Pulmonary Hamartoma Associated With Lung Cancer (PHALC Study): Results of a Multicenter Study

Alfonso Fiorelli (alfonso.fiorelli@unicampania.it)
Universita degli Studi della Campania Luigi Vanvitelli https://orcid.org/0000-0002-0628-613X
Antonio D'Andrilli
Sapienza University of Rome: Universita degli Studi di Roma La Sapienza
Annalisa Carlucci
University of Campania Luigi Vanvitelli: Universita degli Studi della Campania Luigi Vanvitelli
Giovanni Vicidomini
University of Campania Luigi Vanvitelli: Universita degli Studi della Campania Luigi Vanvitelli
Giacomo Argento
Sapienza University of Rome: Universita degli Studi di Roma La Sapienza
Beatrice Trabalza Marinucci
Sapienza University of Rome: Universita degli Studi di Roma La Sapienza
Francesco Ardissone
University of Turin: Universita degli Studi di Torino
Roberta Rapanà
University of Turin: Universita degli Studi di Torino
Simona Sobrero
University of Turin: Universita degli Studi di Torino
Paolo Carbognani
University of Parma: Universita degli Studi di Parma
Luigi Ventura
University of Parma: Universita degli Studi di Parma
Giovanni Bocchialini
University of Parma: Universita degli Studi di Parma
Mark Ragusa
Hospital System of Perugia: Azienda Ospedaliera di Perugia
Valentina Tassi
University of Perugia: Universita degli Studi di Perugia
Francesco Sollitto
Foggia University Hospital: Azienda Ospedaliera Universitaria Foggia
Domenico Loizzi

Foggia University Hospital: Azienda Ospedaliera Universitaria Foggia

Nicoletta Pia Ardò

Foggia University Hospital: Azienda Ospedaliera Universitaria Foggia

Marco Anile

Sapienza University of Rome: Universita degli Studi di Roma La Sapienza

Francesco Puma

University of Perugia: Universita degli Studi di Perugia

Erino Angelo Rendina

Sapienza University of Rome: Universita degli Studi di Roma La Sapienza

Federico Venuta

Sapienza University of Rome: Universita degli Studi di Roma La Sapienza

Nicola Serra

Federico II University Hospital: Azienda Ospedaliera Universitaria Federico II

Mario Santini

University of Campania Luigi Vanvitelli: Universita degli Studi della Campania Luigi Vanvitelli

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Research Article

Keywords: pulmonary, hamartoma, surgical resection, lung cancer

Posted Date: May 11th, 2021

DOI: https://doi.org/10.21203/rs.3.rs-502596/v1

Version of Record: A version of this preprint was published at Lung on July 24th, 2021. See the published version at https://doi.org/10.1007/s00408-021-00460-8.

Abstract

PURPOSE

Pulmonary hamartoma is the most common benign tumor of the lung. We analyzed a 20-year historical series of patients with pulmonary hamartoma undergoing surgical resection, aiming to evaluate the characteristics, the outcomes, and the association between hamartoma and lung cancer.

METHODS

It was a retrospective multicenter study including the data of all consecutive patients with pulmonary hamartoma undergoing surgical resection. The end-points were to evaluate: i) the characteristics of hamartoma, ii) outcomes, iii) whether hamartoma was a predictive factor for lung cancer development

RESULTS

Our study population included 540 patients. Upfront surgical or endoscopic resection was performed in 385 (71%) cases while in the remaining 155 (29%) cases, the lesions were resected 20±3.5 months after diagnosis due to increase in size. In most cases, lung sparing resection was carried out including enucleation (n=259; 48%) and wedge resection (n=230; 43%) while 5 (1%) patients underwent endoscopic resection. Only two patients (0,2%) had major complications. One patient (0.23%) had recurrence after endoscopic resection, while no cases of malignant degeneration were seen (mean follow-up: 103.3±93 months). Seventy-six patients (14%) had associated lung cancer, synchronous in 9 (12%) and metachronous in 67 (88%). Only age > 70-year-old (p=0.0059) and smokers >20 cigarettes/day (p<0.0001) were the significant risk factors for cancer development on logistic regression analysis.

