Vol.45, No.4 April 2002

JMAJ

Japan Medical Association Journal

CONTENTS

Correction: Error in Author Name

In the article titled, "Protein Restriction Diet as an Essential Tool in Treating Uremia: Myth or Truth?" published in the JMAJ Vol.45, No.2 (pp. 80–83), and in the *Correction* which appeared at the foot of the contents page in the JMAJ Vol.45, No.3, the second author's name was misspelled. The correct spelling of the author's name is Tatsuo SHIIGAI. We apologize for the misspelling that occurred in the above two issues.

Key Points and Pitfalls in Electrocardiographic Diagnosis of Acute Myocardial Infarction

JMAJ 45(4): 135–142, 2002

Toshihisa ANZAI and Satoshi OGAWA

Cardiopulmonary Division, Department of Medicine,
Keio University School of Medicine

Abstract: Since electrocardiographic features of acute myocardial infarction vary temporally and spatially among patients, there are many pitfalls in electrocardiographic diagnosis of this condition. In order to avoid overlooking acute myocardial infarction, it is necessary to consider characteristic findings, such as augmentation of T wave amplitude, ST elevation, and the appearance of abnormal Q waves, in light of the time after onset. Observation of time-course changes allows us to noninvasively understand the presence/absence of recanalization and pathological conditions including infarct extension, infarct expansion, and retention of pericardial effusion, as well as to three-dimensionally diagnose the infarct site from changes in waveform in various leads. The latter findings reflect the anatomy of the artery responsible for the infarction. In addition, it is possible to determine the infarct site and the infarct-related artery from the waveforms of premature beats. In recent years, visualized diagnosis of coronary heart disease has become possible by means of improved techniques including coronary angiography and intravascular ultrasound. However, it seems that the well-established qualitative diagnosis of myocardial infarction by electrocardiography will continue to be important.

Key words: Myocardial infarction; Electrocardiogram; Arrhythmia; Reperfusion therapy

Introduction

Although recent years have seen astonishing technological advances in the examination and treatment of cardiovascular diseases, it is still an indisputable fact that electrocardiography (ECG) is the most important examination in diagnosing acute myocardial infarction. If acute myocardial infarction is suspected from symptoms and ECG findings, emergency treatment

This article is a revised English version of a paper originally published in the Journal of the Japan Medical Association (Vol. 125, No. 5, 2001, pages 665–670).

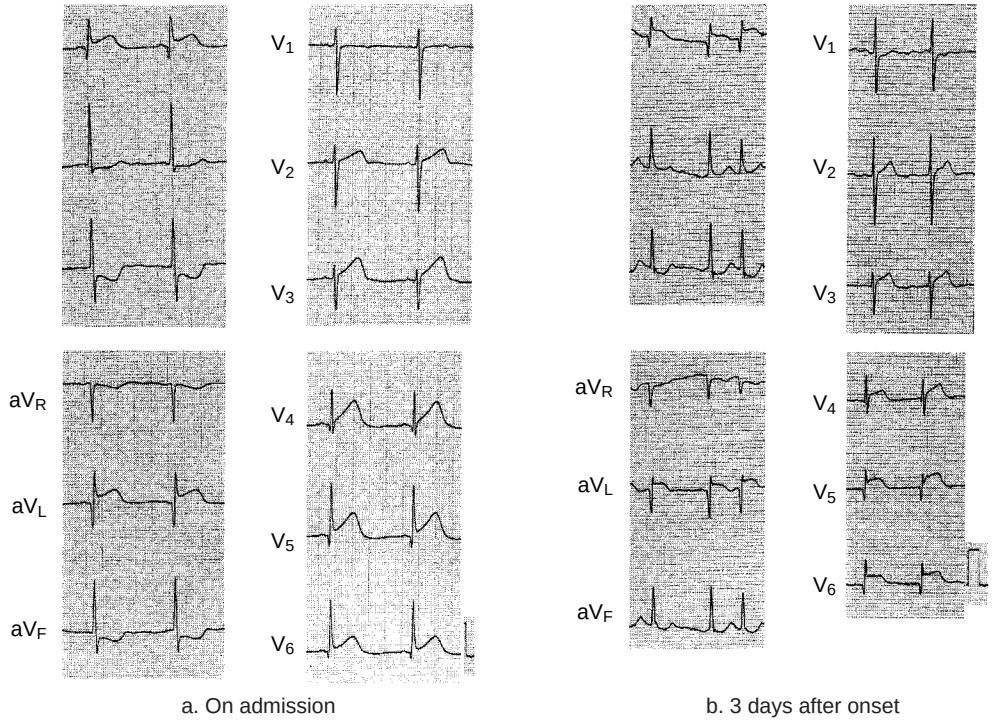


Fig. 1 ECG findings of impending cardiac rupture
a.: ECG findings on admission. There is ST elevation in leads I, aV_L, and V_{3-6}, indicating myocardial infarction of the anterolateral wall. b.: ECG findings at the time of shock occurring 3 days after onset. There is the evidence of atrial fibrillation. Leads I, aV_L, and V_{3-6} show ST re-elevation with an upward convex pattern (infarct expansion), and all leads show decreased potentials (retention of pericardial effusion). Subsequently, rapid retention of bloody pericardial effusion was noted.

based on reperfusion therapy should be administered as promptly as possible. However, electrocardiographic diagnosis is often difficult, such that some patients may not receive timely reperfusion therapy during the acute phase of the disease.

The key points and pitfalls of electrocardiographic diagnosis of acute myocardial infarction are described herein.

Time-course Changes in the Electrocardiogram

1. Time after onset of chest pain and the point of ECG reading

First of all, obtaining a full history is essential to avoid overlooking acute myocardial infarction. Second, ECG examination should be performed with adequate knowledge of possible ECG findings based on time after onset. If the patient is in the hyperacute phase (within a few hours after onset), ST elevation or depression will not necessarily be observed. It is important to determine whether there is Twave amplitude augmentation. On the other hand, if there are no ST changes or abnormal Qwaves 6 or more hours after the onset, differentiation from other diseases, particularly fatal disorders such as acute aortic dissection, is necessary.

2. Importance of observing time-course changes

In addition to the importance of comparing the ECG record taken at the emergency department visit with the patient's previous ECG record, subsequent frequent ECG recordings will also provide important prognostic information.

(1) **Spontaneous recanalization and coronary**

vasospasm: If ST elevation is restored to the baseline after visiting the outpatient clinic, it is possible that spontaneous recanalization has occurred or that coronary vasospasm was involved in the heart attack. This should be confirmed before thrombolytic therapy or emergency coronary angiography is performed.

(2) **Change from incomplete to complete occlusion of the infarct-related artery**: Further incremental ST elevation suggests progression to complete occlusion due to thrombus formation. In this case, reperfusion therapy should be performed immediately.

(3) **Success or failure of reperfusion therapy**: It is known that ST elevation is promptly reversed (50% reduction within 1 hour) if thrombolytic therapy is successful, i.e., recanalization is achieved.[1)] It is also characteristic for negative Twaves to appear in an early phase.[2)] Recently, coronary angioplasty has often been performed as an emergency treatment. Even if recanalization is achieved angiographically, microcirculatory disturbances may persist (no-reflow phenomenon), causing prolonged ST elevation.

(4) **Infarct extension**: Infarct extension occurs if an intracoronary thrombus extends proximally, and ST elevation may be recognized in other leads as well. This finding is said to be relatively common in obese women, after thrombolytic therapy, as well as in those who have diabetes or non-Qwave myocardial infarction.

(5) **Infarct expansion**: ST segment re-elevation occurs if the area of vulnerable and necrotic myocardium is expanded by wall stress following transmural myocardial infarction. ST elevation in this case can be distinguished from ischemia in view of its upward convex form and persistence over time.

(6) **Pericardial effusion**: If infarction is complicated by pericarditis with pericardial effusion, low voltage in all leads will be observed. Subacute cardiac rupture occurring a few or more days after onset often follows infarct expansion or pericardial effusion. Therefore, these findings may facilitate predicting cardiac rupture to some extent (Fig. 1).

Changes in ECG Waveforms

1. Twave augmentation can easily be overlooked

As mentioned previously, Twave augmentation is one of the findings that may be overlooked in the acute phase. Since Twave augmentation is also present in early repolarization, hyperkalemia, left ventricular hypertrophy, and left bundle branch block, differentiation from these conditions is necessary. Whereas such Twaves are bilaterally symmetric and narrow, hyperacute Twaves in myocardial infarction are often relatively broad and their peaks are located posteriorly rather than centrally.

2. Possible diagnoses with ST elevation

Acute myocardial infarction is the first diagnosis to be suspected if there is ST elevation together with chest pain. However, other possibilities should also be considered. In cases of pericarditis, ST elevation is said to be relatively slight, 0.5 mV or less, is not accompanied by mirror-image changes, and is observable in most leads.

3. Diagnosis of the infarction site

As shown in Table 1, it is possible to diagnose the infarct site and the infarct-related artery on the basis of which leads show ST elevation and abnormal Qwaves. However, the combination of leads in which ST elevation and abnormal Qwaves are observed varies somewhat according to individual coronary artery anatomy, and does not necessarily agree with the patterns shown in the table. Therefore, it is important to three-dimensionally understand the infarct site reflected in each lead (Fig. 2).

ST segment changes can often be observed in precordial leads in inferior infarction or in limb leads in anterior infarction. The significance of such changes will be described below.

(1) **ST changes in the precordial leads in inferior infarction**

ST depression: ST depression is seen in the

Table 1 Diagnosis of the Site of Myocardial Infarction

Infarct site	Responsible coronary artery	Sites of abnormal Q waves and ST elevation on ECG											
		I	II	III	aV_R	aV_L	aV_F	V_{4R}	V_1	V_2	V_3	V_4	V_5	V_6
Anterior septum	Proximal LAD								○	○	○	○		
Apex	LAD, RCA, or LCX												○	○
High lateral wall	First diagonal branch of LAD	○				○								
Anterolateral wall	Proximal LAD including diagonal branch	○				○					○	○	○	○
Extensive anterior wall	Proximal LAD	○				○			○	○	○	○	○	○
Anteroinferior wall	LAD going around the apex extensively		○	○			○				○	○	○	○
Lateral wall	Diagonal branch of LAD, extending to the apex	○				○							△	○
High posterior wall	LCX								●	●				
Posterolateral wall	LCX (including obtuse marginal branch) LCX (large obtuse marginal branch)								●	●			○	○
Posteroinferior wall	LCX or large RCA		○	○			○		●	●				
Inferior wall apex	RCA or LCX		○	○			○						△	○
Inferior wall	RCA or LCX		○	○			○							
Inferior wall/right ventricle	RCA, before bifurcation of the anterior branch		○	○			○	○						

Notes: ● denotes R wave augmentation or ST depression
LAD: left anterior descending artery, RCA: right coronary artery, LCX: left circumflex artery

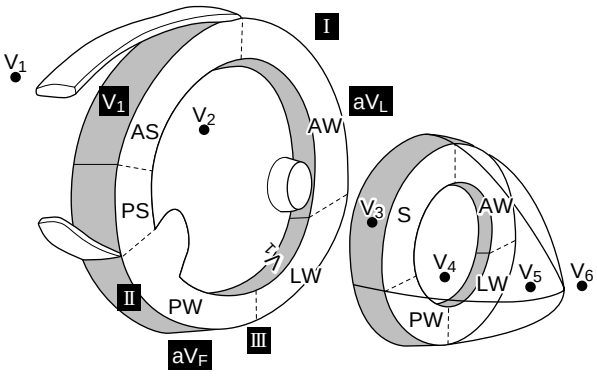


Fig. 2 Site of myocardial infarction and ECG
Leads V_1–V_4 correspond to the anterior wall (AW) and septum (AS, S), and leads II, III, and aV_F correspond to the left ventricular posterior wall (PW) to the posterior septum (PS). Leads I and aV_L correspond to the left ventricular free wall, and have enantiomorphic relations with leads II, III, and aV_F because of their contralateral location. Although there are no available leads directly facing the high posterior wall or lateral wall (LW), changes at these sites appear as mirror-image changes in leads V_1–V_4. Leads V_{5-6} correspond to the left ventricular apex. (Original illustration by Ogawa, S.)

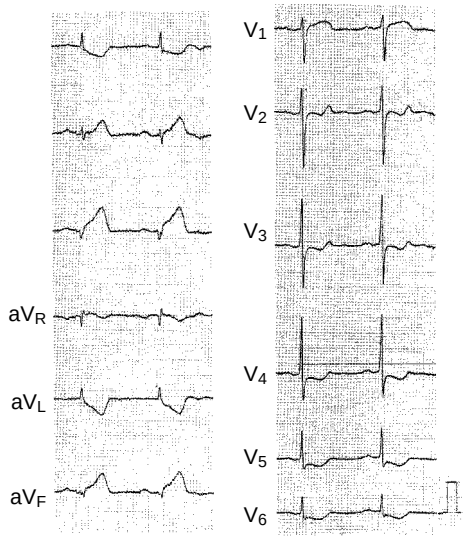


Fig. 3 12-lead ECG of right ventricular infarction
In addition to leads II, III, and aV_F, lead V_1 also shows ST elevation.

precordial leads in about half of all patients with inferior infarction. The prognosis is reportedly poor if ST depression persists. This is probably because most such patients have multi-vessel disease involving the left anterior descending artery or extensive inferior infarction involving the high posterior wall (ST depression occurs in leads V_1–V_3 as a mirror-image change representing transmural infarction in the lateral wall [LW] of the base of the heart, as shown in Fig. 2).[3,4] In particular, when ST depression in the precordial leads is as severe as 3 mm or more, it is strongly suspected that the left anterior descending artery is also affected.[5] ST depression in leads I and aV_L in inferior infarction represents mirror-image changes against ST elevation in leads II, III, and aV_F (the posterior wall [PW] and the anterior wall [AW] at the base of the heart in Fig. 2 are enantiomorphic).

ST elevation: ST elevation may be found in leads V_1 and V_2 in less than 10% of patients with inferior infarction. This finding is known to suggest the presence of right ventricular infarction.[6] Anterior infarction is different from right ventricular infarction in that the degree of ST elevation is greater in lead V_2 than in lead V_1 ($V_1<V_2$) in the former whereas it is greater in lead V_1 than in lead V_2 in the latter ($V_1>V_2$) (Fig. 3). However, the finding associated with the highest sensitivity and specificity in the diagnosis of right ventricular infarction is ST elevation of 1 mm or more in the right precordial lead (V_{4R}).[7] In cases of inferior infarction accompanied by a blood pressure decrease, particularly when there is no angina preceding the infarction, right ventricular infarction is also frequently present.[8] Therefore, ECG findings in the right precordial lead should always be confirmed.

(2) **ST changes in the limb leads in anterior infarction**

ST depression: It is said that, if there is ST depression in the limb leads in anterior infarction, multi-vessel disease is highly probable and the prognosis is thus poor.[9] However, ST changes in the inferior wall lead in anterior infarction are defined by the sum total of mirror-image changes (ST depression) in response to ischemia of the anterior wall and changes due to ischemia of the inferior wall (ST elevation). Therefore, if the left anterior descending artery perfuses an extensive area ranging from the apex to the inferior wall, ST changes in the limb leads may be counterbalanced by mirror-image changes in the anterior wall, such that ST changes may appear to be absent or ST elevation may occur. On the contrary, if the left anterior descending artery perfuses a limited area, prominent ST depression is often seen in leads II, III, and aV_F.[10]

ST elevation: In infarction of the left anterior descending artery long enough to go around the apex of the heart as mentioned above, ST elevation may be found in leads II, III, and aV_F. When infarction has occurred in an area proximal to the diagonal branch, ST elevation is also seen in leads I and aV_L.

