Respir. Med and Res 86 (2024) 101136

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Original article

Incidental pulmonary nodules: Natural language processing analysis of radiology reports

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ARTICLE INFO

Article History:
Received 15 March 2024
Revised 17 July 2024
Accepted 14 August 2024
Available online 22 August 2024

Keywords:
Incidental pulmonary nodule
Natural language processing
Artificial intelligence
Radiology reports
Follow-up

ABSTRACT

Background: Pulmonary nodules are a common incidental finding on chest Computed Tomography scans (CT), most of the time outside of lung cancer screening (LCS). We aimed to evaluate the number of incidental pulmonary nodules (IPN) found in 1 year in our hospital, as well as the follow-up (FUP) rate and the clinical and radiological features associated with FUP.
Methods: We trained a Natural Language Processing (NLP) tool to identify the transcripts mentioning the presence of a pulmonary nodule, among a large population of patients from a French hospital. We extracted nodule characteristics using keyword analysis. NLP algorithm accuracy was determined through manual reading from a sample of our population. Electronic health database and medical record analysis by clinician allowed us to obtain information about FUP and cancer diagnoses.
Results: In this retrospective observational study, we analyzed 101,703 transcripts corresponding to the entire CTs performed in 2020. We identified 1,991 (2 %) patients with an IPN. NLP accuracy for nodule detection in CT reports was 99 %. Only 41 % received a FUP between January 2020 and December 2021. Patient age, nodule size, and the mention of the nodule in the impression part were positively associated with FUP, while nodules diagnosed in the context of COVID-19 were less followed. 36 (2 %) lung cancers were subsequently diagnosed, with 16 (45 %) at a non-metastatic stage.
Conclusions: We identified a high prevalence of IPN with a low FUP rate, encouraging the implementation of IPN management program. We also highlighted the potential of NLP for database analysis in clinical research.

1. Introduction

Lung cancer is the second most common cancer and the leading cause of cancer related deaths worldwide, accounting for 18 % of all cancer related deaths [1]. A recent French study highlighted that non-small cell lung cancer (NSCLC) is diagnosed at a metastatic stage in 60 % of the cases, thus preventing from the outset any curative intent [2]. Studies on Lung Cancer Screening (LCS) have paved the way to earlier diagnosis and showed improvement in lung cancer outcomes [3–6].

However, pulmonary nodules are most often discovered incidentally, outside of LCS [7]. These nodules, detected in patients with no history of cancer are called Incidental Pulmonary Nodules (IPN). An adequate management of IPN, supported by widely accepted recommendations, could lead to a stage shift from late to early-stage disease, and represent a great opportunity to improve lung cancer outcomes. But large population based studies are lacking and the literature is heterogeneous regarding adherence to FUP guidelines [8–12]. A better IPN related knowledge could allow us to evaluate the expected benefits of organized programs of IPN

Abbreviations: IPN, Incidental Pulmonary Nodule; FUP, Follow-Up; NLP, Natural Language Processing; BERT, Bidirectional Encoder Representations from Transformers; HCL, Lyon University Hospital

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https://doi.org/10.1016/j.resmer.2024.101136

management, as it has been suggested by the recent work of Osarogiagbon *et al.* [13].

In this study, we aimed to assess the prevalence of IPN and related FUP outcomes in a large French hospital-based population, through Bidirectional Encoder Representations from Transformers (BERT)-based Natural Language Processing (NLP) detection of nodules in CT reports. NLP is a subset of computer sciences and artificial intelligence, using computational technique to learn, understand, and produce human language content [14,15]. The use of contextual embedding method allows to better understand the sentence's meaning, and to study more complex concepts. Especially, BERT is a pre-trained NLP framework that has shown promising results on a variety of NLP tasks [16].

Our primary endpoint was the assessment of IPN prevalence over one year and the associated FUP rate through healthcare database analysis. We also aimed to describe the main characteristics of IPN in our population and to assess factors associated with the occurrence of FUP. Finally, we evaluated the accuracy of our NLP algorithm through a manual review of radiology reports. This study was conducted during COVID-19 era.

2. Methods

2.1. Study population

We retrospectively identified individuals who had at least one CT at Lyon University Hospital (HCL) during the period from January 1, 2019, to December 31, 2020. CT reports from 2019 were used to train and validate the NLP model. All the CT performed at HCL (regardless of the anatomical zone explored), from January 1, 2020, to December 31, 2020, were included in our study. Radiology reports were semi-structured, with 4 sections, according to the European recommendation [17].

