Original Article

Risks of second primary malignancies among Chinese cancer survivors at a single center during 2002–2016

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Background: The increased survival of patients after a primary cancer diagnosis has led to an increasing number of patients with second primary malignancies (SPMs). Recent studies implied the risk of SPMs among specific survivor groups. However, little is known regarding the risks of developing SPMs across the spectrum of cancer survivors. The present study was undertaken to describe the incidence, common sites, and outcomes associated with SPMs among Chinese cancer survivors at a single center.

Methods: This retrospective study evaluated patients who were ≥18 years old and diagnosed as having a malignancy during 2002–2016 at the Department of Hematology, Tongji Hospital, Tongji Medical College. Factors associated with subsequent SPMs were explored using bivariable and multivariable models.

Results: The study identified 18,257 eligible patients diagnosed with hematological malignancies, including 67 patients (0.37%) who developed SPMs, which mainly consisted of leukemia. Survivors of lymphoma had the highest risk of developing SPMs. Hematological SPMs were more common among patients who received alkylating agents, topoisomerase 2 inhibitors, or allogeneic hematopoietic stem cell transplantation (HSCT) for the first primary malignancy. Non-hematological SPMs were more common among patients who received anti-metabolites, anti-tubulin agents, or radiotherapy for the first primary malignancy. The risks of developing SPMs did not exhibit any significant differences according to age, sex, and latency interval. Hematological malignancy was a non-significant risk factor for SPM development (P>0.05).

Conclusions: Approximately 0.37% of our patients diagnosed with hematological malignancies had SPMs, mainly leukemia. Patients with lymphoma were most likely to develop SPMs. These findings may help identify patients who are at-risk of developing SPMs (e.g., based on the previous treatment and the first primary malignancy), which may help guide the treatment of cancer survivors.

Keywords: Second primary malignancy (SPM); hematological malignancy; cancer survivor; Chinese; treatment

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Introduction

During the last century, continuous developments in surgical procedures, radiotherapy, chemotherapy agents, and combination treatments have enabled people to live longer after a diagnosis of cancer. Between 2005 and 2015, the global number of cancer cases increased by 33%, while the number of deaths decreased for many cancers, such as Hodgkin lymphoma, esophageal cancer, stomach cancer, and chronic myeloid leukemia (1). As these improved outcomes have increased the population of cancer survivors,

an increasing number of people have begun to develop other diseases, including second primary malignancies (SPMs). Second-order or higher-order malignancies now account for approximately 16% of incident cancer, based on data from the National Malignancy Institute's Surveillance, Epidemiology, and End Results Program (2). Furthermore, cancer survivors may be especially susceptible to developing SPMs because of their unique factors, including genetic syndromes, common etiological exposures, and the late effects of chemotherapy and radiotherapy (3). Thus, given the longer duration of cancer survivorship and the substantial increase in the population of survivors who are at risk of developing SPMs, the incidence and mortality from SPMs are expected to increase.

There is ample literature regarding the risk of SPMs among specific survivor groups, such as patients with breast cancer (4) and adult leukemia (5). However, to the best of our knowledge, little is known regarding the risks of developing SPMs across the spectrum of cancer survivors who are diagnosed as having hematological malignancies, as well as the risks of hematological SPMs among patients with other malignances. As screening practices have been widely adopted for several common hematological malignancies [e.g., adult leukemia, myelodysplastic syndrome (MDS), and lymphoma], a better understanding of SPM epidemiology could help achieve better long-term outcomes for cancer survivors, who may not be covered by screening recommendations that are aimed at the broader population. Therefore, the present study aimed to examine the risks of developing SPMs among survivors of the most common hematological malignancies, as well as the risk of developing hematological SPMs among patients with other common malignances. A clearer understanding of these risks may facilitate the design of appropriate long-term surveillance strategies.

Methods

Patients

This retrospective study evaluated all patients who were treated for hematological malignancies between January 2002 and December 2016 at the Department of Hematology, Tongji Hospital, Tongji Medical College. Among the eligible patients, we identified 67 consecutive patients (≥18 years old) with a confirmed diagnosis of SPMs. The study's retrospective protocol was approved by the ethics review board of Tongji Hospital, Tongji Medical College. All patients provided informed consent for the general collection and analysis of their data, and the study's protocol complied with the tenets of the Declaration of Helsinki.

