Thyroid Disease Prevalence in Carabineers Deployed in a War Theater

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ABSTRACT The problem of morbidity in deployed military personnel represents a much-debated topic. Because there have been two cases of thyroid cancer in the Tuscania regiment, the aim of the present study was to investigate the prevalence of all types of thyroid disease in a cohort of carabineers. A total of 673 carabineers, including 501 deployed carabineers (DCs) (29–48 years of age) and 172 nondeployed carabineers (NDCs) (29–51 years of age), of the Tuscania regiment were involved in the study. Thyroid volume, percentages of single nodules and multinodular goiter, percentage of autoimmune thyroid disease, and percentages and histological types of thyroid cancer were all measured. No statistical difference between DCs and NDCs was found for any of the data. Furthermore, when we divided DCs into subgroups according to time spent on deployment and time elapsed since the first deployment, we found no differences. However, a high prevalence of thyroid cancer was found in our cohort (2.0% in DCs and 2.5% in NDCs; not significant), and the prevalence of thyroid cancer in nodules in the cohort of carabineers was higher (10.0%) than the prevalence of thyroid cancer in nodules in the civilian population (5.6%, p < 0.001). No differences regarding the prevalence of thyroid diseases were observed when we compared DCs and NDCs, which suggests that no significant difference in exposure to toxic or carcinogenic substances that could have affected the thyroid occurred during deployments. The high prevalence of thyroid cancer in carabineers may merely reflect an increase of this cancer in the general population, or it may suggest the presence of some carcinogenic event in this specific cohort.

INTRODUCTION

Many studies on morbidity and mortality rates for military personnel deployed in a war theater have been reported in the literature. The data, globally considered, are unequivocal regarding the true extent of increased risk for deployed military personnel.1 A U.S. study on Persian Gulf War veterans2 reported an excess of testicular admissions for tumors (mostly benign) during 1991,1 whereas yet another study reported an excess of hospital admissions for tumors (mostly benign) during 1991,1 whereas yet another study reported increases in some morbidity and genotoxicity rates.3–9 The reasons for the increases in morbidity rates for deployed military personnel could be related to exposure to radioactive substances, such as depleted uranium (DU). DU, which is the best known contaminant found in war theaters, has radiological and chemical properties. Harmful effects of DU in the kidney, the hematopoietic system, the lung, and the brain have been described, and other potential noxious effects are also suspected.10–14 Besides DU, other possible hazardous agents might be made up of unknown environmental substances. Moreover, military personnel receive multiple vaccinations, may suffer from deficiency of some nutrients, and may also be exposed to a radical modification of lifestyle.15–18 Notwithstanding all of these considerations, a review by the Royal Society concluded that, except in particular circumstances, any excess risk regarding tumorigenesis for military personnel is likely to be small.1 However, possible excess morbidity among deployed military personnel represents a relevant problem.

This study was suggested by the Provincial Command of the carabineers because there had been a number of cases of self-reported “thyroid disorders,” as well as two new cases of thyroid cancer, in recently deployed personnel within a period of a few months in the Tuscania Regiment. The aim of the study was to investigate the prevalence of all types of thyroid diseases in carabineers, as well as to examine possible differences between deployed carabineers (DCs) and nondeployed carabineers (NDCs). For this reason, we studied thyroid volume, thyroid function, and the prevalence of nodular goiter, thyroid autoimmunity, and thyroid cancer in carabineers who had been deployed on peacekeeping missions and in carabineers who had not been deployed.

METHODS

We studied carabineers of the Tuscania regiment, including 501 DCs (age range, 29–48 years; average age, 33 years) and 172 NDCs (age range, 30–51 years; average age, 36 years). Carabineers of both groups could choose whether or not to participate in the study, and 2.3% of DCs and 2.8% of NDCs declined. The carabineers came from different parts of Italy, with no region being predominant as place of origin. The time of missions abroad ranged from 3 months to 35 months (median, 21 months), and the time elapsed from the end of the
first mission ranged from 8 months to as long as 15 years (median, 51 months). The places of deployment for carabineers were Somalia, Bosnia, Kosovo, East Timor, Afghanistan, and Iraq, and the majority of subjects (460 subjects, 91.8%) were deployed in all places. All subjects who had been deployed were exposed to DU and had different types and chronology of vaccinations. All carabineers received vaccinations against tetanus, diphtheria, poliomyelitis, and typhoid, whereas DCs also received vaccinations against hepatitis A and B, measles, rubella, mumps, and cholera. Moreover, DCs received malaria chemoprophylaxis. Beyond this, other possible exposures to toxic environmental substances could not be established.