2.2. Ethic

The privacy policy of HCL has been respected. Patient data were considered as anonymous by our local ethic committee, therefore with no need of individual consent. The present study was registered at the «Commission Nationale de l'Informatique et des Libertés » (CNIL) under the number 21_5853.

2.3. NLP algorithm

The NLP algorithm was trained to identify the reports describing the presence of a pulmonary nodule.

To train our model, we first extracted all the sentences from the "findings'' section of each CT report of the 2019 training dataset. It resulted in 1,007,000 independent sentences. Among these sentences, 52,300 were randomly selected and labeled by a clinician and a radiologist according to their semantic meaning. The labels were 'Non-Thoracic", "Healthy Thoracic" and "Pathological Thoracic" related sentence. This latest category was then labeled according to the pathological feature described in the sentence: "Pulmonary embolism", "Non-embolic pulmonary artery pathology", "Heart abnormality", "Mediastinal lymphadenopathy", "Bronchial disorders", "Interstitial syndrome", "Pleural abnormality", "Thoracic wall abnormality', "Aortic dissection", "Aortic aneurysm", "Aortic Atheroma", "Aortic Ulceration", "Congenital aortic pathology", "Sub-clavicular artery or bronchial arteries disorder", "Lung condensation", "Post-surgical aspect", "Pulmonary mass" (opacity $\geq$ 30 mm), "Pulmonary micro-nodule" (opacity < 3 mm), "Pulmonary interstitial micro-nodule" (micro-nodule with associated interstitial features), "Pulmonary nodule" (3−30 mm), "Intrapulmonary lymph node", "Spiculated nodule". In case of disagreement on a label, a review was performed in consensus.

This labelled dataset was then randomly split in 90 % for training, 5 % for validation and 5 % for testing the two classifiers described below.

A BERT-based NLP sentences classifier was built in two steps. First, an unsupervised fine-tuning of the network was performed for Camembert model using a Masked Language Model method on all the sentences extracted from the whole training dataset excepted these of the test dataset [18]. Then, two classifiers were trained successively on the manually labelled sentences. The first one aimed to classify the reports' sentences into three categories ('Non-Thoracic", "Healthy Thoracic" and "Pathological Thoracic" related sentences), the second one to classify the reports' sentences into the pathological sub-categories.

On the test dataset, the final accuracy of these two classifiers was 98.6 % and 94.7 % respectively.

2.4. Application on our study population

All CT performed during the year 2020 in our hospital were included in the analysis, regardless of the presence of chest exploration.

The presence of a nodule was considered when one or more sentences within the same report (in the findings and/or impression section) were classified as "Pulmonary micro-nodule", "Pulmonary nodule", or "Spiculated nodule". We did not consider reports classified as "Pulmonary mass", "Pulmonary interstitial micro-nodule", "Intrapulmonary lymph node" or when no nodule was identified.

The same NLP workflow was then applied on the impression section to determine whether the radiologist who originated the report mentioned the presence of a nodule in the conclusion.

To evaluate the performance of the NLP algorithm we selected a random sample of 475 (0.5 %) patients from our study dataset (2020). We compared the nodule identification findings between NLP algorithm and physician review of reports.

2.5. Nodule characteristics

We performed a keyword analysis using Microsoft Excel version "2206 Build 16.0.15330.20216″ on the text of the CT reports (all keywords are available in supplemental material, Table S1). According to this keyword analysis on the database of patients with a pulmonary nodule identified by the NLP algorithm, those with a history of cancer or nodule mentioned in their CT report were removed from the analysis.

We determined if there was a mention of the nodule in the impression section, if the nodule was related to COVID-19, and its attenuation, through keyword analysis. We assumed that nodules with no specified attenuation were solids. We defined a COVID-19 related CT as any CT performed in a context of microbiologically proven COVID-19, or suspected COVID-19.

Nodule size and location were collected by manual review of all the reports with IPN. In case of multiple nodules, the size of the largest one was retained. In case of single nodule, we reported the lobe in which it was located. Multiple nodules were reported as such, without specification of their location.

2.6. Follow-up (FUP)

We used the international coding system for medical procedures and diagnoses ICD-10 (International Statistical Classification of Diseases and Related Health Problems 10th Revision) to collect the information regarding patients' FUP, from January 1, 2020, to December 31, 2021. Information related to cancer diagnosis and common cancer diagnostic investigations were targeted. Information regarding the occurrence of chest CTs or consultations were also collected.We considered as adequate FUP, a patient who received a chest CT and/or a consultation (in the pulmonology, thoracic surgery and/or radiation oncology departments) during the study period and after the nodule discovery. Other patients were considered as belonging to the No FUP group. Manual review of the patient's medical records was performed for patients with a diagnosis of cancer.

