The incidence, risk factors, and survival of acute myeloid leukemia secondary to myelodysplastic syndrome: A population-based study

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Abstract
To determine the incidence, risk factors, and relative survival of acute myeloid leukemia (AML) secondary to myelodysplastic syndrome (MDS) in the Surveillance, Epidemiology, and End Results (SEER) database. Retrospective analysis of all patients with new MDS onset in the SEER-18 database from 2001 to 2013. We identified 36 558 patients with primary MDS. The rate of secondary AML (sAML) was 3.7% among patients 40 years or younger and 2.5% among those older than 40 (P = .039). The median transformation interval was significantly shorter for the younger group (4.04 vs 13.1 mo; P < .001). For both age groups, median overall and cancer-specific survival were significantly longer for patients who did not develop sAML. Although the younger patients survived longer than the older patients, sAML development had a more negative effect on the survival of younger patients. Female sex, age, and World Health Organization (WHO) type MDS with single lineage dysplasia (MDS-SLD) were associated with a decreased risk of sAML for older but not younger patients. Among older patients with MDS, a married status, Black race, female sex, shorter time to sAML, and WHO type MDS-SLD or MDS with ringed sideroblasts were favorable prognostic factors for survival. In the SEER database, the rate of sAML among patients with MDS is lower than that in previous reports, but these patients still have worse survival. Risk assessment should include clinical and demographic factors.

KEYWORDS
acute myeloid leukemia (AML), epidemiology, myelodysplastic syndrome (MDS), risk factors

1 | INTRODUCTION

The myelodysplastic syndromes (MDSs) are a cluster of clonal hematopoietic disorders. In 2016, the World Health Organization (WHO) issued a revised classification system for MDS with the following types: MDS with single lineage dysplasia (MDS-SLD), MDS with ring sideroblasts (MDS-RS), MDS-RS and single lineage dysplasia (MDS-RS-SLD), MDS-RS and multilineage dysplasia (MDS-RS-MLD), MDS with multilineage dysplasia (MDS-MLD), MDS with excess blasts (MDS-EB), MDS with isolated deletion of chromosome 5q (del(5q)).

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Hematological Oncology, 2019;37:438–446.
Recent epidemiological studies of MDS in Asia, Europe, and the United States have reported divergent incidence rates of MDS ranging from less than 2 to more than 68 per 100,000 people, with a median survival of less than 3 years or 3-year survival of less than 60%. Management of MDS relies on diagnosis, classification, risk assessment, and treatment. The Revised International Prognostic Scoring System (IPSS) (IPSS-R) and WHO-based Prognostic Scoring System (WPSS) are the most commonly used scoring systems, and the WPSS may be more useful for prediction of leukemia-free survival.

MDS can progress to secondary acute myeloid leukemia (sAML), which, currently, is defined as the presence of at least 20% blast cells. The transformation process is most likely driven by successive rounds of mutation and clonal expansion within hematopoietic stem cells (HSCs) and blasts. Mutations in Runt Related Transcription Factor 1 (RUNX1) have been associated with an increased risk of transformation to sAML. sAML is unique from de novo AML and is associated with a poorer response to induction chemotherapy and decreased survival. Recent analyses of two European registries have indicated that sAML causes one-third to one-half of disease-related deaths among patients with MDS.

Although research conducted over the last 5 to 10 years has expanded our knowledge of the underlying genetic causes of MDS and progression to sAML, the incidence and relative survival data are becoming out of date. Moreover, limited information is available regarding the clinical or demographic factors that contribute to these conditions. To fill these gaps in knowledge, we conducted a retrospective study of the National Cancer Institute’s (NCI) Surveillance, Epidemiology, and End Results (SEER) database. Since 1973, the SEER Program has collected demographic and clinical data from cancer registries that span almost one-third of the US population. The size of the SEER database makes it an excellent registry for relatively uncommon cancers, such as MDS.

2 | PATIENTS AND METHODS

2.1 | Data source and ethics statement

This study analyzed data from the SEER Program, which is a collection of state or regional population-based cancer registries established by the United States (US) NCI in 1973. The SEER catchment area includes almost one-third of the US population (www.seer.cancer.gov). Data were extracted from the November 2015 submission of the SEER-18 registries, which contained information collected from 1973 to December 2013.

