Internal Mammary Artery Implantation  
Experimental and Clinical Analysis of the Effects of Implantation on the Ischemic Myocardium

Akira Nonoyama

The effectiveness of internal mammary artery implantation on the ischemic myocardium has been widely recognized, and the fact is now becoming accepted that the implant can give collateral to a coronary artery serving an ischemic area of the myocardium. The author has investigated the presence and the significance of the blood supply carried by the implant immediately after implantation, and demonstrated the immediate effect of implantation in improving the coronary blood flow to some extent in the previous reports.

Now, in the present report, the author shows the clinical and experimental observations that

<table>
<thead>
<tr>
<th>Case</th>
<th>Disease</th>
<th>ECG finding</th>
<th>Coronary ACG</th>
<th>Surgery</th>
<th>Post-op. Course</th>
<th>Post-op. ACG</th>
</tr>
</thead>
<tbody>
<tr>
<td>36 δ</td>
<td>Angina</td>
<td>T flat</td>
<td>positive</td>
<td>l. internal mammary art. implantation</td>
<td>28 months</td>
<td>5 weeks</td>
</tr>
<tr>
<td>48 δ</td>
<td>Angina</td>
<td>almost normal</td>
<td>positive</td>
<td>l. implant, + free omental graft</td>
<td>13 months</td>
<td>good</td>
</tr>
<tr>
<td>57 δ</td>
<td>Angina</td>
<td>T flat</td>
<td>positive</td>
<td>l. implant, + free omental graft</td>
<td>12 months</td>
<td>5 months</td>
</tr>
<tr>
<td>44 δ</td>
<td>Angina</td>
<td>coronary T</td>
<td>positive</td>
<td>l. implant, + free omental graft</td>
<td>4 months</td>
<td>excellent</td>
</tr>
<tr>
<td>62 δ</td>
<td>Angina</td>
<td>T flat</td>
<td>impossible</td>
<td>l. internal mammary art. implantation</td>
<td>3 weeks</td>
<td></td>
</tr>
</tbody>
</table>

Key Words: Internal Mammary Artery Implantation, Myocardial Revascularization, Angina Pectoris, Coronary Arteriography

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Fig. 1. Pre- and Post-operative courses in clinical cases

TABLE II  MYOCARDIAL EXTRACTION OF LACTATE AND PYRUVATE

<table>
<thead>
<tr>
<th>Clinical Cases</th>
<th>Arterial Lactate</th>
<th>Coronary Sinus Lactate</th>
<th>Arterial Pyruvate</th>
<th>Coronary Sinus Pyruvate</th>
</tr>
</thead>
<tbody>
<tr>
<td>pre-op.</td>
<td>4.13 ± 1.19</td>
<td>3.56 ± 0.4</td>
<td>3.70 ± 1.25</td>
<td>2.86 ± 0.64</td>
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<tr>
<td>post-op. (2 weeks)</td>
<td>5.91 ± 1.54</td>
<td>5.56 ± 1.63</td>
<td>5.01 ± 1.70</td>
<td>4.98 ± 1.37</td>
</tr>
<tr>
<td>Control</td>
<td>7.54 ± 0.76</td>
<td>5.08 ± 1.03</td>
<td>0.29 ± 0.04</td>
<td>0.23 ± 0.01</td>
</tr>
<tr>
<td>After ligation</td>
<td>8.07 ± 1.21</td>
<td>6.54 ± 1.27</td>
<td>0.38 ± 0.05</td>
<td>0.24 ± 0.07</td>
</tr>
<tr>
<td>Experimental Cases</td>
<td>immediately after implantation</td>
<td>7.16 ± 0.14</td>
<td>2.55 ± 0.89</td>
<td>0.22 ± 0.076</td>
</tr>
<tr>
<td>2 months after implantation</td>
<td>21.03 ± 4.28</td>
<td>17.04 ± 2.86</td>
<td>1.04 ± 0.18</td>
<td>0.91 ± 0.08</td>
</tr>
<tr>
<td>5 months after implantation</td>
<td>18.53 ± 2.71</td>
<td>12.01 ± 1.91</td>
<td>0.87 ± 0.08</td>
<td>0.70 ± 0.09</td>
</tr>
</tbody>
</table>

\[
Eh = \frac{E_0 + RT}{nF} \times \log_{\text{Red.}} \left( \frac{\text{Oxid.}}{\text{Lactate/Pyruvate}} \right) 
\rightarrow 
Eh = -204 - 30.7 \times \log_{\text{Pyruvate}} \frac{\text{Lactate}}{\text{Pyruvate}}
\]

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principally evaluate how the implant might alter functionally and morphologically until the implant forms a permanent anastomosis with branches of the coronary artery.

