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Coronary Embolization After Balloon Angioplasty or Thrombolytic Therapy: An Autopsy Study of 32 Cases

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Objectives. **This study was undertaken to examine the nature, extent and clinical relevance of coronary embolism after balloon angioplasty or thrombolytic therapy, or both.**

Background. **Histopathologic documentation of postinterventional coronary embolization has been reported in only 10 patients from five studies.**

Methods. **This retrospective autopsy-based study included 32 patients, treated with balloon angioplasty or thrombolysis, or both, who died within 3 weeks of the procedure and underwent autopsy at the Mayo Clinic. Clinical variables included patient age and gender, artery treated, site and type of obstruction, type of intervention, success of the procedure, and postprocedural changes in the electrocardiogram (ECG), cardiac enzymes and hemodynamic status. Histopathologic variables included characteristics of treated plaques, acutely infarcted myocardium and coronary microemboli. Associations between microemboli and clinical and microscopic factors were evaluated by *t* tests and simple and multiple linear regression.**

Results. **Emboli were observed in 26 (81%) of the 32 patients. Among 83 emboli, 95% were thrombotic or atheromatous. The presence of microemboli was associated statistically with the development of postprocedural infarct extension, new myocardial infarction or new ECG abnormalities. Moreover, the greatest number of microemboli were associated with intervention in the left anterior descending coronary artery, multiple interventional sites, postprocedural medial dissection and plaque rupture or extrusion.**

Conclusions. **Among patients undergoing balloon angioplasty or thrombolytic therapy who die and undergo autopsy, coronary microemboli occur in a substantial percent. The frequency in survivors is unknown. However, in living patients who develop acute myocardial ischemia or new ECG abnormalities after these interventions, coronary microembolization should be considered a potential cause.**

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Clinically, coronary embolization is considered to represent a relatively rare complication of coronary balloon angioplasty, especially in elective procedures in patients with stable disease (1–3). The phenomenon is thought to be more prevalent among patients with acute coronary thrombosis and acute myocardial infarction who undergo balloon angioplasty or thrombolytic therapy, or both (4–8). Investigators have also reported embolization of thrombotic or atheromatous material elsewhere in the systemic circulation after these coronary interventions (9–12).

The clinical consequences of coronary embolization depend on both the size and the number of embolic particles. In some cases, the results may be clinically undetectable, whereas in others the process may be responsible for acute myocardial ischemia or infarction, ventricular arrhythmias or sudden death (4,7,13,14). To our knowledge, histopathologic documentation of coronary embolization after balloon angioplasty or thrombolysis, or a combination of the two therapies, has been reported in only 10 patients from five studies (8,15–18).

With these considerations in mind, the present retrospective autopsy-based study was undertaken to evaluate the nature, extent and clinical relevance of postinterventional coronary embolization in a relatively large number of patients from a single institution. This represents an extension of our previous histopathologic study of coronary embolization after balloon angioplasty of aortocoronary saphenous vein bypass grafts (14).

Methods

Study group. In the decade between January 1980 and December 1989, 32 patients were identified who met the following criteria: 1) treatment with coronary balloon angioplasty or thrombolysis, or both; 2) death within 3 weeks of the intervention; 3) no coronary surgery during this time; and 4) autopsy examination at the Mayo Clinic (with cardiac evaluation by W.D.E.). The study group included 20 men

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and 12 women with a mean age of 66 years (range 28 to 88). Twenty-one (66%) had a previous history of chronic ischemic heart disease.

The initial clinical diagnosis was acute myocardial infarction in 23 patients (72%) and stable exertional angina without acute infarction in 9. Among all 32 patients, 17 were treated with balloon angioplasty alone, 10 had both angioplasty and thrombolysis and 5 had thrombolysis alone (either streptokinase or recombinant tissue-type plasminogen activator). For the 27 patients treated with balloon angioplasty, the intervention involved multiple sites in 9 (33%) and multiple arteries in 5 (19%). The time interval between intervention and death was <1 day in 17 patients, 1 day to 1 week in 11, 1 to 2 weeks in 3 patients and 2 to 3 weeks in 1 patient.

