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Clinical Analysis of Multiple Primary Malignant Tumors: A Single-Center Experience

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What is already known on this topic?

- *Multiple primary malignant tumors (MPMTs) are increasingly diagnosed due to prolonged survival and improved diagnostic and treatment methods.*
- *Multiple primary malignant tumors may be misdiagnosed as recurrence or metastasis, which can lead to inappropriate treatment decisions.*
- *Several risk factors such as age, smoking, family history, and obesity are associated with the development of MPMTs.*

What this study adds on this topic?

- *This study presents detailed clinical, demographic, and pathological characteristics of 121 patients with MPMT diagnosed at a single tertiary care center over a 5-year period.*
- *It demonstrates that patients with metachronous MPMT have significantly better survival outcomes compared to those with synchronous or both types of tumors.*
- *It identifies secondary primary lung cancer as the leading cause of death, emphasizing the importance of close monitoring and early diagnosis in high-risk patients.*

Abstract

Objective: Multiple primary malignant tumors (MPMTs) are at least 2 separate malignancies that develop independently. The incidence of patients diagnosed with MPMT is reported to be between 0.52% and 11.7% in various studies in different countries. The study aims to investigate the incidence, clinical features, and survival of patients with MPMT.

Methods: About 121 patients diagnosed with MPMT in the institution were retrospectively analyzed between January 2015 and December 2020. Multiple primary malignant tumors were defined as synchronous tumors if they occurred within 6 months or less, and as metachronous tumors if they occurred more than 6 months. All statistical analyses were performed using SPSS version 25.0.

Results: This study found the incidence of patients with MPMT was 2.6%. Two primary malignancies were detected in 104 (85.9%) patients, 3 primary malignancies in 13 (10.7%), and 4 primary malignancies in 4 (3.3%). In this study, the most common tumor associations were found in patients with MPMT were lung-colorectal 12 (7.1%), lung-prostate 9 (5.3%), and prostate-bladder 9 (5.3%) tumors. Among the patients with MPMT, 38 (31.4%) synchronous MPMT, 72 (59.5%) metachronous MPMT, and 11 (9%) both synchronous and metachronous MPMT were found.

Conclusion: As a result, it was found that lung, colorectal, and prostate cancers were most common in MPMT patients. This study showed that it is very important to distinguish between second primary, recurrence, or metastasis and that treatment methods can be applied to cure patients with the correct diagnosis.

Keywords: Colorectal cancer, lung cancer, metachronous tumors, multiple primary tumor, synchronous tumors

Introduction

Multiple primary malignancies have become an increasingly important topic in oncology. Accurate diagnosis of multiple primary malignant tumors (MPMTs) and their distinction from recurrence or metastasis is of critical importance in determining the most appropriate treatment strategy and improving patient survival.[1] Multiple primary malignant tumors were first described by Billroth in 1889.[2] Multiple primary malignant tumors are defined as at least 2 separate malignancies that develop simultaneously or sequentially, histologically confirmed, independently in the same or different organs.[3] The first study on MPMTs was conducted by Warren and Gates in 1932. Depending on the time of diagnosis of each malignancy, MPMT is divided into 2 categories. Warren and Gates define it as synchronous multiple primary malignant tumors if the interval between primary tumors is 6 months or less, and if this period is longer than 6 months, it is defined as metachronous multiple primary malignant tumors.[4]

Today, the increase of MPMTs is becoming a major medical problem, and the incidence varies widely in many studies.[5,6] The incidence of MPMTs has been reported to be between 0.52% and 11.7% in various studies in different countries.[6,7] Many risk factors are blamed for the development

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of MPMTs; these are the treatment applied for the primary tumor, genetic predispositions, smoking, alcohol, dietary factors, and environmental factors. Survival time in patients with MPMT is variable and is affected by the type of pathology, stage of malignancy, organs involved, the time between malignancies, patient performance, and treatment administered.[8]

Although MPMTs have been increasingly reported in recent years, data from Türkiye remain limited. To the best of the authors' knowledge, this study represents one of the largest single-center retrospective analyses on MPMTs conducted in Türkiye. In this study, the aim was to contribute to the national and international literature by providing real-world data on patients with MPMTs treated at the center and to better describe the epidemiological and clinical features of MPMTs in the Turkish population.