CONCLUSIONS

Surgical resection of hamartoma is a safe procedure; recurrence and malignant degeneration are very uncommon and the association between hamartoma and lung cancer seems to be a spurious phenomenon.

Introduction

Pulmonary hamartoma (PH) is the most common benign tumor of the lung, accounting for 3% of all lung tumors and having an incidence of 0.25% in the general population [1–5]. PH has been initially considered a developmental malformation, but at present it is classified as a true benign mesenchymal tumor [6–9]. Generally, PH presents as a peripheral intraparenchymal solitary nodule incidentally detected during assessments for other diseases [10–12]. Despite the advancement in medical imaging and therapy, surgical resection remains the option of choice for diagnostic and therapeutic purposes [13–16]. However, controversies still exist regarding the indication and timing of surgery, the incidence of recurrence or malignant degeneration of PH and whether PH is a real risk factor for lung cancer development.

In this study, we analyzed a 20-year historical series of patients with PHs undergoing surgical resection, aiming to evaluate the characteristics, the outcomes, and the association between PH and lung cancer.

Materials And Methods

Study design

This was a retrospective multicenter study. All consecutive patients with PH undergoing surgical resection between January 2000-May 2020 were included in the study. Patients with incomplete follow-up were excluded. Data were extracted by data-base and/or medical records of each participant center, and then analyzed. The end-points were to evaluate: i) the characteristics of PH; ii) the outcomes, including recurrence or malignant degeneration; and iii) whether PH could be a risk factor for development of lung cancer.

The study was approved by Local Ethics Committee of University of Campania Luigi Vanvitelli (code number: 17402-20), the coordinating center of the study, and then approved by each participating center.

Patient Data

The following medical and surgical records were reviewed: age at diagnosis; gender; history of tobacco use; previous, concurrent, and subsequent neoplasms; clinical symptoms; location and size of hamartoma; radiological characteristics of PH; rapidity of growth at Chest Computed Tomography (CT) scan; decision for resection; type of resection; histological features, post-operative outcome, follow-up. In case of patients with associated lung cancer, the following information was also collected: time interval between diagnosis of PH and lung cancer, site of lung cancer, stage, histology, and treatment modality.

Statistical Analysis.

Variables were reported as mean ± standard deviation (SD), or median and interquartile range for continuous variables or as number and percentages for categorical variables. Logistic regression analysis was performed to identify prognostic factors influencing the presence of lung cancer. The variables reaching statistically significant difference entered a multivariate regression analysis with forward selection and backward elimination, using lung cancer as endpoint (dependent variable). A $p < 0.05$ was considered statistically significant. We used MedCalc statistical software (Version 12.3, Broekstraat 52; 9030 Mariakerke; Belgium) for analyses

Results

In the study period a total of 555 patients underwent surgical resection of PH. Fifteen of these patients had incomplete follow-up and were excluded from the analysis; thus, our study population included 540 patients. The median age was 61.4 [18–85] year-old, with a peak age at diagnosis between the sixth and the seventh decade (38%); 319 (59%) were male, and 91% were smokers (≥ 20 cigarettes a day). At presentation, 81 (15%) patients were asymptomatic, 444 (82%) patients presented aspecific chest

symptoms (i.e. coughing, expectoration and thoracalgia), and 15 (3%) patients presented specific symptoms as hemoptysis, and pneumonia due to obstruction of the bronchus by PH. Among asymptomatic patients, PH was incidentally discovered on routine follow-up exams for other diseases. The mean diameter of lesion was 18.8 ± 12.4 mm; 98 (19%) patients had tumor larger than 3 cm; 171 (32%) had tumor ≤ 1 cm; in 230 (42%) the tumor size ranged from 10 mm to 20 mm; and in 230 (42%) from 20 to 30 mm. On CT scan, the most common image for tumors was shallow lobulated, high density lesion with clear edges; 112 (21%) patients presented calcification, and 37 (7%) of them had typical popcornlike calcification. 18Fluoro-deoxyglucose positron emission tomography-computed tomography (FDG PET-CT) was performed in 160 (30%) patients. The mean maximum standard uptake value (SUV max) was 1.8 ± 0.88, and in 33 (6%) patients was higher than 2.5 (mean value: 3 ± 0.9). The hamartoma was intraparenchymal in 525 (97%) patients and endobronchial in 15 (3%). No patient had multiple lesions. The tumors were evenly distributed throughout the right and left lungs with a frequency approximately proportional to the volume contribution of each lobe as follows: Right Upper Lobe (n = 111; 21%); Middle Lobe (n = 41; 7%); Right lower lobe (n = 193; 26%); Left Upper Lobe (n = 130; 24%); and Left Lower Lobe (n = 119; 22%).