(3) **The infarct-related artery in inferior infarction (differentiation between the right coronary artery and the left circumflex artery)**:

It is sometimes difficult to electrocardiographically identify the infarct-related artery in

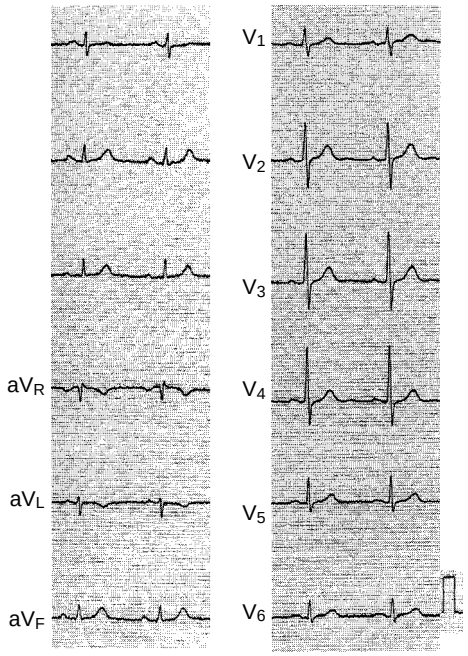


Fig. 4 ECG of high posterior infarction
ECG recording 2 days after onset of infarction. There is R wave augmentation, reflected by mirror-image changes in lead V_1.

inferior infarction, because the anatomy of the coronary arteries varies among patients. However, a pure high posterior wall infarction showing R wave augmentation alone (mirror-image changes) in lead V_1 is a finding characteristic of myocardial infarction in the area of the left circumflex artery, particularly its obtuse marginal branch (Fig. 4). If ST elevation is present in lead I and in at least one of the lateral wall leads (aV_L, V_5, V_6), the lesion is presumed to be located in the left circumflex artery with a sensitivity of 80% and a specificity of 90%.[11)]

4. Meaning of Q waves

Q waves having a width of 0.04 sec or more and corresponding to one-fourth of the voltage of R waves are regarded as abnormal Q waves. This finding is particularly important in diagnosing the infarct site in transmural myocardial infarction. However, Q waves can be induced by conditions other than infarction; the following findings are useful in differential diagnosis.[12)]

(1) **Q waves in lead aV_L**: Such Q waves are often found in the heart with a vertical axis. If there are no Q waves with a width of 0.04 sec in lead I or the left precordial lead, or if there is no abnormality in ST-T, myocardial infarction is unlikely.

(2) **Q waves in leads III and aV_F**: If there is QR in lead aV_R, inferior infarction is highly unlikely (the presence of rS in lead aV_R suggests inferior infarction).

(3) **Q waves in leads V_1-V_3**: The presence of Q waves only in leads V_1-V_2 is often seen in normal cases. If Q waves are observed in leads V_1-V_3, anterior infarction should be suspected, but differentiation from left ventricular hypertrophy, left bundle branch block, and chronic obstructive pulmonary disease is necessary.

Arrythmia in Myocardial Infarction

1. Importance of premature beats

Ventricular premature beats are often seen in acute myocardial infarction. Observation of the waveform may provide important information for diagnosis. For instance, if there are premature beats with a form of bifascicular block (left anterior hemiblock and right bundle branch block) in inferior infarction, the origin of the premature beats is considered to be the ischemic site of the left posterior branch. However, since the left posterior branch is perfused by both the left anterior descending artery and the right coronary artery, such premature beats are unlikely to occur in inferior infarction alone. In this case, multi-vessel disease involving the left anterior descending artery and right coronary artery or the presence of collateral flow from the right coronary artery to the left anterior descending artery should be suspected.

2. Tachyarrhythmia

Ventricular tachycardia and ventricular fibrillation should always be borne in mind as a fatal arrhythmia possibly complicating myocardial infarction. However, accelerated idioventri-

cular rhythm (AIVR) seen in about 50% of reperfused patients[13] is not an indication for antiarrhythmic drug therapy, because the rate is 50–120/min and does not influence hemodynamics. Ventricular tachycardia often begins after a ventricular premature beat, whereas AIVR begins after a long pause. In general, antiarrhythmic medication is given to patients with warning arrhythmia characterized by 6 or more distinct rhythms per minute, R on T, polymorphism, and three or more serial rhythms. To manage potentially fatal arrhythmias such as recurrent sustained ventricular tachycardia or ventricular fibrillation in the chronic phase of myocardial infarction, the use of an implantable defibrillator should also be considered.

A type of supraventricular arrhythmia relatively frequently seen after myocardial infarction is atrial fibrillation. In most cases, such arrhythmia occurs transitorily with hemodynamic worsening, postinfarction pericarditis, or atrial infarction (as represented by elevated PQ segment baseline on ECG) and disappears spontaneously after resolving these problems. If there is hemodynamic disturbance due to atrial fibrillation, cardioversion should be considered promptly. If transient atrial fibrillation is frequent in the chronic phase, the use of antiarrhythmic drugs should also be considered. However, the possibility has been pointed out that the prognosis may be worsened by inhibition of cardiac function or by the proarrhythmic action of antiarrhythmic drugs.[14] Therefore, prudent application of such medications is necessary.

3. Bradyarrhythmia

If atrioventricular block of Mobitz type II or higher, bifascicular block, or symptomatic bradycardia not responding to atropine is found after myocardial infarction, prompt insertion of an intravenous pacemaker is warranted. In these cases of bradycardia, it is necessary to observe the QRS interval of the escape rhythm. If the ventricular escape rhythm has a wide QRS, severe block involving up to the His bundle is suspected, and a permanent pacemaker is often required.

Conclusion

ECG changes in acute myocardial infarction vary among different patients and may cause difficulties in diagnosis. However, it is possible to ascertain the ongoing phenomenon accurately and without difficulty if one copes with waveform changes in each lead in a flexible manner based on a full understanding of the meaning of such changes. Although cardiac catheterization is now frequently used, and visualized diagnosis of myocardial infarction is becoming a common practice, the importance of ECG should never been underestimated in light of the qualitative diagnosis of myocardial infarction.

REFERENCES

1) Shah, P.K., Cercek, B., Lew, A. *et al.*: Angiographic validation of bedside markers of reperfusion. *J Am Coll Cardiol* 1993; 21: 55–61.
2) Matezky, S., Barabash, G.I., Shahar, A. *et al.*: Early T wave inversion after thrombolytic therapy predicts better coronary perfusion: Clinical and angiographic study. *J Am Coll Cardiol* 1994; 24: 378–383.
3) Gibson, R.S., Crampton, R.S., Watson, D.D. *et al.*: Precordial ST-segment depression during acute inferior myocardial infarction: Clinical, scintigraphic and angiographic correlations. *Circulation* 1982; 66: 732–741.
4) Hlatky, M.A., Califf, R.M., Lee, K.I. *et al.*: Prognostic significance of precordial ST segment depression during inferior acute myocardial infarction. *Am J Cardiol* 1985; 55: 325–329.
5) Tendera, M. and Campbell, W.B.: Significance of early and later anterior precordial ST segment depression in inferior myocardial infarction. *Am J Cardiol* 1984; 54: 994–996.
6) Geft, I.L., Shah, P.K., Rodriguez, L. *et al.*: ST elevations in leads V_1 to V_5 may be caused by right coronary artery occlusion and acute right ventricular infarction. *Am J Cardiol* 1984; 53: 991–996.
7) Klein, H.O., Tordijman, T., Ninio, R. *et al.*: The

early recognition of right ventricular infarction: Diagnostic accuracy of the electrocardiographic V_{4R} lead. *Circulation* 1983; 67: 558–565.
8) Haraphongse, M., Tanomsup, S. and Jugdutt, B.I.: Inferior ST segment depression during acute anterior myocardial infarction: Clinical and angiographic correlations. *J Am Coll Cardiol* 1984; 4: 467.
9) Shiraki, H., Yoshikawa, T., Anzai, T. *et al.*: Association between preinfarction angina and a lower risk of right ventricular infarction. *N Engl J Med* 1998; 338: 941–947.
10) Fletcher, W.O., Gibbons, R.J. and Clements, I.P.: The relationship of inferior ST depression, lateral ST elevation, and left precordial ST elevation to myocardium at risk in acute anterior myocardial infarction. *Am Heart J* 1993; 126: 526–535.
11) Bairey, C.N., Shah, P.K., Lews, A.S. *et al.*: Electrocardiographic differentiation of occlusion of the left circumflex vs. right coronary arteries as a cause of inferior acute myocardial infarction. *Am J Cardiol* 1987; 60: 456–459.
12) Ogawa, S. and Akaishi, M.: Examination and treatment of cardiovascular medicine: electrocardiography. *Cardiovascular Medicine Manual*. Nankodo, Tokyo, 1995; pp.177–180. (in Japanese)
13) Cercek, B., Lew, A., Laramee, P. *et al.*: Time course and characteristics of ventricular arrhythmias after reperfusion in acute myocardial infarction. *Am J Cardiol* 1987; 60: 214–218.
14) Cardiac Arrhythmia Suppression Trial: preliminary report: effect of encainide and flecainide on mortality in a randomized trial of arrhythmia suppression after myocardial infarction. *N Engl J Med* 1989; 321: 406–412.

Present Status of Pre-hospital Thrombolytic Therapy for Acute Myocardial Infarction
—Its Indications and Problems—

JMAJ 45(4): 143–148, 2002

Takeshi MOTOMIYA

Vice-Director, Tokyo Metropolitan Ohkubo Hospital

Abstract: Early administration of thrombolytic drugs for acute myocardial infarction may improve survival if safely and appropriately administered. Delays to thrombolytic reperfusion are substantial and are key factors in efforts to improve thrombolytic strategies. Transportation delays vary depending on the patient's distance from the hospital and availability of local ambulance system. In-hospital delay is also a large single component of delay. Intuitively, pre-hospital initiation of thrombolytic therapy is the most promising approach to reducing the overall time to therapy. A meta-analysis of 6 randomized controlled trials of pre-hospital versus in-hospital thrombolysis for acute myocardial infarction indicated significantly decreased all-cause hospital mortality among patients treated with pre-hospital thrombolysis compared with in-hospital thrombolysis. Estimated time to thrombolysis was 104 minutes for the pre-hospital group and 162 minutes for the in-hospital thrombolysis group. However, the time savings can be offset in most cases by an improved hospital triage with resultant "door-to-needle time" reduced to 30 minutes or less. Furthermore only a small percentage (5% to 10%) of patients with chest pain in the pre-hospital setting have acute myocardial infarction and are eligible for thrombolytic therapy. For these reasons, a general policy of pre-hospital thrombolytic therapy cannot currently be advocated and indicated only in cases with transport time greater than 60 or 90 minutes as a Class IIb recommendation in the ACC/AHA Guidelines for the Management of Patients With Acute Myocardial Infarction.

Key words: Acute myocardial infarction; Coronary thrombolysis; Pre-hospital thrombolysis; t-PA

Introduction

Approximately one half of the patients died of acute myocardial infarction (MI) die within 1 hour of onset of symptoms and before reaching a hospital.[1)] Coronary reperfusion therapy in

This article is a revised English version of a paper originally published in the Journal of the Japan Medical Association (Vol. 125, No. 5, 2001, pages 675–678).

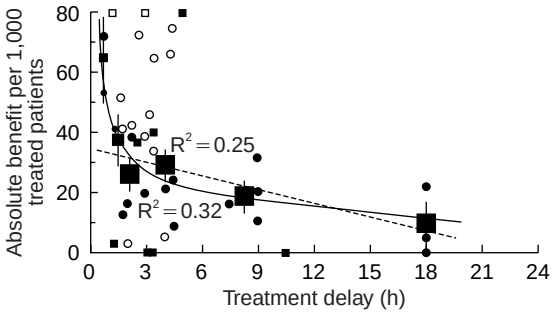


Fig. 1 Absolute 35-day mortality reduction versus treatment delay[2)]

evolving acute MI is an established and effective therapy for reduction of mortality and morbidity. More recent data regarding the time-dependent benefits of reperfusion therapy provide added stimulus to develop more effective means of expediting delivery of medical care to patients with acute MI. The reperfusion therapy is not limited just to the widespread use of thrombolytic agents, but also PTCA, stent and even emergency CABG surgery in suitable patients. Currently PTCA and stent implantation therapy is more frequently performed than thrombolysis in Japan.

Delay in treating patients with acute MI is a critical factor in decreasing the overall survival rate. Boersma *et al.*[2)] reported that the relation between treatment delay and mortality reduction was expressed better by a non-linear than linear regression (Fig. 1), and the beneficial effect of fibrinolytic therapy is substantially higher in patients presenting within 2 hours after symptom onset compared to those presenting later. The components of delay from onset to treatment are (1) patients related (i.e., failure to recognize the seriousness of the symptoms and delay in seeking medical attention); (2) pre-hospital evaluation, treatment, and transport times; and (3) time required for diagnosis and initiation of treatment in the hospital. In most cases, patient-related delay is the longest. Interventions to minimize patient delay are primarily educational in nature. As for the reperfusion therapy, pre-hospital initiation of thrombolytic therapy may be the most promising approach to reducing the overall time to therapy.

In this article, randomized controlled trials of pre-hospital versus in-hospital thrombolysis for acute MI were reviewed and its indications and problems were discussed.

Indications and Contraindications of Thrombolysis

1. Indications of Thrombolysis

Recent ACC/AHA guidelines[3)] are as follows; Class I (conditions for which there is evidence and/or general agreement that given procedure or treatment is beneficial, useful, and effective) are 1) ST elevation, time to therapy 12 hours or less, age less than 75 years, and 2) bundle branch block and history suggesting acute MI. The earlier therapy begins, the better the outcome, with the greatest benefit decidedly occurring when therapy is given within the first 3 hours; proven benefit occurs, however, up to at least within 12 hours of the onset of symptoms.

Class IIa (conditions for which there is conflicting evidence and/or a divergence of opinion about the usefulness/efficacy of a procedure or treatment. And weight of evidence/opinion is in favor of usefulness/efficacy) is 1) ST elevation, age 75 years or older. In persons older than 75 years, the overall risk of mortality form MI is high without and with therapy. Although the proportionate reduction in mortality is less than in patients younger than 75, the absolute reduction results in 10 lives saved per 1,000 patients treated in those over 75.

Class IIb (usefulness/efficacy is less well established by evidence/opinion) are 1) ST elevation, time to therapy greater than 12 to 24 hours, and 2) blood pressure on presentation greater than 189 mmHg systole and/or greater than 110 mmHg diastole associated with high-risk MI.

Class III (conditions for which there is evidence and/or general agreement that a proce-

Table 1 Contraindications and Cautions for Thrombolytic Use in Myocardial Infarction[3)]

Contraindications
• Previous hemorrhagic stroke at any time; other strokes or cerebrovascular events within 1 year
• Known intracranial neoplasm
• Active internal bleeding (does not include menses)
• Suspected aortic dissection
Cautions/relative contraindications
• Severe uncontrolled hypertension on presentation (blood pressure>180/110 mmHg)
• History of prior cerebrovascular accident or known intracerebral pathology not covered in contraindications
• Current use of anticoagulants in therapeutic doses (INR≥2–3); known bleeding diathesis
• Recent trauma (within 2–4 weeks), including head trauma or traumatic or prolonged (>10 min) CPR or major surgery (<3 wk)
• Noncompressible vascular punctures
• Recent (within 2–4 weeks) internal bleeding
• For streptokinase/anistreplase: prior exposure (especially within 5 d–2 y) or prior allergic reaction
• Pregnancy
• Active peptic ulcer
• History of chronic severe hypertension

dure/treatment is not useful/effective and in some cases may be harmful) are 1) ST elevation, time to therapy greater than 24 hours, ischemic pain resolved, and 2) ST-segment depression only.

Pre-hospital thrombolysis is classified as Class IIb recommendation as pre-hospital thrombolysis in special circumstances (e.g. transport time greater than 90 minutes).[3)]

2. Contraindications and Cautions for Thrombolysis

Bleeding represents the most important risk of thrombolytic treatment. Contraindications and cautions for coronary thrombolysis are shown in Table 1.[3)]

Thrombolytic Agents and Routs of Administration

All of the thrombolytic agents currently available are plasminogen activators. However, aside from this similarity, there are many differences among agents in dose, circulating half-life, fibrin-specificity, rates of coronary recanalization, risks of hemorrhage, and cost. Thrombolytic agents available in Japan are urokinase, tissue plasminogen activator (alteplase, tisokinase, nateplase), pro-urokinase (nasaruplase), and mutant or modified plasminogen activator (monteplase, pamiteplase). Among them urokinase, tisokinase, and nasaruplase are approved for intracoronary use as well as intra-venous use, but this intracoronary route of administration for acute MI has been now less frequently performed. Modified plasminogen activators have a longer half-life and can be administered with a single bolus intravenous injection.

