

Investigations into human tracheal cartilage osseocalcineus metaplasia.

I. Radiographic findings

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*Osseocalcineus metaplasia (OCM) of the tracheal cartilages is well known, but no exact data are available relating it to age and sex. To resolve this problem we analysed tracheal telerradiograms of 99 female (age: 0.4–92; $\bar{x} = 59.98 \pm 22.75$ years) and 110 male patients (age: 0–83; $\bar{x} = 53.53 \pm 19.95$ years). As the first step we estimated the percentage of trachea that had complete lesions, those that had trace lesions and those that were unchanged in relation to the patient's age and sex. Secondly we determined the extent and growth of developing lesions during the process of ageing. Data were collected for all the cartilages, with two cartilages with trace lesions considered to be of similar value to one cartilage with complete remodelling. This enabled us to determine the correlation coefficient for changed cartilages and patient age and also the dynamism of OCM in the trachea examined. The χ^2 and Student's *t* tests were used in determining the mean differences between subgroups. The lesions referred to above occurred in 66.35% of men and in 33.33% of women and correlated with age ($r = 0.93$, $p < 0.001$ in men, and $r = 0.27$, $p < 0.01$ in women). Total remodelling of the OCM occurred in the oldest age group, when both sexes were taken into consideration, while cartilages with trace changes were detected in the younger group of patients. The lowest mean patient age was observed in the group without tracheal changes. Osseocalcineus metaplasia of the tracheal cartilages was conditioned by patient age and sex. In male patients it occurred twice as often as in females. Until the age of 50 it occurred as much as nine times as often, while after this age it occurred only twice as often as in female patients. (Folia Morphol 2008; 67: 143–149)*

Key words: tracheal cartilage, metaplasia, ageing, sex, radiographic changes

INTRODUCTION

The trachea, consisting of 16 to 20 cartilages [1], grows with the body until the age of 20 [2]. Kusafuka et al. [10] investigated the tracheae of neonates and observed no ossification, calcification or type I and X collagen presence, or reduction of type II collagen. Leutert [11] observed calcineus remodelling foci in the tracheal cartilages of patients as young

as 25. He only observed the formation of so-called "asbestine needles" or ossification sporadically in elderly patients. In the data available in the literature we found no exact investigations concerning osseous metaplasia and tracheal cartilage calcification in relation to age and sex. University textbooks of human anatomy [4, 5, 9, 16, 21] do not refer to this issue [16], or only enigmatically underline the

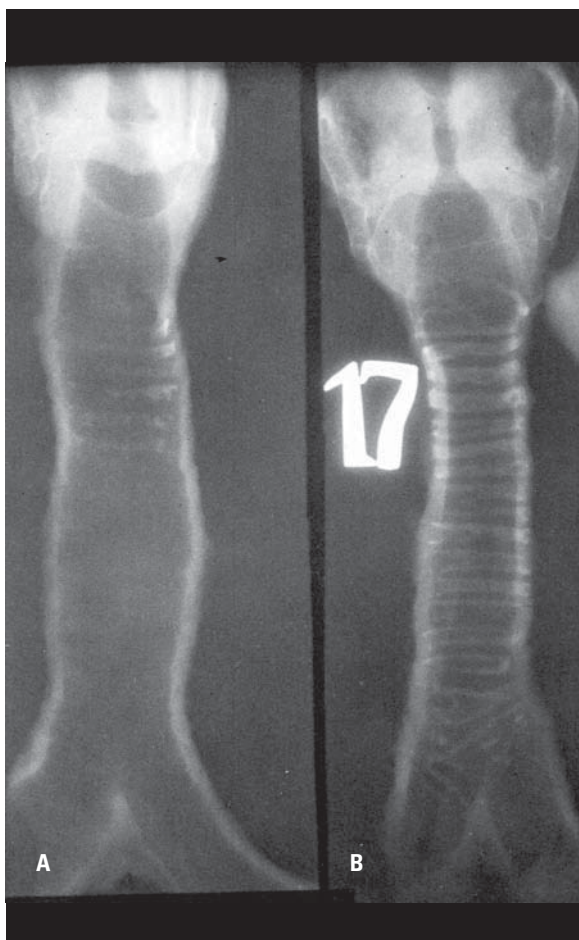


Figure 1. Tracheal radiogram. **A.** 69-year old male (trace lesions of several cartilages); **B.** 65-year old male (complete changes).



Figure 2. Tracheal radiogram. **A.** 71-year old woman (trace lesions); **B.** 82-year old woman (total changes).

fact that in elderly patients [5, 9, 14] or in those near thirty years of age [21] tracheal cartilages are subjected to ossification, calcification and, according to Bloom and Fawcett [4], fibrosis only. Hart and Mayer [9] announced the possible osteogenesis and calcification of tracheal cartilages, which can occur in elderly patients. None of these authors analysed the influence of sex on the occurrence of osseocalcineus metaplasia (OCM), or the dynamism of its development during the process of ageing. We decided to resolve this issue.