All data in the SEER database are deidentified, and thus, analysis does not require approval by an institutional review board (IRB) or informed consent from the included subjects. The NCI granted permission to access the data in the SEER database (reference number 14448-Nov. 2015).

2.2 | Study population

This study included all patients in the database who received a new diagnosis of MDS between January 1, 2001, and December 31, 2013. MDS was defined according to the WHO’s Classification of Tumors of Hematopoietic and Lymphoid Tissues (2016). Patients were stratified by age into two groups: those aged 40 years or younger and those older than 40 years.

2.3 | Study variables

The primary endpoint of the present study was the incidence of leukemic transformation, specifically AML, and its respective transformation time interval. We used the following ICD-O-3.1 histological codes: 9861/3, 9866/3, 9867/3, 9871/3, 9872/3, 9873/3, 9874/3, 9895/3, 9896/3, and 9897/3.

The secondary endpoints were the overall survival (OS) and cancer-specific survival (CSS) of MDS patients who did or did not evolve into AML. OS was calculated from the day of diagnosis to the date of death from any cause; CSS was calculated from the day of diagnosis to the date that the person died of his/her cancer. The vital status indicated whether the patient was alive or dead at the end date in the SEER database. Independent variables for comparison included patient demographics (age at diagnosis, sex, race/ethnicity, and marital status) and histologic classification of the MDS subtype in accordance with the WHO criteria.

2.4 | Statistical analysis

Comparability among the two age groups was tested using an independent two-sample t test for continuous variables and the Chi-square test for categorical variables. Continuous variables are represented as the mean and standard deviation (SD); categorical data are represented as the number count (n) and percentage (%). If continuous variables were obviously not normally distributed, the nonparametric Mann-Whitney U test was used, and the data are represented as the median and interquartile range (IQR). The Kaplan-Meier method with the log-rank test was used to compare OS and CSS between groups. A logistic regression analysis was performed to determine the significant risk factors associated with transformation of MDS into AML. In addition, a Cox proportional hazard regression model was built for analysis of prognostic factors for the survival outcomes of the included patients. All P values were two-sided, and values less than 0.05 were considered statistically significant. The statistical analyses were performed using the statistical software package SPSS version 22 (IBM, Armonk, NY, USA).

3 | RESULTS

3.1 | Study population

A total of 36,558 patients (904 aged ≤40 years old and 35,654 older than 40 years) with primary MDS were identified in the SEER...
database during the study period (2001-2013). The majority of the patients in this cohort were White, and just over half were men. The average age of the patients was 73 years. First, we compared patient demographics and disease characteristics between the younger and older MDS patients (Table 1). The most frequent type of MDS was MDS-U. Significant differences (P < .05) were found in sex, race, marital status, WHO classification, follow-up type, leukemic transformation, and time interval of leukemic transformation between the two age groups. sAML occurred in 3.7% of the younger patients with a median transformation time of 4.04 months and 2.5% of the older patients (P = .039) with a median transformation time of 13.1 months (P < .001).

The median OS for the total patients were 32 months, and the median OS between younger and older patients were significantly different (not reached vs 32 months). Moreover, the median OS was significantly shorter for the patients with sAML than for those without sAML (22 vs 33 months, P = .009). Figure 1 shows the OS (Figure 1A, B) and CSS rates (Figure 1C, D) among patients with or without sAML. Significant differences in both OS (Figure 1A) and CSS (Figure 1C) were found for the younger patients (P < .001). The median OS and CSS for the younger patients who did develop sAML were both 22 months, whereas the median OS and CSS were not reached for the younger patients with MDS that did not transform to AML. Among the patients in the older group, the median OS was

