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Does Life along the Sea Carry Greater Risk of Thyroid Cancer?

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A B S T R A C T

Aim of this study was to determine whether there are any differences between coastal and inland Dalmatia in incidence rates and clinical characteristics of thyroid cancer. Data on 651 persons who suffer from and have undergone surgery for thyroid cancer have been analysed. All patients lived in Dalmatia between 1997 and 2006. Data were collected via surveys, insight into medical histories and results of histopathological analysis. In Dalmatia, in the overall sample, there are no statistically significant differences in incidence between coastal and inland areas (χ^2=3.03; df=1; p=0.082). Somewhat higher overall incidence has been recorded in the inland (8.5%000) than in the coastal Dalmatia (7.3%000). In the overall sample, in Dalmatia, women make up 81.4% of patients and papillary cancer accounts for 80.0% of all thyroid cancers. The ratio of papillary to folicullar cancer is 7.8:1 in coastal and 4.2:1 in inland Dalmatia. Papillary and medullary types are more common in the coastal area and follicular and anaplastic cancer types in the inland area and the differences are statistically significant (p>0.033). Epidemiological characteristics of thyroid cancer in coastal Dalmatia are in accordance with the characteristics of this cancer as described in iodine-sufficient areas: the most common type is papillary cancer, and the ratio of papillary to follicular is 7.8:1. Sex-wise, the coastal area records a higher ratio of male patients (1:3.8) than the inland area (1:7.1). There are no statistically significant differences in thyroid cancer incidence rates between coastal and inland Dalmatia. Epidemiological characteristics of thyroid cancer in inland Dalmatia are in some ways more similar to those of continental Croatia. This result could be the consequence of previous iodine insufficiency in inland Dalmatia.

Key words: *thyroid cancer, epidemiology, Croatia*

Introduction

It is no news that island countries – Hawaii, Japan, Iceland, the Philippines, and some regions of Sicily and Cyprus – have some of the highest thyroid cancer incidence rates: around 20 *per* 100,000 inhabitants[1–3]. The predominant type in these countries is the differentiated – papillary thyroid cancer.

The cause of thyroid cancer is in most cases unknown – as with other forms of cancer. The only proven factor causing differentiated thyroid cancers is ionized radiation of any source[4].

Risk factors are genetic predisposition and female sex. In women in the USA, thyroid cancer accounts for about 3% of all cancers and is the 8th most common cancer[3,5,6]. A rising tendency has been recorded in almost all countries, but increase rates vary: Denmark, a country of some 5 million inhabitants, records around 120 thyroid cancer cases a year[7], while in Croatia, a country of little under 4.5 million, in recent years around 400 new thyroid cancer cases are recorded every year[8]. Age-standardized rate (ASR) of thyroid cancer incidence (Mb *per* 100,000 inhabitants) in Croatia increased 8.6 times in women (1.1:9.4) and 3.6 times in men (0.8:2.9) in the period between 1968 and 2004[9]. Since the year 2000, thyroid cancer ranks among the ten most common cancers in women[8,10], putting Croatia on the list of countries with high incidence and low mortality of thyroid cancer, along with Italy, France, Finland, the USA and Australia[3,5]. Incidence rates differ significantly among different parts of

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Croatia: Slavonia records three times lower thyroid cancer incidence than Dalmatia[11,12].

Thyroid cancer incidence rates are three to four times higher in women than in men, especially in the period between puberty and menopause, indicating a possible link between thyroid cancer aetiology and female sex hormones and reproductive function[3–6,13,14]. The same pattern is often identified in different geographic locations and ethnicities. Incidence in women reaches its peak during the reproduction period, while in men it shows a continuous increase with age[1,2,11,13,14].

Residence in endemic goiter areas, poor diet and pre-existing benign thyroid diseases are factors that, according to Italian authors, could account for up to 60% of thyroid cancer cases[15].

The structure of histopathological types of thyroid cancer in patients partly depends on the amount of iodine in a diet: the papillary type is predominant in iodine-sufficient areas, while the follicular is more common in iodine deficient areas.

In the 1998–2006 period, average thyroid cancer incidence was 9.32‰00 in Dalmatia and 6.02 *per* 100,000 inhabitants in Slavonia (χ^2=56.24, df=1; p<0.001)[16].

