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Application of Symbolic Logic to the Morphometric Study of Coronary Diabetic Microangiopathy

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In order to investigate the involvement of the small intramyocardial arteries in diabetic cardiomyopathy we used histopathologic and morphometric methods. The quantitative analysis was made on 25 diabetic hearts and on a control group of 7 cases. The small arteries of diabetic heart showed following aspects: decreased density/mm^2, increased thickness of arterial wall and perivascular fibrosis. The literature data on the coronarian bed damage in diabetes are numerous and partly contradictory. To work-up an unitary and self-consting model of diabetic heart,we used the symbolic logic language; the computer analysis was based on the Quine-Mc Cluskey decision method. The final model of the literature data supported the hypothesis of a coronary diabetic microangiopathy.

Diabetics have an increased risk of cardiovascular morbidity and mortality (Kannel & Mc Gee:1979) and a high incidence of cardiogenic shock and congestive heart failure with or without myocardial infarct (Dai Rui-Hong et al:1982). The development of the cardiomyopathy in diabetes has been attributed on the one hand to the severe occlusive atherosclerosis of the extramural coronary arteries (Crall & Roberts:1978, Boucher et al:1979).On the other hand epidemiological data from the Framingham study indicated that the diabetic heart disease may be due to small vessel disease in the myocardium. This point of view was supported by the histopathological picture of the heart microvasculature in diabetes (Blumenthal et al:196o, Hamby et al:1974, Zoneraich & Silverman:1978, Gherasim et al:1985, Ledet:1968, 1976, Taşcă et al:1985 b). Moreover, Factor et al.(198o)described capillary and arteriolar microanevrisma in the diabetic hearts analogous with those in the retina and renal glomerulus.

Therefore, the morphological data accumulated in the field of the pathogenesis of diabetic heart disease are numerous and partly contradictory. To incorporate information of this nature into an unitary and self-consisting model of diabetic heart,we used the language of symbolic logic (Moore et al:1977, Riede et al:1979, Taşcă et al:1985a).A formal statement was attached to each study and the final model was elaborated after the computer analysis based on the Quine-Mc Cluskey decision method. This model was compared with the results of our morphometric study on

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25 diabetic hearts.

MATERIAL AND METHODS

The quantitative morphometrical analysis was made on 25 diabetic hearts and on a control group of 7 cases.

Following morphometrical parameters were investigated: arteries number/mm^2, arterial diameter and arterial wall thickness.

The morphometrical method was made by previously described techniques (Gherasim et al.1985).

In order to investigate our morphometrical data we used the symbolic logic which is a decision method on the truth value of a statement. The first step in using symbolic logic in order to obtain a self-consisting model of diabetic heart morphology is the translation of the essential data from natural into a formal language.

Seven parameters were analysed in 25 studies and each parameter was represented by a symbol:

- permeable coronaries	C_p
- arterial(section) area - increased	AA_I
- arterial(section) area - decreased	AA_D
- arterial wall thickening	AT
- endothelial proliferation	E
- arterial microanevrysma	A
- interstitial fibrosis	F

The symbols were assembled in logic statements by operators:

"and"(&); if P,Q are statements, P & Q is true only if both P and Q are true.

"or"(.); statement P . Q is true if and only if either P or Q are true (or both).

"negation"(-); $\overline{P}$ is true when P is false and vice versa.

"implication" ($\longrightarrow$); P $\longrightarrow$ Q is true if and only if whenever P is true, Q is true.

We attached a logic statement to each study on the diabetic heart structure. For a normal heart the statement is:

$$C_p \;\&\; (\overline{AA_D} \;\&\; \overline{AA_I}) \;\&\; \overline{AT} \;\&\; \overline{E} \;\&\; \overline{A} \;\&\; \overline{F}$$

I.e.: permeable coronaries, intramyocardial arteries with: a normal section area (not increased, and not decreased), with a normal wall thickness (no thickening), without endothelial proliferation, without microanevrysma and without interstitial fibrosis.

All the statements were added into a final expression by the "or" (.) operator.

Further we compared our results with the literature data obtained from 25 papers concerning the vascular lesions in diabetic cardiomyopathy (Table 1).

The final result was enormous and impossible to be interpreted in this form. Therefore, in order to find out the truth value of the result, and give an unitary interpretation to the literature data, we applied the Quine-Mc Cluskey decision method. This method is an algorithm of minimizing a symbolic logic expression, which is reducing it at another expression, with few symbols and operators and with the same truth value.

Our original computer program, based on the Quine-Mc Cluskey algorithm, was written in PASCAL and was implemented on a home computer.

