

Dermatoglyphs and Larynx Cancer

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ABSTRACT

Cancer of the larynx is the seventh most common malignant disease among middle-aged men in Croatia. Morbidity ratio between men and women is 17:1. Etiology of disease is directly connected with the tobacco use while genetic influences have not yet been studied enough. Dermo-palmar dermatoglyphs analysis has already been used in studying the genetic etiology of certain malignant diseases (lung, breast, cervical, colorectal, melanoma and gastric cancer). We have analyzed correlation of quantitative and qualitative traits between two groups (group of 40 men with larynx cancer versus control group of 100 phenotypically healthy men). Quantitative statistical analysis (descriptive statistics, multivariate and univariate analysis) has not shown statistically significant difference except for the latent structure using factor analysis. Qualitative analysis has shown statistically significant difference among two investigated groups thus suggesting the faster changes of the qualitative features under the influence of the ecological factors.

Key words: dermatoglyphs, larynx cancer, genetic influences

Introduction

The head and neck oncology shows a special interest in the larynx cancer (*carcinoma laryngis*)^{1,2}. The increase in the incidence of this malignant disease has been notified since the last five decades, mainly among the male population. The highest incidence rates have been reported in Sao Paulo, Brazil (17/100000), USA Connecticut (12.6/100000) and Poona, India (12.9/100000). In Europe the highest incidence has been recorded in the Mediterranean region and the lowest in the northern Europe¹⁻³. In Croatia, every year there are about 400 new diagnosed patients. Morbidity ratio between men and women is 17:1⁴. Planocellular type of carcinoma is the most frequent one, while other types like basalioma and adenocarcinoma are very rare. Carcinoma occurs in 65% of all cases located in the glottic region of the larynx and has the best prognosis. In the 30% of cases tumor is located in the supraglottic region, and in 5% of all cases it is located in the subglottic region and has the worst prognosis⁵⁻⁶. Early diagnosis has an important impact on the therapy decision and the final prognosis. Five-year survival rate for the supraglottic carcinoma without neck metastasis is 80–90%, while with the cervical lymph nodes affected it drops down to 30–50%. Glottic carcinoma has 80–90% five-

year survival rate if the vocal cords are not affected. With the vocal cords affected it drops down to 50–60%⁷⁻⁸. Etiology of the disease is directly connected with the tobacco use, while genetic influences have not yet been studied enough⁷⁻⁹. Histological changes of epithelium found in smokers (hyperkeratosis without atypia) increase the risk of the invasive carcinoma of the larynx by 3%, while hyperkeratosis with atypia increase the risk of invasive carcinoma by 30%^{1,6}. Polycyclic hydrocarbons found in the tobacco smoke are proven to be contact carcinogens, especially in patients with a higher activity of aryl hydrocarbon hydroxylase enzyme^{1-3,6,7}. Other possible factors include alcohol, GERD (gastroesophageal reflux disease) and other carcinogens⁶⁻⁹. Genetic predisposition and the role of genetic factors in the etiology of larynx cancer and other solid malignant head and neck tumors are still unclear and thus have been very actively studied¹⁰⁻¹¹. Mutation in p53 gene has been found in 60% of laryngeal malignoma¹²⁻¹⁴. Alterations of p16 gene are most frequently noticed in the carcinomas of the upper aero-digestive tract¹⁵. Mutations in the chromosome 3 (in Europe) and chromosome 8 (in USA) and, as well as alteration of CENP-F gene, bcl-2

TABLE 1
RESULTS OF THE DERMATOGLYPHS ANALYSIS FOR THE DIFFERENT MALIGNANT DISEASES

Breast cancer ^{29,30}	Lower total finger ridge count, lower a-b rc Significant differences between a-b and c-d rc
Cervix cancer ³¹	Higher frequencies of whorls on fingers, lower atd angle Lower number of finger and palmar ridges
Bronchopulmonary cancer ^{32,33}	Differences in palmar variables, high discriminant classification, biological distance differences
Colorectal cancer ²⁸	Lower atd angle
Gastric cancer ³⁴	Differences in palmar variables, lower atd angle
Melanoma ³⁵	Lower finger ridge count on 1 st , 4 th and 5 th finger and c-d rc and atd angle on both hands in males and females

and p27 further suggest the importance of genetic influences in the larynx cancer development^{16–25}.

