

# We are IntechOpen, the world's leading publisher of Open Access books Built by scientists, for scientists

6,900

Open access books available

186,000

International authors and editors

200M

Downloads

Our authors are among the

154

Countries delivered to

TOP 1%

most cited scientists

12.2%

Contributors from top 500 universities



WEB OF SCIENCE™

Selection of our books indexed in the Book Citation Index  
in Web of Science™ Core Collection (BKCI)

Interested in publishing with us?  
Contact [book.department@intechopen.com](mailto:book.department@intechopen.com)

Numbers displayed above are based on latest data collected.  
For more information visit [www.intechopen.com](http://www.intechopen.com)



# Physiopathology of the Acute Coronary Syndromes

Iwao Emura

*Department of Surgical Pathology, Japanese Red Cross Nagaoka Hospital,  
Japan*

## 1. Introduction

The widespread application of catheter-based interventions, and chronic treatment have contributed to improved long-term prognosis in patients with acute ST-elevation myocardial infarction (STEMI) <sup>1-5</sup>. Despite these indisputable achievements, a large number of individuals remain at substantial risk of severe first attack, recurrent disease and death. Patients with unstable angina were classified into three groups according to short-term risk of death or nonfatal myocardial infarction<sup>6</sup>, and the results of noninvasive tests and the corresponding approximate mortality rates were reported <sup>7</sup>.

Disruption, fissure, or erosion of an atherosclerotic plaque, with residual mural thrombus (RMT) has a fundamental role in the pathogenesis of acute coronary syndromes (ACS) <sup>8-12</sup>. Most of occlusive thrombi had a layered structure indicating an episodic growth by repeated mural deposits <sup>13, 14</sup>. Morphological studies indicated that plaque complications remained clinically silent days or weeks before the fatal event <sup>15-18</sup>. A RMT predisposes patients to recurrent thrombotic vessel occlusion <sup>15, 16, 17</sup>, and plaque disruption, fissure or erosion with thrombus contributes to plaque development and progression <sup>18</sup>. Therefore, a marker that predicts disrupted, fissured or eroded plaque and the coronary thrombus may have practical clinical applications. The diagnosis of these lesions has been tried by several methods <sup>19</sup>. However, plaque disruption itself is asymptomatic, and the associated RMT is usually clinically silent <sup>20</sup>. To the best of our knowledge, markers as a sign of a disrupted, fissured or eroded plaque and a coronary thrombus are not available.

Scavenger receptor-mediated endocytosis of oxidized low-density lipoprotein by macrophages has been implicated in the pathogenesis of atherosclerosis. The differentiation of scavenger receptor A negative (SRA<sup>-</sup>) monocytes in peripheral blood (PB) into SRA positive (SRA<sup>+</sup>) macrophages was believed to take place in atherosclerotic lesions by stimulation of macrophage-colony stimulating factor (M-CSF) <sup>21-24</sup>, and it was reported that freshly isolated blood monocytes were negative for SRA <sup>25</sup>. We surmised that plaque content might be exposed to the blood stream after disruption of plaque, and SRA<sup>-</sup> monocytes might differentiate into SRA<sup>+</sup> cells in PB by stimulation of M-CSF contained in plaque content, and that increased SRA<sup>+</sup> cells in PB might be a useful indication of disrupted, fissured or eroded plaque and coronary thrombus.

Although several scavenger receptors, such as SRA, CD36, scavenger receptor-B1, CD68 and Lox-1 have been shown to bind oxidized low-density lipoprotein, SRA and CD36 are responsible for the preponderance of modified low-density lipoprotein uptake in macrophages<sup>26</sup>. In our study, we evaluated the utility of SRA, since SRA antigen is restrictedly expressed on macrophages<sup>26</sup>, but CD36 is expressed not only on macrophages and monocytes but also on B lymphocytes.

We reported that the SRA index [ number of SRA<sup>+</sup> cells in 10 high power fields (HPF, ×400) of peripheral blood (PB) smear, upper limit: <30 ] greater than 30 was considered to be a useful indication of disrupted, fissured or eroded plaque and coronary thrombus<sup>27, 28</sup>. In this paper, we described the composition of occlusive coronary thrombi obtained from patients with acute ST-elevation myocardial infarction (STEMI), the relationship between the SRA index and these thrombi, and the utility of SRA index as an indication of disrupted, fissured or eroded plaque and coronary thrombus in patients with ACS.

## 2. Study subjects

Eight autopsy cases with acute myocardial infarction, 393 patients with STEMI and 79 patients with unstable angina (UA) were examined. Patients with STEMI were treated with percutaneous intracoronary thrombectomy during primary angioplasty. High-sensitivity C-reactive protein (h-CRP), creatine kinase (CK) and creatine kinase-MB isozyme (CK-MB) were examined in patients with STEMI. PB from 43 apparently healthy men and women in their 20s was examined as a control.

## 3. Thrombectomy procedure

On admission, all patients were treated with 162 mg aspirin (Ebis, Osaka, Japan), and they underwent percutaneous coronary intervention of the infarct-related artery through the femoral access route with a 6F guiding catheter. Thrombectomy was performed with a Rescue™ catheter (Boston Scientific, Natick, MA, USA) or a TVAC catheter (NIPRO, Osaka, Japan). Aspirated blood and intracoronary material were collected in a collection bottle, which was equipped with a filter. Stent implantation was performed in 386 patients and all patients were treated with antithrombotic therapy.

## 4. Tissue processing and histopathological methods

Autopsy was performed 2 or 3 hours after death. Thrombi and organs were fixed in 10 % neutral formalin and embedded in paraffin, and examined using hematoxylin and eosin, and phosphotungstic acid hematoxylin (PTAH) sections. Papanicolaou-stained smears and paraffin-embedded sections were used for the immunohistochemical and immunocytochemical examination, which was performed with the simple stain MAX-PO method (NICHIREI Co., Tokyo, Japan) and with diaminobenzidine as the chromogen using mouse monoclonal anti-human glycoprotein 1b (CD42b, a platelet marker, 1:100; Novo Castra, Newcastle upon Tyne, UK), and mouse monoclonal anti-human SRA (CD204, a macrophage SRA marker, 1:200; Trans Genic Inc., Kumamoto, Japan) antibodies. An antigen retrieval method using citrate buffer and microwave heating was employed. As a negative control, the primary antibody was substituted by phosphate-buffered saline, and a positive stain was not observed in these controls.

## 5. Cytological methods

I believe that the method of cytological examination of peripheral blood is my original method <sup>29</sup>. Briefly, red blood cells were lysed with lysing reagent (826 mg of  $\text{NH}_4\text{Cl}$  + 3.7 mg of  $\text{EDTA-4Na}$  + 100 mg of  $\text{KHCO}_3$  in 100 ml  $\text{H}_2\text{O}$ ), then nucleated cells were suspended in isotonic sodium chloride solution, and the suspensions containing about  $5 \times 10^6$  nucleated cells were smeared on glass slides using Auto smear CF-12 (Sakura Seiki, Tokyo, Japan). Cells that did not adhere to the glass slides were gently washed away with 95% ethanol solution. Smear preparations were fixed in 95% ethanol solution and stained with the Papanicolaou method. A smear preparation of PB is shown in figure 1. About one million and two hundred thousand nucleated cells were smeared in one slide. Nucleated cells are smeared evenly and precise nuclear structures are excellently preserved. About one thousand nucleated cells were observed in one high power field ( $\times 400$ , Figure 2).

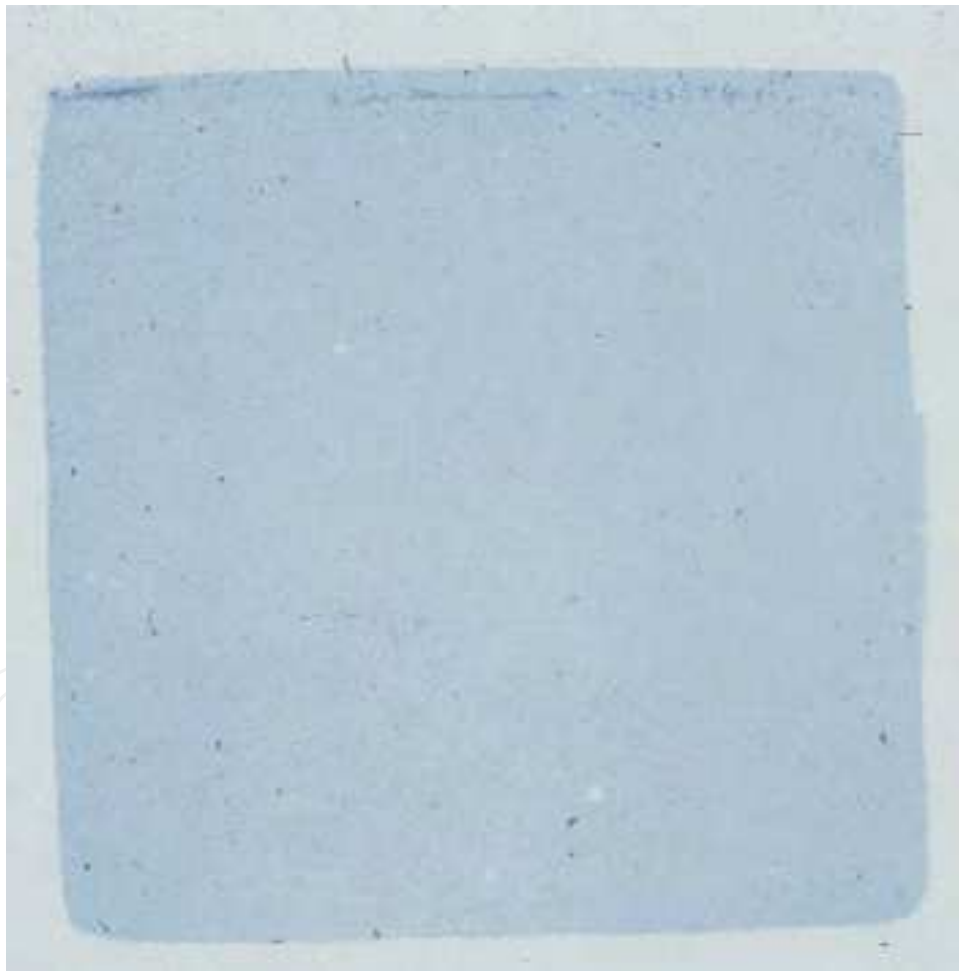


Fig. 1. A cytological preparation of peripheral blood stained with the Papanicolaou method. About one million and two hundred thousand nucleated cells are smeared in one slide. Papanicolaou stain.