Clinical evaluation. *Patients with balloon angioplasty.* Stenotic sites that were subjected to balloon angioplasty were categorized according to coronary artery (left anterior descending, left circumflex, right or their branches), location (proximal, middle or distal), and type of obstruction (discrete, nondiscrete or complete occlusion). The hemodynamic stability of the patient both before and during the procedure was also recorded, as it also was for thrombolytic therapy.

Balloon angioplasty was considered angiographically successful if the postinterventional stenosis was ≤50%. A procedure was considered angiographically unsuccessful if one or more of the following occurred: 1) the postinterventional stenosis remained >50%; 2) the operator was unable to cross the lesion; 3) the artery developed a severe dissection; or 4) the artery immediately reoccluded.

Embolus-related events. To determine whether a new infarction or infarct extension occurred after balloon dilation or thrombolysis (or both), preinterventional and postinterventional clinical findings were compared, with particular emphasis on changes in the electrocardiogram (ECG), cardiac enzymes and hemodynamic status. Postinterventional changes in the ECG that may have resulted from coronary embolization were also recorded, including significant tachybradyarrhythmias, ventricular premature contractions, atrial fibrillation and atrioventricular or bundle branch block.

Specimen evaluation. *Coronary arteries.* Hearts were perfusion fixed in 10% neutral buffered formalin, and the major epicardial arteries were removed and placed into decalcifying solution. Specimens were handled carefully to avoid bending the coronary arteries and thereby dislodging thrombotic or atheromatous material.

After decalcification, the coronary arteries were step-sectioned at 3-mm intervals. For infarct-related arteries and for arteries involved by thrombosis or subjected to balloon angioplasty, the entire length of the vessel was submitted for histologic evaluation. For each of the other coronary arteries, six to eight sections were processed for microscopy. Slides were stained with hematoxylin-eosin and elastic-van Gieson.

Treated coronary arteries were evaluated microscopically (by T.W.M. and W.D.E.) for both chronic and acute features. Chronic plaques were examined for location, degree of stenosis (critical [>75%] or noncritical), shape (eccentric or concentric), consistency (soft and necrotic or hard and fibrocalcific) and the presence of calcification (previous decalcification did not interfere with identification of sites of calcification). Acute alterations that were evaluated included lumen thrombosis, medial dissection and high grade plaque rupture, hemorrhage and atheromatous extrusion.

Myocardium. Hearts were dissected in multiple ventricular cross sections, analogous to echocardiographic short-axis views. From these slices the anatomic location, size and extent of the acute infarction and its relation to the intervened coronary artery were recorded. The frequency with which rupture of an acute infarction occurred was also noted.

Histologic estimations of infarct age were determined using established microscopic criteria, taking into account the accelerated rate of healing that characterizes reperfused myocardium (19,20). A diagnosis of postprocedure infarct extension or new myocardial infarction was rendered when the microscopic age was less than the time interval between intervention and death

Coronary microemboli. In 30 of the 32 patients, at least 11 large sections from the circumference of the left ventricle and two sections from the right ventricle were submitted for routine processing and staining with hematoxylin-eosin. In the other two patients, available tissue was sufficient to obtain only nine sections from one patient and four sections from the other.

For the detection of emboli within intramural coronary artery branches, myocardial sections were evaluated in a blinded manner (by R.S.S. and W.D.E.) using medium-power microscopy and a scanning method similar to that for cytologic screening. The diameter of the artery containing an embolus, as measured with a calibrated scale on an ocular lens, was classified as small (<0.25 mm), medium (0.25 to 0.75 mm) or large (>0.75 mm).

Moreover, each embolus was characterized according to arterial location (within or outside the distribution of the intervened coronary artery); infarct location (within the initial infarct, area of infarct extension or new infarction, or elsewhere); mural location (subendocardial, middle wall or subepicardial); type of embolus (thrombotic, atheromatous, mixed or other), and degree of lumen obstruction (partial or total).

For each patient, the total number of emboli observed by light microscopy was recorded. The number of emboli detected in the two patients with <11 myocardial slides was statistically adjusted for comparative analyses of the mean number of emboli.