### Table 1: Patient demographics and clinical characteristics of the patients in the study

| Variables                        | Age ≤ 40 y old (n = 904) | Age > 40 y old (n = 35 654) | P value |
|----------------------------------|--------------------------|-----------------------------|---------|
| Age, mean ± SD, y                | 24.9 ± 12.8              | 74.9 ± 11.3                 | <.001   |
| Sex, n (%)                       |                          |                             | .040    |
| Male                             | 462 (51.1%)              | 19 447 (54.5%)              |         |
| Female                           | 442 (48.9%)              | 16 207 (45.5%)              |         |
| Race, n (%)                      |                          |                             | <.001   |
| White                            | 620 (68.8%)              | 30 017 (84.2%)              |         |
| Black                            | 163 (18.0%)              | 2686 (7.5%)                 |         |
| American Indian/Alaska Native    | 16 (1.8%)                | 146 (0.4%)                  |         |
| Asian or Pacific Islander        | 83 (9.2%)                | 2341 (6.6%)                 |         |
| Unknown                          | 22 (2.4%)                | 464 (1.3%)                  |         |
| Marital status, n (%)            |                          |                             | <.001   |
| Single                           | 546 (60.4%)              | 3037 (8.5%)                 |         |
| Married (including common law)   | 254 (28.1%)              | 17 703 (49.7%)              |         |
| Separated/Divorced/Widowed       | 43 (4.8%)                | 11 591 (32.5%)              |         |
| Other                            | 61 (6.7%)                | 3323 (9.3%)                 |         |
| WHO classification, n (%)        |                          |                             | <.001   |
| MDS with single lineage dysplasia| 119 (13.2%)              | 3984 (11.1%)                |         |
| MDS with ringed sideroblasts     | 51 (5.6%)                | 2916 (8.2%)                 |         |
| MDS with excess blasts           | 152 (16.8%)              | 4683 (13.1%)                |         |
| MDS with multilineage dysplasia  | 58 (6.4%)                | 2023 (5.7%)                 |         |
| MDS with isolated deletion of 5q | 15 (1.7%)                | 864 (2.4%)                  |         |
| MDS, unclassifiable              | 497 (55.0%)              | 21 044 (59.0%)              |         |
| Therapy-related myeloid neoplasms| 12 (1.3%)                | 140 (0.4%)                  |         |
| Type of follow-up, n (%)         |                          |                             | <.001   |
| Autopsy only or death certificate only case | 4 (0.4%) | 908 (2.5%) |         |
| Active follow-up case            | 900 (99.6%)              | 34 746 (37.5%)              |         |
| Leukemic transformation, n (%)   |                          |                             | .039    |
| Yes                              | 33 (3.7%)                | 909 (2.5%)                  |         |
| No                               | 871 (96.3%)              | 34 745 (97.5%)              |         |
| Time interval of leukemic transform, median, and IQR, mo | 4.04 (2, 18.04) | 13.1 (2.98, 25.99) | <.001 |

Data are presented as No. (%) unless otherwise indicated. Abbreviations: IQR, interquartile range; MDS, myelodysplastic syndrome; SD, standard deviation; WHO, World Health Organization.  
*Indicates a significant factor, P < .05.
significantly shorter for the patients with sAML than for those without sAML (22 vs 32 months, \( P < .001 \), Figure 1B). Moreover, older patients with sAML also had significantly shorter CSS than those who did not (23 vs 80 months, \( P < .001 \), Figure 1D). When comparing patients in the younger and older groups, our analysis indicated that OS and CSS were similar for patients who developed sAML; however, for those who did not, the younger patients had longer OS and CSS than the older patients.

3.2 | Analysis of risk factors for transformation to AML

Table 2 shows the risk factors for transformation to AML for both age groups. None of the analyzed factors were significantly associated with transformation to AML among the younger patients with MDS. However, among the patients older than 40 years, our results indicated that age, sex, race, marital status, follow-up type, and histological MDS type were all significant risk factors for transformation.

Multivariate analysis for the older age group indicated that the risk of experiencing sAML was significantly lower for younger patients (OR: 0.969, \( P < .001 \)) and women (OR: 0.767, \( P < .001 \)). In contrast, patients who did not receive active follow-up (ie, identified at autopsy) were at a higher risk for sAML (OR: 13.872, \( P = .009 \)). Compared with the risk of transformation among patients with MDS-SLD, those with MDS-EB, MDS with isolated deletion of chromosome 5q, and MDS-U had a significantly higher risk. MDS-RS and therapy-related myeloid neoplasms presented no adverse risk compared with the risk of developing sAML from MDS-SLD in MDS patients older than 40 years.

3.3 | Analysis of factors associated with survival

We performed uni- and multivariate analyses with time-dependent Cox proportional hazard models to identify clinical and demographic factors associated with survival. Our results are shown in Tables 3 and 4. Univariate analysis of both OS and CSS revealed that age, sex,
WHO classification, and leukemic transformation were significant prognostic factors in patients 40 years or younger and that all six factors were significant prognostic factors in older patients ($P < .05$).

