Tohoku J. Exp. Med., 1989, **158**, 291-299

Recanalization of Experimental Thrombotic Arterial Occlusion by Radiofrequency Thermal Angioplasty: An Angioscopic Observation

YUSUKE TAMURA, MASARU YAMAZOE, TAKU MATSUBARA, YUTAKA IGARASHI, TOHRU IZUMI, AKIRA SHIBATA, SENJI HAYASHI,* HIDEAKI TOYOSHIMA,* YOSHIAKI SAITO† and HIDEO MAKINO†

*The First Department of Internal Medicine and *Department of Public Health, Niigata University School of Medicine, and †Department of Information Engineering, Faculty of Engineering, Niigata University, Niigata 951*

TAMURA, Y., YAMAZOE, M., MATSUBARA, T., IGARASHI, Y., IZUMI, T., SHIBATA, A., HAYASHI, S., TOYOSHIMA, H., SAITO, Y. and MAKINO, H. *Recanalization of Experimental Thrombotic Arterial Occulusion by Radiofrequency Thermal Angioplasty: An Angioscopic Observation.* Tohoku J. Exp. Med., 1989, **158** (4), 291-299 —— The efficacy of radiofrequency (RF) angioplasty for recanalization of arterial thrombosis was assessed angioscopically in five dogs. A thrombus was induced by balloon injury of the left femoral artery. Within two hr, thrombi led to total occlusion of the artery in three dogs, subtotal occlusion in one, and about 70% obstruction in one. A metal-tipped catheter, with a tip size of 2.0 mm × 5.7 mm, was advanced into the thrombus and RF at 13.56 MHz was delivered repeatedly with gradually increased energies. The arterial lumina were recanalized or enlarged in all dogs. The thrombus surface had a shaggy appearance, and were dark (charring), or mixed dark and white in color. There were relatively large variations in the energies required; 140 J in one, 200 J in two and 250 J in two. The present results suggest that thrombotic arterial occlusion, such as acute occlusion complicating balloon angioplasty, can be treated with RF thermal angioplasty. Angioscopy provided detailed information about thrombus surfaces. The variations in required energies indicate the inability to control the thermal effect by energy settings alone. A more sophisticated method such as measurement of tip temperature will be able to overcome this difficulty. ——— radiofrequency current; thermal angioplasty; laser angioplasty; angioscopy; thrombosis

Balloon angioplasty, since its introduction into clinical practice, has proved to be a very effective method for the treatment of patients with peripheral, as well as coronary, atherosclerotic disease. However, there remain several limitations to

Received February 6, 1989; revision accepted for publication August 2, 1989.

Correspondence: Yusuke Tamura, M.D., the First Department of Internal Medicine, Niigata University School of Medicine, 1-754 Asahimachi-Dori, Niigata 951, Japan.

be solved. Complications such as acute arterial occlusion do occur in spite of advanced balloon technology and increased experience of the operator (Ellis et al. 1988 ; Steffenino et al. 1988). Dilatation of chronic total occlusion and long tight stenosis is difficult (Melchior et al. 1987). Restenosis, which occurs in about 30% of patients, is also one of the major drawbacks of balloon angioplasty (Nobuyoshi et al. 1988). To counteract these limitations of conventional balloon angioplasty, the feasibility of laser angioplasty has been explored (Litvack et al. 1988b ; Sanborn 1988). Since it was shown that direct laser irradiation causes vessel perforation at unacceptably high rates (Abela et al. 1985a ; Crea et al. 1986), the "hot tip" method or laser thermal angioplasty has been developed (Abela et al. 1985b ; Sanborn et al. 1985).

Laser, however, is not the only way to heat the catheter tip (Litvack et al. 1988b). For the treatment of cardiac arrhythmias, radiofrequency (RF) current has been used to ablate normal or accessory conduction pathways (Borggrefe et al. 1987 ; Huang et al. 1987). The advantage of RF is that it is considerably less expensive than laser and that the equipment is compact. Thus, thermal angioplasty energized by RF merits validation. In fact, there have already been several reports on RF thermal angioplasty in both experimental and clinical settings (Litvack et al. 1987, 1988a ; Hoeher et al. 1988). In the present study, we tried to recanalize experimental thrombotic occlusions of canine femoral arteries by RF thermal angioplasty and evaluated the effect by fiberoptic angioscopy (Tomaru et al. 1987).

