Original Article

Prognostic role of subsolid ground-glass opacity, pure ground-glass opacity, and solid nodules of the lung: a retrospective observational study

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Background: Lung nodules can be classified as solid nodules and ground-glass opacity nodules (GGO-GGN). A GGO nodule is a radiological finding characterized by a faded opacity that may hide a preinvasive or invasive adenocarcinoma. GGOs can be divided into two categories: pure GGO (pGGN) and mixed/subsolid GGO (mGGN). The transformation of GGO into solid nodules is a strong indicator of malignancy. Current guidelines suggest a 5-year chest computed tomography (CT) follow-up (FU) for both pure and subsolid GGOs. This study aimed to analyze the prognosis of patients undergoing major lung resection at our center in relation to the radiological characteristics of the resected nodule to assess how much the nodule density in GGO may affect the prognosis.

Methods: This retrospective observational study analyzed 133 patients underwent lobectomy at our center between 2010 and 2020. The nodule density was assessed by CT images, classifying into three groups according to the consolidation tumor ratio (CTR): group 1: pure GGO (pGGN; CTR <0.5, n=30); group 2: subsolid nodule (mGGN; 0.5≤ CTR <1, n=37), group 3: solid nodule (CTR =1, n=66). Overall survival (OS) was calculated from the date of surgery until death or last FU. The OS was estimated through Kaplan-Meier curves, the log-rank test was used for univariate analysis, and Cox regression was used for multivariate analysis. Values with P<0.05 were considered statistically significant.

Results: Of 133 patients, the OS, 5 years after surgery and related to the nodule density, has been classified into three groups as: group 1 contained 30 patients with pure GGO nodules, with a 5-year survival rate of 96% [95% confidence interval (CI): 73–99%]; group 2 contained 37 patients with subsolid GGOs, with a 5-year survival rate of 76% (95% CI: 56–88%); group 3 contained 66 patients with solid nodules, with a 5-year survival rate of 78% (95% CI: 62–88%) with median survival time was 95 months. Multivariate analysis with age and FU lasting for over 6 months in the Cox model confirmed that density was a risk factor, with hazard ratio (HR) =8.37 (95% CI: 1.03–68.12) for group 2 *vs.* group 1 and HR =8.66 (95% CI: 1.06–70.90) for group 3 *vs.* group 1. A FU exceeding 6 months after diagnosis was not a significant risk factor (P=0.57), whereas age was a significant risk factor (HR =1.07, 95% CI: 1.001–1.13).

Conclusions: For pure GGO long-term FU is justified, whereas surgery should be considered as the first option for subsolid nodules. This retrospective study provides a foundation for further research to better define the most appropriate approach to subsolid nodules.

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Keywords: Ground-glass opacity (GGO); nodule; non-small-cell lung cancer (NSCLC); lung resection; overall survival (OS)

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Introduction

In Italy, reports of lung cancer deaths in 2017 totaled about 34,000, with 23,400 men and 10,000 women affected. For men, lung cancer is the most common cause of cancer-related deaths, while for women, it ranks second. An estimated 41,000 new cases of lung cancer (27,550 in men and 13,300 in women) were reported in Italy in 2020. In men, it is the second most common neoplasia (14%) and in women, it is the third most common (7%) (1). Histologically, lung cancer can be divided into non-small-cell and small-cell tumors (2). Small-cell tumors or microcytomas are strictly smoke-related. Non-small-cell lung cancers (NSCLCs) comprise squamous cell carcinomas, adenocarcinomas, carcinoids, and large-cell tumors (2). The neoplasia is often discovered incidentally through radiological imaging (chest X-ray; CXR) or computed tomography [high-resolution computed tomography (HRCT) or contrast-enhanced computed tomography (CE-CT)]. Once a lung nodule is determined, the most important test to establish the staging is CE-CT, which, according to the latest guidelines, should be extended to the encephalon and upper abdomen to exclude secondary cancers that would make the patient inoperable. Currently, the only practicable screening for lung cancer in Italy is a CXR. On the other hand, the National Lung Screening Trial (US) formally reported for the first time that low-dose CT, as opposed to a standard CXR, could reduce lung cancer mortality in high-risk populations by 20% (1).

