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Original Articles

Aortic and Coronary Atherosclerosis in a Hamburg Autopsy Series

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Summary. Morphometrical examinations were carried out on 116 male and 117 female cadavers in order to quantify arteriosclerotic lesions of the aorta and coronary arteries. None of these cases died of natural causes. The age range was between 5 and 64 years. Two defined segments of the descending thoracic aorta and the abdominal aorta were examined from every cadaver, the coronary arteries were dissected out and divided into 3 defined segments. After the vessels had been stained with Sudan IV the point-counting-method was used to evaluate the following arteriosclerotic lesions: fatty streaks, fibrous plaques and complicated lesions. The raised lesions are considered to be the sum of the fibrous plaques and complicated lesions. The frequency of the various lesions as well as their absolute and relative surface areas were evaluated. – The following were also taken into account: relative body weight, absolute and relative heart weight, absolute vessel surface area. The characteristics were correlated statistically and variance analyses were carried out. The most important results are:

1. The absolute increase in surface area of all vessels shows an age-dependent rise in both sexes.

2. The relative heart weights are constant in all age groups; the absolute heart weights increase over all age groups.

3. Fatty streaks occur in all age groups, with increasing frequency up to the third decade. The absolute increase in streak surface area increases in almost all vessels and during all decades, however the relative increase in streak surface area is not influenced uniformly by age. The absolute and relative extent of the fatty streaks correlates significantly with the relative body weight.

4. Complicated lesions are first observed in the 4th decade and have a relatively small area of spread, with the exception of the abdominal aorta. Fibrous plaques are first observed in the 2nd decade. The frequency and extent of these lesions increases over all decades. Males regularly show more pronounced lesions than females.

5. The comparison with three non-German autopsy studies of European

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origin, as well as with a comprehensive study of the international Arteriosclerosis-Project shows: fatty streaks are quantitatively less pronounced in the male coronary arteries than in most of the so-far examined random groups. The difference in occurence and in the spread of fatty streaks is not very large in the other vessels or in the female group. Raised lesions are quantitatively substantially more strongly pronounced in the male coronary arteries than in all other previously examined random groups. The differences are less pronounced in the other vessels and in females.

Key words: Arteriosclerosis, morphometry – Coronary arteries, aorta – Violent deaths.

Arteriosclerosis and its complications continue to hold a leading position in mortality statistics of industrial countries (WHO, 1977). Lately there has been a rise in infarct rates and the incidence of ischaemic heart disease in younger age groups (Hauss, 1976), although trends in the opposite direction are also discussed (Schettler and Greten, 1978). The inadequacy of morbidity and mortality statistics is almost certainly one of the reasons for such contradictions (Zschoch, 1966; Lange, 1977). A rise in mortality associated with ischaemic heart disease (IHD) might be associated with a greater quantitative spread of arteriosclerosis, or to an increase in the complications alone.

Precise quantitative measurement of the extent of arteriosclerotic lesions in the various social classes is necessary as a basis for such discussions. This was one of the goals of the International Arteriosclerosis Project (IAP), in which the individual investigating groups first practised quantification of vessel arteriosclerosis with the naked eye and then examined post mortem material from various random samples (Tejada et al., 1968). With the same goal in mind, in a random sample of Finnish post-mortems, Rissanen (1972) used the points-system developed by Mitchell and Cranston (1965), which has the advantage of having shown better reproduceability.

The group of patients suffering a violent death has – with regard to the extent of arteriosclerosis – the advantage that they are most likely to be at random. This investigation is therefore limited to this group and will try to measure the extent of arteriosclerosis in the various age groups of a sample of North German post-mortems.

Material and Methods

The coronary arteries and aortas of 116 male and 117 female cadavers, whose ages varied between 5 and 64 years, were examined. Post-mortem examinations were done on the cadavers between September 1974 and January 1977 in the Institute of Forensic Medicine. All the causes of death were violent (murders, accidents, suicides) with a short death struggle, and without clinical treatment between trauma and death. The cases were assigned to decades, according to age (see Table 2). After post-mortem and microscopic examinations 4 male and 1 female case were omitted, as infarct scars were present in the myocardium.

The aortas and coronary arteries were dissected out and examined morphometrically as laid out be the IAP (Guzman et al., 1968) and Rissanen (1972):

1. Aorta. The longitudinally opened aorta was divided into two segments: (a) descending part of the thoracic aorta (A.th.): the segment between the exit of the second pair of intercostal arteries and the upper edge of the exit of the coeliac trunk; (b) abdominal aorta (A.abd.): the segment between the dividing line to the thoracic aorta and the horizontal dividing line through the upper border of the aortic bifurcation.

2. Coronary Arteries. The coronary arteries were opened longitudinally as far as possible with a fine pair of scissors (coronary scissors). They were then dissected out and divided into three segments: (a) Right coronary artery (R): the length of vessel from the opening of the main branch, including the right marginal artery and occasionally including the posterior interventricular artery; (b) Anterior interventricular artery (Rda): the length of vessel between the opening of the left main branch and the periphery of the Rda; (c) The left circumflex artery (Rc): the length of vessel between the branching point and the periphery of the Rc.

3. Preparation and Evaluation. All vessel segments were freed from adventitial connective tissue and cleaned with running water, then stretched on cardboard and fixed in 10% neutral formalin for 1–2 days. Following this, the vessel specimens were coloured with Sudan IV. Either a set of 6 aorta segments or of 9 coronary artery segments was suspended for 16–18 h in 1 liter of photometric, freshly made and constantly stirred dye-solution. The solution consisted of 38% isopropylalcohol, which was equilibrated with a saturated solution of Sudan IV at 524 mm and 20° C to an absorption of 0,23. Decolourisation of the vessel specimens was achieved by washing. The vessel segments were then remounted on cardboard and packed into plastic foil.

