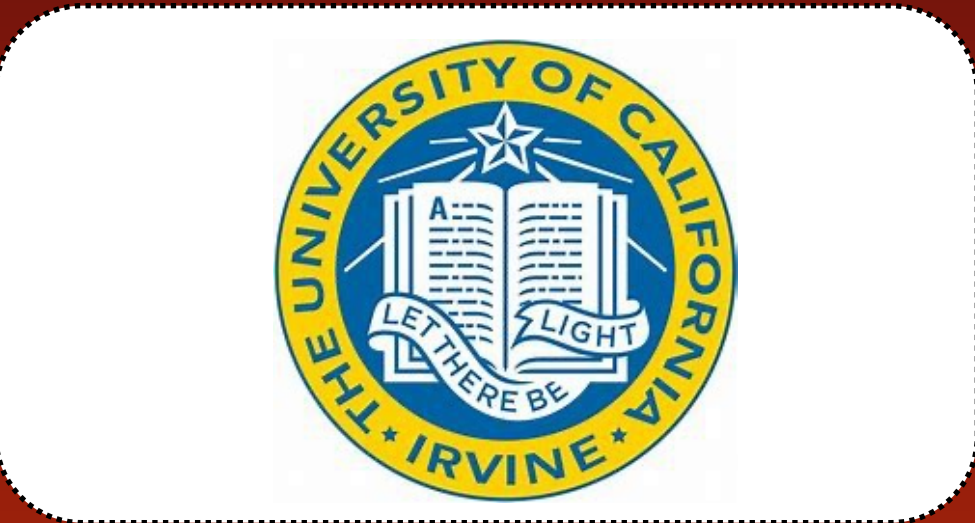




Clinical Characteristics and Outcomes of Indolent B-Cell Lymphoid Malignancies in Carcinogen-Exposed vs. Unexposed US Veterans: A Matched Case–Control Study



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Abstract

Environmental carcinogens are associated with lymphoid malignancies, and Veterans are especially at high risk of exposures while deployed in theaters of conflict. This is a matched case-control study at a VA hospital comparing patients with indolent lymphomas including chronic lymphocytic leukemia who had known exposures vs no exposures. Of 217 Veterans included, 56 (25.8%) had exposures and they had a younger median age of diagnosis (63 vs 68 years) and shorter time from enlistment until diagnosis of lymphoid malignancies (42 vs 47 years). More work needs to be done to substantiate these findings.

Background

Military personnel and civilians living in theaters of conflict were exposed to environmental carcinogens, such as Agent Orange and Burn Pits, which are associated with increased risk of lymphoid malignancies [1]. There is a need to understand how exposures have impacted disease presentation and outcomes.

Objective

To determine whether clinical presentations and outcomes of indolent B-cell lymphoid malignancies differ in persons exposed to carcinogens compared to matched unexposed persons.

Table 1. Characteristics of Patients with Indolent Lymphomas

Patient characteristics	All, n=217	Dioxin, n=56	Unexposed, n=161
Male, n (%)	208 (96)	54 (96)	154 (96)
Race, n (%)			
White	146 (67.3)	40 (71.4)	106 (65.8)
Black	22 (10.1)	6 (10.7)	16 (9.9)
Native American	4 (1.8)	2 (3.5)	2 (1.2)
Asian or Pacific Islander	3 (1.4)	0	3 (1.9)
Unanswered	42 (19.4)	8 (14.3)	34 (21.1)
Histology, n (%)			
CLL/SLL	87 (40.1)	24 (42.9)	63 (39.1)
Follicular Lymphoma	60 (27.6)	17 (30.4)	43 (26.7)
Marginal Zone Lymphoma	37 (17.1)	6 (10.7)	31 (19.3)
Mantle Cell Lymphoma	17 (7.8)	2 (3.5)	15 (9.3)
LPL	16 (7.37)	7 (12.5)	9 (5.60)
Tour of Duty, n (%)			
Vietnam War	117 (53.9)	54 (96)	63 (39.1)
World War 2	37 (17.1)	1 (1.8)	36 (22.4)
Korean War	22 (10.1)	0	22 (13.7)
Post-Korean	17 (7.83)	0	17 (10.6)
Post-Vietnam	11 (5.07)	0	11 (6.8)
Persian Gulf	10 (4.61)	1 (1.8)	9 (5.6)
Multiple	3 (1.38)	0	3 (1.9)
Toxin exposure, n (%)	56 (25.8)	56 (100)	0
Median No. Treatment, (range)	1 (0-8)	1 (0-8)	1 (0-8)
Frontline Treatments			
Chemotherapy	109 (50.2)	32 (57.1)	77 (47.8)
Targeted Therapy	27 (12.4)	7 (12.5)	20 (12.4)
Other Treatments	15 (6.9)	1 (1.8)	14 (8.7)
Untreated	60 (27.6)	14 (25)	46 (28.6)
Unknown	6 (2.8)	2 (3.6)	4 (2.5)

Abbreviations: CLL/SLL - chronic lymphocytic leukemia/small lymphocytic lymphoma; LPL - lymphoplasmacytic lymphoma; No. - number

