Myocardial Response to Infarction in the Rat

Morphometric Measurement of Infarct Size and Myocyte Cellular Hypertrophy

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For determination of the effects of myocardial infarction on the recovery potential of muscle mass in the surviving tissue, ligation of the left coronary artery was performed in 3-month-old rats, and the infarcted ventricles were analyzed morphometrically a month after surgery. Comparisons were made with 4-month-old control rats that underwent sham operations and with 3-month-old control rats that were not operated upon for evaluation of the magnitude of infarct size and discrimination of the relative contribution of tissue growth that occurred in the surviving myocardium solely as a result of the change in age, from 3 to 4 months (postoperative tissue growth, or POTG), from the additional growth induced by infarction (hypertrophic growth, or HG). Coronary occlusion induced a 276-cu mm loss of ventricular tissue volume that corresponded to 43% of the total left ventricular mass, 648 cu mm. Over a 30-day period the remaining 372 cu mm of viable tissue expanded by 90% with an overall volume gain of 334 cu mm. This tissue augmentation consisted of 20% POTG, 67 cu mm, and 80% HG, 267 cu mm. Total myocyte volume increased 89%, from 302 cu mm to 571 cu mm, and average myocyte cell volume per nucleus increased 92%, from 16,500 cu μ to 31,600 cu μ. The expansion of the myocyte mass was the result of a 21% POTG and a 79% HG. Corresponding values for the myocyte population were 19% and 81%. (Am J Pathol 1985, 118:484–492)

ISCHEMIC LOSS of myocardial tissue places a demand on the surviving myocardium to sustain the pumping action of the heart, to initiate reparative processes, and to undertake regenerative replacement for the deficiency in muscle mass and function. Ultimate recovery of cardiac function relies mainly on cellular processes that augment the volume of surviving myocardium, characteristically by hypertrophy of myocytes[1–3] and hypertrophy and hyperplasia of interstitial fibroblasts and endothelial cells.[4] The adaptive and growth capacities of myocardium are not known quantitatively under the condition of myocardial infarction. Measurement of total myocardial hypertrophy during or after recovery from infarction is a practical impossibility on the basis of tissue weight or volume measurement alone. This is because there are variable and unknown amounts of swelling in cells and interstitial space[5,6] and a progressive lateral and radial shrinkage of the infarcted region.[7] The aim of the present study was to evaluate morphometrically the magnitude of tissue and myocyte growth occurring in the spared myocardium following ligation of the left coronary artery in rats. This required the measurement of absolute infarct size, ie, the amount of tissue loss induced by coronary occlusion, so that we could estimate the initial volume of still viable myocardium. A recovery period of 1 month was selected on the assumption that the most significant changes would occur during the completion of the healing process, although myocardial response to infarction may continue for several months.

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Materials and Methods

Thirty-two male Wistar Kyoto rats (Charles River Breeding Laboratories, North Wilmington, Mass) were obtained for this study and at 3 months of age were divided into three groups of 12, 10, and 10 animals. The heart of each animal in the first group, representing control animals not operated upon was fixed by perfusion and prepared for microscopic examination. At the same ages, the second group of rats was subjected to a sham operation by placement of an incomplete ligature around the left coronary artery, and left ventricular myocardial infarction was produced in rats of the third group by ligation of the left coronary artery by a technique described in detail elsewhere.[8] Briefly, with the animal under ether anesthesia, the thorax was opened by incision to the left of and parallel to the sternum, and the heart was exteriorized by application of light pressure upon the thorax. The left coronary artery was then ligated 1–2 mm from its origin for production of a large infarct of the left ventricle.[7] The chest was closed, and the animals were allowed to recover. All rats in the second and third groups were sacrificed 30 days after the operation, at which time their hearts were fixed by perfusion. All infarcts in this study were transmural. It should be noted that the animals in the second and third groups, with the exception of 1 animal, were the same as those in which the changes in the right ventricle have previously been reported.[9]

Just prior to sacrifice, all animals were anesthetized, and the hearts were fixed by perfusion with a solution of glutaraldehyde and paraformaldehyde via a polyethylene cannula inserted into the abdominal aorta.[9,10] Subsequently, the hearts were excised; and the weights of the left ventricle, including the septum, and right ventricle were recorded. Each left ventricle and its chamber were supported with agar (5% agar in distilled water) and serial-sectioned into 1-mm-thick rings perpendicular to the axis of the heart from the apex to the base. These individually numbered slices of the left ventricle, including the septum, were then processed for electron microscopy and flat-embedded in Araldite with the basal side exposed to the surface of the embedding molds.