Definitions

The patients' diagnoses were reviewed and reclassified according to the World Health Organization's 2016 classification. Patients with acute myeloid leukemia (AML) were diagnosed and classified according to the French-American-British Classification, and their prognoses were analyzed according to the 2016 Revised International Prognostic Scoring System (*Table 1*). The exact dates of diagnosis and bone marrow examination were documented. The Warren and Gates criteria (6), with the National Cancer Institute modification (7), were used to define SPMs as a metachronous malignancy that developed ≥6 months after the first primary malignancy. We subsequently excluded 30 patients in whom the SPM was diagnosed within 6 months after the first malignancy, and 2 patients in whom the latency period was unknown, in order to prevent misclassification of metastatic primary malignancies as SPMs. Individuals with >1 pathological diagnosis of malignancy were identified and categorized as the SPM group. The latency interval was defined as the period between the diagnoses of the first malignancy and the SPM.

Clinical data

Clinical and treatment-related data were collected from the patients' medical records. The 3-year survival distribution of SPMs in the study population was calculated using death as a competing event. Chemotherapy agents were classified according to the mechanism of action: alkylating agents, topoisomerase 2 inhibitors, anti-metabolites, and anti-tubulin agents (8). The study population was stratified according to sex, age, first primary malignancy, and SPM, the associations of these variables with the cumulative incidence of SPMs were determined.

Statistical evaluation

Statistical analyses of the patients' clinical characteristics and SPMs were performed for the 67 patients who developed SPMs. The statistical analyses were performed using SPSS software (version 22; IBM Corp., Armonk, NY,

Table 1 Risk status based on validated cytogenetics

Risk status	Cytogenetics
Favorable-risk	Core binding factor: inv(16) or t(16;16) or t(8;21)
	t(15;17)
Intermediate-risk	Normal cytogenetics
	+8 alone
	t(9;11)
	Other non-defined
Poor-risk	Complex (≥3 clonal chromosomal abnormalities)
	Monosomal karyotype
	-5,5q-, -7,7q-
	11q23-non t(9;11)
	inv(3),t(3,3)
	t(6;9)
	t(9;22)

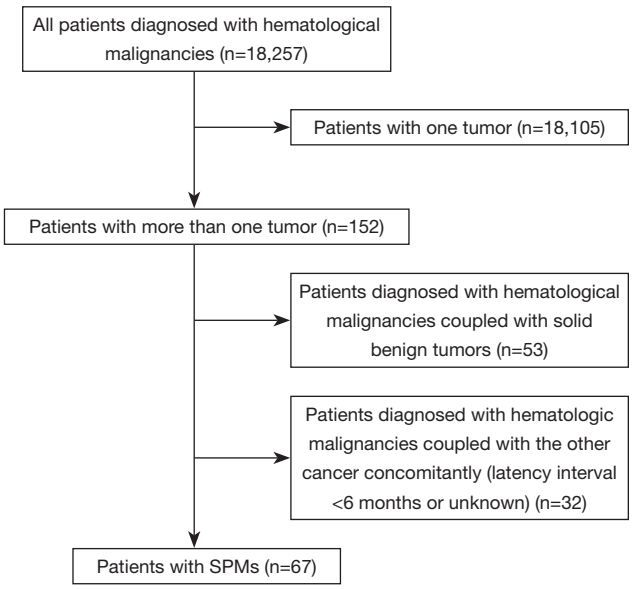

Figure 1 Flowchart depicting all patients at the center from January 2002 to December 2016 and those who developed second primary malignancies (SPMs). Patients with (I) one tumor, (II) hematologic malignancies coupled with solid, benign tumors, and (III) hematologic malignancies coupled with the other cancer concomitantly (latency interval <6 months or unknown) were excluded because of the strong specific influence that these conditions have on outcome.

USA), and the best discriminator threshold was detected using the minimal P value approach, with P values <0.05 being considered statistically significant. All tests were two-sided. Categorical variables were reported as number and frequency, and the incidence of SPMs was assumed to follow a Poisson distribution. Inter-group comparisons were performed using a non-parametric approach with the Mann-Whitney test. Comparisons of the categorical variables' distributions were performed using the chi-square test. Survival analyses were performed using the Kaplan-Meier method and log-rank test.

Results

SPMs among cancer survivors

Between January 2002 and December 2016, 18,257 patients diagnosed with hematological malignancies were treated at our center. Of these, 152 patients (0.83%) had hematological malignancies with other tumors, including 67 patients (44.1%) with SPMs, 32 patients (21.1%) with other concomitant cancer (latency interval of <6 months), and 53 patients (34.9%) with concurrent benign tumors (mainly uterine fibroids) (*Figure 1*). Among the 67 patients with SPMs, 5 patients had a history of solid benign tumors before the first primary malignancy, 8 patients had multiple primary malignancies, and 28 patients (41.8%) had hematological malignancies as their first malignancy.

