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Soft Tissue Sarcoma and Military Service in Vietnam: A Case Comparison
Group Analysis of Hospital Patients

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Abstract

Soft tissue sarcoma and military service in Vietnam: A case comparison group analysis of hospital patients. The possibility that exposure to Agent Orange or phenoxy herbicides may have increased the risk of soft tissue sarcoma (STS) has been of genuine concern to Vietnam veterans and their families. A hospital-based case comparison group study was undertaken to examine, through a comprehensive review of medical records and military personnel records, the association between previous military service in Vietnam and soft tissue sarcoma. The case group comprised 234 Vietnam-era veteran patients who served in the U.S. military between 1964 and 1975 and were treated in one of the 172 VA hospitals between 1969 and 1983 with a histologically confirmed diagnosis of soft tissue sarcoma. The comparison group consisted of 13,496 patients who were systematically sampled from the same Vietnam-era veteran patient population from which the cases were drawn. Military service information, in particular Vietnam service status, for each case and control patient was obtained from a review of the patient's military personnel records archived at the National Personnel Records Center in St. Louis, Missouri. No significant association of soft tissue sarcoma and previous military service in Vietnam was observed: odds ratio was 0.83 with a 95% confidence interval of 0.63-1.09.

Key word: Agent Orange, dioxin, phenoxy herbicides, TCDD, Vietnam veterans, and Vietnam era veterans.

Introduction

Two Swedish case-control studies have suggested that persons reporting exposure to phenoxy herbicides have a 5 to 6 fold higher risk of developing soft tissue sarcoma compared to persons without such exposure (Hardell et al., 1979; Erikson et al., 1981). In addition, several cases of soft tissue sarcoma have been reported in the U.S. among workers involved in the manufacturing or use of phenoxy herbicides (Cook, 1981; Honchar and Halperin, 1981; Moses and Selikoff, 1981).

These studies have generated much concern in the United States for Vietnam veterans that, as a result of their exposure to Agent Orange in Vietnam, they may be at increased risk for soft tissue sarcoma (STS) in addition to several other medical and psychological problems. Agent Orange, a mixture of two commercial phenoxy herbicides 2,4-dichlorophenoxyacetic acid (2,4-D) and 2,4,5-trichlorophenoxyacetic acid (2,4,5-T), was the herbicide most commonly used by the U.S. military in Vietnam. The principle concern over exposure to Agent Orange stems from the fact that during the manufacture of 2,4,5-T trace amounts of a highly toxic dioxin, 2,3,7,8-tetrachlorodibenzo-para-dioxin (TCDD), appeared as a contaminant.

During the five-year period from 1965 to 1970, the U.S. Air Force sprayed more than 11 million gallons of Agent Orange in South Vietnam. Approximately two million U.S. military personnel served one-year tours during the same period.

Studies published subsequent to the Swedish studies have not yet demonstrated the association between STS and either exposure to phenoxy herbicides or military service in Vietnam (Riihimaki, 1982; Greenwald et

al., 1984; Smith, et al., 1982, 1984; U.S. Air Force, 1983; University of Sidney, 1984). Two of the 7 industrial workers previously reported to be cases of STS were also found to have not sarcoma but carcinomas (Fingerhut et al., 1984).

In view of the public concern about potential health risk among Vietnam veterans and conflicting research findings in the scientific literature, a case comparison group analysis of hospital patients for soft tissue sarcoma was undertaken to determine the association between previous military service in Vietnam and soft tissue sarcoma.

Materials and Methods

The Veterans Administration Patient Treatment File (PTF) was used to identify all Vietnam era veterans who were diagnosed as having soft tissue sarcoma from 1969 through 1983. The PTF is a computerized hospital data base of in-patient records including patients' demographic data, surgical and procedural transactions, and patient movement and diagnoses. A record is created for each in-patient discharged from one of the 172 VA medical centers. The Vietnam era veterans are defined as veterans who served in the U.S. military sometime during August 5, 1964 and May 7, 1975.

