EXHIBIT 1013
Intraoperative Coronary Angiography Using Fluorescein

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Intraoperative coronary angiography using fluorescein was applied to evaluate the patency of saphenous vein grafts just after completion of the distal anastomosis. By this technique, the area of the revascularized myocardium was well estimated in real time. This intraoperative direct-vision examination gives us more timely and precise information during coronary artery bypass grafting.

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Intraoperative measurement of the amount of graft flow by magnetic flow meter is the only way to determine the area of revascularized myocardium and graft patency. To obtain more precise and direct information during coronary revascularization, a reliable intraoperative visual examination method is desirable. Intraoperative coronary angiography using fluorescein was applied for this purpose in 29 consecutive cases of coronary artery bypass grafting.

Methods

As a contrast medium, 3 mL of 10% fluorescein sodium was diluted with 500 mL of normal saline solution (0.06% fluorescein solution) and 5 mL of 0.7% sodium bicarbonate; 3 mL of heparin was added to adjust the pH and to keep the anticoagulability. A 6-W black fluorescent light bulb was used as the fluorescence-evoking source.

After the distal anastomoses using saphenous vein graft were performed, all lights in the operating room were turned off, and the fluorescent black light bulb was hung 10 cm over the heart to illuminate the cardiac wall. Then 20 to 40 mL of fluorescent contrast media was injected from the proximal end of the saphenous vein graft using a pressure of 150 mm Hg (Fig 1).

Results

In all cases, bright green-yellow fluorescence was clearly observed in real time in the following order: bypass graft, anastomosis, coronary artery, its branch, myocardial wall, and coronary vein. The revascularized area through the graft showed bright fluorescence in clear contrast with the nonperfused adjacent area. The distribution of the graft flow and the anastomotic state could be easily recognized by the naked eye. Prolongation of the aortic cross-clamp time by this examination was only 1 to 2 minutes.

In Figure 2, a saphenous vein graft was anastomosed to the left anterior descending artery (LAD). A large perfused area including the first and the second diagonal branches of the LAD was clearly observed.

Figure 3 shows the sequential bypass graft to the posterior descending branch of the right coronary artery and the posterolateral branch of the circumflex artery. The fluorescein perfused the inferior and lateral cardiac walls through two anastomoses, and it showed bright fluorescence with a clear border. The first diagonal branch of the LAD was also detected by collateral flow from the poste-
In Figure 4, the saphenous vein was anastomosed to the LAD just distal to the second diagonal branch. At fluorescein angiography, the diagonal branches were well visualized first by the retrograde flow from the anastomosis (Fig 4A), and the antegrade stream to the LAD was observed with delay (Fig 4B). Through these findings, the pronounced stenosis at the anastomosis was strongly suspected. Because the extent of the fluorescence at the LAD area finally seemed to be enough (Fig 4B), no additional procedure was performed. The flow volume of this bypass graft measured by the magnetic flow meter was 65 mL/min, and the postoperative course was quite uneventful without showing any ST change on the electrocardiogram. Through findings in postoperative coronary angiography as well as in intraoperative examination, the preferential flow to the diagonal branches and the more than 50% stenosis of the anastomosis were confirmed (Fig 5A, B).

Fig 3. (A) Sequential bypass grafting to the posterior descending artery from right coronary artery (4-PD) and the posterolateral branch of the circumflex artery (PL). Fluorescein perfused through both anastomoses and also through the area of the first diagonal branch (D1) of the left anterior descending artery. (B) The schema. (SV = saphenous vein graft.)
Comment

There is no other conventional method except magnetic flow meter to evaluate the surgical results intraoperatively in coronary artery bypass grafting. If the graft flow volume measured by magnetic flow meter is unexpectedly low, the question arises whether it is due to anastomotic stenosis or to poor peripheral run-off. Surgeons cannot get any information until postoperative coronary angiography is performed.

The results of intraoperative thermography [1] for this purpose are sometimes misunderstood owing to many kinds of artifacts such as cold saline solution used for topical cooling, cardioplegic solution, and the surgeon's finger. Furthermore, the necessity of special equipment makes this method unpopular.

Intraoperative coronary angiography using fluorescein was performed for indirect myocardial revascularization by Armellini and colleagues [2], but it was not applied to visualize directly the coronary arteries. Through our method, exact quantitative evaluation of the stenosis such as given by coronary angiography was difficult but enough clinical information as to whether the stenosis of the anastomosis is critical or whether the distribution of the graft flow is normal could be obtained by observing the passage and smoothness of the fluorescent stream through the anastomosis.

The safety of the fluorescein has been fully studied in the field of the ophthalmography [3]. Sodium bicarbonate was added to the contrast media to adjust the pH between 7.0 and 9.0, at which fluorescein showed best contrast. The 6-W fluorescent black light evoked enough fluorescence from the contrast medium. Application of this method is now limited to the vein graft because of the difficulty of finding feasible access for the fluorescein injection into arterial grafts.

In conclusion, this technique was quite easy and reproducible within a minimum time without any special equipment. We believe intraoperative coronary angiography using fluorescein is a useful and practical examination for performing more precise coronary artery bypass grafting.
Fig 5. Postoperative coronary angiography of the patient shown in Figure 4. (A) Initial phase: the diagonal branches were visualized before the left anterior descending artery (LAD) distal to the anastomosis. (B) Late phase: LAD now well seen. (C) Schema of (A). (D2 = second diagonal; SV = saphenous vein graft.)

References