In younger patients with MDS, the multivariate time-dependent Cox regression analysis indicated that the female sex had a favorable prognostic impact on survival compared with that of the male sex. Older age and development of sAML were significant prognostic factors for poor survival. Among the MDS types, MDS-EB had the worst prognosis for OS and CSS (Tables 3 and 4).

Among patients older than 40 years, all factors remained significant independent prognostic factors for both OS and CSS when tested in a multivariate analysis with a time-dependent Cox proportional hazard model. Female sex, Black race, and being married all had a favorable prognostic impact on survival versus being male, White, and single, separated, divorced, or widowed, respectively. An older age and development of sAML were prognostic factors for poor survival (Tables 3 and 4).

In contrast to the younger group, MDS-RS was a significant prognostic indicator of longer OS (HR, 0.819; $P < .001$) but was an insignificant factor for CSS for the older group. The negative impact on survival of a subtype other than MDS-SLD was greater for patients under 40 years than for those over 40, particularly for CSS. However, the risk factors could have been amplified by the inclusion of 35000 patients in the older age group compared with only 900 in the younger age group.

### 4 | DISCUSSION

MDS is a group of heterogeneous myeloid clonal diseases with a risk of transformation to AML. Available data on the incidence, survival, and risk factors of sAML are not up-to-date. To shed light on these issues, we conducted a retrospective study of the SEER database. We analyzed data for more than 36000 patients with MDS; as such, this study provides a valuable update to the field. We determined that the incidence of sAML was less than 5% and that the time interval to leukemic transformation ranged from months to years. However, patients younger than 40 years had a significantly higher incidence of sAML and developed sAML much more quickly than older patients.

Finally, our study confirms the negative impact of male sex, older age, and sAML on overall and CSS. However, the positive effects of young age are lost in patients with sAML. Taken together, the data suggest that risk assessment of patients with MDS should be expanded to include demographic information on marital status, sex, age, and race.

### TABLE 2 Logistic regression for risk factors of transformation into acute myeloid leukemia (AML) for patients aged greater than 40 years

|                        | Univariate |          |          |          | Multivariate |          |          |
|------------------------|------------|----------|----------|----------|--------------|----------|----------|
|                        |            | Crude HR (95% CI) | $P$ value | Adjusted HR (95% CI) | $P$ value |
| Age at diagnosis       | 0.964 (0.959-0.970) | .<.001 | 0.969 (0.964-0.975) | .<.001 |
| Sex                    | Female vs Male | 0.658 (0.573-0.755) | .<.001 | 0.767 (0.664-0.887) | .<.001 |
| Race                   | Black vs White | 0.839 (0.641-1.099) | .204 | 0.799 (0.606-1.054) | .122 |
|                        | American Indian/Alaska Native vs White | 0.798 (0.254-2.509) | .699 | 0.670 (0.211-2.129) | .497 |
|                        | Asian or Pacific Islander vs White | 1.294 (1.019-1.641) | .034 | 1.226 (0.962-1.561) | .099 |
| Marital status         | Married vs Single | 1.066 (0.849-1.340) | .581 | 1.100 (0.870-1.392) | .426 |
|                        | Separated/Divorced/Widowed vs Single | 0.600 (0.466-0.773) | .<.001 | 0.878 (0.673-1.145) | .337 |
| Type of follow-up      | Active follow-up case vs Autopsy only or death certificate only case | 24.338 (3.421-173.157) | .<.001 | 13.872 (1.946-98.913) | .009 |
| WHO classification     | MDS-RS vs MDS-SLD | 1.469 (0.907-2.379) | .118 | 1.445 (0.892-2.342) | .134 |
|                        | MDS-EB vs MDS-SLD | 9.198 (6.383-13.256) | .<.001 | 8.208 (5.689-11.843) | .<.001 |
|                        | MDS-MLD vs MDS-SLD | 4.079 (2.665-6.243) | .<.001 | 3.715 (2.424-5.693) | .<.001 |
|                        | MDS with isolated deletion of 5q vs MDS-SLD | 6.025 (3.772-9.624) | .<.001 | 6.482 (4.049-10.375) | .<.001 |
|                        | MDS unclassifiable vs MDS-SLD | 2.361 (1.645-3.390) | .<.001 | 2.484 (1.729-3.569) | .<.001 |
|                        | Therapy-related myeloid neoplasms vs MDS-SLD | 0.870 (0.118-6.413) | .891 | 0.773 (0.105-5.710) | .800 |

Abbreviations: CI, confidence interval; MDS, myelodysplastic syndrome; MDS-EB, MDS with excess blasts; MDS-MLD, MDS with multilineage dysplasia; MDS-RS, MDS with ring sideroblasts; MDS-SLD, MDS with single lineage dysplasia; OR, odds ratio; vs, versus; WHO, World Health Organization.