Since the majority of island countries have higher incidence rates, the aim of this research was to determine whether there are differences in thyroid cancer incidence rates between coastal and inland Dalmatia, where the coastal belt has the geographical characteristics of an island country.

Patients and Methods

The retrospective epidemiological clinical survey focused on patients from Dalmatia who had been treated for thyroid cancer between 1st January 1997 and 31st December 2006. A detailed analysis was conducted on 701 patients (531 women and 170 men) whose data were obtained from the archives of the Split University Hospital Centre, General Hospital Zadar and General Hospital Dubrovnik. Another set of data was obtained from County Institutes of Public Health in Zadar, Šibenik, Split and Dubrovnik, and from the Croatian National Cancer Registry (CNCR) of the Croatian National Institute of Public Health.

The research included only newly diagnosed cancers, while recurrences and metastases of other malignancies to the thyroid gland have been excluded. This survey also excluded patients who have been diagnosed with thyroid cancer but had no permanent residence in Dalmatia, who lived in the observed area only temporarily and originated from other regions. Following such a selection, a group of 651 persons suffering from thyroid cancer was formed, of which 530 were women (81.41%) and 121 men (18.59%).

Geographically and politically, the term »Dalmatia« covers the area of four present-day counties: Zadar, Šibenik-Knin, Split-Dalmatia and Dubrovnik-Neretva counties. For the purpose of this research, Dalmatia has been divided into two areas based on regional lifestyle and direct influence of the sea: coastal and inland Dalmatia. The coastal area encompasses the islands and a narrow coastal strip directly affected by the sea. Inland Dalmatia covers all municipalities in Dalmatia that have no contact or border with the sea. Total surface area of Dalmatia stretches around 11,960 km^2[2,17]. According to this division, and based on the 2001 census, 659,755 inhabitants of Dalmatia lived in the coastal area (76.6%) and 201,305 (23.4%) in inland Dalmatia[18].

In order to facilitate comparison and determine the statistical significance of possible differences, data were age-standardized to the World Standard Population (WSP) and the European Standard Population (ESP). Age standardized rates were used due to the fact that crude rates can be due to different age structures in a population[19].

In order to calculate age-standardized incidence rates, age structure based on sex and on 2001 census population estimates were used[18]. Crude and standardized incidence rates were calculated with a 95% confidence interval (CI). Also calculated were patient age and sex structure and the structure of histopathological types in the 651 patients treated in Dalmatian hospitals between 1997 and 2006. Trends were used to show movement dynamics, and the threshold for statistical significant was p≤0.05.

Results

Thyroid cancer incidence in Dalmatia

According to the data of the CNCR of the Croatian National Institute of Public Health, data have been recorded since 1998. During that time, 723 patients have been recorded as suffering from thyroid cancer, with an average incidence of 9.32 *per* 100,000 inhabitants.

Research data (N=651) show that average incidence for the period 1997–2006 was 7.27 *per* 100,000 inhabitants in the coastal area, which was a little under the average in inland Dalmatia where it was 8.49 *per* 100,000 inhabitants (Table 1).

Although incidence rates might at first seem slightly higher in inland Dalmatia, there are no statistically significant differences between the two observed areas (χ^2= 3.03; df1; p=0.082). Statistically significant differences were recorded only in 1997 (χ^2=8.91; df1; p=0.003) and 2006 (χ^2=4.5; df1; p=0.034) due to higher rates in inland Dalmatia.

Morbidity for different types of thyroid cancer according to sex in Dalmatia, for the period 1997–2006

Crude morbidity rates (Mb *per* 100,000 inhabitants) have been analysed for each sex according to four main histopathological types of thyroid cancer. Papillary thyroid cancer accounts for the highest rates (Table 2).