A consistent proportion of lung nodules accidentally found are not completely solid, showing a component not solid, defined as mixed ground-glass nodule (mGGN), or totally not solid, called pure ground-glass nodule (pGGN) (3-5). These aspects must be strongly considered regarding the incidence of cancer in GGN, which has been reported as high as 63%. GGNs have extremely complex and primarily very varied etiology and imaging features, which can underlie a wide spectrum of observed pathologies. They can develop quickly or very slowly.

The Fleischner Society in 1996 proposed the concept of ground-glass opacity (GGO), referring to shadows with slightly increased density compared to the surrounding parenchyma detected on HRCT. However, GGO areas may represent not only cancerous formations but also the consequences of various disease processes, such as infections, local hemorrhages, and interstitial fibrosis (5,6).

The ground-glass shape of a nodule can be caused, at the histopathological level, by morphological changes such as thickening of the alveolar septum, edema of the terminal air sacs, reduced air content in the alveoli, increased number of cells, and proliferation of alveolar epithelial cells (2-6).

The scientific community now defines pulmonary GGO nodules based on their density as mGGN when the low-

Highlight box

Key findings

- Lung nodules can be classified as solid nodules and ground-glass opacity nodules (GGO-GGN).
- Current guidelines suggest a 5-year chest computed tomography (CT) follow-up (FU) for both pure and subsolid GGOs.
- We aim to analyze the prognosis related to the nodule density.
- Patients with solid and subsolid nodules instead had an almost identical survival rate.

What is known and what is new?

- We highlight that prognosis of patients with subsolid and solid nodule is similar.
- Current guidelines suggest a 5-year chest CT FU for both pure and subsolid GGOs.
- Common guidelines are not yet established for GGNs, we strongly suggest considering surgery as the best treatment in cases of mixed ground-glass nodule.

What is the implication, and what should change now?

- Beside the limitations of this observational retrospective study, we would highlight the importance of considering subsolid nodules and if the nodule detected at the check-up CT scan has changed in dimension or even shown changes in density but not size, a surgical strategy is preferable and must be considered. This study would be a point of reference for further studies and guidelines in this field.

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density component exceeds 50% of the total nodule mass (6-10). To better define this concept, a consolidation tumor ratio (CTR) has been calculated as the index that assesses the proportion of the ground-glass component of a nodule. Specifically, when the non-solid density exceeds 50% of the nodule, the CTR is <0.50, and the nodule can be defined as pGGN. When the CTR is between 0.50 and 0.75, the nodule is defined as partially solid or m GGN, and when the CTR is equal to 1, the nodule is solid (3).

The latest guidelines of the Fleischner Society of Radiology indicate that no routine follow-up (FU) is recommended for pure GGNs under 6 mm in diameter (i.e., 5 mm or smaller), and a 1-year FU is recommended only for high-risk cases (3). A 6–12-month FU is recommended for pGGO nodules with a diameter of 6 mm or more, and then every 2 years for a total of 5 years (3).

For solitary part-solid nodules with a diameter of 6 mm or more, with a solid component having a diameter below 6 mm, a 3–6-month FU is recommended and then annually for a minimum of 5 years. If the nodule is unchanged after 3 months, the patient may become surgical because a nodule with both components underlies a high degree of malignancy (3,8).

Few patients experience distant metastases from pGGN lung cancer, which is typified by a painless course of disease progression. With a 100% 5-year survival rate following surgery, the prognosis is good (4-6). For mGGN, this is untrue. An editorial about the prognosis of GGO based on the predominant or main lesion was published by Sihoe *et al.* in 2018 (11). There is growing evidence that the one main or predominant lesion with the worst prognosis should be the one to guide management in a patient with multiple GGOs due to their independent characteristics. According to a Japanese study, the primary lesion's size and solidity matter (12). A solid-dominant main GGO lesion with a size greater than 25 mm is associated with a poorer 5-year OS prognosis compared to a GGO-dominant lesion with a size of less than 25 mm (12-21).

