

Lifestyle and Dietary Factors in Relation to Risk of Chronic Myeloid Leukemia in the NIH-AARP Diet and Health Study

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Abstract

Background: Aside from exposure to ionizing radiation and benzene, little is known about lifestyle risk factors for chronic myeloid leukemia (CML) in the general population.

Methods: We examined the relation between lifestyle and dietary risk factors for CML in 493,188 participants (294,271 males and 198,917 females) aged 50 to 71 years who completed a baseline questionnaire in the National Institutes of Health-AARP Diet and Health Study in 1995 to 1996. Over a median of 10.5 years of follow-up, 178 incident cases of CML (139 males and 39 females) were ascertained from state registries. We used Cox proportional hazards models to estimate hazard ratios and 95% confidence intervals for exposures of interest, adjusting for potential confounding variables.

Results: In multivariable analysis of all participants combined, female sex, years of education, and vigorous physical activity (HR for ≥ 3 times/week vs. < 1 time/week 0.70; 95% CI, 0.49–0.99) were inversely associated with risk of CML, whereas smoking intensity (HR for smokers of ≥ 20 cigarettes per day vs. never smokers: 1.53; 95% CI, 1.03–2.27) and body mass (HR for BMI ≥ 30 vs. < 25 kg/m² 1.46; 95% CI, 0.95–2.23) were associated with increased risk. A range of dietary factors was not associated with disease.

Conclusions: This study adds to the sparse information about lifestyle factors, which affect the risk of CML in the general population.

Impact: If these findings are confirmed, it would suggest that CML may be amenable to preventive strategies. *Cancer Epidemiol Biomarkers Prev*; 22(5); 848–54. ©2013 AACR.

Introduction

Chronic myeloid leukemia (CML) is a malignant clonal disorder of the hematopoietic stem cells that results in unregulated growth of myeloid cells in the bone marrow and their accumulation in the blood (1). The median age at diagnosis is 53 years; however, the disease occurs in all age groups, including children (1). CML has a reported incidence of 1 to 2 cases per 100,000, accounting for 15% to 20% of newly diagnosed leukemia cases in adults (2); approximately 4,870 new cases are diagnosed each year in the United States (3). However, it is possible that its incidence is underreported (4). Incidence rates are higher in males compared with females among both blacks and whites, and higher among blacks of both genders compared with whites, a pattern that is unique among the leukemias (5).

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In spite of recent dramatic advances in the treatment, long-term prognosis for patients with CML is unknown (2). Therefore, insight into potential preventive strategies is urgently needed. Aside from exposure to ionizing radiation and benzene, little is known about risk factors for CML (5). Most previous studies that examined the role of cigarette smoking in relation to risk of CML have found no association (6–11), with only one exception (6). In contrast, studies have consistently showed increased risk of CML with increasing body mass index (BMI; refs. 8, 9, and 11–13). In addition, 2 meta-analyses are suggestive of a positive association of obesity with CML incidence (14, 15).

Because of the paucity of knowledge regarding risk factors for CML, we used data from the National Institutes of Health-AARP (NIH-AARP) Diet and Health Study to examine the association of lifestyle and dietary factors with risk of CML.

Materials and Methods

Study population

The NIH-AARP Diet and Health Study (www.clinicaltrials.gov; NCT00340015) is a large prospective cohort study of AARP members initiated in 1995 to 1996. The rationale for and design of the study have been described

in detail previously (16). In brief, a baseline questionnaire was mailed to 3.5 million AARP (formerly the American Association of Retired Persons) members between the ages of 50 and 71 years, residing in 6 states (California, Florida, Louisiana, New Jersey, North Carolina, or Pennsylvania) or in 2 metropolitan areas (Atlanta, GA or Detroit, MI), with existing population-based cancer registries. In total, 617,119 questionnaires were returned, and 566,398 were satisfactorily completed. The study was approved by the National Cancer Institute Special Studies Institutional Review Board, and return of the questionnaire signified consent.

Among those with completed questionnaires, we excluded subjects who had questionnaires completed by proxy respondents ($N = 15,760$), who had a previous history of cancer ($N = 49,318$), who died or moved out of the study area before study entry ($N = 1,961$), who were identified as having cancer through death reports only ($N = 2,152$), or whose daily log-transformed calorie intake was greater or less than 3 SDs beyond the mean (i.e., <436 or $>6,575$ calories/day) ($N = 4,019$). Our final analytic cohort consisted of 493,188 subjects (294,271 males and 198,917 females).