Determination of the Volume of the Left Ventricular Wall and of the Volumes of Uninjured Myocardium and Scar Tissue

For evaluation of ventricular wall volume the mean thickness of each embedded serial section of each left ventricle was determined before sectioning by averaging five individual measurements made at a magnification of ×28 with a dissecting microscope having an ocular micrometer accurate to 0.03 mm. Sections from the basal side of each serial slice were cut at a thickness of 2.0-2.5 μ with a glass knife, 38 mm in length (LKB 2078 Histo Knife Maker), and the Sorvall JB-4 microtome (Dupont Company, Newtown, Conn) and mounted on glass slides. These sections, representing 12–14 uniformly spaced parallel planes through the whole left ventricle, were stained with toluidine blue and photographed; prints at a final magnification of ×12 collected. A 172 × 232-mm grid containing 1598 points was superimposed on each print. The uncompressed tissue area represented by each point was 0.1845 sq mm. The area occupied by ventricular myocardium in each section was measured morphometrically by counting the number of points overlying the tissue and multiplying this value by the area per point. Similarly, in the infarcted ventricles the areas of uninjured myocardium and scarred tissue were calculated in each micrograph from the number of points lying over these two regions of the ventricular wall, respectively. Before point counting, the boundaries between scarred and still viable myocardium were carefully drawn on each micrograph after the corresponding tissue section was viewed with the light microscope. The area measurements multiplied by the previously determined thickness of the embedded tissue slice yield the volume of myocardium in each slice of the ventricle in both groups of control rats, and the volumes of viable and scarred myocardium in operated animals. The summation of these data derived from each serial section of the ventricle gives the overall ventricular volume and the volumes of the ventricle represented by viable and nonviable myocardium.

Determination of the Average Number of Myocyte Nuclei in the Left Ventricle and of the Mean Myocyte Cell Volume per Nucleus

From the serial reconstruction of surviving and infarcted myocardium, four sites in each of the middle 8 serial sections in each animal were selected, at least 1 mm removed from damaged tissue, and 4 small tissue samples cut free with a razor blade from the thick embedded sections. The 32 samples collected from each animal were then reembedded in small flat molds so that we could obtain sections for light-microscopic observation in which the myofibers were precisely oriented in either the longitudinal or transverse direction. Because the infarct region comprised most of the free wall of the left ventricle, the tissue samples were obtained from the portion of the wall adjacent to the septum and from the interventricular septum. Corresponding areas were collected from both groups of control animals.

