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Ultrastructural Morphometric Analysis of Human Myocardial Left Ventricles with Mitral Insufficiency

A Comparison with Normally Loaded and Hypertrophied Human Left Ventricles

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Summary. 15 biopsies of dilated and hypertrophied human left ventricles in mitral insufficient hearts were morphometrically investigated. On light and electron microscopical level the results were compared with those received from normally loaded human left ventricles and from hypertrophied human left ventricles found in hearts with aortic valve disease. The results demonstrate alterations when compared with the results from normally loaded left ventricles. The differences between normally loaded and volume loaded left ventricles are smaller than those in pressure loaded left ventricles from aortic valve diseased hearts.

Key words: Electron microscopy – Morphometry – Human left ventricle – Mitral insufficiency.

Introduction

Many ultrastructural investigations on human heart muscle have been performed in order to examine the variety of cellular damages caused by different heart diseases (Dowlatshahi and Hunt 1969; Ferrans et al. 1972; Kajihara et al. 1973; Maron et al. 1975a, b; Olsen 1975; Saetersdal 1976). Changes in the mitochondria have been used to express the degree of heart failure. Morphometric investigations were first carried out on normally loaded human left ventricles and on hypertrophied human left ventricles where the hypertrophy was caused by aortic valve diseases (Fleischer et al. 1978; Warmuth et al. 1978).

In the present study dilated and hypertrophied human left ventricles found in hearts with mitral insufficiency were analysed morphometrically. The results were compared with those published from normally loaded human left ventricles and from hypertrophied human left ventricles found in hearts with aortic valve disease.

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Table 1.

No.	Age	Sex	Indication	Preoperative left ventricular, left atrial + right ventricular pressure	OP report and intraoperatively estimated heart weight
1	17	m	mitral insufficiency IV^0	125/0–10 25/10 −/−	Cor bovinum, cavities of heart very dilated
2.	25	f	mitral insufficiency IV^0	100/2–9 30/8 65/0–6	h.w. = 800 g, dilated left atrium and extensive hypertrophied left ventricle
3.	34	m	mitral insufficiency III^0 hypertonia because of stenosis of renal artery	130/4–8 13/8 40/5–7	h.w. = 750 g
4.	34	m	mitral insufficiency IV^0		left ventricular hypertrophy
5.	37	f	mitral insufficiency IV^0 accompanied by slight mitral stenosis and aortic insufficiency	125/0–8 25/8 30/0–4	distinct left ventricular hypertrophy
6.	42	m	mitral insufficiency IV^0	120/0–23 65/15 30/0–17	gigantic dilatation and left ventricular hypertrophy
7.	43	f	mitral insufficiency IV^0 mitral stenosis I^0	105/5–17 35/18 25/2–5	indicated left ventricular hypertrophy
8.	44	f	mitral insufficiency IV^0 DOE, orthopnea, hepatomegaly, pulmonary congestion	105/5–17 −/− 60/0–44	concentric left ventricular hypertrophy, art. pulmonalis twice the diameter of the aorta
9.	46	m	mitral insufficiency IV^0 mitral stenosis III^0	110/3–10 −/− 36/0–6	h.w. = 800 g
10.	46	m	mitral insufficiency IV^0 pulmonary congestion	90/0–3 35/10 35/0–3	h.w.%750 g right hypertrophied heart
11.	47	f	mitral insufficiency III^0 cardiac dyspnea since 6 years	130/5–12 25/12 35/0–6	hypertrophied left heart
12.	48	m	mitral insufficiency III^0 mitral stenosis	100/0–5 30/15 40/0–7	hypertrophy of the whole heart h.w. = 1000 g
13.	49	m	mitral insufficiency IV^0 cardiac symptoms since 10 years	90/0–6 48/5 55/0–5	h.w. = 700 g
14.	50	m	mitral insufficiency IV^0	90/0–4 −/− 26/10–2	concentric hypertrophy of the left heart h.w. = 700 g
15.	62	m	mitral insufficiency IV^0	100/0–4 −/− 34/0–5	h.w. = 700 g

Material and Methods

The biopsies were taken transmurally under identical conditions during heart surgery on 15 patients (Harmjanz et al. 1971). The diagnosis in all patients was insufficiency of the mitral valve accompanied in 6 cases by a slightly expressed stenosis of the mitral valve (Table 1). The age of the patients ranged between 17 and 62 years. 9 of these patients were between 40 and 50 years of age. The values of blood pressure in the left ventricle were measured by heart catheterisation. The O_2-partial pressure of aortic blood was within the normal range.

All patients possessed a hypertrophied and dilated heart with displacement to the left. The myocardial weights measured as described before (Fleischer et al. 1978) were beyond the "critical heart weight" (Linzbach 1948; Schoenmackers 1958).

