

The morbidity and mortality of non-small cell lung cancer in low risk areas of the COVID-19

Minhao Yu (✉ 503071468@qq.com)

Sichuan Science City Hospital

Yalin Cheng

the Third People's Hospital of Mianyang•Sichuan Mental Health Center

Research Article

Keywords: non-small cell lung cancer, morbidity, mortality, COVID-19

Posted Date: September 16th, 2020

DOI: <https://doi.org/10.21203/rs.3.rs-78352/v1>

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Abstract

Objective: To analyze the morbidity and mortality of non-small cell lung cancer and evaluate treatment strategies for non-small cell lung cancer patients in low-risk areas of the COVID-19.

Materials and methods: We selected patients in the hospital in Sichuan Science City Hospital from September 2019 to February 2020 as research subjects and divided them into experimental and control groups. The evaluation of treatment strategy was based on morbidity and mortality.

Results: There were 9010 patients hospitalized. The total morbidity was 0.699%, which was 0.504% in the control group and 0.991% in the experimental group ($P=0.024$). The total mortality was $0.887/10^3$, which was $0.840/10^3$ in the control group (4/4764) and $0.942/10^3$ in the experimental group ($P=0.998$). The patients discontinued therapy or follow-up and cancer progression in the experimental group was significantly higher than that in the control group ($P=0.001$, $\chi^2=0.007$). Most of the discontinued and progressive cancer patients were elderly and in late stage.

Conclusion: The morbidity of NSCLC during the COVID-19 pandemic was significantly high. The mortality in the experimental group was slightly higher than that in the control group, while the difference in cancer progression was significant. It is practicable to perform surgery for early-stage NSCLC patients and undesirable to suspend treatment for late-stage patients in low-risk areas.

Introduction

COVID-19 was first reported by the Wuhan Municipal Health Commission on December 8, 2019, and then was confirmed that it emerged as early as December 1, 2019^[1]. As of this writing, the COVID-19 has been leading to thousands of people died all over the world. Since its outbreaks, the Chinese government has taken strict quarantine actions and high standard testing methods, including chest CT and viral nucleic acid detection^[2,3]. When people are going to in the hospital, they are required to test chest CT and respiratory virus nucleic acid^[3] for the purpose of detecting infected persons in time. Our hospital began to carry out the command in early January 2020. When running a chest CT scan, people are likely to find some lung space-occupying lesions (LSOLS) unexpectedly, such as ground-glass nodules (GGNs), solid nodules, part-solid nodules or pulmonary masses, which have never been found before. There is no evidence to prove the direct relationship between COVID-19 and non-small cell lung cancer (NSCLC), but in theory, the more widespread chest CT scan performed, the more LSOLS found, and correspondingly, the more NSCLC diagnosed.

Cancer patients are a special group amidst this pandemic for their advanced age, complex health conditions and low immune function, and the risk of COVID-19 infection is higher^[4]. In cancer patients on active treatment or even during watchful observation, lymphopenia, which is an independent poor prognostic indicator in COVID-19 patients, is common and the required immune response is impaired^[5,6]. In turn, cancer patients have a higher mortality rate than the general population. Rogado J et al.^[7] found