3. Statistical analysis

Analyses were performed using R, version "2022.02.1 + 461″ (The R Foundation for Statistical Computing, Vienna, Austria). We utilized a Bonferroni correction to adjust for multiple testing, separately for the two sets of comparisons after which p-values ≤ 0.006 (for univariate) and p-values ≤ 0.004 (for multivariate) were considered as statistically significant. Continuous variables were reported as mean with standard deviation (SD) and categorical variables as count with percentages and their 95 % confidence intervals (CI95 %). Variables of interest were compared between the FUP group and the No FUP group, using $\chi 2$ test for categorical variables and Wilcoxon-Mann-Whitney *U* test test for continuous variables that did not have a normal distribution according to Shapiro test. Logistic regression analysis was performed to examine the association between the independent variables and the follow up, using "glm" function and "forrestmodel" package. New categorical variables were created from quantitative variables. Cutoff were chosen for their clinical relevance. Missing data were reported as such and included as a value of the concerned variables in the multivariate analysis. Only relevant variables, statistically significant in univariate analysis, were included in the multivariate analysis. Interactions and multicollinearity were systematically evaluated.

Table 1
Patient and nodule characteristics in the IPN population. SD: standard deviation. COVID-19: coronavirus disease 2019. IPN: Incidental Pulmonary Nodule.

Patient and nodule characteristics	*N* = 1991 (%)
Patient age	
Mean age ± SD	64.67 ± 19.60
Age 50–75 years-old	890 (44.70)
Patient sex	
Females	892 (44.80)
Males	1099 (55.20)
Nodule size	
Mean size in mm ± SD	7,75 ± 5.47
≥ 6 mm	949 (47.71)
Not available	414 (20.80)
Number	
Single	1145 (57.51)
Multiple	534 (26.82)
Not available	312 (15.67)
Lobe*	
Right upper lobe	298 (14.97)
Middle lobe	147 (7.38)
Right lower lobe	263 (13.21)
Left upper lobe	195 (9.79)
Left lower lobe	242 (12.15)
Nodule type	
Solid	1860 (93.42)
Ground glass	93 (4.67)
Part-solid	38 (1.91)
Nodule mentioned in the impression part (conclusion section)	
Yes	971 (48.77)
No	1020 (51.23)
COVID-19 related CT	
Yes	410 (20.59)
No	1581 (79.41)

* Among single nodules.

4. Results

4.1. Population and nodule characteristics

The NLP algorithm identified 15,996 (16 %) positive nodule cases during the study period, out of the 101,703 CT performed in HCL in 2020 (Fig. 1). This corresponds to 8108 patients. Among these, 1991 were IPN. All characteristics are figured in Table 1.

Mean nodule size was 8 mm (SD ± 5 mm). 48 % of the nodules were ≥ 6 mm. 27 % of the patients had multiple nodules. Most nodules were solid (93 %). 49 % of the nodules were mentioned in the impression part, whereas 51 % were only mentioned in the text body of the CT report. 21 % were related to COVID-19.

4.2. Accuracy of the NLP algorithm to identify IPN in radiology reports

A physician manually reviewed the radiology reports from a random sample of 475 patients. We compared these results (considered as the reference) to NLP detection of IPN (Table 2). We evaluated that the NLP sensitivity, specificity, and accuracy were respectively 98 %, 99 % and 99 %.

