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HISTOMORPHOMETRIC PARAMETERS OF THE CARDIAC CONDUCTION SYSTEM AND THE MYOCARDIUM: CORRELATING RESULTS OF POSTMORTEM FORENSIC ANALYSIS ON ALCOHOLIC CARDIOMYOPATHY AND CORONARY HEART DISEASE

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ABSTRACT — The article presents results of a study on the correlation of histomorphometric parameters of the heart in case of death from alcoholic cardiomyopathy (ACM), ischemic heart disease (IHD) and mechanical injury (control group) by the method of correlation analysis. The previous studies show that normally with age, the myocardium of the sinoatrial node (SAN) is most worn out and fibrosed. In case of IHD the His bundles are most worn out and fibrosed. In case of ACM, histomorphological changes are uniform in all areas of the myocardium. This indicator can be used in practice when providing differential diagnosis of the above-described types of pathology and causes of death. In addition, the results of our study confirm that myocardial lipomatosis is more typical of ACM, which increases its diagnostic value.

KEYWORDS — cardiac conduction system, alcoholic cardiomyopathy, ischemic heart disease, forensic histology, correlation analysis.

INTRODUCTION

Differential diagnosis of various diseases in order to establish the cause of death is an important issue of pathological anatomy and forensic pathology. Currently, a lot of individual signs and their complexes that are observed for various causes of death have been described, but only a few of them are absolutely specific [5].The signs of one pathological condition often differ from the signs of another, not in character, but only in the frequency of their occurrence and the degree of their severity. This greatly complicates the establishment of the cause of death during the autopsy and histological examination [4].

One of the methods to solve this problem is to assess the severity of a diagnostic signs. In order to increase the objectivity of the result it is advisable to use the morphometric method. To increase the reliability of the results, the data from other research methods, for example, biochemical and immunohistochemical are used [3–5].

According to modern scientific methodology, a systematic approach is considered to be optimal for differential diagnostics [3]. A system is most often understood as a set of elements that are related to each other, therefore the essence of the system approach is the real or mental division of the studied object into its parts and the study of these parts, their interaction and the behavior of the whole system in general [2, 7]. There are also functional systems, where the interaction of their parts is subordinated to certain functions. The systems of the body in normal condition have been studied for a long time, but in pathology their structure and behavior, as well as the properties and interaction of their elements, change in different ways in different nosological forms. Sometimes the very set of pathological processes is considered to be a system, since the processes are also related to each other [3]. In practice, first of all this is achieved, through a mathematical study of the relationships (correlations) between the measured parameters of the system as whole and its elements. Therefore, the first and main mathematical tool of systems analysis of pathology is correlation analysis, and then other mathematical research methods should be chosen based on its results [7].

Aims

We aimed to study the correlation between the micromorphological parameters characteristic of

death from ischemic heart disease (IHD), alcohol cardiomyopathy (ACM) and mechanical injury (control group) and to use these data for more objectivity in diagnosis of these causes of death in accordance with the requirements of evidence-based medicine.

The study of the age dynamics of the studied parameters was of particular interest, since it is impossible to estimate it by the methods of descriptive statistics or by comparing the groups. One can only compare different age intervals, which is methodologically incorrect, because the parameters do not change *in leaps*. Only correlation analysis makes it possible to investigate age dynamics [6].

MATERIAL AND METHODS

105 cases were performed (for detailed characteristics, see Table 1). The diagnosis of IHD or ACM was established by macro- and micromorphological signs. For the control group we selected cases of rapid death from mechanical trauma in the absence of signs of IHD, ACM and cardiac trauma.

Table 1. *Characteristics of the studied materials*

Cause of death	IHD	ACM	Trauma
Age	35–85 years old	29–58 years old	18–28 years old
Ethanol in blood	0‰	0,5–1,0‰	0‰
Ethanol in urine	0‰	0,3–1,5‰	0‰
Number of cases	41 (women – 14, men – 27)	40 (women – 8, men – 32)	24 (men – 22, women – 2)
Total	105 cases		

The sinoatrial node (SA or SAN) was singled out according to the generally accepted method [1], and a sample of the myocardium was also taken from the interventricular septum and His bundles. Standard histological and computerized histostereometric studies of these structures were carried out.