Persistent GGNs are those that do not go away after 3.4–5.6 months of FU (22,23). These GGNs have the potential to be malignant and may turn that way after a protracted developmental period. As a result, following the discovery of a pGGN, a specific amount of FU should be applied. In agreement with recent literature, we believe that FU is justified only for pGGO lesions in low-risk patients; otherwise, resection may be the safest path for the patient (22-24).

In the current Italian Association of Medical Oncology guidelines for lung cancer (25), the density criterion is not addressed. GGNs are assimilated with solid nodules, leaving doctors and surgeons with free will regarding the approach to monitoring or removing these nodules. However, overtreatment and overdiagnosis with consequent excessively long FU often occur (11).

This study aimed to present our experience regarding the treatment and management of GGNs by analyzing a population of patients with early-stage NSCLC (IA-IB-IIA) who underwent lobectomy and ilo-mediastinal lymphadenectomy at our center from 2010 to 2021 to confirm that a significant difference exists, in terms of prognosis and survival, between patients with pGGNs and those with mGGNs and solid nodules. We present this article in accordance with the STROBE reporting checklist (available at https://jtd.amegroups.com/article/view/10.21037/jtd-24-1825/rc).

Methods

Patients' characteristics

This was a monocentric, retrospective, observational cohort study enrolling 133 patients undergoing major lung resection for pGGOs, mGGOs, or solid nodules from 2010 to 2020.

Patients were recruited according to the following criteria. (I) The inclusion criteria were: age 18–85 years; a diagnosis of NSCLC with histology as squamous cell or adenocarcinoma at stage IA-IB-IIA according to the 8th edition TNM (tumor-node-metastasis); single nodule; all patients underwent lobectomy via video-assisted thoracic surgery (VATS), robotic-assisted thoracic surgery, or thoracotomy, with a postoperative FU of at least 12 months. (II) The exclusion criteria were synchronous neoplasms and patients undergoing lung resections other than lobectomy (e.g., segmentectomies, atypical resections, bilobed). The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the local Ethics Board Committee of Romagna (CEROM) (ID 2970, date of approval: 11.11.2022), Italy; patients' consent has been taken according with the local Ethics Board Committee regulations.

Radiological evaluation

All patients underwent radiological checks by total-body CT with contrast enhancement before surgery. In particular,

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HRCT images were used to assess the GGO nodules. Every chest CT scan was performed at maximum inspiration, and any GGO nodules were detected after the fact. The largest axial diameter of the nodule on the lung window setting was used to determine the tumor's diameter, and an area of increased opacification that completely covered up underlying bronchial structures and vascular markings was used to define consolidation. Two thoracic surgeons and an imaging specialist anonymously reviewed each nodule on the preoperative CT scans.

The GGNs were then classified into three groups based on the CTR as per Fleischner Society guidelines: solid nodules (CTR =1.0) and partially solid tumors divided into pGGN-predominant (0.5≤ CTR <0.75), and solid-predominant (0.75≤ CTR <1.0) groups. The impact of the tumor size was assessed based on the CTR using the Cox model.

All patients with solid nodules or mGGO underwent positron emission tomography/computed tomography with 18F-fluorodeoxyglucose (^{18}F-FDG PET/CT).

Flexible fiberoptic bronchoscopic examination and diagnosis

We used endobronchial ultrasonography with a guide sheath (EBUS-GS) to perform a bronchoscopic biopsy in an attempt to diagnose GGO-predominant-type lesions. Lesions of the GGO-predominant type have a lower diagnostic rate than lesions of the solid type. This could be explained by the lesions not being visible with X-ray fluoroscopy. It is difficult to determine the bronchial routes to GGO lesions in a constrained amount of time during an examination. We define only possible GGO with this procedure. Alternatively, a CT-guided biopsy was performed in selected cases.

Histological evaluation

Two pathology specialists inspected and documented every clinical specimen. The International Association for the Study of Lung Cancer/American Thoracic Society/European Respiratory Society (IASLC/ATS/ERS) (26) was used to evaluate each nodule's size, location, differentiation, lymph node status, pleural invasion, and lymphatic invasion.

