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HAND OSTEOARTHRITIS AND AGING: THE RESULTS OF A LARGE-SCALE CROSS-SECTIONAL STUDY

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ABSTRACT

Background: Because osteoarthritis (OA) is associated with morbidity and mortality, we hypothesized that radiographic hand OA would generally be associated with chronic systemic morbidity and it will be less prevalent in longevity populations than in non-longevity populations.

Aims: 1) to evaluate the association between chronic systemic morbidity and radiographic hand OA; 2) to compare the prevalence and the mode of the development of radiographic hand OA in three longevity populations (Abkhazian, Azerbaijani and Georgian) vs. two non-longevity populations (Russian and Chuvashians).

Methods: Radiographic hand OA was evaluated using the left hand radiograms in 14 joints according to the Kellgren and Lawrence's (K-L) grading system. Each individual was characterized by the total number of affected (K-L≥2) joints (NAJ). The prevalence of hand OA was defined as the presence of at least one affected joint.

Morbidity data were attained from their medical records and divided into 9 categories by a research physician. The longevity index was calculated as a ratio of the number of individuals aged >90 years versus the number of people aged >60, expressed in per mills (‰). The population with the longevity index >40‰ was considered as the longevity population. Statistical analyses included the prevalence estimation and ANOVA.

Results: Radiographic hand OA was statistically significantly and positively associated with the ischemic heart disease. A significant

difference in the age standardized prevalence of hand OA was found between each pair of the studied samples, except between the Chuvashians, Russians and Georgians and between the Azerbaijanis and Abkhazians. The lowest prevalence was found in the Abkhazians followed by the Azerbaijanis and Georgians. The highest prevalence was found in the Chuvashians. ANOVA showed significant differences between the age-adjusted means of NAJs. The lowest age-adjusted NAJ was found in the Abkhazian population followed by the Azerbaijanis and Georgians. The highest NAJ was found in the Chuvashians.

Conclusions: The results of our study showed association between ischemic heart diseases and hand OA. Longevity populations showed lower hand OA prevalence and NAJ compared to a non-longevity population, that can be interpreted as that longevity populations age slower. Additional follow-up studies are needed to verify this hypothesis.

***Key words*:** *Ageing, hands, longevity, osteoarthritis, biological ageing.*

INTRODUCTION

Osteoarthritis (OA) is the most common form of joint disease and one of the most frequent morbidities in the elderly [17]. Radiographic hand OA is a particularly frequent condition in any population, and its prevalence and severity have been shown to be associated with age [15] and ageing [8]. Livshits et al. [18] performed a standard three-factor variance decomposition analysis on Chuvashian pedigrees and found that the main factor influencing the extent of OA development was age, contributing about 73% of the total variance. A study employing samples from the TwinsUK Adult Twin Registry [26] found significant differences in leucocyte telomere length between the subjects with and without hand OA. The authors suggested that there were potential shared mechanisms between OA and ageing, thus implicating oxidative stress and low-level chronic inflammation in both conditions. In addition, there are numerous studies that found the association of OA with chronic morbidity [7, 10, 11] and even with increased mortality [9]. Schellevis et al. [23] found that OA had the highest rate of comorbidity. As the population ages, individuals with arthritis may represent a subgroup with disproportionate increases in disability relative to the general population [5]. Based on aforementioned studies, we postulated that the individuals

suffering from some form of chronic systemic morbidity would show higher levels of hand OA.

If, as we showed before, hand OA is associated with age, chronic morbidity and mortality, the logical assumption can be that in longevity populations radiographic hand OA generally is less prevalent and would develop at a later age in longevity populations versus non-longevity populations. Longevity populations were comprehensively studied [1, 3] and many studies have reported that centenarians escape the major age-related diseases [2, 6]. However, we found no studies of the prevalence and the severity of OA in the longevity population.

The aims of our study were: 1) to evaluate the association between chronic systemic morbidity and radiographic hand OA; 2) to compare the prevalence and the mode of the development of radiographic hand OA in three longevity populations (Abkhazian, Azerbaijani and Georgian) vs. two non-longevity populations (Russian and Chuvashians);

METHODS

Sample

In the present study, we benefited from the unique data collection from the Institute and Museum of Anthropology, Moscow University. Several ethnic samples were collected from different rural areas of the USSR using the same selection and data collection procedures. There were no significant differences in the level and the accessibility of medical services between samples. Data were collected during several annual expeditions undertaken by the Institute and the Museum of Anthropology in the 1980s. The aim of these expeditions was to collect data for the USSR countrywide study of environmental adaptation in humans. The samples chosen were representative of the general population in each specific area. The focus was on the historical stability of a traditional farming community with little occupational diversity. For generations, most of the population lived under the same environmental conditions and were unexposed to an outside genetic flow [21].