The following parameters were measured in all the structures:

1) the diameter of 10 cardiomyocytes in 3 fields of vision in each section at x400 magnification, then the average diameter of the cardiomyocyte in the structure was calculated;

2) the average area of connective tissue structures (fibrosis) outside the areas of postinfarction cardiosclerosis in 3 fields of vision at x400 magnification (area of fibrosis in 3 fields of view/total area of 3 fields of view);

3) the average area of lipomatosis in 3 fields of vision at x400magnification (area of lipomatosis in 3 fields of view/total area of 3 fields of view).

At the first stage, the statistical processing of the data was carried out using the methods of descriptive statistics. Then the closeness of the distribution of each parameter to normal was determined using the indices of asymmetry and kurtosis, as well as by comparing the mode, median and arithmetic mean. The distribution of all the studied parameters was close to normal; therefore, at the final stage, we used the calculation of the parametric correlation coefficients according to Pearson [6].

RESULTS AND DISCUSSION

The obtained correlation coefficients between the studied parameters are presented in Table 2.

In case of death from trauma (conditional norm), no strong correlation was found between any of the studied parameters. A positive correlation of average strength was noted for the following pairs of parameters: the share of fibrosis in the SAN and the share of lipomatosis in the SAN; the proportion of fibrosis in the contractile myocardium and the share of lipomatosis in it; the share of fibrosis in the contractile myocardium and the share of SAN lipomatosis. In addition, the share of lipomatosis in the contractile myocardium was found to be related with the share of lipomatosis of the SAN and His bundle. When comparing these data with the information about the average values of these parameters, it becomes clear that fibrosis and lipomatosis of the myocardium of different departments are normally insignificant, especially in the area of the His bundle, and tend to grow in parallel to each other. Meanwhile, lipomatosis grows evenly in all departments. This is probably due to the early forms of cardiac pathology, which are usually not yet recorded during routine histological examination.

The proportion of SAN lipomatosis is related with the average diameter of the cardiomyocyte in His bundle. This possibly reflects compensatory hypertrophy of cardiomyocytes of the underlying parts of the conducting system during structural changes in the SAN that can disturb its function. Then it implies that lipomatosis disturbs the function of the elements of the conducting system more severely than fibrosis, which is understandable taking into account the pronounced dielectric properties of adipose tissue. There were no other correlations of the average diameter of the cardiomyocyte in the studied sections with other parameters.

With age, only the share of fibrosis in the SAN and the average diameter of the cardiomyocyte increases.

In case of ACM, the picture is completely different. Most of the parameters correlate with each other moderately or strongly, all the correlations are positive.