Surgery

After the patient was positioned laterally, a double-lumen tracheal intubation was carried out.

A VATS approach was performed in all the patients enrolled. In case of technical difficulties, the surgical approach was converted into an open posterolateral thoracotomy. Using a preoperative CT-guided hook wire or finger exploration, the precise location of the nodule was determined. Cutting staplers at least 2 cm from the nodule edges allowed the lesions to be wedged. Based on the intraoperative histopathological findings, the surgeon decided on a surgical intervention, such as a lobectomy, after carefully evaluating the patient's lung function.

FU

Every case was monitored beginning on the day of surgery. A physical examination and CXR were administered two weeks following the procedure. They also received chest HRCT every 3–6 months for the first 2 years, then, in case of non-modification of the radiological findings, every 1 year for 5 years. Every case was routinely monitored to evaluate quality of life, survival, long-term complications, and perioperative complications.

Statistical analysis

Overall survival (OS) was calculated from the date of surgery until death or the last FU. The OS was estimated using Kaplan-Meier curves, with log-rank tests for univariate analysis and Cox regression for multivariate analysis. Values of $P<0.05$ were considered statistically significant.

Results

We analyzed 133 patients, of whom 74 women (mean age 73 years, range 18–85 years) and 59 men (mean age 71 years, range 18–85 years) underwent surgery for stage I and IIA NSCLC (8th edition TNM). The patients' characteristics are shown in *Table 1*.

Among all the patients, 79 (59%) had no declared previous cancer history, and 51 (39%) showed previous neoplasms; 3 (3%) patients had no data. Of these patients, 31 (23%) were former smokers, and 68 (52%) were active cigarette smokers.

We considered three groups of patients according to the nodule density based on the radiological findings, as described in the methods. In particular, of all the patients who underwent lobectomy, 66 (49%) showed a solid

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Table 1 Descriptive data of the general population, according to the nodule density

Variables	Solid (N=66)	GGN pure/mixed (N=67)	Total (N=133)
Patients' characteristics			
Sex			
Male	30 [45]	29 [43]	59 [44]
Female	36 [55]	38 [57]	74 [56]
Smoking history			
Smokers	44 [67]	24 [36]	68 [52]
Ex-smokers	7 [11]	24 [36]	31 [23]
Non-smokers	15 [22]	19 [28]	34 [25]
Remote anamnesis			
Positive for cancer	23 [35]	28 [42]	51 [39]
Negative for cancer	40 [61]	39 [58]	79 [59] +3 patients no data
Pathological stages (VIII TNM Ed. Lung Cancer)			
IA	40 [61]	49 [73]	89 [67]
IB	24 [36]	11 [16]	35 [26]
IIA	2 [3]	7 [11]	9 [7]
Preoperative findings			
^{18}F-FDG PET/CT			
Positivity (SUVmax >2.5)	47 [71]	36 [54]	83 [62]
Negativity (SUVmax ≤2.5)	19 [29]	31 [46]	50 [38]
FOB			
PREOP	48 [73]	26 [39]	74 [56]
No PREOP	18 [27]	41 [61]	59 [44]
EBUS			
EBUS positive	15 [23]	9 [13]	24 [18]
No EBUS	51 [77]	58 [87]	109 [82]

Descriptive data of the general population were divided according to the density of the nodules; specifically, two columns showing patients' characteristics with solid and ground glass/subsolid (mixed) nodules and the total number of patients' characteristics analyzed. Data are presented as n [%]. EBUS, endobronchial ultrasound; FOB, fiberoptic bronchoscopy; GGN pure/mixed, ground glass nodules pure/mixed; PREOP, preoperative; TNM, tumor-node-metastasis; ^{18}F-FDG PET/CT, positron emission tomography/computed tomography with 18F-fluorodeoxyglucose.

nodule, with a mixed nodule for 29% [37] and pGGO for 23% [30]. The data showed that nodules were followed for 3 months on average before re-evaluation with a CT scan and subsequent surgery.

All 133 patients underwent preoperative study and staging. The most common pathological stage was IA with 89 (67%) cases, followed 35 (26%) by IB and 9 (7%) by IIA.