Information on lifestyle and diet and exposure assessment

At baseline, participants completed a questionnaire that elicited information about demographics including race/ethnicity and education, lifestyle factors such as current weight and height, physical activity at work and outside of work, smoking history, and intake of 124 food items with portion size plus information on intake of low-fat, high-fiber foods and food preparation (16). Women were asked about their use of postmenopausal hormones.

Participants were asked whether they had ever smoked as much as 100 cigarettes during their lifetime; those who responded "yes," were asked whether they smoked currently or if they had quit, and how long ago. Smokers were asked how many cigarettes they usually smoked per day. Assessment of physical activity was based on the average frequency (never; rarely; 1–3 times per month; 1–2 times per week; 3–4 times per week; and 5 or more times per week) during the past year that participants engaged in activities of any type that lasted 20 minutes or more and caused either increases in breathing or heart rate or working up a sweat. To assess dietary intake, participants were asked about their usual frequency of intake and portion size over the past 12 months according to 3 predefined categories of portion size and 10 predefined frequency categories ranging from "never" to " ≥ 6 times/day" for beverages and from "never" to " ≥ 2 times/day" for foods. The nutrient database for this food frequency questionnaire was constructed using the US Department of Agriculture 1994–1996 Continuing Survey of Food Intake by Individuals (17). Of the many hundreds of potential dietary exposures computed in the NIH-AARP study, we focused on a limited number of important indicator variables, such as intake of various types of

meat, total intake of fruits, total intake of vegetables, etc. The total meat category included all types of beef, poultry, fish, pork, and processed meats. The red meat category included bacon, beef, cold cuts, ham, hamburger, regular hot dogs, liver, pork, sausage, and steak. The white meat category included all forms of poultry, fish, and low-fat turkey hot dogs, and sausages. All types of cold cuts, bacon, ham, hot dogs, and sausages from red and white meats were included in the processed meat variable.

Follow-up and ascertainment of cases

In the NIH-AARP study, vital status was determined by linkage of the cohort to the Social Security Administration Death Master File in the United States, the National Death Index Plus (for participants who could also be matched to the Death Master File), and cancer registry records. Participants' responses to questionnaires and other mailings were also used to confirm vital status. Follow-up time extended from the date of receipt of the questionnaire (between 1995 and 1996) to date of death, date of diagnosis of incident primary CML, participant relocation out of the registry ascertainment area, or December 31, 2006, whichever date was earliest (18).

CML cases were defined using International Classification of Diseases for Oncology, Third edition (ICD-O-3) codes 9863, 9875, 9876, 9945, and 9946. Incident cases were identified from cancer registries in the original 6 states and 2 metropolitan areas plus Texas and Arizona, states to which participants most commonly moved during follow-up. A validation study indicated that study procedures identified approximately 90% of all incident cancers within the 8 registries (18). A total of 218 CML cases were identified over a median follow-up of 10.5 years. After the above-mentioned exclusions, 178 cases (139 males, 39 females) were available for analysis.

Statistical analysis

Cox proportional hazards models, with person-years as the underlying time metric, were used to estimate HR and 95% confidence intervals (95% CI) for factors that may be associated with risk of CML. Because the number of cases was limited, especially among women, we analyzed the data in 2 stages. First, we examined the age- and multi-variable-adjusted associations of demographic and lifestyle factors (not including diet) with risk of CML in men and women separately as well as in both sexes combined. To maximize statistical power, we created a parsimonious model containing those variables that showed statistically significant associations with CML. The parsimonious model included the following variables: age (years-continuous), years of education (<12 , 12–15, ≥ 16 , missing), smoking intensity (never, <21 , and ≥ 21 cigarettes/day), BMI (continuous and, alternatively <25 , 25– <30 , ≥ 30 kg/m²), and vigorous physical activity (<1 , 1–2, ≥ 3 times/week, missing); a term for sex was included in the model combining males and females. Participants with missing information were included in the analysis by including a dummy variable for those with missing responses on a

particular variable. We tested for interactions of risk factors with sex by including product terms for each potential interaction (e.g., BMI dichotomized at the median \times sex) in a separate model with all covariates included in the parsimonious model and examined the *P*-value of the coefficient for the interaction term.