Recent trials with alteplase have used an accelerated or frontloaded dosing regimen.[4)] Because the accelerated regimen leads to greater early patency rates without an increase in hemorrhagic risk, it has become the preferred method of administration in the United States and Europe. Modified t-PA monteplase has also proved to produce a higher rate of early recanalization of the infarct-related coronary artery without fatal bleeding complications.[5)]

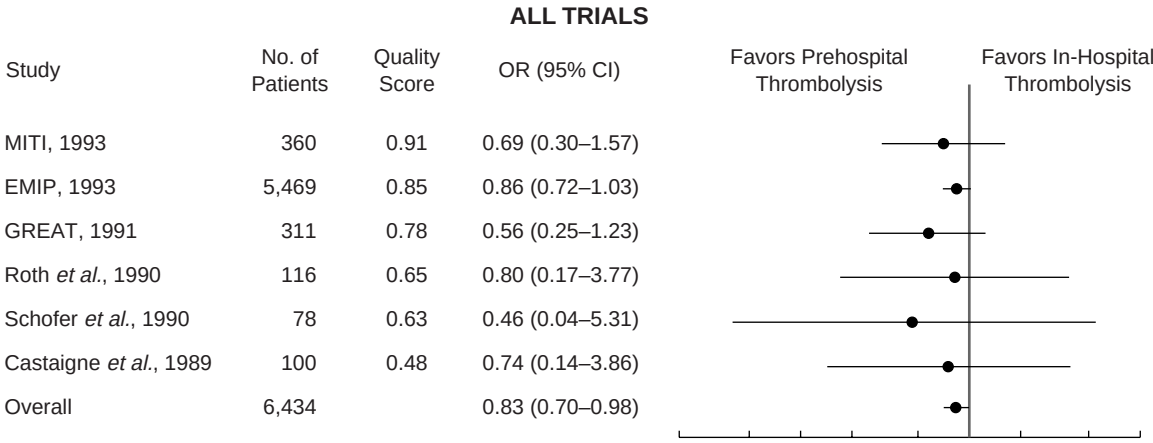


Fig. 2 Results of randomized trials of prehospital thrombolysis on hospital mortality[8]

Pre-hospital Thrombolysis

In the randomized Seattle Myocardial Infarction Triage and Intervention (MITI) study, cardiac function and infarct size were assessed in rather small number of patients who received either in-field or in-hospital treatment with t-PA.[6] Though the time savings for the pre-hospital thrombolysis conducted by paramedics *per se* was small (about 30 minutes), treatment initiated in less than 70 minutes of onset of symptoms was found to result in a distinct advantage in left ventricular function, infarct size, and mortality. The larger European Myocardial Infarction Project (EMIP) study randomized 5,454 patients to pre-hospital versus in-hospital treatment with APSAC (anisoylated plasminogen streptokinase activator complex) and assessed mortality outcome.[7] Patients were treated somewhat later in-field in EMIP (at about 2 hours) than in MITI (about 1 hour), but about 1 hour was saved by in-field treatment compared with in-hospital therapy. This study showed a significant reduction of cardiac mortality and non-significant total mortality at 1 month.

Morrison *et al.*[8] reviewed randomized controlled trials of pre-hospital versus in-hospital thrombolysis for acute MI and performed meta-analysis measuring in-hospital mortality in 6 randomized trials including MITI and EMIP ($n = 6,434$). Results were similar regardless of trial quality or training and experience of the provider among the trials and all-cause mortality was significantly decreased in pre-hospital thrombolysis group as compared with in-hospital group (Fig. 2). Estimated time to thrombolysis was 104 minutes for the pre-hospital group and 162 minutes for the in-hospital group. However, the time savings can be offset in most cases by an improved hospital triage with resultant "door-to-needle time" reduced to 30 minutes or less. Furthermore, only a small percentage (5% to 10%) of patients with chest pain in the pre-hospital setting have acute myocardial infarction and are eligible for thrombolytic therapy. For these reasons, a general policy of pre-hospital thrombolytic therapy cannot currently be advocated and indicated only in cases with transport time greater than 90 minutes as a Class IIb recommendation in the ACC/AHA Guidelines for the Management of Patients with Acute Myocardial Infarction.[3]

Choice of Agent

Three mega-trials randomizing a total 103,069 patients have compared the effects on mortality of various thrombolytic agents. In the Interna-

tional Study including GISSI-2 20,891 patients were randomized to receive either streptokinase or alteplase.[9] Mortalities at 30 days were similar (8.9% with streptokinase versus 8.5% with alteplase). The ISIS-3 trial randomized 41,299 patients to receive either streptokinase, anistreplase, or duteplase.[10] Mortality was similar with all three thrombolytic regimen: 10.5% with streptokinase, 10.3% with duteplase, and 10.6% with anistreplase. The GUSTO-I trial randomized 41,021 patients to receive one of four thrombolytic regimens.[11] The lowest mortality rate at 30 days (6.3%) was achieved with accelerated administration of alteplase as compared with 7.2% for streptokinase. Why did ISIS-3 and International Study fail to demonstrate any mortality difference between streptokinase and t-PA, as GUSTO-I trial did? The failure to use intravenous heparin in the former trials may have disadvantaged alteplase in International Study and duteplase in ISIS-3. Secondly a standard 3-hour infusion of alteplase has been shown to produce less 90-minute patency than an accelerated alteplase regimen, which delivers substantially more of the drug to average-weight patients in the first 60 minutes.

Recently the ASSENT-2 trial assessed the efficacy and safety of modified t-PA tenecteplase compared with alteplase.[12] Tenecteplase and front-loaded alteplase were equivalent for mortality. And the ease of administration of tenecteplase may facilitate more rapid treatment in and out of hospital. Similarly the InTIME-II trial demonstrated that 30 day mortality was equivalent but long-term mortality tended to be lower in the nPA (lanoteplase) group as compared with accelerated alteplase.[13] Both of these agents have the advantage over alteplase of bolus intravenous administration, and therefore could easily be given in the community or pre-hospital phase.

New Adjunctive Therapy

The disadvantage of thrombolytic therapy over primary angioplasty has been said to be a relatively low TIMI-3 flow of approximately 50%. In the TIMI-14 study, however, TIMI-3 flow was obtained in 77% at 90 minutes after start of the fibrinolytic regimen.[14] The TIMI-14 regimen consisted of half the standard dose of alteplase, a low dose of intravenous heparin, monoclonal antibody of platelet glycoprotein IIb/IIIa receptor, abciximab, and aspirin. At 60 minutes 65% of patients had TIMI-3 flow. These findings are significant since only 54% of patients given alteplase in the GUSTO-I angiographic substudy[15] had TIMI-3 flow at 90 minutes, and since coronary angioplasty commonly takes longer than an hour and a half of complete.

REFERENCES

1) Report of a WHO Expert Committee: *Service for Cardiovascular Emergency.* WHO, Geneva, 1975.
2) Boersma, E., Maas, A.C.P., Deckers, J.W. *et al.*: Early thrombolytic treatment in acute myocardial infarction: Reappraisal of the golden hour. *Lancet* 1996; 348: 771–775.
3) ACC/AHA guidelines for the management of patients with acute myocardial infarction. A report of the American College of Cardiology/American Heart Association task force on practice guidelines (Committee on management of acute myocardial infarction). *J Am Coll Cardiol* 1996; 28: 1328–1428.
4) Neuhaus, K.-L., Feuerer, W., Jeep-Tebbe, S. *et al.*: Improved thrombolysis with a modified dose regimen of recombinant tissue-type plasminogen activator. *J Am Coll Cardiol* 1989; 14: 1566–1569.
5) Kawai, C., Yui, Y., Hososa, S. *et al.*: A prospective randomized double blind multi-center trial of a single bolus injection of the noble modified t-PA E6010 in the treatment of acute myocardial infarction: comparison with native t-PA. *J Am Coll Cardiol* 1997; 29: 1447–1453.
6) Weaver, W.D., Cerqueira, M., Hallstrom, A.P. *et al.*: Prehospital initiated versus hospital-initiated thrombolytic therapy. The Myocardial Infarction Triage and Intervention (MITI) trial. *JAMA* 1993; 270: 1211–1216.
7) The European Myocardial Infarction Project

(EMIP) Group: Prehospital thrombolytic therapy in patients with suspected acute myocardial infarction. *N Engl J Med* 1993; 329: 383–389.
8) Morrison, L.J., Verbeek, P.R., McDonald, A.C. *et al.*: Mortality and prehospital thrombolysis for acute myocardial infarction. A meta-analysis. *JAMA* 2000; 283: 2686–2692.
9) The International Study Group: In-hospital mortality and clinical course of 20,891 patients with suspected acute myocardial infarction randomized between alteplase and streptokinase with or without heparin. *Lancet* 1990; 336: 71–75.
10) ISIS-3 (Third International Study of Infarct Survival) Collaborative Group: A randomized comparison of streptokinase versus tissue plasminogen activator versus anistreplase and of aspirin plus heparin versus aspirin alone among 41,299 cases of suspected acute myocardial infarction: ISIS-3. *Lancet* 1992; 339: 753–770.
11) The GUSTO Investigators: An international randomized trial comparing four thrombolytic strategies for acute myocardial infarction. *N Engl J Med* 1993; 329: 673–682.
12) Assessment of the Safety and Efficacy of New Thrombolytic (ASSENT-2) Investigators: Single-bolus tenecteplase compared with front-loaded alteplase in acute myocardial infarction: the ASSENT-2 double-blind randomized trial. *Lancet* 1999; 354: 716–722.
13) Antman, E.M., Wilcox, R.G., Gingliano, R.P. *et al.*: Long-term comparison of lanoteplase and alteplase in ST elevation myocardial infarction: 6 months follow-up in InTIME II trial. *Circulation* 1999; 100: I-498.
14) De Lemos, J.A., Antman, E.M., Gibson, C.M. *et al.*: Abciximab improves both epicardial flow and myocardial reperfusion in ST-elevation myocardial infarction. Observations from the TIMI 14 trial. *Circulation* 2000; 101: 239–243.
15) The GUSTO Angiographic Investigators: The effects of tissue plasminogen activator, streptokinase, or both on coronary artery patency, ventricular function, and survival after acute myocardial infarction. *N Engl J Med* 1993; 329: 1615–1622.

Complications of Acute Myocardial Infarction

—Diagnosis and Treatment—

JMAJ 45(4): 149–154, 2002

Hiroshi NONOGI

Director, Division of Cardiology and Emergency Medicine, National Cardiovascular Center

Abstract: For the past 20 years, the in-hospital mortality rate of acute myocardial infarction has significantly decreased to less than 10%. This reduction can be attributed mainly to the development of acute-phase treatment such as reperfusion therapy. However, cardiogenic shock and cardiac rupture dominate more than 70% of the causes of death. CCUs have made efforts to treat these problems whose mortality rate is still high. For cardiogenic shock, maintenance of circulation followed by reperfusion therapy is necessary before it causes irreversible impairment of organ function. For cardiac rupture, a critical care system should be established to implement emergency surgical intervention following the early detection of cardiac tamponade, in addition to the emphasis on prevention in high-risk populations for cardiac rupture.

Key words: Acute myocardial infarction; Cardiogenic shock; Cardiac rupture; Mortality; Complication

Introduction

The mortality rate of acute myocardial infarction in our CCUs has decreased from 12% in the early period (before the era of reperfusion therapy, 1977–1986), through 8% in the middle period (thrombolytic treatment widely adopted, 1987–1992), to 5% in the late period [PTCA (percutaneous transluminal coronary angioplasty) adopted as the main reperfusion therapy, 1993–1998]. The improved prognosis can be attributed to the progress of treatment of complications of acute myocardial infarction. Pump failure and cardiac rupture (including ventricular septal rupture) dominate approximately 70% of the causes of death in the acute period. Prognosis has been improved, but the mortality rate is still high. Therefore, CCUs are making efforts to improve treatment effectiveness.[1)]

The diagnosis and treatments against the two main causes of death will be discussed along with the major complications in the acute period

This article is a revised English version of a paper originally published in the Journal of the Japan Medical Association (Vol. 125, No. 5, 2001, pages 683–687).

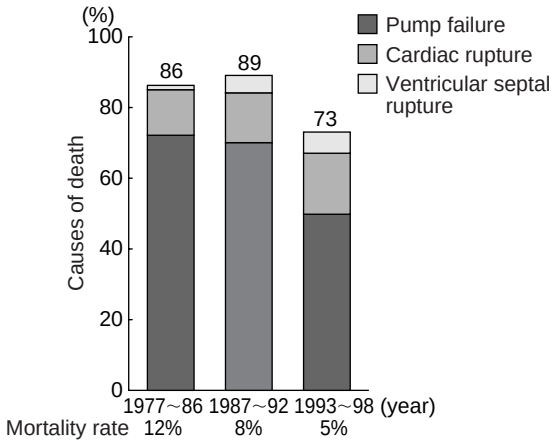


Fig. 1 Serial changes of causes of death in acute myocardial infarction (National Cardiovascular Center)

Table 1 Major Complications of Acute Myocardial Infarction

1. Pump failure (cardiogenic shock, heart failure)
2. Cardiac rupture (free wall rupture, ventricular septal rupture, papillary muscle rupture)
3. Arrhythmia
4. Post-infarction angina
5. Right ventricular infarction
6. Pericarditis
7. Left ventricular thrombus and complicated embolism

Table 2 Severity Classification of Acute Myocardial Infarction (Killip Classification)

Killip class	Mortality rate in the original article
Type I : no sign of CHF (no rales in lung)	6%
Type II : pulmonary congestion limited to basal lung segments (bi basilar rales)	17%
Type III: acute pulmonary edema (rales in more than 50% of lung)	38%
Type IV: cardiogenic shock	81%

CHF: congestive heart failure

listed in Table 1.

Evaluation of the Severity

The classic Killip classification,[2] one of the available methods for evaluating the severity of acute myocardial infarction, is still helpful for the estimation of prognosis. As shown in Table 2, the severity can be easily judged from physical findings according to the Killip classification. Killip *et al.* reported that the mortality rate increased with the rise of the type of the disease, and that mortality rate in class IV (cardiogenic shock) was as high as 81%. In our facility, the mortality rate was the same as that of Killip-class IV before the era of reperfusion therapy (Fig. 2), suggesting that the mortality rate would not improve without reperfusion even when using assisted circulation such as IABP (intra-aortic balloon pumping).

Cardiogenic Shock

1. Definitions (Table 3)

Pump failure is defined as the condition in which cardiac output is insufficient to perfuse various body organs because of acute left ventricular contractile dysfunction caused by myocardial infarction. Cardiogenic shock is defined as myocardiogenic shock, except for when it is caused by underlying diseases before the onset of infarction, mechanical complications, and arrhythmia. Shock includes not only a low arterial blood pressure, but also severe, prolonged

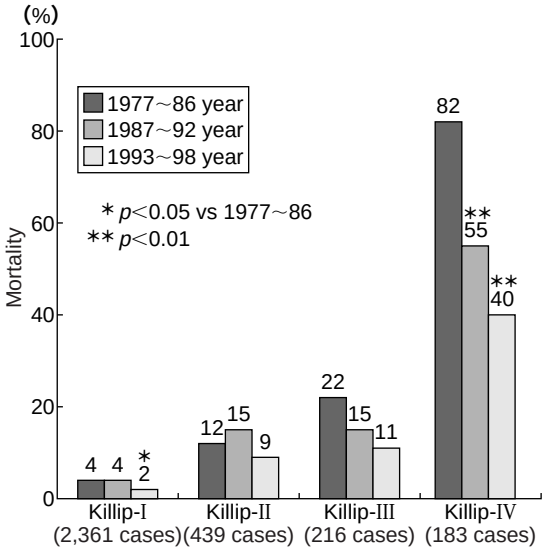


Fig. 2 Serial changes of the mortality rate of acute myocardial infarction (National Cardiovascular Center)

Table 3 Definitions of Cardiogenic Shock

1. Systolic pressure: less than 90 mmHg
2. Existence of tissue hypoperfusion
   (1) oliguria (less than 20 m*l*/h)
   (2) mental obtundation
   (3) peripheral vessel contraction (cool, clammy skin, cyanosis)

Exceptions: hypotension accompanying conditions such as chest pain, hypotension of parasympathetic nerves (bradycardia-hypotension syndrome: Bezold-Jarisch reflex), arrhythmia, drug abuse, hypovolemia (e.g. dehydration and long-term administration of diuretics).