Method

Equipment

The RF generator (RA50 ; Inter Nova, Tokyo) was developed by Saito and his colleagues, and its prototype had been reported previously (Arai et al. 1987). It consists of a power generator and an automatic impedance matching device to enable constant power delivery. The generated frequency is 13.56 MHz with a maximal output of 50 W. The RF power is adjusted manually using an internal load before applying to animals. Duration of RF delivery is preset with a built-in timer, but can also be turned off prematurely when required.

A metal-tipped unipolar catheter was constructed as follows : a piece of metal, 2.0 mm in diameter and 5.7 mm in length, was mounted on the tip of a 0.035 inch guidewire (USCI, Billerica, MA, USA) and the shaft was insulated with a plastic tube.

A fiber angioscopic system, FCA-8000B (Fukuda Denshi Co. Ltd., Tokyo), was used to observe the canine arteries (Fig. 1). Angioscopic images were delivered to the video processor, displayed on color CRT monitor and recorded in VTR. The fiberoptic angioscopic catheter (AS001 ; Fukuda Denshi Co. Ltd.) has a diameter of 0.75 mm, and contains 3,000 silica fibers as image guide and 50 fibers as light guide. It was inserted into the artery through a 5 Fr. multipurpose catheter (American Edwards Laboratories, Irvine, CA, USA).

Animal preparation

After premedication with i.m. morphine hydrochloride, five adult mongrel dogs of either sex, weighing 7.5 to 10 kg, were anesthetized by i.v. administration of a solution of urethane and α-chloralose, intubated and artificially ventilated with room air. The abdominal aorta

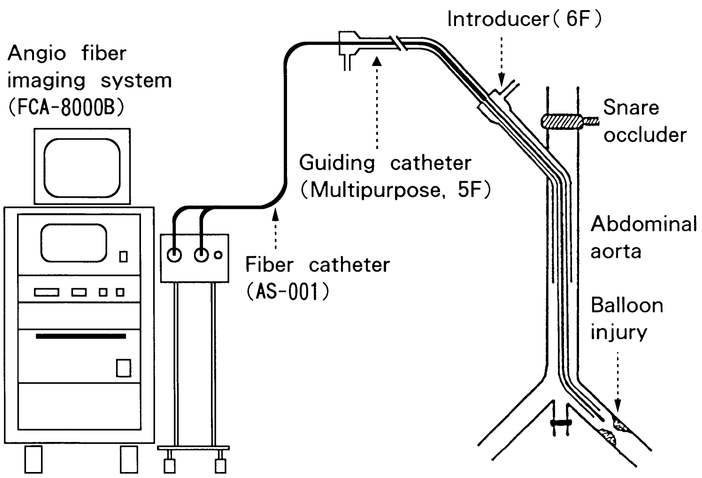

Fig. 1. Schematic representation of the experiment. The abdominal aorta was cannulated with a 6 Fr. introducer for insertion of catheters. In this figure, the angioscopic catheter is introduced through a 5 Fr. multipurpose catheter.

was dissected free from surrounding tissue with all side branches ligated and incised. A 6 Fr. catheter introducer (Argon Medical Corp., Athens, TX, USA) was cannulated into the aorta distal to the renal arteries through an incision and fixed by a purse-string suture. A snare occluder was placed around the aorta proximal to the catheter introducer (Fig. 1). Systemic heparinization was avoided to encourage thrombus formation.