that there was a significant increase in the mortality rate in lung cancer patients with Covid-19 compared to all Covid-19 patients, which may be because most of them had a greater predisposition to respiratory infections and a previous diagnosis of COPD and metastatic disease. Therefore, providing care to patients suffering from lung cancer has been extremely challenging^[8]. Many researchers have proposed several guidelines to manage this vulnerable population. Kumar S et al.^[9] suggested that if surgical resources were limited or the risks of perioperative care were high, locally advanced NSCLC patients with resectable disease could be treated with definitive non-operative management, such as chemotherapy, chemoimmunotherapy, radiation therapy, and immunotherapy. A consensus statement suggested that during the pandemic, the annual screening exam and treatment of clinical stage I NSCLC should be delayed, and it was acceptable to delay the surveillance CT scan for approximately 3-6 months for patients with an incidentally detected any size pure GGN, part-solid lung nodule with the solid component 6 mm to 8 mm or solid nodule that was less than 8 mm in diameter^[10]. Raskin J et al.^[11] recommended delaying surgery for up to 3 months in small size NSCLC that appear not to grow fast and follow-up of growth rate with chest CT. All these conservative guidelines are proposing potential approaches to reduce the risk of infecting with COVID-19 for NSCLC patients, but there are still some problems. Whether are these guidelines applicable for all NSCLC patients? Do NSCLC patients in low-risk areas benefit from them? To our knowledge, there are still no studies to reckon it. To do that, we carried out a retrospective study to analyze the morbidity and mortality of NSCLC and evaluate treatment strategies for NSCLC patients in low-risk areas of the COVID-19.

Materials And Methods

1 Patients

We selected patients in our hospital from September 2019 to February 2020 as the research subjects and divided them into an experimental group and a control group. Patients in the experimental group were those who were hospitalized from December 2019 to February 2020, and the control group contained those who were hospitalized from September 2019 to November 2019. All hospitalized patients were included and patients in the pediatrics and obstetrics department, under 18 years old and had previous cancer were excluded. The evaluation of the treatment strategy was based on morbidity and mortality. The study protocol was approved by the Ethics Committee of our hospital and informed consent was obtained from patients.

2 Treatment strategy

In the control group, our treatment strategies obeyed the guides of the Chinese Society of Clinical Oncology (CSCO). We chose patients in stage I-II and resectable stage IIIA-IIIB to perform surgical treatment. Nonsurgical treatments, such as chemotherapy, targeted therapy, radiation therapy, and immunotherapy, were performed for postoperatively locally advanced NSCLC patients and those who were not suitable for surgical treatment. During the pandemic, we generate ourselves' treatment strategies after consulting several guidelines. Therefore, in the experimental group, patients in stages I and II are

advised to undergo surgery as usual, while patients in stages III-IV are told to delay any therapy, including surgery, chemotherapy, radiation therapy and immunotherapy, whereas targeted therapy is not, because it can go on in outpatient settings. All the patients during the pandemic are asked for testing chest CT and respiratory virus nucleic acid, and all treatments should be suspended if one is a suspected infected person.

3 Statistical analysis

SPSS 22.0 (IBM Corp., Armonk, NY, USA) software was used for the statistical analysis. Measured data were expressed as the mean \pm standard deviation or the median. A t-test was used to compare normally distributed data according to whether the variance was equal. The Mann-Whitney U test was used to compare non-normally distributed data sets. Countable data were expressed as absolute values or percentages, and comparisons between groups were performed using the chi-square test or Fisher's exact probability method. The difference was statistically significant at $P < 0.05$.

Results

1 The morbidity of NSCLC

There were 9010 included patients hospitalized in our hospital between September 2019 and February 2020, including 4518 men and 4492 women. There were 63 newly confirmed NSCLC patients and the total morbidity was 0.699% (63/9010). The morbidity in the control group was 0.504% (24/4764), and in the experimental group, it was 0.919% (39/4246). In the control group, 1694 patients underwent chest CT scans, and 713 patients were found to have LSOL, among which 77 cases had unclear diagnoses and 49 cases had malignant lesions. In the experimental group, 2729 patients underwent chest CT scans, and 1743 patients were found to have LSOL, among which 174 cases had unclear diagnoses and 76 cases had malignant lesions. The line chart of the total number of hospitalizations, chest CT scan, LSOLS findings, unclear diagnosis LSOLS, malignant LSOLS, and pathologically confirmed NSCLC from September 2019 to February 2020 is shown in Figure 1. The clinical characteristics are shown in Table 1.