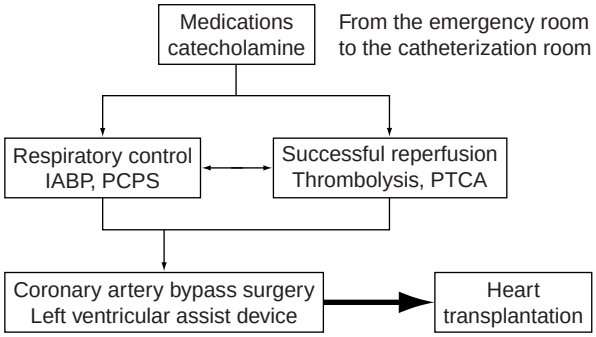


Fig. 3 Medical guidelines for cardiogenic shock in acute myocardial infarction support

IABP: intra-aortic balloon pumping, PCPS: percutaneous cardiopulmonary system, PTCA: percutaneous transluminal coronary angioplasty.

tissue hypoperfusion.[3)]

2. Treatment strategies[4)]

Because impairment of organ function caused by shock rapidly develops and becomes irreversible within a short period, the most suitable treatment should be adopted as early as possible. Prolonged tissue hypoperfusion makes prognosis worse, leading to death from multiple organ failure even if hemodynamics is improved. Immediately after admission, respiratory control should be implemented for significant hypoxemia with the administration of catecholamines. If 5–20μg/kg/min of dopamine cannot achieve pressor effects, 5–20μg/kg/min of dobutamine (DOB), or 0.05–0.2μg/kg/min of noradrenaline (NAd) should be administered.

At the same time, the femoral artery and vein should be secured with a 5 Fr sheath to enable use of assisted device at any time. Puncturing is often difficult if the femoral artery is not palpable. In principle, the internal jugular or subclavian vein should not be punctured in case of shock. The reason is that there are cases in which even one or two mispunctures can lead to fatal bleeding because of thrombolytic therapy or heparinization. If systolic pressure does not rise to more than 80 mmHg within 15 minutes, assisted device should be implemented.

Treatment requiring a combination of reperfusion therapy and maintenance of peripheral circulation is continued while in transit from the emergency room (or CCU) to the catheterization room. The reperfusion method of choice is PTCA. Prolonged shock with unavailability of a catheterization room should be treated with intravenous thrombolysis.

3. Assisted devices

(1) **Intra-aortic balloon pumping (IABP)**: The results of IABP treatment without reperfusion therapy for cardiogenic shock in acute

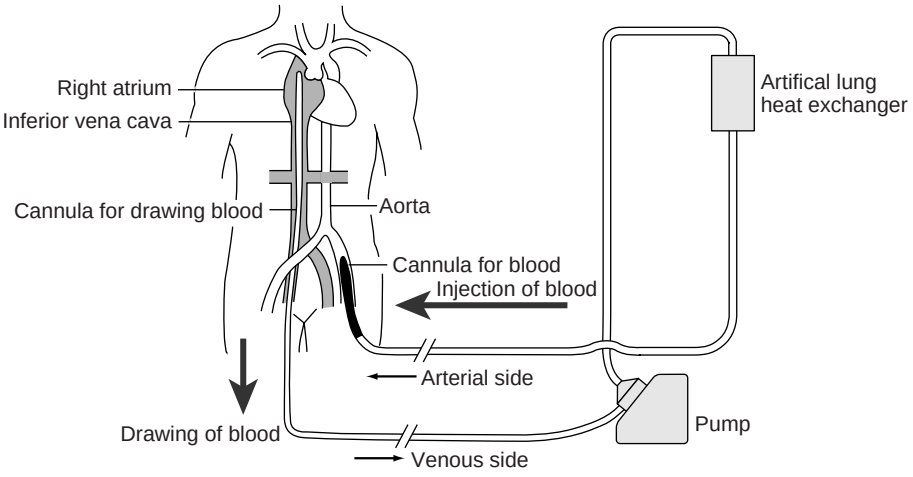


Fig. 4 Percutaneous artificial cardiopulmonary system (PCPS)
In case of a shock, 5 Fr sheath is inserted into femoral artery and vein to prepare for the initiation of PCPS. Priming (circuit filling) is completed within 5 minutes. Routine training is required.

myocardial infarction have not been encouraging. However, IABP is still an indispensable assisted device method when combined with reperfusion therapy. If systolic pressure is less than 80 mmHg, and cardiac index is less than 2.2 l/min/m^2 even with catecholamines, IABP should be used. IABP serves as a pressure-support device, supporting only 15% of cardiac output. Therefore, if cardiac output by own beat cannot be expected, the following PCPS should be used.

(2) **Percutaneous cardiopulmonary support system (PCPS)**: PCPS is a method in which an artificial cardiopulmonary device enabling assisted circulation can be made available by inserting a cannula percutaneously. Perfusion is maintained by delivering oxygen to venous blood derived from right atrium by means of an artificial lung, and by delivering the blood retrogradually into the femoral artery (Fig. 4). It is possible to deliver blood at 2–4 l/min. If systolic pressure is less than 50 mmHg, or repeated ventricular fibrillation or tachycardia requiring cardioversion is observed, PCPS should be used, rather than IABP. To support coronary perfusion, it should be combined with IABP.

Because PCPS should be implemented quickly, our CCU is always equipped with PCPS with a circuit organized in sanitary conditions. In order to enable a few night staff members to deal with it, every nurse has routine training to complete circuit filling within 5 minutes as a part of lessons on cardio-pulmonary resuscitation.

If these types of assisted circulation and reperfusion are insufficient, the use of a left ventricular assist device to take care of part of the cardiac pumping function should be considered. Because reduced cardiac function will be prolonged even after successful reperfusion, assisted circulation should be continued. Intensive care is required to maintain assisted circulation for a long period, and to prevent complications such as infection, bleeding, and lower limb ischemia.

4. Efficacy of treatments for Cardiogenic shock

In cardiogenic shock, tissue hypoperfusion and acute myocardial infarction should be treated at the same time. Failing in either treatment would be lethal. Reperfusion of occluded coronary artery is essential to improve prognosis. Moreover, it is important to achieve reperfusion within a short period from the development of shock. If reperfusion cannot be achieved, the mortality rate is as high as 80% even with

assisted device (Fig. 2). If a major vessel causing occlusion is reperfused irrespective of the type of reperfusion therapy, the in-hospital mortality rate is less than 40%, suggesting the importance of successful reperfusion.

A guideline of the ACC/AHA (American College of Cardiology/American Heart Association) strongly recommends the use of PTCA.[5] If PTCA is not available, or if it takes over 30 minutes to start it, intravenous infusion of tissue plasminogen activator (t-PA) should be performed. However, because the mortality rate of cardiogenic shock is still high, new therapies such as myocardial protection methods should be reviewed in addition to reperfusion therapy.

Cardiac Rupture

Cardiac rupture occurs through an area of transmural neurosis and expansion in the acute phase of myocardial infarction. It is classified as left ventricular free wall rupture, ventricular septal perforation or papillary muscle rupture, depending on the site of the lesions. The incidence of rupture shows two peaks: within 24 hours after the onset of infarction, and one week later. The mortality rate of free wall rupture is high. It is one of the concerns for CCUs in parallel with death from pump failure. The frequency is low, but it does have a noticeable incidence. The frequency of the oozing type has been increasing compared with the sudden rupture type, which is lethal and requires preventive measures.

1. Free wall rupture

In cases of successful reperfusion, the second peak of cardiac rupture is reported to decrease, while the possibility of increased cardiac rupture caused by thrombolytic therapy is pointed out. Therefore, for patients over the age of 70 complicated with hypertension, PTCA is often the reperfusion method used.

Attention should be paid to suppress systolic pressure under 120 mmHg in the acute phase of myocardial infarction, and under 20 mmHg increase in the rehabilitation. Because patients showing significant retention of pericardial effusion in echocardiogram over time and patients with rapidly thinning of the infarction wall are highly susceptible to cardiac rupture, they are carefully monitored and the rehabilitation process is delayed.

An oozing type of rupture with gradual retention of bloody pericardial effusion leading to cardiac tamponade can be diagnosed by echocardiography before the patient goes into shock. Cardiac tamponade can be treated by performing a surgical repair after drainage of pericardial cavity. A sudden rupture, which immediately leads to electro-mechanical dissociation, is lethal. It is treated by PCPS immediately after the rupture to secure general circulation before stepping up, but the prognosis for sudden rupture is unfavorable.

2. Ventricular septal perforation

Like free wall rupture, the peak incidence of septal rupture appears to be within a week after infarction. When a new, harsh, loud holosystolic murmur is heard between the third and the fourth intercostal of the left parasternum, ventricular septal perforation is strongly suspected. It can be diagnosed by confirming the existence of a left-to-right interventricular shunt using two-dimensional echocardiography, and by confirming a significant increase in oxygen saturation from the right atrium to pulmonary artery. The frequency of ventricular septal perforation in our facility is approximately 1% of all myocardial infarction. Out of 33 patients, 18 underwent an operation, and 12 of them survived and were discharged from the hospital. Only 2 out of 15 patients who did not undergo surgery survived and were discharged from the hospital. Therefore, the operation should be performed whenever possible. Especially for shock, early surgical intervention is essential.

3. Papillary muscle rupture

Severe mitral regurgitation occurs after acute myocardial infarction in papillary muscle rup-

ture, rapidly progressing to shock from left-sided heart failure. As cardiac murmur associated with mitral regurgitation is brief or even completely absent in patients with reduced cardiac function, echocardiography is an effective diagnostic tool. Because significant mitral regurgitation is an indication to perform early surgical correction, valve replacement or repair should be performed.

Conclusion

The prognosis for acute myocardial infarction after admission has improved for the past 20 years because of the progress in treatments such as reperfusion therapy. However, as mentioned in the present paper, the mortality rate of cardiogenic shock and cardiac rupture is still high, and further efforts should be made to improve treatment effectiveness. The mortality rate before admission is higher, and 30–50% is estimated to die outside the hospital. Establishment of a cardiovascular critical care system is urgently required to reduce the general mortality of acute myocardial infarction.

REFERENCE

1) Nonogi, H.: Therapeutic strategies to improve long-term prognosis in acute myocardial infarction. *J Jpn Soc Intensive Care Med* 1999; 6: 189–195.
2) Killip, T. and Kimball, J.T.: Treatment of myocardial infarction in a coronary care unit. A two year experience with 250 patients. *Am J Cardiol* 1967; 20: 457–464.
3) Nonogi, H.: Definition and diagnostic standard of cardiogenic shock. *ICU and CCU* 2000; 24: 211–221. (in Japanese)
4) Residents of National Cardiovascular Disease Center Eds: *CCU Manual*. Chugai Igakusya, 2000. (in Japanese)
5) Ryan, T.J., Antman, E.M., Brooks, N.H., *et al.*: ACC/AHA guidelines for managements of patients with acute myocardial infarction: Executive summary and recommendations: A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee on Management of Acute Myocardial Infarction). *Circulation* 1999; 100: 1016–1030.

Acute Coronary Syndromes

JMAJ 45(4): 155–160, 2002

Hirofumi YASUE

Director, Kumamoto Aging Research Institute

Abstract: Recently, unstable angina, acute myocardial infarction, and sudden cardiac death have often been put together under the name "acute coronary syndromes", because almost all of these conditions have been shown to be caused by thrombotic occlusion of a coronary artery following atherosclerotic plaque disruption. Acute coronary syndromes occur more frequently in the coronary arteries with no significant organic stenosis than in those with a high degree of stenosis. A plaque prone to disruption has a thin fibrous cap, a large lipid core, and increased infiltration of macrophages and T lymphocytes. The elimination or control of risk factors for atherosclerosis such as dyslipidemia, hypertension, smoking, diabetes mellitus, obesity, and lack of exercise is essential for the prevention of acute coronary syndromes.

Key words: Acute myocardial infarction; Atherosclerotic plaque; Coronary spasm; Coronary thrombosis; Unstable angina

Introduction

Ischemic heart diseases, including angina pectoris and myocardial infarction, are the leading cause of death in Europe and America. They have also been increasing in Japan and are currently the second highest cause of death in this country as the result of the westernization of Japanese dietary habits, the increased use of automobiles, obesity, lack of exercise, and increased stress induced by our complex society.

Angina pectoris develops by transient ischemia of myocardium, while myocardial infarction is the necrosis of myocardium caused by prolonged ischemia. It has therefore been considered that a precise line should be drawn between the two diseases. Angina pectoris is divided into stable (organic) and unstable angina. The former is stable because advanced organic stenosis is extensively distributed in the coronary artery, but develops only when effort increases oxygen demand. The latter develops even at rest and is characterized by the increased severity and duration of the attack and reduced response to nitroglycerin. The latter has been considered to be at high risk of acute myocardial infarction or sudden death.

Recent studies have revealed that unstable angina, acute myocardial infarction, or ischemic cardiac sudden death develop mostly as a result of plaque disruption in the coronary artery followed by thrombotic formation, thereby com-

This article is a revised English version of a paper originally published in the Journal of the Japan Medical Association (Vol. 125, No. 5, 2001, pages 703–707).

pletely or incompletely occluding the coronary lumen. Based on a similar onset mechanism, unstable angina, acute myocardial infarction, and ischemic cardiac sudden death have come to be referred to collectively as acute coronary syndromes.[1–3] This concept was generated based on rapid advances in clinical medicine, pathology, and molecular biology. At the same time, these advances force us to make a paradigm shift in the existing way of thinking about these ischemic heart diseases and the nature of the corrective actions to be instituted.

Clinical Advances

The angina syndrome proposed by Heberden includes various diseases. James Herrick (1912) considered acute myocardial infarction to be an independent disease and inferred that it might result from coronary occlusion by thrombi. Since then, coronary thrombosis has been considered an important potential cause of myocardial infarction. In the 1970's, however, there were investigators, and pathologists in particular, who believed that coronary thrombosis was not a cause of myocardial infarction. The almost simultaneous introduction of coronary angiography during the early stages of acute coronary infarction in major medical institutions throughout the world in the 1980s has allowed clinicians to identify the responsible artery.

The experience of the authors shows that the artery responsible for myocardial infarction was spontaneously recanalized in the early stages of the disease in 18% of the cases examined, and that it was recanalized by the intracoronary injection of nitroglycerin in 16%, and by a thrombolytic agent (urokinase) in 46%.[1] These results indicate that most acute myocardial infarction develop as a result of occlusion by coronary thrombosis, and that coronary spasm also causes myocardial infarction directly. The thrombotic occlusion rate of the coronary artery is higher in the earlier stages of the disease, and the spontaneous re-canalization rate increases over time.

It has been considered that coronary atherosclerosis develops at an early age and progresses slowly over several decades to cause the stenosis of the coronary lumen, and that advanced stenosis is prone to causing myocardial infarction. However, coronary angiograms conducted prior to the attack of myocardial infarction revealed that few cases had significant organic stenoses in the responsible coronary artery. Rather, myocardial infarction frequently occurs in the coronary lesions with no significant stenosis.[1,4] A working group of the Ministry of Health and Welfare reported that the coronary artery responsible for myocardial infarction had no significant stenosis before the onset of the disease in 86% of the patients examined. Improved intravascular echography has disclosed that most coronary arteries that appear normal on angiograms have been affected by atherosclerosis. It has also been shown that plaque progress eccentrically toward the adventitia and do not cause the stenosis of the lumen in the early stages of the disease. This has been confirmed by autopsy and is known as compensatory growth.

Recent studies have indicated that reducing plasma cholesterol with hydroxymethyl glutaryl CoA (HMG-CoA) reductase inhibitors markedly lowers the incidence of cardiovascular accidents, such as cardiac death and acute myocardial infarction, without producing significant changes in stenotic lesions on coronary angiograms. This suggests that the quality of plaque may be more closely involved in the pathogenesis of myocardial infarction than the degree of coronary stenosis.[1–3]

Recent advances in coronary endoscopy and intravascular echography have revealed that coronary thrombi or plaque disruption frequently appear also in unstable angina.[3–5]

Plaque Prone to Disruption

Advanced pathological techniques have revealed that the coronary lumen was occluded or narrowed by thrombi in most autopsied cases

with acute coronary syndrome, and that plaque had been disrupted with fissures in approximately two-thirds of such cases, and had been disrupted with erosion in the remaining third.[4,6] The disrupted plaque showed inflammation with the infiltration of macrophages and T lymphocytes.