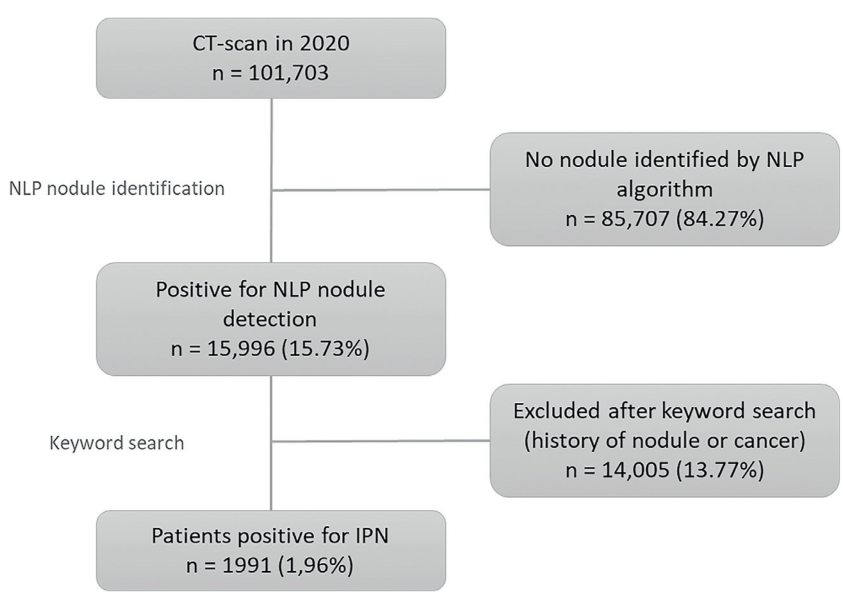

Fig. 1. flowchart of the study. CT: Computed Tomography, NLP: Natural Language Processing, IPN: Incidental Pulmonary Nodule.

Table 2
Performance of our NLP algorithm to identify IPN on the study dataset.

	Value	CI95 %
Sensitivity	97.8 % (44/45)	94 % - 100 %
Specificity	99.3 % (427/430)	98 % - 100 %
Positive Predictive Value	93.6 % (44/47)	87 % - 100 %
Negative Predictive Value	99.8 % (427/428)	99 % - 100 %
Accuracy	99.2 % (471/475)	97 % - 99 %

4.3. Follow-up

Overall, 41 % of patients with IPN were followed up in our population (Fig. 2).

4.4. Comparison between followed and unfollowed patients in univariate analysis

In univariate analysis, patients belonging to the 50–75 years-old category were over-represented in the FUP group whereas the > 75 years-old category was under-represented (Table 3).

Even if the difference is weak, nodules were significantly larger in the FUP group in comparison to the No FUP group (8.1 mm vs 7.5 mm respectively, $p < 0.001$). Moreover, in the FUP group, 33 % and 21 % had nodules larger than 6 mm and 10 mm respectively, whereas it was only 29 % and 15 % in the No FUP group ($p < 0.001$).

In addition, the proportion of reported nodules in the conclusion by the radiologist was significantly higher in the FUP group (57% vs 43 %, $p < 0.001$).

COVID-19-related CT were under-represented in the FUP group in comparison to the No FUP group (15% vs 24 %, $p < 0.001$).

Part-solid nodules were over-represented in the group of patients with FUP, but without reaching the significance level after Bonferroni correction (2.85% vs 1.27 %, $p = 0.0489$)

4.5. Comparison between followed and unfollowed patients in multivariate analysis

We performed a multivariate analysis to refine our model for assessing factors associated with the likelihood of patient FUP (Fig. 3). We selected the analysis parameters according to their clinical relevance.

Among the included variables, being aged between 50 and 75 years-old (OR = 1.57, 95 %CI 1.24–2, $p < 0.001$) and the mention of the nodule in the impression section were significantly associated with FUP (OR = 1.45, 95 %CI 1.19–1.76, $p < 0.001$). Marginally significant association between nodule size (>10 mm) and FUP was observed (OR = 1.53, 95 %CI 1.14–2.05, $p = 0.004$). In contrary, CT performed in a context of COVID-19 were associated with a lower proportion of FUP (OR = 0.62, 95 %CI 0.49–0.79, $p < 0.001$). Patients over 75 years-old were less likely to be followed, although the threshold for significance was not reached (OR = 0.75, 95 %CI 0.57–0.98, $p < 0.033$). Other variables were not significantly associated with the likelihood of FUP in our model.

4.6. Cancer

In our population, we identified 127 cancer cases (Fig. 4). Lung cancer diagnosis was more frequent among patients with a FUP in comparison to their counterpart (37 % and 10 % respectively). Detailed characteristics of patients with a cancer diagnosis are available in Table 4.

Among lung cancer patients, 44 % were diagnosed with a lung adenocarcinoma, 33 % with a squamous cell carcinoma (SCC), 11 % with a small cell lung cancer and 11 % with other histological types (Fig. 4). Sixteen (44 %) were diagnosed at a non-metastatic stage (Table 4).