Fig 1 The line chart of the total number of hospitalizations, chest CT scan, LSOLS findings, unclear diagnosis LSOLS, malignant LSOLS, and pathologically confirmed NSCLC

2 The mortality of NSCLC

There were 196 pathologically confirmed NSCLC patients treated in our hospital, including the 63 newly confirmed NSCLC patients. The age of the control group was significantly higher than that of the experimental group, while the number of therapy or follow-up discontinued and cancer progression patients was significantly lower than that of the experimental group. The total mortality was $0.887 / 10^3$ (8/9010), which in the control group was $0.840 / 10^3$ (4/4764) and in the experimental group was $0.942 / 10^3$ (4/4246). The death tolls in both groups were 4, and the mortality between them was not significantly different ($P = 0.998$). The bar chart of pathologically confirmed, therapy or follow-up

discontinued, cancer progression, outpatient, and inpatient patients of each month is shown in Figure 2. Treatment methods for each month are shown in Figure 3. The clinical characteristics of the 196 NSCLC patients are shown in Table 2. The details of the fifty-five therapy or follow-up discontinued patients are shown in Table 3. The number of early stage (I+II) patients was 23, the number of late stage (III+IV) patients was 32, and the mean age was 67.75 ± 10.11 years old.

Fig 2 The bar chart of pathologically confirmed, therapy or follow-up discontinued, cancer progression, outpatient, and inpatient patients

Fig 3 Different treatment methods of each month

Discussion

The city our hospital located in had a population of more than 5.3 million, and a total of 22 cases were confirmed to be infected with COVID-19 at the end of February 2020. To date, all have been cured and discharged, and no new cases have been reported. The city is a genuine low-risk area, and fortunately, there are no COVID-19-infected patients in our hospital. Our hospital started strict testing methods and limited the number of hospitalizations as soon as the government sounded a warning. In addition, we have projected a series of prevention programs in the operating room, such as checking body temperature, wearing medical face masks or protective clothing, and operating in laminar flow operation rooms. Treatments must be suspended, and quarantine action must be taken if a patient is suspected to be infected with COVID-19 before being in the hospital. During the pandemic, we prefer a positive surgical treatment strategy for early-stage patients and a negative non-surgical strategy for patients in the late stage. This is because early-stage patients have less respiratory disease and less surgical trauma, so they can recover and be discharged more quickly, while late-stage patients always have complex health conditions and low immune function, which can easily lead to complications and cause a longer length of stay, increasing the risk of infection.

We could learn from the line chart (Fig. 1) that since January 2020, the number of hospitalizations has decreased considerably, while patients who test chest CT scans have increased simultaneously, and the number of LSOLs detected by chest CT increased correspondingly. The reason why there were still a large number of patients in the hospital and a small number of patients testing chest CT in December 2019 might be that people did not realize the seriousness of the virus at the very beginning. Furthermore, in December 2019 and before, the change tendency of pathologically confirmed NSCLC was nearly consistent with that of unclear diagnosis and malignant LSOLs, while after that, its increment was lower than that of unclear diagnosis and malignant LSOLs. This indicates that some high-risk patients delay further examination and treatment.

The total morbidity of NSCLC for the 9010 patients was 0.699%, which was dramatically higher than that reported from 2009 to 2011^[12-14] in China. This might be because, on the one hand, this study looked at hospitalized patients, who had a relatively high prevalence rate, rather than at the general population at large. On the other hand, patients in hospitals have a high probability of obtaining CT scans, which results

in more LSOLS. Therefore, the high morbidity is reasonable. The key to these data was that the morbidity in the experimental group was significantly higher than that in the control group. This may be because more people received CT scans. Chest CT is of great significance in lung cancer screening. The National Lung Screening Trial Research of America found that 96.4% of the positive screening results in the low-dose CT group and 94.5% in the radiography group were false positive results, and the rate of death from any cause was reduced in the low-dose CT group^[15]. An Early Lung Cancer Action Project study showed that 85% of the CT-detected cancers were stage I, and the curability rate of these malignancies was in excess of 80%^[16]. Therefore, the data not only support the importance of chest CT in lung cancer screening, but also illustrate the significance of developing a rational treatment strategy for NSCLC during the pandemic.