The clinical characteristics of all patients are shown in *Table 2*. SPMs were most common among survivors of lymphoma (mainly the diffuse, large B-cell type), which was followed by breast cancer, leukemia, colorectal cancer, and lung cancer (P<0.05) (*Figure 2A*). The most common SPM was leukemia (43.3% of patients), followed by lymphoma (23.9%), multiple myeloma (7.5%), uterine cancer (6.0%), and colorectal cancer (4.5%) (P<0.05) (*Figure 2B*). Among survivors of lymphoma, 28.6% of the SPMs were another type of lymphoma. Among survivors of breast cancer, leukemia was the most common SPM (81.8%). The most common SPMs among survivors of leukemia were lymphoma, colorectal cancer, and uterine cancer. Among patients with a second leukemia, AML-M5 was the most common French-American-British type (33.3%), followed by chronic lymphocytic leukemia, acute lymphocytic leukemia and AML-M3 (P<0.05) (*Figure 2C*).

Table 2 Clinical characteristics of second primary malignancies

Covariate	All patients (n=67) (%)	Patients diagnosed as having hematological second malignancies (n=50) (%)	Patients diagnosed as having non-hematological second malignancies (n=17) (%)	P
Age at diagnosis of second malignancy, years				0.218 (>0.05)
18–29	3 (4.5)	2 (4.0)	1 (5.9)	
30–39	7 (10.4)	6 (12.0)	1 (5.9)	
40–49	11 (16.4)	6 (12.0)	5 (29.4)	
50–59	17 (25.4)	12 (24.0)	5 (29.4)	
60–69	17 (25.4)	14 (28.0)	3 (17.6)	
70–79	6 (9.0)	5 (10.0)	1 (5.9)	
≥80	6 (9.0)	5 (10.0)	1 (5.9)	
Gender				0.357
Male	32 (47.8)	24 (48.0)	8 (47.1)	
Female	35 (52.2)	26 (52.0)	9 (52.9)	
Latency interval, months				0.316
6–11	6 (9.0)	5 (10.0)	1 (5.9)	
12–23	10 (14.9)	7 (14.0)	3 (17.6)	
24–59	25 (37.3)	20 (40.0)	5 (29.4)	
60–119	12 (17.9)	9 (18.0)	3 (17.6)	
≥120	14 (20.9)	9 (18.0)	5 (29.4)	
Year of diagnosis				0.037
2002–2005	1 (1.5)	0 (0.0)	1 (5.9)	
2006–2009	11 (16.4)	7 (14.0)	4 (23.5)	
2010–2013	30 (44.8)	21 (42.0)	9 (52.9)	
2014–2016	25 (37.3)	22 (44.0)	3 (17.6)	
First primary cancer				<0.001
Lymphoma	14 (20.9)	7 (14.0)	7 (41.2)	
Leukemia	8 (11.9)	2 (4.0)	6 (35.3)	
Multiple myeloma	3 (4.5)	1 (2.0)	2 (11.8)	
Other hematologic malignancies	3 (4.5)	2 (4.0)	1 (5.9)	
Breast cancer	11 (16.4)	10 (20.0)	1 (5.9)	
Uterine cancer	2 (3.0)	2 (4.0)	0 (0.0)	
Lung cancer	6 (9.0)	6 (12.0)	0 (0.0)	
Stomach and esophageal cancer	2 (3.0)	2 (4.0)	0 (0.0)	
Colorectal cancer	6 (9.0)	6 (12.0)	0 (0.0)	
Prostate cancer	2 (3.0)	2 (4.0)	0 (0.0)	
Thyroid cancer	1 (1.5)	1 (2.0)	0 (0.0)	

Table 2 (*continued*)

Table 2 (*continued*)