Table 1

	C_p	AA_D	AA_I	AT	E	A	F
1. Bell:1952	-	-	-	+	+	-	+
2. Saphir et al:1956	-	+	-	+	+	-	-
3. Blumenthal et al: 1960	-	+	-	+	+	-	-
4. Warren et al:1966	+	-	-	+	-	-	-
5. Ledet:1968	+	-	-	+	-	-	-
6. Waxler et al.:1971	+	+	-	-	-	-	-
7. Bulloch et al:1971	+	+	-	+	+	-	+
8. Richardson et al.: 1971	+	-	-	-	-	-	-
9. Tambe et al:1972	+	+	-	-	-	-	-
10. Halkin & Ravid: 1976	+	+	-	+	+	-	-
11. Hamby et al:1974	+	+	-	+	-	-	-
12. Rubler et al:1972	+	-	-	-	+	-	+
13. Pearce et al:1973	+	+	-	+	+	-	+
14. Rider et al:1974	-	+	-	+	-	-	+
15. Seneviratne:1977	+	-	-	+	+	-	-
16. Zoneraich & Silverman:1978	+	+	-	+	+	-	+
17. Badeer & Zoneraich:1978	-	+	-	+	-	-	+
18. Crall & Roberts: 1978	-	-	-	-	-	-	-
19. Weinrauch et al: 1978	+	+	-	+	+	-	+
20. Boucher et al: 1979	-	-	-	-	-	-	-
21. Fischer et al.: 1979	+	+	-	-	-	-	-
22. Shirey et al:1980	+	-	-	-	-	-	-
23. Factor et al:1980	+	-	-	+	+	-	+
24. Dai Rui-Hong et al:1982	+	-	-	+	+	-	+
25. Gherasim et al: 1985	+	-	-	+	+	-	+

RESULTS

In our quantitative investigation we found that the mean number of arteries in the diabetic myocardium is much smaller as compared to the mean number of arteries in the control group.

The mean arterial diameter was not significantly increased in the diabetic myocardium. On the contrary, an increase of the vascular wall thickness in the diabetic heart was present (Table 2).

Table 2
Morphometric values of intramyocardial arteries in diabetic heart

Morphometrical parameters	Diabetic heart M.V.	S.D.	Control heart M.V.	S.D.
1. Arteries number/mm^2	2,51	±o,65	5,82	±o,54
2. Arterial diameter (μm)	29,45	±8,25	24,61	±7,7
3. Arterial wall thickness (μm)	7,37	±1,98	5,1o	±1,71

M.V. = mean value
S.D. = standard deviation
1 and 3 = the differences are statistically significant for a probability of 95%

In the small intramyocardial arteries ($<$ 1oo μm diameter) we also found a proliferation of endothelial cells with protuberances in the form of cushions , humps and bridges across the lumen. Frequently, we found areas of perivascular and interstitial fibrosis. The extramural coronary atherosclerosis was moderate ($<$ 70%) in both diabetic and control hearts.

The symbolic logic expression resulted after the computer analysis was:

$$C_p \ \& \ AA_D \ \& \ AT \ \& \ E \ \& \ F$$

I.e.: permeable coronaries, intramyocardial arteries with decreased section area, increased wall thickness, endothelial proliferation and interstitial fibrosis.

DISCUSSION

The two major aims of this study were: (1) to investigate, by histopathological and morphometrical methods, the involvement of intramyocardial arteries in diabetic heart disease and (2) to compare these results with a symbolic-logic model obtained after the computer analysis of the literature data.

The endothelial proliferation and the significant thickening of the vascular wall confirmed the findings of Blumenthal et al.(196o), Ledet (1968), Zoneraich & Silverman (1978) and Factor et al.(198o). These alterations, as well as the interstitial fibrosis are the probable basis for the diminished compliance and the impaired left ventricular function without coronary disease (Dai Rui-Hong et al:1982). Recent ultrastructural observations showed some similarities between the increased thickness of the small vessels wall in diabetics (due to the thickening of the basement membrane) and the modifications occuring in the normal process of ageing (Vracko: 1982).

The histopathological model obtained after the computer analysis of the literature data gives further support to the hypothesis that the microangiopathy could play a role in the pathogenesis of diabetic cardiomyopathy.

In our personal morphometrical results as well as in the symbolic-logic model the extramural coronaries were permeable. Our observations of the arterial wall thickening, the endothelial proliferation and the interstitial fibrosis were also confirmed. The important decreasing of the intramyocardial arteries density that we noticed in the diabetic hearts was not considered in our symbolic-logic analysis because we found no similar information in the literature data.

The data obtained in the present study indicate that the diabetes involves the heart not only by coronary atherosclerosis, but also in form of intramyocardial microangiopathy.

It is possible that an unsignificant narrowing of the extramural coronaries becames important in the presence of an impaired vascular bed, with an exceeded compensatory capacity (Taşcă et al.: 1985 b).

The concept of diabetic microangiopathy involving not only the retina, the skeletal muscle and the kidney but also the heart can be of practical importance: if the changes in the microcirculatory bed of the skeletal muscle (Camerini-Davalos et al: 1983) are reversed by early drug treatment and the control of blood glucose (Siperstein:1983), similary results can be probable expected in the myocardium.

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