All patients underwent thyroid ultrasonography (10-MHz probe, Esaote MyLab 50; Esaote, Genova, Italy), with measurement of the thyroid volume and with evaluation of the echoic pattern (with respect to the surrounding tissue, following the literature) and of nodularity.19 Serum measurements were made for all subjects in thyroid function tests and in thyroid autoimmunity tests, including thyroid-stimulating hormone (TSH), free thyroxine, free triiodothyronine, antithyroid peroxidase antibodies, and antithyroglobulin antibodies. The serum marker of medullary thyroid cancer, calcitonin, was also measured. All biochemical tests were performed with an Immulite 2000 system (Diagnostic Products, Los Angeles, California).

Fine-needle aspiration (FNA) was performed under ultrasonographic guidance for all single nodules and for dominant nodules in multinodular goiters when the maximal size was >1.0 cm. Nodules (single or in multinodular goiters) with a maximal size of <1.0 cm underwent FNA when, following the literature,19,20 there were at least two of the following ultrasonographic features: hypoechogenicity, irregular margins, microcalcifications, or intranodular vascularization. FNA was performed with a 21-gauge needle, and the sample was smeared, fixed, and stained through the Papanicolaou method.

All of the parameters studied, as already stated, were compared between DCs and NDCs Moreover, DCs were further subdivided according to the time elapsed from the end of the first mission (<5 or >5 years) and the duration of the mission (<12 or >12 months).

Data regarding the prevalence of cancer in the carabineers with thyroid nodules were compared with data regarding the prevalence of thyroid cancer in patients with thyroid nodules from the civilian population. The latter patients were outpatients seen at our ambulatory clinic who had undergone FNA during the past year, using the same ultrasonographic criteria; 1,345 subjects underwent FNA, and positive cytological results were found for 76 (5.6%).

Thyroid volume was reported in milliliters, with the mean and SE, and Student’s t test was used for the comparison among the groups. The other data were reported in percentages, and statistical analysis was performed with the χ² test.

**RESULTS**

Thyroid volume was 11.7 ± 0.8 mL in the group of DCs and 12.1 ± 0.9 mL in the group of NDCs (not significant). Results of ultrasonography revealed pathological features as follows: single nodule, 16.6% in DCs and 16.8% in NDCs (not significant); multinodular goiter, 4.81% in DCs and 6.20% in NDCs (not significant); simple cysts, 2.2% in DCs and 3.12% in NDCs (not significant); hypoechoic aspect, 7.8% in DCs and 6.6% in NDCs (not significant) (Fig. 1 summarizes all ultrasonography data).

Abnormal serum test results were as follows: increased TSH level, 1.38% (4.21–9.73 mU/L) in DCs and 1.0% (5.0–8.81 mU/L) in NDCs (not significant).

**FIGURE 1.** Prevalence of nodular goiter and hypoechogenicity in the cohort of carabineers. The p values were nonsignificant for all data.
mU/L) in NDCs (not significant); decreased TSH level, 0.98% (0.12–0.28 mU/L) in DCs and 1.4% (0.10–0.30 mU/L) in NDCs (not significant; normal values for TSH levels, 0.30–4.0 mU/L); anti-thyroid peroxidase antibody and antithyroglobulin antibody positive (>20 IU/mL), 15.91% in DCs and 17.49% in NDCs (not significant; normal values for TSH levels, 0.30–4.0 mU/L); anti-thyroid peroxidase antibody and antithyroglobulin antibody positive (>20 IU/mL), 15.91% in DCs and 17.49% in NDCs (Fig. 2). Free thyroxine and free triiodothyronine levels were normal for all subjects.