Before resection, 78 (14%) patients underwent CT-fine needle biopsy (FNAB), while in 15 (3%) patients bronchoscopy was performed for diagnosis. Of the 78 FNAB performed, 49 (62%) were diagnostic, 28 (36%) were inconclusive for a diagnosis, and 1 (2%) was considered positive for malignancy, but turned out to be a hamartoma after excision. Bronchoscopy diagnosed hamartoma in 13 out of 15 (87%) patients with bronchial obstruction.

Upfront surgical (n = 380) or endoscopic resections (n = 5) were performed in a total of 385 (71%) cases due to the suspicion of malignancy (n = 83; 21%) (i.e. lesion was suspected to be a metastatic lesion, but turned out to be a hamartoma after resection); patient's decision (n = 170; 44%); presence of synchronous lung cancer (n = 9; 3%) or symptoms (n = 123; 32%). In the remaining 155 (29%) cases, the lesions were resected due to increase in size during follow-up (mean increase size: 10 ± 2.9 mm; mean follow-up: 20 ± 3.5 months). In most cases, lung sparing resection was carried out by enucleation (n = 256; 47%) and wedge resection (n = 228; 43%). Anatomic pulmonary resections were performed in 51 patients with hilar PH or with lung cancer and associated PH. Lobectomy was performed in 43 (7.8%) patients associated with partial bronchoplastic resection in 3 cases; segmentectomy in 7 (1%); and bilobectomy in 1 (0,2%). The procedures were performed via thoracotomy (n = 160; 27%); and VATS (n = 375; 73%). In 21 (6%) cases, VATS was converted to thoracotomy due to the difficulty in detecting the lesion. All of the three main tissue types including mature hyaline cartilage, fibromyxoid stroma, and mature adipose tissue were present in every individual lesion, but mature hyaline cartilage represented the major constituent (more than 50%) in 282 out of 540 (52%) tumors.

Outcome and follow-up

No complications occurred during surgery. The length of chest drainage and of hospital stay was 4.0 ± 2.6 days and 5.5 ± 2.8 days, respectively. Twenty/two (4%) patients presented postoperative

complications occurring after lobectomy (n = 20; 91%), enucleation (n = 1; 4.5%) and wedge resection (n = 1; 4.5%). Thirteen (2.4%) patients had persistent air-leaks that resolved spontaneously in all but one which was successfully treated with endobronchial valves; 7 (1.3%) had atrial fibrillation; and 2 (0.3%) had hemothorax requiring surgical exploration by thoracotomy. The mean follow-up time was 103.3 ± 93 months [1-370 months]. None of the patients undergoing surgical resection of PH had recurrence while one of the five patients treated with endoscopic resection via rigid bronchoscope had recurrence of PH 11 months later; he underwent a second resection via rigid bronchoscope and no further recurrence was observed.

Cancer associated to Hamartoma

One hundred forty-three out of 540 (26%) patients had associated cancer (Table 2). Sixty-seven (12%) out of 540 patients had associated extrapulmonary malignancies that were metachronous in all patients but one, while 76 (14%) had associated lung cancer. It was synchronous in 9/76 (12%) (Fig. 1), and metachronous in 67/76 (88%) patients. Most patients with associated lung cancer were male (56%), and all but two were smokers (97%). The mean interval time between the diagnosis of hamartoma and lung cancer was 20 ± 4.5 months. Twenty-eight lesions (36%) involved the ipsilateral lung, and 20 of these (26%) the same lobe of the hamartoma; while 48 (64%) the contralateral lung of the hamartoma. The mean size of hamartoma was 17 ± 9.3 mm; it had a shallow margin in 50 cases (66%), and mature hyaline cartilage represented the major constituent in 41 (54%) cases. Hamartoma was resected in association with synchronous lung cancer by lobectomy in 6 cases (8%), by enucleation in 55 (72%) and by wedge resection in 24 (20%). For resection of lung cancer, lobectomy was performed in 60 patients (79%), and segmentectomy in 16 patients (21%) due to limited respiratory function.