In the second phase, we examined dietary factors and beverages (alcohol, coffee, tea) in the presence of covariates included in the parsimonious model. Alcohol intake was categorized as never, <1, 1–2, and ≥ 3 drinks/day. Coffee (caffeinated and decaffeinated combined) and tea intake were categorized into tertiles (coffee: 0–<376, ≥ 376 to <957, ≥ 957 g/day; tea: 0 to <34, ≥ 34 to <315, ≥ 315 g/day). For dietary exposures that were expressed as continuous variables (e.g., grams of red meat per day), we created quartiles based on their distribution among the noncases. In alternative models, we also entered dietary variables as continuous variables to maximize statistical power. The results of the 2 approaches were similar, and we present the results for the dietary variables in terms of quartiles. The meat and other dietary variables were energy adjusted using the density method, with energy included in the model, because most dietary variables were correlated with total energy intake (19). Models using unadjusted dietary intake but with calories as a covariate were also fitted; these models gave similar results to those derived from use of the multivariable nutrient density method. Models assessing specific meat groups simultaneously controlled for the remaining meat groups for total meat consumption (white and red; processed and non-processed). Tests for trend across categorical variables were conducted by assigning the median value of each category and modeling this variable as a continuous variable. All analyses were done using SAS version 9.1 (SAS Institute). All tests were 2-sided and *P*-values were assessed at the α -level of 0.05 for statistical significance.

Results

Cases were predominantly male (78%) and white (94%). Fifty-one percent of cases were 65 years of age or older, 27% had never smoked, 26% were obese (BMI ≥ 30 ; Table 1).

In the age-adjusted model, women were at reduced risk of CML, and in the sex-adjusted model age (≥ 65) was associated with increased risk of malignancy (Table 1). After adjustment for both age and sex, being a former or current smoker and being obese were positively associated with risk. In contrast, engaging in vigorous physical activity and higher education level were inversely associated with risk. Race and alcohol intake were not associated with CML.

Table 2 presents multivariable-adjusted hazard ratios for the variables retained in the parsimonious model for both sexes combined (tests for interaction with sex were not statistically significant). Education was inversely associated with risk for CML (HR for ≥ 16 vs. <12 years of

Table 1. Association of selected demographic and lifestyle characteristics at baseline with risk of CML in the NIH-AARP Diet and Health Study, 1995 to 2006

	N = 493,188			
	Cases	Person-years	HR	95% CI
Age (years)				
<60	50	1,700,268	1.00 ^a	Ref.
60–65	37	1,260,345	0.99	0.65–1.52
≥ 65	91	1,525,551	2.00	1.42–2.83
Sex				
Male	139	2,625,367	1.00 ^b	Ref.
Female	39	1,860,798	0.40	0.28–0.57
Education (years)				
<12	21	261,095	1.00 ^c	Ref.
12–15	95	2,363,407	0.57	0.36–0.92
≥ 16	57	1,733,067	0.42	0.25–0.69
Missing	5			
Race				
White	167	4,085,600	1.00 ^c	Ref.
Black	4	176,855	0.70	0.26–1.90
Other	7	223,710	0.78	0.37–1.66
Smoking				
Never	47	1,623,495	1.00 ^c	Ref.
Former	104	2,185,523	1.38	0.97–1.96
Current	24	508,640	1.50	0.89–2.50
Missing	6			
Alcohol (drinks/day)				
Never	41	1,084,438	1.00 ^c	Ref.
>0–<1	87	2,386,138	0.94	0.65–1.37
≥ 1 –<3	35	685,172	1.13	0.72–1.78
≥ 3	15	330,417	0.94	0.52–1.70
BMI (kg/m²)				
<25	45	1,558,044	1.00 ^c	Ref.
25–<30	85	1,863,465	1.37	0.95–1.97
≥ 30	46	958,766	1.65	1.09–2.49
Missing	2			
Vigorous physical activity (times per week)				
<1	63	1,388,497	1.00 ^c	Ref.
1–2	39	971,078	0.83	0.56–1.24
≥ 3	73	2,079,673	0.68	0.48–0.95
Missing	3			

^aAdjusted for sex.

^bAdjusted for age.

