

Coronary and Aortic Atherosclerosis in Chronic Alcoholics

Viljo Rissanen*

Department of Forensic Medicine, University of Helsinki, Helsinki (Finland)

Received July 19, 1974

Summary. The severity of the atherosclerotic involvement of the coronary arteries and the abdominal aorta was compared in a medico-legal autopsy series of chronic alcoholics and violent deaths. Atherosclerosis was quantitated by surface area measurements made by the point-counting technique. Coronary fatty streaks were less extensive in chronic alcoholics than in violent deaths. The extent of coronary and aortic raised lesion and the severity of coronary stenosis did not differ in medico-legally autopsied chronic alcoholics from that in persons who died of violent causes.

Zusammenfassung. Atherosklerose der Herzkranzschlagadern und der abdominalen Aorta wurde bei Alkoholikern und bei Unfalltoten in einem gerichtsmedizinischen Sektionsmaterial untersucht. Die Fetteinlagerungen in der Intima der Coronararterien waren leichter bei Alkoholikern als bei Unfalltoten. Es war keine signifikante Differenz zwischen Alkoholikern und Unfalltoten in der Stärke der Atheromatose und Coronarstenosen.

Key words: Alcoholism — Atherosclerosis, in chronic alcoholics.

Introduction

Ethyl alcohol in large quantities can produce profound metabolic and hemodynamic abnormalities in the cardiovascular system (Robin *et al.*, 1969; Gould, 1970). A well established long-term cardiac effect of alcohol is the development of alcoholic cardiomyopathy (Burch *et al.*, 1969; Bulloch *et al.*, 1972). It has been suggested that abuse of alcoholic beverages may delay the development of arterial atherosclerosis (Cowdry, 1933). The post-mortem studies on the relationship of the excessive use of alcohol to atherosclerotic involvement of the arteries have, however, led to conflicting interpretations (Creed *et al.*, 1955; Parrish *et al.*, 1961; Hirst *et al.*, 1965; Restrepo *et al.*, 1968; Sackett *et al.*, 1968; Viel *et al.*, 1968).

In the present study the atherosclerotic involvement of the coronary arteries and the abdominal aorta was compared in a medico-legal autopsy series of chronic alcoholics and violent deaths. The quantitation of the atherosclerosis was based on the measurements made by the point-counting technique (Rissanen, 1972; Rissanen and Pyörälä, 1972).

Material and Methods

The present series consisted of 39 medico-legally autopsied males from the Department of Forensic Medicine, University of Helsinki whose previous history suggested chronic excessive abuse of alcoholic beverages. The majority (28) were Skid-Row alcoholics. Patho-anatomical findings characteristic of chronic alcoholics (Ponsold, 1967) were demonstrated at the autopsy

* Present address: Second Department of Medicine, University Central Hospital, 00290 Helsinki 29, Finland. Investigation was supported by a grant from the Finnish Heart Association.

in the liver, kidneys, ventricle, respiratory tract, meninges or other organs in these males. Cirrhosis was found in only 5 men. The cause of death in 10 males was chronic alcoholism, in 10 males pneumonia, in 2 males pancreatitis, in 5 males other diseases and 12 males violent causes. The age range in this series was from 28 to 64 years.

The control series of the study comprised 145 males, aged 25 to 64 years, who had died of violent causes, as a result of an accident, suicide or homicide. Males whose previous history or autopsy findings suggested the possibility of chronic alcoholism were excluded from the control series.

In order to assess the degree of obesity, the mean values of and standard deviations from the ratio of body weight in kg to the square of height in cm $\times 10000$ (Khosla and Lowe, 1967) were calculated in the ten-year age groups of chronic alcoholics and violent deaths. The values for the chronic alcoholics were somewhat lower in all age groups.

Evaluation of Atherosclerosis

The quantitation of the severity of atherosclerosis was based on the assessment of the areas of atherosclerotic lesions by the point-counting technique from the longitudinally opened arteries. The method has been described in detail in previous papers (Rissanen, 1972; Rissanen and Pyörälä, 1972).