Arteriosclerotic lesions were evaluated with the help of the point-counting-method of Mitchell and Cranston (1965) with the modification of Rissanen (1972). In this method transparent foil printed with a point grid was laid on the vessel intima. By palpation and inspection of the vessel intima the lesions present at every point on the scanner were registered separately with the help of a counter. The scanner points for counting were arranged photomechanically in the form of isosceles triangles (sides 6.35 resp. 2 mm) on thin plastic foil. Every point of the aortic scanner represents a total area of 0.349 cm^2 and 0.0346 cm^2 in the coronary grid. Between 100 and 150 scanner points per vessel segment were evaluated.

4. Definition of Arteriosclerotic Lesions. The arteriosclerotic lesions were defined in accordance with the IAP (Guzman et al., 1968): as (a) Fatty streaks (FS), (b) Fibrous plaques (FP), (c) complicated lesions (CL), (d) raised lesions (RL) as the sum of FP and CL.

5. Reproduceability and Reliability. In order to check the macroscopic definition of the various lesions, specific samples were taken during the study and the macroscopic diagnosis confirmed histologically. In an earlier study, carried out with the help of Dr. V. Rissanen[1] the definition of arteriosclerotic lesions was practiced on selected vessel specimens until conformity occurred.

In order to check the reliability of the point-counting-method 40 aortas and 30 coronary arteries from the total of 116 previously evaluated male vessel specimens were recounted.

6. Statistical Evaluation. All data were transmitted to Hollerith cards and statistically evaluated using the "SPSS"-Program (Nie et al., 1975) on a TR 440 Computer of the Computing Center of the University of Hamburg.

Quantitative attributes were examined descriptively by means of the usual sample statistics. After checking the plausibility of the data and assessing the empirical distributions, the Pearson coefficients of correlation were determined for all suitable pairs of attributes, and for triplets of special interest the partial correlation coefficients were calculated. The significance of all correlation coefficients was examined. All differences of mean values of relevant variables were considered by means of 1-way analyses of variance, classifying the patients according to their age into 1 of 6 age decades. Where the test results were significant on the 5% level, the Multiple-Range-Test of Scheffé (Weber, 1972) was used in addition to track down homogenous groups; analyses of trend were performed for more precise estimation of age dependency.

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[1] We thank Dr. V. Rissanen for his friendly assistance and helpful advise

Results and Discussion

The results found can be seen in the tables and diagrams. In order to give a better comparison, our results were put together with those from two random samples from the IAP, as well as results from a Finnish study, in diagrams Fig. 4 to Fig. 6.

The Representativity, Comparability and Reliability

For various reasons even violent deaths are not unselected (Rissanen, 1972). Results from such studies should therefore not be transferred to the living population without reservation. However, in comparison with those causes of death evaluated in the IAP-study, this material seems relatively unselected with regard to arteriosclerosis (Sternby, 1967; McMahan, 1968; Rissanen, 1972). A disadvantage is that forensic autopsy material differs from clinical material in the absence of a detailed history and the diagnosis is based exclusively on the morphological findings. In order to keep the study material as free as possible from IHD, cases with myocardial scars of over 0.5 cm diameter were eliminated. Thus we assumed, that our random samples were almost completely IHD-independent, but other risk-factors such as diabetes mellitus and lipid-metabolism diseases cannot be excluded. Our results can best be compared with those of Rissanen (1972). This material was also composed of violent deaths and

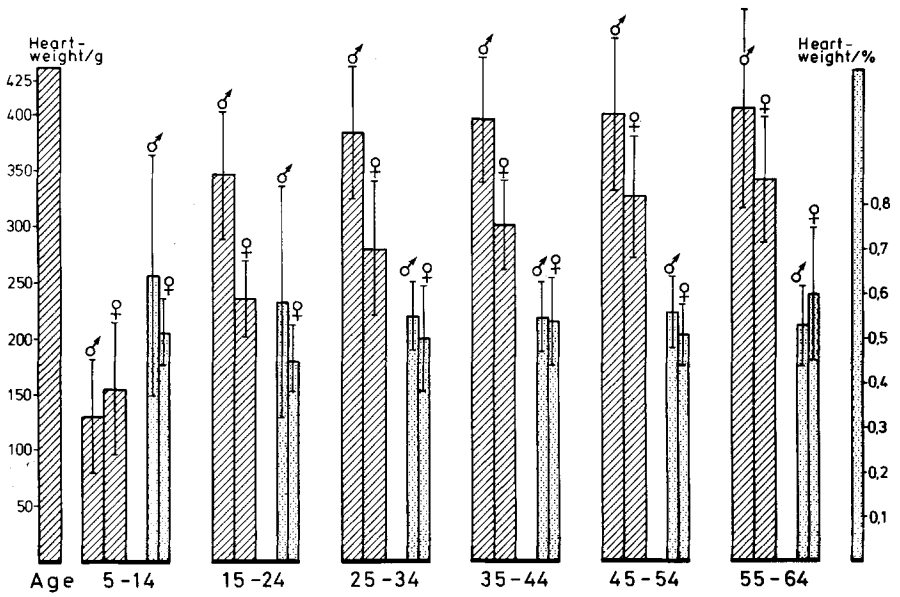

Fig. 1. Means and standard deviations of relative and absolute heart weights in males and females grouped according to six age classes