Table 2. *Correlation coefficients between the studied parameters*

Parameter	Parameter	ACM	IHD	Trauma
Age	Mean diameter of CMC of SAN	-0,01915	-0,07705	0,56015
Age	Mean diameter of CMC of IVS	-0,1837	-0,12895	0,068338
Age	Mean diameter of CMC of HB	-0,10855	-0,31091	0,189366
Age	Share of fibrosis of SAN	0,577441	-0,0131	0,440411
Age	Share of fibrosis of CM	0,401407	-0,22162	-0,08205
Age	Share of fibrosis of HB	0,55489	0,336179	0,099953
Age	Share of lipomatosis of SAN	0,514922	-0,33163	0,098228
Age	Share of lipomatosis of CM	0,694397	-0,41735	0,086459
Age	Share of lipomatosis of HB	0,44691	-0,36281	0,076928
Mean diameter of CMC of SAN	Mean diameter of CMC of IVS	0,432466	0,135603	0,213257
Mean diameter of CMC of SAN	Mean diameter of CMC of HB	0,624463	0,438395	0,092965
Mean diameter of CMC of SAN	Share of SAN fibrosis	0,06973	0,342186	0,289918
Mean diameter of CMC of SAN	Share of CM fibrosis	0,233645	0,033839	-0,22381
Mean diameter of CMC of SAN	Share of HB fibrosis	0,132708	-0,09977	0,104599
Mean diameter of CMC of SAN	Share of SAN lipomatosis	-0,16196	0,068105	0,165477
Mean diameter of CMC of SAN	Share of CM lipomatosis	0,003739	0,062196	-0,02811
Mean diameter of CMC of SAN	Share of HB lipomatosis	0,008463	0,290362	0,181051
Mean diameter of CMC of IVS	Mean diameter of CMC of HB	0,520119	0,272227	0,229797
Mean diameter of CMC of IVS	Share of SAN fibrosis	-0,10524	-0,11804	0,186659
Mean diameter of CMC of IVS	Share of CM fibrosis	0,06376	0,059361	-0,10747
Mean diameter of CMC of IVS	Share of HB fibrosis	-0,30426	-0,2468	0,003386
Mean diameter of CMC of IVS	Share of SAN lipomatosis	-0,27271	0,130516	-0,11304
Mean diameter of CMC of IVS	Share of CM lipomatosis	-0,17088	0,318842	0,159252
Mean diameter of CMC of IVS	Share of HB lipomatosis	-0,06361	0,170291	0,053979
Mean diameter of CMC of HB	Share of SAN fibrosis	-0,23683	0,092784	0,356616
Mean diameter of CMC of HB	Share of CM fibrosis	0,046677	0,377867	0,354733
Mean diameter of CMC of HB	Share of HB fibrosis	-0,17172	0,022028	-0,38942
Mean diameter of CMC of HB	Share of SAN lipomatosis	-0,26734	-0,11221	0,502604
Mean diameter of CMC of HB	Share of CM lipomatosis	-0,13138	0,188885	0,339385
Mean diameter of CMC of HB	Share of HB lipomatosis	0,014732	0,235344	0,096292
Share of SAN fibrosis	Share of CM fibrosis	0,706444	0,438847	0,08339
Share of SAN fibrosis	Share of HB fibrosis	0,707119	0,337486	0,189159
Share of SAN fibrosis	Share of SAN lipomatosis	0,218152	-0,08301	0,370806
Share of SAN fibrosis	Share of CM lipomatosis	0,435002	-0,09602	0,012553
Share of SAN fibrosis	Share of HB lipomatosis	0,074173	0,170852	0,151901
Share of CM fibrosis	Share of HB fibrosis	0,634753	0,276595	-0,30082
Share of CM fibrosis	Share of SAN lipomatosis	-0,09279	-0,08896	0,536248
Share of CM fibrosis	Share of CM lipomatosis	0,348407	0,080652	0,466173
Share of CM fibrosis	Share of HB lipomatosis	-0,10567	0,123727	0,259238
Share of HB fibrosis	Share of SAN lipomatosis	0,262653	-0,17877	-0,04005
Share of HB fibrosis	Share of CM lipomatosis	0,436198	-0,47464	-0,13218
Share of HB fibrosis	Share of HB lipomatosis	0,182928	-0,39382	0,062725
Share of SAN lipomatosis	Share of CM lipomatosis	0,685566	0,513181	0,370733
Share of SAN lipomatosis	Share of HB lipomatosis	0,509615	0,485938	0,221327
Share of CM lipomatosis	Share of HB lipomatosis	0,499242	0,669926	0,533854

Note: *CM — cardiomyocytes, IVS — interventricular septum, CM — contractile myocardium, HB — His bundle; bold type indicates correlation coefficients from 0.3 to 0.6, bold type and italics indicate strong correlation (more than 0.6).*

In case of ACM the share of fibrosis and lipomatosis increase in all the studied areas, especially the proportion of lipomatosis of the contractile myocardium with age (the correlation with age is strong). It is quite natural that in this case they all correlate with each other, especially the share of lipomatosis in the SAN and the contractile myocardium (strong correlation). In particular, the shares of fibrosis in all departments are related with each other, and this correlation is also strong. There is a correlation between the share of lipomatosis of the contractile myocardium with the share of fibrosis in all three sections, but the correlation between the proportion of fibrosis and lipomatosis of the contractile myocardium is weak. In addition, the mean diameters of cardiomyocytes in all three areas, especially in the SAN and the His bundle, correlate with each other.

These data reflect the dynamics of myocardial reactions to the toxic effect of alcohol and its metabolites. These substances are capable of affecting both the vascular bed and the parenchymal elements of the heart. They reduce the value of each parameter separately (parameters that correlate with each other are considered uninformative), while not changing their differential diagnostic role in each particular case. If fibrosis, lipomatosis, and changes in the diameter of cardiomyocytes are significant and affect uniformly both the conductive and contractile myocardium, this is an argument in favor of the diagnosis of ACM.