In the overall number of patiens, thyroid cancer is four times more common in women than in men and

TABLE 1
THYROID CANCER INCIDENCE – A COMPARISON OF COASTAL AND INLAND DALMATIA

Year	Coastal area			Inland Dalmatia					
	No. of Patients	No. of Inhabitants	Incidence/ 100,000	No. of Patients	No. of Inhabitants	Incidence/ 100,000	χ^2	df	p
1997	26	659755	3.94	19	201305	9.44	8.91	1	0.003
1998	33	659755	5.00	10	201305	4.97	0	1	0.985
1999	46	659755	6.97	17	201305	8.44	0.46	1	0.500
2000	60	659755	9.09	17	201305	8.44	0.07	1	0.787
2001	62	659755	9.40	12	201305	5.96	2.12	1	0.146
2002	41	659755	6.21	15	201305	7.45	0.36	1	0.547
2003	47	659755	7.12	14	201305	6.95	0	1	0.937
2004	49	659755	7.43	15	201305	7.45	0	1	0.991
2005	57	659755	8.64	23	201305	11.43	1.29	1	0.256
2006	59	659755	8.94	29	201305	14.41	4.5	1	0.034
Total	480	659755	72.75	171	201305	84.95	3.03	1	0.082

df = degrees of freedom

women make 81.41% (530/651) of patients. Of all papillary cancer cases, women account for 82.53% (430/521). Papillary thyroid cancer is the most common type in men as well, where it accounts for 75.2% of all patients (91/121). Differences are not statistically significant (p=0.318).

There are no statistically significant differences between men and women in the frequency of other types of thyroid cancer.

Cases of the anaplastic type of thyroid cancer are rare – none were recorded in patients in Dalmatia in 1998, 1999, 2004 and 2005.

Increased incidence rates and morbidity trends are due exclusively to papillary cancer types. The other three thyroid cancer types show a stagnating trend (Figure 1).

Age of thyroid cancer patients in Dalmatia

In overall 651 thyroid cancer patients, there were no children under the age of 14, there were three (0.46%) adoloescents (between 15 and 19 years old) and the rest (N=648) were categorized as adults (≥20 years old). All three adolescents lived in the coastal area.

Age structure of patients according to permanent residence (Coastal/Inland Dalmatia) is shown Figure 2.

TABLE 2
THYROID CANCER RATES IN DALMATIA, PER HISTOLOGICAL TYPE AND SEX, PERIOD 1997 – 2006

Thyroid cancer	Year	No. of newly diagnosed patients – incidence (per 100,000 inhabitants)									
		1997	1998	1999	2000	2001	2002	2003	2004	2005	2006
Total	Total	5.22	4.99	7.31	8.94	8.59	6.5	7.8	7.43	9.29	10.21
	Male	1.91	1.43	4.29	1.67	2.86	2.38	2.14	3.33	4.05	4.76
	Female	8.38	8.38	10.19	15.85	14.04	10.42	11.77	11.32	14.26	15.4
Papillary	Total	4.06	3.37	6.04	6.5	7.43	5.11	6.15	5.8	7.43	8.59
	Male	1.19	0.71	3.1	1.19	2.62	1.67	1.67	2.38	2.86	4.29
	Female	6.79	5.89	8.83	11.55	12	8.38	10.42	9.06	11.77	12.68
Follicular	Total	0.35	1.28	1.04	1.63	0.46	0.81	0.7	1.04	1.28	0.81
	Male	0.24	0.71	0.71	0.48	0	0.24	0.24	0.48	0.48	1.13
	Female	0.45	1.81	1.36	2.72	0.91	1.36	1.13	1.58	2.04	0.81
Medullary	Total	0.7	0.35	0.23	0.7	0.58	0.35	0.12	0.58	0.58	0.7
	Male	0.48	0	0.48	0	0.24	0.24	0	0.48	0.71	0
	Female	0.91	0.68	0	1.36	0.91	0.45	0.12	0.68	0.45	1.36
Anaplastic	Total	0.12	0	0	0.12	0.12	0.23	0.12	0	0	0.12
	Male	0	0	0	0	0	0.24	0.24	0	0	0
	Female	0.23	0	0	0.23	0.23	0.23	0	0	0	0.23

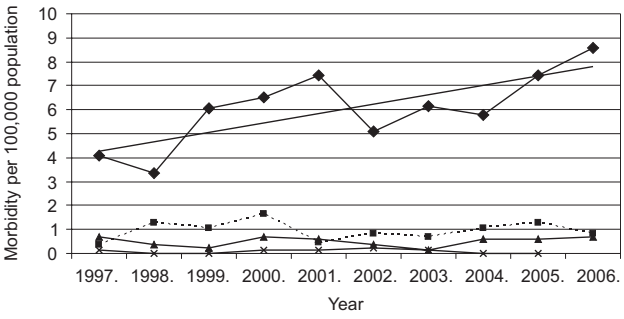

Fig. 1. Thyroid cancer incidence rates according to histological types, Dalmatia, 1997–2006.