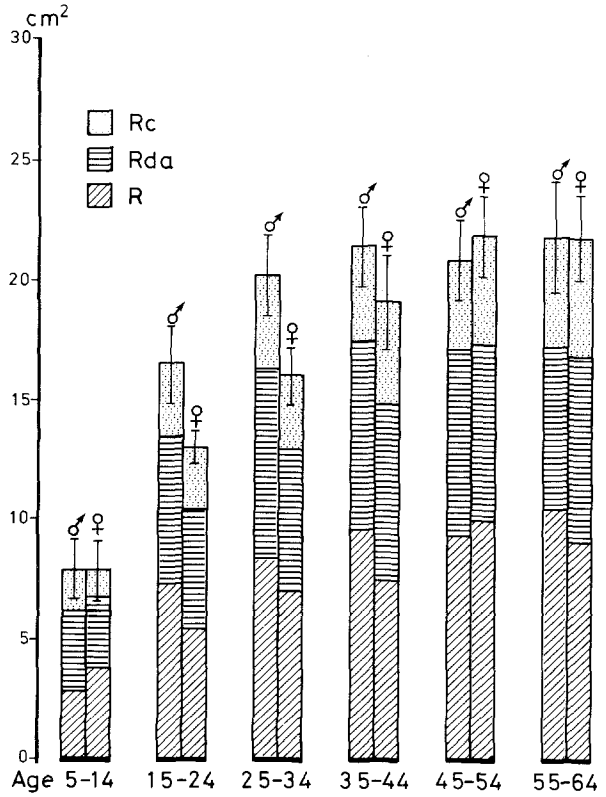

Fig. 2. Means of the absolute areas of the total intimal surfaces of three coronary arteries in males and females grouped according to six age classes. Standard deviations of the total surface of all three vessels combined

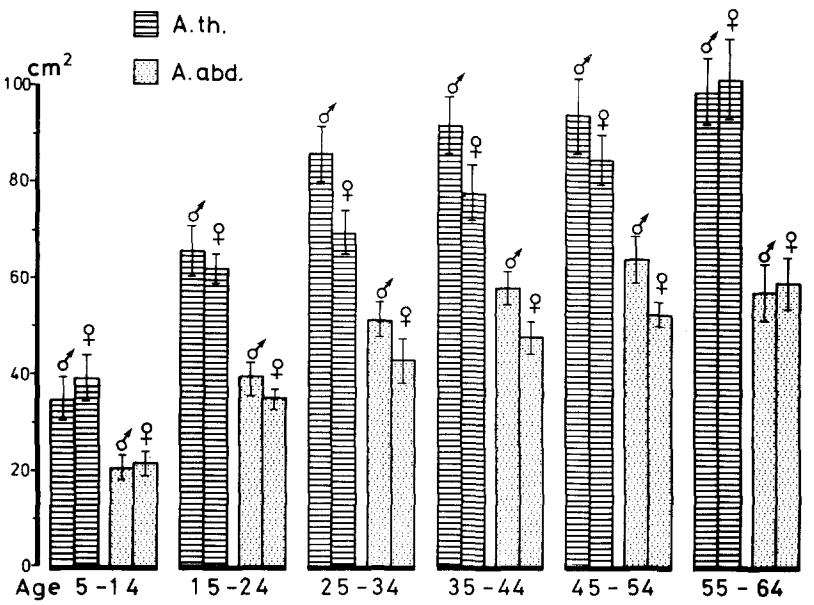

Fig. 3. Means and standard deviations of the absolute areas of intimal surfaces of two aortic specimens in males and females grouped according to six age classes

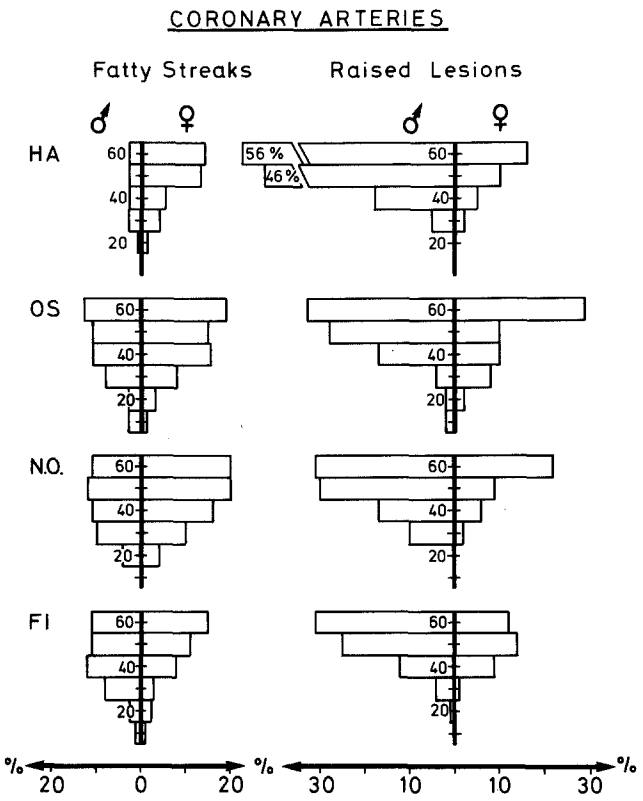

Fig. 4. Means of the relative extent of intimal surfaces involved with fatty streaks (*FS*) and raised atherosclerotic lesions (*RL*) in coronary arteries in males and females at different ages. Comparison of four autopsy series. *HA* = Hamburg, *OS* = Oslo, *N.O.* = New Orleans, *FI* = Finland. The diagrams of the Oslo and New Orleans series are adopted from Tejada et al. (1968), those of Finaland are adopted from Rissanen (1972)

the point-counting-method was also used for evaluation. Rissanen also found a high degree of conformity between two consecutive evaluation studies. Comparison with the IAP-study is not simple, as the autopsy material is differently composed and the method of quantification also varies. In the IAP-study the graduation of the extent of arteriosclerotic lesions was performed by the naked eye. Accidental deaths, cancer deaths, deaths from infectious diseases and various other causes of death were gathered together into a so-called basis-group.

