our Department of General Surgery of the University of Milan. Of these, 370 were VTS resections performed for a pulmonary nodule (276 by wedge resections and 94 lobectomies).

The other VTS operations are detailed in Table 1.

The patients were 295 males and 75 females, with an average age of 69 (range 36–87 years), bearing nodules ranging from 0.6 cm to 3 cm. The mean nodule diameter was 2.5 cm.

The decisional algorithm followed for managing the solitary pulmonary nodule is reported in Fig. 1.

2.2. Wedge resection

A total of 276 wedge resections (220 males and 56 females) were performed for a pulmonary nodule of unknown origin. The average age was 70 years (range 36–87) with 59 patients over 75 years old. Twenty-seven patients had a

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Table 1
VTS procedures 1991–2006

2921 VTS procedures
284 major pulmonary resections
538 wedge resections
249 procedures for pleural pathologies
240 procedures for pneumothorax
165 procedures for mediastinal pathologies
117 procedures for emphysema
1224 videothoroscopic operative staging
104 procedures for other pathologies

Table 2
Histology of pulmonary nodules removed by wedge resection

77 primary malignancy	138 benign lesion	61 metastasis
50 adenocarcinoma	28 TB	30 from colon carcinoma
17 squamous carcinoma	7 mycetoma	6 from renal carcinoma
4 bronchioloalveolar carcinoma	7 sarcoidosis	12 from breast carcinoma
4 small cell lung cancer	4 anthracosis	6 from lung carcinoma
2 carcinoid	10 pulmonary fibrosis	2 from ovarian carcinoma
	16 chronic aspecific phlogosis	2 from bone neoplasm
	59 pulmonary amartoma	3 fibrosarcoma
	7 fibrous tumour of pleura	

nodule between 0.5 cm and 1 cm, 158 had a nodule ranging between 1 cm and 2 cm, and 92 patients had a nodule ranging between 2 cm and 3 cm. The mean nodule diameter was 2.3 cm (range 0.7–3). Post-resection histology revealed 77 primary malignant neoplasms, 138 benign lesions and 61 metastases. The details are reported in Table 2.

In the 138 cases in which frozen section examination indicated a benign or inflammatory nodule and in the 61 cases it evidenced the presence of a metastatic neoplasm, the intervention was concluded with a wedge resection. In 50 of the 77 cases in which the frozen section examination revealed a primary carcinoma, the intervention was converted to a lobectomy in the same operative session;

25 times via VTS and 28 by thoracotomy due to technical difficulties. In 24 cases the intervention was limited to a wedge resection owing to the presence of one or more high surgical risk conditions that contraindicated a wider pulmonary resection. After the introduction of a wire hook, which was positioned in 39 cases, we had no difficulty in localising the nodule in 34 patients, while we observed the rupture of the wire hook in 3 cases and the displacement of the device in another 2 patients. No intra or postoperative mortality or morbidity was recorded. The average post-operative hospitalisation was 3 days (range 2–7).