FNA results were positive for papillary thyroid cancer for nine subjects in the DC group (1.85%); in this group we also found one case of follicular neoplasia and two cases of microfollicular nodules. In the NDC group, FNA results were positive for four subjects (2.5%), and we found a microfollicular nodule in one case. Subjects with positive FNA results and the subject with FNA results suggesting follicular neoplasia underwent operations, which yielded papillary cancer in all cases; we found the histological prevalence of thyroid cancer to be 2.0% in DCs and 2.5% in NDCs (not significant; power of the test, 0.6). All data regarding the prevalence of thyroid cancer are reported in Figure 3. For subjects with microfollicular nodules, the decision was to carefully monitor the patients without submitting them for surgery.

The histological types (International Union Against Cancer, 6th Edition) of papillary cancer are reported in Figure 3. No statistical difference was found regarding the prevalence of more aggressive cancer or the prevalence of a specific histological type.

The analyses of the prevalence of hypoechogenicity, nodular goiter, and thyroid cancer in the different subgroups (with respect to time elapsed from the end of the first mission and the overall duration of the mission) of DCs did not show any differences, and results are reported in Table I. Regarding the prevalence of cancer in all patients with thyroid nodules who underwent FNA during the previous year, the comparison between the civilian population and the cohort of carabiners showed a higher prevalence in the latter group (10.0% in carabiners vs. 5.6% in the civilian population, p < 0.001).

**DISCUSSION**

Several reports have suggested possible increases in rates of morbidity, of genotoxicity, and of some malignancies in military personnel deployed in a war theater. However, the data in the literature are not unanimous regarding the real incidence of the various types of morbidity and, above all, the rates of cancer morbidity and death in these subjects. Data on thyroid volume showed no difference between DCs and NDCs, suggesting that there was no significant difference in exposure to substances with antithyroid activity or to an important and prolonged iodine deficiency. We have no data regarding urinary iodine levels, but urinary iodine levels reflect only iodine intake in the short term and would have given us only limited information. Furthermore, results concerning nodular goiter showed no differences among the groups studied. Nodular goiter has a complex and still imperfectly known pathogenic development. Genetic and environmental factors contribute to produce goiter, which usually develops (throughout the sequence of hyperplasia) small multiple nodules, which are often cystic, and then nodules of various sizes. When we considered only cystic nodules or small nodules, we found no differences among the various groups, and this corroborates the hypothesis that no difference

**FIGURE 2.** Prevalence of abnormal serum test results in the cohort of carabiners. AbTPO e/o AbTg+, positive results for anti-thyroid peroxidase antibodies and/or antithyroglobulin antibodies. The p values were nonsignificant for all data.
in exposure to important goitrogenic environmental factors took place between the DC and NDC groups.

Data regarding the prevalence of thyroid autoimmunity showed no difference among the groups studied. Modification of lifestyle and especially an increase in stress might be factors that could trigger thyroid autoimmunity, although in these cases no difference was found. Thyroid autoimmune diseases can produce different clinical manifestations of hypothyroidism and hyperthyroidism, with different degrees of severity. When we considered hypothyroidism or hyperthyroidism and their severity, we found no statistical differences among the various groups.

The final data regard thyroid cancer. There was no difference in the prevalence of thyroid cancer between DCs and NDCs; moreover, there was no difference between carabineers deployed on missions abroad that terminated ≥5 years before the study and those recently deployed, just as there was no correlation with the overall duration of the mission. These results could be especially important if we consider the long natural time frame generally needed for the development of cancer. The absence of a difference in rates of cancer between DCs and NDCs, as well as within the subgroups of DCs, strongly corroborates the notion that no difference in exposure to carcinogenic factors occurred, at least for thyroid cancer. We have no data regarding the rates other neoplasias in this cohort.

All thyroid cancers were papillary cancer (classical or follicular variant), which is not surprising, considering that this malignancy is the most frequent. Thyroid papillary cancer is a particular type of cancer in which the histological findings, in many cases, do not show aggressive features, so much so that there has been a proposal to designate as papillary tumors papillary cancers without multifocality and without extracapsular extension or locoregional diffusion. For these reasons, another important feature that had to be considered was the histological type of papillary cancer. Our results showed no difference in the percentages of aggressive cancers between DCs and NDCs (Fig. 3).