Control group. To determine whether microscopic coronary emboli in the study group were the result of an interventional procedure or, instead, may have resulted from spontaneous plaque rupture or may represent an artifact due to perfusion fixation, a control group of perfusion-fixed hearts was obtained from the Mayo Clinic tissue registry.

This group consisted of specimens from 39 patients matched according to age, gender and the presence and age of acute myocardial infarction with the study group. None of the patients had undergone coronary angioplasty or thrombolytic therapy or had ever had heart surgery of any kind.

Statistical analysis. Data were evaluated by a biomedical statistician (K.R.B.). Comparison of the incidence of coronary emboli between study patients and control subjects was based on the Pearson chi-square test. Clinicopathologic factors, patient demographic factors and procedural factors were compared between patients with and without coronary emboli either by the Pearson chi-square test for discrete variables or by *t* tests for continuous variables.

To establish associations between the presence and number of emboli and patient or procedural factors or outcomes, either linear regression analysis or *t* tests were utilized. Multiple linear regression was used to relate the number of emboli to multiple baseline or procedural factors. Factors considered in the multiple regression analysis were artery of intervention, single- or multiple-artery intervention, single- or multiple-site intervention, type or types of intervention and patient age and gender.

A p value < 0.05 was used to judge statistical significance, although values between 0.05 and 0.20 were noted as potentially interesting associations.

Results

Control group. The 39 perfusion-fixed control hearts were normal in 12, had coronary atherosclerosis without acute infarction in 13, and were involved by acute myocardial infarction in 14. In only one subject, who had a calcified aortic valve, was an intramural coronary artery embolus detected, and it represented a dense calcific nodule (presumably of aortic valve origin).

Thus, in no case, including those with acute coronary plaque rupture or thrombosis and those with acute myocardial infarction, was thrombotic or atheromatous embolic material identified in the coronary circulation. Consequently, such emboli within hearts in the study group were considered to be causally related to the interventional therapy (either balloon angioplasty or thrombolysis, or both).

Cause of death. The cause of death was determined for each of the 32 study patients on the basis of a review of clinical and autopsy information. In 31 (97%), death was due to ischemic heart disease. Death in the other patient was attributable to a cerebrovascular accident.

Features of microemboli. *Number of emboli.* Of the 32 study patients, 26 (81%) had evidence of one or more emboli within the intramural coronary artery branches, compared with only 1 of the 39 control subjects ($p < 0.0001$). In these 26 patients, the number of emboli per patient ranged from 1 to 6, with a mean of 3 and a total of 83.

Of the 83 emboli, 67 (81%) were small, 11 medium and 5 large. Diameters of the involved coronary arteries ranged from 0.045 to 1.250 mm (mean 0.25). Among the 83 emboli, 68 (82%) were identified within branches of the intervened coronary artery. Eighteen (22%) were found in areas of recent infarction; 24 (29%) involved areas of new infarction or infarct extension; and 41 (49%) involved myocardium without acute infarction (Fig. 1).

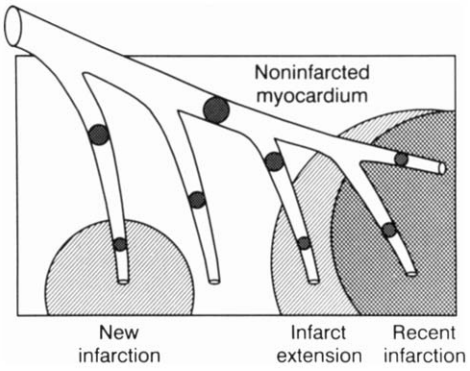

Figure 1. Schematic diagram of postinterventional coronary microembolization. Emboli (small circles) within branches of the treated coronary artery may involve not only areas of recent infarction, infarct extension or new infarction but also areas of noninfarcted myocardium.