MATERIAL AND METHODS

Extra situ tracheal telerradiograms performed on 99 women aged between 0.4 and 90 years (mean age 59.98 ± 22.75 years; median = 64 years), and 110 male patients, aged between 0 and 83 years (mean age 53.53 ± 19.95 years; median = 55 years) were the basis for determining the frequency of occurrence and dynamism of OCM of the tracheal

cartilages in relation to patient age and sex. Investigations were performed in phases. During the first phase we estimated the percentage of the trachea with complete or trace foci and without foci in relation to patient age and gender. In the second phase we determined the extent and growth of developing lesions during the process of ageing. Cartilages with complete remodelling (Fig. 1B, 2B, 3A) and those with trace elements of remodelling (Fig. 1A, 2A) were counted. Where one cartilage proved to be completely changed, regardless of the number of cartilages with trace lesions, the case was accounted in the complete change group. Afterwards data was assembled for all the cartilages, with two cartilages with trace lesions considered to be of similar value to one cartilage with complete remodelling. This enabled us to determine the correlation coefficient between changed cartilages and patient age. Additionally, we estimated the relationship between the number of changed cartilages for each



Figure 3. Tracheal radiogram. **A.** 55-year old male (total changes); **B.** 44-year old male (trace lesions).

decade of life (n), and each trachea examined (N). The results obtained enabled us to determine the dynamism and extent of OCM in the investigated tracheae. The χ^2 and Student's t tests were used. $P < 0.05$ was considered as statistically significant in determining the mean differences between subgroups.

RESULTS

Osseocalcineus remodelling of the tracheal cartilages significantly differed in relation to patient age and sex ($p < 0.001$) (Table 1). In male patients the correlation coefficient between changed cartilages and patient age was $+0.93$ ($p < 0.001$), while in female patients it was only $+0.27$ ($p < 0.01$). The lesions referred to were twice as common in male (66.35%) as in female patients (33.33%), occurring in the group with complete changes 2.5 times as often, and in the group with trace lesions twice as often. The mean age of all the female patients investigated was 59.98 ± 32.8 years, and was significantly higher than that of the male patients (53.53 ± 19 years; $p < 0.05$). Analysis of the mean age demonstrated that total remodelling of OCM cartilages occurred in the oldest age group with regard to both sexes, while trace elements of remodelling were observed in the younger patient group. The lowest mean patient age was observed in the group without tracheal changes (Table 1). When both sexes were considered, the differences in mean patient age in particular groups proved highly significant. In male patients the differences between the group with unchanged tracheae and those with trace changed trachea were of a significance of $p < 0.001$, while the differences between the latter and those with complete tracheal cartilage changes had a significance of $p < 0.01$. With regard to female patients the mean age differences between the first two groups amounted to $p < 0.02$ and between the trace and completely changed groups to $p < 0.001$ significance.

The mean age of the female patients was significantly higher than that of the male patients (Table 1). Table 2 shows the frequency of occurrence

Table 1. Tracheal cartilage osseocalcineus metaplasia occurrence, depending on patient age and gender

Changes	Men					Women					P
			Age (years)					Age (years)			
	N	%	Min.	Max.	$\bar{x} \pm SD$ (Me)	N	%	Min.	Max.	$\bar{x} \pm SD$ (Me)	
No changes	37	33.64	0	84	42.40 ± 24.10 (46)	66	66.67	0.4	66	55.40 ± 24.90 (60)	0.02
Trace lesions	50	45.45	28	77	56.78 ± 10.40 (54)	25	25.25	42	86	65.40 ± 12.80 (64)	0.01
Total changes	23	20.90	44	84	64.52 ± 10.20 (54.5)	8	8.08	66	90	77.88 ± 5.60 (78)	0.01
Summary	110	100.00	0	84	53.53 ± 19.00 (55)	99	100.00	0.4	90	59.98 ± 22.80 (64)	0.05

N — number of cases, % — percentages of cases with tracheal cartilage lesions, Min. — minimal age, Max. — maximal age, $\bar{x} \pm SD$ — mean arithmetic \pm standard deviation, Me — age median in years