In the context of COVID-19, controlling the pandemic is the most common, but managing cancer patients is also vital. To date, many researchers have proposed several recommendations to solve this problem. The European Society of Medical Oncology (ESMO)^[17] agreed to principles to classify three levels of priorities for cancer care management, namely, high priority, medium priority and low priority, and it recommended high priority for advanced NSCLC by applying to neoadjuvant treatment in potentially resectable stage IIIA. This is worth our learning. Figure 2 shows that the therapy or follow-up discontinued patients showed an upward trend, and it was significantly higher in the experimental group than in the control group (Table 2), which might be the reason why there was a significant difference between the two groups in cancer progression patients (Table 2). Table 3 shows that most of the discontinued and progressive cancer patients were elderly and in stage III or IV. This means that we delayed the treatment of these patients. Although there was no statistically significant difference in the mortality between the two groups, the mortality in the experimental group was still higher than that in the control group, and the difference might be more significant over time. So, a positive non-surgical strategy should be applied to advanced NSCLC patients. However, the ESMO recommendations were not based on risk classification, and it preferred to delay operation in early stage NSCLC, while Cafarotti^[18] suggested surgical treatment for I-IIa stage NSCLC in low risk of infection. The latter is almost identical to our strategy. Although the number of hospitalizations in the experimental group was lower, the number of inpatient NSCLC patients (Fig. 2) and surgical treatment patients (Fig. 3) was significantly higher than that in the control group. It manifests that a positive surgical strategy is feasible for early-stage patients without increasing the risk of infection in low-risk areas under the premise of strict testing and prevention measures.

Although this is a retrospective study, it is significant because it is unwise to blindly carry out a prospective study as things are. As far as it goes, the pandemic is almost impossible to end in a short time, so we should prepare a long struggle against it. It is advisable for different areas to set out treatment strategies according to the actual situation of different risks. Based on this study, we will improve our treatment strategy for NSCLC in the future.

Conclusion

The morbidity of NSCLC during the COVID-19 pandemic was significantly high as a result of CT scan expansion. The mortality in the experimental group was slightly higher than that in the control group, while the difference in cancer progression was significant. It is practicable to perform surgery for early-stage NSCLC patients and undesirable to suspend the treatment for late-stage patients in low-risk areas under the premise of strict testing and prevention measures.

Declarations

Acknowledgements

None.

Conflict of Interest Statement

Minhao Yu has no conflict of interest. Yalin Cheng has no conflict of interest.

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Tables

Table 1 Clinical characteristics of the 9010 hospitalized patients

Items	Control group (n)	Experimental group (n)	P Value
Sex			
Male	2364	2154	0.301
Female	2400	2092	
Age (years)	60.85±17.65	61.49±17.40	0.080
Patients test CT scan	1694	2729	0.001
Total LSOL	713	1743	0.001
Unclear diagnosis LSOL	77	174	0.001
Malignant LSOL	49	76	
New Confirmed NSCLC	24	39	0.024

Abbreviation: LSOL: lung space-occupying lesions; NSCLC: non-small cell lung cancer.

Table 2 Clinical characteristics of the 196 NSCLC patients

Items	Control group (n)	Experimental group (n)	P Value
Sex			
Male	66	47	
Female	46	37	0.393
Age (years)	66.75±11.14	63.04±11.53	0.024
Tumor types			
AAH	1	1	
Ais	1	1	0.971
ADC	93	71	
SCC	17	11	
Stage			
AAH	1	1	
Ais	1	1	
I	52	42	0.952
II	13	8	
III	11	11	
IV	34	21	
Therapy/follow-up discontinued	18	37	0.001
Cancer progression	9	18	0.007
Dead	4	4	

Abbreviation: AAH, atypical adenomatous pyperplasia; Ais, adenocarcinoma in situ; ADC, adenocarcinoma; SCC, squamous cell carcinoma.