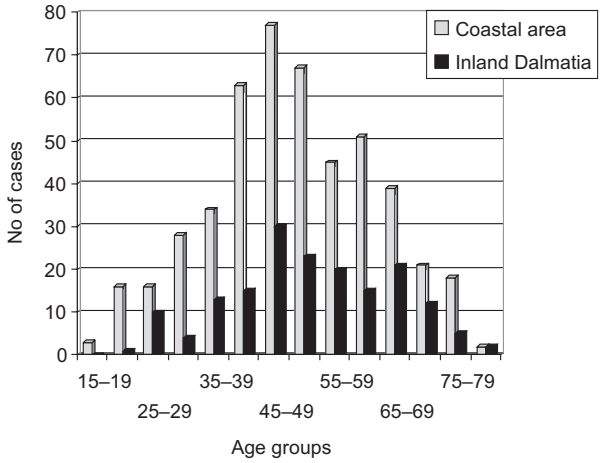

Fig. 2. Age structure of thyroid cancer patients in Dalmatia – a comparison of coastal and inland Dalmatia, 1997–2006 period.

In the coastal area, average patient age at the time of diagnosis was 50.28, with the youngest patient being 16 and the oldest 50 years old – giving a median of 50.

In inland Dalmatia, average patient age was higher – 52.71, with the youngest patient a 22-year-old and the oldest an 84-year-old – giving a median of 51.

In the observed sample (N=651), average age of thyroid cancer patients in inland Dalmatia was 2.5 years higher than the coastal average, which is a statistically significant difference (p=0.044).

Patient age at the time of diagnosis according to histological type of cancer

In the overall sample (N=651), 50.33 was the average age for papillary cancer patients, 50.67 for follicular, 55.62 for medullary, and 69.71 for anaplastic cancer patients. The differences are statistically significant (χ^2= 14.630; df=3; p=0.002) and patients suffering from the anaplastic type comprise the oldest group of all four (Table 3).

Sex structure of thyroid cancer patients in Dalmatia

When looking at the occurrence and sex structure of thyroid cancer in Dalmatia and comparing coastal with inland Dalmatia, one can see no statistically significant differences. What can be observed, however, is a slightly higher ratio of women in papillary cancer cases in coastal than in inland Dalmatia and a slightly lower ratio of the follicular type, but differences are again not statistically significant (Table 4).

Histopathological types of thyroid cancer in the two observed areas of Dalmatia (coastal and inland) are equally present in both men and women.

Thyroid cancer in coastal and inland Dalmatia – a comparison of histological types

Papillary cancer is the most common type in both observed areas, accounting for 80.03% (521/651) of the overall sample (N=651). The coastal area has a somewhat higher ratio of this type of cancer. Second in line but far rarer is the follicular type, which is also somewhat more frequent in inland Dalmatia. In the overall structure, papillary and follicular (differenciated) types of thyroid cancer account for 92.1% of cases in coastal and 93.56% in inland Dalmatia.

Papillary and medullary thyroid cancers are more common types in coastal Dalmatia, whilst follicular and anaplastic types occur somewhat more frequently in inland Dalmatia, and these differences are statistically significant (p>0.033) (Table 5).