Plaque that is prone to disruption is characterized by (1) large lipid nuclei generated by fused lipids, such as cholesterol, accumulated outside the cells in plaque, (2) thin fibrous cap that separates lipid nuclei and vascular lumen, (3) increased infiltration of macrophages and T lymphocytes, and (4) a decreased number of smooth muscle.[3,4,6] The plaque is prone to undergo mechanical stress and disrupt at the border between plaque and normal tissue, known as the shoulder, where a particularly large infiltration of macrophages occurs. The mechanical stress becomes stronger as the diameter of the lumen increases.

Since macrophages produce interstitial metalloprotease that decomposes interstitial collagen and elastin, which are constituents of fibrous caps, they make the caps thin and prone to breaking. Similarly, T lymphocytes secrete interferon-γ to inhibit the production of collagen from smooth muscle cells, thereby making the fibrous caps even more prone to breakage.[3] Furthermore, the tissue factor, which triggers blood coagulation, is expressed in macrophages and lipid nuclei. Therefore, once plaque is disrupted to expose the tissue factor to blood, it activates blood coagulation cascades, which produces fibrin and thrombotic formation.[7]

Factors Precipitating Acute Coronary Syndromes

(1) **Plaque disruption**

It has been shown that plaque disruption followed by thrombotic formation is the origin of acute coronary syndromes. ST-elevated myocardial infarction develops when thrombi completely occlude the coronary lumen. When the occlusion is incomplete, non-ST-elevated myocardial infarction or unstable angina develops.

(2) **Coronary spasm**

Various factors other than plaque condition may induce acute coronary syndromes. The onset of acute coronary syndromes tends to develop in the early morning. This is related to the circadian variation of blood coagulation and fibrinolysis systems and blood platelet aggregation. Blood is prone to coagulate, fibrinolytic activity is reduced, and platelet aggregation is accelerated in the early morning. Coronary spasm tends to develop at night and in the early morning. When it develops, it increases the tissue factor and fibrinopeptide in blood and reduces the fibrinolytic activity, thereby making it easier for thrombi to develop and stimulating platelet aggregation. It is therefore considered that coronary spasm triggers acute coronary syndromes through thrombotic formation. Moreover, coronary spasm itself causes unstable angina and acute myocardial infarction.[1,8]

(3) **Stress**

Stress triggers acute coronary syndromes by increasing blood pressure to increase the mechanical stress on plaque, by accelerating blood coagulation and platelet aggregation, and by causing coronary spasm. It is well known that the incidence of acute myocardial infarction increased in Israel after the Gulf War and in Hanshin after the Great Hanshin Earthquake.

Pathogenesis and Treatments of Acute Coronary Syndromes

1. Pathogenesis of acute coronary syndromes

Figure 1 summarizes the pathogenesis of acute coronary syndromes.[1] Thrombi are formed after plaque disruption or coronary spasm. Acute coronary syndromes develops when the thrombi become sufficiently large to occlude the coronary artery. In some cases, coronary spasm may induce plaque disruption or directly cause coronary occlusion. It is also

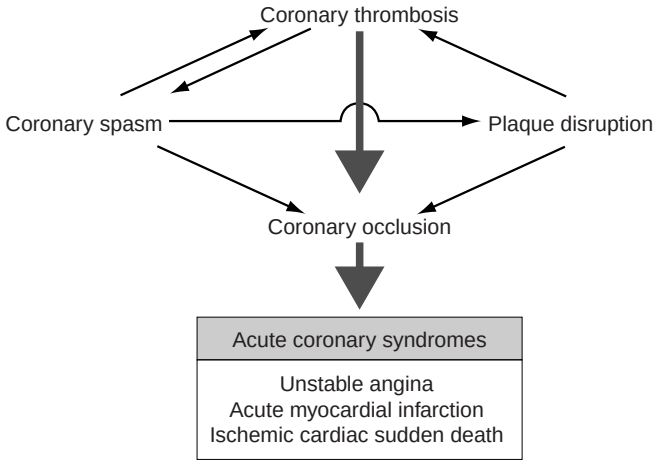


Fig. 1 Pathogenesis of acute coronary syndromes
Acute coronary syndromes (unstable angina, acute myocardial infarction, and ischemic cardiac sudden death) mostly result from coronary occlusion by thrombi. However, in some cases they may develop due to coronary spasm or mechanical occlusion by plaque disruption (quoted from Reference 1)

possible that a small artery running through the plaque is ruptured to cause a hemorrhage, which suddenly increases the size of the plaque to mechanically occlude the coronary lumen. It is also known that thrombi cause coronary spasm by serotonin or thromboxane A_2 secreted from blood platelets.

2. Treatment of acute coronary syndromes

Since the pathogenesis of acute coronary syndromes is now well understood, it has become possible to apply appropriate treatment for the syndromes. That is, acute coronary syndromes should be treated by combining the treatments for coronary thrombosis, spasm, and plaque disruption. Among such treatments, the treatment for coronary thrombosis is most important.

(1) Treatment for coronary thrombosis

Anti-platelet drugs, such as aspirin and ticlopidine, and anti-coagulants, such as heparin, are now most frequently used to treat coronary thrombosis. The effect of aspirin is relatively weak and inhibits only one platelet coagulation pathway by thromboxane A_2. Ticlopidine inhibits the pathway through ADP (adenosine 5′-diphosphate), but may have adverse effects.

The GPIIb/IIIa (platelet glycoprotein IIb/IIIa) receptor antagonists, which block the common final pathways of platelet aggregation, have recently attracted a great deal of attention. Its efficacy and safety have been established via the many clinical trials conducted in Europe and America.[1,9] It has been demonstrated to be particularly useful when intravenously administered in percutaneous coronary interventions, such as percutaneous transluminal coronary angioplasty (PTCA). However, the effectiveness of these anti-clotting agents when orally administered over long periods have yet to be demonstrated. Its efficacy for acute coronary syndromes by an intravenous route also remains controversial when used without PCI.

Heparin is effective only when it combines with antithrombin III, and is not effective for thrombin combining with fibrin. Heparin is inactivated by platelet factor 4. Therefore, hirudine and hirulog, which acts directly on thrombin, and low-molecule heparin with more stable activity have been studied in clinical settings. Clinical studies on activated protein C, which inhibits thrombotic formation, and the

tissue factor pathway inhibitor (TFPI), which inhibits the tissue factor itself, are also under going trials.

It has been established that thrombolytic therapy using tissue plasminogen activator (t-PA) or urokinase is effective for transmural myocardial infarction with elevated ST on ECG. PTCA or stent insertion without thrombolytic therapy is also performed for quick re-perfusion. However, it should be noted that thrombolytic therapy is ineffective for, or rather aggravates unstable angina.[1,9)]

(2) **Treatment for coronary spasm**

Nitrates, calcium antagonists, and nicorandil are effective for coronary spasm.[1)] Most cases with unstable angina can be successfully controlled by these medications. However, some cases require percutaneous coronary intervention or coronary bypass. In such cases, PTCA itself can cause plaque disruption, thereby worsening acute coronary syndromes. Therefore, plaque in unstable angina that is prone to thrombi formation, should be stabilized by medical therapy as far as possible before PTCA. The recent introduction of stent insertion techniques has contributed to the prevention of acute coronary occlusion due to PTCA in a considerable number of cases.

3. Prevention of acute coronary syndromes

Although various treatments for acute coronary syndromes have been developed as described above, it is still often difficult to treat these syndromes once they develop. Therefore, preventing the syndromes is quite important. It is necessary to suppress atherosclerosis in order to prevent acute coronary syndromes because atherosclerosis is the base of the syndromes. It is also important to eliminate or control risk factors, such as hypertension, smoking, diabetes mellitus, hyperlipemia, obesity, and lack of exercise.[10)] The importance of eliminating or controlling such factors was fully established by several multi-center prospective randomized studies which demonstrated that correcting hyperlipemia with HMG-CoA reductase inhibitors markedly reduced cardiovascular events, such as acute myocardial infarction and cardiac death.

Moreover, recent studies have shown that the following therapies are effective for preventing acute myocardial infarction and sudden death: anti-platelet drugs, such as a small amount of aspirin, anti-coagulants, such as warfarin, angiotensin converting enzyme (ACE) inhibitors, anti-oxidants, such as vitamin E, and estrogen replacement therapy for post-menopausal women.

Conclusion

Recent studies have revealed that most cases with unstable angina, acute myocardial infarction, or ischemic cardiac sudden death result from coronary plaque disruption followed by formation of thrombi, which occlude or narrow the coronary lumen. These diseases have therefore come to be referred to collectively as acute coronary syndromes. The syndromes are characterized by its frequent onset from mildly narrowed coronary arteries and easily disrupted plaque with large lipid nuclei, thin fibrous caps, together with marked infiltration of macrophages and T lymphocytes. Coronary spasm not only triggers acute coronary syndromes, but also occludes the coronary arteries to directly cause acute coronary syndromes.

Eliminating or controlling coronary risk factors including hypertension, diabetes mellitus, smoking, hyperlipemia, and lack of exercise is crucial for preventing acute coronary syndromes. Anti-platelet drugs, such as aspirin, and anti-coagulants, such as warfarin, are also useful. Calcium antagonists are effective for coronary spasm.

REFERENCES

1) Yasue, H.: Pathogenesis and treatment of acute coronary syndromes. *Journal of Japanese Society of Internal Medicine* 1998; 87: 296–301. (in Japanese)

2) Fuster, V., Badimon, L., Badimon, J.J. *et al.*: The pathogenesis of coronary artery disease and the acute coronary syndromes. *N Engl J Med* 1992; 326: 242–250.
3) Libby, P.: Molecular basis of the acute coronary syndromes. *Circulation* 1995; 91: 2844–2850.
4) Falk, E., Shah, O.K. and Fuster, V.: Coronary plaque disruption. *Circulation* 1995; 92: 657–671.
5) Mizuno, K., Satomura, K., Miyamoto, A. *et al.*: Angioscopic evaluation of coronary artery thrombi in acute coronary syndromes. *N Engl J Med* 1992; 326: 287–291.
6) Davies, M.J.: Stability and instability: two faces of coronary atherosclerosis. *Circulation* 1996; 94: 2013–2020.
7) Kaikita, K., Ogawa, H., Yasue, H. *et al.*: Tissue factor expression on macrophages in coronary plaques in patients with unstable angina. *Arterioscler Thromb Vasc Biol* 1997; 17: 2232–2237.
8) Oshima, S., Ogawa, H., Yasue, H. *et al.*: Fibrinopeptide A is released into the coronary circulation after coronary spasm. *Circulation* 1990; 82: 2222–2225.
9) Braunwald, E., Antman, E.M., Beasley, J.W. *et al.*: ACC/AHA guidelines for the management of patients with unstable angina and non-ST segment elevation myocardial infarction. *Circulation* 2000; 102: 1193–1209.
10) AHA Medical/Scientific Statement: Guide to primary prevention of cardiovascular diseases. *Circulation* 1997; 95 : 2329.

Social Security Viewed from a Demographic Perspective: Prospects and Problems

JMAJ 45(4): 161–167, 2002

Naohiro OGAWA

Deputy Director, Population Research Institute,
Professor, College of Economics, Nihon University

Abstract: This paper discusses the impact of population aging on the social security system, with particular reference to Japan. One of the primary findings of this paper is that although coresidence has been considered for a long time Japan's latent asset in providing in-home care to the elderly, the demographic feasibility of continuing such a care-giving pattern will be increasingly difficult in the years to come, largely due to the low fertility trends persisting over the last few decades. In addition, norms of filial piety among middle-aged women have substantially weakened since the late 1980s.

Key words: Population aging; Social security system; Family organization; Value shift

Introduction

In the recent past, the birth rate in Japan has been falling substantially, with the total fertility rate for 1998 being 1.38 children per woman. Although this figure is not likely to fall below the 1.3 mark during 1999, it is considered almost certain to drop to a historic low during the year.

As the fertility rate continues to fall, debates concerning not only the long-term shortage of labor but also the social security system are displaying a new intensity. This is particularly true of those relating to contributions to and benefits from the public pension system.

In the first half of this paper, the relationship between the aging of the Japanese population and the social security system will be examined. The second half will deal with an analysis of the problems the Japanese social security system is likely to face in the 21st century, from the viewpoint of the family.

As is well known, the Japanese social security system is wide-ranging, covering medical care, old-age pensions, and unemployment compensation programs. Among these programs, it is the public pension system that distributes income from the younger generations

This article is a revised English version of a paper originally published in the Journal of the Japan Medical Association (Vol. 124, No. 2, 2000, pages 207–212).
The paper is a transcription of a presentation given at the JMA Health Policy Symposium on Social Security held at the JMA office in Tokyo on February 5, 2000.

to the older ones to a substantial extent. Thus, when the age structure of the population shifts, this clearly affects the solvency of the pension system.

In the medical care program, income flows from the healthy to the ill. This latter group does of course contain a significant proportion of elderly people, resulting in another flow of earnings from the young to the elderly. However, some young people also suffer from health problems, so that a certain amount of the flow is diverted back to the young themselves. In this manner, the medical care program induces both inter-generational and intra-generational resource transfers.

It should be noted, however, that in the case of the public pension system, methods of financing play a part in determining whether or not changes in age structure affect public pension systems. An example of a method not having an effect in this way would be reserve financing. Some experts on the public pension system in Japan assert that in order to overcome the negative effects of the aging of society, Japan's public pension system should be converted to reserve financing. At present though, pay-as-you-go components are predominant, and when this is the case, changes in age structures have a direct impact on the public pension system.

Clearly, in a country such as Japan, with its rapidly aging population, there are major differences in the financial implications of age structure shifts between the pension and the medical care systems. It should also be borne in mind that the effect of population age structural change differs considerably, depending on the methods of financing adopted for these social security programs.

The Relationship Between Medical Costs and Population Aging

First of all, let us compare a variety of countries from around the world in terms of the percentage of the population consisting of people aged 65 and over and the percentage of GDP taken up by health-related costs. This comparison is based on OECD data for 1997.

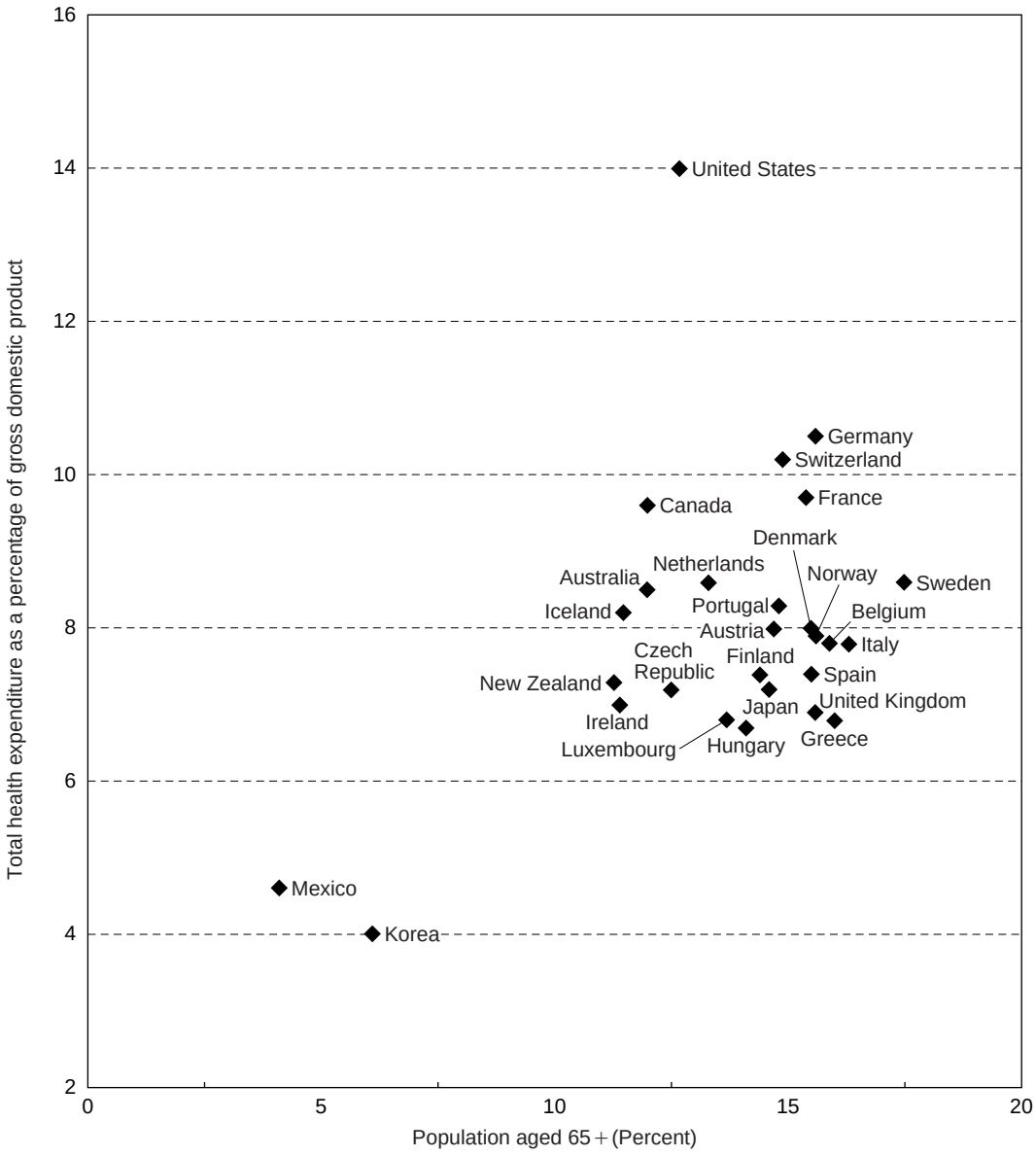
As is clearly presented in Fig. 1, there appears to be, broadly speaking, a positive correlation between these two variables. However, if we take the U.S., Mexico, and South Korea out of the analysis, we find that this correlation is not statistically significant; indeed, it is very close to zero.