At the autopsy the opened main trunks of the right coronary artery, the left anterior descending coronary artery and the left circumflex coronary artery and the opened abdominal aorta from the coeliac artery to the bifurcation were dissected out, flattened on cardboard and fixed in 10% formalin. The fixed arterial specimens were stained with Sudan IV solution (Uemura *et al.*, 1964). The areas of the arterial specimens and the absolute and percentage areas of atherosclerotic lesions were assessed from the specimens using point-grids (Rissanen, 1972; Rissanen and Pyörälä, 1972). Fatty streak and raised lesion, which were defined according to the specifications given by the study group of the International Atherosclerosis Project (Guzman *et al.*, 1968), were used as parameters of atherosclerosis. *Fatty streak* is a flat intimal lesion that is stained distinctly by Sudan IV. *Raised lesion* is a firm, pale grey elevated intimal lesion which may be covered with sudanophilic material and may exhibit calcification, ulceration, haemorrhage or thrombosis. Thus raised lesion represents the total extent of advanced atherosclerosis. As shown in previous papers, the results obtained with the point-counting technique were well reproducible in both the coronary arteries and the aorta and the accuracy of the technique was comparable to that of planimetry (Rissanen, 1972; Rissanen and Pyörälä, 1972).

The degree of obstruction in the coronary arteries was evaluated using the following score:

- 0 = no stenosis;
- 1 = less than 50% stenosis;
- 2 = 50% stenosis at one site but no occlusion;
- 3 = 50% stenosis at more than one site but no occlusion;
- 4 = almost total or total occlusion at one site;
- 5 = almost total or total occlusion at more than one site, or occlusion for a distance of several centimetres.

The scores for the right coronary artery, left anterior descending coronary artery and left circumflex coronary artery were summed up to a *stenosis score* expressing the degree of obstruction in the whole coronary arterial tree. The range of this score was thus from 0 to 15. The reproducibility of the assessment of the score proved to be fairly good (Rissanen, 1972).

The statistical significance of the difference between chronic alcoholics and the control series in the variables used as estimates of atherosclerosis was tested as follows: The mean values and standard deviations denoting the extent of fatty streak and raised lesion and denoting the stenosis score were calculated for 10-year-age groups of chronic alcoholics and violent deaths. The unilateral t-test was applied to each age group. The probabilities of these mutually independent tests were combined using the formula

$$Z = - \sum_{i=1}^I 2 \ln(1-P(t_i))$$

where I is the number of tests, t_i the t value of Student's test in age group i , and $P(t_i)$ the corresponding p value. Z has a χ^2 distribution with $2 \times I$ degrees of freedom (Pearson, 1938; Fisher, 1944). In order to obtain the accurate p value for the test for each age group, these values were calculated from the t functions with relevant degrees of freedom; the p values of Z were obtained from χ^2 tables.

Results

Atherosclerosis of the Coronary Arteries

The mean weight of the heart was slightly higher in age groups of chronic alcoholics than in those of violent deaths (Table 1). There was, however, no consistent difference between chronic alcoholics and control persons in the total area of the specimens of the right coronary artery, left anterior descending coronary artery and left circumflex coronary artery (Table 1). The mean area of fatty streak was in coronary arteries smaller in all age groups of chronic alcoholics than in age groups of violent deaths (Table 2). The difference was significant ($P < .01$). No consistent or significant difference was found between chronic alcoholics and violent deaths in the absolute area of raised lesion (Table 2). The mean value of stenosis score was higher in the three oldest age groups of chronic alcoholics than in the corresponding age groups of the control series (Table 3). The difference between the two series was, however, small and did not attain the level of statistical significance.

Table 1. Mean values and standard deviations for the heart weight (Gr) and the total area of the coronary arteries (sq. cm) in age groups of chronic alcoholics and violent deaths

Age	Chronic alcoholics					Violent deaths				
	No. of cases	heart weight		area of coronary arteries		No. of cases	heart weight		area of coronary arteries	
		mean	s.d.	mean	s.d.		mean	s.d.	mean	s.d.
25—34	3	390	78	21.41	3.40	38	365	51	18.61	4.86
35—44	9	423	23	21.60	4.62	39	395	47	22.58	5.29
45—54	18	412	73	24.85	7.68	30	408	84	23.38	5.92
55—64	9	442	95	21.35	6.46	38	424	77	22.60	6.77

Table 2. Mean values and standard deviations for the absolute area (sq. cm) of fatty streak and raised lesion in the coronary arteries of chronic alcoholics and violent deaths by age

AGE	Chronic alcoholics					Violent deaths				
	No. of cases	fatty streak		raised lesion		No. of cases	fatty streak		raised lesion	
		mean	s.d.	mean	s.d.		mean	s.d.	mean	s.d.
25—34	3	1.06	0.33	0.89	0.43	38	1.59	1.80	0.76	1.13
35—44	9	2.34	1.73	3.76	2.76	39	2.90	2.30	2.71	2.28
45—54	18	1.94	1.48	5.36	4.68	30	2.93	1.92	5.70	3.79
55—64	9	1.65	0.76	8.40	4.88	38	2.54	2.26	6.31	4.35