At death from IHD, in contrast to the results described above, many correlation coefficients are negative. Particularly, only the share of fibrosis of the His bundle increases. At the same time the average diameter of the cardiomyocyte in the same area and the share of lipomatosis in all studied areas, decrease with age. In this case, the share of lipomatosis in different areas correlate with each other positively. There is also a positive relationship of average strength between the share of fibrosis of the SAN and the share of fibrosis in other departments. This result seems paradoxical, because IHD is a typical age-related disease, and pathological changes in it should increase with age. However, the facts have an explanation that is important for practical needs. Diffuse fibrosis affecting the conducting system, and lipomatosis, are not the characteristic signs for the most common forms of coronary artery disease and are caused by other reasons. Therefore they do not have positive age-related dynamics, and are also little related to each other. For ischemic heart disease, according to the data obtained, a typical predominant violation of the His bundle is typical, and the share of fibrosis of the His bundle correlates inversely with the proportions of lipomatosis of the same area and contractile myocardium. It is fibrosis, not lipomatosis, that is characteristic of IHD, which is understandable, given the metabolic characteristics of alcoholic intoxication in comparison with ischemic heart disease. The share of fibrosis of the His bundle in IHD increases with age in response to atrophy and death of cardiomyocytes. Therefore, the average diameter of cardiomyocytes in this area decreases with age. And, finally, there is a positive relationship of average strength between the average diameters of cardiomyocytes in the bundle of His and in the SAN, which obviously reflects compensatory hypertrophy of less damaged parts of the conducting system.

CONCLUSION

Thus, the correlation analysis of the histomorphometric parameters of the heart helped to establish that normally, with age, the myocardium of the SAN is worn out and fibrosized most. In case of IHD the His bundles are most worn out and fibrosed. In case ACM, histomorphological changes are uniform in all areas of myocardium. This conclusion is not only of theoretical significance, it can be used in practice in the differential diagnosis of these causes of death. In addition, our data confirm that among the causes of death studied, myocardial lipomatosis is typical only of ACM, which increases its diagnostic value.

From a thanatogenetic point of view, our data make it possible to explain the mechanisms of death of elderly people with insignificant alcohol intoxication with ACM or with coronary artery disease through edema of worn-out structures of the conducting system, associated with both hemodynamic and toxic damaging factors.

REFERENCES

1. **Bogomolova I. N., Saperovskaya V. E., Orlovskaya A.V.** Application of the Bayes-Wald-Gubler method for differential diagnosis of causes of death at low ambient temperature. Sudebnaya meditsina. 2015; 58(1):44–48 [In Russ.]
2. **Bogomolova I. N., Bogomolov D. V., Perepelkin A.V., Saperovskaya V. E., Orlovskaya A.V.** Microscopic differential diagnostic signs of fatal cold injury. Methodical recommendation. – M. – Federal state budgetary institution "RCSME of the Ministry of health and social development of Russia". 2014. – 26 p. [In Russ.].
3. Madea, Burkhard. Injuries due to Cold. In book: Handbook of Forensic Medicine. 2014: pp. 468–476. DOI: 10.1002/9781118570654.ch23.
4. **Bogomolova I. N.** The role of a systematic approach in establishing a forensic histological diagnosis. Sudebnaya meditsina. 2014; 57(5): 7–12 [In Russ.].
5. **Dettmeyer R.B.** Forensic–Histological Diagnosis of Species, Gender, Age, and Identity. In: Forensic

Histopathology. Springer, Cham. 2018. – pp. 289–230 DOI: 10.1007/978-3-319-77997-3_12

6. **Dorandeu A., de la Grandmaison G.L., Coulibaly B., Durigon M., Piercecchi-Marti M.D., Baccino E., Leonetti G.** Value of histological study in the fronto-sphenoidal suture for the age estimation at the time of death. Forensic Sci Int 2009; 191:64–69. DOI: 10.1016/j.forsciint.2009.06.010
7. **Avtandilov G.G.** Fundamentals of pathoanatomic practice. M: RMAPO 1998; 115–117 [In Russ.].
8. **Antonov, A.V.** System analysis. Students book for universities – M.: Higher school, 2004. – 454 p. [In Russ.].
9. **Glants S.** Medico-biological statistics. Translated from English. – M. Practice. 1998; 459 p. [In Russ].
10. **Slavin M. B.** Methods of system analysis in medical research. – Moscow. – Medicine. 1989. – 304 p. [In Russ.].