Table 3 Details of the fifty-five therapy or follow-up discontinued patients

Patients	Treat time (month)	Sex	Age	Diagnosis	Stage	Discontinued time (month)	Follow up	
							Prognosis	Time
1	9	M	53	SCC	III	1	Progression	Dec.2019
2	9	F	70	ADC	IV	1	Progression	Sep.2019
3	9	M	67	ADC	□	1	Progression	Jan.2020
4	9	M	65	SCC	III	1	Progression	Jan.2020
5	9	M	63	ADC	I	1	Metastasis	May.2020
6	9	M	76	ADC	I	1	Progression	Feb.2020
7	9	M	74	SCC	I	2	Progression	Feb.2020
8	9	M	45	ADC	III	9	Progression	Oct.2019
9	9	M	66	ADC	IV	9	Dead	Sep.2019
10	9	M	64	ADC	III	9	Well	
11	9	M	69	ADC	II	9	Well	
12	9	M	73	ADC	II	9	Well	
13	9	M	63	ADC	IV	10	Dead	May.2020
14	9	M	41	ADC	II	11	Progression	Oct.2019
15	9	M	85	ADC	III	11	Well	
16	9	M	63	SCC	III	12	Well	
17	10	F	74	ADC	III	10	Progression	Jan.2020
18	10	F	67	ADC	I	10	Well	
19	10	M	80	ADC	IV	10	Well	
20	10	F	55	ADC	II	11	Progression	Nov.2019
21	10	M	78	SCC	III	12	Progression	Dec.2019
22	10	M	81	ADC	IV	12	Dead	Jan.2020
23	11	M	81	ADC	I	1	Well	
24	11	M	63	SCC	II	2	Progression	Nov.2019
25	11	M	57	ADC	IV	11	Progression	Nov.2019
26	11	M	63	ADC	II	11	Well	
27	11	F	74	ADC	IV	11	Well	

28	11	M	80	ADC	IV	11	Well	
29	11	F	58	ADC	IV	11	Well	
30	11	M	71	SCC	IV	12	Dead	Dec.2019
31	11	M	79	SCC	IV	12	Well	
32	12	M	90	SCC	I	1	Well	
33	12	M	78	SCC	I	1	Well	
34	12	M	68	ADC	II	12	Progression	Jul.2020
35	12	F	76	ADC	II	12	Progression	Jan.2020
36	12	M	44	ADC	IV	12	Progression	Feb.2020
37	12	M	61	ADC	III	12	Progression	Jan.2020
38	12	M	67	ADC	I	12	Well	
39	12	M	66	SCC	II	12	Dead	Feb.2020
40	1	M	56	SCC	III	1	Progression	Jan.2020
41	1	F	78	ADC	IV	1	Well	
42	1	M	61	ADC	I	1	Well	
43	1	M	79	ADC	I	1	Well	
44	1	M	74	ADC	IV	1	Well	
45	1	M	72	ADC	II	1	Well	
46	1	M	78	ADC	IV	1	Well	
47	1	M	69	ADC	III	2	Dead	May.2020
48	1	F	58	SCC	II	2	Well	
49	1	M	63	SCC	IV	2	Well	
50	1	M	68	ADC	III	12	Well	
51	2	M	63	ADC	IV	2	Progression	Apr.2020
52	2	M	66	ADC	IV	2	Well	
53	2	M	68	SCC	IV	2	Well	
54	2	M	69	ADC	IV	2	Well	
55	2	M	56	SCC	I	2	Well	

Abbreviation: M, male; F, female; ADC, adenocarcinoma; SCC, squamous cell carcinoma.