In the preoperative study, 83 (62%) patients showed an uptake in the PET scan, and 50 (38%) were ^{18}F-FDG PET/CT-negative. pGGO nodules had a greater tendency to PET negativity *vs.* mixed and solid nodules, as already indicated in the literature (12,27).

A study with FOB was performed in only 74 out of 133 patients (56%) due to the distance from the bronchi or the absence of bronchial involvement.

Finally, EBUS was performed in only 24 patients:

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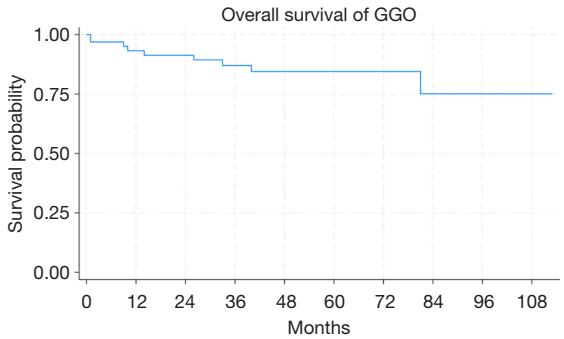

Figure 1 The curve shows the mortality rate for the GGO patients (group 1 and group 2) in relation to the months of post-surgery follow-up. GGO, ground-glass opacity.

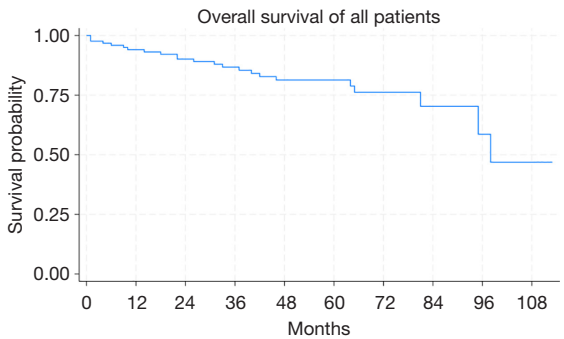

Figure 2 The curve shows the OS of all patients recruited for the study. OS, overall survival.

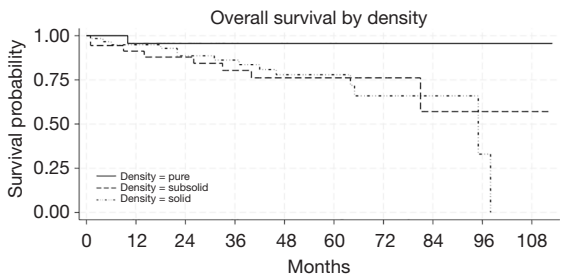

Figure 3 The curves show the OS of the patients split into the three groups based on the density of the nodules. OS, overall survival.

15 solid and 9 mixed. These were mainly patients with solid nodules, and only a few mixed, because the echo methodology cannot distinguish pGGO nodules from the surrounding lung parenchyma.

After the FU and preoperative study, all 133 patients underwent pulmonary lobectomy and ilo-mediastinal lymphadenectomy, with 81 VATS and 52 open approaches, all at our center. They were then followed for varying FU times, averaging 5 years.

Figure 1 shows the mortality curve for patients with solid nodules in relation to postoperative FU time. A 25% mortality was observed only around year 6 of FU. This is consistent with the current literature, which indicates 5-year survival for more than 75% of patients (28).

As shown in *Figure 2*, of 133 patients analyzed, the OS was 81% [95% confidence interval (CI): 72–88%] 5 years after surgery, much better than for solid nodules. The mean survival time was 98 months. Specifically in relation to the density of nodules, *Figure 3* shows the OS for each group of patients. In particular, in the pGGN group, two deaths occurred, including one within 5 years, for a survival rate of 97%, far exceeding the national survival averages for lung cancer (28). Additionally, the 5-year survival rate was 96%. In the group of partially solid nodules with a GGO component below 50%, nine deaths occurred, of which eight were within 5 years, for a survival rate of 80.5% (*Figure 3*).