5. Discussion

We trained a BERT-based NLP algorithm to detect pulmonary nodules on CT reports and demonstrated its high accuracy in processing a large database with 98 % sensitivity and 99 % specificity. The performance of our NLP tool is comparable to those reported in previously published works [19–21]. IPN prevalence was 2 % among all CT reports of 2020, with a FUP rate of 41 % in the study period. Patient age, nodule size and the mention of the nodule in the impression part were significantly associated with FUP in multivariate analysis, while nodules related to COVID-19 were less followed.

IPN prevalence in the European population is poorly known. In the literature, this prevalence depends on the CT type, ranging from <10 % for abdominal CT, to almost 50 % for chest CT angiograms [22].

The FUP rate of IPN was yet not really explored. With our NLP-based detection method coupled with healthcare software database interrogation, we obtained a FUP rate of 41 %. When considering only the nodules ≥ 6 mm, the FUP rate increased to 45 %. Blagev and colleagues reported that 29 % of IPN discovery led to further evaluation when nodules were discovered in pulmonary angiograms, especially

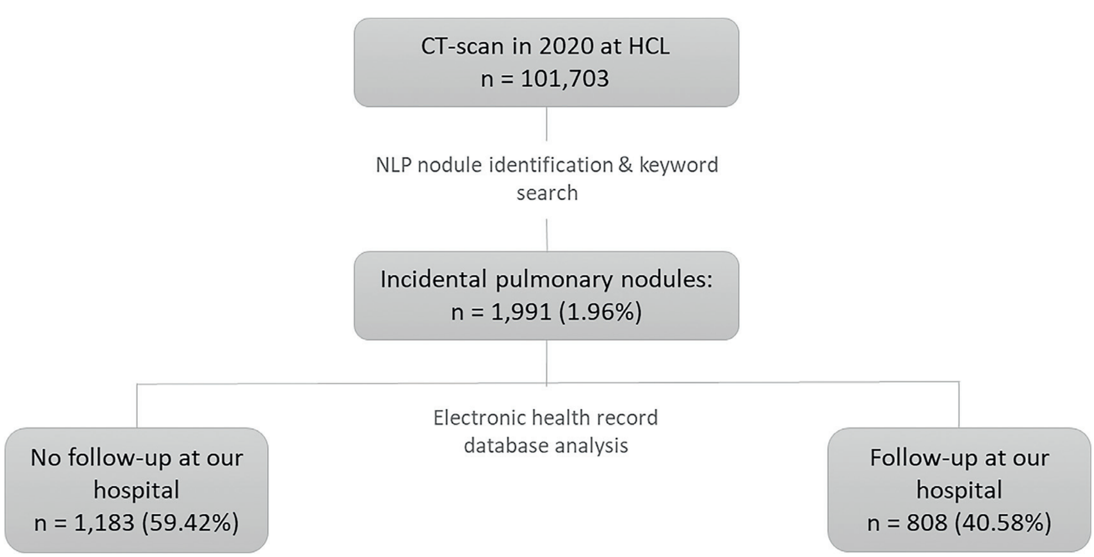

Fig. 2. Flowchart depicting the outcome after incidental pulmonary nodule detection. HCL: Lyon university Hospital.

Table 3
comparison of patients' and nodules' characteristics in univariate analysis, between the followed and unfollowed patients. SD: standard deviation, COVID-19: coronavirus disease 2019, IPN: Incidental Pulmonary Nodule, FUP: Follow-UP.

	FUP *N* = 808	%	No FUP *N* = 1183	%	p
Age (mean ± SD)	63.76 ± 16.32	–	65.28 ± 21.54	–	< 0.001
Age < 50	160	19.8	271	22.91	< 0.001
Age 50–75	441	54.58	449	37.95	
Age > 75	207	25.62	463	39.14	
Total	808	100	1183	100	–
Females	357	44.18	535	45.22	0.679
Males	451	55.82	648	54.78	
Total	808	100	1183	100	–
Size (mm)	8,08	5.43	7.52	5.5	< 0.001
< 6	233	28.84	395	33.39	< 0.001
6 - 10 mm	265	32.8	343	29	
> 10	165	20.42	176	14.88	
Not available	145	17.95	269	22.74	
Total	808	100	1183	100	–
Single	456	56.44	689	58.24	0,359
Multiple	226	27.97	308	26.04	
Not available	126	15.59	186	15.72	
Total	808	100	1183	100	–
Solid	745	92.20	1115	94.25	0.034
Ground glass	40	4.95	53	4.48	
Part-solid	23	2.85	15	1.27	
Total	808	100	1183	100	–
Mentioned in the impression part	463	57.30	508.00	42.94	< 0.001
Mentioned only in the findings	345	42.70	675.00	57.06	
Total	808	100	1183	100	–
Non COVID-19 related IPN	687	85.02	894.00	75.57	< 0.001
COVID-19 related IPN	121	14.98	289.00	24.43	
Total	808	100	1183	100	–