A total of 418 cases with International Classification of Disease (ICD) 171 diagnosis, i.e., malignant neoplasm of connective and other soft tissue, were identified by computer search of the PTF for Vietnam era veterans who were hospitalized between 1969 and 1983. A pathology report for each ICD 171 case was requested from each treating VA medical center. A review of 394 pathology reports received for these cases was made by a pathologist (L.W.) who has particular interest and experience in this

group of malignancies. During the review he had no knowledge of Vietnam service status of any of the cases.

On the basis of the review of the pathology reports, 151 ICD 171 cases were excluded as not likely being soft tissue sarcoma because of miscoding or misclassification and 9 ICD 171 cases were put in a doubtful STS category, leaving 234 histologically confirmed diagnoses of STS. All diagnoses were classified according to the WHO classification system for soft tissue sarcomas (Enzinger et al., 1969).

The comparison group consisted of 14,931 patients who were systematically sampled from the same Vietnam era veterans patient population from which the STS cases were identified. Vietnam era veteran patients who have predetermined numbers in the last two digits of their social security numbers were selected among all Vietnam era veteran patients.

Military service information, in particular Vietnam service status, for STS cases and control patient was obtained from a comprehensive review of the patient's military personnel records archived at the National Personnel Records Center (NPRC) in St. Louis, Missouri. The General Services Administration (GSA) under an agreement with the Department of Defense maintains the military personnel records of veterans including those from the Vietnam era. Military personnel records were located and abstracted for all of the 234 soft tissue sarcoma cases and 13,496 of the 14,931 (90%) control patients.

Results and Discussion

Eighty-six of the 234 histologically confirmed soft tissue sarcoma cases, or 36.8%, had served in Vietnam. As Table 1 indicates there was no one predominant type of soft tissue sarcoma. Distribution of tumor type of the 234 STS cases was similar to the results from the recently published NY state study of 281 cases of soft tissue sarcoma and Vietnam service (Greenwald et al., 1984). Greenwald et al., reported that percentage distribution of malignant tumor of muscle tissue, fibrous tissue, adipose tissue, and other soft tissue were 23.8, 17.8, 16.4 and 42.0 respectively among the men with soft tissue sarcoma diagnosed from 1962 through 1980, who were between the ages of 18 and 29 years anytime between 1962 and 1971 and in the New York State Cancer Registry.

Age distribution of STS cases was similar to the control group. No unusual influx of STS cases was observed at any interval as indicated by percent distribution of STS cases and control groups by hospitalization year (Table 2).

Of the sample of 13,469 PTF Vietnam era patients, 5,544 or 41% had served in Vietnam (Table 3). No significant association of soft tissue sarcoma and previous military service in Vietnam was observed among the Vietnam era veterans who come to the VA hospital for inpatient medical care. The odds ratio was 0.83 with a 95% confidence interval of 0.63-1.09. This suggests that the chance of having diagnosis of STS among Vietnam veteran patients was not greater than that among veteran patients who did not serve in Vietnam.

A differential ascertainment of military service status between the STS cases (100%) and the control patients (90%) should be noted. We believe, however, that the difference is primarily a reflection of levels of efforts and man-hours allocated for the personnel record search rather than any difference in availability of the military records between STS

cases and control patients, or Vietnam veterans and non-Vietnam veterans. For example, when the same levels of record search efforts as for the control patients were employed for the STS cases, the military record searchers at the NPRC were able to locate 214 of the 234 STS cases (91%); the yield for the control patients was 13,496 of the 14,931 (90%). Additional time-consuming manual tracking efforts were made for the 20 STS cases whose Vietnam service status was not determined because their personnel folder were misplaced, missing or on loan to other agencies. Of the 20 STS cases, 12 did not serve in Vietnam and 8 did serve in Vietnam: a ratio of 5:4. Prior to this exhaustive manual search the ratio among the 214 STS cases was 5:3.