The different times at which this study and the work of Rissanen and the IAP took place, must also be considered when a comparison is made.

In this study, the results of the repeated count of the 40 aortas and 30 coronary arteries showed a high degree of conformity with the first count (see Table 1), so that the examination method used can be described as reliable. Using the earlier study of another researcher (Rissanen) and random histological sampling, the comparability of the results with other authors was demonstrated, as was the internal homogeneity of the study.

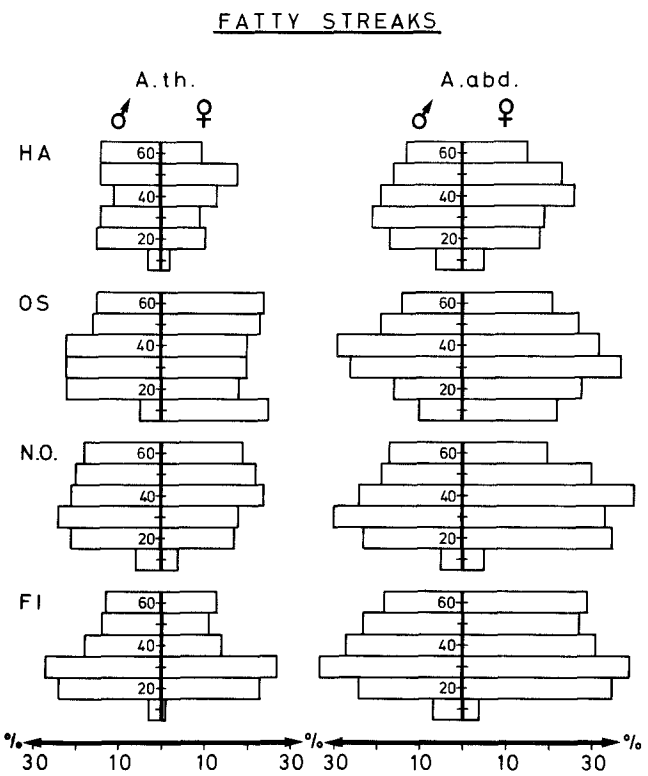

Fig. 5. Mean relative extents of intimal surfaces involved with FS in two aortic specimens. Comparison of four autopsy series (for abbreviations and references see Fig. 4). The results are grouped according to age-classes and sexes

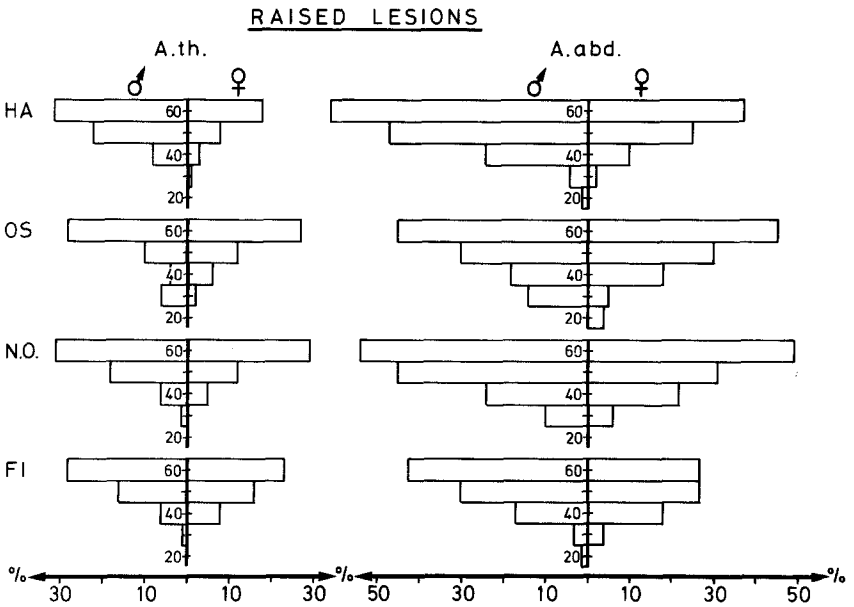

Fig. 6. Mean relative extents of intimal surfaces involved with RL in two aortic specimens. Comparison of four autopsy series (for abbreviations and references see Fig. 4). The results are grouped according to age clsses and sexes

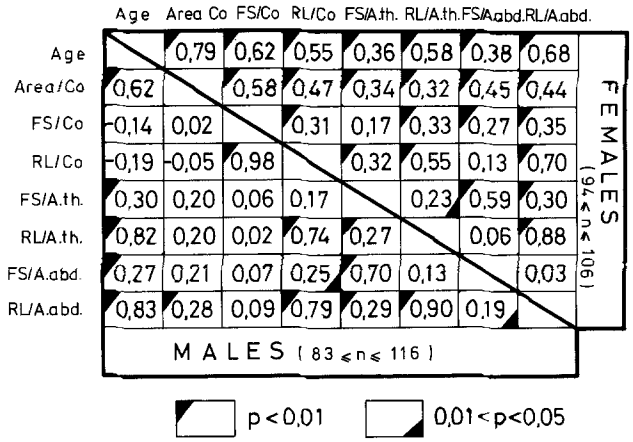

Fig. 7. Pearson correlation coefficients of various traits in males and females

Table 1. Reproduceability of the pointcounting method. Results of two independent examination series