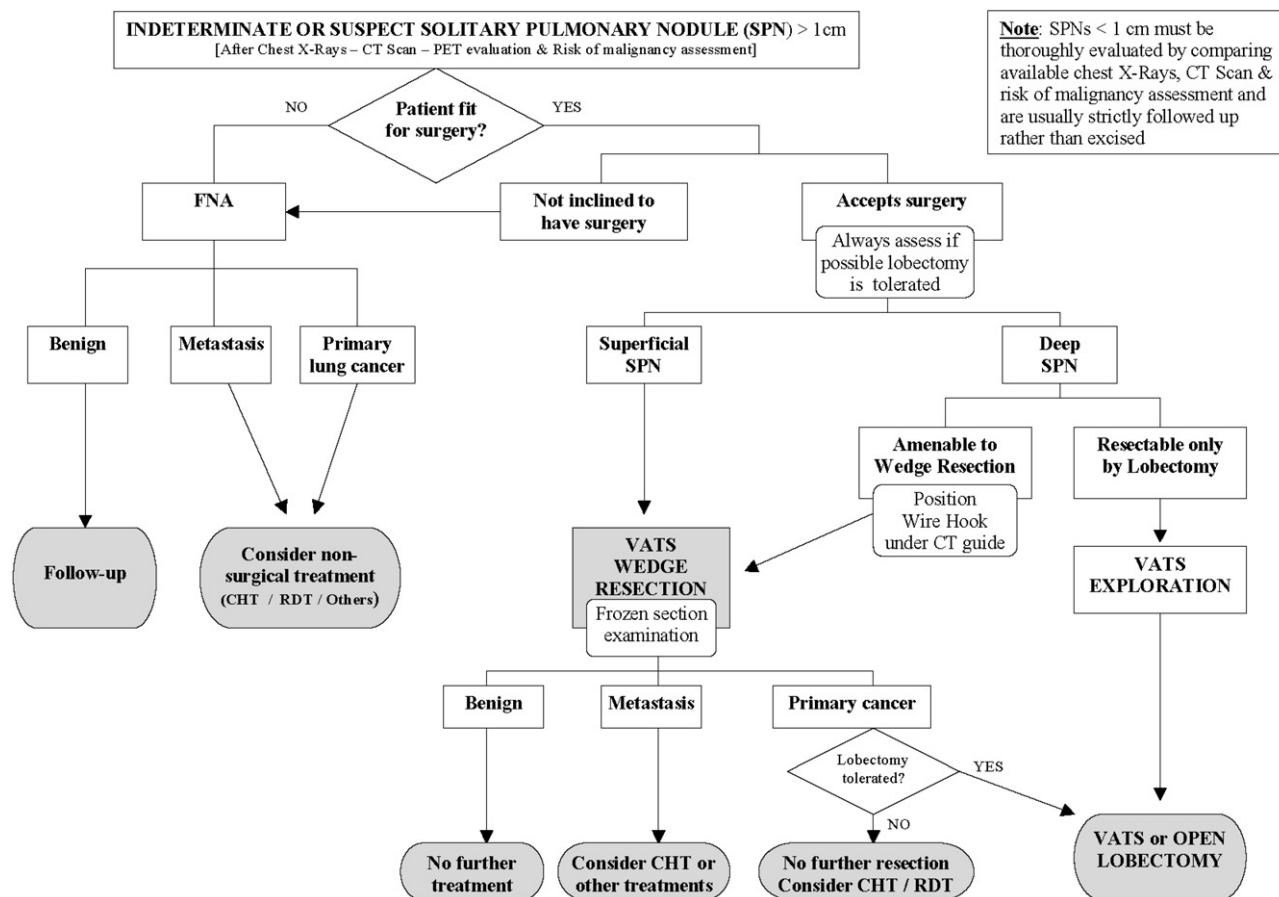


Fig. 1. Indeterminate or suspect solitary pulmonary nodule (SPN) > 1 cm. (After chest X-rays–CT scan–PET evaluation and risk of malignancy assessment.) Note: SPNs < 1 cm must be thoroughly evaluated by comparing available chest X-rays, CT scan and risk of malignancy assessment and are usually strictly followed up rather than excised.

Table 3
Histology of pulmonary nodules removed by lobectomy

65 primary malignant	10 metastasis	19 benign lesion
29 adenocarcinoma	6 from colon carcinoma	8 chronic aspecific phlogosis
31 squamous carcinoma	4 from breast carcinoma	4TB
5 carcinoid		3 mycetomas
		4 hamartomas

2.3. VTS lobectomy

A VTS lobectomy was performed in 94 patients because of the technical impossibility of performing a wedge resection owing to the deep location of the nodule and its relation with hilar structures. The average age of these patients was 67.5 (range 41–83). Histology is reported in Table 3.

Relevant postoperative complications were protracted air loss (8 cases) and the formation of pleural empyema without fistula (1 case). Average postoperative hospital stay was 5 days (range 3–10).

2.4. Technical notes

The operation is performed under general anaesthesia with the patient in lateral decubitus and intubated with a double lumen Carlens' tube that ensures selective one-lung ventilation. The trocar for the optics is inserted in the 7th intercostal space along the mid-axillary line, and another port is positioned in the 5th interspace posteriorly. A 3 cm inframammary utility thoracotomy is performed along the 4th interspace for the insertion of operating instruments and the withdrawal of the resected specimen. Identification of the nodule is the crucial step of the operation: the area of the nodule is palpated with an endoscopic instrument to locate a hard area, an index of the presence of the lesion. Such a manoeuvre gives optimal results when the nodule is superficial and when its consistency is increased with respect to that of the surrounding parenchyma. In cases of difficult localisation of the nodule, it may be useful to mobilise the lung by sectioning the triangular ligament and opening the mediastinal pleura anteriorly and posteriorly to the hilum. In this way it is possible to bring the lung near to the anterior wall by means of traction with Duval's forceps and to palpate also the posterior segments with an instrument. When even this manoeuvre is not sufficient, it is possible to enlarge the utility thoracotomy and introduce one or more fingers for digital palpation.

In all the cases in which the deep position of the nodule predicts a difficult intra-operative localisation, a percutaneous wire hook is positioned under CT guide, immediately before surgery. This allows intra-operative localisation and traction of the nodule to facilitate its resection [7].

Once identified, the nodule is resected with the aid of one or more shots of an endoscopic automatic stapler, which provides an airtight suture.