To evaluate the association between OA morbidities, we used the data collected in native Chuvashians residing in small villages in the Chuvasha Autonomies of the Russian Federation.

To evaluate the association between hand OA and longevity, five population samples were chosen. The population samples with a

longevity index (LI) of >40‰ were considered longevity populations [21]. According to Kozlov et al. [16], who conducted extensive research on longevity in the same area, among the four samples chosen, three were longevity populations: Abkhazian, Azerbaijani, Georgian, and one non-longevity sample: Russian [16]. LI is calculated as a ratio of the number of individuals >90 years versus the number of people >60 years old, expressed in per mills (‰). This index was previously used in numerous publications including the recent [16, 19, 21].

Data on age, chronic morbidity and medical treatment were obtained from the participants' medical records and completed during the interview. Age was also verified by an identification document. Various anthropological measurements and left hand x-rays were taken. There were no individuals using hormone replacement therapy in the studied samples. Individuals with known posttraumatic, rheumatoid or psoriatic arthritis were not included in this study.

Morbidity definitions

An experienced research physician divided the morbidity data into 9 categories, similar to the previously used categories in several comorbidity investigations [6, 24–26), without noting the physiologic severity of each chronic condition (see Appendix 1).

Appendix 1: Diseases included in each studied group of morbidities

Ischemic heart diseases	Angina pectoris, Ischemic heart disease, Myocardial infarction
Organic heart deceases	Cardiosclerosis, Myocarditis, Rheumatoid myocarditis
Rheumatologic diseases	Rheumatism, Ankylosing spondylitis, Systemic lupus erythematosus
Diabetes	Diabetes
Renal diseases	Pyelonephritis, Nephrolithiasis
Hepatitis	Hepatitis
Hypertension	Hypertension
Pulmonary diseases	Chronic bronchitis, Emphysema
Gastrointestinal diseases	Chronic colitis, Chronic gastritis, Peptic ulcer, Gastroectomy

Radiographic assessment of OA: Single plain radiographs of the left hand, in the postero-anterior position with the x-ray source located

60 cm above, using a standard radiographic technique as described in detail by Pavlovsky [21], were obtained from each study participant The same equipment was used in all the expeditions. An experienced and specially trained researcher read each x-ray. The intra-observer reliability of the K-L scores (kappa statistics) was at least 0.84 ($p<0.01$), based on 20 repeated measurements.

OA development was evaluated according to Kellgren and Lawrence's (K-L) grading scheme, utilizing the photographs from the Atlas of Standard Radiographs [14]. The K-L score for each joint (ranging from 0 to 4) represented the accumulation of degenerative changes. OA development was separately evaluated on 14 joints of the left hand, i.e., 4 distal interphalangeal (DIP), 4 proximal interphalangeal (PIP), 5 metacarpophalangeal (MP), and 1st interphalngeal (IP-1). Joints scored as K-L$\geq$2 were considered affected. Each individual was characterized by the number of affected joints (NAJ). The prevalence of hand OA was defined as the presence of at least one affected joint.

Statistical Analysis

To evaluate the difference in the mean values of age-adjusted NAJ between the individuals affected vs. non-affected with the specific disease, we used one-way analysis of variance (ANOVA) with hand NAJ as a dependent variable and the individuals affected vs. non-affected with the specific disease as an independent (grouping) variable. This analysis was performed only in the Chuvashian sample, because most detailed and reliable information on morbidity was collected in this sample.

The prevalence of OA (at least one affected joint) and the mean NAJ were then calculated according to age groups ($\leq$35, 36–50, 51–65, >65 years). Using the χ^2 test, we compared the prevalence of hand OA between longevity and non-longevity samples, after the standardization for age, in each sample. The age distribution in the total sample was used as the standard. Applying the one-way ANOVA (Scheffe) procedure, we compared the NAJ, adjusted for age and sex, between the studied population samples.