Study protocol

After confirming by angioscopy that the arterial lumen was intact before induction of the thrombus, a 4 Fr. Berman angiographic catheter (Critikon Inc., Tampa, FL, USA) was introduced through the catheter introducer into the left femoral artery and inflated with 0.2 to 0.3 ml of saline, then pulled back twice over about 1 cm. Growth of thrombus was observed with the angioscope immediately after balloon injury and at 15, 30, 60, 90 and 120 min. During each observation the abdominal aorta was clamped with the snare and saline was flushed manually through the guiding catheter to displace blood. When the arterial lumen became completely occluded or 120 min had passed, the metal-tipped catheter was advanced into thrombus and RF was applied between the catheter and a patch electrode placed on the back of the dog. The RF energy was initially set at 140 J, with a power of 7 W and a duration of 20 sec. After completion of the RF delivery, the metal-tipped catheter was withdrawn and angioscopic observation was done to see the effect of RF angioplasty. If the thrombus was not recanalized, RF angioplasty was repeated with gradually increasing energies; the power was increased with 1 W increments up to 10 W while the duration was kept constant at 20 sec, but the enegry settings were individualized at higher ranges.

Results

Serial angioscopic observations revealed complete occlusions of the arterial lumina with thrombi in three of the five dogs within 120 min after balloon injury (dogs 1, 3 and 5; Table 1). Dog 2 showed subtotal occlusion 120 min after balloon injury and dog 4 about 70% obstruction. All of the thrombi were ablated

TABLE 1. *Result of RF thermal angioplasty*

Dog	Degree of lumen obstr. before RF	RF Energy: Power (W) × time (sec)	Degree of lumen obstr. after RF	Thr. surface after RF
1	Total	7×20	60%	Dark and whitish
2	Subtotal	10×20 (twice)	Thr. retarded*	
		$8 \times 30 + 25 \times 10$	90%	Dark
3	Total	10×20	50%	Dark
4	70% Obstr.	10×20	40%	Dark and whitish
5	Total	10×25†	<80%	Dark and whitish

*No vigorous reflow was observed.
†Long thrombus extended distally was ablated at multiple sites. Obstr., obstruction; RF, radiofrequency; Thr., thrombus.

by RF thermal angioplasty and the arterial lumina were recanalized or enlarged. However, there were relatively large variations among dogs in the energies required to recanalize the thrombi. Energy of 140 J was sufficient only in dog 1. In dogs 3 and 4, 200 J was needed. In dogs 2 and 5, much higher energy, 250 J, was required.

Fig. 2 shows the examples of the angioscopic findings from dog 2 (panels a through d) and dog 5 (panels e and f). In panel a, the arterial lumen is subtotally occluded with thrombus two hours after balloon injury. Panel b shows the result of RF angioplasty with a power of 10 W for 20 sec (200 J); the thrombus is somewhat retarded and is displaced laterally, but there is no vigorous reflow at this time, indicating that mere advancement of the catheter or RF of low energy is not capable of recanalizing the thrombus. Panel c is the result of further RF application, 8 W for 30 sec plus 25 W for 10 sec. The thrombus was charred and changed to dark in color. A new lumen was created as seen at the center of the picture. A vigorous reflow was observed as in panel d. There was no charring of the arterial wall. Panel e shows the result of RF angioplasty at 10 W for 25 sec on total occlusion in dog 5. The thrombus was ablated and the lumen reopened. The surface of the thrombus looked whitish rather than dark. In this dog the thrombus extended distally to the level of the knee, so this long thrombus was ablated at multiple sites with energy of 250 J (10 W for 25 sec) at each site. The long thrombus was successfully recanalized as shown in panel f. The surface of the thrombus looked shaggy, and dark and whitish appearances were intermixed.

Fig. 3 is a histologic section (Mallory's stain) from dog 5. The vessel lumen is occupied by a large thrombus. The cleft at the upper portion is an artifact of tissue processing. A new lumen is seen at the lower left of the figure. Debris-like material attaches to the inner surface of the recanalized lumen. The thrombus around the new lumen stains yellowish and this was thought to represent the thermal effect. There seems to be, however, no apparent changes in the arterial wall, suggesting that the thermal effect is relatively confined to the thrombus.

Discussion

Laser thermal angioplasty is considered to be a relatively safe method because it is accompanied by less frequent vessel performation than direct laser irradiation (Abela et al. 1985b ; Sanborn et al. 1985). In an animal experiment (Sanborn et al. 1987), the restenosis rate was lower after laser thermal angioplasty than after balloon angioplasty. A recent report on its clinical use (Sanborn et al. 1988) showed satisfactory results; long lesions could be recanalized and the chronic patency rate was relatively high.