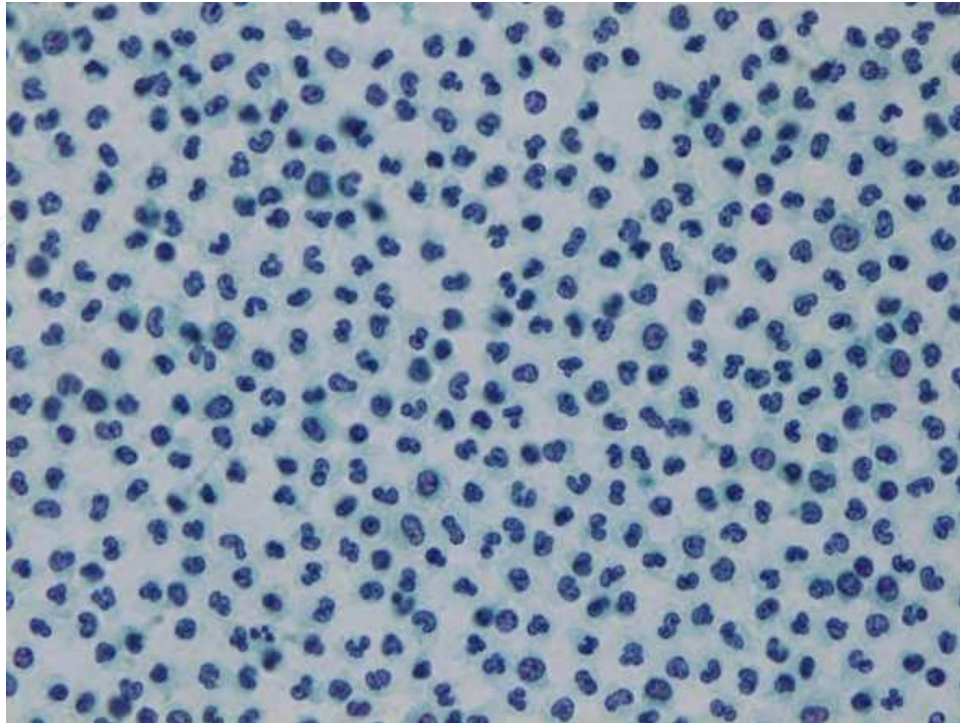


Fig. 2. About one thousand nucleated cells are observed in one high power field ( $\times 400$ ). Nucleated cells are smeared evenly and precise nuclear structures are excellently preserved. Papanicolaou stain.

## 6. Definitions

Thrombi were classified into 4 groups according to previously published definitions considering age and constituents of thrombus<sup>13, 30</sup> : 1) an eosinophilic mass with neo-vascularization (organizing thrombus: OT), 2) a structureless eosinophilic (hyalin) mass (fibrin-rich thrombus: FT), 3) Thrombus containing significant quantities of platelets, erythrocytes, fibrin and leukocytes (mixed thrombus: MT), and 4) tightly packed but individually discernible platelets (platelet thrombus: PT). In this paper, we defined MT and FT as RMT. Plaque components were identified based on the presence of foamy macrophages, cholesterol crystals, collagen tissue, and/or calcification. Since the aspirated material was fragmented, and PT seemed to be the freshest thrombus, contact between PT and other types of thrombus (PT and MT: P-M, PT and FT: P-F,) and contact between PT and plaque content (P-C) were examined in all cases to investigate the process of coronary occlusion. Cases were classified into 3 groups according to the composition of the thrombus: group A, containing PT only and P-C; B, a MT only, P-M and P-C+P-M; C, P-F, P-M+P-F, P-C+P-F, and P-C+P-M+P-F. SRA<sup>+</sup> cells in PB that had the same size and nuclear shape as blood monocytes were defined as SRA<sup>+</sup> cells. The SRA index was defined as the number of SRA<sup>+</sup> cells in 10 HPFs of PB smear samples. Based on the SRA index of apparently healthy people in their 20s, we temporarily set the normal upper limit of the SRA index at 30<sup>27</sup>.

## 7. Autopsy cases

P-C was observed in 4 autopsy cases, P-M in 3 and P-M + P-F in 1. Numerous emboli of PT were observed in peripheral small arteries and capillaries of the infarct-related artery in 6 cases. SRA index exceeded 30 in 5 cases. A typical case with acute myocardial infarction is presented in figure 3 to 7. This patient is a forty-three year old male. He died suddenly. Postmortem examination revealed disruption of the plaque and occlusive thrombus in the left anterior descending artery (Figure 3). Thrombus is composed of platelet thrombus and mixed thrombus + fibrin-rich thrombus (Figure 4 and 5). Platelet thrombus was adhered on the inner side of mixed thrombus + fibrin-rich thrombus (Figure 4). Immunohistochemistry for CD 42b revealed that platelet thrombus was deeply stained than mixed thrombus + fibrin-rich thrombus (Figure 4). Fibrin mesh is contained in mixed thrombus + fibrin-rich thrombus but not in platelet thrombus (figure 5). SRA<sup>+</sup> cells are infiltrated in mixed thrombus + fibrin-rich thrombus but not in platelet thrombus (Figure 6). Numerous emboli of fragments of platelet thrombi were observed in small arteries and capillaries at the distal portion of the left anterior descending artery (Figure 7).

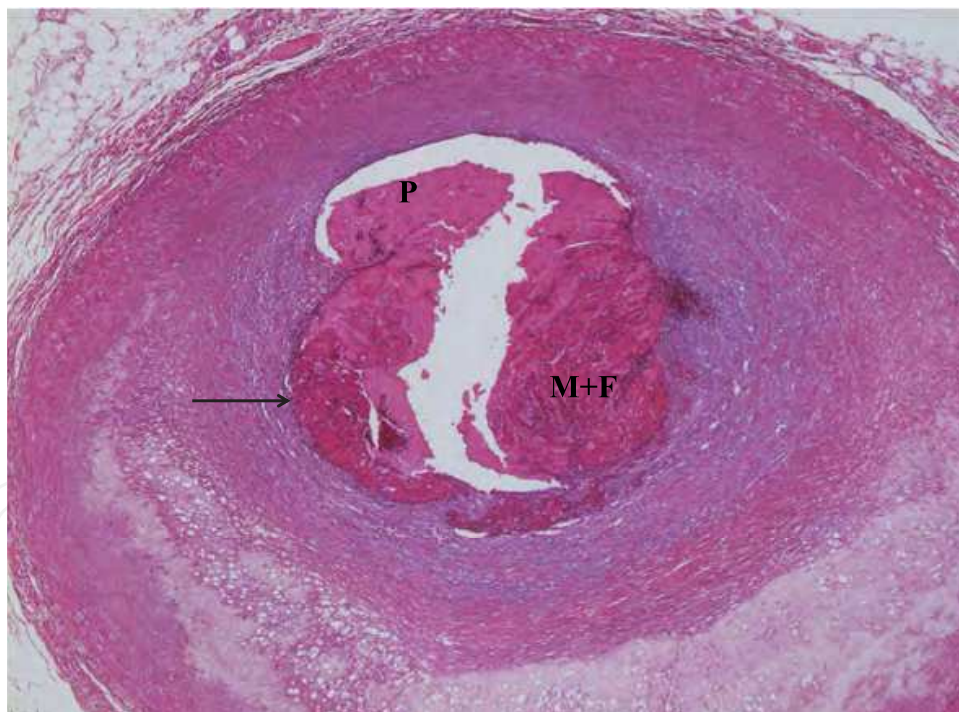


Fig. 3. Plaque disruption (arrow) and thrombus formation in the left anterior descending artery of the patients who died suddenly. Thrombus is composed of platelet thrombus (P) and mixed thrombus + fibrin-rich thrombus (P+M). hematoxylin and eosin.



Fig. 4. Serial section of figure 1. Platelet thrombus is deeply stained than mixed thrombus + fibrin-rich thrombus, and adhered on the inner side of mixed thrombus + fibrin-rich thrombus. Immunochemistry for CD42b.