In the solid nodule group, 16 deaths occurred overall from disease recurrence, with 14 within 5 years and a survival rate of 79%, consistent with ISS statistics for lung cancer (*Figure 3*).

The log-rank test to assess the OS based on density was significant (Pr > chi^2 =0.0440). The multivariate analysis through the Cox model confirmed density as a risk factor, with hazard ratio (HR) =8.37 (95% CI: 1.03–68.12) for group 2 *vs.* 1 and HR =8.66 (95% CI: 1.06–70.90) for group 3 *vs.* group 1. Extending the FU to over 6 months after diagnosis was not indicated as a significant risk factor (P=0.57), whereas the patient's age was very important (HR =1.07, 95% CI: 1.001–1.13).

To summarize, in terms of OS, whereas pGGN differed significantly from solids, mGGN did not. This is very important to consider, suggesting more attention when a nodule is not totally pure. Although common guidelines are not yet established for GGNs, we strongly suggest considering surgery as the best treatment in cases of mGGN.

Discussion

Because no official guidelines exist for the approach to GGO nodules, every center tends to treat them uniquely,

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according to their experience (29,30). The GGO nodule, especially if pure, could hide a benign pathology, and the diagnosis can be challenging even if the radiology and pneumology innovations are invaluable. However, the necessity to standardize levels of care is urgent, using the correct approach even for mixed GGO as well as in terms of long-term FU (31).

Some critiques exist regarding the approach used, especially when faced with a new-onset pulmonary nodule measuring >6 mm and with GGN aspects (32). Several studies suggest long radiological FUs for GGO nodules without making distinctions based on the proportion of density and without differentiating between pure and mixed (22,23). However, some studies have highlighted the high importance of performing a more complete study with total-body PET-FDG (26), and others have proposed a more aggressive approach with early surgical treatment (27-29), which seems to be closest to our concept.

The objective of our study was to demonstrate, using data collected from over 10 years' experience treating GGO nodules, that they may be controlled with long-term FU when pure and small (below 7 mm). However, we showed that, when GGNs contain a solid component, their trend in mortality and recurrence overlaps completely with solid nodules (*Figure 3*). Therefore, we believe that, even in mGGN, the most correct approach is early surgery, which seems also to be the safest option (29).

Our data showed that preoperative FUs for mGGNs that are performed too late (over 3 months) from when they have been noted by chest CT may lead to adverse events in patients' prognoses, as illustrated in the results section.

In our study, minor resections, such as wedges and anatomical segmentectomies, were deliberately eliminated from the database to standardize the approach, the FU period, and the surgical treatment, to focus our attention on the density of the nodules as the only variant.

We strongly believe that the nodule density should be the variable considered first over the nodule location, size, and metabolic activity. Additionally, for pGGNs and mGGNs at stage I, for the dimension and density of the nodule, total-body PET-FDG is inconclusive. For this reason, mixed GGN may indicate a more aggressive approach by surgery.

Many studies agree with this thought process and have assigned key importance to nodule density (30-32). We believe that with the same histology and size, the nodule density is an element that can strongly influence prognosis, as supported by several studies (15-18).

In accordance with the previous literature, we analyzed the OS of patients who were resected with pulmonary lobectomy and subsequently underwent FU in our center (30-32). The outcome showed a trend for patients with both solid and mixed nodules that was almost identical, although patients with pGGOs differed greatly (*Figure 3*). Thus, albeit with some limitations linked to our retrospective cohort study and the limited population of 133 patients, for nodules of this size, the surgical method (e.g., lobectomy) has been almost completely replaced by anatomic segmentectomies. We are conscious that this represents a limitation of our study, and further research will need to compare the surgical approach in terms of anatomic segmentectomies *vs.* lobectomies concerning the possible impact of mGGNs on prognosis, in terms of recurrence and survival.

Beyond the surgical approach, the density, like the other variables of a nodule, is arguably an important prognostic factor, and its CTR should always be calculated.

We believe that when a GGN appears, a 3-month FU is always justified since it could conceal a benign or malignant pathology. However, if the nodule detected at the check-up CT scan has changed in dimension or even shown changes in density but not size, a surgical strategy is preferable and must be considered.