Methods

We retrospectively analyzed patients diagnosed with cancer who were treated or followed up in the Medical Oncology Department of Cerrahpaşa Faculty of Medicine between January 2015 and December 2020. Retrospective data were obtained using the archives of the Department of Cerrahpaşa Faculty of Medicine, Department of Medical Oncology. Outpatient clinic visits provided follow-up for the patients. Patients who met the criteria for diagnosis of MPMT were included in the study. Warren and Gates' diagnostic criteria were used to diagnose MPMTs.[4] The diagnostic criteria are: 1) all primary tumors are malignant, 2) each of the tumors has its pathological features, and 3) tumors are formed in different regions or organs. Exclusion criteria are: 1) patients younger than 18 years of age, 2) patients with tumor recurrence or metastasis, and 3) patients with missing data or insufficient follow-up periods. Patients' age, gender, family history, body mass index, smoking habits, number of primary tumors, tumor location, and intervals between tumors were recorded. The patients were divided into 3 groups: synchronous, metachronous, and both synchronous and metachronous multiple primary tumors. Synchronous multiple primary tumors describe tumor associations occurring over 6 months or less, and metachronous multiple primary tumors describe tumor associations occurring for more than 6 months.[9] If the patients had both synchronous and metachronous tumors, they were included in the group of synchronous and metachronous tumors. The patients were divided into 3 groups according to the World Health Organization age classification. The age groups were determined as under 65 years old, 65-80 years old, and over 80 years old. The survival time of the patients was calculated from the time of diagnosis of the first cancer, considering the death of the patient or the last follow-up.

Statistical Analysis

In statistical comparisons, chi-square or Fisher exact tests were used for qualitative variables, the Kruskal–Wallis test for quantitative variables, and the Mann–Whitney *U* test for post hoc analyses. Overall survival was estimated using the Kaplan–Meier method, and the difference in survival was calculated using the log-rank test. Categorical variables are presented as percentages. Continuous variables are expressed as a range (min-max) and medians. *P* values less than .05 were considered statistically significant. All statistical analyses were performed using SPSS version 25.0 (IBM SPSS Corp.; Armonk, NY, USA).

Ethics Statement

Before starting the study, approval was obtained from the İstanbul University–Cerrahpaşa institutional ethics committee (Approval No.: [E-83088843-604.01.01-22845]). Informed consent was obtained from the participants included in the study. The Helsinki Declaration was followed during the study's execution.

Results

In the center, 4570 patients followed between 2015 and 2020 were screened, and MPMTs were detected in 121 patients. Two primary malignancies were seen in 85.9% (n = 104) of patients, 3 primary malignancies were seen in 10.7% (n = 13) of patients, and 4 primary malignancies were seen in 3.3% (n = 4) patients (Table 1).

There were 31.4% (n = 38) synchronous tumors, 59.5% (n = 72) metachronous tumors, and 9.1% (n = 11) synchronous and metachronous tumor groups (Table 2). The median age of patients with MPMT was 68 (range, 62-75). The majority of patients with MPMTs (60.3%) were 65 years of age or older. Of the patients with MPMT, 62.8% (n = 76) were male and 37.2% (n = 45) were female. The male-to-female patient ratio was 1.68:1. A family history of cancer was present in 63.6% of the patients. The majority of the patients (65.1%) were either former or current smokers. Of the patients, 22.2% had a BMI greater than 30 (Table 3).

The 3 most common tumor sites in patients with MPMT were lung 19.7% (n = 52), colorectal 19.3% (n = 51), and prostate 13.3% (n = 35), respectively. Breast cancer was found to be significantly more common in female patients, with a prevalence of 21.5% (n = 20) ($P < .001$). Lung cancer was found to be significantly more common in male patients, with a prevalence of 24.7% (n = 42) ($P = .002$) (Table 4).

The most common tumor sites in the first primary cancer were breast 14.9% (n = 18), lung 14% (n = 17), colorectal 12.4% (n = 15), and prostate 9.9% (n = 12), respectively (Figure 1A). The most common tumor sites in the second primary cancer were lung 23.1% (n = 28), colorectal 16.5% (n = 20), prostate 16.5% (n = 20), and stomach 7.4% (n = 9), respectively (Figure 1B).