Table 1
Characteristics of study population (n = 540)

Variables	Value
Age (year-old; median)	61.4 [18–85]
• 20–30	8 (1%)
• 31–40	12 (2%)
• 41–50	80 (15%)
• 51–60	150 (28%)
• 61–70	180 (33%)
• > 70	110 (21%)
Smokers (yes/no)	493/47 (91%)
Sex (male/female)	319(59%)/221 (41%)
Previous comorbidity	81 (15%)
• Diabetes	115 (21%)
• Hypertension	120 (22%)
• Cardiac	27 (5%)
• Cerebral	220 (41%)
• BPCO	67 (12%)
• Neoplastic	
Symptoms	81 (15%)
• None	220 (41%)
• Cough	79 (14%)
• Thoracalgia	145 (27%)
• Expectoration	13 (2%)
• Hemoptysis	2 (0,3%)
• Pneumonia	27 (5%)
• Pyrexia	31 (6%)
• Weight loss	

Variables	Value
Size mm (mean)	18.8 ± 12.4
• ≤ 10 mm	171 (32%)
• > 10–20 mm	230 (42%)
• > 20–30 mm	41 (7%)
• > 30 mm	98 (19%)
CT findings	112 (21%)
• Calcification	37 (7%)
• Popcornlike calcification	
PET	160 (30%)
• Mean value SUV value	1.8 ± 0.88
• Patients with SUV > 2.5	33 (6%)
Preoperative FNAB	78 (14%)
• Diagnostic	49 (62%)
• Inconclusive	28 (36%)
• Positive for malignancy	1 (2%)
Preoperative bronchoscopy	15 (3%)
• Diagnostic	13 (87%)
• Inconclusive	2 (13%)
Localization	111 (21%)
• RUL	41 (7%)
• ML	139 (26%)
• RLL	130 (24%)
• LUL	119 (22%)
• LLL	

Variables	Value
Decision for surgical resection	83 (21%)
• risk of malignancy	170 (44%)
• patient's decision	9 (23%)
• synchronous lung cancer	123 (12%)
• symptoms	155 (29%)
• increase in size during follow-up	
Surgical resection	535
• Enucleation	256 (47%)
• Wedge resection	228 (43%
• Lobectomy	43 (7.9%)
• Bilobectomy	1 (0.1%)
• Segmentectomy	7 (1%)
Endoscopic resection	5 (1%)

Table 2
Malignancy associated with PH (n = 143)

Variables	Total number	Synchronus	Metachronus	
			Antecedent	Subsequent
Lung Cancer				
Number	76 (53%)	9 (12%)	-	67 (41%)
Age	63.4 ± 9.8	60 ± 8.7	-	63.1 ± 7.8
Sex (male)	43 (56%)	7 (9%)	-	36 (47%)
Smokers	74 (97%)	9 (12%)	-	65 (85%)
Interval between amartoma and tumor (months)	20 ± 4.5	-		20 ± 4.5
Site	8 (10%)	3 (3%)	-	5 (7%)
• Ipsilateral	20 (26%)	6 (8%)	-	14 (18%)
• Same lobe	48 (64%)	0	-	48 (62%)
• Controlateral				
Histology	47 (62%)	5 (7%)	-	42 (55%)
• Adenocarcinoma	26 (34%)	4 (5%)	-	22 (29%)
• Squamous cell carcinoma	3 (4%)	0	-	3 (4%)
• Large Cell carcinoma				
pStage	53 (70%)	7 (10%)	-	46 (60%)
• Stage I	19 (25%)	2 (3%)	-	17 (22%)
• Stage II	4 (5%)	0	-	4 (5%)
• Stage III				
Type of resection (amartoma/lung cancer)	6 (8%)	6 (8%)	-	0
• Lobectomy	45 (59%)	3 (4%)	-	42 (55%)
• Enucleation + Lobectomy	9 (12%)	0	-	9 (12%)
• Wedge resection + Lobectomy	16 (21%)	0	-	16 (21%)
• Wedge resection + segmentectomy				