Variables	First examination $\bar{X}/(s)$	Second examination $\bar{X}/(s)$
Aorta ($n=40$)		
NI	218.6 (40.9)	218.3 (41.0)
FS	64.2 (20.5)	65.7 (20.7)
FP	80.5 (21.9)	81.5 (22.3)
CL	8.0 (9.4)	8.0 (8.8)
Coronary arteries ($n=30$)		
NI	90.4 (67.3)	90.5 (67.2)
FS	3.9 (7.6)	3.9 (7.0)
FP	125.2 (69.7)	123.4 (69.8)
CL	1.7 (4.6)	1.8 (4.6)

Vessel Surface Areas, Heart Weights, Body Weights

Vessel surface areas (Tables 2 and 6; Figs. 2 and 3). The surface area of the coronary arteries, of both parts of the aorta and of the total aorta showed a significant increase with age in all groups of both sexes. Growth causes

Table 2. Unweighted means and standard deviations of the total intimal surfaces grouped according to age groups and sexes. Corresponding numerical designation of the decades

Age	Decade	*n*		Area (cm^2): $\bar{X}(s)$											
				A.th.		A.abd.		R		Rda		Rc		Co	
		m	f	m	f	m	f	m	f	m	f	m	f	m	f
5–14	1	8	8	34.5 (9.1)	38.9 (9.5)	20.1 (5.4)	21.5 (5.4)	2.79 (1.26)	3.71 (1.82)	3.39 (1.28)	2.95 (0.79)	1.70 (0.82)	1.15 (0.82)	7.8 (2.5)	7.81 (2.38)
15–24	2	30	18	65.6 (10.2)	61.6 (6.3)	38.8 (6.6)	34.8 (4.2)	7.27 (1.97)	5.40 (1.89)	6.18 (1.59)	4.97 (0.78)	3.04 (1.36)	2.61 (1.11)	16.5 (3.3)	12.98 (1.41)
25–34	3	19	16	85.7 (11.2)	69.3 (8.8)	51.1 (6.8)	42.2 (7.1)	8.33 (2.47)	6.99 (1.10)	7.98 (1.57)	5.86 (1.54)	3.97 (1.72)	3.12 (1.10)	20.3 (3.4)	15.97 (2.45)
35–44	4	28	19	91.6 (10.4)	77.9 (11.4)	57.9 (6.9)	47.6 (5.6)	9.60 (3.18)	7.46 (2.34)	7.85 (1.89)	7.37 (2.24)	3.97 (1.84)	4.30 (1.56)	21.3 (3.4)	19.13 (4.07)
45–54	5	19	21	93.8 (15.8)	84.8 (9.8)	64.1 (10.2)	52.3 (5.2)	9.25 (2.48)	9.90 (2.63)	7.80 (1.96)	7.32 (1.54)	3.68 (1.60)	4.52 (1.67)	20.6 (3.4)	21.75 (3.43)
55–64	6	12	24	98.8 (15.6)	100.1 (16.7)	57.3 (12.3)	58.9 (10.5)	10.38 (2.84)	9.03 (3.18)	6.86 (1.85)	7.69 (2.08)	4.51 (1.70)	4.89 (2.20)	21.7 (4.7)	21.59 (3.56)

an especially large increase in these measurements up to the age of 24. Thereafter only a small increase occurs up to the oldest age group, and neighbouring decades no longer differ significantly. One exception is the aorta in females, which shows a significant increase in surface area between the last and next-to-last decades. The first growth decade was excluded in the statistical consideration. For both sexes, the analysis of variance shows unequivocal differences between both mean values, a significant age dependence of the mean curve of both sexes and a significant difference in the age-related curve for the coronary arteries and the abdominal aorta. –

Differential study of the coronary artery branches shows that the increase in surface area is most likely to be dependent on the right coronary artery, but a significance test was not carried out because of the wide scatter of the single values. Growth and increase in weight of the arteries continues throughout life, in comparison to other body organs (Linzbach, 1959). The coronary arteries can compensate for the increased metabolic requirements of the myocardium by growth, up to a so-called critical heart weight (Linzbach, 1947). With increasing age these physiological processes are also joined by pathomorphological changes such as senile ectasia of the vessels or fibrosis of the media (Doerr, 1970), which may also play a large part in the increase in weight and surface area of the artery walls. The age group differences found by analyses of variance in this study show that in men, after the end of the physiological growth process after the age of 25, there is a relative consolidation of the increase in surface area. In women a second striking increase in growth of surface area was found in the last decade, when the total area of both aortic segments

Table 3. Means and standard deviations of heart weights and relative body weights expressed as Broca-Indices (%) in males and females at different ages

Age	*n*		Heart-weights				Broca-Indices	
			absolute/g $\bar{X}/(s)$		relative/% $\bar{X}/(s)$		$\bar{X}/(s)$	
	m	f	m	f	m	f	m	f
5–14	8	7	129 (53)	155 (60)	0.64 (0.27)	0.51 (0.07)	– –	– –
15–24	29	15	346 (57)	236 (35)	0.58 (0.26)	0.45 (0.07)	4 (16)	0.1 (20)
25–34	23	16	384 (59)	280 (61)	0.55 (0.08)	0.50 (0.12)	6 (15)	3 (20)
35–44	25	18	396 (55)	313 (40)	0.55 (0.08)	0.54 (0.10)	13 (15)	11 (23)
45–54	12	25	401 (68)	328 (54)	0.57 (0.08)	0.51 (0.07)	12 (13)	23 (22)
55–64	9	24	406 (93)	343 (57)	0.53 (0.09)	0.60 (0.15)	22 (15)	9 (19)

even exceeded those of the men. The expansion in area of the thoracic aorta was especially marked. There is an obvious conformity with the research of Rissanen (1972) and Mitchell and Schwarz (1962).