Eight tissue blocks from each left ventricle were sec-

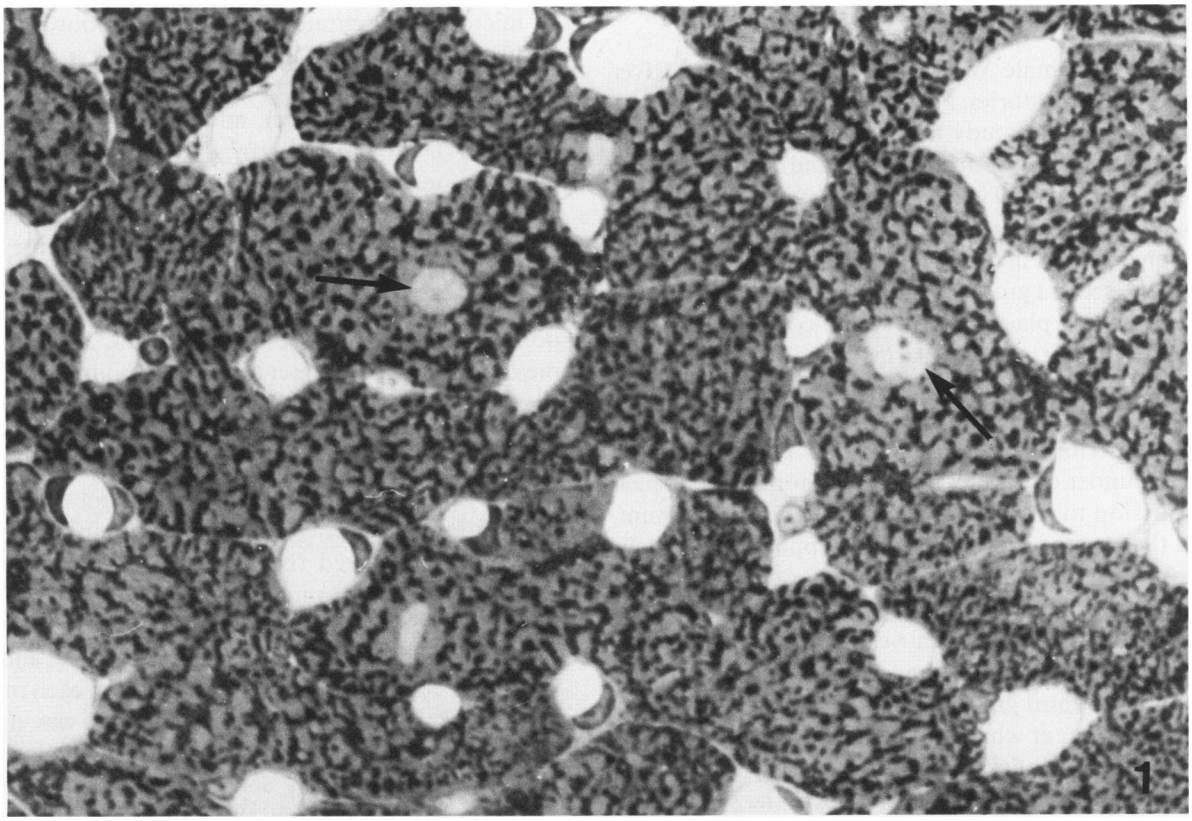

Figure 1—Semithin section of ventricular myocardium with myofibers oriented transversely, prepared from the spared tissue of an infarcted ventricle. Several myocyte nuclei (*arrows*) are present in the tissue area shown. (Methylene blue and safranin, × 1250) **Figure 2**—Semithin section of ventricular myocardium of an infarcted ventricle with myofibers oriented in the longitudinal direction. Three mid-sections of myocyte nuclei are shown (*arrows*). The nuclear envelope is defined at both ends, and clusters of mitochondria are visible at the nuclear poles. (Methylene blue and safranin, × 1250)

tioned for light-microscopic nuclear counting at a nominal thickness of 0.75 μ with the use of an MT-1 Porter-Blum microtome (Ivan Sorvall, Inc., Norwalk, Conn). The sections were stained with methylene blue and safranin and mounted on glass slides (Figure 1). Morphometric sampling at a magnification of ×630 consisted of counting the total number of myocyte nuclear profiles, N(n), in a measured area, A, in transversely oriented tissue sections. A square uncompressed tissue area equal to 21,609 sq μ was delineated in the microscopic field by an ocular reticle (#105844, Wild Heerbrugg Instruments, Inc., Farmingdale, NY), and laterally adjacent fields were examined in each section. A total of 24 such fields were evaluated in each animal for determination of the mean number of nuclear profiles per unit area, $N(n)_A$.

Table 1—Comparisons of Gross Cardiac Parameters Among Group 1, Group 2, and Group 3

	Group 1	Group 2	% Difference	Group 3	% Difference Versus Group 1	% Difference Versus Group 2
Age	3 months	4 months		4 months		
Number of rats	12	10		10		
Body weight (g)	266 ± 27	321 ± 28	21*	313 ± 17	18*	−2
Heart weight (mg)	901 ± 107	1119 ± 96	24*	1231 ± 121	37*	10
Right ventricular weight (mg)	191 ± 28	248 ± 32	30*	325 ± 53	70*	31*
Left ventricular weight (mg)	710 ± 90	871 ± 68	23*	906 ± 123	28*	4
Left ventricular volume (cu mm)	648 ± 92	763 ± 89	18	706 ± 199 (viable) 102 ± 29 (scar)	9	−7

Results are expressed as means ± SD.
* Indicates a percent change that is statistically significant ($P < 0.05$).