Table 3. Mean values and standard deviations for stenosis score (range 0 to 15) of the coronary arteries in age groups of chronic alcoholics and violent deaths

Age	Chronic alcoholics			Violent deaths		
	No. of cases	mean	s.d.	No. of cases	mean	s.d.
25—34	3	0.7	0.5	38	0.7	0.9
35—44	9	2.7	1.4	39	1.9	1.2
45—54	18	3.8	3.2	30	3.2	2.0
55—64	9	6.2	4.2	38	4.6	3.1

Table 4. Mean values and standard deviations for the area of the abdominal aorta (sq. cm) in age groups of chronic alcoholics and violent deaths

Age	Chronic alcoholics			Violent deaths		
	No. of cases	mean	s.d.	No. of cases	mean	s.d.
25—34	3	45.8	6.5	38	42.2	5.7
35—44	9	53.1	6.0	39	49.6	6.6
45—54	18	55.4	6.0	30	58.2	9.8
55—64	9	62.3	9.6	38	62.1	9.8

Table 5. Mean values and standard deviations for the absolute area (sq. cm) of fatty streak and raised lesion in the abdominal aorta of chronic alcoholics and violent deaths by age

Age	Chronic alcoholics					Violent deaths				
	No. of cases	fatty streak		raised lesion		No. of cases	fatty streak		raised lesion	
		mean	s.d.	mean	s.d.		mean	s.d.	mean	s.d.
25—34	3	9.80	5.45	2.34	2.58	38	13.86	6.67	1.36	3.00
35—44	9	12.94	8.94	10.17	9.91	39	14.07	8.40	8.20	8.56
45—54	18	11.10	6.88	20.30	15.12	30	12.51	7.48	18.70	13.68
55—64	9	12.39	6.47	25.61	13.21	38	11.03	5.78	28.35	14.63

Atherosclerosis of the Abdominal Aorta

There was no consistent difference between chronic alcoholics and violent deaths in the mean area of aortic specimens (Table 4). The mean extent of aortic fatty streak was smaller in the three youngest age groups of chronic alcoholics than in the corresponding age groups of violent deaths (Table 5). In the same age groups the area of raised lesion was higher in chronic alcoholics than in the controls (Table 5). In the oldest age group, however, the direction of the difference was opposite. The difference between chronic alcoholics and violent deaths was not statistically significant with regard to either of these parameters of aortic atherosclerosis.

Discussion

The point-counting technique which was applied in the present study for the quantitative assessment of atherosclerosis enables reliable comparisons with regard to the severity of arterial atherosclerosis (Mitchell and Cranston, 1965; Rissanen, 1972; Rissanen and Pyörälä, 1972). When the significance of the results is interpreted, the most important source of bias is obviously the selective composition of autopsy materials. This problem has been discussed by many authors (Mainland, 1953; McMahan, 1962; Sternby, 1968; Rissanen, 1972). There is considerable consensus that persons dying of violent causes constitute the best possible cross-sectional sample of population for the study of atherosclerosis (Strong and McGill, 1962; Sternby, 1968; Vihert *et al.*, 1970). Violent deaths may thus best represent the situation in the general population, which is the logical control when the relationship between certain factors and atherosclerosis is investigated. It is evident that the population of chronic alcoholics which is studied postmortem is always highly selected, representing extreme stages of alcoholism. The majority of the present cases were Skid-Row alcoholics, comprising a sample of asocial population which mainly includes persons originating from the lower social classes. Historical information concerning the duration and degree of alcoholism is in these persons either unavailable or recorded in nonstandardized fashion. Some authors have studied the relationship between alcoholism and atherosclerosis in a series of cirrhotic patients (Creed *et al.*, 1955; Restrepo *et al.*, 1968). The selection of the material in this way may be fallacious if chronic alcoholism is the object of the study. The prevalence of cirrhosis was rather low in the present series.