Limitations

The study is retrospective and observational. We are conscious that the small sample has led to considerable uncertainty in the estimates of relative risks, as evidenced by the wide confidence intervals, which, however, do not include the null value for the factor under study (density). In multivariate analysis, the limited sample size and the limited availability of data prevented the adjustment of the density effect for any other confounding factors, however the results obtained seem suggestive and preparatory to the design of further multicenter studies with "greater power".

Conclusions

The patients we examined appeared to form a population homogeneous with the general population in terms of age, sex, and many other descriptive variables. Our three subgroups formed according to nodule density were alike and shared histology and tumor staging as well as the numbers of individuals in the subgroups.

The statistical analysis of OS showed that patients with pGGO nodules had a 5-year postoperative survival rate

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that differed greatly from the other two groups. Patients with solid and subsolid nodules instead had an almost identical survival rate, as shown in *Figure 3*. This seems to indicate that the GGO component is a positive prognostic index in NSCLC, but only for those nodules with a GGO component exceeding 50% with 0.5< CTR <0.75. When the solid component dominates, the tumor adopts a pattern comparable to a purely solid tumor.

To summarize, FU can be applied for nodules with pGGO characteristics, although an early radical surgery is preferable for nodules that, while having a GGO component, show a solid portion exceeding 50%, even if they are small.

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Footnote

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References

1. National Lung Screening Trial Research Team; Aberle DR, Berg CD, et al. The National Lung Screening Trial: overview and study design. Radiology 2011;258:243-53.
2. Travis WD, Brambilla E, Burke AP, et al. WHO classification of tumours of the lung, pleura, thymus and heart. 4th ed. Geneva: WHO Press; 2015.
3. MacMahon H, Naidich DP, Goo JM, et al. Guidelines for Management of Incidental Pulmonary Nodules Detected on CT Images: From the Fleischner Society 2017. Radiology 2017;284:228-43.
4. Kakinuma R, Noguchi M, Ashizawa K, et al. Natural History of Pulmonary Subsolid Nodules: A Prospective Multicenter Study. J Thorac Oncol 2016;11:1012-28.
5. Shigefuku S, Shimada Y, Hagiwara M, et al. Prognostic Significance of Ground-Glass Opacity Components in 5-Year Survivors With Resected Lung Adenocarcinoma. Ann Surg Oncol 2021;28:148-56.
6. Zhang Y, Fu F, Chen H. Management of Ground-Glass Opacities in the Lung Cancer Spectrum. Ann Thorac Surg 2020;110:1796-804.
7. Liu B, Zhang Y, Su L, et al. Treatment options for pulmonary multifocal ground glass opacity type adenocarcinoma: Surgery combine thermal ablation? J Interv Med 2020;3:180-3.
8. Handa Y, Tsutani Y, Okada M. Transition of Treatment for Ground Glass Opacity-Dominant Non-Small Cell Lung Cancer. Front Oncol 2021;11:655651.
9. Lee JH, Hong JI, Kim HK. Guidelines for the Investigation and Management of Ground Glass Nodules. J Chest Surg 2021;54:333-7.
10. Wang SB, Mao YS. Progress in screening and follow-up studies of pulmonary ground glass nodules. Zhonghua Zhong Liu Za Zhi 2022;44:123-9.
11. Sihoe ADL, Petersen RH, Cardillo G. Multiple pulmonary ground glass opacities: is it time for new guidelines? J