Variables	Total number	Synchronus	Metachronus	
			Antecedent	Subsequent
Extrapulmonary Malignancy	67 (47%)	1 (1%)	60 (42%)	6 (4%)
• Breast	17 (26%)	0	15 (22%)	2 (4%)
• Thyroid	2 (3%)	0	2 (3%)	0
• Gastric	10 (15%)	0	10 (15%)	0
• Colon	14 (21%)	0	13 (19%)	1 (2%)
• Kidney	15 (22%)	1 (1%)	12 (18%)	2 (3%)
• Lymphoma	5 (7%)	0	5 (7%)	0
• Skin	4 (6%)	0	3 (5%)	1 (1%)

Logistic regression analysis reported in Table 3 found that only age > 70-year-old (odds ratio: 0.469; p = 0.0059) and smokers more than 20 cigarettes/day (odds ratio: 5.083; p < 0.0001) were significant risk factors for cancer development.

Table 3
Logistic regression analysis for development of lung cancer

Variables	Odds Ratio	95% CI	p-value
Age > 70 year-old (yes/not)	0.469	0.273 to 0.803	0.0059
Sex (male/female)	1.447	0.836 to 2.50	0.18
History of cancer (yes/not)	1.706	0.838 to 3.47	0.14
Smokers more than 20 cigarettes/day (yes/not)	5.083	3.001 to 8.60	< 0.0001
Size ≥ 30 mm (yes/not)	1.018	0.492 to 2.10	0.96
SUV > 2.5 on PET scan (yes/not)	2.057	0.812 to 5.21	0.12
Smooth margin (yes/not)	0.817	0.449 to 1.48	0.50
Calcification (yes/not)	1.205	0.639 to 2.27	0.56
Increase in size during follow-up (yes/not)	1.358	0.871 to 2.11	0.17
Hamartoma condroma histology (yes/not)	0.877	0.373 to 2.06	0.76

Discussion

The term "hamartoma" derives from the Greek word which means “error”. It was first used in 1904 by Albrecht [17] to define certain tumor like malformations resulting from a presumed error in development

or mixing of tissues normally present in the involved organ. In 1934, Goldsworthy defined as PH the benign tumor composed of a combination of adipose tissue and cartilage [1, 2]. The significance of PH remains intriguing. Malignant degeneration of PH to carcinoma or sarcoma has been reported in literature, as well as the association between PH and lung cancer. However, these evidences are supported by small series or sporadic case reports, and thus they are still under debate. To evaluate these issues, we planned a multicenter study collecting the largest number of patients with PH undergoing surgical resection published so far.

First, our findings confirmed the previously published data on PH. This tumor occurred most frequently between the sixth and seventh decade of life, with a male preponderance. In most of cases, it appeared as a small, solitary pulmonary nodule, uniformly distributed in the two lungs. Only few patients with endobronchial obstruction presented specific symptoms related to airway obstruction by PH, and in most cases PH was incidentally detected by CT scan performed for other diseases. In 112 cases, there were calcifications on CT findings, and only 33 out of 160 lesions were FDG-avid (SUV uptake > 2.5). Pre-operative FNAB was not routinely performed probably due the difficulty in aspirating adequate cytological or histological samples due to the dense structure of the lesion [18, 19]. In asymptomatic patients the decision for upfront surgical resection was based on (i) the difficulty in distinguishing PH from malignant lesions, particularly in patients with history of malignancy; (ii) the increase in size during follow-up; and (iii) patient's decision, owing to unclear diagnosis. Lung sparing resections (i.e. enucleation or wedge resection) were the main surgical strategy, while anatomic resections were performed only in selected cases due to tumor extension.