Dermatoglyphs (epidermis patterns on fingers, palms and soles) start developing between the 5th and the 6th week of the intrauterine development and by the 21st week they are completely formed, and remain unchanged²⁶. They are relevant for the understanding of the human development and for the differentiation in the early stages of the embriogenesis, which makes them important in studies of the human medical pathology^{26,27}. So far, digito-palmar dermatoglyphs have been used in many studies attempting to understand the genetic etiology of different malignant diseases²⁸ (Table 1). The results have shown differences of the dermatoglyphics features between patients and healthy subjects.

In the present study we tested the hypothesis of genetic predisposition of larynx cancer. Embryological development of the larynx starts at about the same time and from the same embryological layers as the development of the skin, from which the dermatoglyphs develop. Changes in embryological period could have influences on development of the cancer but they could also have reflection on the expression of the dermatoglyphic patterns. We tested this hypothesis by comparing the dermatoglyphs of digito-palmar complex of group of larynx cancer patients versus group of healthy individuals.

Materials and Method

In our research we have analyzed digito-palmar dermatoglyphs of 40 male patients with the confirmed di-

TABLE 2
FACTOR ANALYSIS FOR THE VARIABLES IN THE GROUP OF PATIENTS DIAGNOSED WITH LARYNX CANCER

Variables	Factor I	Factor II	Factor III	Factor IV	Factor V	Factor VI
<i>FRR 1</i>	-0.085	0.103	0.156	0.009	-0.018	0.814
<i>FRR 2</i>	0.305	0.068	0.267	0.038	0.738	0.128
<i>FRR 3</i>	0.706	-0.292	0.074	0.138	0.412	-0.075
<i>FRR 4</i>	0.861	0.005	0.180	0.019	-0.103	0.247
<i>FRR 5</i>	0.572	-0.066	0.381	-0.078	0.196	0.468
<i>a-b rcR</i>	-0.029	-0.096	0.920	0.100	0.012	0.130
<i>b-c rcR</i>	0.146	0.178	-0.042	0.915	0.015	0.027
<i>c-d rcR</i>	0.175	0.319	0.461	0.411	-0.002	-0.443
<i>atd R</i>	-0.061	0.927	0.149	0.121	0.023	-0.014
<i>FRL 1</i>	0.226	0.042	0.027	0.025	0.543	0.542
<i>FRL 2</i>	0.062	0.105	-0.019	-0.004	0.904	-0.073
<i>FRL 3</i>	0.778	0.029	-0.024	0.167	0.264	-0.220
<i>FRL 4</i>	0.858	0.053	0.051	-0.219	0.119	-0.164
<i>FRL 5</i>	0.668	0.086	0.042	0.144	0.125	0.493
<i>a-b rcL</i>	0.269	0.204	0.775	0.108	0.185	0.077
<i>b-c rcL</i>	-0.108	0.056	0.248	0.892	0.019	-0.007
<i>c-d rcL</i>	-0.041	0.524	0.347	0.424	0.197	-0.464
<i>atd L</i>	0.031	0.912	-0.100	0.100	0.104	0.146
Variance percentage	20.299	12.677	11.995	11.955	11.450	11.322

agnosis of planocellular carcinoma of the larynx, age ranging from 29–78 (mean age 62.2 ± 10.2). Control group consisted of 100 phenotypically healthy subjects of the same population, age ranged from 50–74 years (mean age 60.4 ± 5.0) and who have never been diagnosed with any type of malignant disease³⁶. The digito-palmar prints were taken and quantitative and qualitative dermatoglyphs features were analyzed according to the standard Cummins and Midlo methods^{26,37}.

The analysis of quantitative digito-palmar dermatoglyphs features (descriptive statistics, multivariate and univariate variance analysis, discriminate and factor analysis) included 18 variables (finger ridge counts on the right and the left hand: FRR1, FRR2, FRR3, FRR4, FRR5, FRL1, FRL2, FRL3, FRL4, FRL5; palmar ridge-counts on the right and left hand: a-b rcR, b-c rcR, c-d rcR, a-b rcL, b-c rcL, c-d rcL; and the atd angles: atdR, atdL). Separately we analyzed qualitative features of the fingers, palms and the axial triradius. In order to evaluate differences between the two investigated groups we used the χ^2 test.