Figures

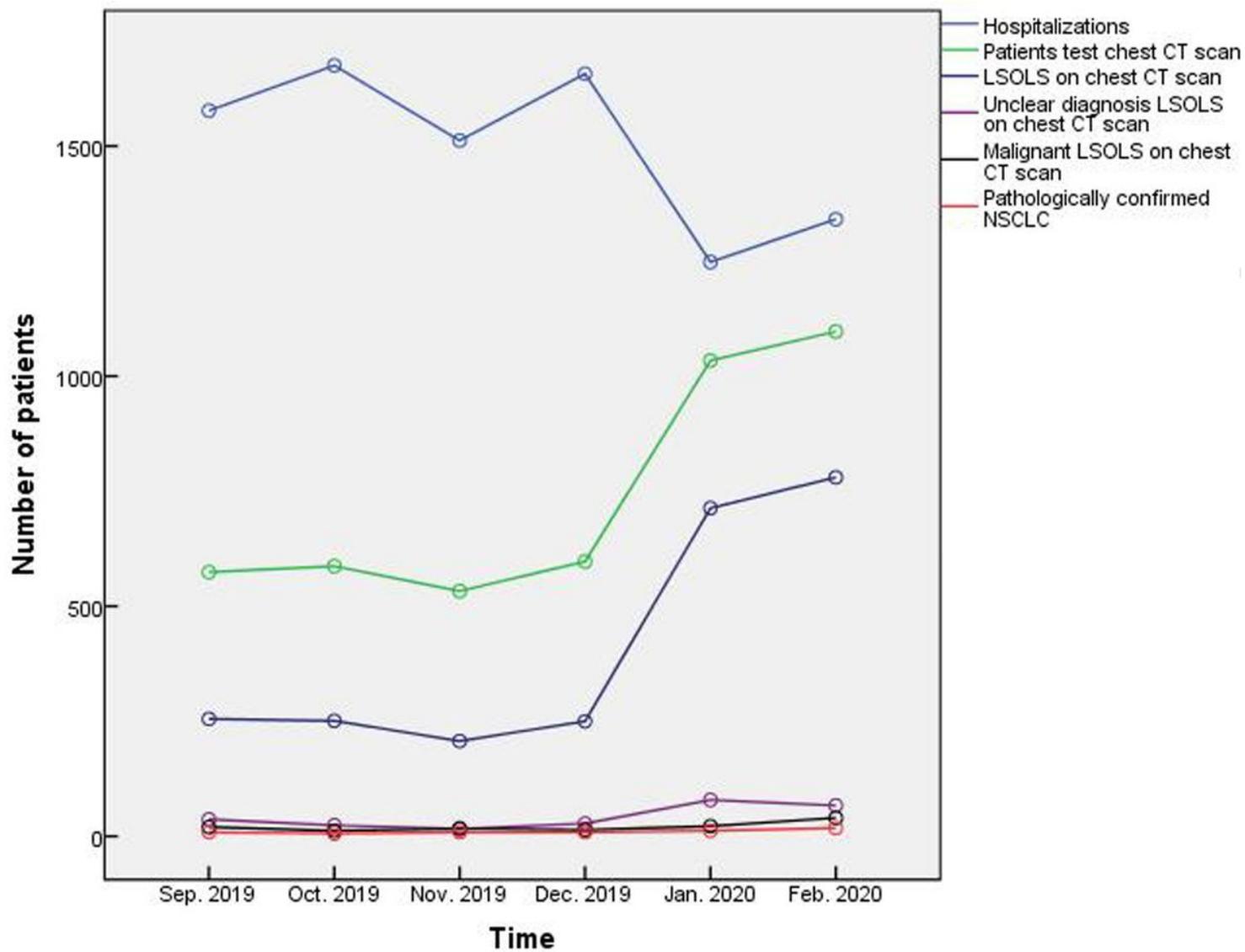


Figure 1

The line chart of the total number of hospitalizations, chest CT scan, LSOLS findings, unclear diagnosis LSOLS, malignant LSOLS, and pathologically confirmed NSCLC