Covariate	All patients (n=67) (%)	Patients diagnosed as having hematological second malignancies (n=50) (%)	Patients diagnosed as having non-hematological second malignancies (n=17) (%)	P
Other digestive system malignancies	2 (3.0)	2 (4.0)	0 (0.0)	
Other urological malignancies	3 (4.5)	3 (6.0)	0 (0.0)	
Other malignancies	4 (6.0)	4 (8.0)	0 (0.0)	
Second primary malignancy				<0.001
Lymphoma	16 (23.9)	16 (32.0)	0 (0.0)	
Leukemia	29 (43.3)	29 (58.0)	0 (0.0)	
Multiple myeloma	5 (7.5)	5 (10.0)	0 (0.0)	
Other hematologic malignancies	0 (0.0)	0 (0.0)	0 (0.0)	
Breast cancer	1 (1.5)	0 (0.0)	1 (5.9)	
Uterine cancer	4 (6.0)	0 (0.0)	4 (23.5)	
Lung cancer	2 (3.0)	0 (0.0)	2 (11.8)	
Stomach and esophageal cancer	1 (1.5)	0 (0.0)	1 (5.9)	
Colorectal cancer	3 (4.5)	0 (0.0)	3 (17.6)	
Prostate cancer	0 (0.0)	0 (0.0)	0 (0.0)	
Thyroid cancer	1 (1.5)	0 (0.0)	1 (5.9)	
Other digestive system malignancies	1 (1.5)	0 (0.0)	1 (5.9)	
Other urological malignancies	2 (3.0)	0 (0.0)	2 (11.8)	
Other malignancies	2 (3.0)	0 (0.0)	2 (11.8)	
Exposure to alkylating agents				0.018
Yes	22 (32.8)	17 (34.0)	5 (29.4)	
No	45 (67.2)	33 (66.0)	12 (70.6)	
Exposure to topoisomerase 2 inhibitors				0.018
Yes	22 (32.8)	17 (34.0)	5 (29.4)	
No	45 (67.2)	33 (66.0)	12 (70.6)	
Exposure to anti-metabolites				<0.001
Yes	7 (10.4)	5 (10.0)	2 (11.8)	
No	60 (89.6)	45 (90.0)	15 (88.2)	
Exposure to anti-tubulin agents				0.001
Yes	18 (26.9)	12 (24.0)	6 (35.3)	
No	49 (73.1)	38 (76.0)	11 (64.7)	
Radiation				<0.001
Yes	14 (20.9)	10 (20.0)	4 (23.5)	
No	53 (79.1)	40 (80.0)	13 (76.5)	

Table 2 (*continued*)

Table 2 (*continued*)

Covariate	All patients (n=67) (%)	Patients diagnosed as having hematological second malignancies (n=50) (%)	Patients diagnosed as having non-hematological second malignancies (n=17) (%)	P
Operation				0.307
Yes	29 (43.3)	27 (54.0)	8 (47.1)	
No	38 (56.7)	23 (46.0)	9 (52.9)	
Allogeneic hematopoietic stem cell transplantation				<0.001
Yes	2 (3.0)	2 (4.0)	0 (0.0)	
No	65 (97.0)	48 (96.0)	17 (100.0)	