The most common tumor associations in patients with MPMT were lung-colorectal 7.1% (n = 12), lung-prostate 5.3% (n = 9), and prostate-bladder 5.3% (n = 9). Lung-colorectal cancer was the most frequent tumor combination in male patients 8.6% (n = 10), with a significantly higher prevalence compared to female patients ($P = .043$). Breast-colorectal cancer was the most frequent tumor combination in female patients 11.7% (n = 6), with a significantly higher prevalence compared to male patients ($P = .001$) (Table 5).

Table 1. Distribution of Patients by Number of Primary Malignancies

Primary Malignancies	N (%)
2 Primary malignancies	104 (85.9)
3 Primary malignancies	13 (10.7)
4 Primary malignancies	4 (3.3)

Table 2. Distribution of Synchronous, Metachronous, and Both Synchronous and Metachronous Tumor Groups

Tumor Groups	N (%)
Metachronous tumor	72 (59.5)
Synchronous tumor	38 (31.4)
Synchronous and metachronous tumor	11 (9.1)

Table 3. Demographic Information and Clinical Characteristics of the Patients

Variables		N (%)
Gender	Women	45 (37.2)
	Men	76 (62.8)
Age groups	<65	48 (39.7)
	65-80	65 (53.7)
	>80	8 (6.6)
BMI	<18.5	5 (5.1)
	18.5-24.9	34 (34.3)
	25-29.9	38 (38.4)
	>30	22 (22.2)
Smoke	Non-smoker	38 (34.9)
	Ex-smoker	39 (35.8)
	Smoker	32 (29.4)
Family history	Yes	77 (63.6)
	No	44 (36.4)

The most common cause of death in the study was secondary primary lung cancer. The median survival was 71.85 months (range, 55.13-88.57 months) for synchronous tumors, 140.26 months (range, 77.76-202.76 months) for metachronous tumors, and 93.26 months (range, 83.72-102.81 months) for synchronous and metachronous tumors. In Kaplan–Meier analysis, median survival in patients with metachronous tumors was significantly higher than in patients with synchronous tumors and both synchronous and metachronous tumors ($P < .001$) (Figure 2). In the Kaplan–Meier analysis, median survival was significantly longer in female patients ($P = .015$). Median survival was significantly shorter in patients with a history of smoking ($P = .012$). Median survival was found to be statistically significantly longer in patients diagnosed with breast cancer ($P = .007$), whereas it was significantly shorter in those diagnosed with lung cancer ($P = .026$). In the multivariate Cox regression analysis for overall survival, having a metachronous tumor type was identified as a favorable independent prognostic factor ($P < .001$), whereas smoking was demonstrated to be an unfavorable independent prognostic factor ($P = .005$).

Table 4. Most Common Types of Cancer in Men and Women, All Patients

	Women	Men	All Patients	
Cancer Type	**N (%)**	**N (%)**	**N (%)**	***P***
Lung cancer	10 (10.7)	42 (24.7)	52 (19.7)	.002*
Breast cancer	20 (21.5)	**0 (0)**	20 (7.6)	<.001*
Colorectal cancer	14 (15)	37 (21.7)	51 (19.3)	.995
Prostate cancer	**0 (0)**	35 (20.5)	35 (13.3)	<.001*
Bladder cancer	1 (1)	15 (8.8)	16 (6)	.009*
Ovarian cancer	11 (11.8)	**0 (0)**	11 (4.1)	<.001*
Gastric cancer	5 (5.3)	12 (7)	17 (6.4)	.279
Uterus cancer	9 (9.6)	**0 (0)**	9 (3.4)	<.001*
Other cancer	23 (24.7)	29 (17)	52 (19.7)	.312

*P-value < .05.

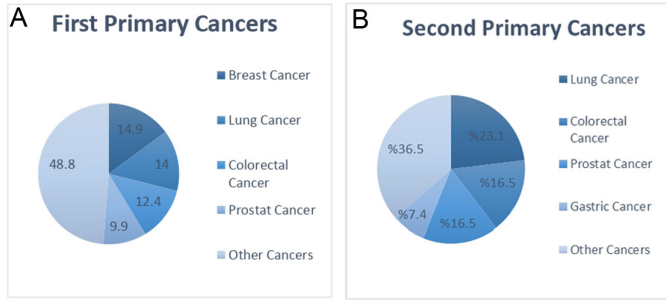

Figure 1. A and B: Most common tumor sites in first primary cancer and second primary cancer.