TABLE 3
PATIENT AGE AT THE TIME OF DIAGNOSIS ACCORDING TO HISTOLOGICAL THYROID CANCER TYPE IN DALMATIA, 1997–2006

Histological type of tumor	Patients	Average age at time of diagnosis	χ^2-test	df	p
Papillary	521	50.33			
Follicular	81	50.67			
Medullary	42	55.62	14.630	3	0.002
Anaplastic	7	69.71			
Total	651				

(N=651)
df = degrees of freedom

TABLE 4
SEX STRUCTURE OF THYROID CANCER PATIENTS IN DALMATIA, PER OBSERVED AREA, IN THE PERIOD 1997–2006

Histological type of cancer	Total patients	Of which				p
		Coastal area		Inland Dalmatia		
		M N %	F N %	M N %	F N %	
Papillary	521	75 (75)	317 (83.4)	16 (76.2)	113 (75.3)	Coastal Dalm. p=0.170
Follicular	81	13 (13)	37 (9.7)	4 (19)	27 (18)	
Medullary	42	11 (11)	23 (6.1)	0 (0)	8 (5.3)	Inland Dalm. p=0.452
Analplastic	7	1 (1)	3 (0.8)	1 (4.8)	2 (1.3)	
Total	651	100 (100)	380 (100)	21	150	

TABLE 5
PATIENT STRUCTURE ACCORDING TO HISTOPATHOLOGICAL TYPE OF THYROID CANCER, PER OBSERVED AREA OF DALMATIA, 1997–2006

Histological type of cancer	Area				p
	Coastal Dalmatia		Inland Dalmatia		
	N	%	N	%	
Papillary	392	81.67	129	75.44	
Folicular	50	10.42	31	18.13	
Medullary	34	7.08	8	4.68	0.033
Anaplastic	4	0.83	3	1.75	
Overall	480	100.0	171	100.0	

Occurrence of metastases

Metastases were found in 94 of the 651 surgically treated patients (14.43%) (Table 6). Most common are metastases to neck lymph nodes (88/94; 93.62%). A somewhat higher percentage of metastases has been recorded in coastal (15.63%) than in inland Dalmatia (11.11%), but differences are not statistically significant (p=0.212).

Distribution of metastases according to sex

In our sample, there were no statistically significant differences in the distribution of metastases according to sex between the two regions – they were equally distributed in coastal and in inland Dalmatia (Fisher's exact test p>0.950) – Table 7.

A comparison of some epidemiological and clinical indicators of thyroid cancer between coastal and inland Dalmatia

The two observed areas differ statistically significantly in the structure of patients according to sex, the structure of histopathological types of cancer and in average patient age: more women are diagnosed with thyroid cancer in inland Dalmatia (p=0.001), follicular cancer occurs more often in inland Dalmatia (p=0.021) and average patient age is higher in inland Dalmatia (p=0.044). There are no statistically significant differences in average incidence rates (p=0.082) and occurrence of metastases (p=0.212) (Table 8).

Discussion

For the purpose of analysing the possible impact of life on the seaside as a risk factor for cancer of the thy-

TABLE 7
METASTASES ACCORDING TO SEX AND PER OBSERVED AREA OF DALMATIA, BETWEEN 1997–2006

Area	Sex		Overall	Fisher's exact test p
	M N %	F N %		
Coastal area	27 38.0	44 62.00	71	
Inland Dalmatia	6 35.3	11 64.7	17	p>0.950
Overall	33 37.5	55 62.5	88	

TABLE 6
OCCURRENCE AND LOCATION OF METASTASES IN THYROID CANCER PATIENTS IN DALMATIA, DURING THE 1997–2006 PERIOD

Area	Total patients	Of which with metastases N %	Location of metastasis		Fisher's exact test p
			Neck lymph node N %	Lungs N %	
Coastal area	480	75 15.63	71 14.79	4 0.83	
Inland Dalmatia	171	19 11.11	17 9.94	2 1.17	0.212
Overall/average	651	94 14.43	88 13.51	6 0.92	

TABLE 8
COMPARISON OF SOME THYROID CANCER INDICATORS IN THE TWO OBSERVED AREAS OF DALMATIA DURING THE PERIOD 1997–2006

	Dalmatia		p
	Coastal area	Inland Dalmatia	
Inhabitants in 2001	659,755	201,305	–
Observed period	1997–2006	1997–2006	–
Surgically treated patients	480	171	–
Average incidence per 100,000 inhabitants (1997–2006)	7.27	8.49	0.082
Average age	50.28 years	52.71 years	0.044
Patient sex structure – ratio women:men	3.8:1 (380/100)	7.1:1 (150/21)	0.001
Regional lymph node metastases	14.8%	9.9%	0.212
Remote lymph node metastases	0.8%	1.2%	
Ratio of papillar/ follicular cancer in overall number of thyroid cancer patients	7.8:1	4.2:1	0.021
Papillary ca (M+F)	81.67 %	75.44%	0.033
Follicular ca (M+F)	10.42 %	18.13%	
Medulary ca (M+F)	7.08%	4.68%	
Anaplastic ca (M+F)	0.83%	1.75%	