Composition of emboli. Emboli represented thrombus in 41 (49%), atheromatous plaque in 24 (29%), a mixture of thrombus and atheroma in 14 (17%) and foreign material, presumably derived from the interventional procedure, in 4 (5%) (Fig. 2). In three of the four, the foreign substance was admixed with thrombus, and in the fourth case, it occurred alone. The refractile and polarizable foreign material was consistent with cotton fibers and talc (glove powder).

Statistics of microemboli *Statistically related variables (Table 1).* Although the left anterior descending coronary artery was no more likely to be associated with microemboli than were the left circumflex and right coronary arteries ($p = 0.24$), the number of emboli did tend to be greater when the left anterior descending artery was the artery of intervention ($p = 0.035$). In multiple regression analysis of the effects of age, gender, artery, number of sites and type of intervention, only the artery (left anterior descending vs. other) and number of sites (multiple vs. single) showed an independent association with the number of emboli.

Infarct extension or new infarction was also related to the presence of postinterventional coronary microemboli. Among 29 patients with microscopic evidence of infarct extension or new infarction, 26 (90%) had emboli compared with none of the 3 patients without these changes ($p = 0.0002$). Moreover, the mean number of emboli was also significantly higher in the 26 patients than in the other 3 (3.01 vs. 0, $p = 0.01$).

Similarly, important new ECG abnormalities were strongly associated with the presence of emboli. Of the 22 patients with ECG changes, 21 (95%) had emboli, but only 5 (50%) of the 10 patients without these ECG changes had

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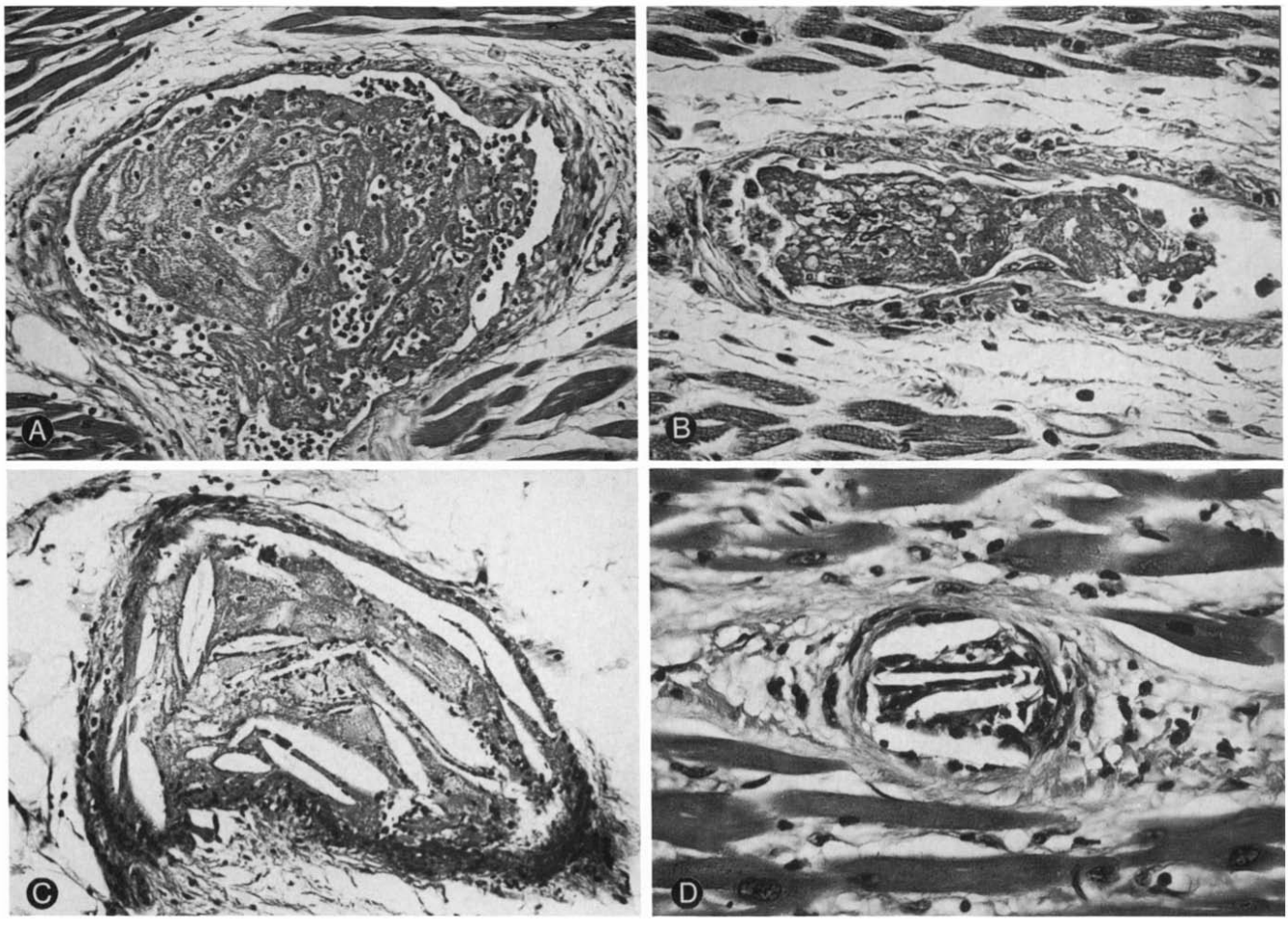