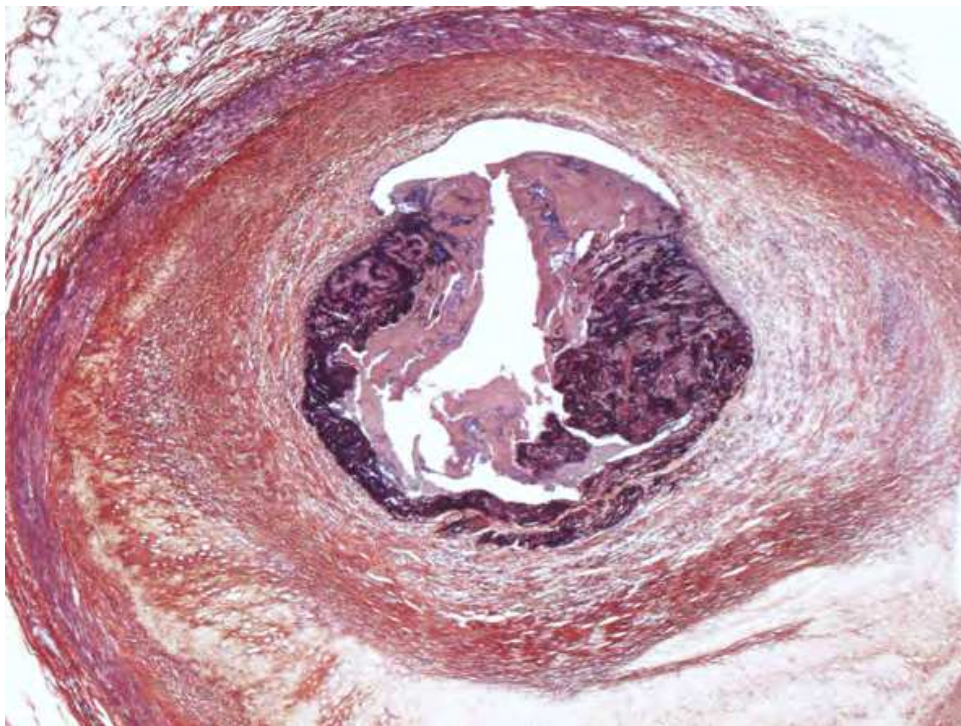


Fig. 5. Serial section of figure 1. Fibrin mesh is contained in mixed thrombus + fibrin-rich thrombus but not in platelet thrombus . phosphotungstic acid hematoxylin stain.

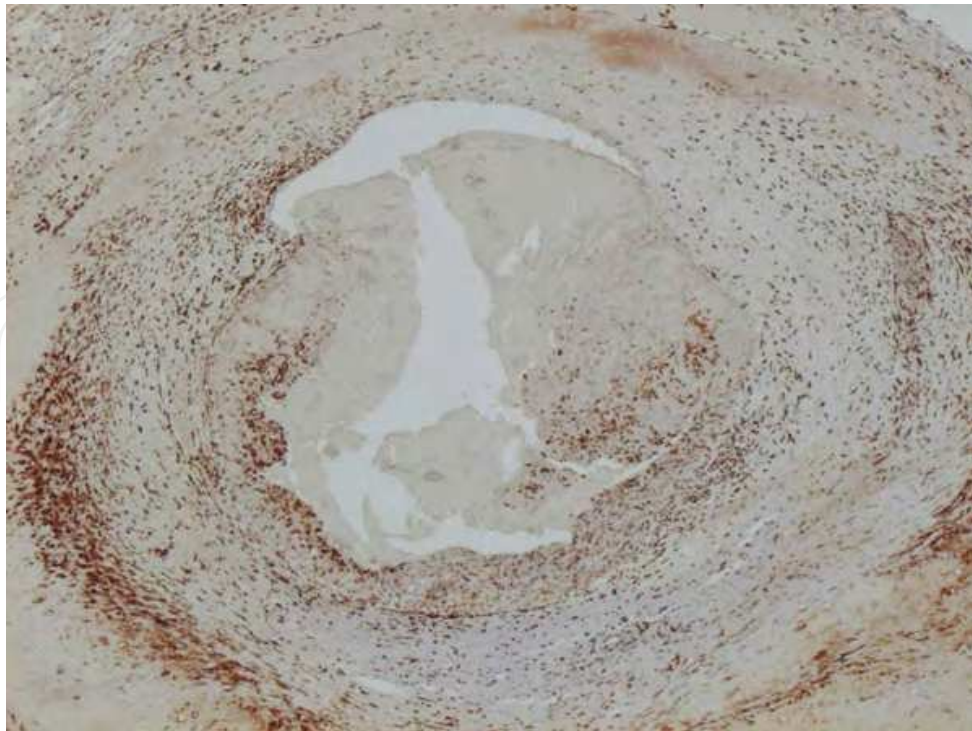


Fig. 6. Serial section of figure 1. Scavenger receptor A positive cells are infiltrated in mixed thrombus + fibrin-rich thrombus but not in platelet thrombus. Immunohistochemistry for scavenger receptor A.

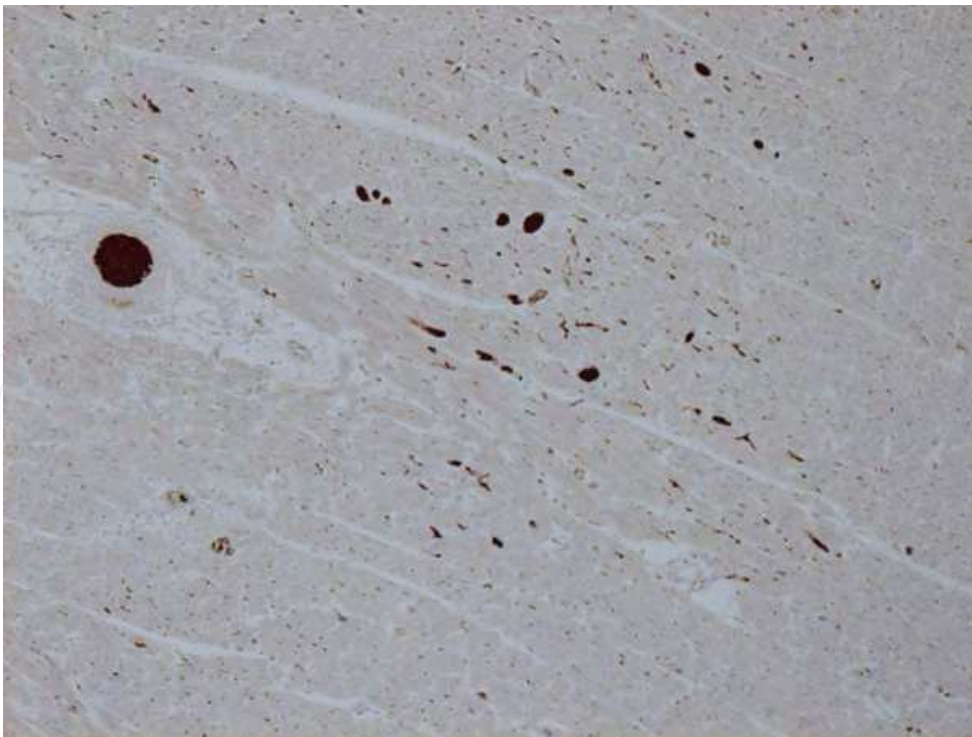


Fig. 7. Numerous emboli of fragments of platelet thrombi are observed in small arteries and capillaries at the distal portion of the left anterior descending artery. Immunohistochemistry for CD 42b.



## 8. Patients with STEMI

### 8.1 SRA index and CK, CK-MB, h-CRP

Abnormally increased levels of CK and CK-MB were observed in 53.8 % and 55.6% cases respectively at the hospitalization, and all cases showed abnormally high levels of CK and CK-MB within 24 hours after hospitalization. There was a strong correlation between CK and CK-MB ( $r=0.986$ ), but no correlation between the SRA index and CK ( $r=0.025$ ), CK-MB ( $r=0.005$ ), and h-CRP( $r=0.085$ ) were seen (all, Student's t-test).

### 8.2 Pathological findings of thrombus

Thrombus was observed in 389 (99%) of the 393 patients, plaque contents alone were detected in 2, and neither thrombus nor plaque contents was identified in 2. In 270 patients, only thrombus was found; and both thrombus and plaque content were identified in 119. PT was found in 387 of 389 (99.5%) patients, MT in 269 (69.2%), FT in 57 (14.7%), and OT in 29 (7.5%). Results of the histopathological examination of thrombus are shown in table 1. RMT was detected in 300 (77.1 %) patients (Table 1). One type of contact was detected in 285 (73.3 %) patients, 2 types in 61 (15.7 %) and 3 types in 12 (3.0 %), and PT, or MT alone was found in 29 and 2 patients respectively. Contact between PT and OT was not observed. There was no gradual morphological transition from PT to MT or FT, but there were gradual transitions from MT to FT, and FT to OT in some cases.

Group	Contact		Thrombus n/n (%)	SRA index >30 n/n (%)
	Pattern	n		
A	P	29	89/389(22.9)	46/89 (51.7)
	P-C	60		
B	M	2	243/389(62.5)	181/243(74.5)
	P-M	202		
	P-C+P-M	39		
C	P-F	23	57/389(14.7)	49/57(86.0)
	P-M+P-F	14		
	P-C+P-F	8		
	P-C+P-M+P-F	12		

Table 1. Brief title: Relationships between contact patterns of thrombus and SRA index at hospitalization<sup>1</sup>.

<sup>1</sup>P: Platelet thrombus. P-C: Contact between platelet thrombus and plaque content. M: Mixed thrombus. P-M: Contact between platelet thrombus and mixed thrombus. P-F: Contact between platelet thrombus and fibrin-rich thrombus.