^cAdjusted for age and sex.

education 0.51; 95% CI, 0.30–0.86). Current and former smoking were not associated with increased risk; however, relative to never smokers, smokers of ≥ 21 cigarettes per day had significantly increased risk (HR = 1.53; 95% CI, 1.03–2.27). Obesity showed a nonsignificant positive association with risk in the combined group (HR = 1.46 for BMI ≥ 30 vs. <25; 95% CI, 0.95–2.23), whereas vigorous physical activity showed a significant inverse association

Table 2. Multivariable-adjusted associations of demographic and lifestyle factors and risk of CML in the total population (males and females combined), in the NIH-AARP Diet and Health Study, 1995 to 2006

	Total ($N_{\text{cases}} = 178$)		
	No. of cases	HR ^a	95% CI
Education (years)			
<12	21	1.00	Ref.
12–<16	95	0.56	0.34–0.91
≥16	57	0.51	0.30–0.86
Unknown	5		
<i>P for trend</i>		0.01	
Smoking			
Never	47	1.00	Ref.
Former	104	1.35	0.95–1.93
Current	21	1.41	0.83–2.39
Missing	6		
Amount smoked			
Never	47	1.00	Ref.
<21 cpd	62	1.23	0.84–1.82
≥21 cpd	63	1.53	1.03–2.27
Missing	6		
<i>P for trend</i>		0.03	
Body mass index (kg/m ²)			
<25	45	1.00	Ref.
25–<30	85	1.31	0.90–1.90
≥30	46	1.46	0.95–2.23
Missing	2		
<i>P for trend</i>		0.08	
Vigorous physical activity			
<1×/wk	63	1.00	Ref.
1–2×/wk	39	0.88	0.58–1.32
≥3×/wk	73	0.70	0.49–0.99
Missing	3		
<i>P for trend</i>		0.04	

^aAdjusted for age and sex and for remaining variables where appropriate: body mass index (<25, 25–<30, ≥30 kg/m²), smoking intensity (never, <21 cigarettes per day, ≥21 cigarettes per day), physical activity (<1, 1–2, ≥3 times per week), and years of education (<12, 12–<16, ≥16 years).

(HR = 0.70 for ≥ 3 times per week vs. <1 time per week; 95% CI, 0.49–0.99).

In analyses restricted to women, in both univariate and multivariable analyses, postmenopausal hormone use showed no association with CML in women (multivariable-adjusted HR = 1.20; 95% CI, 0.62–2.33; data not shown).

In a sensitivity analysis of the combined data, excluding the first 2 years of follow-up (leaving 137 cases and 467,861 noncases), the positive association with BMI was strength-

ened, with an HR of 2.06; 95% CI, 1.25 to 3.39 for ≥30 versus <25 kg/m²; *P* for trend 0.005, whereas the association with smoking intensity was attenuated (HR = 1.36 for ≥21 cigarettes per day; 95% CI, 0.88–2.10). The inverse association with vigorous physical activity was no longer statistically significant: HR = 0.75 for ≥3 times per week versus <1 times per week; 95% CI, 0.50 to 1.12; *P* for trend 0.15.

When subjects who rated their health status at baseline as "poor" were excluded ($N_{\text{cases}} = 4$), the associations with BMI, level of smoking, and physical activity were unchanged except for a slight loss of precision (HR for ≥30 kg/m² = 1.51; 95% CI, 0.98–2.32; HR for ≥21 cigarettes per day = 1.56; 95% CI, 1.04–2.32; and HR for physical activity ≥3 times per week = 0.73; 95% CI, 0.51–1.05).

After adjustment for covariates in the parsimonious model, no dietary factors were associated with risk of CML (Table 3). Results were similar when dietary intake was not adjusted for energy intake but a term for calories was entered as a covariate (data not shown).

Discussion

In this study, analysis of the total study population (males and females combined) indicated that, after adjusting for covariates, younger age, female sex, having a college education or higher, and a higher level of physical activity were associated with significantly reduced risk of CML, whereas intensity of smoking was a significant risk factor. BMI showed a nonsignificant positive association, whereas dietary factors and alcohol intake showed no associations with disease. Differences in the associations between men and women were not statistically significant. When the first 2 years of follow-up were excluded, only the positive association of BMI remained statistically significant. When those with poor health were excluded, the associations in the main analysis were unchanged.

Established leukemogenic exposures, such as ionizing radiation and benzene, are likely to account for only a small proportion of CML incidence (3), yet few studies have investigated demographic, lifestyle, and dietary risk factors for this disease. Of 6 studies that examined smoking in relation to CML risk (7–12), a cohort study of U.S. veterans reported a significant positive association (7), and second cohort study (8) showed a borderline positive association in men but not in women based on small numbers of cases. In this study, in the analysis combining men and women, relative to never smokers, ever smokers of ≥21 cigarettes per day had a significantly increased risk after adjustment for other risk factors. However, the association was attenuated and no longer significant when the first 2 years of follow-up were excluded, suggesting that preclinical disease may have been responsible for the association.

Findings regarding the association of BMI with CML have been somewhat more consistent. A large cohort study from Norway (14) in which height and weight were measured in 2 million men and women at baseline showed a significant positive association in both sexes.