Looking at the way the figures for these countries change over time, we can see that each country conforms to one of three different patterns. As shown in Fig. 2, the countries showing the first pattern include the U.S., Canada, France, Switzerland, and Greece. Here, the proportion of GDP taken up by health-related costs increases along with the increase in the proportion of the elderly in the total population.

The second pattern, as displayed in Fig. 3, represents those countries where the ratio of health-related costs to GDP shows little change over time, of which Japan is one. Finally, the third pattern corresponds to those countries where health-related costs expressed as a proportion of GDP have actually fallen over time. This third pattern is shown in Fig. 4, and Denmark, Ireland, and Sweden are some of the countries which fall into this category.

Based on the cross-sectional and time-series data presented so far, it is clear that the conclusion commonly arrived at with regard to aging, i.e. that the arrival of an aging society will be accompanied by an increase in health-related costs, is not necessarily valid. The reason for this result lies in a number of factors affecting the two variables in question. These include economic growth performance, political stability, and the tax system. Moreover, there is another important factor to be noted: the significant differences in family structures observed in the countries sampled in the present study.

Take, for example, the second pattern, which shows little change over time, and to which Japan belongs. It should be clear that in spite of this consistency over time, the proportion of Japan's population consisting of elderly people



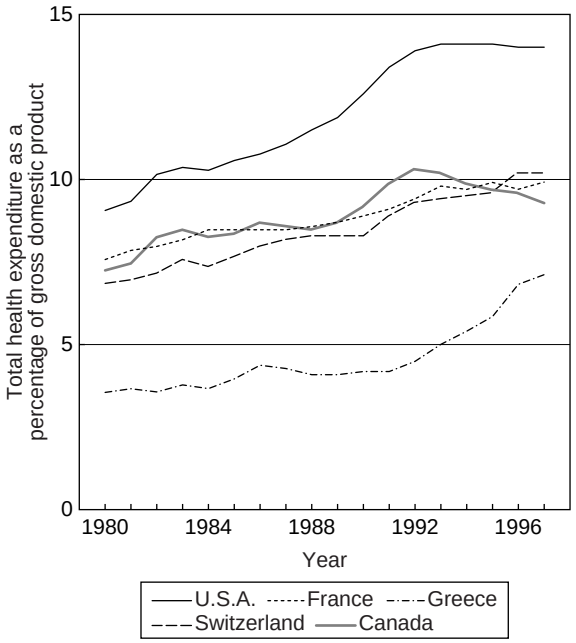
Source: OECD Health Data 99, OECD, 2000.

Fig. 1 Relationship between population aged 65 and over and total health expenditure

grew considerably over the time period under review. The fact that relative health-related spending remained virtually unchanged over time may be intimately linked with the advancement of the Japanese-style welfare system introduced in the 1970s by the Ohira administration. This point will be further discussed in the next section.

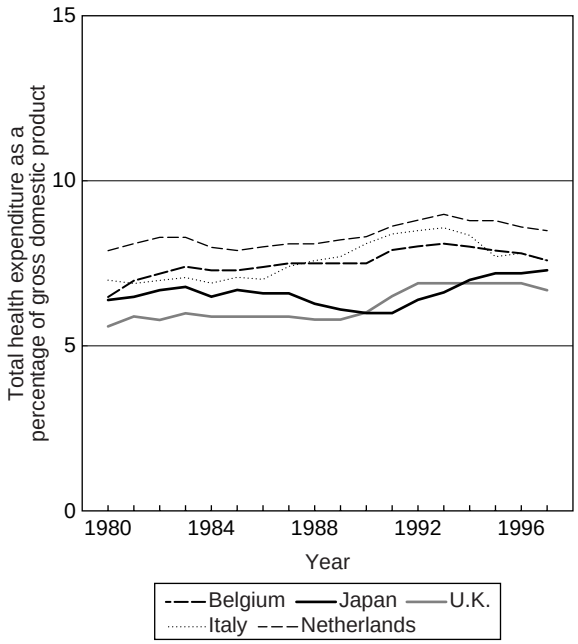
Limits to the Japanese-Style Welfare Society

Figure 5 shows the changes in Japan's total fertility rate since World War II. Inspecting this graph reveals that the years 1947–1949 constituted a so-called 'baby boom,' with an average of 2.7 million births a year over that three-year



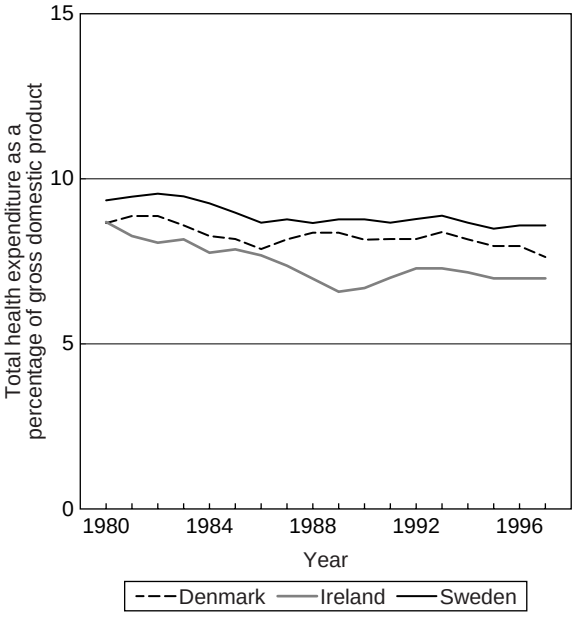
Source: OECD Health Data 99, OECD, 2000.

Fig. 2 Countries in which total health expenditure as a percentage of GDP is increasing



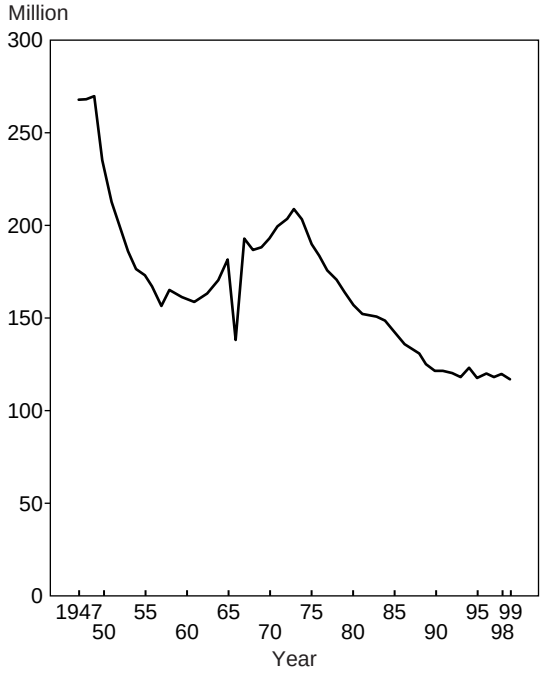
Source: OECD Health Data 99, OECD, 2000.

Fig. 3 Countries in which total health expenditure as a percentage of GDP is constant



Source: OECD Health Data 99, OECD, 2000.

Fig. 4 Countries in which total health expenditure as a percentage of GDP is decreasing



Source: Vital Statistics, various years.

Fig. 5 Trend in number of births in Japan

period. Over the next several years, however, the fertility rate nearly halved, with the annual number of births falling to 1.5 million in 1957.

This was the first occurrence of such a phenomenon in the history of mankind, and was largely responsible for inducing the aging of the Japanese population. Putting it differently, we may say that in that unprecedented 10-year period when the total fertility rate nearly halved (1947–1957), Japan moved onto a course leading to another historical first — the arrival of the first super-aged society, in the 21st century.

The 1978 Health and Welfare White Paper says that 'coresidence is Japan's latent asset.' This suggests that Japan's coresidence should somehow allow her to overcome various problems arising from population aging. Will this observation turn out to be valid, however, as family structure undergoes a rapid transformation?

According to survey data gathered over a period of half a century by the Population Problems Research Council of Mainichi Newspapers, the probability of adult children coresiding with parents at the time they get married has been decreasing. It is of interest to note that this trend goes hand in hand with the decrease in the proportion of arranged marriages; one could say that changes in attitudes towards marriage and family organization have been developing along similar paths. Particularly notable is the way in which, as those coresiding with the husband's parents at the time of marriage have been becoming less common, those coresiding with the wife's parents at this time have actually been becoming slightly more so (figure not shown). It is quite conceivable that, within several years, those elderly coresiding with a married daughter will become more numerous than those living with a married son. This must be considered one of the most important changes with which Japanese society is faced.

Next, let us turn our attention to care potential as viewed from a demographic perspective. Taking the population aged 65–84 as the denominator and the female population aged 40–59 as the numerator, the demographic feasibility of the elderly being cared for by the female population they had given birth to can be examined. It should be mentioned here that these computed values are quoted not with the conviction that women should bear all the responsibility for taking care of the elderly, but due to the fact that approximately 90% of all in-home care for old persons is carried out by middle-aged women. These values have been computed for a total of approximately 3,400 administration units (cities, towns, and villages) throughout Japan since 1955.

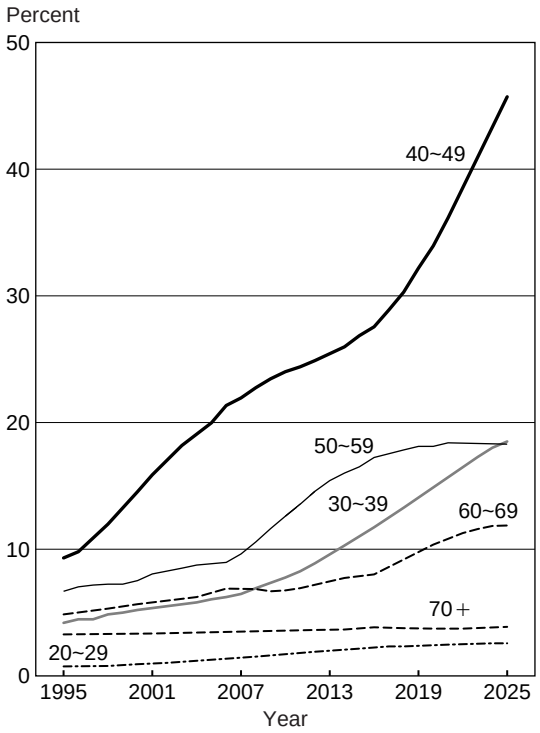
The computed results (relevant graphs omitted) clearly show that the care potential of middle-aged women fell between 1955 and 1975 and again between 1975 and 1995. Indeed, in 1995, administrative areas in which the computed values were less than 0.5 increased significantly.

Furthermore, the projected results for 2010 suggest that the potential for caregiving on the part of middle-aged women will decrease yet further, and those areas where the computed values are 0.25 or less will increase dramatically. In addition, the majority of the approximately 3,400 areas are projected to have computed values below 0.25 in 2025.

As the numbers used for this calculation refer to people already born, it can safely be said that these projected values are likely to be highly realistic. They therefore pose the question of just how practical the long-term care insurance system will be, and make absolutely clear how important it is to ensure that this problem is fully discussed at a range of political levels.

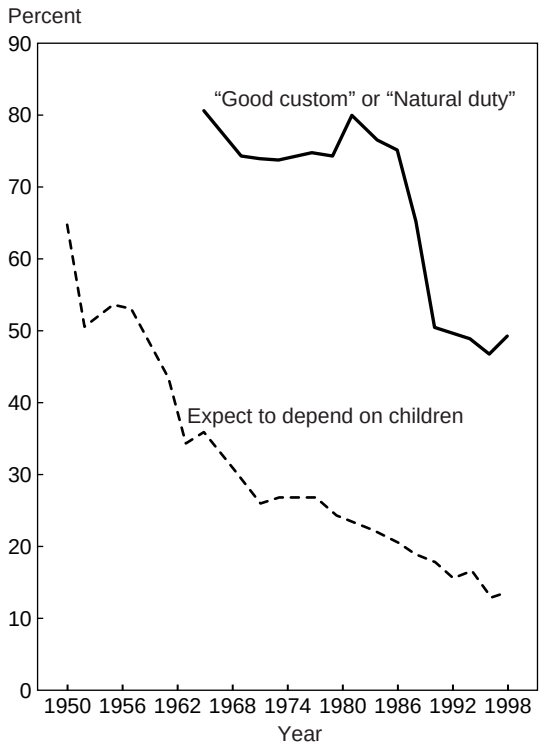
There is another key point to be dealt with here. The United Nations' 1998 population projections suggest that the computed value for Japan as a whole will become lower than anywhere else in the world during the period from 2006 to 2018. This projected result can also be considered highly accurate for the reasons outlined in the paragraph above.

Figure 6 shows the calculations of the burden due to fall on full-time housewives looking after



Source: Calculated by the author using the NUPRI long-term macroeconomic-demographic-social security model.

Fig. 6 Projected ratio of the elderly population who suffer from senile dementia or are bedridden to non-working women at various ages: Japan, 1995–2025



Source: Calculated from various rounds of the National Survey on Family Planning.

Fig. 7 Trends in norms and expectations regarding care for the elderly: Japan, 1950–1998

elderly persons who are bedridden or suffering from senile dementia. It can be seen by inspecting the graphical presentation that the burden to be placed on those women in their 40s will rise quickly. At present, one out of every seven or eight full-time housewives in their 40s takes care of a bedridden or senile elderly person. In 2025, however, nearly 50% of this group are projected to be in such a position. Needless to say, these projected results suggest an extremely gloomy situation.

The burden will increase even more when the baby boom generation shift from being the care providers to the care recipients. In other words, the current stage in the lifecycle of the baby boom generation exerts a considerable effect on the care needs of the country as a whole.

A point that needs to be mentioned here is that those women who will be in their 40s in 2025 consist of girls currently attending elementary school and junior high school. Whether or not these girls will have the same values when they grow up as we do now remains to be seen. Therefore, changes in values are as crucial as population changes when considering the various problems related to caregiving in the 21st century.

To shed some more light on this issue, let us examine data collected from various rounds of the National Survey on Family Planning conducted by the Population Problems Research Council of Mainichi Newspapers. In each round of the survey, the question 'How would you feel about looking after your elderly parents?' was asked to married women under 50. As seen in Fig. 7, from 1963–1986, 80% of Japanese women affirmed the practice, answering that taking care of elderly parents was either 'a good custom' or 'a natural duty.' However, from 1988 onwards, the corresponding figure has been

rapidly falling.

It is conceivable that the reason for this sudden fall is the emphasis the government has placed on the creation of a new care system since the mid-1980s, in which in-home care plays a central role. Up until that point, the government had assumed the bulk of the responsibility for looking after the elderly. Presumably, most of the married women asked thought that this would continue into the future, and it would be sufficient for the family to provide support for these efforts. However, with the release of the White Paper on Health and Welfare in 1986, the government made clear that it should not be relied upon to pay for nursing and other care, and the White Paper published the following year stressed that the government would not be able to meet manpower requirements for providing care to the elderly either.