Eighty-nine patients were classified into group A, 243 into group B, and 57 into group C (Table 1). Typical findings of group A (P-C) are shown in figure 8. Macrophages in plaque content were positive for SRA, and SRA positive cells were not found in platelet thrombus. Figure 9 to 12 are typical findings of group B (P-M). Platelet thrombus is adhered on the mixed thrombus (Figure 9, 10), and fibrin mesh is not observed in platelet thrombus (Figure 11). SRA positive cells are infiltrated into mixed thrombus along the boundary zone (Figure 12). Typical findings of group C (P-F) are shown in figures 13 and 14. SRA positive cells are diffusely infiltrated in fibrin-rich thrombus (Figure 14). Fragments of PT are frequently found in MT in many cases (Figure 15). SRA<sup>+</sup> cells infiltrated into 147 (54.6%) of 269 MT. These cells and SRA<sup>+</sup> cells in PB were nearly equal in size, and infiltrated into MT along the boundary zone between PT and MT in most cases. SRA<sup>+</sup> cells were diffusely infiltrated into all FT and OT. Some of these SRA<sup>+</sup> cells were large in size. Foam cells in plaque content were positive for SRA. SRA<sup>+</sup> cells were not infiltrated into PT.

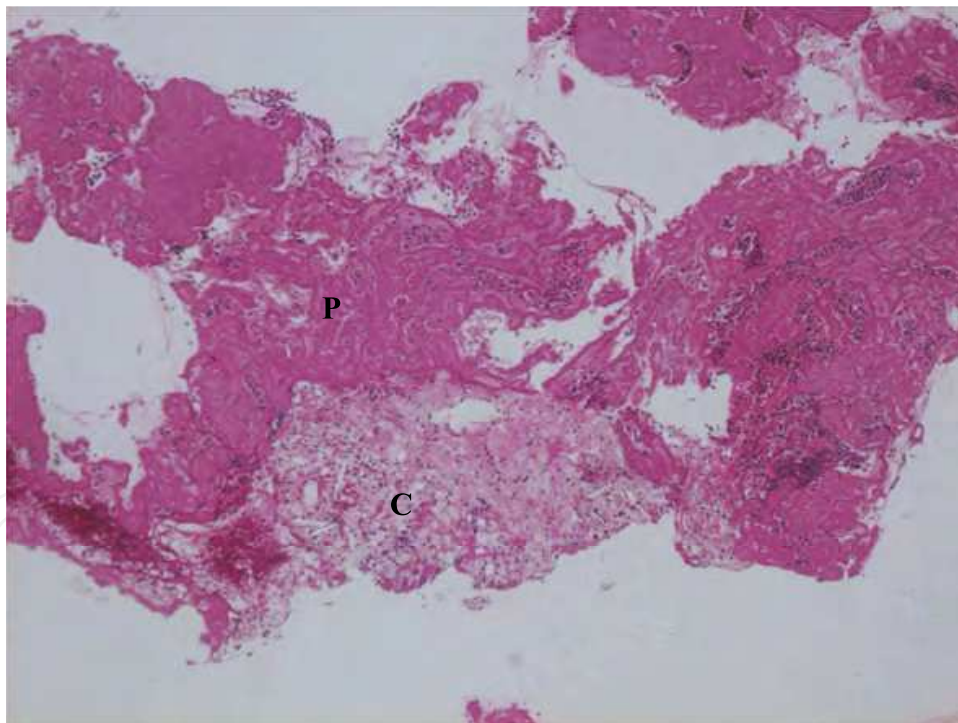


Fig. 8. Contact between platelet thrombus (P) and plaque content (C).

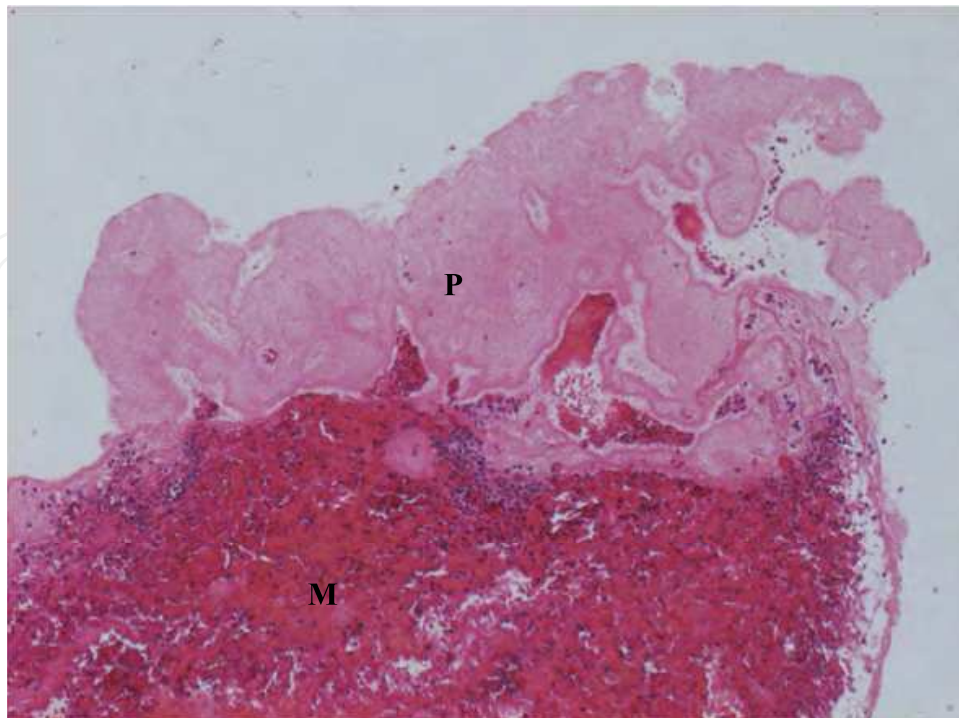


Fig. 9. Contact between platelet thrombus (P) and mixed thrombus (M).

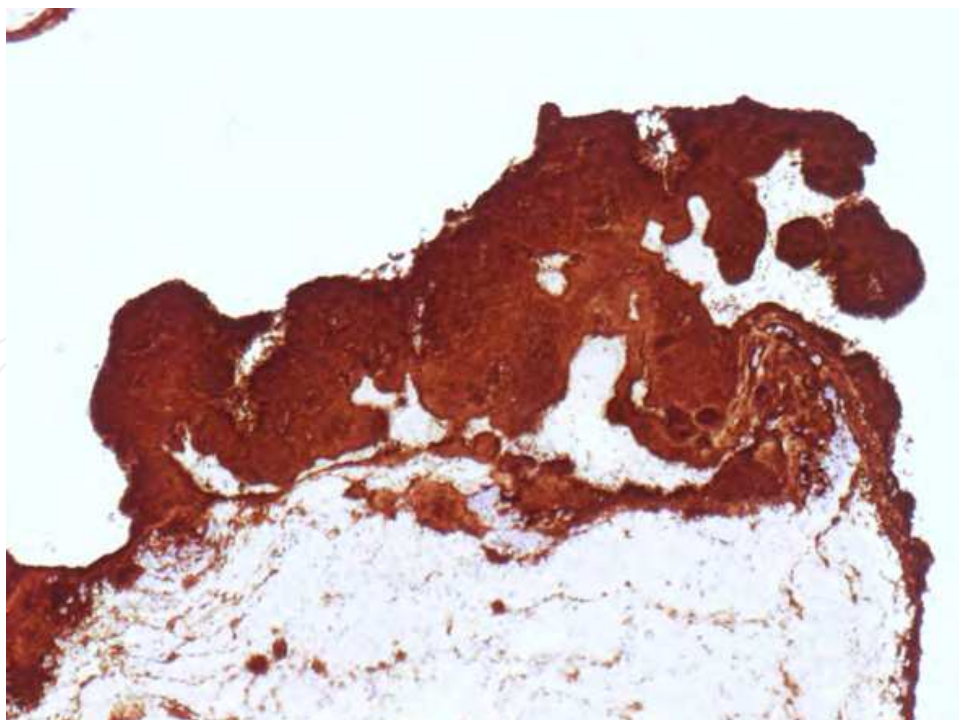


Fig. 10. Serial section of figure 9. Platelet thrombus is strongly stained. Immunohistochemistry for CD42b.

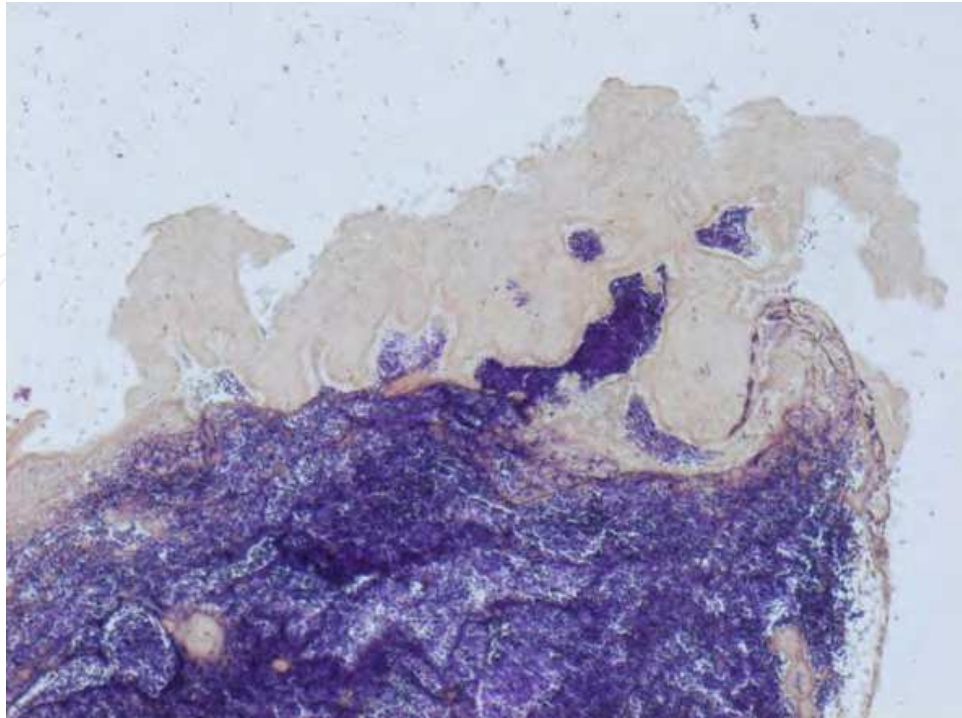


Fig. 11. Serial section of figure 9. Fibrin mesh is not observed in platelet thrombus. phosphotungstic acid hematoxylin stain.