Table 3. Association of dietary factors with risk of CML in the NIH-AARP Diet and Health Study, 1995 to 2006

	No. of cases	No. of person-years	Multivariable model ^a	
			HR	95% CI
Red meat (g/day)^b				
<27.3	33	1,228,647	1.00	Ref.
27.3–<51.3	42	1,119,335	1.20	0.74–1.95
51.3–<87.6	50	1,108,332	1.36	0.85–2.17
≥87.6	53	1,101,246	1.33	0.83–2.13
<i>P for trend</i>			0.25	
Total meat (g/day)				
<67.9	39	1,116,426	1.00	Ref.
67.9–<106.9	47	1,112,529	1.12	0.72–1.74
106.9–<161.3	48	1,114,098	1.23	0.80–1.90
≥161.3	44	1,114,509	1.11	0.71–1.73
<i>P for trend</i>			0.65	
White meat (g/day)^b				
<25.8	39	1,101,159	1.00	Ref.
25.8–<46.0	50	1,110,974	0.82	0.53–1.26
46.0–<77.8	48	1,118,285	1.15	0.76–1.72
≥77.8	41	1,127,144	0.94	0.61–1.46
<i>P for trend</i>			0.89	
Processed meat (g/day)^b				
<2.8	41	1,127,532	1.00	Ref.
2.8–<6.6	38	1,123,322	0.80	0.50–1.26
6.6–<15.4	52	1,111,307	1.01	0.65–1.59
≥15.4	47	1,095,399	0.62	0.36–1.07
<i>P for trend</i>			0.14	
Fish (g/day)				
<4.2	55	1,110,495	1.00	Ref.
4.2–<7.9	51	1,113,299	0.91	0.62–1.35
7.9–<14.2	34	1,113,995	0.63	0.41–0.98
≥14.2	38	1,119,773	0.73	0.48–1.11
<i>P for trend</i>			0.11	
Total fruit (cup equivalents/day)				
<0.97	37	1,093,153	1.00	Ref.
0.97–<1.69	50	1,128,735	1.45	0.93–2.25
1.69–<2.65	55	1,110,765	1.68	1.09–2.60
≥2.65	96	1,124,909	1.12	0.69–1.81
<i>P for trend</i>			0.84	
Total vegetables (cup equivalents/day)				
<1.14	30	778,204	1.00	Ref.
1.14–<1.71	53	1,391,457	1.12	0.70–1.80
1.71–<2.48	56	1,330,487	1.28	0.80–2.04
≥2.48	39	957,414	1.26	0.76–2.08
<i>P for trend</i>			0.35	
Total grains (oz. equivalents/day)				
<3.37	39	1,107,879	1.00	Ref.
3.37–<4.78	42	1,112,903	1.02	0.65–1.60
4.78–<6.57	44	1,120,035	1.02	0.65–1.59
≥6.57	53	1,116,745	1.17	0.76–1.80
<i>P for trend</i>			0.45	

(Continued on the following column)

Table 3. Association of dietary factors with risk of CML in the NIH-AARP Diet and Health Study, 1995 to 2006 (Cont'd)

	No. of cases	No. of person-years	Multivariable model ^a	
			HR	95% CI
Total fat (g/day)				
<38.6	37	1,126,983	1.00	Ref.
38.6–<55.3	37	1,114,083	0.95	0.59–1.53
55.3–<78.5	49	1,114,679	1.21	0.78–1.89
≥78.5	55	1,101,816	1.21	0.78–1.90
<i>P for trend</i>			0.26	
Total fiber (g/day)				
<12.7	43	1,103,170	1.00	Ref.
12.7–<17.7	37	1,129,612	0.89	0.56–1.40
17.7–<24.0	49	1,102,684	1.19	0.78–1.82
≥24.0	49	1,122,097	1.14	0.74–1.75
<i>P for trend</i>			0.36	
Alcohol intake (drinks/day)				
Never	41	1,076,913	1.00	Ref.
>0–<1	87	2,372,482	1.04	0.70–1.52
≥1–<3	34	680,675	1.19	0.74–1.93
≥3	16	327,493	1.03	0.57–1.86
<i>P for trend</i>			0.69	
Coffee intake (g/day)				
0–<376	55	1,571,313	1.00	Ref.
376–<957	53	1,420,635	1.20	0.82–1.78
≥957	70	1,494,217	1.00	0.68–1.46
<i>P for trend</i>			0.64	
Tea intake (g/day)				
0–<34	66	1,481,435	1.00	Ref.
34–<315	53	1,500,004	0.92	0.63–1.33
≥315	59	1,504,726	1.00	0.69–1.44
<i>P for trend</i>			0.88	

^aAdjusted for age, sex, body mass index (<25, 25–<30, ≥30 kg/m²), smoking intensity (never, <21 cigarettes per day, ≥21 cigarettes per day), physical activity (<1, 1–2, >3 times per week), and years of education (<12, 12–<16, ≥16 years), energy intake (kcal/day—continuous).