RESULTS

The descriptive statistics of the studied samples is presented in Table 1. As mentioned above, three sampled populations fulfilled the criterion

for longevity populations (LI >40‰): Abkhazians (LI=60–70‰), Azerbaijanis (LI=50–60‰) and Georgians (LI=40–50‰); and two samples were of a non-longevity population: Russians and Chuvashians (LI=10–20‰). The samples in tables 1, 2 and 3 were arranged in accordance with their LI. Each sample comprised individuals with a wide range of ages. The mean age (±SE) for Abkhazians was 43.47±0.62; Azerbaijanis 48.29±0.98; Georgians 52.11±1.14, Russians 43.75±0.45 and the Chuvashians 48.93±0.58. The prevalence of at least one joint with OA and the mean NAJs in each studied sample is presented in Table 1.

Table 1. Description statistics of the studied samples

Studied group	Longevity index* 90+/60+ (‰)	Sample size	Sex (% of males)	Mean age±SE [years]	Age range [years]	Prevalence of hand OA (%)	# of affected joints mean ± SE
Chuvashians	10–20	819	52.99	48.93±0.58	18–86	48.00±0.49	2.33±0.14
Russian	10–20	1071	43.60	43.75±0.45	18–90	49.86±0.76	1.74±0.08
Georgians	40–50	271	32.84	52.11±1.14	18–99	61.99±1.43	2.27±0.16
Azerbaijanis	50–60	290	44.48	48.29±0.98	19–90	29.15±1.21	1.28±0.12
Abkhazian	60–70	590	52.37	43.47±0.62	18–94	43.10±1.01	0.72±0.06

* The intervals of longevity index as were estimated in an extensive screening study [16].

Table 2 presents the prevalence of radiographic hand OA (at least one affected joint) in the studied ethnic samples according to four age groups (≤35, 36–50, 51–65, >65). The prevalence of hand OA in each age group was lower in populations with high LI and vice versa. The results of the χ^2 test (data not presented) showed significant differences ($p<0.003$) in the age-standardized prevalence of hand OA between each pair of the studied samples, except between Chuvashians, Russians and

Georgians and between Azerbaijanis and Abkhazians ($p>0.05$). The lowest age-standardized prevalence was found in Abkhazians followed by Azerbaijanis and Georgians. The highest prevalence was found in the Chuvashian population.

Table 2. Prevalence (%) of radiographic hand OA in different ethnic samples according to age groups

Sample	≤35	36–50	51–65	>65
Chuvashians	5.30	21.60	72.40	94.60
Russians	21.70	45.52	81.90	99.06
Georgians	13.79	40.58	89.47	94.03
Azerbaijanis	8.22	26.74	66.29	88.09
Abkhazians	3.89	21.95	60.71	82.69

Table 3 shows the mean NAJ (±SE) in the studied samples according to age groups and age-adjusted means in each sample. In each age group, the samples with a higher LI showed lower mean values of NAJs. ANOVA showed significant differences ($p<0.01$) between the age-adjusted standardized means of NAJs. The post-hoc comparison (the Scheffe test) demonstrated a significant difference ($p<0.01$) between each pair of samples, except between Azerbaijanis and Abkhazians ($p>0.05$). The lowest age-adjusted mean NAJ was found in Abkhazians followed by Azerbaijanis and Georgians. The highest NAJ was found in Chuvashians.

Table 3. Mean number of affected joints (±SE) of radiographic hand OA in different ethnic samples according to age groups

Sample	≤35	36–50	51–65	>65
Chuvashians	0.06±0.02	0.36±0.09	3.42±0.21	6.55±0.45
Russians	0.32±0.04	0.89±0.06	3.24±0.18	6.72±0.29
Georgians	0.22±0.08	0.83±0.16	2.32±0.20	5.44±0.34
Azerbaijanis	0.08±0.03	0.39±0.08	1.82±0.20	4.04±0.45
Abkhazians	0.04±0.01	0.33±0.05	1.55±0.19	3.15±0.31

The most common morbidities in the Chuvashian population were gastrointestinal diseases (107 individuals or 13%), the ischemic heart disease and hypertension (79 individuals or 9.6%). The results of ANOVA are also shown in Table 4. Statistically significant differences

between the mean radiographic hand OA scores in affected vs. non-affected individuals were found only for the ischemic heart disease (p=0.022) and a group of gastrointestinal diseases (p=0.043). The mean values of hand OA scores were higher in the individuals affected by the ischemic heart disease and lower in the individuals affected by the gastrointestinal disease compared to non-affected persons.