*Indicates a significant factor, $P < .05$. 

**DISCUSSION**

MDS is a group of heterogeneous myeloid clonal diseases with a risk of transformation to AML. Available data on the incidence, survival, and risk factors of sAML are not up-to-date. To shed light on these issues, we conducted a retrospective study of the SEER database. We analyzed data for more than 36 000 patients with MDS; as such, this study provides a valuable update to the field. We determined that the incidence of sAML was less than 5% and that the time interval to leukemic transformation ranged from months to years. However, patients younger than 40 years had a significantly higher incidence of sAML and developed sAML much more quickly than older patients. We also report the novel finding that marital status and race are significant predictors of OS and CSS. Finally, our study confirms the negative impact of male sex, older age, and sAML on overall and CSS. However, the positive effects of young age are lost in patients with sAML. Taken together, the data suggest that risk assessment of patients with MDS should be expanded to include demographic information on marital status, sex, age, and race.
Use of the SEER database has allowed us to update and substantially expand upon previous studies of the sAML incidence and the clinical and demographic risk factors associated with its development. The size of the population we included (36,000) is among the largest of any population-based study of MDS or sAML, and this feature of our research provides a high level of reliability. We found that the overall rate of sAML was 3.7% among younger patients and 2.5% for older patients. These rates are much lower than the historically cited rates of 15% to 30%. Several factors could have contributed to this difference in the sAML rates. First, the MDS type at highest risk for transformation (MDS-EB) comprised just 13% of our population; second, we have not taken into account the effects of treatment on progression to sAML.

To the best of our knowledge, our study is the first to use a population-based registry to determine the time interval for transformation to AML. The median intervals observed among the 942 patients who progressed to AML in our study (4.04 mo for younger patients and 13.1 mo for older patients) were in agreement with those of other smaller studies (5-17.8 mo). More recently, Rollison et al reported a mean time to sAML of 26.9 months among a cohort of American patients diagnosed with any MDS risk category, who were enrolled in a study of the efficacy of lenalidomide. Collectively, the data indicate that many patients with MDS progress to AML within 1 or 2 years of their diagnosis. Given the inferior outcomes associated with sAML, further research is needed to optimize treatment protocols and improve survival.

The large number of patients in the SEER database has allowed us to discover previously unknown aspects of MDS among younger patients. Kuendgen et al and Marisavljevic et al compared patients younger and older than 50 years in Germany and Serbia, respectively, and reported remarkably similar OS times for the two age groups. The median survival of the younger groups was almost twice that of the older groups (39 and 40 mo vs 19 and 23 mo, respectively). Our analysis revealed that superior OS among younger patients was seen only for those who did not develop sAML. Younger patients with sAML had poor OS and CSS that was similar to that of older patients with sAML. In addition, younger patients developed sAML more quickly than older patients. Importantly, the transformation interval is shorter for younger patients even though older patients have a greater burden of comorbidities.

Younger patients are also more likely to undergo cytogenic assessment and risk stratification and receive active therapies, including stem cell transplantation. However, our research lacked the mentioned above. Accordingly, we suggest that young patients who develop sAML may comprise a unique clinical population.