Second, the outcome observed in our series confirmed the benign nature of PH. No case of malignant transformation of PH was found, and only one patient had recurrence (0,2%) 11 months after endoscopic resection. Thus, an incomplete excision likely explained this event. Previously published series in the English literature [1–16], considered collectively with the present in Table 4, confirmed our results. Among 1,733 patients evaluated, recurrence after excision was found in only 4 cases (0.23%). In all cases, it occurred in the same pulmonary segment after enucleation, pointing out that excision with a minimal margin of normal lung was mandatory to prevent the recurrence. No cases of malignant transformation were found suggesting that this event is highly exceptional or impossible. Rare isolated reports showed the possibility of malignant degeneration of PH, but these findings were contradicted by other authors. Hayward and Carabasi [20] found that most papers either lacked evidence that original tumor was a hamartoma or provided weak evidence of malignant change. In histological findings of some reports hamartoma and carcinoma cell lines seemed to be independent from each other, suggesting a coexistence of the two tumors rather than a degeneration of PH [21]. In others, PH involved the pleura and this unusual growth pattern was considered a sign of malignant transformation, but no malignant cells were detected in any of these cases [22]. Furthermore, there was no evidence of malignant transformation in surveillance of patients with non-resected PH. Sinner et al. [23] analyzed 61 patients with asymptomatic FNAB-proven peripheral pulmonary hamartoma. Forty-one patients had a 5-year follow-up (the longest surveillance reported in literature), and they developed no malignant transformation.

Similarly, in our series 116 patients were followed up for a mean time of 25 months before resection. The tumor increased in size, but no malignant degeneration was found.

Table 4
Review of the literature regarding recurrence and malignant transformation of PH

Authors	No. of PH	Recurrence	Malignant transformation
Koutras et al. [1]	19	0	0
Karasik et al. [2]	52	0	0
Fudge et al. [3]	29	0	0
van Den Bosch et al. [4]	154	2	0
Crouch et al. [5]	19	0	0
Salminen et al. [6]	77	0	0
Hansen et al. [7]	89	0	0
Ribet et al. [8]	65	0	0
Gjevre et al. [9]	216	0	0
Lee et al. [10]	29	0	0
Lien et al. [11]	62	0	0
Guo et al. [12]	39	1	0
Çaylak et al. [13]	20	0	0
Wang [14]	226	0	0
Ekinci et al. [15]	73	0	0
Haberal et al. [16]	24	0	0
Our series	540	1	0
Total	**1,733**	**4 (0.23%)**	**0**

Third, we found that PH was associated with synchronous or metachronous lung cancer in 14% of our population that is likely higher compared to the incidence of lung cancer in general Italian population considering that about 41,500 new cases of lung cancer have been estimated in 2018 as reported by the Italian Association of Medical Oncology and the Italian Association of Tumor Registries [24]. The association between PH and lung cancer has been previously reported, with an incidence ranging from 1–23% in previous studies [1–9, 15], summarized in Table 5. Furthermore, Karasik et al. [2], and Ribet et al. [8] calculated that the risk for lung cancer in patients with PH were 6.3 and 6.7 times respectively, higher than that expected for the general Israeli and French population. However, it is still under debate whether PH is a real risk factor for lung cancer development or just an associated phenomenon. Karasik