Average nuclear length, $\overline{D}n$, was determined in each animal from 100 measurements made at a magnification of ×630 in longitudinally oriented myocytes (Figure 2) viewed with a microscope having an ocular micrometer accurate to 0.002 mm. Ten blocks were cut from each animal with the myofibers sectioned perpendicular to their length for avoidance of longitudinal compression. Sections, approximately 2.0 μ in thickness, were collected and stained, and 10 measurements of nuclear length were recorded from each tissue section. Only those nuclei were measured for which the nuclear envelope was sharply defined at both ends and also where clusters of mitochondria were clearly visible in the areas adjacent to the nuclear edges.

Measurements of the number of myocyte nuclei per unit volume of myocardium, $N(n)_V$, were obtained with the equation[9,11]:

$$N(n)_V = N(n)_A/\overline{D}n$$

The total number of myocyte nuclei in each ventricle, $N(n)_T$, was computed from $N(n)_V$ and the corresponding total ventricular volume of viable myocardium, V_T, previously determined by serial section reconstruction:

$$N(n)_T = N(n)_V \times V_T$$

Transverse myocardial sections were also employed for determination of the volume fraction of myocytes in the myocardium. The myocardial slices were examined by light microscopy at a magnification of ×630 with an ocular reticle (#105844, Wild Heerbrugg Instruments) containing a uniform distribution of 42 sampling points. Starting at one corner of each slice five successive laterally adjacent fields, each completely filled by myocardial tissue, were brought into view and the numbers of sampling points overlying myocyte profiles and the remainder of the field were recorded. A total of 40 such fields were examined in each animal, for a total of 1680 points per animal.

The aggregate volume of myocytes in the ventricle of each animal, $V(m)_T$, was then computed from the ventricular volume measurement, V_T, and the volume fraction of myocytes in the myocardium, $V(m)_V$:

$$V(m)_T = V_T \times V(m)_V$$

The total myocyte volume, $V(m)_T$, divided by the total number of myocyte nuclei in the ventricle, $N(n)_T$, yields the average myocyte cell volume per nucleus, $\overline{V}(m)_n$, in each animal:

$$\overline{V}(m)_n = V(m)_T/N(n)_T$$

All morphometric data were collected blind, and the code was broken at the end of the experiment. All the results in each table show the mean ± SD of values determined for the individual animals in each group. Statistical significance in multiple comparisons among independent groups of data, in which analysis of variance and the F test indicated the presence of significant differences, was determined by the Bonferroni method.[12] Significance levels for comparisons between two measurements were evaluated with the use of the unpaired two-tailed Student t test.

Results

Table 1 shows that the weight of the left ventricle including the septum increased 23% in 1 month after the sham operation and 28% following surgical ligation of the left coronary artery near its origin. Left ventricular volume measurements demonstrated a corresponding 18% and 25% expansion (ventricular volume in infarcted animals, 808 ± 219 cu mm), but only the latter change was statistically significant ($P < 0.05$). Volume determinations indicated that 13% of the whole ven-

Table 2—Numeric Density of Myocyte Nuclei in Left Ventricular Myocardium

	Group 1	Group 2	% Difference	Group 3	% Difference Versus Group 1	% Difference Versus Group 2
A	6.22	5.19		5.19		
N(n)	5331	3893		2594		
$N(n)_A$	857 ± 74	750 ± 47	−12*	500 ± 61	−42*	−33*
$\overline{Dn}$	17.46 ± 0.69	17.58 ± 0.36	1	19.44 ± 0.92	11*	11*
$N(n)_V$	49,049 ± 5964	42,660 ± 3097	−13*	25,712 ± 2664	−48*	−40*
Number of nuclei in the whole ventricle (millions)	31.76 ± 3.54	32.55 ± 3.43	2	18.25 ± 5.57	−43*	−44*

Results are expressed as means ± SD.
* Indicates a percent change that is statistically significant ($P < 0.05$).

tricle in the infarcted animals consisted of scarred tissue (102 cu mm versus 808 cu mm).