Results

Quantitative statistical analysis (descriptive statistics, multivariate and univariate analysis) of the two investigated groups did not reveal any statistically significant difference, except for the latent structure by factor analysis. The results of the factor analysis for the patients and the healthy control subjects are presented in Table 2 in male patients and Table 3 in control group.

In the latent structure six factors were extracted in the male patients' group and five factors in the control group. The total variance percent in the group of male patients was 79.69%, while for the control group was 71.85%. The largest variance percent was found in the first factor for the both groups and it was 20.29% in the group of male patients, while in the control group it was 25.91%, which is five percent higher.

The analysis of the qualitative traits of the digito-palmar dermatoglyphs (in which the χ^2 test was used) showed statistically significant differences. The finger

TABLE 4
RESULTS OF THE CHI SQUARE FOR THE FINGER PATTERNS

Finger patterns	χ^2	p
Right	$\chi^2=6.475$	p<0.091
Left	$\chi^2=7.308$	p<0.063
Total	$\chi^2=26.76$	p<0.005

TABLE 5
RESULTS OF THE CHI SQUARE TEST FOR THE PALMAR PATTERNS

	χ^2	p
Thenar and 1st interdigital area	$\chi^2=3.111$	p<0.078
2nd interdigital area	$\chi^2=0.583$	p<0.445
3rd interdigital area	$\chi^2=86.889$	p<0.001
4th interdigital area	$\chi^2=1.645$	p<0.1997
Hypothenar	$\chi^2=2.158$	p<0.1418

TABLE 3
FACTOR ANALYSIS OF VARIABLES IN THE GROUP OF THE HEALTHY CONTROL SUBJECTS

Variables	Factor I	Factor II	Factor III	Factor IV	Factor V
<i>FRR 1</i>	0.530	-0.198	0.142	0.633	-0.025
<i>FRR 2</i>	0.801	-0.061	0.219	0.124	0.045
<i>FRR 3</i>	0.824	0.027	-0.054	0.170	0.019
<i>FRR 4</i>	0.692	0.223	0.460	-0.096	0.057
<i>FRR 5</i>	0.392	0.039	0.795	0.065	-0.048
<i>a-b rcR</i>	-0.240	0.706	0.305	0.144	-0.103
<i>b-c rcR</i>	0.159	0.264	0.067	0.762	0.152
<i>c-d rcR</i>	0.095	0.780	-0.103	-0.068	0.181
<i>atd R</i>	-0.058	0.079	0.039	-0.035	0.937
<i>FRL 1</i>	0.559	-0.015	0.111	0.466	-0.163
<i>FRL 2</i>	0.792	-0.017	0.197	0.193	0.060
<i>FRL 3</i>	0.831	0.094	0.189	0.009	-0.098
<i>FRL 4</i>	0.687	0.097	0.498	-0.027	0.040
<i>FRL 5</i>	0.407	-0.025	0.708	0.221	0.006
<i>a-b rcL</i>	-0.087	0.669	0.163	0.312	-0.103
<i>b-c rcL</i>	-0.044	0.508	0.142	0.640	0.183
<i>c-d rcL</i>	0.237	0.787	-0.218	0.035	0.037
<i>atd L</i>	0.051	-0.079	-0.057	0.186	0.888
Variance percentage	25.912	14.303	10.851	10.628	10.158

analysis revealed difference between the two investigated groups at the probability level of $p < 0.005$ (Table 4). Difference for the palm was detected at the probability level of $p < 0.001$ mainly for the III interdigital area (Table 5). Statistically significant difference was also detected for the frequency of the axial triradius, ($\chi^2 = 38.685$, $p < 0.001$).

Discussion

Larynx cancer is the seventh on the malignant diseases incidence list among men in Croatia, which is 3% of all malignant diseases in the male population⁴. The role of genetic and hereditary influences on the etiology of the disease is lately very actively studied and needs to be more evaluated. In the present study while evaluating the dermatoglyphic features of the two different groups (40 patients diagnosed with planocellular type of the larynx cancer and 100 phenotypically healthy subjects), we have tried to investigate the hypothesis of genetic predisposition of the disease. The descriptive statistical analysis did not show any difference between

the investigated groups except for the latent structure using factor analysis. In the latent structure six factors were extracted in the male patients' group with the total variance percent of 79.69, and five factors in the control group with the total variance percent of 71.85. The analysis of the qualitative traits of the digito-palmar dermatoglyphs shows the following statistically significant differences: for the finger variables at the probability level of $p < 0.005$, for the palm variables at $p < 0.001$, and for the position of axial triradius at $p < 0.001$.