However, an energy source other than laser can be used to heat the catheter tip. Litvack et al. (1987, 1988a) applied RF thermal angioplasty on experimentally induced chronic occlusions of canine arteries and occlusions of human femoropopliteal arteries. The temperature at the catheter tip was measured and controlled in their RF angioplasty system. Hoeher et al. (1988) successfully dilated ten out of thirteen human coronary arteries with a ring-shaped tip electrode catheter. Therefore, RF thermal angioplasty seems to be a potential alternative to laser thermal angioplasty.

In this study, we used the RF thermal angioplasty to treat thrombotic occlusion induced by balloon injury instead of atherosclerotic obstruction. The thrombi grew rapidly during the two hours' observation period and were successfully recanalized by RF angioplasty. The clinical relevance of this experimental thrombosis might be the acute arterial occlusion complicating balloon angioplasty. Although arterial dissection seems to be a major cause of acute arterial occlusion (Ellis et al. 1988), there is no doubt that thrombosis also plays an important role in the pathogenesis of acute occlusion (Holmes et al. 1983 ; Hickey et al. 1986 ; Lam et al. 1986 ; Barnathan et al. 1987 ; Kohchi et al. 1987). Repeated balloon inflations often fails to resolve acute occlusions (Steffenino et al. 1988) ; thus, simple mechanical compression seems inadequate to treat acute occlusions. Although our experimental model of arterial injury is not identical to balloon angioplasty (Lam et al. 1986), the result of the present study suggests that RF thermal angioplasty may be used for the treatment of acute occlusions in a certain group of patients.

We evaluated the result of RF angioplasty by means of angioscopy. It provides much more detailed information on arterial surface than angiography (Hickey et al. 1986 ; Sherman et al. 1986 ; Tomaru et al. 1987). In the present study, the surface of the thrombus changed dark or whitish after RF application. The dark color indicates charring and the whitish appearance probably represents "desiccation" of the thrombi. Another finding to be noted is the shaggy appearance of the thrombus surface. This seems to correspond to the debris-like material seen on the surface of the neolumen in the histologic specimen. We speculate that the shagginess resulted from the detachment of the catheter tip which had become firmly stuck to the thrombus by the RF application. It remains to be determined whether the continuous to-and-fro movement of the catheter (Sanborn et al. 1988) can smooth the luminal surface.

Although there may be concern about untoward effects on the normal arterial wall, charring of the arterial wall was not noted by angioscopy. Histologic specimen also showed no apparent change in the arterial wall. These findings may imply that the thermal injury produced by RF is relatively limited to the near field around the electrode. But a long term follow up study may be required to see the chronic effect of sub-vaporizing energy.

Another and probably the most important result of our study is that there were relatively large variations in the energies required for thrombus ablation. So we think it difficult to accurately predict the extent of the thermal effect from the amount of the applied RF energy alone (Haines et al. 1987). Theoretically the temperature increase by RF is related to current density (Budde et al. 1987). So even when an identical electrode is used, the temperature increase will vary depending on the net area of the electrode that is in contact with the tissue ; that is, when only a small part of the electrode is in contact with the thrombus, the increase in temperature may be larger than when the entire electrode is in contact. This mechanism seems to contribute to the variations in RF energies. Since it has been shown that the extent of thermal injury is related to temperature at the catheter tip (Arai et al. 1987 ; Haines et al. 1987), measurement of the catheter tip temperature (Litvack et al. 1987, 1988a) will be a valuable method to regulate the thermal effect of RF.

In conclusion, the present results show that RF thermal angioplasty can be effective in treating thrombotic arterial occlusion, such as acute occlusion complicating conventional balloon angioplasty. Angioscopic observation provided detailed information about the thrombus surface. The effect of RF could not be predicted by the RF energy alone, and it was considered that a more sophisticated method such as measurement of the electrode temperature will enable us to control the thermal effect.