Figure 2. Photomicrographs of coronary emboli. Thrombotic microemboli in large (**A**) and small (**B**) intramural coronary artery branches. Atheromatous microemboli in large (**C**) and small (**D**) intramural arteries. Hematoxylin-eosin. **A and C,** ×125; **B and D,** ×250.

microscopically detectable emboli (p = 0.002). From another perspective, new ECG disturbances developed in 21 (81%) of 26 patients with emboli but in only 1 (17%) of 6 patients without emboli. The presence or absence of ECG changes did not correlate significantly with the mean number of emboli (2.99 vs. 2.13, p = 0.26).

Plaque rupture was associated with both the presence and number of emboli. In the 14 patients with plaque rupture, 100% had emboli (mean 3.87 emboli/patient). In contrast, in the 18 patients without plaque rupture, only 67% had emboli (p = 0.02), and the mean number of emboli was 1.87 (p = 0.002).

For plaque extrusion, the mean number of emboli was 5.60 compared with 2.19 for the 27 patients without this microscopic finding (p = 0.0001). However, the presence of emboli was not significantly different between the two groups (100% vs. 78%, p = 0.24).

Medial dissection was also associated with the mean number of microemboli. The number was 4.13 for the 10 patients with dissection and 2.09 for the 22 patients without dissection (p = 0.005). Emboli were observed in all 10 patients with dissection but in only 73% of those without medial injury (p = 0.07).

Possibly related variables (Table 1). Comparisons with a p value between 0.05 and 0.20 were considered potentially interesting associations. The presence of emboli was greater in patients treated with both balloon dilation and thrombolysis (100%) than in those with angioplasty alone (76%) or thrombolysis alone (60%) (p = 0.132). The mean number of emboli was greater among patients with interventions in multiple arteries (4.07) than in a single artery (2.48) (p = 0.10) and among those with interventions at multiple sites in the same artery (3.48) than at only a single site (2.43) (p = 0.18).

Patients with microscopic evidence of plaque hemorrhage were somewhat more likely to have detectable emboli (100% vs. 74%, p = 0.09) and to have a greater number of emboli (3.65 vs. 2.36, p = 0.097) than those without such hemorrhage. Although arteries with acute thrombosis were no more likely to be associated with microemboli than were those without, the number of emboli was greater in arteries with thrombosis (3.33 vs. 2.12, p = 0.08).