This study is also the first to assess the influence of marital status on the outcomes of patients with MDS. We found that married patients had significantly better OS and CSS than those who were not married.

| TABLE 3 | Multivariate time-dependent Cox proportional hazard model for overall survival |
|---------|--------------------------------------------------------------------------------|
|         | Age ≤ 40 y old                                                               | Age > 40 y old                                                               |
|         | Adjusted HR (95% CI) P value                                                 | Adjusted HR (95% CI) P value                                                 |
| Age at diagnosis | 1.015 (1.005-1.024) .002* | 1.036 (1.035-1.037) <.001* |
| Sex     | 0.704 (0.563-0.881) .002* | 0.806 (0.783-0.830) <.001* |
| Race    |                               |                               |
| Black vs White | – – | 0.929 (0.881-0.979) .006* |
| American Indian/Alaska Native vs White | – – | 1.081 (0.868-1.347) .485 |
| Asian or Pacific Islander vs White | – – | 0.995 (0.942-1.051) .857 |
| Marital status |                                |                                |
| Married vs Single | – – | 0.811 (0.773-0.852) <.001* |
| Separated/Divorced/Widowed vs Single | – – | 0.971 (0.923-1.022) .263 |
| WHO classification |                               |                               |
| MDS-RS vs MDS-SLD | 1.261 (0.640-2.485) .502 | 0.819 (0.767-0.875) <.001* |
| MDS-EB vs MDS-SLD | 3.601 (2.206-5.879) <.001* | 2.547 (2.412-2.691) <.001* |
| MDS-MLD vs MDS-SLD | 2.152 (1.173-3.948) .013* | 1.347 (1.254-1.447) <.001* |
| MDS with isolated deletion of 5q vs MDS-SLD | 2.380 (0.958-5.911) .062 | 1.272 (1.154-1.402) <.001* |
| MDS, unclassifiable vs MDS-SLD | 1.849 (1.173-2.916) .008* | 1.292 (1.234-1.352) <.001* |
| Therapy-related myeloid neoplasms vs MDS-SLD | 3.263 (1.385-7.685) .007* | 1.719 (1.413-2.091) <.001* |

Leukemic transformation (time-dependent covariate)

| Yes vs No | 2.832 (1.767-4.539) <.001* | 3.617 (3.321-3.939) <.001* |

Note. — Not included in the multivariate analysis model

Abbreviations: CI, confidence interval; HR, hazard ratio; MDS, myelodysplastic syndrome; MDS-EB, MDS with excess blasts; MDS-MLD, MDS with multilineage dysplasia; MDS-RS, MDS with ring sideroblasts; MDS-SLD, MDS with single lineage dysplasia; vs, versus; WHO, World Health Organization.

* Indicates a significant factor, P < .05.
single. Although the effect may not be as large as that of clinical factors, such as the marital status, can influence the survival of patients with cancer. Over the past 10 years, studies by multiple groups have revealed that the survival of married patients is significantly better than that of nonmarried patients for several types of cancer.29-31 Because the population we assessed was more than 80% White, the effect of marital status could be race-specific. Recent studies by Martinez et al support this idea, because these authors found that race had a significant influence on the effect of marital status on all-cause and cancer-specific mortality among 800 000 patients in the California Cancer Registry (CCR).31 The most viable explanations for the effect of marriage on survival are that married patients have more support (emotionally, physically, or financially) or are less likely to make lifestyle choices that are detrimental to their health.32 For example, Davidoff et al reported that single patients with MDS were less likely to use erythropoiesis-stimulating agents.33 Regardless of the underlying reasons, the strength of the evidence dictates that both marital status and race or ethnicity must be taken into account when determining the risk category of a patient with MDS.

Although we did not compare the survival advantage of being married for each of the races and ethnicities included in our study (White, Black, American Indian/Alaska Native, and Asian or Pacific Islander), we did include an assessment of the prognostic value of race on OS and CSS. Our analysis revealed that Black patients with MDS were likely to survive longer than White patients. This finding did not support the conclusion of Ma et al, whose multivariate analysis of 3200 patients in the SEER-17 registry found no difference in the risk of death among Blacks and Whites.7 We suspect that we were able to identify an association between race and survival because we analyzed a much larger number of patients (36 000 vs 3200) and because Ma et al considered relative survival. Race-related differences in survival were observed by Komrokji et al, Sridharan et al, and Zandberg et al, who all found that Black men with MDS survived longer than White men. However, the differences were not statistically significant.34-36 Confirmation of the results from these smaller studies highlights the importance of using large databases, such as SEER, to characterize patients with rare cancers, such as MDS.

This study had several limitations. First, the SEER database does not collect information on the use of chemotherapy by patients with MDS and/or sAML. As a result, we could not assess how treatment affected the outcomes of this study. Second, the database does not collect information on complex demographic issues, including education, insurance, or economic status. Third, the database does not collect information on cytogenetics or molecular biology, which both have a large influence on the outcomes of sAML. As a result, scoring systems, such as IPSS-R and WPSS, were not mentioned.