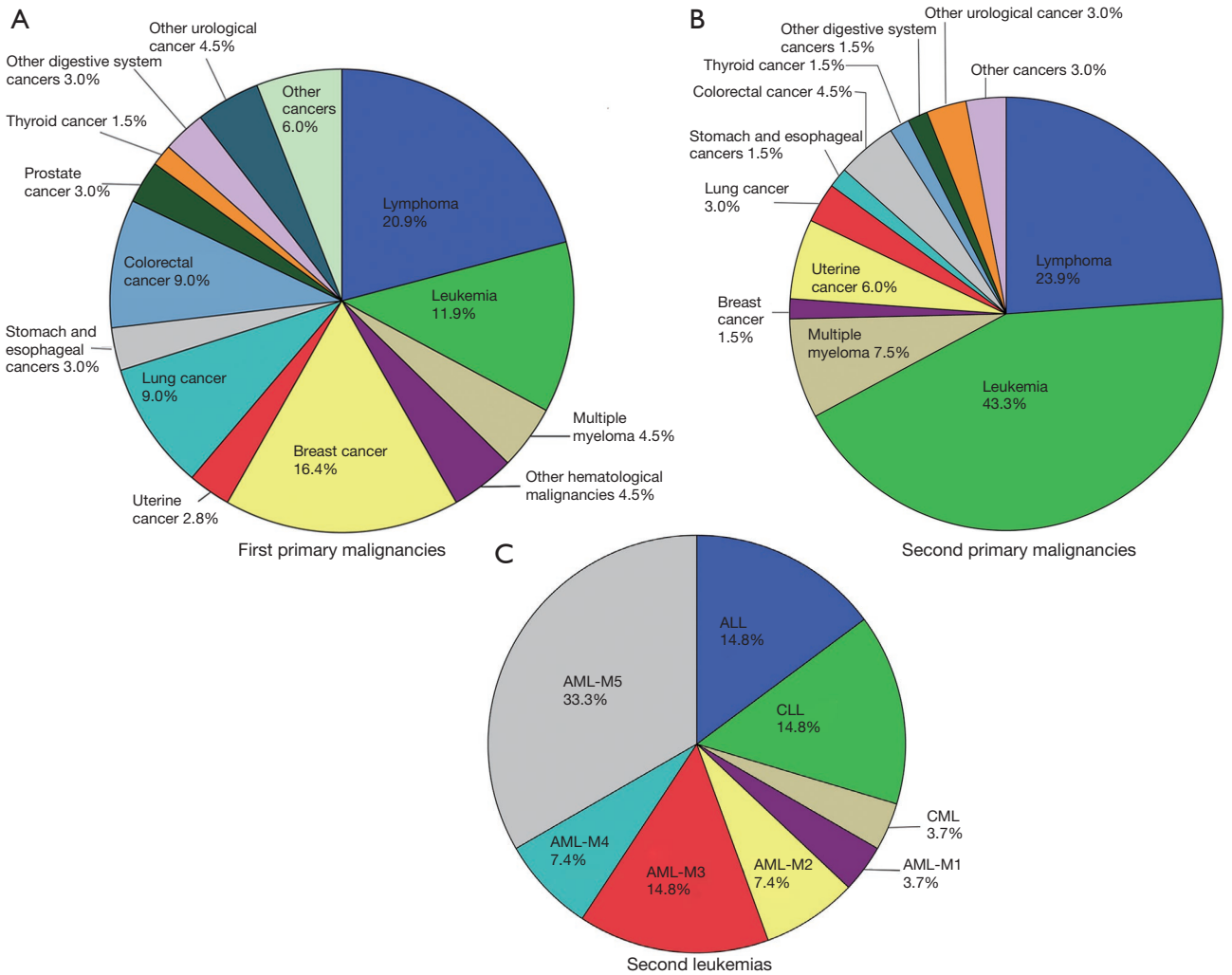

Figure 2 Classification of the first primary malignancies (A), second primary malignancies (B), and second leukemias (C). ALL, acute lymphoblastic leukemia; CLL, chronic lymphoblastic leukemia; CML, chronic myeloid leukemia; AML, acute myeloid leukemia; AML-M1, acute myeloid leukemia without maturation; AML-M2, acute myeloid leukemia with maturation; AML-M3, acute promyelocytic leukemia; AML-M4, acute myelomonocytic leukemia; AML-M5, acute monocytic leukemia.