Table 1. Associations Between Variables and the Presence or Number of Postinterventional Coronary Microemboli

Statistically related variables ($p < 0.05$)
Intervention in left anterior descending artery
Infarct extension or new infarction
New electrocardiographic abnormalities
Plaque rupture
Plaque extrusion
Medial dissection
Possibly related variables ($p = 0.05$ to 0.20)
Both balloon angioplasty and thrombolysis
Multiple arteries of intervention
Multiple sites of intervention
Plaque hemorrhage
Recent coronary thrombosis
Unrelated variables ($p > 0.20$)
Age or gender
History of ischemic heart disease
Hemodynamic status before or during procedure
Success of intervention
Site or type of arterial obstruction
Plaque shape or consistency
Plaque calcification
Rupture of acute myocardial infarction

Discussion

Among patients undergoing coronary balloon angioplasty or thrombolytic therapy (or both), the potential exists for embolization of thrombotic or atheromatous material into the distal coronary artery circulation. However, to our knowledge, this phenomenon has been previously documented microscopically in only 10 patients from 5 studies (8,15–18).

In the current retrospective autopsy-based investigation, postinterventional coronary embolization was studied in 32 patients. Observations that warrant further discussion include 1) the nature of the microemboli, 2) the variables associated with the presence or number of microemboli, and 3) the limitations of this study.

Nature of microemboli. One or more emboli were identified within the intramural coronary arteries in 81% of the 32 patients. Although the number of emboli per patient only ranged from 1 to 6, 5 of the 83 emboli obstructed relatively large intramural arterial branches.

Microscopically, the emboli were thrombotic or atheromatous in 95% of the patients. Four emboli (5%) consisted of foreign material, all of which were refractile or polarizable. These presumably were derived from the catheters, glove powder, cotton sponges or other materials used during the interventional procedure. Similar material can occasionally be identified within small pulmonary arteries after right-sided cardiac catheterization.

Variables associated with emboli. One of the most important clinical observations in this study was the statistically significant correlation between the presence of coronary emboli and the development of postprocedure infarct extension, a new myocardial infarction or new ECG abnormalities. The occurrence of new ECG abnormalities after balloon angioplasty or thrombolysis probably results from a complex interplay of several factors, among which the effects of coronary embolization may be important (21–24).

In the current study, the greatest number of emboli was associated statistically with intervention in the left anterior descending coronary artery, multiple interventional sites, postinterventional medial dissection, and plaque rupture and extrusion. These findings support intuition that embolization would be most extensive among cases in which the degree of coronary artery injury is also the greatest. Other investigators have also noted that myocardial infarction due to coronary embolization is related to the number, size and location of the emboli (4,13,18).

Limitations of the study. This represents a retrospective autopsy-based investigation and is subject to the same limitations inherent in any such study. The results of the current study indicate that coronary microemboli occur in a substantial number of patients undergoing balloon angioplasty or thrombolysis (or both) who die and who undergo autopsy. However, the frequency of this postinterventional phenomenon among the much larger cohort of survivors is unknown. Notwithstanding, in living patients who develop acute myocardial ischemia or new ECG changes after these interventions, coronary microembolism should be considered as a potential cause.

References

1. Holmes DR Jr, Vlietstra RE, Mock MB, et al. Angiographic changes produced by percutaneous transluminal coronary angioplasty. Am J Cardiol 1983;51:677–83.
2. Dorros G, Cowley MJ, Simpson J, et al. Percutaneous transluminal coronary angioplasty: report of complications from the National Heart, Lung, and Blood Institute PTCA Registry. Circulation 1983;4:723–30.
3. Cowley MJ, Dorros G, Kelsey SF, Van Raden M, Detre KM. Emergency coronary bypass surgery after coronary angioplasty: the National Heart, Lung, and Blood Institute's Percutaneous Transluminal Coronary Angioplasty Registry experience. Am J Cardiol 1984;53:22C–6C.
4. MacDonald RG, Feldman RL, Conti CR, Pepine CJ. Thromboembolic complications of coronary angioplasty. Am J Cardiol 1984;54:916–7.
5. Weyne AE, Heyndrickx GR, Vandekerckhove YR, Clement DL. Embolization complicating coronary angioplasty in the presence of an intracoronary thrombus. Clin Cardiol 1986;9:463–5.
6. Saenz CB, Harrell RR, Sawyer JA III, Hood WP Jr. Acute percutaneous transluminal coronary angioplasty complicated by embolism to a coronary artery remote from the site of infarction. Cathet Cardiovasc Diagn 1987;13:266–8.
7. Cameron J, Buchbinder M, Wexler L, Oesterle SN. Thromboembolic complications of percutaneous transluminal coronary angioplasty for myocardial infarction. Cathet Cardiovasc Diagn 1987;15:100–6.
8. Richardson SG, Callen D, Morton P, Murtagh JG, Scott ME, O'Keefe DB. Pathological changes after intravenous streptokinase treatment in eight patients with acute myocardial infarction. Br Heart J 1989;61:390–5.
9. Ueda M, Fujimoto T, Ogawa N, Shoji S. An autopsy case of cholesterol embolism following percutaneous transluminal coronary angioplasty and aortography. Acta Pathol Jpn 1989;39:203–6.
10. Stafford PJ, Strachan CJL, Vincent R, Chamberlain DA. Multiple microemboli after disintegration of clot during thrombolysis for acute myocardial infarction. Br Med J 1990;299:1310–2.
11. Zahger D, Weiss AT, Anner H, Waksman R. Systemic embolization following thrombolytic therapy for acute myocardial infarction. Chest 1990;97:754–6.