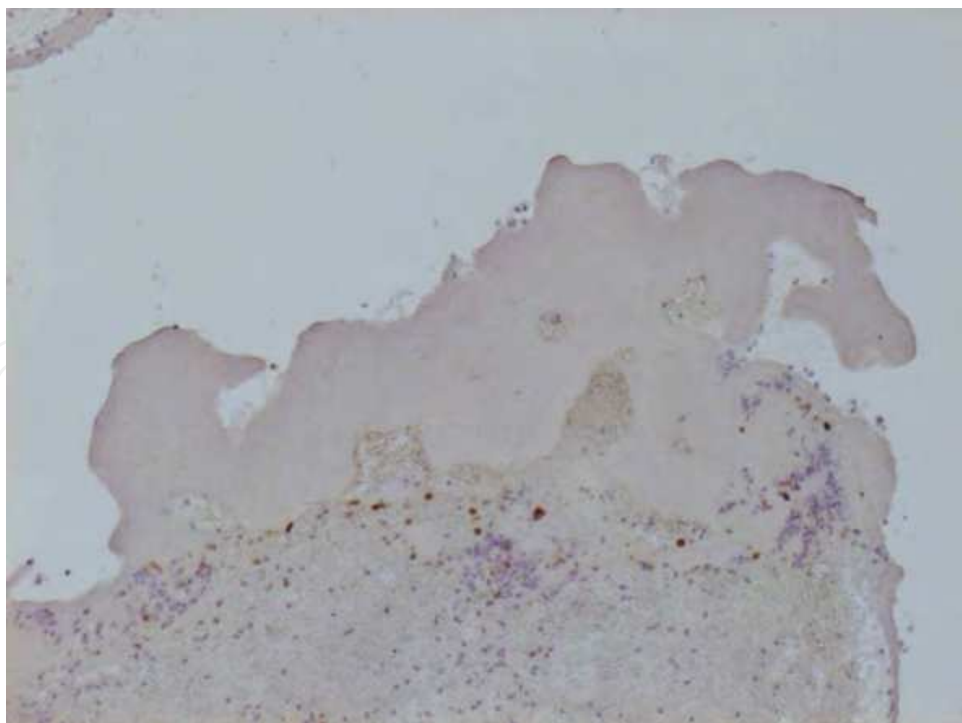


Fig. 12. Serial section of figure 9. Scavenger receptor A positive cells infiltrate into mixed thrombus along the boundary zone. Immunocytochemistry for CD204.

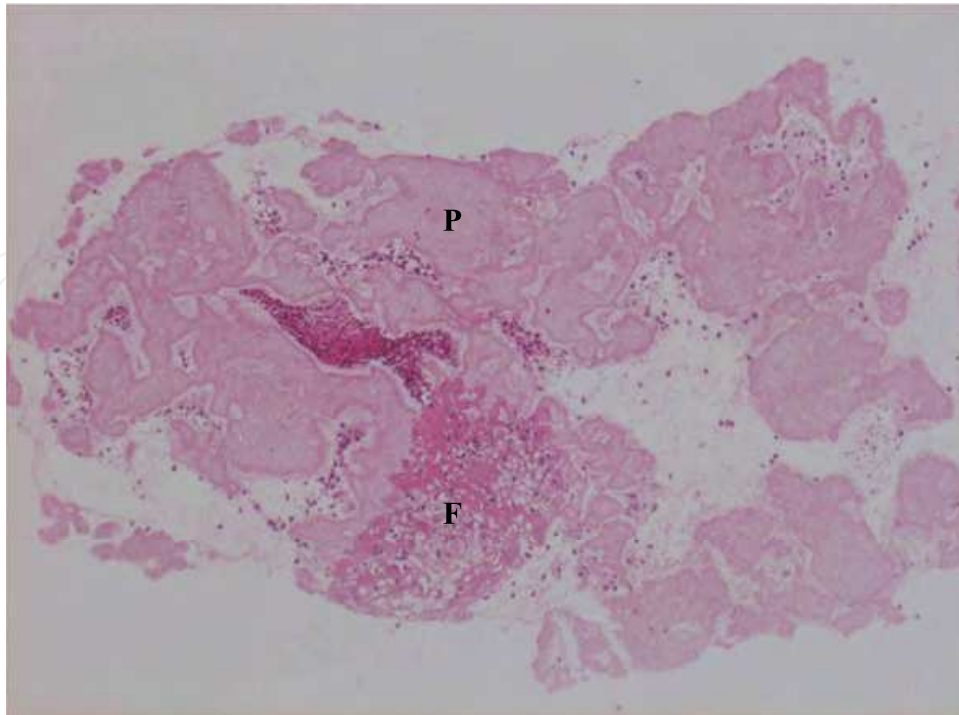


Fig. 13. Contact between platelet thrombus (P) and fibrin-rich thrombus (F).

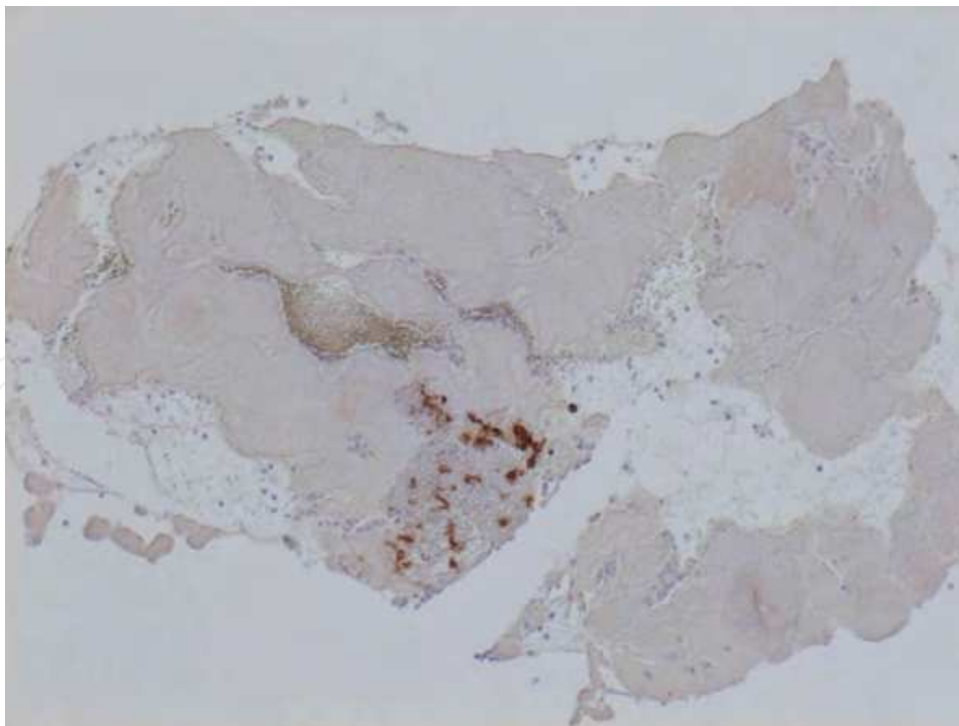


Fig. 14. Serial section of figure 13. Scavenger receptor A positive cells infiltrate into fibrin-rich thrombus. Immunohistochemistry for CD204.

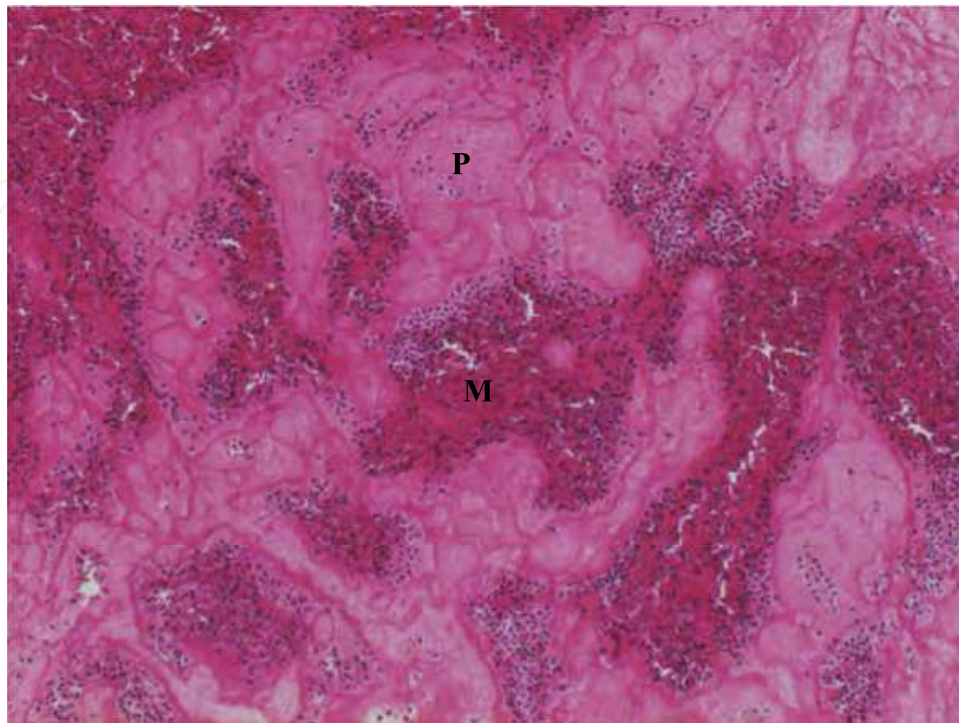


Fig. 15. Small fragments of platelet thrombus (P) are intermingled with mixed thrombus (M).