It seems fair to say that women were put in a position where they were forced to change their opinion of the merits of taking care of elderly parents. In short, shifts in the concepts underlying the social security system were responsible for corresponding shifts in Japanese women's attitudes relating to family nursing.

There is one more point made by Fig. 7 worth remarking upon. In the various rounds of the National Survey on Family Planning, the following question was included: 'Would you expect your children to look after you in your old age?' The proportion of married women who answered that they would expect their children to provide care in old age had been in long-term decline ever since Japan had started to expand economically. In addition, in the early 1960s, the proportion fell dramatically, due to the implementation of universal pension and medical care systems in 1961. It is well-known that old age security can play a large part in a married couple's decision to have children. When the new social security system was implemented, the motivation for having children was sharply reduced.

These time-series changes demonstrate how changes in the social security system affected both fertility behavior and the criteria regarding how families look after their elderly members. It is clear that if our social security system is not reorganized effectively in the 21st century, attitudes to family and in-home care will be bent further still, perhaps to breaking point or beyond.

REFERENCES

1) Ogawa, N. and Retherford, R.D.: Shifting costs of caring for the elderly back to families in Japan. *Population and Development Review* 1997; 23: 59–94.
2) Retherford, R.D., Ogawa, N. and Sakamoto, S.: Values and fertility change in Japan. *Dynamics of Values in Fertility Change*, Oxford University Press, Oxford, 1999; pp. 121–147.

Agenda for Japanese Social Security

JMAJ 45(4): 168–171, 2002

Yoshinori HIROI

Associate Professor, Faculty of Law and Economics, University of Chiba

Abstract: Reform of Japan's social security systems (health insurance, welfare, and pensions) has become a major issue as its population is rapidly growing older. This article examines Japanese Social Security in international perspective, and along with identifying key features of its social security system, develops two directions for reform: (1) Social security with emphasis on health care and welfare, and (2) social security based on support for individual life-cycles.

Key words: Japanese social security; International comparison; Models of social security; Health care and social security reform

Three Models of Social Security

If we examine different social security systems in countries around the world, we can find three general models, or basic patterns, as shown in Table 1.

The first model (Model A in Table 1) is known as the universalistic model, and is the typical model in Sweden, other Scandinavian countries and the United Kingdom. It is comprised of social protections based primarily on general taxes, which covers all citizens (not only employees), and is strongly grounded in the principle of equality.

The second model (Model B in Table 1) is the social insurance model, and as I will discuss later, it was the basic form of social security first introduced in Japan. The classic expression of this model can be found in Germany and France. Its features include a social insurance system, based largely around white collar and blue collar employees, and contribution-based benefits particularly in the case of pension system.

The third model (Model C in Table 1) is the market model, of which the typical expression is in the United States. Public social security is kept to a minimum, the market or private insurance is the main feature, and self-reliance, self-help, and volunteerism are expected to play a large role.

These three models are linked to three types of basic values and principles of social security. Model A places a high value on public support. The social insurance system of Model B in both Germany and France emphasizes instead solidarity and mutual assistance, thus placing emphasis on the notion of community The third model, Model C, the market model, is built on the

This article is a revised English version of a paper originally published in the Journal of the Japan Medical Association (Vol. 124, No. 2, 2000, pages 221–224).
The paper is a transcription of a presentation given at the JMA Health Policy Symposium on Social Security held at the JMA office in Tokyo on February 5, 2000.

Table 1 Three Models of Social Security

		Example
A. Universalistic model	• General tax basis • All citizens covered • Principle of equality	Scandinavian Countries, (United Kingdom)
B. Social Insurance model	• Social insurance basis • Employment-based coverage • Benefits based on income	Germany, France
C. Market model	• Private insurance basis • Minimum public provision • Self-reliance, self-help, and volunteerism	United States

• Differences in models are related to the idea of a spectrum ranging from self-reliance (Model C) to solidarity/mutual aid (Model B) to public support (Model A).

Table 2 Features of Japan's Social Security System

(1) Mixed model
- Japan developed from a social insurance model (Model B) gradually into a universalistic model (Model A)
- The different principles of both models have been mixed, and the difficulty of resolving the two sets of basic principles has grown (for example, in the public pension system)

(2) Low spending on social security
- Spending on social security as a share of GDP reached 38.5% in Sweden by 1993, 27.9% in France, 25.3% in Germany, 21.1% in the United Kingdom, and 15% in the United States, but only 11.9% in Japan (and in 1996 13.4%)
- Why does Japan spend so little on social security?
  ⟶ Reliance on "informal" social security, particularly corporate welfare based on life-long employment
- Currently, the community basis for this "informal" system (especially large corporations and the nuclear family) is falling apart quickly

principle of self-help and self responsibility.

Features of Japan's Social Security System

Based on the assumptions listed above, there are two noteworthy features in Japan's social security system (see Table 2).

The first point is that social security in Japan is a "mixed" model. As mentioned before, the early social security system in Japan was based on the German social insurance model for both health insurance and pensions, but then gradually became more like a universalistic system. For example, the public basic pension (*kiso nenkin*) system introduced in 1985, is not like the social insurance pension system of Germany or France, but more like a universalistic system. And all citizens take part in the basic pension system which provides flat-rate benefits. For health insurance, a separate old-age health scheme was introduced in 1982 which was to cover both salaried employees and self-employed alike. At earlier times, the National Health Insurance (*Kokuho*) program, which is a community-based health insurance for self-employed and farmers, was subsidized by national general taxes for 50% of its spending, thus contributing to the realization of universal coverage in 1961. All of these represent departures from the original social in surance model as seen in Germany and France.

Table 3 Future Directions in Social Security Reforms

(1) Social security with strong emphasis on health and welfare
- Public support in areas of health and welfare, which is likely to have market failure
- Restructuring and strengthening basic pension as a tax-based public pension

(2) Social security based on individual life-cycle
- Towards an individual-based society, acknowledging more fluid labor market and growing female workforce participation
- More unemployment compensation and childcare support benefits
- Clear division between tax and insurance
  - Children and elderly—mostly tax-based (strong income redistribution character)
  - Adults (active labor force)—mostly insurance based

What is important is that until recently, this mixed model has functioned rather well, but now the problems from conflicting principles have become much more serious. In other words, the current system is not based on a clear philosophy or basic set of principles.

For example, the basic pension (*kiso nenkin*) uses a mixed finance, in which one-third of the program is financed by general tax revenue, and two-thirds by pension contributions. Thus it is not clear what kind of basic character the system has. Is it the kind of system in which the young support the old, since it is close to a tax-based system, or is it more of an insurance system, in which the money contributed while young will be paid out later? Accordingly, the question of how to make the role of taxes and insurance clear will be a major issue in setting the future direction of the system.

Another feature of the Japanese social security system is that the level of spending on social security is quite low.

For example, if we compare the level of social security spending to GDP, Sweden, France, and other European countries have by far the highest level of spending. Japan is even lower than the United States. It has been said that one reason for this gap is that aging has not progressed as rapidly in Japan as in the other countries, but in 2000, Japan became the most aged country in the world surpassing Sweden. Therefore, the difference in the rate of aging is not able to explain why social security spending in Japan is so low.

So we are left with the question of why the level of social security spending in Japan is so low. I believe the answer lies in the fact that social security in Japan has long relied in large part on "informal support" provided by companies and families.

In the system of lifetime employment in Japanese corporations, not only the employees but also their families are supported through company benefits for family support and housing. As a result, Japanese social security has come to rely on corporations and families, and the level of social security spending has remained low.

But if we look at the changing social conditions in Japan, we see that the corporations and nuclear families that underpinned this system of informal support have rapidly become much weaker. That is to say, the system of lifetime employment in large corporations has ended, and large-scale layoffs have become much more common. Within families, more and more women work outside their homes and family structure is becoming a more individualized one. Therefore, it is extremely important to discuss the policy response of the social security system to the dissolution of the community in Japan.

Directions for the Future of Social Security in Japan

Based on the previous points, it is possible to

identify two possible directions for future social security reforms in Japan (see Table 3).

The first possible direction is a social security system with a strong emphasis on health and welfare, rather than pension.

In international perspective, the share of pension benefits in Japan's social security system is unusually high. From now resources should be shifted more into health care and welfare. One reason for this is that if health care and welfare are left to the private market, they do not function well as market failure is likely to occur in these areas. On the other hand, market failure is less likely to take place in the area of pension, and so the pension system could be reduced to a basic public pension which provides minimum equal support, and supplemental income-based pension might best be left to market provision.

But in this case, a stronger basic public pension system would be required, and in order to assure a basic livelihood, tax rather than insurance revenues should properly play a role.

Another direction that the social security system could take would be a system based on an individual life-cycle. As mentioned above, the labor market is becoming much more fluid, and women are working outside their homes in greater numbers than ever before. As a result, individuals are becoming the basis of society, and a social security system that takes this into account may become necessary.

Still another feature of the Japanese social security system is that there is almost no unemployment compensation. In Europe, the level of unemployment insurance is quite high, and it is possible that it will play a larger role in Japan in the future as well. The reason for this is that unemployment benefits will be more important as corporations become more flexible. And as family structures also become more flexible and society becomes more individualized, it will be necessary to improve child benefits. These benefits have been very low in Japan in comparison to other countries, and both child care and unemployment benefits may have to become much more generous than before.

Based on this discussion, while considering the principles of tax-based and insurance-based social security, the total picture of social security is likely to take the following direction.

Supporting children and the elderly will be based for the most part on taxes, since they are age groups which do not earn income, but at the same time require the most health services and other benefits. Accordingly, insurance-based system, which presupposes the balance between benefits and contributions, is unlikely to be sustainable and so the tax-based system should be adopted. On the other hand, for the people of production age, it would be most desirable to link benefits and contributions more directly so the insurance-based may be more desirable and efficient. In total, the future direction of social security should be the one based on an individual life-cycle.

Adrenal Preclinical Cushing's Syndrome

JMAJ 45(4): 172–174, 2002

Toshihiro SUDA

Professor, Third Department of Medicine, Hirosaki University School of Medicine

Key words: ACTH; Cortisol; Adrenal; Incidentaloma; Pituitary

Introduction

Cushing's syndrome results from chronic glucocorticoid excess with characteristic clinical signs and symptoms. Cushing's syndrome is divided into 2 groups, ACTH-dependent or ACTH-independent. Varieties of ACTH-dependent Cushing's syndrome are Cushing's disease (primary hypersecretion of pituitary ACTH), ectopic ACTH syndrome (inappropriate secretion of ACTH from non-pituitary tumors), and ectopic CRH syndrome (inappropriate secretion of CRH from non-hypothalamic tumors causing hypersecretion of pituitary ACTH). ACTH-independent Cushing's syndrome is caused from primary adrenocortical disorders. They are adrenocortical adenoma or carcinoma, ACTH-independent macronodular adrenocortical hyperplasia (AIMAH), and primary pigmented micronodular adrenocortical dysplasia (PPMAD).

Incidentaloma of the adrenal gland is the new endocrine epidemic as a result of a wider application of imaging techniques (CT, MRI, ultrasonography . . . etc.). About 10% of the adrenal incidentaloma secrete cortisol in at least a partially autonomous condition (abnormal cortisol response to dexamethasone suppression test.[1,2] These patients do not show specific features of Cushing's syndrome and are defined as having preclinical Cushing' syndrome. Adrenal preclinical Cushing's syndrome has the autonomic cortisol secretion that is insufficiently abnormal to cause a clinically manifested Cushing's syndrome.[3,4]

Pathophysiology

Adrenal preclinical Cushing's syndrome is mainly caused by adrenocortical adenoma, and is sometimes caused by AIMAH.[5] In these adenoma or hyperplasia cells, cortisol production by each cell seems to be very low. Therefore, an increase in cell number is necessary before excessive cortisol production occurs and causes Cushing's syndrome and inhibition of ACTH secretion. In contrast to these cells, large cortical cells in micronodules have potent cortisol production in PPMAD.

In primary aldosteronism, the aldosterone-producing adenoma often produces cortisol as well as aldosterone and shows preclinical Cushing's syndrome. In these patients, we have to be careful because these patients cause mild adrenal failure after removal of adrenal tumor.

Patients with preclinical Cushing's syndrome are frequently found in middle-aged women in Japan. Total weight of adrenal glands

This article is a revised English version of a paper originally published in the Journal of the Japan Medical Association (Vol. 125, No. 4, 2001, pages 530–531).

Table 1 Criteria for Diagnosis of Adrenal Preclinical Cushing's Syndrome

1. Presence of adrenal incidentaloma
2. Lack of specific clinical findings of Cushing's syndrome
3. Examination
(1) Normal early morning plasma cortisol levels[*1]
(2) Autonomic secretion of cortisol[*2]
(3) Inhibition of ACTH secretion[*3]
(4) Suppression of uptake on the non-tumor side in adrenocortical scintiscan
(5) Abnormal circadian rhythm
(6) Low plasma DHEA-S level[*4]
(7) Postoperative adrenal insufficiency or attached atrophic non-neoplastic part of the adrenal cortex
In the examination, if (1) and (2) are completed and (7) or at least one among (3)–(6) is positive, results of examination are considered as positive.
When 1, 2, and 3 are positive, a patient is diagnosed as preclinical Cushing's syndrome.

*1: Plasma cortisol levels should be determined at least twice. Plasma cortisol levels should be always within normal limit.
*2: Overnight 1 and 8 mg dexamethasone suppression test
Screening test (1 mg) : $>3\mu g/dl$ is positive
Diagnostic test (8 mg): $>1\mu g/dl$ is positive
*3: Basal plasma ACTH levels are <10 pg/ml
Low or no response of ACTH to CRH stimulation
*4: Age matched DHEA-S level

(adenomas) are 10–15 g.

Diagnosis

Recently, diagnostic criteria for adrenal preclinical Cushing's syndrome have been reported[6] as shown in Table 1. General obesity, hypertension, and glucose intolerance are considered as non-specific findings of Cushing's syndrome. Specific signs and symptoms of Cushing's syndrome are not found in this syndrome, such as central obesity, moon face, buffalo hump, purple striae, atrophic skin, and so on.

Early morning plasma cortisol levels are within the normal limit, while late evening levels are often elevated. This means abnormal circadian rhythm. If the late evening cortisol levels are higher than $5\mu g/dl$, preclinical Cushing's syndrome is strongly suggested. Urinary free cortisol excretion is usually between 100–150μg/day. Early morning plasma ACTH levels are often low or less than normal (less than 10 pg/ml). To confirm the inhibition of ACTH secretion, CRH test is recommended. If the peak plasma ACTH level remains less than 150% of the basal level after CRH administration, ACTH secretion is thought to be inhibited. Plasma DHEA-S levels are ACTH-dependent after puberty and such levels gradually decrease with age. So age-matched plasma DHEA-S levels should be examined and these levels are usually suppressed in these patients. In scintiscans with ^{131}I-labeled cholesterol of ACTH-inhibited patients, asymmetrical uptake indicates a functional adenoma, whereas symmetrical uptake indicates bilateral hyperplasia. These data indicate autonomous secretion of cortisol and inhibition of ACTH secretion.

Single dose (overnight) dexamethasone suppression test is useful to demonstrate autonomic secretion of cortisol. Overnight mg dexamethasone suppression test is recommended for screening for preclinical Cushing's syndrome. If the next early morning plasma cortisol level is higher than $3\mu g/dl$ after 1 mg dexamethasone administration (at 11 pm previous day), such a patient has a possibility of this syndrome. Then, the overnight 8 mg dexamethasone suppression test should be examined. If the next early morning plasma cortisol level is higher than $1\mu g/dl$ after 8 mg dexamethasone administration, the patient has a strong possibility of this syndrome.

Treatment

Surgical criteria for this syndrome are as follows;

1. Tumor size is more than 5 cm.
2. Even if the tumor size is less than 5 cm, tumor size is increasing with time.
3. Malignancy is suspected from the results of CT, MRI, etc.
4. Demonstration of autonomic secretion of

cortisol and inhibition of ACTH secretion.