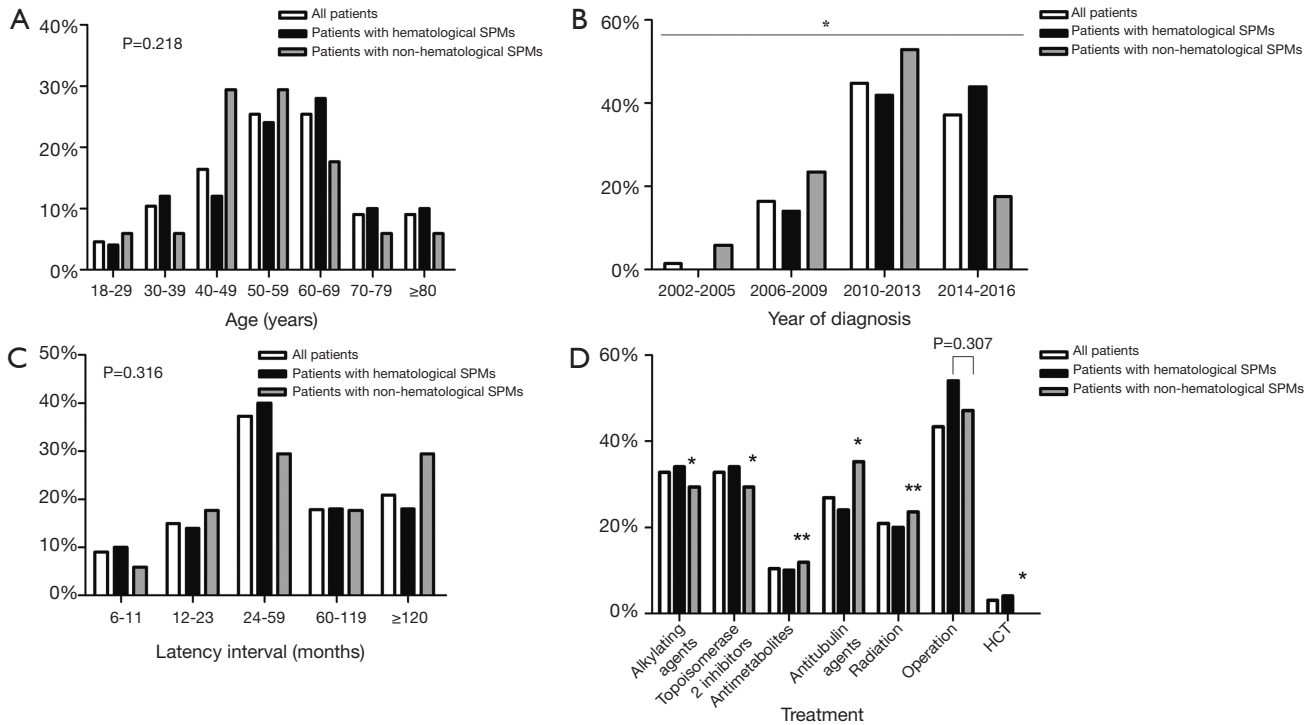

Figure 3 Comparison of clinical characteristics of patients with different second primary malignancies (SPMs) using the chi-square test. (A) Age distribution at the diagnosis of SPMs; (B) time at the diagnosis of SPMs; (C) latency interval from the first malignancies to SPMs; (D) treatment for the first malignancies. *, P<0.05; **, P<0.01 *vs.* patients diagnosed as having non-hematological second malignancies. HSCT, hematopoietic stem cell transplantation.

Risks among cancer survivors

The median age at the SPM diagnosis was 56.7 years (range, 18–96 years), and most patients with SPMs were 40–69 years old (67.2%) (*Figure 3A*). Of the 67 patients, 32 men (47.8%), although no significant sex-related differences were observed (P>0.05). There was no significant age-related difference between hematological and non-hematological malignancies (P>0.05). The diagnoses of SPMs increased during recent years (*Figure 3B*). The mean latency period for SPMs was 77.6 months, and the median time was 36 months, with 37.3% of the patients diagnosed with their SPMs at 24–59 months after the first diagnosis. Compared to the latency period between the first and SPMs, the latency period between the second and third malignancies was shorter (mean: 32.3 months, median: 33 months, range, 5–60 months), although the difference was not statistically significant (P>0.05). Compared to patients with first hematological malignancies, patients with non-hematological first malignancies had a longer latency period, and a similar result was observed for patients with non-hematological second malignancies (*Figure 3C*). However, these differences were not statistically significant (P>0.05).

Fourteen patients (20.9%) had received radiotherapy, 35 patients (52.2%) had undergone surgery, 29 patients (43.3%) had received chemotherapy, and 2 patients (3%) had undergone allogeneic hematopoietic stem cell transplantation (HSCT). Twenty-two patients (32.8%) had received alkylating agents, 22 patients (32.8%) had received topoisomerase 2 inhibitors, 7 patients (10.4%) had received anti-metabolites, and 18 patients (26.9%) had received anti-tubulin agents. Patients with hematological SPMs had received alkylating agents and topoisomerase 2 inhibitors (34%) or undergone allogeneic HSCT (4%). These rates were significantly higher than the rates for patients with non-hematological SPMs (P<0.05). Compared to patients with hematological SPMs, patients with non-hematological SPMs had higher rates of exposure to anti-metabolites (11.8%), anti-tubulin agents (35.3%), and radiotherapy (23.5%) (P<0.05) (*Figure 3D*).

Table 3 Cytogenetic characteristics of patients with second leukemia

Case	Cytogenetics	Risk status
1	Complex	Poor-risk
2	inv(3)(q21;q26)	Poor-risk
3	t(11;12)(p14;q12)	Intermediate-risk
4	t(4;5)(p16;q11q23)	Intermediate-risk
5	t(9;11)(p22;q23)	Intermediate-risk
6	t(9;11)(p22;q23)	Intermediate-risk
7	t(9;22)(q34;q11)	Poor-risk
8–17	Normal cytogenetics	Intermediate-risk

Cytogenetic characteristics of SPMs

Among the 29 patients with a second leukemia, 2 patients (6.9%) had rearrangements of the *MLL* (11q23) gene. Seventeen patients with a second leukemia were subjected to karyotype analysis, which revealed that 14 patients (82.4%) had intermediate cytogenetics and 3 patients (17.6%) had poor cytogenetics (*Table 3*).

Survival analysis

Although data regarding patients with SPMs were available up until 2016, we only analyzed the 3-year survival rate among 43 patients who were diagnosed as having SPMs before 2014. *Figure 4* shows that the median follow-up was 29 months (range, 0–120 months). Longer survival was observed for patients with non-hematological first (*Figure 4A*) and second malignancies (*Figure 4B*) (*vs.* hematological first and second malignancies), although these differences were not statistically significant (P=0.235 and P=0.700).

Discussion

In this large population-based study at a single center, we identified 67 patients with SPMs, all of whom were diagnosed with at least one hematological malignancy. We further evaluated the risk factors for developing SPMs, and found that SPMs were more common among survivors with hematological malignancies than those with non-hematological malignancies. Patients with lymphoma had the highest risk of SPMs, and leukemia was the most common SPM. However, we did not detect any significant differences in the risks of SPMs according to age, sex, and the latency interval. To the best of our knowledge, this is the first large-scale study to systematically evaluate the characteristics of Chinese patients at a single center who were diagnosed with hematological malignancies and who experienced SPMs.