All biopsies were fixed with 3% glutaraldehyde in a 0.05 m phosphate buffer with a pH of 7.2, rinsed in this buffer solution, postfixed with 1.33% OsO_4, dehydrated after washing in graded ethanol series and embedded in Epon 812.

The tissue blocks were cut with a diamond knife on a LKB Ultrotome III for light and electron microscopic analysis (Leitz-Ortholux with Orthomat; Philips EM 301, equipped with a 35-mm-camera). The counting procedures and parameter transformations into stereological data were performed as described previously (Fleischer et al. 1978). 1182 micrographs were analysed in all. The volume densities were expressed as a percentage of the test volume (cm^3 heart tissue for light microscopy and cm^3 heart muscle cells for electron microscopy) for better understanding. Student's t-test was used as the statistical test.

Results

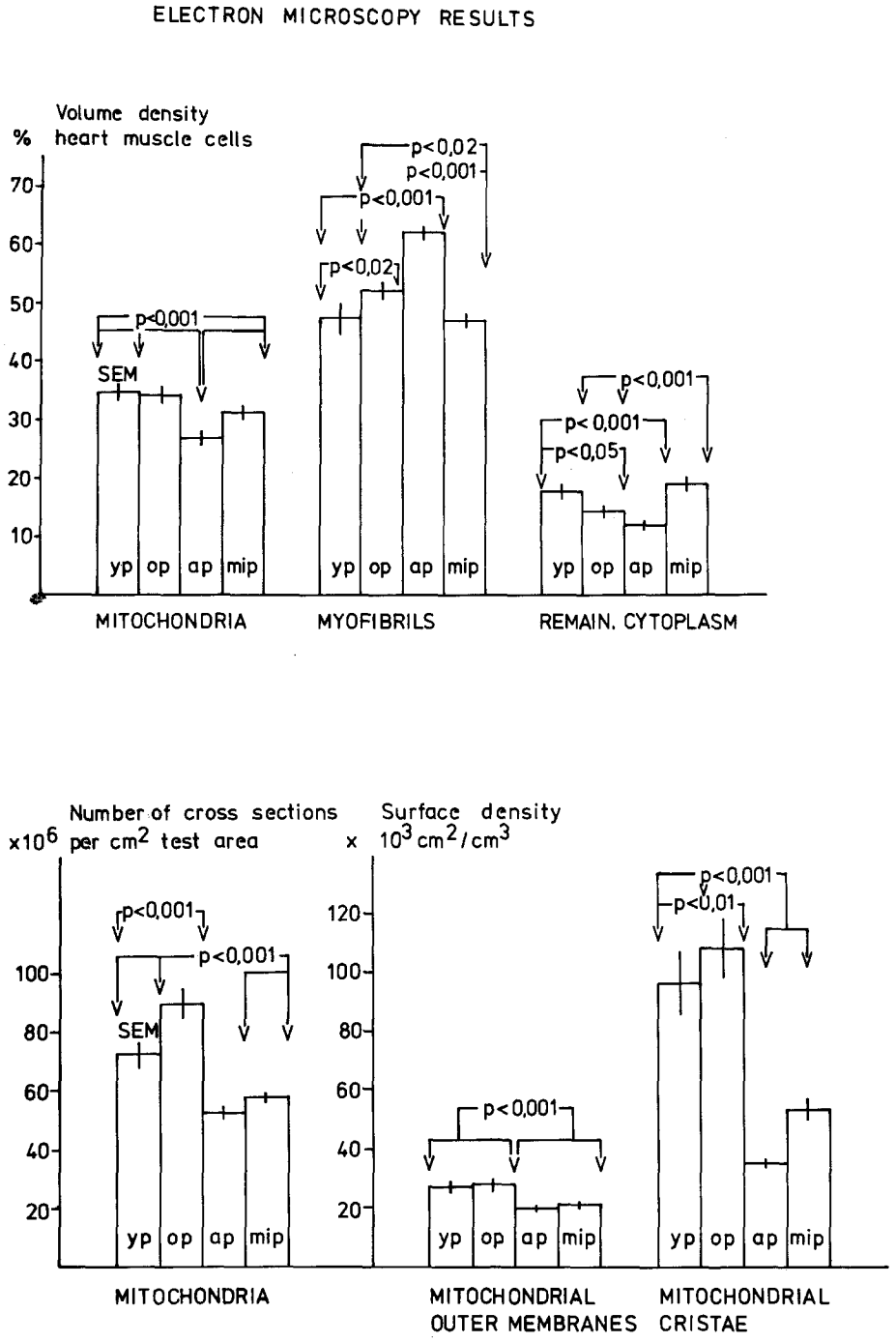
Light Microscopy

On light microscopical level, the volume density (V_v) of heart muscle cells was 80.08% per cm^3 heart tissue and that of the interstitial space was 19.92% per cm^3 heart tissue. The number of heart muscle cell nuclei per cm^2 test area was 33.99×10^3. The volume density of these nuclei reached 1.31% per cm^3 heart tissue.