et al. [2], and Ribet et al. [8] supported the first hypothesis. In Karasik's series [2], all four associated lung cancers occurred in the same lobe of the hamartoma. It has been reported that 5–25% of all lung cancer are associated with scars, and the most common example is adenocarcinoma arising from tuberculosis scar. Thus, the authors [2] supposed that the association between PH and lung cancer was another example of the so-called scar carcinomas, because the fibrosing process sustained by PH favored the development of malignancy. By contrast, van den Bosch et al. [4] and Gjevre et al. [9] considered as fortuity this association. In the series of van den Bosch et al. [4] only 45% of associated lung cancer were localized in the same lobe of hamartoma, making likely doubtful any spatial correlation between two tumors. Thus, the authors [4] explained this association by the possibility that the existence of cancer could lead to the discovery of an asymptomatic hamartoma that would have remained unknown otherwise. Furthermore, Gjevre et al. [9] pointed out that PH and lung cancer were associated to the same exposures and risk factors, that could explain their association. Our results were in line with these. In our series only 26% of associated lung cancers were localized in the same lobe of PH, and similar results were also observed in series from literature review reported in Table 5 where associated lung cancer and hamartoma were localized in the same lobe in 42% of cases. Yet, all patients but two were smokers and our logistic regression analysis found that only smoking and advanced age were significantly associated with lung cancer occurrence. Furthermore, also in the Ribet's series [8] most patients with lung cancer were smokers. Thus, patients with PH should undergo a complete evaluation and to regular follow-up, especially if they are smokers and elderly, as it could lead to the discovery of early stage lung cancer.

Table 5
Review of literature regarding PH associated with lung cancer

Authors	No. of PH	No. Of Associated Lung Cancer			Same lobe
		Total number	Synchronous	Metachronous	(Lung cancer and PH)
Koutras et al. [1]	19	1 (5.2%)	1 (5.2%)	0	0
Karasik et al. [2]	52	4 (7.6%)	1 (1.9%)	3 (5.7%)	4 (100%)
Fudge et al. [3]	29	5 (17.2%)	1 (3.4%)	4 (13.8%)	N/A
van Den Bosch et al. [4]	154	11 (7.1%)	6 (3.8%)	5 (3.3%)	5 (45.4%)
Crouch et al. [5]	19	2 (10.5%)	2 (10.5%)	0	2 (100%)
Salminen et al. [6]	77	1 (1.2%)	0	1 (1.2%)	N/A
Hansen et al. [7]	89	1 (1.1%)	1 (1.1%)	0	1 (100%)
Ribet et al. [8]	65	3 (4.6%)	0	3 (4.6%)	0
Gjevre et al. [9]	216	45 (1.1%)	39 (18%)	6 (2.8%)	16 (35.5%)
Ekinci et al. [15]	73	17 (23%)	13 (17.8%)	4 (5.2%)	4 (23.5%)
Our series	540	76 (14%)	9 (1.6%)	67 (12.4%)	20 (26%)
Total	**1,333**	**166 (12.4%)**	**73 (5.4%)**	**94 (7%)**	**52 (42%)***

*This value was calculated on the total of 1,227 cases as in 106 cases it was not reported which lobe was affected by lung cancer.

Obviously, our results should be evaluated with caution, before drawing definitive conclusions. Due to the retrospective and multicenter nature of the study, there was not a standardized protocol for the timing of surgical resection, the extent of resection, the histological diagnosis and the clinical follow-up modality. The lack of a surveillance control group made impossible to know whether all PHs undergoing upfront surgery in our series would remain stable in size over the time.

In conclusion, resection of PH is a safe procedure. The recurrence and malignant degeneration are likely uncommon and the association between PH and lung cancer seems to be a spurious phenomenon related to common risk factors as smoking and advanced age.

Declarations

Author Contributions

Conceptualization, A.F. and A.D.; methodology, A.C. and G.A.; software, N.S.; validation, B.T.M, F.A. R.R. and S.S.; formal analysis, N.S.; investigation, P.C. and L.V.; resources, A.F.; data curation, G.B., M.R., V.T, D.L., N.A, M.A; writing—original draft preparation, A.F. and A.D; writing—review and editing, A.F and A.D..; visualization, A.F.; supervision, F.A., M.R., F.P., E.A. R,. F.V. and M.S.; project administration, A.F.; funding acquisition, A.F. All authors have read and agreed to the published version of the manuscript.

Funding

The authors disclose no funding for the present paper

Conflicts of Interest

The authors declare no conflict of interest.