An American study indicated that the most common SPM was lung cancer, and patients with bladder cancer had the highest risk of being diagnosed as having SPMs (8). There are several possible explanations for these discrepancies. First, we evaluated SPMs in patients diagnosed with at least one hematological malignancy at a single center, while the previous study evaluated SPMs in the general population of cancer survivors in United States (3). Thus, our SPM rate may have been underestimated. Second, there may have been bias given that these SPMs could represent misclassified metastases from the primary tumor. However, we believe that this risk was minimized by our exclusion of patients who had their second malignancy diagnosed within 6 months after the first malignancy. Third, the present study evaluated a group of Chinese patients, whereas the previous study evaluated American patients and 85% of those patients were white people (3). Thus, racial and regional differences may explain the discrepancies between our findings and the previous findings. Last, we performed a retrospective study and could not control for various factors (e.g., smoking, diet, radiotherapy, surgery, HSCT, or chemotherapy), which could have influenced the incidence of SPMs. Therefore, unmeasured covariates may have affected both the primary cancer and development of SPM.

The present study's results revealed that the risk of hematological SPMs (*vs.* non-hematological SPMs) was increased among patients who had been treated using alkylating agents, topoisomerase 2 inhibitors, or allogeneic HSCT for the first cancer. In contrast, the risk of non-hematological SPMs was increased among patients who had been treated using anti-metabolites, anti-tubulin agents, or radiotherapy for the first cancer. To the best of our knowledge, our study is the first one to observe this difference.

Chemotherapy using anthracyclines for breast cancer or topoisomerase inhibitors for leukemia can increase the risk of SPMs, especially AML. This is because the treatment kills cancer cells through DNA damage, although hidden latent damage to the DNA of normal cells can eventually cause new cancers (9). For example, a study of 234 patients receiving fludarabine-based, cyclophosphamide-based, and rituximab-based first-line regimens revealed that their risk of second cancers was 2.38× higher than the expected risk in the

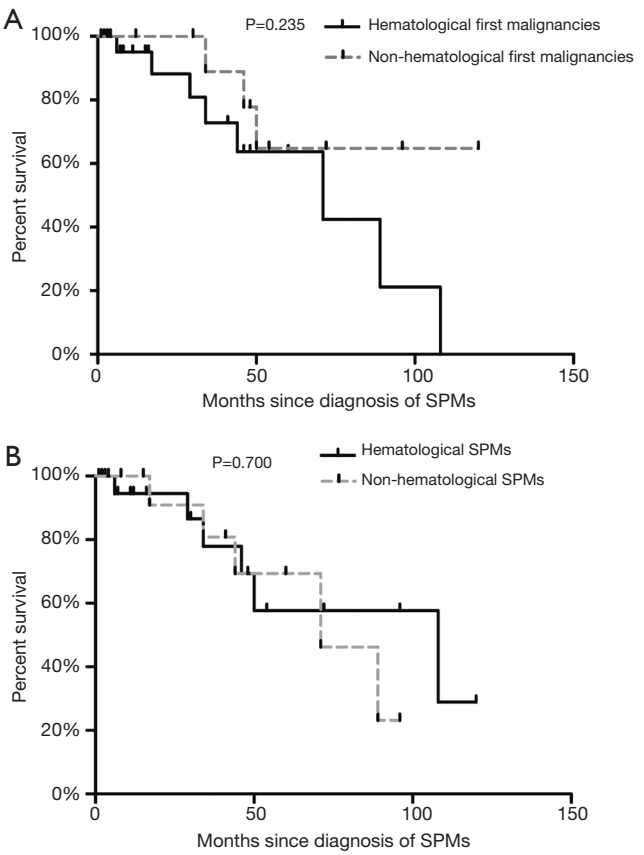

Figure 4 Survival analysis of patients with second primary malignancies (SPMs) using the Kaplan-Meier method and log-rank test. Longer survival was observed for patients with non-hematological first (A) and second malignancies (B) (*vs.* hematological first and second malignancies). These differences were not statistically significant (P=0.235 and P=0.700).

general population (10). Long-term radiation exposure is also associated with carcinogenesis, despite being an important part of multimodality therapy for many malignancies, and 14 of our patients with SPMs (20.9%) had received radiotherapy. Kamran *et al.* (11) also reported that radiotherapy appeared to increase the risk of SPMs in primary hematological, breast, gynecological, and pediatric malignancies. Radivoyevitch *et al.* (5) reported that patients who underwent radiotherapy for prostate cancer had an increased risk of AML and MDS that peaked at 1.5–2.5 years. This increased risk is also associated with age, hormone levels, chemotherapy use, environmental factors, genetic predisposition, infection, and immunosuppression, although it is difficult to define the dose-response relationship for developing SPMs after radiotherapy (11).