Table 2 lists first the tissue area of myocardium sampled and the number of nuclei counted from the light-microscopic transverse sections of ventricular myocardium. The number of myocyte nuclei per square millimeter in infarcted ventricles (Group 3) was found to be decreased 42% and 33% in comparison with the controls that were not operated upon (Group 1) and the controls that underwent a sham operation (Group 2), respectively. Relative to both control groups, average nuclear length was increased by 11%. Because of this change in nuclear length, decreases in the numerical density of myocyte nuclei, the number per cubic millimeter of myocardium, were greater than those seen per unit area of tissue. The total number of myocyte nuclei per ventricle is presented last in Table 2. Similar values were observed in control animals, approximately 32 million, whereas only 18 million were found in the viable myocardium of the infarcted ventricles. These data demonstrate a loss of 14 million myocyte nuclei, 43%, as a result of the ligation of the left main coronary artery.

Table 3 shows first the computation of absolute infarct size and then the overall growth adaptation that has occurred in the surviving myocardium during the 1-month interval. These determinations required first the evaluation of the mean percent and standard deviation of nuclei spared and nuclei lost in the infarcted ventricles. Such values were obtained from the quotient of the total number of myocyte nuclei measured in the animals constituting the third group and the total number of nuclei evaluated in Group 1. Furthermore, the product of the aggregate volume of myocardium in Group 1 times the percent of nuclei lost in Group 3 gives the average volume of myocardium that will be lost by coronary occlusion. In a complementary way, the volume of myocardium that will be spared can be calculated. Statistical treatment of stereologic measurements, based on the quotient or the product of two variables, was derived with application of the equation previously described.[1]

Loss of 43% of myocyte nuclei after infarction (Group 3) implies that the original 648 cu mm of myocardium in the 3-month-old rats (Group 1) was divided by coronary artery ligation into 276 cu mm destined for ischemic death and 372 cu mm that would survive. One month after infarction the necrotic tissue had become 102 cu mm of scar, 37% of its original tissue volume, 276 cu mm. This difference was highly significant ($P < 0.001$). The 276-cu mm loss of ventricular volume induced a tissue response in the remaining 372 cu mm of surviving ventricle which resulted in a total volume gain of 334 cu mm throughout the entire experimental period, from 3 to 4 months (706 cu mm − 372 cu mm = 334 cu mm). Such a change indicates a 90% tissue expansion ($P < 0.001$), which is, however, less than the 105% overall growth that would have been required for realization of a fully regenerative adaptation, represented by the 763 cu mm of ventricular volume measured in control animals that underwent sham operations (Table 1).

Table 3—Determination of Absolute Infarct Size

	Group 1	Group 3
Number of nuclei in the whole ventricle (millions)	31.76 ± 3.54	18.25 ± 5.57
Percent of nuclei spared		57.47 ± 18.76
Percent of nuclei lost		42.53 ± 18.76
Volume of myocardium (cu mm)	648 ± 92	808 ± 219
Volume of myocardium infarcted (cu mm)	276 ± 127	102 ± 29
Volume of myocardium spared (cu mm)	372 ± 132	706 ± 199
Hypertrophic growth of the myocardium (cu mm)	372 ± 132	639 ± 180

Results are expressed as means ± SD.

Table 4—Changes in Mean Myocyte Cell Volume per Nucleus as a Result of Physiologic Growth and Myocardial Infarction

	Group 1	Group 2	% Difference	Group 3	% Difference Versus Group 1	% Difference Versus Group 2
Volume percent of myocytes in the myocardium	81.12 ± 1.82	82.22 ± 1.57	1	80.67 ± 2.28	−1	−2
Total volume of myocytes in the ventricle (cu mm)	525 ± 76	627 ± 77	19	571 ± 168	9	−9
Myocyte volume spared (cu mm)	302 ± 107			571 ± 168	89*	
Myocyte cell volume per nucleus (cu μ)	16,500 ± 2700	19,300 ± 1550	17	31,600 ± 4500	92*	64*

Results are expressed as means ± SD.
* Indicates a percent change that is statistically significant ($P < 0.05$).