Although the results of the quantitative analysis, except latent structure, do not show significant differences, the genetic influences on the development of the larynx cancer cannot be underestimated. The explanation might be in a possible influence of the different set of genes in the formation of the quantitative features of the digito-palmar dermatoglyphs, other than those, which might influence the etiology of the disease. The results of the qualitative analysis reveal statistically significant differences thus suggesting faster changes of the qualitative features under the influence of the environmental factors.

REFERENCES

1. LEBOVICS, R. S., Neoplasms of head and neck. In: Harrison's principles of internal medicine. (Mc Graw-Hill, New York, 1994). — 2. CUMMINGS, W. C., J. M. FREDRICKSON, L. A. HARKER, C. J. KRAUSE, D. E. SCHULLER: Otolaryngology-head and neck surgery. (Mosby Year Book, St. Louis, 1998). — 3. BAILEY, B. J.: Otolaryngology-head and neck surgery. (Lippincott Williams and Wilkins, Philadelphia, 2001). — 4. HRVATSKI ZAVOD ZA JAVNO ZDRAVSTVO: Incidencija raka u Hrvatskoj 2000. (Bilten br. 25, Zagreb, 2002). — 5. VINCENT, T. H. SAMUEL, A. R. STEVEN: Cancer: Principles and practice of oncology. (Lippincott Williams and Wilkins, Philadelphia, 2001). — 6. LUIS, B. H., B. S. ROY, K. I. H. WAUN, B. BERNARD, B. W. BRUCE: Head and neck cancer. (Lippincott Williams and Wilkins, Philadelphia, 1998). — 7. CARVALHO, A. L., J. PINTOS, N. F. SCHLECHT, B. V. OLIVEIRA, A. S. FAVA, M. P. CURADO, L. P. KOWALSKI, E. L. FRANCO, Arch. Otolaryngol. Head Neck Surg., 3 (2002) 318. — 8. RAFFERTY, M. A., J. E. FENTON, A. S. JONES, Clin. Otolaryngol., 26 (2001) 442. — 9. NELS, R. O., Am. J. Med., 103 (1997) 97. — 10. WEINBERG, R. A.: Oncogenes and the molecular origins of cancer. (Cold Spring Harbor Laboratory Press, Cold Spring Harbor, 1989). — 11. FRANKS, L. M., N. M. TEICH: Introduction to cellular and molecular biology of cancer. (Oxford University Press, New York, 1991). — 12. VOGELSTEIN, B., K. W. KINZLER, Cell, 70 (1992) 523. — 13. ZHANG, X., L. WANG, S. LIU, X. OUYANG, C. LIANG, Head Neck, 19 (2002) 61. — 14. PIFFKO, J., A. BANKFALVI, K. TORY, L. FUZESI, M. BRYNE, D. OFNER, F. KUSCH, U. JOOS, K. W. SCHMID, Head Neck, 20 (1998) 8. — 15. YARBROUGH, G. W., Laryngoscope, 112 (2002) 2114. — 16. FRIEDMAN, M., J. W. LIM, E. MANDERS, A. D. SCHAFFNER, L. G. KIRSHENBAUM, H. TANYERI, D. D. CALDARELLI, J. S. COON, Head Neck, 23 (2001) 280. — 17. BOCKMUHL, U., G. WOLF, S. SCHMIDT, A. SCHWENDEL, V. JAHNKE, M. DIETEL, I. PETERSEN, Head Neck, 20 (1998) 145. — 18. BRZOSKA, P. M., N. A. LEVIN, K. K. FU, M. J. KAPLAN, M. I. SINGER, J. W. GRAY, M. F. CHRISTMAN, Cancer Res., 55 (1995) 3055. — 19. SPEICHER, M. R., C. HOWE, P. CROTTY, S. DU MANOIR, J. COSTA, D. C. WARD,