The size and the site of the lesion affect the number of cartridges required. When the nodule is localised near an acute edge of the pulmonary lobe, or near a fissure, or along the costo-diaphragmatic margin, positioning of the endo-

stapler is easy. On the other hand, when the nodule is on the convex surface of the lung, appropriate traction on the parenchyma containing the lesion must be exerted to ensure tangential positioning of the stapler beneath the nodule. This is not always easy as the thickness of the parenchyma, and the limited opening of the stapler jaws hinder the proper positioning of the stapler when the nodule is deeply located. In these cases an inviting stapling shot can be conducted obliquely to the lung surface to facilitate the exposure of the nodule and the positioning of the stapler.

The surgical specimen is then retrieved through the minithoracotomy protected with an endoscopic plastic bag and sent for the frozen section examination. If histology reveals the presence of a primary lung cancer, and there is no contraindication to a wider lung resection, the procedure is converted to a formal lobectomy in the same session. Conversely, or in cases of benign disease, surgery is limited to a wedge resection.

Lobectomy can be performed via VTS or thoracotomy depending on the technical feasibility, specific experience and philosophy of the surgeon. The technique of VTS lobectomy has already been described elsewhere [8].

3. Discussion

The finding of a pulmonary nodule always presents diagnostic and therapeutic problems. Such lesions are usually benign, but the possibility of a malignant aetiology (30% according to the literature, 55% in our series) makes it mandatory to obtain a definitive diagnosis as quickly as possible. For primary cancer of the lung, early surgical excision is the only therapy currently offering a reasonable guarantee of cure [9]. Even when dealing with secondary localisations of neoplastic diseases in patients already submitted to radical excision and with apparent control of the primary disease, surgical removal of the secondary lesion is considered the therapy of choice [9]. Obviously, in the presence of a pulmonary nodule of unknown origin, the clinical history of previous resection of cancer suggests a pulmonary metastasis; but there are exceptions. In fact, in our experience there were 5 out of 61 cases in which the frozen section examination indicated a benign histology (three hamartomas, one fibrous tumour of pleura and one TB). In the same way there were five cases in which frozen section indicated the presence of metastases of unsuspected primary tumours (two from colon carcinomas, two from renal carcinomas and one from breast). Finally, in two patients with previous history of colonic cancer resection and with a pulmonary nodule of possible metastatic nature, frozen section histology of the nodule resected by a VATS wedge resection revealed a primary lung tumour and demanded a formal lobectomy. This was performed in one patient thoracoscopically and in the other with an open thoracotomy approach.

History and availability of previous X-rays can sometimes aid in the diagnosis. High-density CT provides useful information on the presumed nature of the nodule by evaluation of the densitometry, characteristics of the margin, and infiltrating nature of the lesion [10].

However, even the most careful and accurate imaging study does not give a diagnosis of the nature of the nodule, which can be ascertained only by a cyto-histological study.

Bronchoscopy is not definitive, because the parenchymal site of nodule is difficult to reach endobronchially. The possibility of obtaining a correct diagnosis by means of such techniques depends heavily on the specific experience of the physician. Data in the literature are extremely variable, depending on the benign (0–10%) or malignant nature (20–80%) of the lesion, and whether it is >2 cm in diameter and situated between 2 cm and 6 cm from the hilum (71%), or <2 cm in diameter and situated more than 6 cm from the hilum (27%) [11].

At the beginning of the 1980s, the introduction of FNA changed the diagnostic work-up of pulmonary lesions. FNA is mildly invasive and provides material for cytological evaluation. In the study of Li et al. [12], the diagnostic accuracy (calculated by comparing cytological diagnoses based on biopsy with final diagnoses based on histological findings from surgery or autopsy) of large nodules (>1.5 cm in diameter) was 96%, whereas for small nodules (<1.5 cm in diameter) it was 74%. FNA thus has a good diagnostic accuracy for malignant lesions, but is limited in the evaluation of benign lesions. The diagnosis of 'absence of malignant tumour cells' in the sample is always interlocutory and not definitive, in that there is no guarantee regarding the adequacy of the sample itself.

The development of modern techniques of nuclear medicine, with the introduction of PET, has opened new horizons in the diagnostic work-up of pulmonary nodules. It is a non-invasive method with a good diagnostic accuracy, but like FNA, it cannot establish with absolute certainty the aetiology of the disease [13]. PET has a sensitivity, specificity and positive predictive value of 93%, 88%, and 92%, respectively, for detection of malignancy in indeterminate solitary pulmonary nodules. The probability of malignancy with a positive PET scan is 83%, and a negative PET scan has a 5% risk of malignancy [14]. Furthermore, bronchioloalveolar carcinomas can be silent at PET scan. More recent studies have led to the same conclusions.

At present the only certain diagnosis of the nature of the nodule is obtained by histological examination of the surgical sample [15–18].