Thorac Dis 2018;10:5970-3.
12. Fu F, Zhang Y, Wen Z, et al. Distinct prognostic factors in patients with stage I non-small cell lung cancer with radio- logic part-solid or solid lesions. J Thorac Oncol 2019;14:2133-42.
13. Yip R, Li K, Liu L, et al. Controversies on lung cancers manifesting as part-solid nodules. Eur Radiol 2018;28:747-59.
14. Miyoshi T, Aokage K, Katsumata S, et al. Ground-Glass Opacity Is a Strong Prognosticator for Pathologic Stage IA Lung Adenocarcinoma. Ann Thorac Surg 2019;108:249-55.
15. Hattori A, Matsunaga T, Takamochi K, et al. Importance of Ground Glass Opacity Component in Clinical Stage IA Radiologic Invasive Lung Cancer. Ann Thorac Surg 2017;104:313-20.
16. Ye T, Deng L, Xiang J, et al. Predictors of Pathologic Tumor Invasion and Prognosis for Ground Glass Opacity Featured Lung Adenocarcinoma. Ann Thorac Surg 2018;106:1682-90.
17. Butnor KJ, Travis WD. Recent advances in our understanding of lung cancer visceral pleural invasion and other forms of minimal invasion: implications for the next TNM classification. Eur J Cardiothorac Surg 2013;43:309-11.
18. Hattori A, Matsunaga T, Takamochi K, et al. Neither Maximum Tumor Size nor Solid Component Size Is Prognostic in Part-Solid Lung Cancer: Impact of Tumor Size Should Be Applied Exclusively to Solid Lung Cancer. Ann Thorac Surg 2016;102:407-15.
19. Kim H, Goo JM, Kim YT, Park CM. Consolidation-to-tumor ratio and tumor disappearance ratio are not independent prognostic factors for the patients with resected lung adenocarcinomas. Lung Cancer 2019;137:123-8.
20. Hamada A, Suda K, Fujino T, et al. Presence of a Ground-Glass Opacity Component Is the True Prognostic Determinant in Clinical Stage I NSCLC. JTO Clin Res Rep 2022;3:100321.
21. Kodama K, Higashiyama M, Yokouchi H, et al. Prognostic value of ground-glass opacity found in small lung adenocarcinoma on high-resolution CT scanning. Lung Cancer 2001;33:17-25.
22. Lee HW, Jin KN, Lee JK, et al. Long-Term Follow-Up of Ground-Glass Nodules After 5 Years of Stability. J Thorac Oncol 2019;14:1370-7.
23. Naidich DP, Bankier AA, MacMahon H, et al. Recommendations for the management of subsolid pulmonary nodules detected at CT: a statement from the Fleischner Society. Radiology 2013;266:304-17.
24. MacMahon H, Austin JH, Gamsu G, et al. Guidelines for management of small pulmonary nodules detected on CT scans: a statement from the Fleischner Society. Radiology 2005;237:395-400.
25. Passiglia F, Pilotto S, Facchinetti F, et al. Treatment of advanced non-small-cell lung cancer: The 2019 AIOM (Italian Association of Medical Oncology) clinical practice guidelines. Crit Rev Oncol Hematol 2020;146:102858.
26. 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;6:244-85.
27. Shao X, Niu R, Shao X, et al. Application of dual-stream 3D convolutional neural network based on (18) F-FDG PET/CT in distinguishing benign and invasive adenocarcinoma in ground-glass lung nodules. EJNMMI Phys 2021;8:74.
28. Kakinuma R, Kodama K, Yamada K, et al. Performance evaluation of 4 measuring methods of ground-glass opacities for predicting the 5-year relapse-free survival of patients with peripheral nonsmall cell lung cancer: a multicenter study. J Comput Assist Tomogr 2008;32:792-8.
29. Chen KN. The diagnosis and treatment of lung cancer presented as ground-glass nodule. Gen Thorac Cardiovasc Surg 2020;68:697-702.
30. Yotsukura M, Asamura H, Motoi N, et al. Long-Term Prognosis of Patients With Resected Adenocarcinoma In Situ and Minimally Invasive Adenocarcinoma of the Lung. J Thorac Oncol 2021;16:1312-20.
31. Shimizu K, Ohtaki Y, Nakazawa S, et al. Neither the maximum tumor size nor solid component size is prognostic in part-solid lung cancer: to be ground-glass opacity or not to be, is that really the question? J Thorac Dis 2016;8:2334-6.
32. Asamura H, Hishida T, Suzuki K, et al. Radiographically determined noninvasive adenocarcinoma of the lung: survival outcomes of Japan Clinical Oncology Group 0201. J Thorac Cardiovasc Surg 2013;146:24-30.

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