^bRed meat additionally adjusted for intake of white meat and visa versa; processed meat additionally adjusted for intake of unprocessed meat.

Two case-control studies also reported a positive association (9, 12). Two other cohort studies found no association (10, 13); however, it should be noted that in the study by Fernberg and colleagues (10) there were only 8 cases in the >30 kg/m² category. In addition, one meta-analysis (15) reported a positive association of obesity with CML in men and women combined, with no evidence of heterogeneity among studies. A second meta-analysis (16) found a statistically significant association for men and women combined but not when men and women were analyzed separately. Only a few of the previous studies controlled

for a number of potential confounding variables identified in this study, including education, smoking, and physical activity (12–14). Hazard ratios in the study by Engeland and colleagues (14) were adjusted only for age and birth cohort. Kassim and colleagues (9) adjusted for sex, passive smoking, pack-years of smoking, residence, and ethnicity, whereas Strom and colleagues (12) adjusted for age, gender, ethnicity, and agrochemical exposure. The study by Fernberg and colleagues (10) took only age into account whereas that by Samanic and colleagues (13) included only age and calendar year as covariates.

In this analysis, the associations of BMI and physical activity with CML were each statistically significant and somewhat stronger when each was entered in the parsimonious multivariable model without the other variable (HR for BMI $\geq 30 = 1.54$; 95% CI, 1.01–2.35, compared to 1.46; 95% CI, 0.95–2.23; HR for physical activity ≥ 3 times per week = 0.68; 95% CI, 0.48–0.96, compared to 0.70; 95% CI, 0.49–0.99). When both variables were included simultaneously each association was somewhat attenuated. No previous study has presented data on physical activity in relation to risk of CML. In any event, our finding of a borderline association with BMI is in agreement with the results of most previous studies (9, 12, 14) and with those of 2 meta-analyses (15, 16).

Although a number of studies have examined dietary factors in relation to risk of leukemia and AML and CLL (4, 5), the only study (9) that examined dietary factors in relation to CML had information only on intake of fruits and vegetables. In agreement with our findings, that study found no evidence of an association. Of the wide range of dietary factors investigated in this study, none was associated with risk of CML.

Strengths of this study include the fact that the NIH-AARP Diet and Health Study obtained information on a wide range of lifestyle and dietary factors. Our study is larger than all but one previous study (13). In addition, we were able to carry out sensitivity analyses to examine the potential effects of reverse causation and poor health on our results.

Our analysis is subject to a number of limitations. In spite of its having a larger sample size than all but one previous study, the number of cases was limited, particularly among women, making it difficult to tease apart the associations of a number of different variables, including education, smoking, BMI, and physical activity. The number of cases was further reduced in the sensitivity analyses. Furthermore, because of the age requirement of the NIH-AARP study (age range 50–71 years), our study

population is not representative of the full age range of CML. Risk factors were only assessed at baseline, so there is potential misclassification of exposure; however, such misclassification is likely to have been nondifferential and therefore the observed associations may have been underestimated. The low representation of non-whites among cases prevented us from examining risk factors for CML among blacks compared to whites. In addition, height and weight were reported by the participants, rather than measured, although in a cohort study any bias in reporting of height and weight is unlikely to be associated with disease status. Finally, despite controlling for covariates, there is potential for residual confounding that might affect the relationship of lifestyle or dietary factors with risk of CML.

In conclusion, this study found suggestive positive associations of smoking and BMI with risk of CML as well as inverse associations with vigorous physical activity, female sex, and years of education. We found no evidence of associations with a variety of dietary factors. This study adds to the sparse information about factors, which affect the risk of CML in the general population and suggests that lifestyle modifications may affect the risk of this disease. In view of the low incidence of this type of leukemia, epidemiologic studies should be carried out within cohort consortia to achieve an adequate sample size for CML and to compare risk factors across the different subtypes of leukemia.

Disclosure of Potential Conflicts of Interest

No potential conflicts of interest were disclosed.

Authors' Contributions

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