Institutional Review Board Statement

The study was conducted according to the guidelines of the Declaration of Helsinki, and approved by Local Ethics Committee of University of Campania Luigi Vanvitelli (code number: 17402-20), the coordinating center of the study,

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Figures

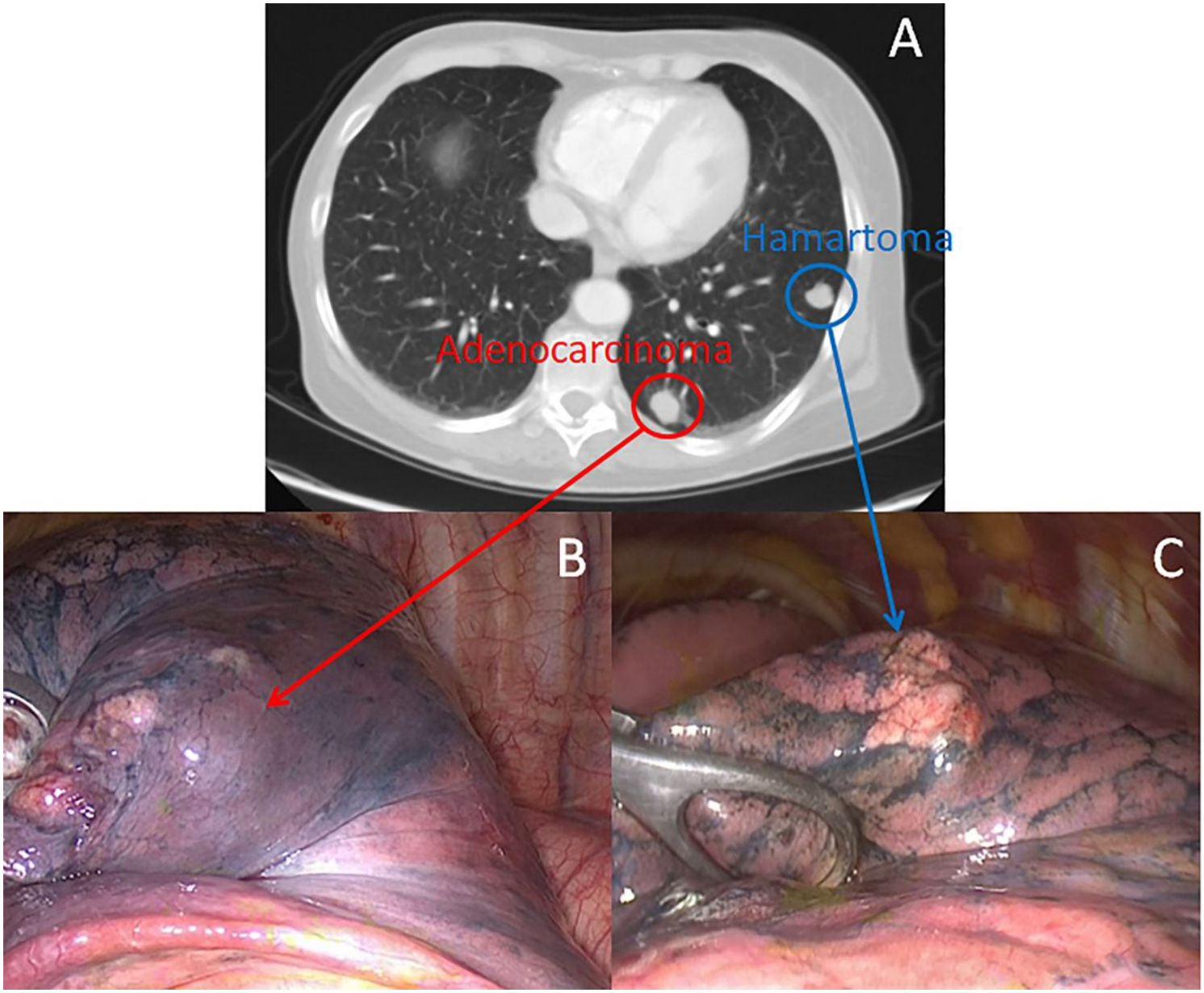

Figure 1

A 57 year-old woman had hamartoma and adenocarcinoma in the left lower lobe. She underwent thoracoscopy left lower lobectomy. Part A=CT scan; Part B and Part C=operative view of adenocarcinoma (B) and hamartoma (C)