Discussion

Multiple primary cancers are seen more frequently as patients live longer as a result of advances in screening, diagnostic methods, and new treatments.[10] Schoenberg and colleagues found that patients diagnosed with cancer were 1.29 times more likely to develop new cancer than patients without a cancer diagnosis.[11] This study showed that more than 1 primary cancer may develop after the diagnosis of the first primary cancer in a large number of patients. Multiple primary cancers can pose many challenges for clinicians in treatment management. At the same time, MPMTs can be confused with recurrence or metastases in clinics. Therefore, identifying the characteristics of multiple primary cancers may contribute to more accurate treatment planning for these patients**.** In support of this, [Pk et al] highlighted in their 2024 study that the presence of dual malignancies often leads to diagnostic delays and therapeutic dilemmas, particularly in patients with overlapping symptomatology or atypical presentations.[12]

The incidence of MPMTs has been reported between 0.52% and 11.7% in various studies in different countries.[6,7] Genetic factors, environmental factors, diagnostic methods, and follow-up frequencies cause different incidence results. In the study performed

Table 5. The Most Common Tumor Associations in Women, Men, and All Patients

Tumor Association	Men, N = 116, n (%)	Women, N = 51, n (%)	All Patients, N = 167, n (%)	*P*
Lung – colorectal tumor	10 (8.6)	2 (3.9)	12 (7.1)	.043*
Lung - prostate tumor	9 (7.7)	**0 (0)**	9 (5.3)	.011*
Prostate – bladder tumor	9 (7.7)	**0 (0)**	9 (5.3)	.011*
Breast – colorectal tumor	**0 (0)**	6 (11.7)	6 (3.5)	.001*
Breast – ovary tumor	**0 (0)**	3 (5.8)	3 (1.7)	.136
Ovary – uterus tumor	**0 (0)**	3 (5.8)	3 (1.7)	.018*

*P-value < .05.

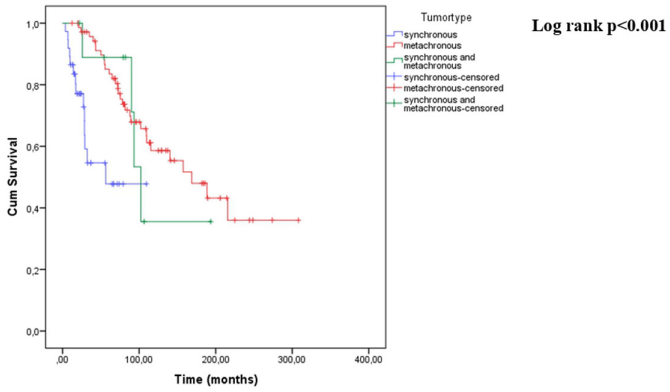

Figure 2. Survival in synchronous, metachronous, and both synchronous and metachronous tumors.

in the clinic, the incidence of MPMTs was found to be 2.6%. In this study, patients with metachronous tumors were more common than patients with synchronous tumors. This result was similar to most studies in the literature. In most previous studies, patients with MPMTs were around 70 years of age.[13,14] The age at which primary tumors appeared in the patients ranged from 37 to 87, and the median age at diagnosis was 68. Of the patients with MPMTs, 60.3% were 65 years of age or older. According to Pan et al,[15] aging leads to cumulative exposure to environmental and iatrogenic carcinogens, while age-related immune suppression and chronic inflammation also predispose individuals to multiple malignancies. In this study, male patients were more common than female patients among multiple primary cancer patients, similar to what was reported in the literature.[16] Family history is an important risk factor for the development of multiple primary tumors; if there is a family history in patients, a hereditary tumor should be suspected and genetic evaluation should be performed.[17] In line with previous studies, 63.6% of the patients included in the study reported a positive family history. It is known that smoking causes p53 point mutations and is one of the most important risk factors for multiple primary cancers.[18] In this study, 65.1% of the patients were either former or current smokers. In the multivariate Cox regression analysis for overall survival, smoking was identified as an independent unfavorable prognostic factor (P = .005). Breast, female reproductive organs, and gastrointestinal cancers are more common in obese patients.[19] In this study, 47.6% (n = 10) of patients with breast cancer had a BMI ≥ 30, and this association was statistically significant (P < .001).

