Clinical and Experimental Observation of Serum Enzyme Changes Occurring after Surgical Myocardial Revascularization*

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The activity of SGOT and LDH was studied in a selected group of patients and in experimental animals undergoing anterior and posterior myocardial revascularization. In both series, enzymatic elevation patterns similar to those seen in acute myocardial infarction were observed. The SGOT level reached its peak on the first postoperative day and returned to normal by the sixth or seventh day. The LDH level reached its peak 48 hours after surgery, followed by a gradual fall to normal between the tenth and 14th day. Having eliminated the influence of massive surgical stress or extracorporeal circulation, it was concluded that direct trauma to the wall of the left ventricle during construction of a myocardial tunnel is the primary factor responsible for a rise of serum enzyme activity as observed in the following revascularization procedures.

The introduction, by La Due and collaborators,† of serum SGOT activity measurement for detection of tissue necrosis has facilitated early diagnosis and follow-up of myocardial infarction. The enzymes which have emerged to date as routine diagnostic adjuvants in myocardial disease are serum glutamic oxaloacetic transaminase (SGOT), serum lactic dehydrogenase (LDH), and more recently, creatinine phosphokinase (CPK).

The considerable operative trauma associated with intracardiac surgery has been advanced as a possible cause for observed transient serum enzyme elevations. Several investigators have studied the pattern of serum enzyme changes associated with general, thoracic§–¶ and cardiovascular surgery, both with and without the use of extracorporeal circulation.$–^{12}$

We have observed the pattern of serum enzyme alterations during and after anterior and posterior myocardial revascularization procedures which involve direct implantation of arterial vessels into the myocardium. SGOT and LDH levels were examined in both human and animal subjects.

![Graph showing SCOT and LDH levels over post-operative days](http://journal.publications.chestnet.org/pdfaccess.ashx?url=/data/journals/chest/21472/)

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CASE 12—The peak of SCOT and LDH levels on the second postoperative day was preceded by the appearance of an electrocardiographic pattern compatible with acute diaphragmatic infarction.
cardiographic changes compatible with acute myocardial infarction (case 12, Fig 1, case 24, Fig 2, and case 14, Fig 3). Case 14 had demonstrated SCOT elevation two days after selective coronary angiography and evidence of very recent myocardial infarction was visible at surgery. The preoperative enzyme levels of all the other patients were within normal limits. All patients had showed evidence of coronary artery disease clinically and this was confirmed by cineangiography.

To obtain a meaningful experimental correlation, six mongrel dogs weighing approximately 30 kg each, were operated on in controlled fashion. Serial enzymatic studies of SCOT and LDH were carried out before and after myocardial implant revascularization. Both the clinical and the experimental procedures involved implantation of the right gastroepiploic artery into the diaphragmatic (posterior) wall of the left ventricle and implantation of the left internal mammary artery into the anterior wall of the left ventricle.

The animals were anesthetized by intravenous injections of 60 mg of pentothal per kilogram of body weight. Controlled respiration was achieved by intubation and use of mechanical respirator. A left lateral sixth intercostal space thoracotomy was made to expose the heart and mobilize the left internal mammary artery. For mobilization of the right gastroepiploic artery the abdomen was opened by incising the left hemidiaphragm.

In the clinical patients, anesthesia was induced with intravenous pentothal, followed by nitrous oxide-halothane closed circuit inhalation. Intravenous succinyl choline was administered as a muscle relaxant. A median sternotomy incision, extending into the abdomen for a distance of 5 to 8 cm below the xyphoid process was used. By incising the diaphragm for two thirds of its anteroposterior extent, the diaphragmatic surface of the heart was exposed. The right gastroepiploic artery was mobilized from the stomach, its distal 5 cm was skeletonized, and it then was implanted within the thickness of the diaphragmatic wall of the left ventricle. The internal mammary artery was implanted anteriorly close to the course of the anterior descending branch of the left coronary artery.

The myocardial tunnel was extended 5 cm within the substance of the left ventricular wall. Our clinical and experimental work suggests that a longer tunnel offers a better chance for patency of implanted arteries and, thus, aids the development of collateral circulation to the original coronary artery. Enzyme studies were carried out immediately prior to surgery and on each postoperative day until normal levels were reached. Creatinine phosphokinase and lactic dehydrogenase isoenzyme determinations were undertaken in some of the later patients, but sufficient data is not yet available for final evaluation. LDH values were determined by the Wroblewski and LaDue method. SCOT levels were measured by a modified Reitman-Frankel method. The normal range of SCOT and LDH levels was designated at 8 to 40 and 200 to 450 units per milliliter respectively in both species.

**RESULTS**

Typically, postoperative enzyme levels in our patients followed a pattern similar to that seen with an acute myocardial infarction of moderate size. The mean SCOT activity reached a peak of 122 units on the first day, declining to normal values by the seventh day. The mean high LDH peak was
SERUM ENZYME CHANGES AFTER REVASCULARIZATION

Figure 4. Mean SGOT and LDH values of the group of uneventful revascularization cases studied.