Cancer Res., 55 (1995) 1010. — 20. PARTRIDGE, M., G. EMILION, J. D. LANGDON, Br. J. Cancer, 73 (1996) 366. — 21. EL NAGGAR, A. K., M. S. LEE, G. WANG, M. A. LUNA, H. GOEFFERT, J. G. BATSAKIS, Cancer, 72 (1993) 881. — 22. REID, C. B., G. B. SNOW, R. H. BRAKENHOFF, B. J. BRAAKHUIS, Aust. N. Z. J. Surg., 67 (1997) 410. — 23. GUARDIA, C., C. CASIANO, J. TRINIDAD-PIENO, A. BAEZ, Head Neck, 23 (2001) 104. — 24. FAN, G. K., S. FUJIEDA, H. SUNAGA, H. TSZUKI, N. ITO, H. SAITO, Laryngoscope, 109 (1999) 815. — 25. ELL, R. S., J. E. ASHMAN, D. N. STAFFORD, J. GREENMAN, Laryngoscope, 112 (2002) 1094. — 26. MILIČIĆ, J., P. RUDAN, LJ. SCHMUTZER, I. ŠKRINJARIĆ: Dermatoglyphs in anthropological researches. In Croat. (Laboratory of biological Anthropology. Anthropological Bibliotheca, 13, Zagreb, 1989). — 27. SCHAUMAN, B., M. ALTER: Dermatoglyphs in medical disorders. (Springer-Verlag, New York, 1976). — 28. MILIČIĆ, J., R. PAVIČEVIĆ, M. HALBAUER, B. ŠARČEVIĆ: Analysis of qualitative dermatoglyphic traits of the digito-palmar complex in carcinomas. In: DURHAM, N. M., K. M. FOX, C. C. PLATO (Eds.): The state of dermatoglyphs-the science of finger and palm prints. (The Edwin Mellen Press, Lewiston, 2000). — 29. BASAURI, L. A., L. BARNEO, J. CARNELLA, Oncology, 32 (1975) 27. — 30. RUDAN, P., Z. PIŠL, B. BAŠEK, I. ŠKRINJARIĆ, F. BUDIMAN, P. NOLA, N. RUDAN, Z. MARIČIĆ, I. PRODAN, Acta. Med. Iug., 35 (1980) 5. — 31. BEJERANO, M., K. YAKOVENKO, M. B. KATZNELSON, E. KOBLYANSKY, Z. Morphol. Anthropol., 83 (2001) 75. — 32. MILIČIĆ, J., R. PAVIČEVIĆ, Med. Jad., 24 (1994) 39. — 33. MILIČIĆ, J., R. PAVIČEVIĆ, Int. J. Anthropol., 13 (1998) 24. — 34. ŽIVANOVIĆ-POSILOVIĆ, G., J. MILIČIĆ, D. BOŽIČEVIĆ, Coll. Antropol., 27 (2003) 213. — 35. POPOVIĆ, Š., The analysis of quantitative dermatoglyphic traits of the digito-palmar complex in patients with melanoma malignant. In croat. Mr. Sc. Thesis. (Postgraduate study of Natural History, University of Zagreb, Zagreb, 1981). — 36. LETINIĆ, D., J. MILIČIĆ, Liječ. Vjesn., 120 (1998) 53. — 37. CUMMINS, H., C. MIDLO: Fingerprints, palms and soles. (Dover Publications, New York, 1961).

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DERMATOGLIFI I RAK GRKLJANA

SAŽETAK

Rak grkljana zauzima sedmo mjesto na ljestvici incidencije karcinoma u muškaraca u Hrvatskoj. Javlja se uglavnom u srednjoj i starijoj životnoj dobi. Odnos obolijevanja muškaraca naspram žena iznosi 17:1. Razvoj bolesti direktno se povezuje s pušenjem, dok genetski utjecaji još nisu do kraja razjašnjeni. Analiza digito-palmarnih dermatoglifa već je korištena u procjenama genetske osnove nekih malignih bolesti (karcinom dojke, pluća, melanom, karcinom debelog crijeva te želuca). U ovom radu analizirana je korelacija kvalitativnih i kvantitativnih svojstava dermatoglifa digito-palmarnog kompleksa između skupine 40 muškaraca oboljelih od karcinoma grkljana i kontrolne skupine 100 fenotipski zdravih muškaraca. Statističkom obradom kvantitativnih svojstava (deskriptivna statistika, multivarijantna i univarijantna analiza varijance) nije dobivena signifikantna razlika, osim prikazom latentne strukture faktor-skom analizom. Analiza kvalitativnih svojstava pokazala je heterogenost između dviju ispitivanih skupina što ukazuje na njihovo brže mijenjanje pod utjecajem okolinskih faktora.