Hearth Weights (Tables 3 and 6, Fig. 1). With the exception of the growth decades there was no significant difference between the mean absolute heart weights of neighbouring decades. However, an age-dependent increase over all decades and for both sexes accurs. The total mean values related to sex show definite differences, the sex-independent mean value curve is definitely age-dependent, furthermore there is an obvious difference in both curve characteristics ("reciprocal effect", men-women). On the other hand, an age-dependence for the relative heart weights is not detectable, the analysis of variance indicates a significant sex-difference only.

Linzbach and Akuamoa-Boateng (1973) differentiate two phases of growth in the increase in mass of the heart up to the third decade. The first depends on the age-dependent increase in stroke volume, the second on an increase in blood pressure. The mean absolute and relative heart weights found in this study agree in the main with those of Linzbach and Akuamoa-Boateng, the same goes for the corresponding values of the Finnish random samples (Rissanen, 1972). An obvious correlation between heart weight and arteriosclerotic lesions under the exclusion of age influence is merely indicated in the male coronary arteries. A weak positive correlation such as this does not allow further interpretation.

Body Weights (Table 3). The Broca Indices showed a significant increase in mean weights over all age groups and in both sexes; neighbouring decades did not differ significantly. The analyses of variance for both sexes did not show any obvious differences. In the IAP study (Montenegro and Solberg, 1968) weight loss was more likely to be noted in the older age groups; the groups of various geographical and racial origins differed but slightly.

Intima Lesions

Introduction. For the macromorphological classification and quantification of the arteriosclerotic lesions, we followed the definitions of the IAP (Guzman et al., 1968) as well as comparable study groups. Therefore attempts by other authors to differentiate certain "types" or "courses" of arteriosclerosis could not be taken into account. The first synoptic studies of this type were carried out by Hueck (1920) and were continued by Ruehl (1929), with the definition of various courses ("Gangarten"). Hempel (1957) differentiates 4 types of arteriosclerosis from the purely pathological-anatomical point of view.

Most recently a subtle differentiation into two main forms and numerous subdivisions was carried out by Doerr (1976). The author uses histological criteria to differentiate numerous morphologically varying forms of the intimal lesion. In the continuation of these studies Höpker and Co-Workers (1977a, b), using qualitative and quantitative methods of investigation, managed to prove that various types of manifestation and patterns of spread of arteriosclerosis exist ("bundle pattern"), which allows a substantially more differentiated evaluation of the illnes, when considering the aetiological aspects. This study, however, is limited exclusively to macromorphological evaluation which does not allow an adequate subtyping. The main objective of our study lies in the comparison with other previously examined European populations.

Fatty Streaks (FS). Fatty streaks are observed in all age groups and in all vessel specimens. Their frequency (Table 4) increases up to the third decade and then remains nearly constant. – The *total* area of spread shows a monotonous increase with age (Table 8). On inspection of the *relative* areas (Table 5) decreases as well as increases are observed; in the male group some p-values are found to be below the 1% level (Table 8). The joint analysis of variance of both sexes shows significant sex differences between the total mean values, a significant age-dependence of the mean value curve of both sexes and significant sex differences in the curve characteristics (Table 6). Two points of interest emerge from our data. The relative extent of fatty streaks in the coronary arteries shows a striking sex difference, the female group exhibiting noticeably larger areas of this type of lesion. The male group in the same vessels only shows low figures of involvement with FS.

Comparing our data with the literature findings we may conclude: In both sexes the aortic FS lie in the lower scatter area when compared to three other autopsy series (Fig. 5). The age profiles in the same samples, however, are fairly similar within the different groups of each sex.

Table 4. Prevalence (%) of FS, FP and CL in 5 arterial specimens in males and females at different ages[a]

Age	*n*		Lesion	R		R.da		Rc.		A.th.		A.abd.	
	m	f		m	f	m	f	m	f	m	f	m	f
5–14	8	8	FS	12	–	37	28	–	–	75	50	88	63
			FP	–	–	–	–	–	–	–	–	–	–
15–24	30	18	FS	69	40	83	53	34	20	100	100	100	100
			FP	–	6	34	6	3	6	7	17	20	25
25–34	19	16	FS	91	69	96	87	74	50	100	100	100	100
			FP	39	19	52	44	30	12	16	13	53	25
35–44	28	19	FS	80	88	80	93	56	75	100	100	100	100
			FP	68	50	88	75	68	43	64	80	86	73
			CL	4	–	–	6	–	–	4	–	29	–
45–54	19	21	FS	67	100	75	100	36	80	100	100	100	100
			FP	100	84	100	96	100	60	100	86	100	95
			CL	11	–	8	4	–	6	26	14	58	29
55–64	12	24	FS	78	96	33	100	33	92	100	100	100	96
			FP	100	80	100	96	89	75	100	100	100	100
			CL	11	21	33	8	–	–	85	29	100	54

[a] Because of the relatively small samples, the percentage is to be considered as (rough) approximations

Table 5. Unweighted means of percentage of intimal surface involved with fatty streaks (FS) and raised atherosclerotiv lesions (RL) in three arterial specimens. $s_{\bar{x}}$-values are put in ( )[a]