Clinically, as of the end of March, 1970, five patients afflicted with angina pectoris have undergone the internal mammary artery implantation on the left ventricle. They suffered from repeated and frequent chest pain attacks over a period of a year, and, at the same time, in whom the constrictive alterations in 2 or more of 3 major coronary arteries were demonstrated by the coronary arteriography (Table I). As implant, a pedicle consisting of left internal mammary artery and its surrounding soft tissue was obtained and was trimmed away 6 to 7 centimeters in length and then drawn through a tunnel into the ischemic myocardium according to the combined method of Vineberg-Sewell. Moreover, in 3 of 5 patients, the free omental grafting by epicardectomy of the posterior left ventricular wall according to the method of Vineberg was performed at the same time.

Postoperatively, all five patients are alive and their conditions have been uneventful up to this date. However, in respect of their courses after surgery, their complaints disappeared until 5 to 7 days after implantation, and thereafter, they complained of chest pain on exertion in particular, for which sometimes medication was a necessity, although their complaints were less than preoperatively. The period when they complained of chest pain continued for 4 to 5 weeks and then their complaints gradually disappeared (Fig. 1).

On the other hand, the difference between the redox potential of coronary sinus and arterial blood, that is the change in redox potential across the heart (ΔEh), was measured at the resting state 2 weeks after surgery to determine the effect of implantation on the myocardial oxidative metabolism by means of measuring the serum concentration of lactate and pyruvate. ΔEh was positive after surgery, although it was negative before surgery as shown in Table II. This change might be of significance, because a negative ΔEh is considered to be indicative of anaerobic metabolism in the myocardium.

Therefore, judging from these results, it would probably be indicated that the implantation is responsible for improving the ischemic myocardium after surgery, although it is not sufficient to correspond to any effort for at least 5 to 6 weeks after implantation.

In addition, the alteration in ΔEh across the heart is the best one among the objective index in order to determine the effectiveness of the implantation in clinical cases, although the determination of the effectiveness could be made by the other methods, such as the comparisons of the degree of the patients' complaints or the administrated doses of drugs before and after surgery as shown in Fig. 1.

The results of the selective implant angiographies at 5 weeks or 5 months after implantation showed the patencies of implant, but did not yet reveal the evident intramyocardial anastomoses between the implant and the coronary artery or the retrograde fillings of coronary artery from the implant.

The results obtained from the clinical observations as mentioned above seem to correspond with the following experimental results.

For the experiment, a series of adult mongrel dogs, weighing 14 to 16 kilograms were used. Ischemia of the left ventricle was produced by ligating 3 or 4 diagonal branches of the anterior descending artery at these origins except the first branch of the artery. As implant, a pedicle was used according to the combined method of Vineberg-Sewell, the same as in clinical cases.

Firstly, the implant flow was measured by means of a non-cannulating electromagnetic flow-

\[
\begin{array}{ccc}
\text{arterial} & \text{coronary} & \Delta E_h \\
\text{L/P} & \text{sinus} & \text{L/P (CS}_{Eh} - A_{Eh}) \\
1.14 \pm 0.06 & 1.27 \pm 0.09 & -1.46 \\
1.20 \pm 0.09 & 1.11 \pm 0.09 & +1.06 \\
28.65 \pm 0.22 & 22.07 \pm 0.22 & +4.03 \\
25.08 \pm 0.41 & 27.84 \pm 0.26 & -3.63 \\
27.05 \pm 1.74 & 18.76 \pm 2.86 & +3.35 \\
20.2 \pm 0.48 & 18.9 \pm 0.96 & +0.71 \\
21.23 \pm 0.94 & 17.21 \pm 1.74 & +2.82 \\
\end{array}
\]

\[\text{ΔEh} = \text{CS}_{Eh} - \text{A}_{Eh}\]
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Fig. 2. Changes of flow pattern and average flow rate in internal mammary artery implant immediately after implantation to 5 to 6 months after implantation.