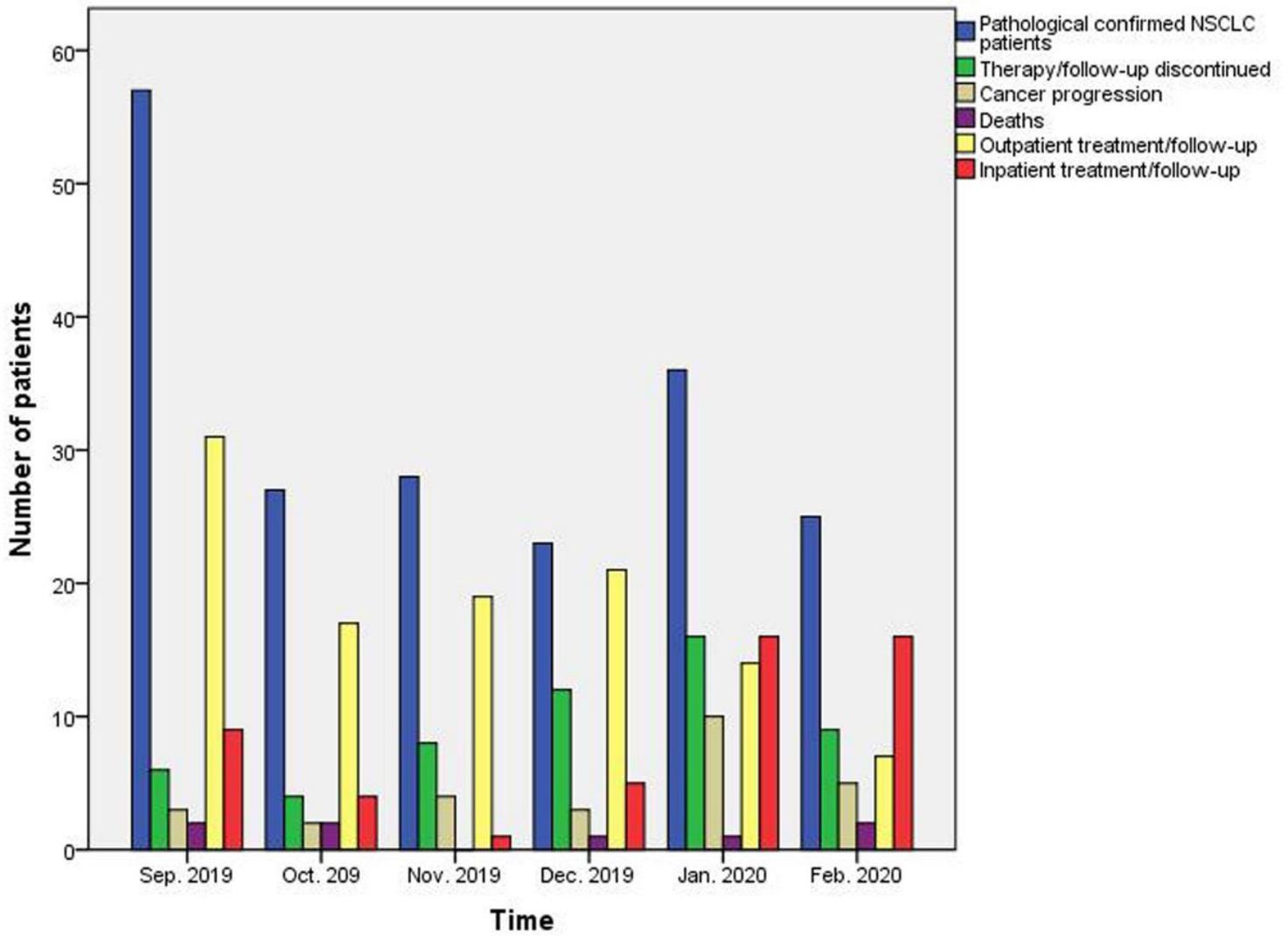


Figure 2

The bar chart of pathologically confirmed, therapy or follow-up discontinued, cancer progression, outpatient, and inpatient patients