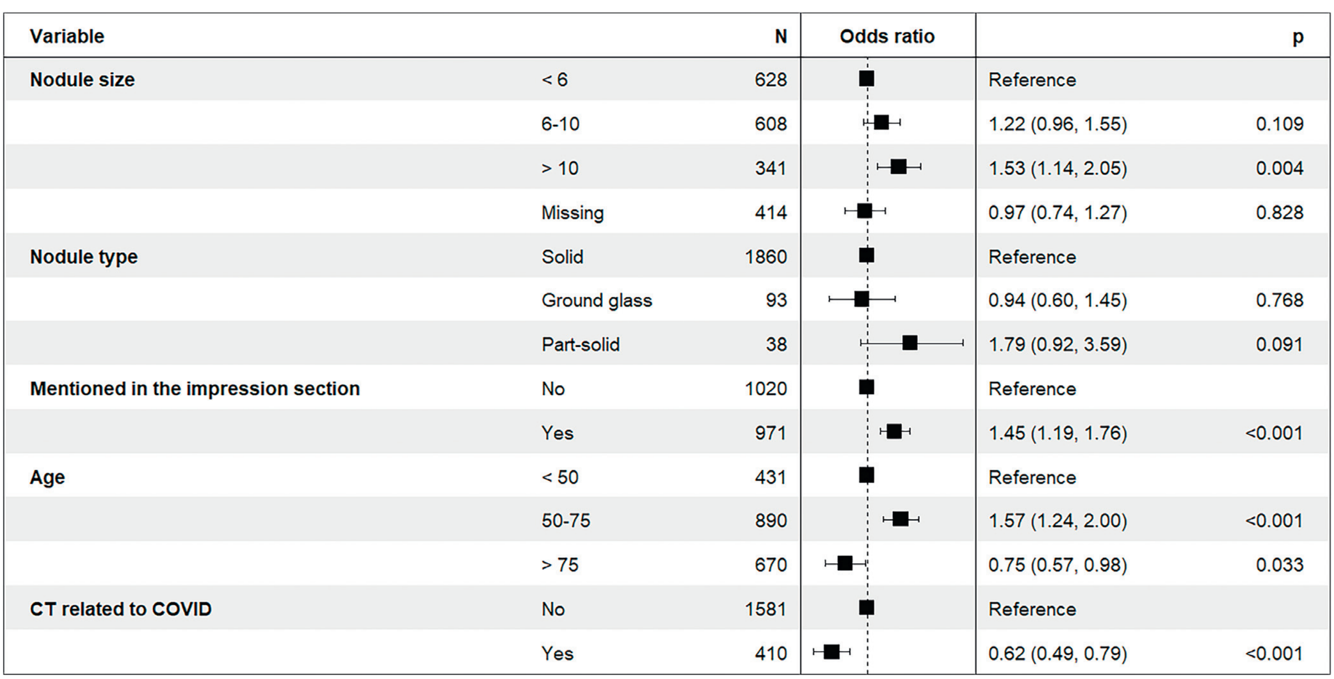

Fig. 3. Multivariate analysis. CT: Computed Tomography, COVID: coronavirus disease.

when they were mentioned in the impression section [8]. Iqbal et al. studied the impact of the terminology used by radiologists to report IPN on FUP. They showed that only 41 % of the nodules resulted in a subsequent FUP [23]. In a retrospective cohort study using NLP to identify nodules in CT reports, Lee et al. reported that 61 % of the patients were followed. Among patients with inadequate FUP a majority had delayed surveillance [19]. We did not study here the adequacy between timely recommended FUP and actual work-up.