It should be pointed out, however, that the magnitude of tissue expansion, measured by comparing the total volume of viable myocardium in the infarcted ventricles with that estimated to survive at the time of coronary artery ligation, was an expression of the cumulative effect of two simultaneously occurring processes: 1) postoperative tissue growth (POTG) resulting from the change in age of the animals, from 3 to 4 months, and 2) hypertrophic growth (HG) associated with the stress of myocardial infarction. The extent of POTG, therefore, was estimated from the change in volume of the whole left ventricle between the 3-month-old Group 1 animals and the 4-month-old Group 2 animals (Table 1). Thus, the real extent of tissue hypertrophy could be measured from the values above and found to be 72% (372 cu mm × 1.18 postoperative growth factor = 439 cu mm; 439 cu mm −372 cu mm = 67 cu mm = amount of tissue expansion due to POTG; 706 cu mm −67 cu mm = 639 cu mm = amount of tissue present in the infarcted ventricles corrected for POTG) as shown last in Table 3 ($P < 0.005$). Finally, the magnitude of actual tissue replaced by HG after the ischemic injury can be derived, 267 cu mm (639 cu mm −372 cu mm = 267 cu mm), and seen to amount to approximately 82% of the anticipated 326-cu mm aggregate myocardial volume that would have been attained by the infarcted portion of the ventricular wall in 1 month (276 cu mm × 1.18 postoperative growth factor = 326 cu mm).

Table 4 shows the volume fraction of myocytes in the myocardium, the total volume of the contractile compartment of the ventricle, and the mean myocyte cell volume per nucleus. In comparison with Group 1 and Group 2, average cell size per nucleus in infarcted ventricles increased 92% and 64%, respectively. The former change is the result of both postoperative and induced myocyte growth, whereas the latter change indicates the magnitude of cellular hypertrophy achieved by the myocyte population under the stress of myocardial infarction. The product of total myocyte volume in the ventricle and the fraction of nuclei spared after infarction (Table 3) gives the aggregate volume of the contractile compartment that remained viable after the ischemic injury. Again, it was found that the extent of cellular (92%) or total myocyte volume expansion (89%) was less than that expected for a complete reconstitution of the muscle mass of the ventricle following coronary occlusion (108%).

Discussion

The findings of the present study indicate that ligation of the left coronary artery near its origin in 3-month-old Wistar Kyoto rats produces an ischemic loss of myocardial tissue that comprises an average 43% of the total left ventricular mass. This tissue loss evokes a hypertrophic response in the surviving myocardium that results in a nearly 80% replacement of the original necrotic tissue. In a 1-month interval the viable portion of the ventricle increases its volume by 90%, still less than the 105% overall growth that would have been required for a fully regenerative adaptation. These morphometric results suggest that infarctions of 40% of the left ventricle in rats are too great to be completely compensated by the residual myocardium. Infarcts affecting 40% or more of the left ventricle in humans lead to cardiogenic shock and irreversible myocardium dysfunction.[13] Compared with the rat heart, the more limited tolerance of the human heart may be found in a coexisting vascular disease that may impair the capability of the viable tissue to offset the large destruction in muscle mass.

Although anatomic,[14] hemodynamic, and wall motion abnormalities[15] may all play a role in the outcome of myocardial infarction, a direct relationship has been found between healed infarct size and ventricular per-

formance in animal models[16,17] and in humans as well.[18,19] Ultimate recovery, in fact, relies mostly on the extent of tissue hypertrophy achieved by the uninjured tissue to compensate for the deficiency in muscle mass and function. The demonstration that a significant but still inadequate tissue growth has occurred in the surviving myocardium is consistent with observations showing a reduced cardiac output and pressure-generating capacity following large infarcts of the left ventricle in rats.[16,17] Furthermore, alterations in the structural integrity of the myocyte population[20,21] or in the capillary parameters controlling oxygen availability, diffusion, and transport,[10] or both, in the hypertrophied myocardium could also contribute to the deterioration of the physiologic properties of the infarcted ventricle.

A further indication of the insufficient reconstitution of myocardial tissue after infarction is seen in the concurrent development of right ventricular hypertrophy (Table 1). This adaptation of the heart has been observed previously in several studies with the same animal model in which the hypertrophic growth of the right ventricle was explained on the basis of an increased pressure load on the ventricle.[16,22,23] The enlarged ventricle would tend to maintain the pressure gradient across the pulmonary bed in left-side pump failure[16] and may also constitute a functional unit with the infarcted left ventricle, contributing to the emptying of the left ventricular chamber during systole.[22,23] However, the significantly greater stress imposed on the surviving myocardium of the left ventricle induced a hypertrophic tissue response, 72%, that was more than twofold larger than that detected in the right ventricle, 31%.