Materials & Methods

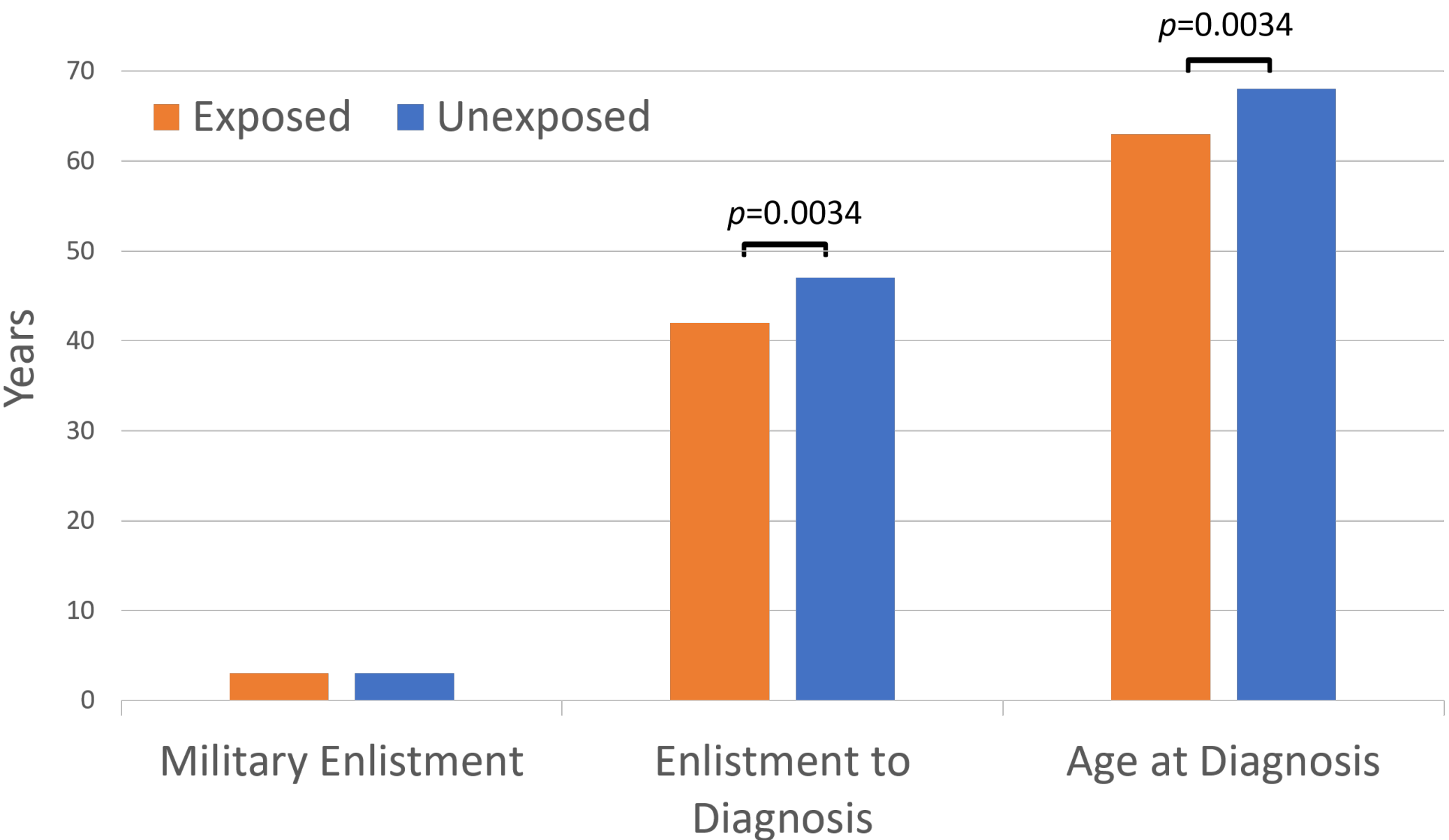
Matched case–control study at a single Veteran Affairs Medical Center (January 1, 1994 – August 15, 2020). Data abstraction through January 31, 2021. Descriptive statistics were used to summarize the data, and the Mann-Whitney test was used to compare differences between the two groups.

Results

We studied 217 veterans. Median age at diagnosis was 66 years (range, 32–91), 208 (96%) were male, median duration of time in military service was 3 years (range, 0.26–28), and median time from enlistment until diagnosis of lymphoid malignancy was 47 years (range, 10–71). First-line management consisted of chemotherapy (n=109), targeted therapy (n=27), other treatments (n=15), untreated (n=60), or unknown (n=6).

Fifty-six patients reported carcinogen exposures, and 161 patients did not have documented exposures; both groups were mostly male, 54 (96%) and 152 (95%), respectively. Median age at diagnosis was lower (63 years; range, 33–76) in exposed vs. 68 years (range, 32–91) in unexposed patients (p=0.0034), and median time from enlistment until diagnosis of lymphoid malignancy was shorter (42 years; range, 13–55) in exposed vs. 47 years (range, 10–71) in unexposed patients (p=0.0034). Median duration of time in service (3 years; range, 0–28; p=0.11) and median number of therapies (1; range, 0–8) were not statistically different for both groups.

Comparing Median Times Between Exposed and Unexposed Patients with Lymphoid Malignancies



Discussion

Veterans who developed indolent B-cell lymphoid malignancies after prior exposure to chemical carcinogens had a younger age at diagnosis and shorter time from enlistment in military service to diagnosis. Our findings provide the rationale for larger clinical, epidemiological, and mechanistic investigations to understand underlying pathophysiological mechanisms and identify targets for treatment.

Reference

[1] National Academies of Sciences & Medicine, Veterans and Agent Orange: Update 11 2018

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