5. Improvement of hypertension, general obesity or glucose intolerance is expected.

Adenomectomy or adrenalectomy is recommended when criteria are completed. When inhibition of ACTH secretion is severe (the plasma ACTH level is less than 10 pg/m*l* or no ACTH response to CRH), a surgery should be careful about adrenal failure after removal of the tumor.

REFERENCES

1) Kloos, R.T., Gross, M.D., Francis, I.R., Korobkin, M. and Shapiro, B.: Incidentally discovered adrenal masses. *Endocr Rev* 1995; 16: 460.
2) Ross, N.S.: Epidemiology of Cushing's syndrome and subclinical disease. *Endocrinol Metab Clin North Am* 1994; 3: 539.
3) Osella, G., Terzolo, M., Borretta, G. *et al.*: Endocrine evaluation of incidentally discovered adrenal masses (incidentalomas). *J Clin Endocrinol Metab* 1994; 79: 1532.
4) Reincke, M., Nieke, J., Krestin, G.P., Seager, W., Allolio, B. and Winkelmann, W.: Preclinical Cushing's syndrome in adrenal incidentalomas: Comparison with adrenal Cushing's syndrome. *J Clin Endocrinol Metab* 1992; 75: 826.
5) Suda, T.: Preclinical Cushing's syndrome and adrenocorticotropic hormone-independent bilateral adrenocortical macronodular hyperplasia. *Int Med* 1997; 36: 601.
6) Nawata, H., Demura, H., Suda, T. and Takayanagi, R.: Preclinical Cushing's syndrome. *In:* Annual report of the Ministry of Health and Welfare "Disorders of Adrenal Hormones" (Nawata, Ed.) 1996, p. 223. (in Japanese)

Characteristics of Multislice CT

JMAJ 45(4): 175–179, 2002

Kazuhiro KATADA

Professor, Department of Radiology, Fujita Health University, School of Medicine

Key words: Multislice CT; Isotropic voxel; Volume visualization; CT scanning

Introduction

The multislice CT (MSCT), or multi-detector-row CT (MDCT), is a CT system equipped with multiple rows of CT detectors to create images of multiple sections. This CT system has different characteristics from conventional CT systems, which have only one row of CT detectors. The introduction of this advanced detector system and its combination with helical scanning has markedly improved the performance of CT in terms of imaging range, time for examination, and image resolution. At the same time, the time for scanning (the time required for 1 revolution) has been shortened to 0.5 sec. and the width of the slice (tomographic plane) reduced to 0.5 mm. Thus, dramatic improvements have been made in CT-based diagnostic techniques.[1] Since its excellent clinical effects have been demonstrated, MSCT has become rapidly widespread: more than 500 systems are now in use in Japanese medical institutions. This paper outlines the basics and characteristics of MSCT.

Basics of MSCT

The most important aspect of MSCT is the detectors (multislice detectors). The multislice CT systems with 2 or 4 rows of detectors are widely used, however, those systems with 8 and 16 rows of detectors are now to be released. The most basic 4-row MSCT detectors are divided into 3 types (Fig. 1), although they are structurally divided into 2 types. One is known as the matrix type in which small detectors (cells) are arranged at equal intervals in grid formation. The other is the adaptive array type, in which detector units with increasing widths toward both ends are arranged symmetrically. Multiple slice widths can be selected with both types, by combining the number of rows of detectors used.

MSCT is also different from conventional single slice CT in terms of the image (reconstruction algorithm) calculation method it employs.[2] The helical scanning with 4-row detectors provides data which are several times as large as those of conventional single slice CT and have higher density. These data are used to calculate a high-resolution section image of the target site using a technique called Z-axis multiple-point weighed interpolation.

To obtain high image quality with multislice helical scanning, it is important to determine the distance moved by the patient table during one rotation of the scanner. A concept known as pitch (helical pitch) is usually used as an index of the distance of table movement. The

This article is a revised English version of a paper originally published in the Journal of the Japan Medical Association (Vol. 125, No. 11, 2001, pages 1772–1775).

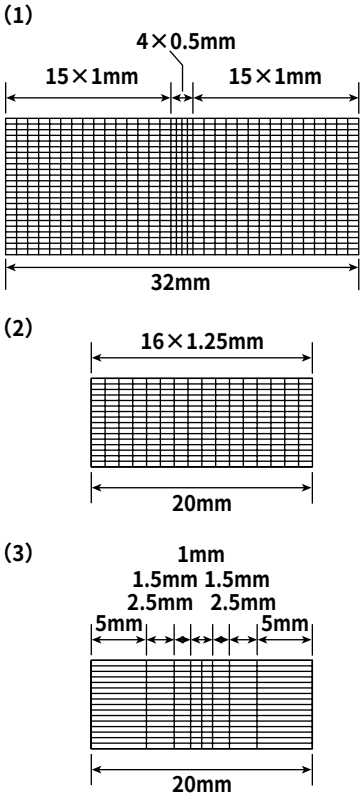


Fig. 1 Multislice CT detectors
Matrix type (1, 2) and adaptive array type (3)

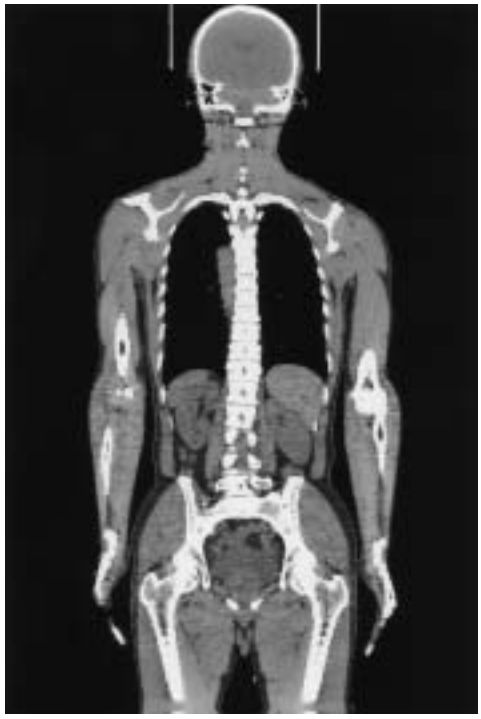


Fig. 2 Wide-range imaging (of a normal volunteer)
The range from the head to thighs is covered with one scanning.

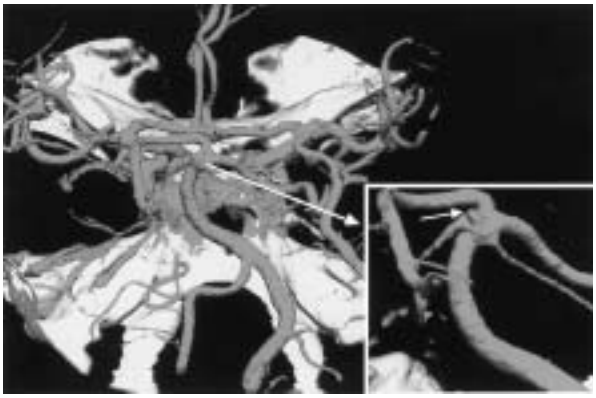


Fig. 3 Example of high quality three-dimensional images
Three-dimensional image of the circle of Willis with an intravenous injection of contrast medium (volume rendering technique). A cerebral aneurysm with a diameter of ≤1 mm (arrow) can be clearly identified at the origin of the superior cerebellar artery.

helical pitch is determined by dividing the distance of the table movement per rotation of the X-ray tube by the detector width equivalent to 1 slice. In conventional helical scanning, the table moves for a distance equal to the slice width during 1 rotation of the X-ray tube (that is, pitch 1). In contrast, the pitch can be adjusted up to 6 in MSCT: the table can be moved by a half channel per rotation (pitch 3.5 or 4.5) or by 1 channel per rotation (pitch 3). The pitch is closely correlated with image quality and exposure dose. In general, image quality is improved and exposure dose is increased as the pitch is reduced, while image quality is worsened and the exposure dose is reduced as the pitch is increased.[3)]

Characteristics of MSCT

The defining characteristic of MSCT is the dramatic increase in the imaging range per rotation due to the combination of multiple rows of detectors with helical scanning. This allows clinical technicians to obtain an image for a range

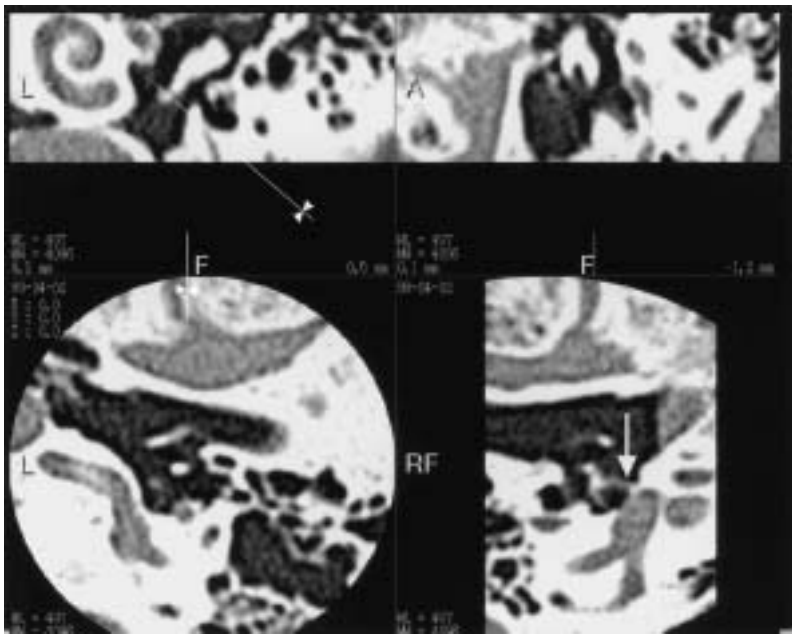


Fig. 4 Visualization of auditory ossicles with a 0.5 mm slice
The microstructure of the middle ear including stapes (arrow) can be clearly visualized.

exceeding 1 meter during single breath holding (Fig. 2). At the same time, the scanning time of MSCT can be reduced by up to one-tenth that of single slice CT when an image with the same scanning range is required.

Another characteristic of MSCT is its excellent Z-axis resolution. Single slice CT covers only a narrow range when helical scanning is performed with a thin slice (for example, a 1-mm slice). In contrast, MSCT can fully cover the whole target organ even with a thin slice because it has a wider scanning range per scan, as described above. These characteristics have enhanced the usefulness of MSCT in three-dimensional imaging diagnosis using computer graphics (Fig. 3). Since a very thin slice of 0.5 mm can be used, MSCT can visualize microstructures which could not be achieved with conventional scan techniques (Fig. 4).

When MSCT is used with thin slices of 1 or 0.5 mm, resolution is equal among the directions of X, Y, and Z axis of a voxel that is the minimum unit of an image. This minimum unit is called an isotropic voxel.[1] The partial volume

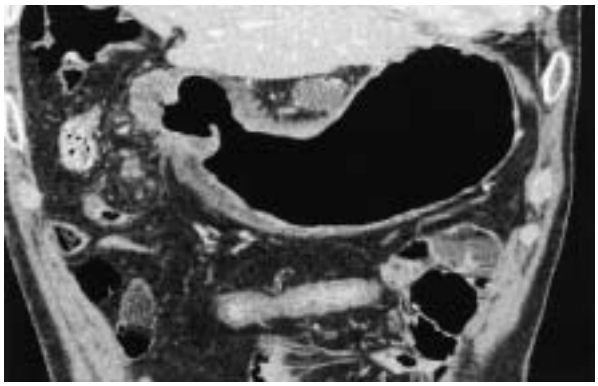


Fig. 5 High resolution coronal section of the abdomen with isotropic voxels
It clearly shows Borrmann's type III gastric cancer and swollen lymph nodes.

effect based on slice width, which was a serious problem with conventional CT diagnosis, can be avoided in images based on the isotropic voxels. Therefore, reproducible images can be obtained, irrespective of the direction and size of the target structure of diagnosis. MSCT has other advantages including reduced artifacts,

improved reliability of CT values, and reformatted sagittal or coronal sections that can be obtained with the same axial resolution as axial sections (Fig. 5). Thus, MSCT with isotropic volumetric data has revolutionized imaging diagnosis.

Problems with MSCT

The most significant shortcomings with MSCT are the increase in the volumetric data produced by the increased use of thin slices. The increase in data directly influences the patient throughput because it prolongs the time required for image reconstruction[4–6] and transferring and indicating data. Therefore, MSCT requires processing units, network environment, and display systems with higher speed capacities. It also requires hard disks, memories, and image storage devices with much larger capacities. As MSCT images have increased the number of images, it has become unrealistic to observe them on films. Instead, diagnosis with the images displayed on the monitor (so-called CRT or monitor diagnosis) has become essential. Furthermore, as the use of sagittal and coronal sections has increased, it has become necessary for clinicians to have a knowledge of both axial anatomy and longitudinal anatomy. The increased burden on radiologists who are required to interpret a large number of images is also a serious problem.[7]

Future of MSCT

Although 4-row MSCT systems have just started to become widespread, the development of next-generation MSCT systems is already in progress and it is considered certain that 8- or 16-row multislice systems will be released at the end of 2001. What is the true clinical significance of these advanced multi-row detectors? Since current 4-row systems have already provided sufficient scanning range and speed, the primary significance of the 8- or 16-row detector system is to improve the Z-axis resolution with thin slices. It is possible that very thin slices of 0.5 or 1 mm, which are now limited due to small coverage, will be used as a standard parameter.

Another issue of clinical significance in introducing the 8- or 16-row systems is to simplify scanning conditions. With the existing 4-row systems, it is necessary to select the scanning parameters on the basis of the clinical situation. However, the next-generation multislice detectors system will be able to employ scan parameters that will continually ensure optimum image quality thanks to their dramatically increased speed. In emergency situations at night, for example, even those not specialized in CT can use the system since the operator is not required to execute complicated parameter selection. Initial images can be provided as a thick slice and, if necessary, re-processed to generate high resolution images for further investigation using the raw data. That is, one scanning enables both screening and detailed examination. This is one of the most significant advances in the history of CT.

Apart from the above commercially available products, a CT system with multiple-row detectors has been developed for research purposes. This is an experimental system equipped with 256-row area detectors and developed under the project of the "High-speed Cone Beam 3-dimensional X-ray CT (Energy Use Rationalization) Development Committee" supported by the New Energy and Industrial Technology Development Organization (NEDO).[8] A clinical study on the experimental system is scheduled to be conducted at the end of 2001 in order to develop a "four-dimensional scanner" that obtains real-time three-dimensional information. It is considered promising as a prototype of the next-generation systems.

Conclusion

The diagnostic ability of MSCT systems is far higher than that of conventional single slice CT systems. Such systems have been developed and are now more widespread than ever, and

the advances have been much more rapid than was expected by most physicians. The present 4-row systems are clinically quite useful, but only represent the earliest stage of MSCT development. After its clinical application, area detector CT employing several-hundred rows of detectors will have the potential to replace conventional radiography in a number of examinations, and as a consequence, it is currently difficult to accurately define the indications and limitations of MSCT. All clinicians will need to watch closely the future of the diagnostic revolution that has been brought about by MSCT.

REFERENCES

1) Katada, K.: Half-second submillimeter real-time multi-row helical CT — CT diagnosis by aquilion. *Medical Review* 1999; 72: 62–70.
2) Taguchi, K. and Aradate, H.: Algorithm for image reconstruction in multislice helical CT. *Med Phys* 1998; 25(4): 550–561.
3) Tsujioka, K.: Principle of multislice CT. *Journal of Japanese Association of Radiology* 2000; 56(12): 1391–1396. (in Japanese)
4) Akabane, M.: Imaging diagnosis with multislice CT — Possibility and future prospect. *New Medicine* 1999; 293: 53–56. (in Japanese)
5) Kadota, M., Yamashita, Y. and Takahashi, M.: Application of multi-row detector CT. *Image Information (M)* 1999; 31(20): 1117–1126. (in Japanese)
6) Kobayashi, S., Shiragami, N. and Hiramatsu, K.: Dynamic study with multiple detector row CT. *Image Information (M)* 1993; 31(20): 1146–1153. (in Japanese)
7) Katada, K.: Multislice CT. *Clinical Neuroscience* 2000; 18(9): 1009–1012. (in Japanese)
8) Edited by Medical Welfare Equipment Research Center: *1999 Results Report*. High-speed corn beam three-dimensional X-ray CT (energy use rationalization). 2000. (in Japanese)