Table 2. Morphometrical results of 4 different groups of patients

Parameters	y.p.	o.p.	a.p.	mi.p.
Light microscopy results:				
V_V interstitial space in % of the unit volume	23.91	23.17	25.79	19.92
V_V heart muscle cells in % of the unit volume	76.09	76.83	74.21	80.08
V_V heart muscle cell nuclei in % of the unit volume	4.79	2.18	1.33	1.31
Number of heart muscle cell nuclei $\times 10^3$ per cm^2 test area	60.57	20.83	20.68	33.99
Electron microscopy results:				
V_V myofibrils in % of the unit volume	47.1	52.0	62.0	47.6
V_V mitochondria in % of the unit volume	34.5	34.1	26.6	31.6
V_V remaining cytoplasm in % of the unit volume	17.4	13.2	11.2	18.6
Number of mitochondria $\times 10^6$ per cm^2 test area	74.61	89.43	52.82	56.79
S_V of outer mitochondrial membranes $\times 10^3$ cm^2/cm^3 test volume	26.60	26.90	20.51	21.10
S_v of mitochondrial cristae $\times 10^3$ cm^2/cm^3 test volume	92.61	107.05	35.37	53.10

y.p. = young patients, *o.p.* = old patients, *a.p.* = patients with aortic valve disease, *mi.p.* = patients with mitral insufficiency



Figs. 1 and 2. Diagrammatic representation of the electron microscopic results. *SEM* standard error, *yp* young patients, *op* old patients, *ap* patients with aortic valve disease, *mip* patients with mitral insufficiency

These results are compared in Table 2 with those of the normally loaded left ventricles and those of the hypertrophied human left ventricles caused by aortic valve diseases.

Electron Microscopy

The volume density of the myofibrils was 47.62% per cm^3 heart muscle cells. The mitochondria occupied a volume density of 31.61% per cm^3 heart muscle cells. For the remaining cytoplasm – including hyaloplasm, vacuoles, sarcoplasmic reticulum, lipofuscin and glycogen areas – the volume density was 18,99% per cm^3 heart muscle cells (Fig. 1).

The number of cross-sections of mitochondria amounted to 56.79×10^6 per cm^2 test area. The surface density (S_v) of these mitochondria reached 21.1×10^3 cm^2/cm^3 heart muscle cells and that of the mitochondrial cristae 53.1×10^3 cm^2/cm^3 heart muscle cells. The standard error was always under 5% (Fig. 2).

Table 2 demonstrates the electron microscopic values obtained in comparison with those of normal loaded human left ventricles and the hypertrophied left ventricles caused by aortic valve diseases.

Discussion

In all operation reports the surgically treated hearts were described as hypertrophied and dilated. The heart weights were always more than the "critical heart weight". Hyperplasia of the heart muscle cells and of the single heart muscle cell was assumed. This assumption was verified by light microscopic analysis.

Results for myofibrils can be accepted as normal when compared with those on normally loaded human left ventricles. No statistically significant differences between both groups of patients exist. Laguens (1971) reported values from rat heart muscle cells in the same range. This accordance was not unexpected because the human left ventricles investigated were volume and not pressure loaded. The pressure loading of the ventricles caused by aortic valve diseases requires a greater amount of force generation for an efficient contraction. This explains the higher volume density of myofibrils in the cells of the aortic valve diseased hearts.

Although the heart weights were in conformity with those hypertrophied from aortic valve diseases, the variations from normal were not so extensive. This may be a consequence of the normal blood pressure in the left ventricles. Degeneration of the myofibrils or Z-band aberrations as described in pressure hypertrophied left ventricles were never observed.

The volume densities of the mitochondria showed a statistically significant decrease ($p < 0.001$) in comparison with those of the normally loaded left ventricular muscle cells. The reduction is also recognizable in the surface density of the mitochondria ($p < 0.001$) and in the mitochondrial cristae ($p < 0.001$). There are two reasons for the decrease in the surface density of the mitochondria: first a decline in the volume density of the mitochondria and in the number

of the mitochondria; second and in a direct relationship, there was a degeneration of the mitochondria, which was present in the form of cristolysis and a loss of substance in the matrix.

Significantly more signs of degenerative processes were found in the hypertrophied heart muscle cells caused by aortic valve diseases. The volume loading induced hypertrophy of mitral insufficient hearts and produced no increase in content of contractile material. This variable was interpreted by Meessen and Poche (1967) as one of the limiting factors for growth of the cells. This restriction in the hypertrophy of volume loaded ventricles was caused by a decrease in capillary density and by the long diffusion distance (Wearn et al. 1933; Linzbach 1948; Rakusan and Poupa 1964; Doerr 1974).

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