The present chronic alcoholics did not differ with regard to the severity of advanced coronary and aortic atherosclerosis from persons who died of violent causes. Negative association of the severity of the atherosclerotic involvement of coronary arteries with chronic alcoholism or cirrhosis has been reported in a few other surveys in which the severity of arterial lesions has been estimated (Parrish and Eberly, 1961; Restrepo *et al.*, 1968; Viel *et al.*, 1968). Negative association has been shown also between aortic atherosclerosis and alcoholism (Restrepo *et al.*, 1968; Sackett *et al.*, 1968). The series of Viel *et al.* consisted of persons who died of violent causes. The other above-mentioned studies have been based on hospital materials. In comparing persons with "chronic excessive alcoholism" with "total abstainers and moderate consumers of alcohol" studied at autopsy, Wilens (1947) noted considerably less "generalized atherosclerosis" in the former than in the latter. Decreased prevalence of coronary lesions in patients with portal cirrhosis as compared with autopsied persons in whom no cirrhosis was found, was observed by Hall *et al.* (1953). Creed *et al.* (1955) have concluded that males with Lannec's cirrhosis had significantly less severe aortic involvement of atherosclerosis than was found in the control series. Hirst *et al.* (1965) compared the extent of intimal atheroma among chronic alcoholics without cirrhosis and cirrhotics with or without alcoholism with the control series of other autopsied persons. They concluded that patients with cirrhosis showed some "immunity" to atherosclerosis that was not shared by subjects who had chronic alcoholism without cirrhosis. Decreased incidence of myocardial infarction or coronary heart disease in patients with cirrhosis has also been reported (MacDonald *et al.*, 1958;

Grant *et al.*, 1959; Howell *et al.*, 1960). It may, however, be dangerous to study in autopsy material the association of two diseases of severe prognosis (Viel *et al.*, 1968).

Malnutrition is often associated with chronic alcoholism. The present chronic alcoholics were indeed somewhat thinner than males who died of violent causes. Metabolic derangements resulting from alcoholism and malnutrition may cause sudden death and degenerative changes in the myocardium (Nevins *et al.*, 1972). It has been suggested that extensive wasting may be responsible for the reversal of atherosclerotic lesions (Wilens, 1947; Eilersen *et al.*, 1960). Sackett *et al.* (1968) have discussed that the wasting secondary to excessive alcohol intake may explain the decreased severity of arterial involvement that has been found in a few surveys in patients with chronic alcoholism or cirrhosis of the liver. It is possible that the tendency to less extensive fatty streaks which was found in the coronary arteries of the present chronic alcoholics as compared with violent deaths was a reflection of malnutrition in these persons. Although the males in the series of chronic alcoholics were somewhat thinner than those in the series of violent deaths there was no difference between these two series in the extent of advanced atherosclerotic lesions, raised lesions or in the severity of coronary stenosis. This is in agreement with the results of several studies which have shown that the degree of obesity is not related to the severity of coronary and aortic atherosclerosis (Giertsens, 1966; Montenegro and Solberg, 1968; Sternby, 1968).

The present results give grounds for a conclusion that in the population of chronic alcoholics which comes to medico-legal autopsy the severity of coronary and aortic atherosclerosis does not differ from that in the general population.

References

- Bulloch, R. T., Pearce, M. B., Murphy, M. L., Jenkins, B. J., Davis, J. L.: Myocardial lesions in idiopathic and alcoholic cardiomyopathy. Study by ventricular septal biopsy. *Amer. J. Cardiol.* **29**, 15 (1972)
- Burch, G. E., DePasquale, N. P.: Alcoholic cardiomyopathy. *Amer. J. Cardiol.* **23**, 723 (1969)
- Cowdry, E. V.: Arteriosclerosis. New York: The MacMillan Co., Publ. 1933
- Creed, D. L., Baird, W. F., Fisher, E. R.: The severity of aortic arteriosclerosis in certain diseases. A necropsy study. *Amer. J. med. Sci.* **230**, 385 (1955)
- Eilersen, P., Faber, M.: Human aorta VI. Regression of atherosclerosis in pulmonary tuberculosis. *Arch. Path.* **70**, 103 (1960)
- Fisher, R. A.: Statistical methods for research workers, § 21.1. Edinburgh: Oliver and Boyd 1944
- Giertsens, J. C.: Atherosclerosis in an autopsy series. X. Relation of nutritional state to atherosclerosis. XI. General summary and conclusions. *Acta path. microbiol. scand. Sect. A* **67**, 305 (1966)
- Gould, L.: Cardiac effects of alcohol. *Amer. Heart J.* **79**, 422 (1970)
- Grant, W. C., Wasserman, F., Rodensky, P. L., Thomson, R. V.: The incidence of myocardial infarction in portal cirrhosis. *Ann. intern. Med.* **51**, 774 (1959)
- Guzman, M. A., McMahan, C. A., McGill, H. C., Jr., Strong, J. P., Tejada, C., Restrepo, C., Eggen, D. A., Robertson, W. B., Solberg, L. A.: Selected methodologic aspects of the International Atherosclerosis Project. *Lab. Invest.* **18**, 479 (1968)
- Hall, E. M., Olsen, A. Y., Davis, F. E.: Portal cirrhosis. *Amer. J. Path.* **29**, 993 (1953)
- Hirst, A. E., Hadley, G. G., Gore, I.: The effect of chronic alcoholism and cirrhosis of the liver on atherosclerosis. *Amer. J. med. Sci.* **249**, 143 (1965)