### Table 4

|                      | Age ≤ 40 y old | Age > 40 y old |
|----------------------|---------------|---------------|
|                      | Adjusted HR (95% CI) | P value | Adjusted HR (95% CI) | P value |
| Age at diagnosis     | 1.013 (1.002-1.025) | .025* | 1.026 (1.025-1.028) | <.001* |
| Sex                  |               |             |                        |         |
| Female vs Male       | 0.700 (0.528-0.930) | .014* | 0.787 (0.756-0.819) | <.001* |
| Race                 |               |             |                        |         |
| Black vs White       |               |             | 0.792 (0.732-0.857) | <.001* |
| American Indian/Alaska Native vs White |       |             | 1.276 (0.971-1.676) | .080 |
| Asian or Pacific Islander vs White | |             | 1.014 (0.941-1.092) | .720 |
| Marital status       |               |             |                        |         |
| Married vs Single    |               |             | 0.920 (0.859-0.985) | .017* |
| Separated/Divorced/Widowed vs Single | |             | 1.061 (0.987-1.141) | .108 |
| WHO classification   |               |             |                        |         |
| MDS-RS vs MDS-SLD    | 1.435 (0.321-6.420) | .637 | 0.958 (0.859-1.069) | .447 |
| MDS-EB vs MDS-SLD    | 15.584 (5.642-43.048) | <.001* | 5.219 (4.799-5.676) | <.001* |
| MDS-MLD vs MDS-SLD   | 9.659 (3.263-28.595) | <.001* | 2.106 (1.892-2.343) | <.001* |
| MDS with isolated deletion of 5q vs MDS-SLD | 10.357 (2.773-38.679) | .001* | 2.355 (2.065-2.686) | <.001* |
| MDS, unclassifiable vs MDS-SLD | 5.413 (1.987-14.742) | .001* | 1.909 (1.767-2.063) | <.001* |
| Therapy-related myeloid neoplasms vs MDS-SLD | 9.736 (2.431-38.986) | .001* | 2.045 (1.503-2.782) | <.001* |
| Leukemic transformation (time-dependent covariate) | |             |                        |         |
| Yes vs No            | 3.245 (1.954-5.388) | <.001* | 5.346 (4.885-5.850) | <.001* |

Note. —Not included in the multivariate analysis model. *Indicates a significant factor, P < .05.

Abbreviations: CI, confidence interval; HR, hazard ratio; MDS, myelodysplastic syndrome; MDS-EB, MDS with excess blasts; MDS-MLD, MDS with multilineage dysplasia; MDS-RS, MDS with ring sideroblasts; MDS-SLD, MDS with single lineage dysplasia; vs, versus; WHO, World Health Organization.
In conclusion, we conducted a retrospective analysis of the SEER cancer registry database. Our results indicate that although only a small percentage of patients with MDS go on to develop AML, these patients have significantly poorer survival than those without sAML, especially for those younger than 40 years. Survival of patients with MDS is influenced by demographic factors, including race, marital status, age, and sex. Accordingly, the accuracy of current risk assessment systems may be improved by including these types of data.

CONTRIBUTIONS
Xingnong Ye, Dan Chen, Yan Zheng, Cai Wu, and Xiaojiong Zhu performed the data acquisition; Xingnong Ye, Dan Chen, and Jian Huang performed the conception and design; Xingnong Ye and Jian Huang drafted the manuscript. All authors approved the manuscript.

ACKNOWLEDGEMENTS
This study was supported by funding from the Science and Technology Department of Zhejiang Province, China (2016C33160), the Medical and Health Science and Technology Plan of Zhejiang Province, China (2019R330020), the Public Technology Research Projects of Yiwu, China (2016-5-05), and the Key Medical Discipline of Yiwu, China (Hematology, 2018-2020).

CONFLICT OF INTEREST
The authors have no competing interests.

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How to cite this article: Ye X, Chen D, Zheng Y, Wu C, Zhu X, Huang J. The incidence, risk factors, and survival of acute myeloid leukemia secondary to myelodysplastic syndrome: A population-based study. Hematological Oncology. 2019;37:438-446. https://doi.org/10.1002/hon.2660