### 8.3 SRA<sup>+</sup> cells in PB

SRA<sup>+</sup> cells were observed in all control cases and in all patients with STEMI and UA. Neither SRA<sup>+</sup> large macrophages nor foamy cells could be observed in PB of all examined cases. SRA index of control cases ranged 1 to 24 (mean±SD=11.1±7.5). The relationships between SRA index and contact patterns of thrombus at hospitalization were shown in table 1. At hospitalization, SRA index exceeded 30 in 276 of 393 patients with STEMI (Figure 16). Thrombus was identified in all these patients with more than 30 SRA index. PT was identified in 274 (99.3 %), and RMT in 230 (83.3 %) cases. From the viewpoint thrombus, SRA index exceeded 30 in 230 of 300 (76.7 %) cases with RMT and 46 of 89 (51.7 %) cases with PT alone (Table 1). The percentage of patients with a SRA index more than 30 was significantly lower in group A patients than other groups of patients ( $P<0.001$ ). Significant differences were observed between group A and B, and A and C (both,  $P<0.001$ ).

Peripheral blood of 109 of 117 patients with less than 30 SRA index at hospitalization were examined repeatedly, and SRA index of all 109 cases exceeded 30 within 2 to 3 days after hospitalization. The maximum SRA indices of STEMI patients during 3 days after hospitalization were significantly higher than those of STEMI patients at hospitalization.

The SRA index of 60 of 79 UA (75.9%) cases were 30 or more at hospitalization. The differences in the SRA index were not significant between STEMI and UA (Table 2,  $P=0.218$ , Welch's test).

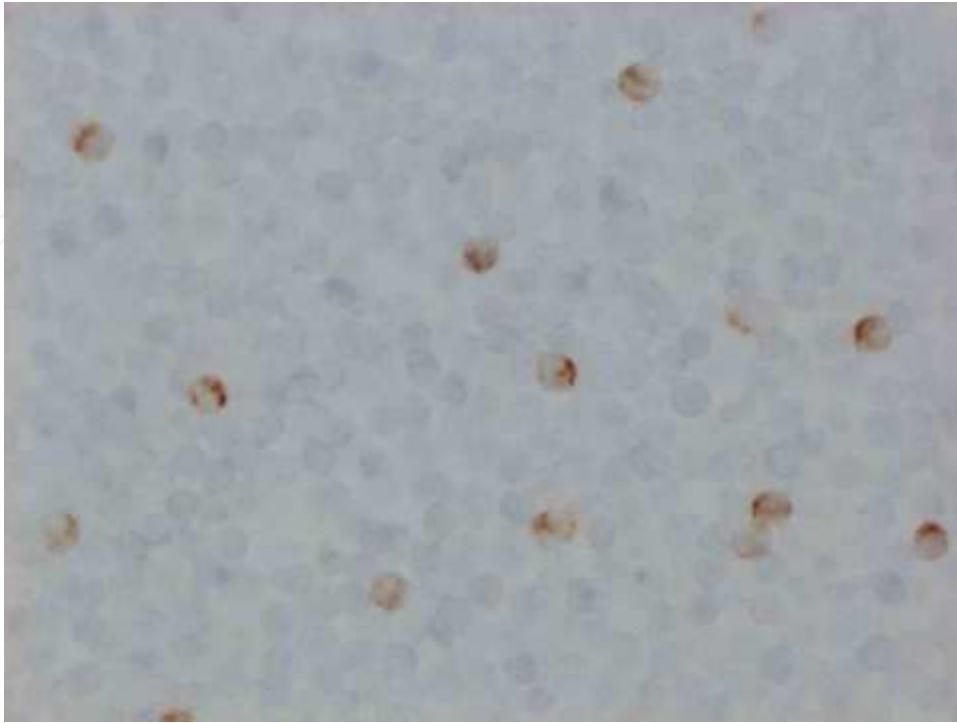


Fig. 16. Scavenger receptor A positive cells in peripheral blood (SRA index: 187/10HPFs).

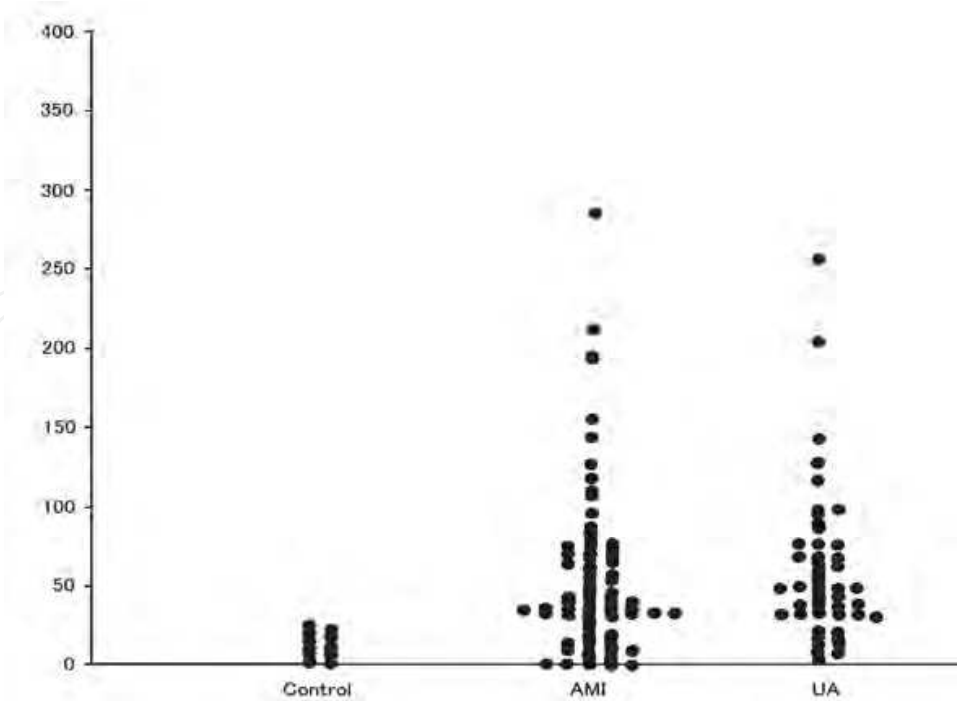


Table 2. The scattered plots of the SRA index of controls, AMI, UA.

## 9. Differentiation of SRA<sup>+</sup> cells in PB

It is reported that freshly isolated blood monocytes were negative for SRA<sup>+</sup><sup>25</sup>; however, a few reports have indicated that SRA<sup>-</sup> monocytes can differentiate into SRA<sup>+</sup> cells in PB by various stimuli<sup>32, 33, 34</sup>. SRA<sup>+</sup> cells were observed in all control cases. We, therefore, surmised that a small number of SRA<sup>-</sup> monocytes differentiated into SRA<sup>+</sup> cells in PB of healthy men and women by various stimuli. Fuster et al. classified the progression of coronary atherosclerotic diseases into five phases<sup>35</sup>. Phase 1 is represented by a small plaque that is present in most people under the age of 30 years. We set the normal upper limit of the SRA index at 30<sup>27</sup>, since plaque disruption, fissure, or erosion and RMT might not develop in healthy men and women in their 20s, and SRA index of these control cases ranged 1 to 24 (mean±SD=11.1±7.5).

We considered two possibilities on the pathophysiologic mechanisms underlying the differentiation of SRA<sup>+</sup> cells in patients with STEMI (myocardial infarction or plaque disruption, fissure or erosion). With the recognition that atherosclerosis is an inflammatory process<sup>36</sup>, h-CRP has been evaluated as a potential tool for predicting the risk of AMI<sup>37, 38, 39</sup>, and CK and CK-MB are good markers of myocardial injury. Macrophages are known to arise from monocytes, and become larger over twice as large as monocytes with differentiation. SRA<sup>-</sup> monocytes became positive for SRA after 5 days in culture with M-CSF<sup>40</sup>, and differentiated into large macrophages by 10 days<sup>41</sup>. Cytokines elevate in PB after insult<sup>42</sup>. Myocardial infarction is severe insult, so SRA<sup>+</sup> cells may increase in PB as a result of myocardial infarction. However, differentiation of SRA<sup>+</sup> cells in PB was not considered to result from myocardial injury, because there was no correlation between SRA indices and CK, CK-MB, and h-CRP.