Table 2. Percentage of tracheal cartilages lesions during given decades of life

Decades of life (years)		0-10	11-20	21-30	31-40	41-50	51-60	61-70	71-80	> 80
MEN	Number of trachea without lesions	4	2	7	3	10	8	10	5	1
	Number of changed trachea	0	0	1	1	10	14	18	12	2
	Percentage of changed trachea	0.00	0.00	12.56	25.00	50.00	63.64	64.29	70.55	66.67
WOMEN	Number of trachea without lesions	5	5	2	3	15	8	15	14	11
	Number of changed trachea	0	0	0	0	1	6	4	8	5
	Percentage of changed trachea	0.00	0.00	0.00	0.00	6.25	42.86	21.05	36.36	31.25

of tracheal cartilage change in relation to decade of life. Figure 4 presents the results of the investigation. It is easily noticeable that in the case of male patients OCM changes had already developed during the third decade of life, while the highest values were observed in patients in the eighth decade of life. In female patients the changes developed twenty years later than in males. The results were much lower than for men during all the decades referred to. The highest values for females were observed during the sixth and eighth decades of life, although none came close to the lowest

values noted in men. The highest percentages of tracheal metaplasia were thus observed in the eighth decade of life in men (70.6%) and in sixth decade of women (42.86%). Table 3 shows the proportion of changed cartilages in relation to the number of trachea investigated during particular decades of life. Figure 5 presents the results. In contrast to Figure 4, this shows a two-phase development in tracheal changes in men. The most significant changes were noted in the sixth and ninth decades of life. In women the opposite was the case. The curve had a tendency towards mild

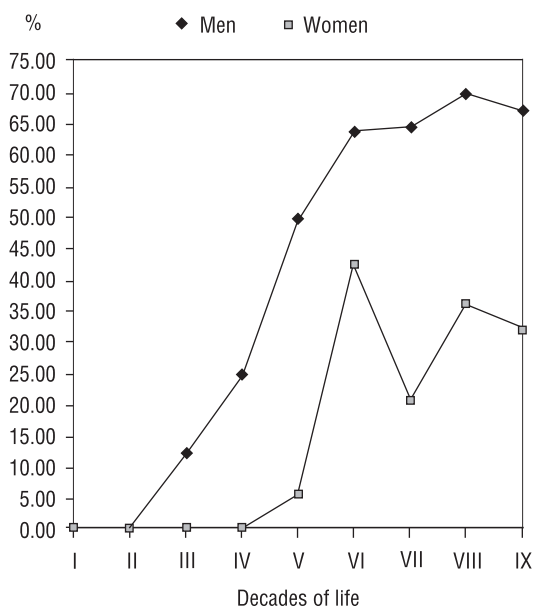


Figure 4. Frequency of tracheal cartilage ossification in male and female.

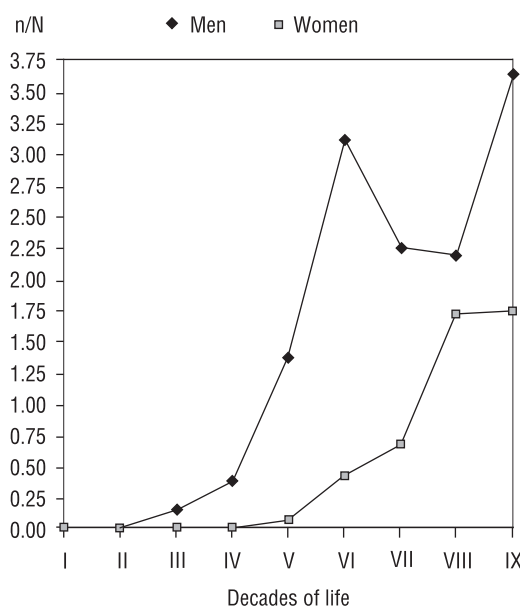


Figure 5. Dynamics of tracheal cartilage ossification in male and female.

Table 3. Dynamism of tracheal cartilage osseocalcineus metaplasia depending on particular age and gender

Decades of life	I	II	III	IV	V	VI	VII	VIII	IX
n/N	0/5	0/2	1/7	2/5	29.5/21	73/23	59/27	36/17	11/3
Men	0.00	0.00	0.14	0.4	1.4	3.17	2.19	2.12	3.67
n/N	0/5	0/5	0/2	0/3	1.0/12	7.5/16	12.5/18	39.5/22	29.5/16
Women	0.00	0.00	0.00	0.00	0.08	0.47	0.69	1.8	1.84

n/N — relationship between the number of changed cartilages and number of investigated trachea during a given decade of life

growth, attaining the highest values during the ninth decade of life. However, none of these peak values reached the lowest values observed in male patients.