roid gland, Dalmatia has been divided into two regions: the coastal strip, bigger in size and in the number of inhabitants, and inland Dalmatia, or the continental part separated from the coast by hills and mountains. Inland Dalmatia is characterized by a somewhat different diet (though increasingly less different) and is not directly exposed to and influenced by the sea and possible radiation from the sea. It is worth noting that only two islands (Jabuka and Brusnik) on the Croatian side of the Adriatic Sea are of volcanic origin, both uninhabited[19]. One of the reasons why island countries have high thyroid cancer incidence rates is volcanic lava radiation and the diet – higher iodine intake with seafood. The highest quantities of iodine are taken in with fish and milk[20,21].

Since differences between the two observed regions are negligible, as seen above, no differences were expected in incidence rates – which was also confirmed by the research. At first sight, thyroid cancer incidence rates in inland Dalmatia are somewhat higher, but no statistically significant differences between the two observed areas of Dalmatia have been established ($\chi^2=3.03$; df=1; p=0.082). According to CNCR, average morbidity rate for thyroid cancer in Dalmatia is 9.32 *per* 100,000 inhabitants. Research has shown that incidence rates are around 8.5 *per* 100,000 inhabitants in inland Dalmatia and 7.3 *per* 100,000 inhabitants in coastal Dalmatia. This difference between the »official« (CNCR) and research rate is due to the fact that not all patients were included in the study and some (registered) patients most likely underwent surgery in other hospitals in Croatia (Zagreb, Rijeka).

However, some differences in epidemiological and clinical characteristics of thyroid cancer between these two narrow and highly interconnected regions do exist. Thus, coastal area sees a higher percentage of male patients (ratio men : women is 1:3.8) than inland Dalmatia (1:7.1). The real cause of this difference is unknown. One assumption is that men in the coast seek medical assistance more often, but there could be other reasons as well.

Inland Dalmatia sees more follicular cancer than the coastal area. Papillary to follicular cancer ratio is 7.8:1 in coastal and 4.2:1 in inland Dalmatia. A statistically significant difference (p=0.033) has also been observed in the structure of histopathological types of cancer: papillary cancer is more common in coastal (81.7%) than in inland (75.4%) Dalmatia, but the follicular type is more common in inland (18.1% of all thyroid cancers) than in coastal (10.4%) Dalmatia, which could have been caused by previous iodine insufficiency in inland Dalmatia. Average patient age in inland Dalmatia is 52.7, meaning that there was no systematic salt iodization during their childhood. Life expectancy in male patients living in inland Dalmatia is also lower, the reason for which could be men's reluctance to use healthcare, as shown by Hall et al.[22].

From the histopathological point of view, research has shown that papillary thyroid cancer occurs three to four times more often in women than in men[23–25].

This research confirms that fact: of the total 651 patients, 521 (80.0%) suffered from the papillary type, of which 430 women. Women suffer both from thyroid cancer and from papillary cancer more frequently than men: loking at patient structure according to histopathological types, papillary cancer accounts for 81.1% of all female patients (430 of overall 530 women suffering from all thyroid cancer types).

Most authors have found that the papillary type occurs three or four times more frequently than other thy-

roid cancers. Papillary cancer has proven to be highly predominant in this research as well, with a ratio of 4.7:1 (430/91). In a study conducted in a different part of Croatia, T. Jukić established a 4.5:1 ratio[26].

Thyroid cancer is four times rarer in men than in women. Papillary cancer is the most common type of thyroid cancer in men as well and accounts for 75.2% of all male thyroid cancer patients. Our research has confirmed other authors's findings: thyroid cancer does not occur in men as often as in women, but when it does occur it is more likely to be followed by metastases than is the case with women and the difference is statistically significant ($p<0.001$).

Numerous authors have tried to explain why thyroid cancer occurs more frequently in women than in men. Some claim it is due to thyroid gland's sensitivity to stress which, assuming that women are more sensitive than men, could be the reason behind different ratios[3,5,21,23].