In this work, we highlighted different factors associated with patient FUP. A Higher FUP rate was observed in the 50–75 years-old group whereas older patients are under-represented in the FUP group (Table 3, Fig. 3). This trend might be driven by the lower

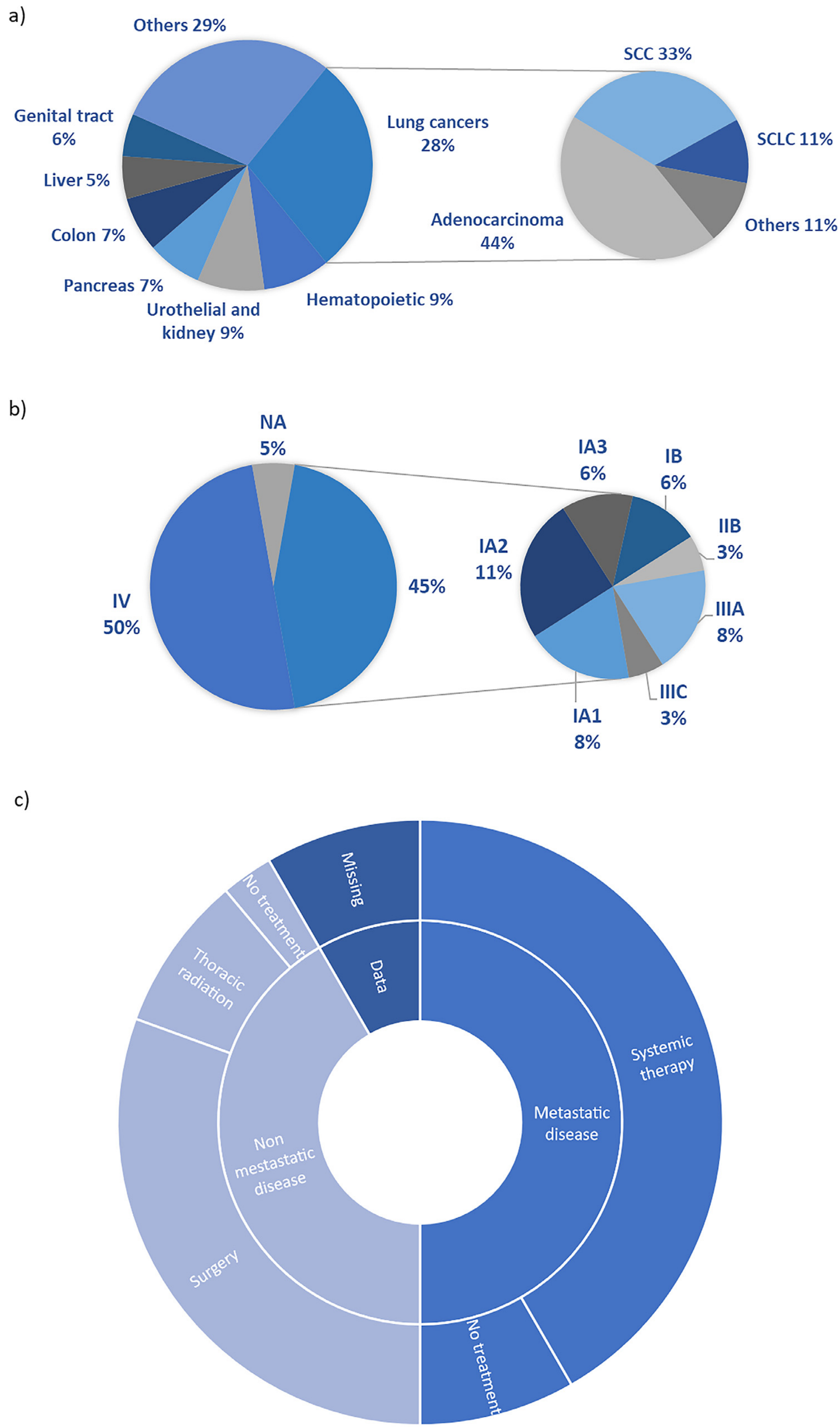

Fig. 4. Cancer diagnosis in the study population. a) Histological types b) Stage distribution among lung cancers. c) Distribution of treatment strategy among lung cancer patients. NA: Not Available. SCC: Squamous Cell Carcinoma. SCLC: Small Cell Lung Cancer.

Table 4
Cancer diagnosis in the study population. SD: standard deviation. COVID-19: coronavirus disease 2019, FUP: Follow-UP, NA: Not Available.