Even if one makes an extreme assumption, that is, that all of the remaining 10% of the control patients (1,435), whose military personnel records were not located, did not serve in Vietnam, the conclusion of the study would not be altered. This assumption results in the odds ratio of 0.98. The other extreme assumption, that is, that all of the 1,435 patients had served in Vietnam, results in the odds ratio of 0.66.

There seems to be no propensity of ground troops (Army or Marines) among the STS cases as compared to the comparison group (Table 4). It has been suggested that ground troops, by nature of their military operation through defoliated zones and by practice of base perimeter spraying, might have a higher probability of direct or indirect contact with Agent Orange than Air Force or Navy personnel.

The findings of this study are consistent with a case control study recently published by Greenwald et al. (1984). Greenwald et al. (1984) reported no significant association between STS among Vietnam era veteran age males and military service in Vietnam.

Other studies of Vietnam era veterans published to date also have failed to find an excess of STS among Vietnam veterans. A study of RANCH HAND personnel, a group of approximately 1,260 men who conducted the fixed wing aerial herbicide spraying missions in Vietnam from 1962 through 1971, did not reveal a single death from STS (USAF, 1983). A proportionate mortality analysis of deaths among New York State Vietnam era veterans between 1965 and 1980, exclusive of 1968 and 1969, also failed to show excess STS deaths among Vietnam veterans. Two of the 555 deaths reported among Vietnam veterans were due to cancer of connective and soft tissue (ICD 171), whereas 3 of 941 deaths among non-Vietnam veterans resulted from the same type of cancer. The mortality odds ratio (MOR) was 1.09 with a 95% confidence interval of 0.08-15.09 (Lawrence et al., 1985). A mortality study of Australian Vietnam era veterans reported 260 deaths among 19,205 Vietnam veterans and 263 deaths among 24,677 non-Vietnam veterans when followed from the end of their military service to January 1, 1982. There was no statistically significant difference in the death rates from STS (University of Sidney, 1984). However, in all three mortality studies, it should be recognized that the design of the study is such that only very high risks for STS were likely to be detected: the number of person years followed or number of deaths available for analysis was too small to detect moderately elevated relative risks of STS from Vietnam service.

The absence of positive association between STS and Vietnam service might be a result of insufficient observation time since Agent Orange exposure in Vietnam. In general, it takes more than a decade for cancer to manifest itself if it is induced by a chemical carcinogen. Over 80% of STS cases in the study were observed less than 10 years after the last troops were exposed to Agent Orange in Vietnam. Another possibility is that although Agent Orange or dioxin can induce STS, Vietnam veterans as a

group, were exposed to such small amounts that the conventional epidemiologic study cannot detect the excess risk resulting from Agent Orange exposure in Vietnam. Or, of course, there is the possibility that Agent Orange does not induce STS in humans after all.

In conclusion, a study of STS cases and a comparison patients group in VA hospitals did not reveal a statistically significant positive association between STS and previous military service in Vietnam.