Hall et al. claim that this could also be due to the tendency in women to seek more healthcare by the age of 60 and to undergo diagnostic methods more often than men[22]. Women get thyroid gland checks for certain clinical symptoms indicating thyroid gland disorders: tahychardia, bradychardia, nervosness, which symptoms are often attributed to the thyroid gland due to the current frequency of thyroid diseases[22].

This analysis of epidemiological characteristics of thyroid gland cancer in two very close areas is the result of a search for other indicators, related to the direct impact of sea on the population living in coastal areas. Thus, the population of inland Dalmatia is separated from the sea by a mountain or hill chain. This division and search for differences between the two areas is due to the fact that some authors believe higher thyroid cancer incidence could be caused by radiation and the possible effect of volcanic lava on volcanic islands. According to the available data, of the 982 islands, islets and reefs in Dalmatia, only two are of volcanic origin: Jabuka and Brusnik, and both are uninhabited. Geological characteristics of the rest of the islands are similar to those of coastal and inland areas – and are not of volcanic origin[17].

Not so long ago, it was believed that high thyroid cancer incidence in island countries (Iceland, Hawaii, the Philippines, etc.) was due to increased iodine intake. Today, however, the cause is believed to lie in the natural radiation of volcanic rocks that form the geological structure of the islands[27]. A research by Pelegritti et al. conducted on Sicily and the Province of Catania including the Etna volcano area showed that a higher incidence of papillary thyroid cancer in Catania than in the population comprised of the remaining eight regions of Sicily[28]. The research was flawed in that the conclusion on increased incidence due to volcanic lava influence was drawn without evidence and without volcanic contamination or radiation measurements.

As a rule, in iodine-sufficient areas papillary cancer is the most common type of thyroid cancer. Research has shown that the introduction of a iodine prophylaxis has in many countries lead to a reduction in anaplastic and follicular thyroid cancers and an increase in papillary cancers, resulting in a higher ratio of papillary/follicular cancer[3,5,21,23,25].

In our research, in a iodine-sufficient area, papillary cancer is the most common type and occurs four times more often in women than in men, which is in line with the findings of other authors[3,5,29].

Follicular cancer is less common and, according to data from literature, acccounts for 10–15% of all thyroid cancers. In our sample, this type was on average found in 12.4% of patients. The percentage is somewhat higher in inland Dalmatia with 18.1%, but ranges around 10.4% in coastal Dalmatia. According to other authors' studies, it is more common in women and tends to occur in the fifties. In our sample, this type was slightly more common in men (14.0%) than in women (12.1%) but the difference is not statistically significant. Average patient age for follicular cancer is 50.67.

As far as metastases are concerned, in our sample their occurrence was proven in 11.8% (71/602) of patients with papillary and follicular cancer.

In our sample, medullary cancer accounts for 6.5% (42/645) of cases. Average patient age is 55.6. It occurs somewhat more often in men (9.1%; 11/121) than in women (5.8%; 31/530). Occurrence of metastases in patients with medullary cancer is somewhat higher in our sample (31%; 13/42) than in papillary and follicular cancer cases (11.8%).

Anaplastic cancer is fortunately rare and is found in only 1.1% (7/651) of our patients. No statistically significant differences in occurrence have been established between coastal and inland Dalmatia. Average patient age is 69.7. In overall patient structure, it accounts for 1.7% (2/121) male and 0.9% (5/530) female patients. From the point of frequency and average patient age, our results are in line with the results in literature. Anaplastic cancer is the most aggressive and fastest progressing type of thyroid cancer. It usually occurs in patients from iodine-insufficient areas and is associated with persisting goiter[30,31].

The ratio of papillary/follicular is 7.8:1 in coastal and 4.2:1 in inland Dalmatia. According to these values, the ratio for inland Dalmatia is closer to Slavonian values (3:1)[11] than the Dalmatian average (6.4:1), which could be the consequence of previous iodine defficiency in inland Dalmatia. The characteristics of thyroid cancer in inland Dalmatia are somewhere between its characteristics in Slavonia and in coastal Dalmatia.