12. Queen M, Biem HJ, Moe GW, Sugar L. Development of cholesterol embolization syndrome after intravenous streptokinase for acute myocardial infarction. Am J Cardiol 1990;65:1042–3.
13. Roberts WC. Coronary embolization: a review of causes, consequences, and diagnostic considerations. Cardiovasc Med 1978;3:699–710.
14. Saber RS, Edwards WD, Holmes DR Jr, Vlietstra RE, Reeder GS. Balloon angioplasty of aortocoronary saphenous vein bypass grafts: a histopathologic study of six grafts in five patients, with emphasis on restenosis and embolic complications. J Am Coll Cardiol 1988;12:1501–9.
15. Menke DM, Jordan MD, Aust CH, Storer W, Waller BF. Histologic evidence of distal coronary thromboembolism: a complication of acute proximal coronary artery thrombolytic therapy. Chest 1986;90:614–6.
16. de Morais CF, Lopes EA, Checchi H, Arie S, Pileggi F. Percutaneous transluminal coronary angioplasty: histopathologic analysis of nine necropsy cases. Virchows Arch A 1986;410:195–202.
17. Colavita PG, Ideker RE, Reimer KA, Hackel DB, Stack RS. The spectrum of pathology associated with percutaneous transluminal coronary angioplasty during acute myocardial infarction. J Am Coll Cardiol 1986;8:855–60.
18. Walley VM, Higginson LAJ, Marquis J F, Williams WL, Morton BC, Beanlands DS. Local morphologic effects of coronary artery balloon angioplasty. Can J Cardiol 1988;4:17–24.
19. Edwards WD. Pathology of myocardial infarction and reperfusion. In: Gersh BJ, Rahimtoola SH, eds. Acute Myocardial Infarction. New York: Elsevier, 1991:14–48.
20. Reichenbach D, Cowan MJ. Healing of myocardial infarction with and without reperfusion. In: Virmani R, Atkinson JB, Fenoglio JJ, eds. Cardiovascular Pathology. Philadelphia: WB Saunders, 1990:86–99.
21. Vlietstra RE, Holmes DR Jr. Percutaneous transluminal coronary angioplasty. J Cardiac Surg 1988;3:53–66.
22. Steffenino G, Meier B, Finci L, et al. Acute complications of elective coronary angioplasty: a review of 500 consecutive procedures. Br Heart J 1988;59:151–8.
23. Rosen RM, Janse MJ, Myerburg RJ. Arrhythmia induced by coronary artery occlusion: what are the electrophysiological mechanisms? In: Hearse D, Manning A, Janse M, eds. Life Threatening Arrhythmia During Ischemia and Infarction. New York: Raven, 1987:11–47.
24. Cranefield PF, Aronson RS. Arrhythmias induced by ischemia and myocardial infarction. In: Cranefield PF, Aronson RS, eds. Cardiac Arrhythmias: The Role of Triggered Activity and Other Mechanisms. Mount Kisco, NY: Futura, 1988:481–505.