Our data appear to suggest that there is no difference concerning thyroid disease between DCs and NDCs, although

![FIGURE 3. Prevalence of thyroid cancer and histological types in the cohort of carabineers (DCs vs. NDCs) and prevalence of thyroid cancer in thyroid nodules in a civilian population. PCCV, papillary cancer classical variant; PCFV, papillary cancer follicular variant. The p values were nonsignificant for all data.](https://academic.oup.com/milmed/article-abstract/173/11/1098/4265800)
there are some considerations to be made. As already stated, DCs might have been exposed to a myriad of toxic substances, and it is impossible to correlate an individual mission with a specific toxic substance with any certainty. Furthermore, theoretically, some groups deployed on particular missions might have been exposed to different risks, which our analysis was unable to take into consideration.

DU is a well-known contaminant found in war theaters and, although we did not perform measurements of urinary DU levels, we can surely suppose that DCs were exposed to some quantity of this substance. Beyond this, DCs experienced an extreme change of lifestyle, with exposure to stressful events, and they were given more vaccinations than NDCs. At least with respect to these factors, our data suggest the absence of any relationship with thyroid disease. Another consideration concerns the long latent period seen in the development of thyroid cancer, and one possibility could be that too few years have passed to perceive any difference. Continued follow-up monitoring will be necessary to clarify this point, although all data to date appear to rule out a role for deployment in a war theater in the development of thyroid disease and cancers.

Our data raise other important considerations about the epidemiological features of thyroid cancer. The prevalence of thyroid cancer was surprisingly high in our cohort, and this finding is probably more surprising if we consider that we studied young male subjects. There are no data concerning the prevalence of thyroid cancer in a cross-sectional study of the general population, and the only reports on the prevalence of thyroid cancer regard patients surgically treated for goiter (therefore, groups with a bias in selection). Data from autopsy studies could prove more comparable. Apart from autopsy reports from Nagasaki and from a single area in Finland where the prevalence of thyroid cancer was extraordinarily elevated, all other reports have shown a prevalence of thyroid cancer that is essentially, but in our opinion only in appearance, comparable to our data. The large majority of neoplasms found in autopsy studies were, according to a histological review, papillary microtumors, whereas in our cohort, as shown in Figure 3, we found mainly true aggressive cancer with locoregional spread.

A comparison with patients who came under our observation within the past year showed a percentage of thyroid cancer in thyroid nodules that was lower than what we observed in the carabineers. These two groups were not perfectly comparable, for two reasons; the first is that the civilian patients who came under our observation were mainly from the province of Livorno and the second is that the ages of the patients, as well as the proportions of female patients, were different between the two groups. At the moment, it is impossible to say whether the increase in papillary cancer in carabineers represents a true increase in this cancer in this particular group or whether our study has merely allowed us to observe the general increase in this cancer in the general Italian population. The possibility that some groups (i.e., professional firefighters and flight personnel in Florida) may see an increase in some cancers, including thyroid cancer, has already been described, and this suggests that there may exist some unknown risk factors for thyroid cancer that may be relevant.

Possible limitations of this study, as already stated, are the difficulty of correlating specific toxic exposures with a particular mission, the long latent period for thyroid cancer, and the statistical power of the test, which was not so high. These reasons may not allow us, at present, to perceive possible relationships between mission deployment and pathological conditions, and continued follow-up monitoring is required. In light of our results, a possible recommendation might be to pay special attention to the development of thyroid cancer in certain cohorts of military personnel.

In conclusion, exposure to DU, at least when such exposure is within the “normal range” for a war theater, does not appear to introduce an increased risk of thyroid morbidity. Furthermore, neither a change of lifestyle nor increased stress appeared to increase thyroid morbidity, and our data suggest that no particular exposure to environmental substances with thyroid toxicity occurred in carabineers deployed on missions abroad. Data regarding the prevalence of papillary cancer in carabineers might suggest the existence of some unknown risk factor for the carabineers or a general increase, attributable to unknown factors, in the population as a whole.

REFERENCES

and surveillance results of Gulf War I veterans exposed to depleted uranium. Int Arch Occup Environ Health 2006; 79: 11–21.