Lung, prostate, colorectal, and breast tumors are among the most frequently observed malignancies in patients with MPMT, as reported in various studies.[6] In the study by Li et al[20] 175 patients with multiple primary tumors were examined, and the most common tumor association was lung and colorectal cancer. In the current study, it was found that the most common tumor association in patients with MPMT was lung and colorectal cancer. Zheng et al[21] reported that the most common second primary cancer was lung cancer, which is consistent with the findings of this study. Breast cancer is the most common cancer and the leading cause of death among women worldwide.[22] Bazire et al[23] found that the risk of developing a second malignant tumor was high in patients treated for breast cancer. In this study, the most common primary tumor in women was breast cancer, and the most common secondary tumor accompanying breast cancer was colorectal cancer. Approximately 50% of colorectal tumors were identified at a locally advanced or metastatic stage at the time of diagnosis. This result was similar to Corso's study in 21 527 patients with primary breast cancer.[24]

In this study, 39.7% (n = 48) of patients with MPMT died during the follow-up period. This mortality rate is consistent with previously published studies, in which mortality among patients with multiple primary malignancies ranged between 35% and 50%.[16,20,21] In this study, most patients died due to secondary primary tumors, with advanced-stage lung cancer being the most common cause of death. Donin et al[16] reported a similar finding. In this study, patients with metachronous MPMTs had a better prognosis compared to those with synchronous or both synchronous and metachronous tumors. Similarly, Lv et al[25] reported that patients with shorter intervals between tumors had poorer survival outcomes, and Jiao F et al[26] found significantly longer survival in patients with metachronous tumors. One possible explanation is that longer intervals between tumor occurrences may reflect a slower biological tumor behavior or a more indolent disease course, allowing for more effective treatment of the first malignancy before the second 1 emerges. This extended interval may also provide patients with sufficient recovery time, better functional status, and an improved response to subsequent treatments, which could contribute to improved overall prognosis.[27,28]

There are some limitations in this study. The study was retrospective and was conducted in a single center. The study population was heterogeneous, consisting of patients at different stages and with different primary malignancies. There was insufficient screening data for genetic mutations.

As a result, it was found that MPMTs were more common in elderly and male patients, and lung, colorectal, and prostate cancers were most common in MPMT patients. These findings showed that patients with metachronous MPMT had the best survival rate; most patients followed up died of secondary primary tumors, and advanced lung cancer most frequently caused death. This study showed that it is very important to distinguish between second primary, recurrence, or metastasis and that treatment methods can be applied to cure patients. Furthermore, this study is one of the largest single-center retrospective trials on MPMTs in Türkiye, and due to the limited national data, it provides valuable insights into the demographic and clinical features specific to this population. These results may support future national studies, guide clinical decision-making, and contribute to international research on MPMTs.

Data Availability Statement: The data that support the findings of this study are available on request from the corresponding author.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of İstanbul University–Cerrahpaşa, (Date: 03.02.2021; No: E-83088843-604.01.01-22845).

Informed Consent: Written informed consent was obtained from all participants who participated in this study.