The perplexity of the clinician and patient when confronted by surgical exeresis is due to the entity of the trauma linked to thoracotomy for a lesion that in most cases is benign. The advent of VTS surgery has greatly reduced the surgical trauma, the hospitalisation period, postoperative pain, and time to recovery of full activity, thus giving a valid response to these problems [19].

The operative risk with a VTS wedge resection is low, there is no intra-operative mortality, and complications are rare, as predicted by Baldwin et al. in a very important study published in 2002 [20] and as confirmed by large series reported in the literature [21].

From the technical point of view, wedge resection is simple because it is not necessary to isolate hilar structures. However, the lack of manual palpation can sometimes hinder localisation if a lesion is located particularly deep within the parenchyma or when its consistency closely resembles that of the surrounding parenchyma as emphasised by many authors.

Different methods have been developed to avoid the difficulty of localising a deep pulmonary nodule [22–24]. The most widely diffused method is that of the wire hook positioned immediately before the operation under computed tomography guidance [7,25]. The advantages of this method are linked to the fact that the collapse of the lung does not modify the position of the wire hook, which remains anchored to the nodule. Moreover, the presence of the wire hook makes it possible to exert a slight traction and thus facilitate the positioning of the endostapler. Caution is advised because the resistance of the thin metallic wire hook is limited and its possible rupture can lead to the loss of any intra-operative reference.

Sometimes, even when the nodule has been precisely identified, wedge resection is not technically feasible. In some cases, the thickness of the parenchyma does not permit the closure of the stapler jaws. When the nodule is located on the convex surface of the lung, it is considerably difficult to position and close the endostapler, without excessive tension on the suture line at the moment of pulmonary re-expansion. In other cases, the deep nodule is in such strict contact with hilar structures as to render a wedge resection impossible. In such cases, removal of the nodule must be done by a lobectomy. Recourse to a lobectomy for technical reasons should be taken into consideration and evaluated preoperatively, as the feasibility of a wedge resection can be verified only at the operation.

Performing a lobectomy for a pulmonary nodule may appear an excessively aggressive approach for a potentially benign pathology. However, major pulmonary resections are carried out legitimately for lesions that post-operatively turn out to be benign tumours or even for tubercular nodules suspected to be scar cancers. In these cases the aggressive approach is counterbalanced largely by the risk of delaying the diagnosis and radical excision in patients bearing a carcinoma.

VTS exeresis of a pulmonary nodule has a fundamental advantage over non-invasive or micro-invasive diagnostic methods such as bronchoscopy, FNA and PET: i.e. the possibility to obtain by a frozen section an immediate, sure and definitive diagnosis. In this way, it is possible to perform a lobectomy after a wedge resection in the course of the same operative session and initiate the oncologically correct surgical therapy when there is a primary pulmonary carcinoma.

Even though lobectomy is the treatment of choice in the case of small peripheral carcinomas, a wide wedge resection is acceptable in strictly selected cases, such as elderly patients with severe cardio respiratory conditions in whom larger lung resections are absolutely contraindicated and in patients who have already undergone a contra lateral resection for a tumour [15]. In our experience, wedge resection was converted to a lobectomy for cancer in 50 patients, whereas in the other 24 cases lobectomy was absolutely contraindicated.

Surgical exeresis of the nodule definitively resolves the diagnostic doubt. Sometimes, after completing the non-invasive diagnostic work-up, confronted by the possibility of a non-definitive diagnosis even after a FNA it is the patient who prefers to face the limited risks of a VTS intervention rather than be subjected to repeated controls.

As our experience in the field of thoracoscopic surgery has increased, the indication for FNA of nodules has progressively diminished and indications for surgical VTS exeresis increased. The incidence of patients subjected to FNA dropped from 90% a few years ago to 3% today. Such a tendency to reduce recourse to FNA has also been reported by other authors [19]. FNA has maintained its validity in selected cases, such as patients bearing a pulmonary nodule with particularly high operative risk, which can be dealt with only on the basis of a proven malignancy.

4. Conclusions

In conclusion, in accord with other authors [15–18], we believe that VTS surgical exeresis has had an important impact on the diagnostic–therapeutic management of pulmonary nodules. Its fundamental advantage lies in its immediate, precise and sure diagnostic power.

Wedge resection is surely the intervention of first choice in that it implies minimal functional damage and negligible operative risk. With wedge resection it is possible to resolve the diagnostic query definitively removing benign lesions. In the same operative session, the intervention can be extended and the oncologically correct surgical therapy can be applied in cases of malignant disease.

In patients with good respiratory function and at low operative risk, when wedge resection is impossible for technical reasons, a VTS lobectomy should be performed. Even though the pulmonary nodule is a potentially benign pathology, one should not run the risk of losing precious time in cases of malignant disease in its early phase. The marked reduction in surgical trauma linked to minimally invasive techniques and the optimal results render surgical exeresis of the pulmonary nodule the gold standard for patients with such pathology.

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