DISCUSSION

Osseocalcineus metaplasia of the tracheal cartilages is conditioned by patient age and sex and in male patients this occurred twice as often as in females. It took place mainly in the early decades of life and until the age of 50 was diagnosed nine times as often in male patients, while after this age it appeared only twice as often as in female patients. Differences were also observed in the occurrence of tracheal cartilage lesions, depending on patient age. In male subjects a constant increase was observed until the eighth decade of life, while in female subjects two peaks were noted, one during the sixth and the other during the eighth decade of life. Among female patients, therefore, there are two subpopulations susceptible to the occurrence of the lesions referred to here. This raises the question of whether they are hormonally dependent. There is no clear answer to this. On the basis of clinical practice it would appear that the end of the endocrine activity of the female gonads may differ even by years. However, there have been no endocrinological studies to work out a common pathogenetic position.

Animal [7, 12, 18, 19] and human [2, 3, 15, 17, 20] experimental models have considered both sexes, but have involved a small number of cases and have not related tracheal cartilage lesions to patient sex. Of the patients evaluated by Kasafuka et al. [10] 68% were male and 32% female, although the influence of sex on the pathogenesis of OCM of the tracheal cartilages was not examined. Glaser [8] investigated 250 autopsied patients and did not mention the influence of sex on the occurrence of tracheal cartilage ossification. Of 268 trachea investi-

gated by Linzbach [13], 67.83% were of male and 32.15% were of female patients. The authors also mentioned the issue of cartilage ossification, which occurred less frequently in female patients, although no percentages were given.

Female patients have thinner tracheal cartilages than male patients. Tracheal cartilages, especially in athletes and pyknotic patients are thicker than in leptosome and asthenic patients. The percentage of subjects with cartilage ossification increased with the thickness of the cartilages. After 40 years of age the percentage of ossified cartilages in athletes and pyknotic patients ranged from 60% to 75%, and were significantly reduced in asthenics and leptosomes [13]. Glaser [8] also mentioned the relationship between greater weight in male patients and the frequent occurrence of OCM of the tracheal cartilages. However, the authors cited did not clarify the anthropological method used for the determination of body type. There is some doubt about the results presented, since they were estimated during World War II. Our examinations were performed in 1974 without distinguishing the patient body type. However, the poor economic situation of the Eastern block countries should be taken into account, as this did not favour the more athletic pyknotic type. The mean age of autopsied patients who were born during World War I and thereafter did not favour this either, because of world famine and poor economic conditions.

The inferior thyroid, internal thoracic and thoracic aorta branches nourish the trachea [5, 14]. It is well-known that nicotine influences the development of degenerative vascular changes. Thus the primary insufficiency of nutritional substances and the dilated diffusion surface of thick cartilages in male patients might be evidence of the changes observed. On the basis of the data collected during the years of the study it appears that female smokers were rarely observed. After the cultural revolution of 1968 this changed significantly. It would be interesting

to perform investigations in thirty years, when the population of smoking women reach their seventh decade of life, and to determine the percentage of metaplastic tracheae. A positive result might explain the pathomechanism of tracheal cartilage OCM.

As mentioned previously, diffusion of nutritional substances into the central parts of the tracheal cartilages is reduced with increasing age, which leads to "infarctus protachens" [13]. Chondrocytes are surrounded by protein fibres up to 0.5 μm thick. The fibres disappear with age [7], and the degradation products stimulate the penetration of vessels from the perichondrium. A basophil histochemical reaction of chondral matrix changes with age into acidophil, and in 84% of cases chondroid matrix hyalinisation is observed [10]. The following stage consists in the deposition of calcium salts. It is interesting to note that Bonucci et al. [6] never observed ossification, only calcium salt deposition, when considering animal experimental models.

The results obtained by Kasafuka et al. [10] and Glaser [8] in studies of tracheal cartilage OCM were similar, ranging from 52% to 54%. Our own observations differed significantly, especially when male patients were concerned, amounting to 66.4%. However, it must be remembered that the data presented by Kasafuka et al. [10] only consisted of 25 cases with none of the above-mentioned lesions in the sixth decade of life. These results differ from ours. Glaser (250 autopsies) also mentioned that tracheal cartilage calcareous lesions appeared in the fifth decade of life and much earlier in male patients.

The results presented seem to be the first concerning the issue of tracheal cartilage OCM and the dynamism of its development in relation to patient age and sex.

The tracheal cartilage lesions observed can influence the mechanism of maximal expiration and coughing. The average cartilage rigidity to deflexion correlated with patient age. The correlation coefficient was $r = 0.83$, and considered as statistically significant ($p < 0.05$) [15].

CONCLUSIONS

1. Tracheal cartilage osseocalcineus metaplasia is conditioned by patient age and sex.
2. This occurs twice as often in men as in women.
3. Osseocalcineus remodelling of the tracheal cartilages begins in the third decade of life in males, while in female patients it begins in the fifth decade.

4. The dynamism of tracheal cartilage osseocalcineus metaplasia in men has two peaks, with an acute rise during the initial six decades of life. In women, in contrast, one can observe a gradual increase, with peak elevation in the ninth decade of life.

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