HSCT is a double-edged sword that can cause SPMs and/or mortality after successful treatment of the primary disease. For example, the overall risk of secondary MDS/AML is higher among patients who undergo allogeneic HSCT (*vs.* other treatments), and the estimated risk of SPMs after allogeneic HSCT is 3.3× higher that the risk in the general population (12,13). In the present study, 2 patients had undergone allogeneic HSCT for their first malignancy. Local factors (e.g., chronic skin inflammation and radiation damage) and profound immunosuppression (e.g., chronic graft-versus-host disease and immunosuppressive drug use) may have influenced the development of SPMs after bone marrow transplantation (14). Alam *et al.* (15) have also suggested that unrelated donors are a significant risk factor for both greater non-relapse mortality and decreased overall survival.

Only some patients who undergo chemotherapy, radiotherapy, or HSCT develop certain SPMs; this suggests that they may be genetically predisposed to primary and secondary malignancies. Genetic variation in pathways that mediate cellular responses to DNA damage can affect the risk of developing therapy-related AML, presumably by influencing the likelihood that hematopoietic cells survive with leukemogenic mutations. Ellis *et al.* (16) reported that two common functional p53-pathway variants (MDM2 SNP309 and the TP53 codon 72 polymorphism) interact to modulate responses to genotoxic therapy and affect the risk of therapy-related AML. Moreover, mutations in genes that drive hereditary breast cancer syndromes (e.g., *BRCA2*), rare mutations in five genes (*CDH1*, *BMPR1A*, *STK11*, *PRSS1*, and *PMS2*), and mitochondrial dysfunction (influenced by gene expression in CD34+ stem cells) can reduce the ability to neutralize reactive oxygen species that are generated through chemotherapy and radiotherapy, and subsequently lead to cancer-causing mutations (17,18). Two patients in the present study had rearrangements of the *MLL* (11q23) gene, which plays important roles in the regulation of homeotic gene expression and embryonic development (19). Douet-Guilbert *et al.* (20) analyzed 65 patients with secondary acute lymphoblastic leukemia and observed an association with 11q23/MLL rearrangement. Shima *et al.* (21) also suggested that *MLL* is crucial in the initiation of NUP98-HOXA9 leukemia. Translocations of the *MLL* gene also produce fusion proteins, such as MLL-AF4, which are associated with a poor prognosis in patients with leukemia (22). Moreover, genetic alterations of *MLL* are involved in

bladder cancer relapse (23). Thus, we speculate that *MLL* may play a crucial role in the development of SPMs.

Hematological malignancy was the main risk factor in the present study. However, the difference between hematological and non-hematological malignancies did not reach statistical significance, which is likely related to the relatively short follow-up period and limited number of cases available for the survival analysis. Nevertheless, the difference between these two groups was noticeable. The findings of the present study also have various implications for cancer survivors, as the incidence of SPMs has been increasing during recent years. Therefore, lifelong cancer screening is recommended for all cancer survivors. Furthermore, screening and preventative strategies should incorporate the patient's specific risk profile, which includes their age, sex, lifestyle, genetic predisposition, immunosuppression, pre-treatment exposures, and post-treatment complications.

Conclusions

Approximately 0.37% of patients diagnosed with hematological malignancies had SPMs, and the highest rate was observed among survivors with lymphoma. The most common SPM was leukemia (43.3% of all patients with SPMs). Hematological SPMs were associated with previous treatment using alkylating agents, topoisomerase 2 inhibitors, and HSCT, whereas non-hematological SPMs were associated with previous treatment anti-metabolites, anti-tubulin agents, and radiotherapy. However, there were no significant differences in the risks of SPMs according to age, sex, and the latency interval. Therefore, the growing number of Chinese cancer survivors and the high risk of SPMs in the present study suggest that it will be prudent to develop effective detection and treatment strategies for this population.

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Footnote

Conflict of Interest: All authors have completed the ICMJE uniform disclosure form (available at http://dx.doi.org/10.21037/tcr.2018.02.12). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. The study's retrospective protocol was approved by the ethics review board of Tongji Hospital, Tongji Medical College (grant no. TJ-IRB20170709). All patients provided informed consent for the general collection and analysis of their data.

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