			Co.				A.th.				A.abd.			
Age	*n*		FS		RL		FS		RL		FS		RL	
	m	f	m	f	m	f	m	f	m	f	m	f	m	f
5–14	8	8	0.3 (0.1)	0.1 (0.1)	0	0	3.3 (1.4)	1.7 (0.8)	0	0	6.5 (1.9)	5.2 (2.3)	0 –	0 –
15–24	29	18	1.2 (0.2)	0.7 (0.4)	0.2 (0.1)	0.1 (0.1)	15.3 (2.2)	9.8 (2.4)	0.1 (0.1)	0.3 (0.2)	16.9 (2.9)	18.3 (2.9)	0.5 (0.2)	0.4 (0.4)
25–34	19	16	3.3 (0.8)	3.5 (0.8)	5.5 (3.1)	1.7 (1.1)	14.1 (2.5)	9.4 (1.8)	0.3 (0.2)	0.6 (0.3)	21.4 (3.5)	18.7 (3.4)	4.0 (1.3)	1.6 (0.7)
35–44	28	19	3.3 (0.7)	4.6 (1.1)	18.3 (4.5)	4.6 (1.5)	10.8 (1.5)	13.2 (2.3)	8.1 (1.5)	2.7 (0.8)	18.5 (2.1)	25.5 (3.1)	23.7 (4.0)	10.5 (2.7)
45–54	20	21	3.3 (1.1)	12.7 (2.0)	46.2 (6.7)	10.3 (2.3)	13.8 (1.3)	18.1 (3.0)	21.1 (1.6)	8.1 (2.6)	15.9 (1.6)	22.9 (2.5)	47.4 (3.4)	24.9 (5.4)
55–64	12	24	2.9 (1.1)	14.0 (1.8)	55.6 (5.5)	16.4 (3.2)	13.7 (1.9)	9.5 (1.1)	31.3 (2.7)	17.6 (2.6)	13.4 (2.0)	15.3 (1.5)	61.4 (4.0)	36.9 (4.5)

[a] Because of the wide variation of the data we used $s_{\bar{x}}$ instead of s

Table 6. 2-way-analyses of variance[a]

Variables		Sex	Age	Interaction age with sex
Heart-w		0.001 (0.01)	0.001 (0.999)	0.018 (0.16)
Area	Co	0.001	0.001	0.008
Area	A.th.	0.001	0.001	0.071
Area	A.abd.	0.001	0.001	0.020
FS	Co	0.012 (0.006)	0.001	0.001
RL	Co	0.001	0.001	0.001
FS	A.th.	0.999 (0.318)	0.026 (0.158)	0.301 (0.053)
FS	A.abd.	0.999 (0.063)	0.013 (0.054)	0.999 (0.328)
RL	A.th.	0.001	0.001	0.001
RL	A.abd.	0.001	0.001	0.002 (0.001)

[a] Underlined *P*-values are significant on the 1% level. When available the absolute and the relative extent of variables was tested independently. When deviating of the "absolute" values, the results of the latter test are put in ( )

Table 7. Significance of correlations of Broca-Index with the absolute areas of FS and RL. Individuals under 15 years of age are eliminated. Underlined *P*-values are significant on the 1% level

Variables		*P*	
		males	females
FS	Co	0.001	0.026
RL	Co	0.002	0.008
FS	A.th.	0.001	0.005
FS	A.abd.	0.001	0.002
RL	A.th.	0.215	0.332
RL	A.abd.	0.457	0.07

For instance, in the female thoracic aortas the relative extent of FS is almost constant in all age groups (except the youngest), whereas in the abdominal aorta an even decrease can be observed over all decades. – In the male group, the coronary FS in the Hamburg sample, however, show significantly lower figures than in all other samples of Fig. 4. The average areas were in the range of 3%, whereas the other samples showed relative areas in the range of 10–13%. Only few european population samples of the IAP (McGill, 1968) were in the low range as observed here. Other aspects of low FS-areas in male coronary arteries will be discussed lateron.

Raised Lesion (RL). This type of lesion is the group name for various lesions of advanced arteriosclerosis and is composed of the FP and CL. FP, comprising

Table 8. 1-way-analyses of variance (age dependency)

Traits		P (all age groups)		Diff. (between subsets of groups) $P<0.05$	
		Males	Females	Males[a]	Females
Heart-W.	(absol.)	<0.01	<0.01	1/2–6	n.d.
Heart-W.	(relat.)	0.75	0.44	n.d.	n.d.
Co	(intimal surface)	<0.01	<0.01	1/2–6	1/2–6
Aorta	(intimal surface)	<0.01	<0.01	1/2/3–6	1/2–5/6
FS	(aerea, absol.)				
Co		<0.02	<0.01	n.d.	1–4/5–6
Aorta		<0.01	<0.01	n.d.	n.d.
RL	(aerea, absol.)				
Co		<0.01	<0.01	1–4/5–6	1–(5)/(5)–6
Aorta		<0.01	<0.01	1–3/4/5/6	1–5/6

n.d. = no significant differences

[a] Numbers indicating decades according to Table 2. Significant differences ($P<0.05$) between neighbouring age groups are marked by an oblique line

the main part of RL, are first noticed in the second decade. Their frequency rises to nearly 100% in the 5th decade and then stays constant. CL are first observed in the 4th decade and their frequency increases up to the 6th decade (Table 4). A comparison of the vessel samples shows that in the coronary arteries the right coronary artery and the anterior ventricular artery are affected with approximately the same frequency whereas the lesions occur both more rarely and later in the circumflex artery. Similar differences occur in both aortic segments (Table 4). RL (as the sum of FP and CL) occur more frequently in men than in women. – The relative areas of coronary RL show striking sex differences, the male group exhibiting figures four times larger than the females. The analysis of variance shows that significant differences in these vessels were noted earlier in men than in women, in the coronary arteries between the 4th and 5th decades (men) and in the 5th decade (women), see Table 8. In the aortic specimens, the involvement of the male groups with RL was significantly higher than in the females (Fig. 6, Table 6). Significant differences between neighbouring groups occur earlier in the male groups than in the females, this age difference being more pronounced than in the coronary specimens (Table 8). – The 2-way-analyses of variance show significant differences in the total mean values, a significant age-dependence in the mean value curve and significant differences in the curve characteristics (reciprocal effect, males – females), (see Table 6).