Growth of the contractile mass in adult myocardium following an increased workload on the ventricle is the result of the development of larger myocytes.[1-3] The present data indicate that a similar cellular mechanism underlies the expansion of the muscle compartment of the ventricle even under the condition of experimental infarction. Because the volume percent of myocytes in the viable myocardium was similar to control values, the total increase in myocyte volume (89%) was almost identical to the expansion in tissue volume (90%) and to the myocyte cellular hypertrophy per nucleus (92%). Average myocyte size per nucleus was 16,500 cu μ in 3-month-old controls that did not undergo operations, and it became 31,600 cu μ 1 month after coronary occlusion. The overall 92% increase in mean cell size was the result of both postoperative (17%) and induced (64%) myocyte growth. It has recently been reported that septal fiber diameters are increased in infarcts involving more than 15% of the left ventricle in rats.[24]

Infarcts comprising almost the entire free wall of the left ventricle in rats lead to enlargement of the left atrium with hypertrophy of both mononucleated and binucleated myocytes.[25] However, the major response of atrial myocytes to infarction was found to be binucleation, which, in association with an increased ploidy, explained the earlier finding of Rumyantsev and Kassem[26] of a significant enhancement of DNA synthesis in the myocyte nuclei of both atria after infarction. In contrast, the increase in myocyte mass in the injured ventricle occurs with no evident changes in the number of nuclei, as demonstrated by autoradiographic studies showing little or no DNA synthesis within hypertrophying myocytes.[26-29] Furthermore, quantitative analysis of tissue sections of different thickness in independent studies have indicated that the numeric fraction of binucleated myocytes does not change in cardiac hypertrophy.[4]

The morphometric methodology employed here has enabled the direct evaluation of 1) the *real* infarct size; 2) *magnitude* of tissue hypertrophy occurring in the spared myocardium; 3) the *extent* of average cellular hypertrophy of the myocyte population. These tissue and cellular measurements required, first, the estimation of the total volume of surviving myocardium and then the determination of the total number of myocyte nuclei still present in the infarcted ventricles. The absolute loss of myocyte nuclei has provided a measurement of the absolute loss of myocardium following the ligation of the left coronary artery. Recovery of myocardium has been represented by the hypertrophic growth adaptation attained by the still viable tissue, whereas myocyte cellular growth has been represented by the increase in myocyte volume per nucleus. The complexity of the technique used, however, requires several interconnected steps, each of which has the inherent effect of increasing the variability of the mean values. Statistical treatment of the data in terms of quotients and products of mean values also contributes to progressively increase the standard deviation of the resulting values.

Previous estimates of infarct size have relied on methodologies based on the evaluation of the fraction of endocardial circumference[7,16] or endocardial surface[9] bordering the infarcted portion of the ventricle. Such methods, however, contain various sources of error. These include the alterations taking place in the necrotic region during the healing process,[7] the dilatation of the ventricular chamber,[17,30] and, most of all, the unknown magnitude of compensatory growth in the surviving myocardium. Because these variables cannot be predicted and measured by conventional semiquantitative techniques, the approach developed here is the only one at present that can provide information on both actual

infarct size and degree and efficiency of ventricular mass recovery. For example, infarct size measured by the volume of scarred tissue (102 cu mm) underestimates by 67% the real amount of tissue loss (276 cu mm). This discrepancy is the consequence of the progressive thinning of the infarcted portion of the ventricular wall with time,[7] combined with the 90% tissue hypertrophy occurring in the viable myocardium throughout the 1-month interval studied. In contrast, infarct size measured by the fraction of its endocardial area in the same animals (Left ventricular weight in infarcted animals = 906 mg × 0.40 [percent of endocardial surface bordering the infarcted region of the left ventricle] = 362 mg ÷ 1.06 [tissue density] = 342 cu mm) (9) results in a 24% overestimation (342 cu mm versus 276 cu mm). This difference is more difficult to explain, but it might be related, at least in part, to infarct expansion[31] characterized by a progressive thinning and dilation of the infarcted region within the first few days after coronary occlusion. Infarct expansion is an early event that precedes the formation scar tissue.[14]

In conclusion, the potential importance of this study lies in its systematic and quantitative approach to the evaluation of factors that influence the recovery potential of the myocardium to compensate for tissue losses sustained after infarction. Related implications are foreseen in the use of these methods in estimating the efficacy of various pretreatments and therapies in improving the myocardial response to ischemic injury.

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