Conclusion

1. In Dalmatia, in the overall sample, there are no statistically significant incidence rates differences between coastal and inland Dalmatia ($\chi^2=3.03$; df=1; $p=0.082$). Somewhat higher overall incidence has been recorded in inland (8.5%000) than in coastal (7.3 %000) Dalmatia. Women are predominant in patient sex structure,

with four times higher rates than men. In Dalmatia, in the overall sample, women account for 81.4% of all patients, and papillary cancer accounts for 80.0% of all thyroid cancers. There are no statistically significant differences in histological types between men and women in Dalmatia ($p=0.318$). Papillary cancer is the most common type in both sexes and is followed by follicular, medullary and anaplastic types.

2. The ratio of papillary to follicular cancer is 7.8:1 in coastal and 4.2:1 in inland Dalmatia.
3. Coastal area sees more papillary and medullary thyroid cancers than inland Dalmatia, but inland Dalmatia sees more follicular and anaplastic types (than the coastal area), and the differences are statistically significant ($p>0.033$).
4. Thyroid cancer is rarer in men than in women, but when it does occur in men it is followed by metastases more often than in women, showing a statistically significant difference ($p>0.033$). The difference between men and women is even more prominent when comparing coastal ($p<0.001$) and inland ($p=0.026$) Dalmatia.
5. Epidemiological characteristics of thyroid cancer in coastal Dalmatia are in accordance with the characteristics of thyroid cancer in iodine-sufficient areas: the most frequently occurring type is papillary cancer, and the ratio of papillary to follicular is 7.8:1. In coastal Dalmatia, patient sex structure shows a higher ratio of men (1:3.8) than is the case with inland Dalmatia (1:7.1).
6. Epidemiological characteristics of thyroid cancer in inland Dalmatia are in some segments more like the characteristics of thyroid cancer in continental Croatia, which could be the consequence of previous iodine insufficieny in inland Dalmatia.

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NOSI LI ŽIVOT UZ MORE VEĆI RIZIK OD KARCINOMA ŠTITNJAČE?

S A Ž E T A K

Cilj ovog istraživanja bio je utvrditi postoje li razlike između obalnog i kontinentalnog područja Dalmacije u stopi incidencije i kliničkim karakteristikama raka štitnjače. Analizirani su podaci o 651 oboljelom i operiranom od raka štitnjače. Svi su stanovnici Dalmacije, a oboljeli i operirani su u razdoblju između 1997. i 2006. Podaci su prikupljeni anketiranjem oboljelih, uvidom u medicinsku dokumentaciju i histopatološku analizu. U Dalmaciji, u ukupnom uzorku, ne postoje statistički značajne razlike u incidenciji između obalnog i kontinentalnog područja (χ^2=3,03; df=1, p=0,082). Nešto veća ukupna incidencija zabilježena je u unutrašnjosti (8,5 na 100.000 stanovnika) nego u obalnom dijelu Dalmacije (7,3 na 100.000 stanovnika). U ukupnom uzorku, u Dalmaciji, žene čine 81,4% bolesnika,i a papilarni karcinom čini 80,0% svih karcinoma štitnjače.Omjer papilarnog i folikularnog karcinoma je 7,8:1 u obalnom području prema 4,2:1 u unutrašnjosti Dalmacije. Papilarni i medularni karcinomi su češći u obalnom području, dok su i folikularni i anaplastični češći u unutrašnjosti, a razlike su statistički značajne (p>0,033). Epidemiološka obilježja raka štitnjače u obalnom dijelu Dalmacije su u skladu s karakteristikama ovog raka u jod-suficijentnim područjima: najčešći tip je papilarni karcinom, a omjer papilarni/ folikularni je 7,8:1. Glede spola, u obalnom području bilježi se veće učešće muških bolesnika (1:3,8) u odnosu na unutrašnjosti (1:7,1). Nema statistički značajne razlike u stopama raka štitnjače između obalnog dijela i unutrašnjosti Dalmacije. Epidemiološka obilježja raka štitnjače u unutrašnjosti Dalmacije su sličnija onima u kontinentalnom dijelu Hrvatske. Ovakav rezultat bi mogao biti posljedica insuficijencije joda u unutrašnjosti Dalmacije u prošlosti.