Comparing our figures of RL (sum of CL and FP) with the literature we may conclude: In comparison with the IAP (Tejada et al., 1968) the frequency of CL shows that in both sexes the abdominal aorta is affected most markedly.

In the coronary arteries, the anterior interventricular artery and the right coronary artery are affected earlier and more severely than the circumflex artery. The lesions are more advanced in males than in females. Quantitatively there is a definite degree of conformity with the figures from Finland (Rissanen, 1972). – Comparing the relative areas of coronary RL with three other male autopsy series of european origin we have to state that the maximal values of our series are appreciably higher (Fig. 4). It is striking that the development runs similarly until the 4th decade in the groups shown and the steep rise in the Hamburg study only becomes evident thereafter. If it is considered that the spread in surface area of FS is only relatively small in the Hamburg group, then it might be that intermediate forms were grouped together with RL more frequently than in other studies. The additive consideration of FS and RL in the oldest age group gives: 59% (Hamburg), 46% (Oslo), 40% (New Orleans), 40% (Finland). Even omitting a significance calculation this difference must be described as unequivocal. Whether the difference is due to local peculiarities or to the later date of the investigation in comparison with the IAP, must be left open.

In the 4 female groups shown, the age profiles of the coronary RL-areas were similar; in the oldest age groups the studies from Hamburg and Finland showed slight degrees of lesion, however, the differences from other geographical groups were less evident than in the male groups. The additive consideration of FS and RL made no changes in the total picture. The RL-areas in both aortic samples are very similar, both in the age-profile and also quantitatively in both sexes (Fig. 6). More evident sex-differences are merely found within the Hamburg study itself. This is due to the fact that the Hamburg male group overrrides the other male groups slightly, the female group showing a slightly smaller total surface area of involvement.

Finally, we may suggest tentatively that the low extent of coronary FS in males in the presence of extremely high figures of RL in the same group might be of etiological interest. Contrary to aortic FS it has been suggested by various authors that coronary FS are undoubtedly forerunners of arteriosclerotic lesions. This opinion is based on histological evidence of intermediary forms between FS and FP (Geer et al., 1968; McGill, 1968) and the demonstration that lipid composition in coronary arteries differs from that in the aorta (Boettcher and Woodford, 1962). The striking differences of FS and FP in our material might therefore sustain the theory of transformation.

Correlations (Table 7, Fig. 7). As all arteriosclerotic lesions showed a definite age-dependent increase, one should consider age as a separate risk factor for this disease. However, Hauss (1976) sees no risk factor in age per se, but feels that only the duration of action of sclerogenic noxa on the artery wall is of importance. The thesis that FS is always a forerunner of all further intima changes is not strongly supported by this study. After exclusion of age the correlations between FS and RL in the coronary arteries and aorta were only weakly positive and statistically non-significant; a negative correlation (decrease in FS with increase of RL) was not found. These findings give evidence that

FS can partly change into FP, but suggest that a separate pathogenetic mechanism for the development of FP exists. Sternby et al. (1965) and McGill (1968) come to similar conclusions. The development of raised lesions in the coronary arteries and in the thoracic aorta shows an age-independent positive correlation. One can also draw conclusions with a fair degree of probability on the extent of atherosclerosis in the coronary arteries from the extent of advanced atherosclerosis in the aorta and vice versa.

Our most surprising result was that a highly significant connection between overweight and the area of extent of aortic lipoidosis exists (Table 7). Similar relationships exist between overweight and coronary lipoidosis, and coronary RL. Previous investigations did not demonstrate these correlations so positively. In the IAP the connection between overweight and RL was checked and appropriate p-values were found for some populations; but no such investigations for the FS were done (Montenegro and Solberg, 1968). In another investigation the lipid value determined chemically was compared with the body weight (Giertsen, 1966). Rissanen (1975) only found similar associations between coronary and aortic FS and overweight. The relationship to coronary RL was not as pronounced, but a close correlation exists with the coronary stenosis score.

The numerous clinical and epidemiological investigations which assume a direct connection between IHD and overweight (Kannel et al., 1967; Dawber, 1976; Keys, 1970) can therefore be supplemented by the observation that adiposity has a morphological equivalent – more strongly marked arteriosclerosis. However this data must be carefully interpreted as certain atherogenic factors such as hypertension and diabetes mellitus were not considered. The connection found between overweight and coronary RL, in the absence of a correlation with aortic RL, makes it likely that coronary FS is in fact a forerunner of coronary RL unlike lipoidosis in the aorta.

Abbreviations

IAP	= International Atherosclerosis Project
A.th.	= thoracic aorta
A.abd.	= abdominal aorta
Co	= all coronary arteries
R	= right coronary artery
Rda	= anterior interventricular artery
Rc	= left circumflex artery
FS	= fatty streaks
FP	= fibrous plaques
CL	= complicated lesions
RL	= raised lesions (= the sum of FP and CL)
NI	= normal intima
m	= males
f	= females

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