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References

1. Cook, R. R. (1981). Dioxin, chloracne, and soft tissue sarcoma (letter). Lancet 1:618-619.
2. Eriksson, M., Hardell, L., Berg, N. O., Moller, T., Axelson, O. (1981). Soft tissue sarcomas and exposure to chemical substances: A case-reference study. Br. J. Ind. Med. 38:27-33.
3. Fingerhut, M. A., Halperin, W. E., Honchar, P. A., Smith, A. b., Groth, D. H., Russell, W. O. (1984). Review of exposure and pathology data for seven cases reported as soft tissue sarcoma among persons occupationally exposed to dioxin-contaminated herbicides. In Lowrance WW (ed): "Public Health Risks of the Dioxin." The Rockefeller University, pp 187-216.
4. Greenwald, P., Kovasznay, B., Collins, D. N., Therriault, G. (1984). Sarcomas of soft tissue after Vietnam service. JNCI 73:1107-1109.
5. Hardell, L., Sandstrom, A. (1979). Case-control study: Soft tissue sarcoma and exposure to phenoxyacetic acids or chlorophenols. Br. J. Cancer 39:711-717.
6. Honchar, P. A., Halperin, W. E. (1981). 2,4,5-T, trichlorophenol, and soft tissue sarcoma. Lancet 1:268-269.
7. Lawrence, C., Reilly, A. A., Quickenton, P., Greenwald, P., Page, W., Kuntz, A. (1985). Mortality patterns of New York State Vietnam veterans. Am. J. Public Health (in print).
8. Moses, M., Selikoff, I. J. (1981). Soft tissue sarcomas, phenoxy herbicides and chlorinated phenols. Lancet 1:1370.
9. Riihimaki, V., Sisko, A., Hernberg, S. (1982). Mortality of 2,4-dichlorophenoxyacetic acid and 2,4,5-trichloroacetic acid herbicide applicators in Finland. Scand. J. Work Environ. Health 8:37-42.
10. Smith, A. H., Fisher, D. O., Pearce, N., Teague, C. A. (1982). Do agriculture chemicals cause soft tissue sarcoma? Initial findings of a case-control study in New Zealand. Community Health Stud. 6:114-119.
11. Smith, A. H., Pearce, N. E., Fisher, D. O., Giles, H. J., Teague, C. A., Howard, J. K. (1984). Soft tissue sarcoma and exposure to phenoxy herbicides and chlorophenols in New Zealand. JNCI 73:1111-1117.
12. The Commonwealth Institute of Health, University of Sydney (1984). A retrospective cohort study of mortality among Australian national servicemen of the Vietnam conflict era. Australian Government Printing Service, Canberra.
13. USAF School of Aerospace Medicine, An epidemiologic investigation of health effects in Air Force personnel following exposure to herbicide. Baseline mortality study results. Epidemiology Division, USAF School of Aerospace Medicine, Brooks AFB, Texas. June 1983.

Table 1

Soft Tissue Sarcoma Type By Military Service Status

Type	Histology	Non-Vietnam Veteran	Vietnam Veteran	Total (%)
Tumors of muscle tissue	Rhabdomyosarcomas	18	8	26
	Leiomyosarcomas	<u>8</u>	<u>12</u>	<u>20</u>
		26	20	46 (19.7)
Tumors of fibrous tissue	Fibrosarcoma	26	13	39 (16.7)
Tumors of synovial tissue	Synovial sarcoma	21	9	30 (12.8)
Tumors of adipose tissue	Liposarcoma	19	9	28 (12.0)
Tumors of vascular origin	Angiosarcoma	3	1	4
	Malignant hemangio- pericytomas	<u>10</u>	<u>2</u>	<u>12</u>
		13	3	16 (6.8)
Others		43	32	75 (32.0)
Total (%)		148 (63.2)	86 (36.8)	234 (100)

Table 2
 Distribution by Age and Hospital Discharge Year for STS
 Case and Comparison Group

Category	STS Cases	Percentage Comparison Group
Age group, years		
20 - 29	9	6
30 - 34	18	29
35 - 39	42	37
40 - 44	11	11
45 - 49	4	4
50 - 59	10	8
60+	6	5
Hospitalization, year		
Before 1970	6	7
1971 - 75	35	36
1976 - 80	42	41
1981 - 83	17	16

Table 3
 Distribution of STS Cases and a Comparison Group of
 Patients by Vietnam Service Status

Vietnam service	STS Cases (%)	Comparison Group (%)	Total
Yes	86 (37)	5,544 (41)	5,630
No	148 (63)	7,952 (59)	8,100
Total	234 (100)	13,496 (100)	13,730

Odds Ratio: 0.83 (95% confidence interval 0.63-1.09)

χ^2 : 1.78 (P>0.1)

Table 4
 Distribution of STS Cases and a Comparison Group
 of Patients by Branch of Service in Vietnam

Branch	STS Cases (%)	Comparison Group (%)
Army	45 (52)	3,528 (64)
Air Force	6 (7)	367 (7)
Marines	14 (16)	921 (16)
Navy	21 (24)	721 (13)
Coast Guard	—	7 (*)
Total	86 (100)	5,544 (100)

*Less than 1%