	Lung Cancers		Others		Overall	
	N	%	N	%	N	%
Mean age ± SD	67.31 ± 12.99	–	68.37 ± 15.03	–	67.97 ± 14.43	
Sex						
Female	9.00	25.00	48.00	52.75	57.00	44.88
Male	27.00	75.00	43.00	47.25	70.00	55.12
Tobacco status						
Never	5.00	13.89	40.00	43.96	45.00	35.43
Former	18.00	50.00	29.00	31.87	47.00	37.01
Current	13.00	36.11	15.00	16.48	28.00	22.05
Missing	0.00	0.00	7.00	7.69	7.00	5.51
Mean size (SD)	14.17 ± 8.59	–	8.57 ± 7.56	–	10.22 ± 8.30	–
Number						
Single	20.00	55.56	43.00	47.25	63.00	49.61
Multiple	11.00	30.56	35.00	38.46	46.00	36.22
Missing	5.00	13.89	13.00	14.29	18.00	14.17
Nodule type						
Solid	33.00	91.67	87.00	95.60	120.00	94.49
Ground Glass	2.00	5.56	2.00	2.20	4.00	3.15
Mixt	1.00	2.78	2.00	2.20	3.00	2.36
Mentioned in the conclusion	19.00	52.78	44.00	48.35	63.00	49.61
COVID-19						
Non COVID-19 related CT	31.00	86.11	77.00	84.62	108.00	85.04
COVID-19 related CT	5.00	13.89	14.00	15.38	19.00	14.96
Nodule invasive exploration	25.00	69.44	16.00	17.58	41.00	32.28
Non metastatic disease	16.00	44.44	38.00	41.76	54.00	41.73
Lobectomy	8.00	53.33	NA	NA	NA	NA
Segmentectomy	3.00	20.00	NA	NA	NA	NA
Thoracic radiation	3.00	20.00	NA	NA	NA	NA
No treatment	1.00	6.67	NA	NA	NA	NA
Metastatic disease	18.00	50.00	35.00	38.46	53.00	41.73
Systemic therapy	15.00	41.67	NA	NA	NA	NA
No treatment	3.00	8.33	NA	NA	NA	NA
Missing	2.00	5.56	18	19.78	20.00	16.54
Total	**36.00**	**100.00**	**91.00**	**100.00**	**127.00**	**100.00**

benefit for the patient perceived by the radiologist and/or the clinician. The context of LCS implementation might have also favored the over-representation of 50−75 years-old patients in the FUP population [3,4]. A significantly higher rate of FUP was associated with the mention of the nodule in the conclusion (Fig. 3). This observation had already been made by Blagev *et al.* in their review of 1000 CT pulmonary angiography [8]. Finally, COVID-19 associated CT were less likely to be followed, according to univariate and multivariate analyses. A possible explanation is that the French healthcare system has been heavily affected by the pandemic, and many scheduled consultations, surgeries, and imaging procedures were delayed [24,25].

In our population, 36 lung cancers were diagnosed, representing around 2 % of IPN, with a substantial proportion (45 %) of non-metastatic stage, allowing to consider a curative therapy.

Overall, IPN is a frequent finding, not enough monitored [26]. Several avenues for improvement can be further explored: firstly, a structured reporting and the mention of the IPN in the impression part by the radiologist seem very important [8]. Secondly, facilitating the communication between radiologist and care providers could lead to substantial improvement in the FUP rate: NLP tool allowing to extract the radiologist recommendation from the CT report, patient tracking system, or NLP-based generation of FUP recommendations from the CT reports have been reported [20,22,27]. Finally, the caregiver in charge of the patient at the time of nodule discovery is often limited by time, knowledge, and resources in providing the preferred level of care. This could be addressed by the development of lung nodule surveillance programs [21,22].

Our conclusions must be interpreted with some limitations: patient's FUP was considered only within our institution, and we did not consider the external FUP of the patients. Under-estimation of the FUP rate might have been favored by the FUP of some nodules in non-specialized medical departments, not included in our analysis. Misclassification of nodules might have occurred because of incorrectly reported CT scan indication. Even if our NLP tool was not supposed to retain benign nodules, we did not evaluate its accuracy to discriminate this nodule subclass.

6. Conclusions

To our knowledge, our study is the first to provide information regarding pulmonary nodule prevalence, characteristics, and FUP outcome over one year, in a European population. Another strength of this work lies on the innovative method using NLP algorithm, underlining the significant potential of this tool, its feasibility, and its relevance, in database analysis and medical research.

There is a need for further studies, but our findings provide a useful overview of the situation, encouraging the implementation of IPN management program.

Declaration of interests

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgment

The authors are very grateful to Thibault Thalamas (Acute Respiratory Disease and Thoracic Oncology Department, Lyon Sud Hospital, Hospices Civils de Lyon, Pierre-Bénite, France) for his help in the statistical analysis.

Funding information

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Supplementary materials

Supplementary material associated with this article can be found in the online version at doi:10.1016/j.resmer.2024.101136.

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