Table 4. Analysis of variance of hand OA scores in the Chuvashian population. The mean values and standard deviations (SD) of age-adjusted hand OA score of affected vs. non-affected individuals

Disease	P-value	Category	Mean	SD	N
Ischemic heart disease	**0.022**	Affected	0.18	1.34	79
		Non-affected	–0.02	0.95	740
Organic heart diseases	0.202	Affected	–0.32	0.99	38
		Non-affected	0.02	0.99	781
Rheumatologic diseases	0.841	Affected	0.00	0.71	45
		Non-affected	0.00	1.00	774
Diabetes	0.509	Affected	0.29	1.62	6
		Non-affected	0.00	0.99	816
Renal diseases	0.667	Affected	0.10	0.77	21
		Non-affected	–0.00	1.00	798
Hepatitis	0.134	Affected	–0.18	0.91	67
		Non-affected	0.02	1.01	752
Hypertension	0.475	Affected	–0.08	1.22	79
		Non-affected	0.01	0.97	740
Pulmonary diseases	0.455	Affected	–0.02	1.31	61
		Non-affected	0.00	0.97	758
Gastrointestinal diseases	**0.043**	Affected	–0.16	0.85	107
		Non-affected	0.02	1.01	712

N – number of individuals in each category; Significance of variance (p-values) indicated between the means of hand OA scores in affected vs. non-affected individuals. Significant p (<0.05) appear in bold.

DISCUSSION

In every population and at any age, it is possible to find individuals with higher or lower than average hand OA. The main hypothesis underlying

this study was that the extent of age-associated skeletal changes (such as radiographic hand OA) might be, inter alia, under the influence of some adverse functional conditions and morbidities. Different measures of skeletal aging and among them OA, are strongly correlated with the status of the vital health systems and ultimately with survival rates. Indeed, in previous studies, the individuals with OA had a significantly higher risk of comorbid conditions such as the cardiovascular disease [7], hypertension, chronic pulmonary diseases [20], peptic ulcer and renal diseases [5], gastritis and phlebitis [10]. In the present study, we found that radiographic hand OA is positively associated with ischemic heart morbidity. To support this finding, Philbin et al [22] found that the individuals with OA had an adverse profile of metabolic risk factors for the coronary heart disease. Compared with controls, OA patients had a higher mean body mass index, systolic blood pressure and fasting blood glucose, and lower mean high-density-lipoprotein (HDL) cholesterol. Singh et al. [24] also reported that the patients with OA often have risk factors for the cardiovascular disease, including the respiratory disease, hypertension and a low HDL cholesterol level.

In a systematic review, Hochberg [9] found moderate evidence of increased mortality among the persons with OA compared with the general population. The association between the lifespan and OA development can also be seen in animals [25]. The animals with long life expectancy (monkeys) postpone OA development, while the animals with short life expectancy, (mice) show early OA. Primary OA development occurs after a reproductive active life expectancy, indicating that primary OA is not directly time-related. Evolutionary controlled age-related processes are involved in the development of bone and cartilage degeneration and, therefore in primary OA. OA apparently is not a simple wear and tear process but a process of biological ageing [25].

The rate of degenerative changes in the skeleton, such as hand OA, may reflect an individual's biological resistance, immunity, the functional or health status in reference to his or her chronological age. We also believe that chronic morbidities and different body compositions may influence skeletal aging through changes in the metabolism of bone and joints. Therefore, age-related skeletal changes can serve as an index of biological ageing. Unlike the non-skeletal

markers, proposed as biomarkers of aging (such as physiological and blood chemistry measurements), bone characteristics are relatively stable and not prone to circadian or seasonal rhythms [12, 13].

The present study suggests that longevity populations showed lower hand OA prevalence and NAJ compared to a non-longevity population, that can be interpreted as that longevity populations age slower. We suggest that the same phenomenon occurs on an individual level. Franceschi et al., in their comprehesive review on ageing and longevity [4], demonstrated that centenarians (and long-lived individuals, in general) were not the best example for the age cohort, but rather the individuals who better biologically and psycho-socially adapted to the environment. Unfortunately, the cross-sectional design of our study did not allow us to evaluate this hypothesis. Additional follow-up studies are needed to verify this hypothesis.

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