- Howell, W. L., Manion, W. C.: The low incidence of myocardial infarction in patients with portal cirrhosis of the liver. A review of 639 cases of cirrhosis of the liver from 17,731 autopsies. *Amer. Heart J.* **60**, 341 (1960)
- Khosla, T., Lowe, C. R.: Indices of obesity derived from body weight and height. *Brit. J. prev. soc. Med.* **21**, 122 (1967)
- MacDonald, R. A., Mallory, G. K.: The natural history of postnecrotic cirrhosis. A study of 221 autopsy cases. *Amer. J. Med.* **24**, 334 (1958)
- Mainland, D.: The risk of fallacious conclusions from autopsy data on the incidence of diseases with applications to heart disease. *Amer. Heart J.* **45**, 644 (1953)
- McMahan, C. A.: Age-sex distributions of selected groups of human autopsied cases. *Arch. Path.* **73**, 40 (1962)
- Mitchell, J. R. A., Cranston, W. I.: A simple method for the quantitative assessment of aortic disease. *J. Atheroscler. Res.* **5**, 135 (1965)
- Montenegro, M. R., Solberg, L. A.: Obesity, body weight, body length, and atherosclerosis. *Lab. Invest.* **18**, 594 (1968)
- Nevins, M. A., Lyon, L. J.: Sudden death and metabolic derangement in alcoholism with malnutrition. *J. med. Soc. N. J.* **69**, 155 (1972)
- Parrish, H. M., Eberly, A. L., Jr.: Negative association of coronary atherosclerosis with liver cirrhosis and chronic alcoholism — a statistical fallacy. *J. Indiana med. Ass.* **54**, 341 (1961)
- Pearson, E. S.: The probability integral transformation for testing goodness of fit and combining independent tests of significance. *Biometrika* **30**, 134 (1938)
- Ponsold, A.: *Lehrbuch der gerichtlichen Medizin*. Stuttgart: Thieme 1967
- Restrepo, C., Montenegro, M. R., Solberg, L. A.: Atherosclerosis in persons with selected diseases. *Lab. Invest.* **18**, 552 (1968)
- Rissanen, V.: Aortic and coronary atherosclerosis in a Finnish autopsy series of violent deaths. *Ann. Acad. Sci. fenn. A* **5**, 155 (1972)
- Rissanen, V., Pyörälä, K.: Application of point-counting technique to the quantitative assessment of coronary and aortic atherosclerosis. *Acta path. microbiol. scand. Sect. A* **80**, 412 (1972)
- Robin, E., Ravens, K. G., Bing, R. J.: Die Wirkung von Alkohol, Nikotin und Zigarettenrauchen auf das Herz. *Dtsch. med. J.* **20**, 19 (1969)
- Sackett, D. L., Gibson, R. W., Bross, I. D. J., Pickren, J. W.: Relation between aortic atherosclerosis and the use of cigarettes and alcohol. An autopsy study. *New Engl. J. Med.* **279**, 1413 (1968)
- Sternby, N. H.: Atherosclerosis in a defined population. An autopsy survey in Malmö, Sweden. *Acta path. microbiol. scand. Sect. A, Suppl.* **194** (1968)
- Strong, J. P., McGill, Jr., H. C.: The natural history of coronary atherosclerosis. *Amer. J. Path.* **40**, 37 (1962)
- Uemura, K., Sternby, N. H., Vanecek, R., Vihert, A., Kagan, A.: Grading atherosclerosis in aorta and coronary arteries obtained at autopsy. Application of a tested method. *Bull. Wld Hlth Org.* **31**, 297 (1964)
- Viel, B., Donoso, S., Salcedo, D.: Coronary atherosclerosis in persons dying violently. *Arch. intern. Med.* **122**, 97 (1968)
- Vihert, A. M., Zhdanov, V. S., Matova, E. E.: Dynamics of the development of atherosclerosis alterations in the aorta and coronary arteries in practically healthy men. *Arkh. Pat.* **32**, 44 (1970)
- Wilens, S. L.: Relationship of chronic alcoholism to atherosclerosis. *J. Amer. med. Ass.* **135**, 1136 (1947)
- Wilens, S. L.: Resorption of arterial atheromatous deposits in wasting disease. *Amer. J. Path.* **23**, 793 (1947)

Dr. Viljo Rissanen
 Department of Forensic Medicine
 University of Helsinki
 SF-00170 Helsinki 17, Snellmaninkatu 10
 Finland