Figure 5. Pattern of SGOT values obtained in dogs undergoing anterior and posterior implantation revascularization procedures.

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1,073 on the second day, dropping close to normal levels by the ninth day, and returning to normal before the 14th day, if the postoperative course was otherwise uneventful (Fig 4).

The experimental animals demonstrated nearly identical enzyme patterns. Maximum SGOT elevation in dogs also occurred on the first postoperative day at a mean of 134 units and the peak in LDH occurred on the third postoperative day at a mean of 633 units (Fig 5 and 6). The postoperative course in each of the experimental animals was uneventful.

Our series showed no appreciable correlation between the extent of coronary artery disease ascertained by coronary cineangiography and serum enzyme elevation. However, there was a direct relationship between the peak and duration of enzyme elevation and the extent of myocardial damage as demonstrated in patient 14 at the time of surgery and in patients 21 and 24 during postmortem studies, thus tending to confirm the experimental work of Nydick and collaborators.16

With the exception of those patients who developed unquestionable myocardial infarction, postoperative electrocardiographic changes were transient and consistent with sinus tachycardia and nonspecific ST-T changes. Among the patients with extensive myocardial infarction, case 14 (Fig 3) demonstrated an SGOT elevation of 240 units two days after selective coronary angiography was performed. The LDH level was normal at this time and remained so for the three days which were permitted to elapse before revascularization surgery was performed. It rose to a peak of 1,960 units within the first 24 hours following operation. The highest SGOT level in this patient was 2,150 units on the first postoperative day. A normal SGOT level was reached on the seventh day after surgery and a normal LDH on the 19th day.

Two other patients, cases 12 and 24 showed electrocardiographic changes compatible with extensive myocardial infarction respectively 48 and 96 hours after surgery. The highest measured enzyme level in these two cases were 240 and 170 units SGOT on the first and fourth postoperative day and 2,400 and 2,300 units LDH on the fourth and sixth postoperative day (Fig 1 and 2).

In case 21, the clinical diagnosis of acute myocardial infarction was confirmed at postmortem examination, 20 days after surgery. Case 26 died five days after surgery with a persistent elevation of SGOT activity, probably attributable to myocardial infarction. Postmortem examination was not permitted.

It is worthy of emphasis that only those patients who developed the complication of extensive myocardial infarction manifested very elevated enzyme levels (cases 12, 14, 24, 21 and probably case 26).

**DISCUSSION**

Since the immediate postoperative course of patients undergoing myocardial revascularization may be altered by complications such as pulmonary embolism, myocardial infarction, or congestive heart
failure with various degrees of liver congestion conditions which in themselves can account for serum enzyme changes, it is of great importance that the physician be familiar with the uncomplicated postoperative pattern of variation in the level of these enzymes.

The function of the liver in relation to enzyme changes has been assessed by excretion tests and pathologic studies. Sulfobromophthalein (Bromsulphalein) excretion was found to be abnormal in 80 percent of individuals in whom carbamoyl transferase did not show a significant elevation. This determination is believed to be more contributory than the SCPT test in detection of liver dysfunction. Postmortem studies have not revealed any extensive central lobular necrosis to explain this type of impaired function. The evidence suggests that the observed enzyme changes are not secondary to liver damage.

The stress reaction of the body as a whole following cardiac surgery has been considered as another possible cause for any increase of serum enzyme activity. Cardiac surgery without extracorporeal bypass produces mild to moderate serum enzyme elevation depending upon the type and extent of the procedure. With use of extracorporeal circulation, significant elevation is encountered consistently and its height appears to be related directly to the duration of perfusion. Hemolysis, per se, does not appear to be a contributing factor. Although skeletal muscle trauma produced during thoracotomy and the generalized stress response of the body to any nondescript form of surgery conceivably might add a minor contribution to elevation of serum enzyme activity probably as a result of alteration in cell membrane permeability, our beliefs coincide with those of Ayres and William and Person and Judge that these usually do not constitute a sufficient stimulus for enzyme release.

Because of the nature of the surgical procedures, we were able to eliminate the effect of extracorporeal circulation on enzyme activity. Hemolysis was not a problem and the surgical stress was a standardized one comparable to that of other patients undergoing cardiac surgery without bypass. Blood losses were minimal and were promptly and adequately replaced. Hypotension did not present a difficulty. The overall surgical stress to the organism in our revascularization cases was not judged to be significantly greater than that of nondescript exploratory thoracotomy.

The enzyme activity pattern demonstrated by these patients provides basic knowledge which can be useful in the differential diagnosis of myocardial infarction from other conditions involving tissue necrosis. Several of our patients exemplified this by showing further elevation of serum enzymes during episodes of pulmonary embolism or myocardial infarction.

In the absence of complications, behavior of these serum enzymes in postrevascularization patients appears to be similar to that encountered in moderate degrees of myocardial infarction, corroborating earlier observations of Crafoord and co-workers. We conclude that direct operative trauma to the ventricular wall itself constitutes the prime stimulus to serum enzyme elevation in these cases.

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