References

1) Abela, G.S., Normann, S.J., Cohen, D.M., Franzini, D., Feldman, R.L., Crea, F., Fenech, A., Pepine, C.J. & Conti, C.R. (1985a) Laser recanalization of occluded atherosclerotic arteries in vivo and in vitro. *Circulation*, **71**, 403-411.
2) Abela, G.S., Fenech, A., Crea, F. & Conti, C.R. (1985b) "Hot tip" : Another method of laser vascular recanalization. *Lasers Surg. Med.*, **5**, 327-335.
3) Arai, Y., Masani, F., Kato, H., Sasagawa, Y., Shibata, A., Eguchi, S., Nemoto, K., Makino, H. & Saito, Y. (1987) Experimental study of myocardial ablation by radio frequency current. *Cardiac Pacing*, **3**, 29-33. (Japanese)
4) Barnathan, E.S., Schwartz, J.S., Taylor, L., Laskey, W.K., Kleaveland, J.P., Kussmaul, W.G. & Hirshfeld, J.W. (1987) Aspirin and dipyridamole in the prevention of acute coronary thrombosis complicating coronary angioplasty. *Circulation*, **76**, 125-134.

5) Borggrefe, M., Budde, T., Podczeck, A. & Breithardt, G. (1987) High frequency alternating current ablation of an accessory pathway in humans. *J. Am. Coll. Cardiol.*, **10**, 576-582.
6) Budde, T., Borggrefe, M., Podczeck, A., Jacob, B., Langwasser, J., Frenzel, H. & Breithardt, G. (1987) Radiofrequency ablation: An improvement of ablation techniques in comparison to direct-current delivery? In: *Nonpharmacological Therapy of Tachyarrhythmias*, edited by G. Breithardt, M. Borggrefe & D. Zipes, Futura Publishing Company, New York, pp. 221-241.
7) Crea, F., Abela, G.S., Fenech, A., Smith, W., Pepine, C.J. & Conti, C.R. (1986) Transluminal irradiation of coronary arteries in live dogs: An angiographic and morphologic study of acute effects. *Am. J. Cardiol.*, **57**, 171-174.
8) Ellis, S.G., Roubin, G.S., King, S.B., III., Douglas, J.S., Jr., Weintraub, W.S., Thomas, R.G. & Cox, W.R. (1988) Angiographic and clinical predictors of acute closure after native vessel coronary angioplasty. *Circulation*, **77**, 372-379.
9) Haines, D.E., Watson, D.D. & Halperin, C. (1987) Monitoring electrode tip temperature during radiofrequency fulguration of ventricular myocardium is strongly predictive of lesion size. *Circulation*, **76**, Suppl. IV, IV-406.
10) Hickey, A, Litvack, F., Grundfest, W., Sherman, T., Lee, M., Chaux, A., Kass, R., Blanche, C., Matloff, J., Swan, H.J.C. & Forrester, J. (1986) In vivo angioscopy following balloon angioplasty. *Circulation*, **74**, Suppl. II, II-458.
11) Hoeher, M., Hombach, V., Hoepp, H.W., Eggeling, T. & Kochs, M. (1988) Percutaneous coronary "hot tip" angioplasty in man using a radiofrequency catheter. *Circulation*, **78**, Suppl. II, II-296.
12) Holmes, D.R., Vliestra, R.E., Mock, M.B., Reeder, G.S., Smith, H.C., Bove, A.A., Bresnahan, J.F., Piehler, J.M., Schaff, H.V. & Orszulak, T.A. (1983) Angiographic changes produced by percutaneous transluminal coronary angioplasty. *Am. J. Cardiol.*, **51**, 676-683.
13) Huang, S.K., Bharati, S., Graham, A.R., Lev, M., Marcus, F.I. & Odell, R.C. (1987) Closed chest desiccation of the atrioventricular junction using radiofrequency energy — a new mehtod of catheter ablation. *J. Am. Coll. Cardiol.*, **9**, 349-358.
14) Kohchi, K., Takebayashi, S., Block, P.C., Hiroki, T. & Nobuyoshi, M. (1987) Arterial changes after percutaneous transluminal coronary angioplasty: Results at autopsy. *J. Am. Coll. Cardiol.*, **10**, 592-599.
15) Lam, J.Y.T., Chesebro, J.H., Steele, P.M., Dewanjee, M.K., Badimon, L. & Fuster, V. (1986) Deep arterial injury during experimental angioplasty: Relation to a positive indium-111-labeled platelet scintigram, quantitative platelet deposition and mural thrombosis. *J. Am. Coll. Cardiol.*, **8**, 1380-1386.
16) Litvack, F., Grundfest, W., Mohr, F., Jakubowski, A., Goldenberg, T., Strul, B. & Forrester, J.S. (1987) "Hot tip" angioplasty by a novel radiofrequency catheter. *Circulation*, **76**, Suppl. IV, IV-47.
17) Litvack, F., Grundfest, W., Mohr, F., Strul, B., Goldenberg, T., Roth, F.J., Kirchhoff, P.G. & Forrester, J.S. (1988a) Percutaneous "hot tip" angioplasty in man by a radiofrequency catheter. *J. Am. Coll. Cardiol.*, **11**, 108A.
18) Litvack, F., Grundfest, W.S., Papaioannou, T., Mohr, F.W., Jakubowski, A.T. & Forrester, J.S. (1988b) Role of laser and thermal ablation devices in the treatment of vascular diseases. *Am. J. Cardiol.*, **61**, 81G-86G.
19) Melchior, J.P., Meier, B., Urban, P., Finci, L., Steffenino, G., Noble, J. & Rutishauser, W. (1987) Percutaneous transluminal coronary angioplasty for chronic total coronary arterial occlusion. *Am. J. Cardiol.*, **59**, 535-538.
20) Nobuyoshi, M., Kimura, T., Nosaka, H., Mioka, S., Ueno, K., Yokoi, H., Hamasaki, N., Horiuchi, H. & Ohishi, H. (1988) Restenosis after successful percutaneous transluminal coronary angioplasty: Serial angiographic follow-up of 229 patients. *J. Am. Coll. Cardiol.*, **12**, 616-623.