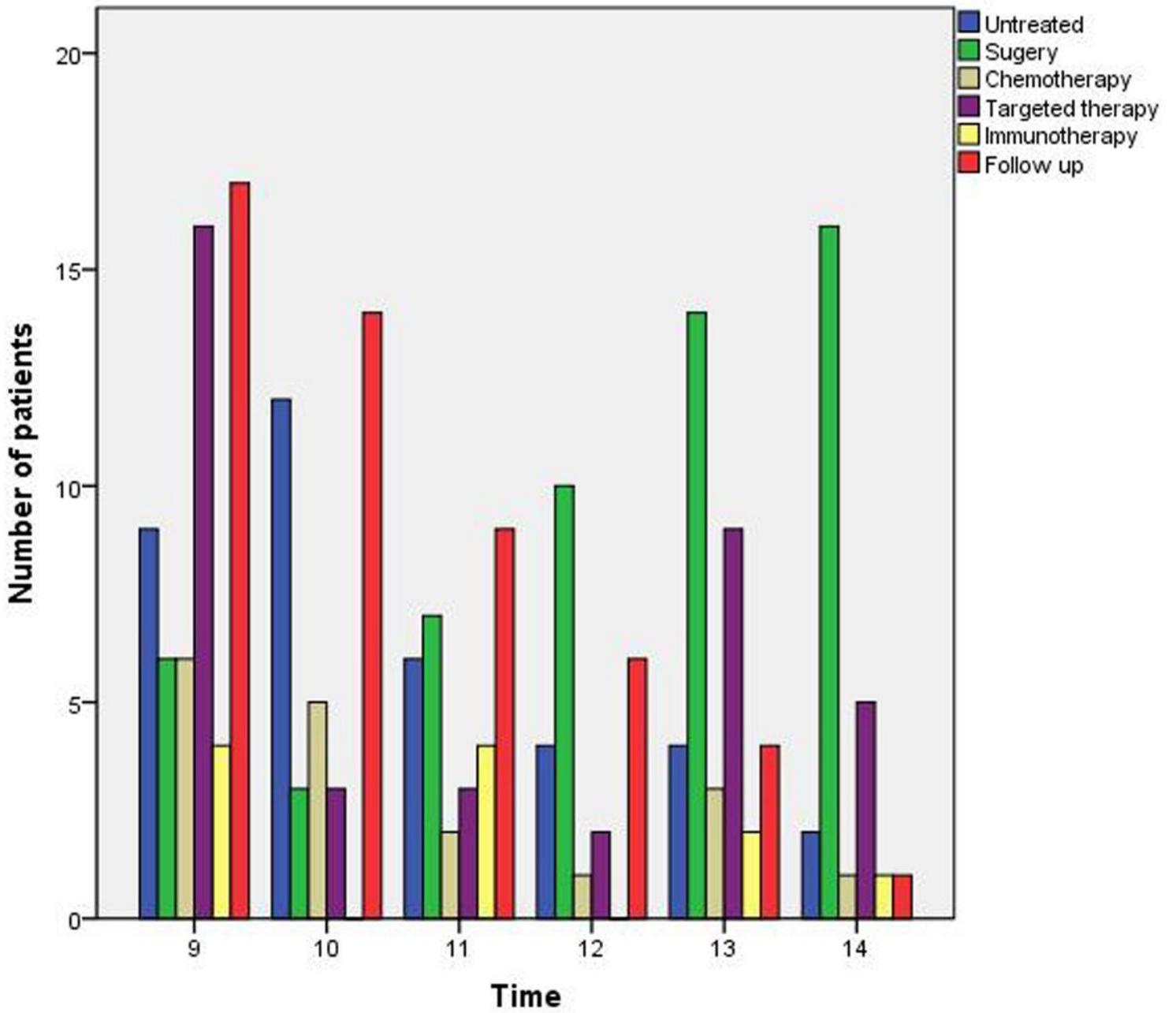


Figure 3

Different treatment methods of each month