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Fig. 3. Selective implant angiographies in 5 months after implantation.
A. in vivo angiography: the evident retrograde fillings of coronary artery from the implant are demonstrated.
B. postmortem angiography in same dog: the abundant arterio-arterial anastomosis between the implant (→) and the coronary artery is demonstrated. a triangular mark (←) shows the portion of ligation in the anterior descending artery.

Meter or ultrasonic flowmeter. The mean flow in the internal mammary artery immediately after implantation was nearly 15 ml per minute with maximal flow during systole which was equivalent to about 35 per cent of pre-implant flow and was proportionate to about 30 per cent of flow in the anterior descending artery. The trace of flow distinctly showed a forward flow in systole. However, the implant mean flow declined to values of 5 to 10 ml per minute with maximal flow during systole afterward. The decreases in implant flow were demonstrated until at least 2 to 3 weeks after implantation. The implant mean flow 1 to 2 months after surgery still remained unchanged with a value of about 5 ml per minute, although the tracing of flow showed a change in the small forward flow with two peaks of both systole and diastole. Moreover, a marked change in the pattern of flow in the implant 5 to 6 months after implantation was demonstrated, which was an alteration in the period of maximal flow from systole to diastole with the increased mean flow of about 15 ml per minute as shown in Fig. 2.

Secondly, in the selective implant angiography in vivo, which was performed by means of cineangiography at the speed of 130 frames per second, the patency of implant was verified, but the
retrograde filling of coronary artery from implant was not yet demonstrated at the stage 1 to 2 months after implantation. However, the post-mortem implant angiography in this stage showed the arterio-arterial anastomosis between the implant and the anterior descending artery distal to the ligation, although it was not abundant. In the advanced stage 5 to 6 months after implantation, in which the implant flow increased again 15 ml per minute during diastole as mentioned above, the selective implant angiography in vivo showed the evident retrograde fillings of coronary artery from the implant and this meant the comprehensive anastomosis between the implant and the coronary artery, while at the same time, the abundant arterio-arterial anastomosis between the implant and the coronary artery in the post-mortem implant angiography was demonstrated as shown in Fig. 3.

Nextly, the ability of implant to increase the flow in response to certain drugs was measured in each stage by means of administration of aramine (2 ml of a solution containing 10 mg in 100 ml of normal saline: 0.2 mg), isoproterenol (isuprel) (5 ml of a solution containing 0.3 mg in 100 ml of normal saline: 0.015 mg), or l-norepinephrine (levophed) (2 ml of a solution containing 1 ml of a 0.1 per cent solution in 100 ml of normal saline), respectively. The implant flow immediately after implantation and 1 to 2 weeks after implantation remained unchanged by the administration of these drugs. The result might show that the implant flow could not respond to any kind of effort in these stages. In the stage 1 to 2 months after implantation, aramine produced an effect on implant flow which increased about 40 per cent, whereas the implant flow did not differ significantly by the administration of isoproterenol and it rather decreased slightly by the administration of l-norepinephrine. The increased implant flow produced by the administration of aramine was attributable to the increase of flow during systole. The alteration of implant flow in response to drugs was more similar to that of systemic flow than that of coronary flow in this stage. However, in the advanced stage 5 to 6
months after implantation, isoproterenol increased implant flow of about 30 per cent, aramine increased implant flow by nearly 10 per cent, and l-norepinephrine increased it by about 5 per cent. The implant flow altered in these manners in response to drugs had more resemblance to that in a coronary rather than a systemic artery.

Furthermore, the alteration in the lactate extraction produced by the administration of isoproterenol as shown in Fig. 5 tended to be negative in each stage from immediately after implantation to 1 to 2 months after surgery like the alteration after the ligation of anterior descending artery, whereas in the stage 5 to 6 months after implantation it was corrected and became almost the same as the control pattern as shown in Fig. 5.

As summary, the experimental results from investigating the completion of anastomoses between implant and coronary artery correspond with that from clinical observations and would verify the effectiveness of internal mammary artery implantation on the ischemic myocardium. However, time is necessary for effective implant function and it is not always sufficient to supply the flow to the ischemic myocardium only by a single artery implantation. Therefore, the double implantation of 2 or more arteries at the same time or the combined methods with the other revascularization is necessary when the ischemic area of myocardium spreads over the anterior and posterior walls of ventricle.