21) Sanborn, T.A. (1988) Laser angioplasty: What has been learned from experimental and clinical trials? *Circulation*, **78**, 769-774.
22) Sanborn, T.A., Faxon, D.P., Haudenschild, C.C. & Ryan, T.J. (1985) Experimental angioplasty: Circumferential distribution of thermal energy with a laser probe. *J. Am. Coll. Cardiol.*, **5**, 934-938.
23) Sanborn, T.A., Haudenschild, C.C., Garber, G.R., Ryan, T.J. & Faxon, D.P. (1987) Angiographic and histologic consequences of laser thermal angioplasty: Comparison with balloon angioplasty. *Circulation*, **75**, 1281-1286.
24) Sanborn, T.A., Cumberland, D.C., Greenfield, A.J., Welsh, C.L. & Guben, J.K. (1988) Percutaneous laser thermal angioplasty: Initial results and 1-year follow-up in 129 femoropoliteal lesions. *Radiology*, **168**, 121-125.
25) Sherman, C.T., Litvack, F., Grundfest, W., Lee, M., Hickey, A., Chaux, A., Kass, R., Blanche, C., Matloff, J., Morgenstern, L., Ganz, W., Swan, H.J.C. & Forrester, J. (1986) Coronary angioscopy in patients with unstable angina pectoris. *N. Engl. J. Med.*, **315**, 913-919.
26) Steffenino, G., Meier, B., Finci, L., Velebit, V., Von Segesser, L., Faidutti, B. & Rutishauser, W. (1988) Acute complications of elective coronary angioplasty: A review of 500 consecutive procedures. *Br. Heart. J.*, **59**, 151-158.
27) Tomaru, T., Uchida, Y., Masuo, M., Kato, A. & Sugimoto, T. (1987) Experimental canine arterial thrombus formation and thrombolysis: A fiberoptic study. *Am. Heart J.*, **114**, 63-69.