The differentiation of SRA<sup>-</sup> monocytes into SRA<sup>+</sup> macrophages was believed to take place in atherosclerotic lesions by stimulation of M-CSF<sup>21-24</sup>. Disruption, fissure or erosion of an atherosclerotic plaque is generally recognized as a proximate event responsible for the development of the ACS<sup>8-12</sup>. The SRA index of the patients with less than 30 SRA index at hospitalization rapidly increased, and the SRA index of all these STEMI patients exceeded 30 within 2 to 3 days. We therefore surmised that SRA<sup>-</sup> monocytes might differentiate into SRA<sup>+</sup> cells as the result of exposure of plaque content that contains M-CSF to the blood stream.

## 10. Coronary occlusion

Examinations of aspirated material have focused on thrombus age<sup>31, 43, 44</sup>. Rittersma et al. classified thrombi into 3 groups: fresh (< 1 day), lytic (1 to 5 days), and organized thrombus (> 5 days)<sup>31</sup>. However it is hard to understand the constituents of thrombus by this classification. PT and some MT seem to correspond to fresh thrombus, and some MT and FT to lytic thrombus. PT was detected in 387 (99.5 %) of 389 patients, MT in 269 cases (69.2 %) and FT in 57 (14.7 %). SRA<sup>+</sup> cells infiltrated into all FT and 147 (54.6 %) of 269 MT, but not PT. These SRA<sup>+</sup> cells in PB were thought to be infiltrated into MT, since SRA<sup>+</sup> cells infiltrated in MT along the boundary zone between PT and MT (luminal side of the coronary artery). From these findings, PT was considered to be most fresh thrombus, and infarct-related coronary artery was totally and rapidly occluded by the formation of PT.

Using their computer-assisted extracorporeal-perfusion system, Badimon et al.<sup>45</sup> and Lassila et al.<sup>46</sup> found that platelet deposition increased significantly with increased stenosis. Sudden



coronary occlusion was often preceded by a period of plaque instability and thrombus formation, initiated days or weeks before the onset of symptoms<sup>15-18</sup>, and total coronary occlusion of the infarct-related artery always results from the growth of RMT<sup>44, 47 - 49</sup>. Considering these reports and the histopathological findings of thrombi, PT was thought to be formed abruptly as a result of severe coronary stenosis due to sudden extrusion of atheromatous debris into vessel lumen in 43 group A patients with a SRA index less than 30 at hospitalization, and due to gradual growth of RMT in group B and C patients. The percentage of patients with SRA index more than 30 at hospitalization was significantly lower in group A patients than other groups of patients. This finding seemed to support the theory, since the SRA index exceeded 30 about 2 days after plaque disruption<sup>27</sup>.

### 11. The fate of platelet thrombus

RMT was observed in 300 of 389 STEMI cases. Meshwork of fibrin was observed in RMT, so RMT was thought not to be fragile. RMT predisposes patients to recurrent thrombotic vessel occlusion<sup>15-17</sup>, and plaque disruption, fissure or erosion with thrombus contributes to plaque development and progression<sup>18</sup>. Gradual growth of RMT plays an important role on the increased stenosis of coronary artery, and total occlusion of coronary artery by platelet thrombus.

Meshwork of fibrin was not contained in platelet thrombus. Consequently, platelet thrombus was considered to be very fragile. Fragments of platelet thrombus were frequently observed in mixed thrombus and numerous emboli of fragments of platelet thrombus were observed in small arteries and capillaries at the distal portion of the infarct related artery of autopsy cases. Platelet thrombus was considered to repeat formation and disintegration with the gradual growth and lysis of RMT, and numerous emboli of fragments of platelet thrombus at the distal portion of the infarct related artery may repeatedly injure cardiac myocytes.

### 12. SRA index and vulnerable plaque

Disruption, fissure, or erosion of an atherosclerotic plaque, with RMT has a fundamental role in the pathogenesis of acute coronary syndromes (ACS)<sup>8-12</sup>.

In general, in case of AMI, a direct relationship between the onset of plaque disruption and acute transmural ischemia is assumed; however pathological studies of autopsy<sup>13, 14</sup> and thrombectomy<sup>18, 31, 43</sup> materials indicated that plaque disruption, fissure or erosion with RMT remain clinically silent days or weeks before the fatal event. The SRA index of the patents with less than 30 SRA index at hospitalization exceed normal level within 2 to 3 days. These findings indicated that SRA index rapidly increases in AMI patients after plaque disruption, erosion, or fissure. A SRA index more than 30 was observed in patients with multiple organ dysfunction syndrome<sup>50</sup>. Therefore, SRA index more than 30 was not a specific finding to ACS. SRA index exceeded 30 in 230 of 300 (76.7 %) cases with RMT and 46 of 89 (51.7 %) cases with PT alone, and 276 of all 389 cases at hospitalization. Thrombus was identified in all 276 patients with a SRA index more than 30 at hospitalization. PT was detected in 99.3 % and RMT in 83.3 % of these patients. SRA index did not exceed 30 in healthy control cases. SRA index of these 276 patients was surmised to exceed 30 before the onset of STEMI. The SRA indices of 75.9 % of unstable angina cases were more than 30 at hospitalization<sup>27</sup>. The pathophysiological substrate of the unstable angina is now considered

to be common with the acute myocardial infarction. We, therefore, believe that the abnormal increase of SRA<sup>+</sup> cells is considered to be a useful finding to gather the presence of disrupted or fissured or eroded plaque, PT, and probably RMT in patients with UA.

### 13. References

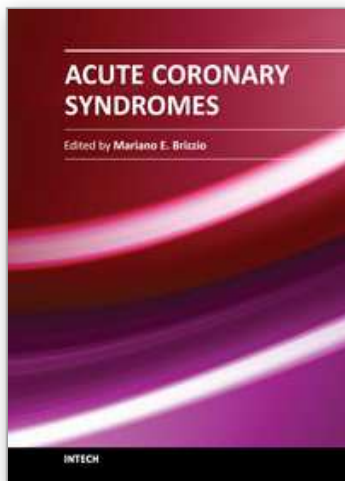
- [1] Keeley EC, Boura JA, Grines CL. Primary angioplasty versus intravenous thrombolytic therapy for acute myocardial infarction: a quantitative review of 23 randomised trials. *Lancet* 2003;361:13-20.
- [2] Freemantle N, Cleland J, Young P, Mason J, Harrison J. Beta blockade after myocardial infarction: systematic review and meta regression analysis. *BMJ* 1999;318:1730-1737.
- [3] Latini R, Tognoni G, Maggioni AP, et al. For Angiotensin-converting Enzyme Inhibitor Myocardial Infarction Collaborative Group. Clinical effects of early angiotensin-converting enzyme inhibitor treatment for acute myocardial infarction are similar in the presence and absence of aspirin: systematic overview of individual data from 96712 randomized patients. *J Am Coll Cardiol* 2000;35:1801-07.
- [4] Schwartz GG, Olsson AG, Ezekowitz MD, et al. Effects of atorvastatin on early recurrent ischemic events in acute coronary syndromes: the MIRACL study: a randomized controlled trial. *JAMA* 2001;285:1711-18.
- [5] Antithrombotic trialists' Collaboration. Collaborative meta-analysis of randomized trials of antiplatelet therapy for prevention of death, myocardial infarction, and stroke in high risk patients. *BMJ* 2002;324:71-86.
- [6] Gibbons RJ, Balady GJ, Bricker JT, et al. ACC/AHA 2002 guideline update for exercise testing: summary article: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee to Update the 1997 Exercise Testing Guidelines). *J Am Coll Cardiol* 2002;40:1531-40.
- [7] Kumar A, Cannon CP. Acute coronary syndromes: Diagnosis and management, Part II. *Mayo Clin Proc* 2009;84:1021-36.
- [8] Falk E. Plaque rupture with severe pre-existing stenosis precipitating coronary thrombosis: characteristics of coronary atherosclerotic plaques underlying fatal occlusive thrombi. *Br Heart J* 1983;50:127-34.
- [9] Davies MJ, Thomas AC. Plaque fissuring—the cause of acute myocardial infarction, sudden ischemic death, and crescendo angina. *Br Heart J* 1985;53:363-73.
- [10] Richardson PD, Davies MJ, Born GVR. Influence of plaque configuration and stress distribution on fissuring of coronary atherosclerotic plaques. *Lancet* 1989;2:941-4.
- [11] Burke AP, Farb A, Malcom GT, Liang Y-H, Smialek J, Virmani R. Coronary risk factors and plaque morphology in men with coronary disease who died suddenly. *N Engl J Med* 1997;336:1276-82.
- [12] Burke AP, Farb A, Malcom GT, Liang Y-H, Smialek J, Virmani R. Effect of risk factors on the mechanism of acute thrombosis and sudden coronary death in women. *Circulation* 1998;97:2110-6.
- [13] Falk E. Unstable angina with fatal outcome: Dynamic coronary thrombosis leading to infarction and/or sudden death: autopsy evidence of recurrent mural thrombosis with peripheral embolization culminating in total vascular occlusion. *Circulation* 1985;71:699-708.