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References

1. Vogt A, Schmid S, Heinimann K, et al. Multiple primary tumors: challenges and approaches, a review. *ESMO Open*. 2017;2(2):e000172. [CrossRef]
2. Billroth T, Reimer G. *Die Allgemeine Chirurgische Pathologic und Therapie. 51 Vorlesungen-Ein Handbuch fur Studierende und Artze*. 14th Auflage. Berlin; 1889:908.
3. *National Cancer Registry. Multiple Primary Neoplasms* [*Krajowy Rejestr Nowotworów*].
4. Warren S, Gates O. Multiple primary malignant tumors. A survey of the literature and statistical study. *Am J Cancer*. 1932;16:1358.
5. Whitworth J, Hoffman J, Chapman C, et al. A clinical and genetic analysis of multiple primary cancer referrals to genetics services. *Eur J Hum Genet*. 2015;23(5):581-587. [CrossRef]
6. Demandante CG, Troyer DA, Miles TP. Multiple primary malignant neoplasms: case report and a comprehensive review of the literature. *Am J Clin Oncol*. 2003;26(1):79-83. [CrossRef]
7. Liu FS, Qin DX, Wang QL. The clinical pathology analysis of 172 cases of multiple primary malignant tumors. *Zhonghua Zhong Liu Za Zhi*. 1979;1(2):113-119.
8. Liu CS, Wang C, Du ZH, Xue H, Liu Z. Clinical features and prognosis of duplex primary malignant neoplasms involving chronic myeloid leukemia. *Medicine*. 2020;99(44):e22904. [CrossRef]
9. Wood ME, Vogel V, Ng A, Foxhall L, Goodwin P, Travis LB. Second malignant neoplasms: assessment and strategies for risk reduction. *J Clin Oncol*. 2012;30(30):3734-3745. [CrossRef]
10. American Cancer Society. *Cancer Facts & Figures 2016*. Atlanta: American Cancer Society; 2016.
11. Schoenberg BS. Multiple primary malignant neoplasms. The Connecticut experience, 1935-1964. *Recent Results Cancer Res*. 1977;58:1-173.
12. Pk K, Prakash GH, Kr S, Naik R. Exploring multiple primary malignancies: an institutional experience with dual malignancy cases. *Asian Pac J Cancer Care*. 2024;9(4):699-704. [CrossRef]
13. Burton KA, Ashack KA, Khachemoune A. Cutaneous squamous cell carcinoma: a review of high-risk and metastatic disease. *Am J Clin Dermatol*. 2016;17(5):491-508. [CrossRef]
14. Siegal T, Bairey O. Primary CNS lymphoma in the elderly: the challenge. *Acta Haematol*. 2019;141(3):138-145. [CrossRef]
15. Pan S-Y, Huang C-P, Chen W-C. Synchronous/metachronous multiple primary malignancies: review of associated risk factors. *Diagnostics (Basel)*. 2022;12(8):1940. [CrossRef]
16. Donin N, Filson C, Drakaki A, et al. Risk of second primary malignancies among cancer survivors in the United States, 1992 through 2008. *Cancer*. 2016;122(19):3075-3086. [CrossRef]
17. Shimatani A, Hoshi M, Oebisu N, Iwai T, Takada N, Nakamura H. Investigation of multiple primary cancers in patients with bone and soft tissue primary malignancies: A retrospective, institution-based study. *Mol Clin Oncol*. 2020;13(3):17. [CrossRef]
18. Yuasa Y. Double cancer. Med prac. 2000;17:698-699.
19. Soerjomataram I, Coebergh JW. Epidemiology of multiple primary cancers. *Methods Mol Biol*. 2009;471:85-105. [CrossRef]
20. Li F, Zhong WZ, Niu FY, et al. Multiple primary malignancies involving lung cancer. *BMC Cancer*. 2015;15:696. [CrossRef].
21. Zheng X, Li X, Wang M, et al. Second primary malignancies among cancer patients. *Ann Transl Med*. 2020;8(10):638. [CrossRef]
22. Sung H, Ferlay J, Siegel RL, et al. Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin*. 2021;71(3):209-249. [CrossRef]
23. Bazire L, De Rycke Y, Asselain B, Fourquet A, Kirova YM. Risks of second malignancies after breast cancer treatment: long-term results. *Cancer Radiother*. 2017;21(1):10-15. [CrossRef].
24. Corso G, Veronesi P, Santomauro GI, et al. Multiple primary non-breast tumors in breast cancer survivors. *J Cancer Res Clin Oncol*. 2018;144(5):979-986. [CrossRef]
25. Lv M, Zhang X, Shen Y, et al. Clinical analysis and prognosis of synchronous and metachronous multiple primary malignant tumors. *Medicine*. 2017;96(17):e6799. [CrossRef]
26. Jiao F, Yao LJ, Zhou J, Hu H, Wang LW. Clinical features of multiple primary malignancies: a retrospective analysis of 72 Chinese patients. *Asian Pac J Cancer Prev*. 2014;15(1):331-334. [CrossRef]
27. Liu YY, Chen YM, Yen SH, Tsai CM, Perng RP. Multiple primary malignancies involving lung cancer-clinical characteristics and prognosis. *Lung Cancer*. 2002;35(2):189-194. [CrossRef]