Fig. 2. Angioscopic findings in dogs 2 (panels a through d) and 5 (panels e and f). a, Subtotal occlusion of the arterial lumen in dog 2; b, The thrombus is somewhat retarded and displaced laterally but not recanalized by RF thermal angioplasty at 10 W for 20 sec; c, Recanalization of the lumen by further RF application, 3 W for 30 sec plus 25 for 10 sec. Note that the surface of the throbus changed dark; d, Vigorous reflow at the next instance (left upper part of the panel); e, Recanalization of the total occlusion after RF at 10 W for 25 sec in dog 5; f, Recanalization of the distally-extended thrombus.

Fig. 3. Histologic section from dog 5. (Mallory's stain.)

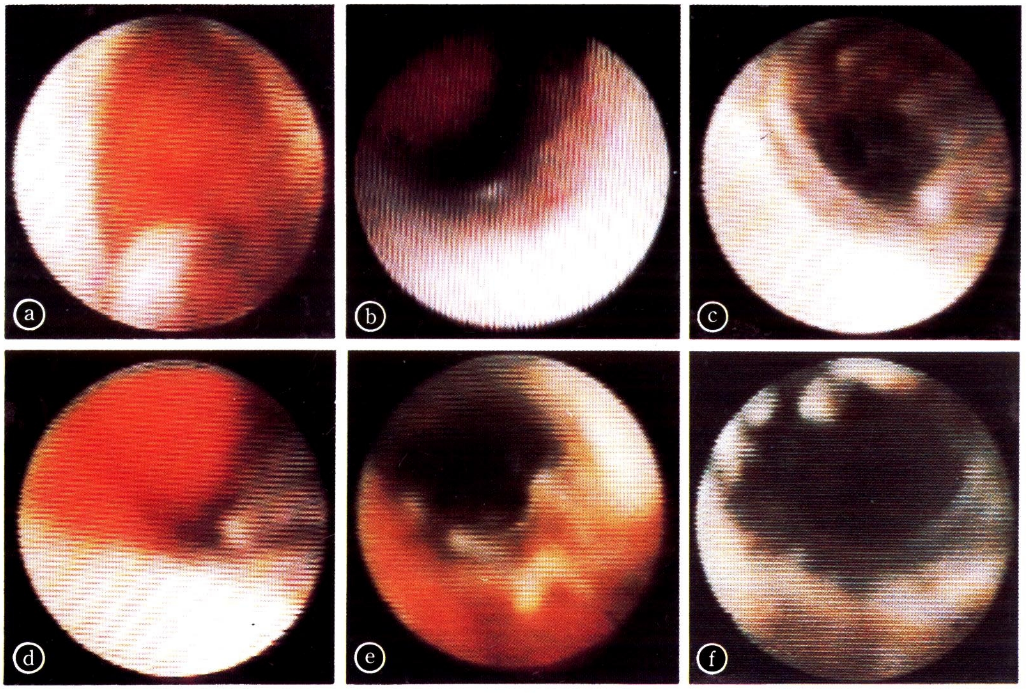

Fig. 2.

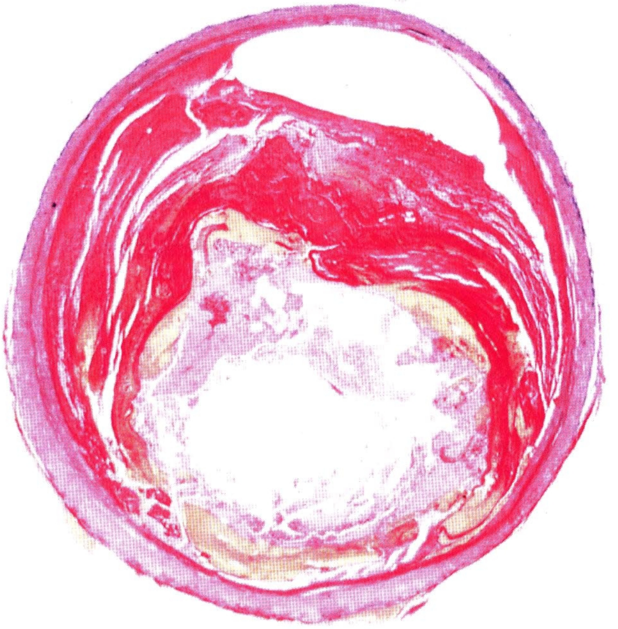

Fig. 3.