- [14] Mailhac A, Badimon JJ, Fallon JT, et al. Effect of an eccentric severe stenosis on fibrin(ogen) deposition on severely damaged vessel wall in arterial thrombosis. Relative contribution of fibrin(ogen) and platelets. *Circulation* 1994;90:988-96.
- [15] Hackett D, Davie G, Chierchia S, Maseri A. Intermittent coronary occlusion in acute myocardial infarction: value of combined thrombolytic and vasodilatory therapy. *N Engl J Med* 1987;317:1055-9.
- [16] Davies SW, Marchant B, Lyons JP, et al. Irregular coronary lesion morphology after thrombolysis predicts early clinical instability. *J Am Coll Cardiol* 1991;18:669-74.
- [17] Ohman EM, Topol EJ, Califf RM, et al. An analysis of the cause of early mortality after administration of thrombolytic therapy. *Cor Art Dis* 1993;4:957-64.
- [18] Burke AP, Kolodgie FD, Farb A, et al. Healed plaque rupture and sudden coronary death. Evidence that subclinical rupture has a role in plaque progression. *Circulation* 2001;103:934-40.
- [19] MacNeill BD, Lowe HC, Takano M, Valentin F, Ik-Kyung J. Intravascular modalities for detection of vulnerable plaque. *Arterioscler Thromb Vasc Biol* 2003;23:1333-42.
- [20] Davies MJ, Bland JM, Hangartner JRW, Angelini A, Thomas AC. Factors influencing the presence or absence of acute coronary artery thrombi in sudden ischemic death. *Eur Heart J* 1989;10:203-8.
- [21] Rajavashisth TB, Andalibi A, Territo MC, et al. Induction of endothelial cell expression of granulocyte and macrophage colony-stimulating factors by modified low-density lipoproteins. *Nature* 1990;344:254-7.
- [22] Liao F, Andalibi A, Qiao J-H, Allayee H, Fogelman AM, Lusis AJ. Genetic evidence for a common pathway mediating oxidative stress, inflammatory gene induction, and aortic fatty streak formation in mice. *J Clin Invest* 1994;94:877-84.
- [23] Clinton SK, Underwood R, Hayes L, Sherman ML, Kufe DW, Libby P. Macrophage colony-stimulating factor gene expression in vascular cells and in experimental and human atherosclerosis. *Am J Pathol* 1992;140:301-16.
- [24] Rosenfeld ME, Ylä-Herttula S, Lipton BA, Ord VA, Witztum JL, Steinberg D. Macrophage colony-stimulating factor mRNA and protein in atherosclerotic lesions of rabbits and humans. *Am J Pathol* 1992;140:291-300.
- [25] Takeya M, Tomokiyo R, Jinnouchi K, et al. Macrophage scavenger receptor: Structure, function and tissue distribution. *Acta Histochem. Cytochem* 1999;32:47-51.
- [26] Kunjathoor VV, Febbraio M, Poderz EA, et al. Scavenger receptor A-I/II and CD36 are the principal receptors responsible for the uptake of modified low density lipoprotein leading to lipid loading in macrophages. *J Biol Chem* 2002;277:49982-8.
- [27] Emura I, Usuda H, Fujita T, Ebe K, Nagai T. Increase of scavenger receptor-A- positive monocytes in patients with acute coronary syndromes. *Pathology International* 2007;57:502-508.
- [28] Emura I, Usuda H, Fujita T, Ebe K, Nagai T. Scavenger receptor A index and coronary thrombus in patients with acute ST elevation myocardial infarction. *Pathology International* 2011;61:351-355.
- [29] Iwao Emura. High incidence of apoptosis in peripheral blood of myelodysplastic syndrome patients determined by Papanicolaou-stained preparations. *Laboratory Hematology* 2003;9:42-6.

- [30] Rittersma SZH, van der Wal AC, Koch KT, et al. Plaque instability frequently occurs day or weeks before occlusive coronary thrombosis. A pathological thrombectomy study in primary percutaneous coronary intervention. *Circulation* 2005; 111: 1160-5.
- [31] Konishi Y, Okamura M, Konishi N, et al. Enhanced gene expression of scavenger receptor in peripheral blood monocytes from patients on cuprophane haemodialysis. *Nephrol Dial transplant* 1997;12:1167-72.
- [32] Villanova JG, Lucena JLD, Arcás NF, Engel AR. Increased expression of scavenger receptor type I gene in human peripheral blood from hyperlipidemic patients determined by quantitative additive RT-PCR. *Biochimica et Biophysica Acta* 1996;1300:135-41.
- [33] Geng Y-j, Kodama T, Hansson GK. Differential expression of scavenger receptor isoforms during monocyte-macrophage differentiation and foam cell formation. *Arterioscler Thromb* 1994;14:798-806.
- [34] Fuster V, Badimon L, Badimon JJ, Chesserbo JH. The pathogenesis of coronary artery disease and the acute coronary syndromes. *N Engl J Med* 1992;326:242-50.
- [35] Ross R. Atherosclerosis – an inflammatory disease. *New Engl J Med* 1999;340:115-26.
- [36] Kuller LH, Tracy RP, Shaten J, Meilahn EN. Relationship of C-reactive protein and coronary heart disease in the MRFIT nested case-control study : Multiple Risk Factor Intervention Trial. *Am J Epidemiol* 1996;144:537-47.
- [37] Koenig W, Sund M, Frohlich M. et al. C-rfeactive protein, a sensitive marker of inflammation, predicts future risk of coronary heart disease in initially healthy middle-aged men : results from the MONICA(monitoring Trends and Determinants in Cardiovascular Disease) Augsburg Cohort Study, 1984 to 1992. *Circulation* 1999;99:237-42.
- [38] Libby P, Ridker PM, Maseri A. Inflammation and atherosclerosis. *Circulation* 2002;105:35-1143.
- [39] Naito M, Kodama T, Matsumoto A, Doi T, Takahashi K. Tissue distribution, intracellular localization, and in Vitro expression of Bovine macrophage scavenger receptor. *Am J Pathol* 1991;139:1411-23
- [40] Young DA, Lowe LD, Clark SC. Comparison of the effects of IL-3, granulocyte-macrophage colony- stimulating factor, and macrophage colony-stimulating factor in supporting monocytes differentiation in culture. *J Immunol* 1990;145:607-15.
- [41] Sakamoto K, Arakawa H, Mita S, et al. Elevation of circulating interleukin 6 after surgery: Factors influencing the serum level. *Cytokine* 1994;6:181-186.
- [42] Henriques de Gouveia R, van der Wal AC, van der Loos CM, Becker AE. Sudden unexpected death in young adults. Discrepancies between initiation of acute plaque complications and the onset of acute coronary death. *Eur Heart J* 2002; 23: 1433-40.
- [43] Murakami T, Mizuno S, Takahashi Y, et al. Intracoronary aspiration thrombectomy for acute myocardial infarction. *Am J Cardiol* 1998; 82: 839-44.
- [44] Badimon L, Badimon JJ. Mechanism of arterial thrombosis in nonparallel streamlines: platelet thrombi grow on the apex of stenotic severely injured vessel wall. Experimental study in the pig model. *J Clin Invest* 1989; 84: 1134-44.
- [45] Lassila R, Badimon JJ, Vallabhajosula S, Badimon L. Dynamic monitoring of platelet deposition on severely damaged vessel wall in flowing blood. Effects of different stenoses on thrombus growth. *Arteriosclerosis* 1990; 10: 306-15.

- [46] Nagata Y, Usuda K, Uchiyama A, Uchikoshi M, sekiguchi Y, Kato H, Miwa A, Ishikawa T. Characteristics of the Pathological images of coronary artery thrombi according to the infarct-related coronary artery in acute myocardial infarction. *Circ J* 2004; 68: 308-14.
- [47] Ruggeri ZM. Platelets in atherothrombosis. *Nat Med* 2002; 8: 1227-34.
- [48] Gawaz M. Role of platelets in coronary thrombosis and reperfusion of ischemic myocardium. *Cardiovasc Res* 2004; 61: 498-511.
- [49] Emura I, Usuda H. Histopathological and cytological examination of autopsy cases with multiple organ dysfunction syndromes. *Pathology International* 2010;60:443-51.

IntechOpen



## **Acute Coronary Syndromes**

Edited by Dr. Mariano Brizzio

ISBN 978-953-307-827-4

Hard cover, 214 pages

**Publisher** InTech

**Published online** 24, February, 2012

**Published in print edition** February, 2012

This book has been written with the intention of providing an up-to-the minute review of acute coronary syndromes. Atherosclerotic coronary disease is still a leading cause of death within developed countries and not surprisingly, is significantly rising in others. Over the past decade the treatment of these syndromes has changed dramatically. The introduction of novel therapies has impacted the outcomes and surviving rates in such a way that the medical community need to be up to date almost on a "daily bases". It is hoped that this book will provide a timely update on acute coronary syndromes and prove to be an invaluable resource for practitioners seeking new and innovative ways to deliver the best possible care to their patients.

### **How to reference**

In order to correctly reference this scholarly work, feel free to copy and paste the following:

Iwao Emura (2012). Physiopathology of the Acute Coronary Syndromes, Acute Coronary Syndromes, Dr. Mariano Brizzio (Ed.), ISBN: 978-953-307-827-4, InTech, Available from:

<http://www.intechopen.com/books/acute-coronary-syndromes/physiopathology-of-the-acute-coronary-syndromes>

# **INTECH**

open science | open minds

### **InTech Europe**

University Campus STeP Ri  
Slavka Krautzeka 83/A  
51000 Rijeka, Croatia  
Phone: +385 (51) 770 447  
Fax: +385 (51) 686 166  
[www.intechopen.com](http://www.intechopen.com)

### **InTech China**

Unit 405, Office Block, Hotel Equatorial Shanghai  
No.65, Yan An Road (West), Shanghai, 200040, China  
中国上海市延安西路65号上海国际贵都大饭店办公楼405单元  
Phone: +86-21-62489820  
Fax: +86-21-62489821

© 2012 The Author(s). Licensee IntechOpen. This is an open access article distributed under the terms of the [Creative Commons Attribution 3.0 License](#), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

IntechOpen

IntechOpen