

REVIEW

Sudden death due to cardiovascular disorders: a review of the studies on the medico-legal cases in Tokyo

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Abstract. The Tokyo Metropolitan Government has a medical examiner system, in which all cadavers classified as "unusual death" in the city of Tokyo should be examined, and if necessary, autopsied to determine the cause of death. Of about 10,000 unusual deaths examined per year, two thirds are usually determined to have died of natural causes. The most common cause of sudden natural death is ischemic heart disease, especially acute myocardial infarction. Pathological examination, however, proves acute myocardial ischemia in only one third of autopsies. Subarachnoid hemorrhage and intracerebral hemorrhage, acute myocarditis and cardiomyopathies and aortic dissection/aneurysm as well as pulmonary thromboembolism are frequent causes of death in medical examiner cases. Both pathological and socio-medical problems associated with these diseases are discussed. (Keio J Med 50 (3): 175–181, September 2001)

Key words: sudden death, unexpected death, medical examiner, medico-legal autopsy, cardiovascular disease

Introduction

The prognosis of several diseases that were once lethal have been improved through developments in clinical medicine. However, the number of patients who die suddenly has not decreased in Japan, and this poses a critical problem in social medicine. In this article the authors present the actual circumstances of sudden death due to cardiovascular disorders in Tokyo, with reference to studies on medico-legal cases that have involved medical examiners.

Sudden Death Investigated by Medical Examiners

The Tokyo Medical Examiner's Office (TMEO) is an administrative body that was established under the direction of the GHQ (General Headquarters) after the second World War. All cadavers classified as unusual according to the Japanese Medical Act in the city of Tokyo, including those whose deaths are due to ectogenic causes and those in which the cause of death is unclear, are examined by medical examiners who were also trained as forensic pathologists. If the cause of

death is not clarified by an external examination, an autopsy is performed, with or without the consent of the family. The number of the examined bodies has recently increased, and has reached about 10,000 per year. Among these, about 2,500 are autopsied.

Natural death accounts for two thirds of the cadavers investigated by medical examiners and most of these are considered to be unexpected death (Fig. 1). More than half of these unexpected deaths are caused by cardiovascular disorders that mainly consist of diseases of the heart, the great and intracranial vessels (Fig. 2). Tokudome *et al.*¹ classified the clinical deaths into those that had had a medical history and those who had apparently been healthy. A significant difference was not presumed in the fraction of deaths due to cardiovascular causes between the two groups.

Ischemic Heart Disease

About 40% of the natural deaths investigated by Tokyo medical examiners are due to ischemic heart disease (IHD) or coronary heart disease. Tokudome, *et al.*¹ examined incidents in which the patient had died

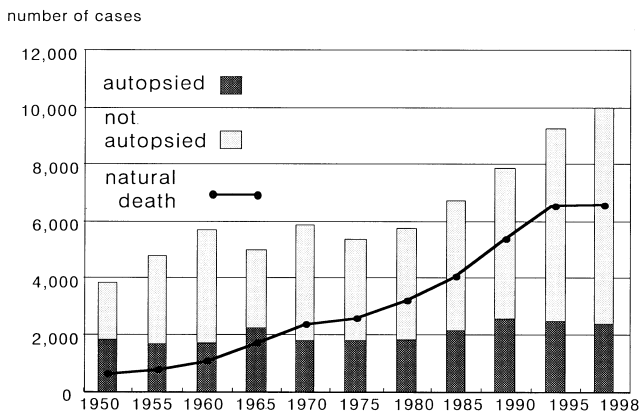


Fig. 1 Annual number of “unusual death” in the city of Tokyo. (Tokyo Medical Examiner’s Office)

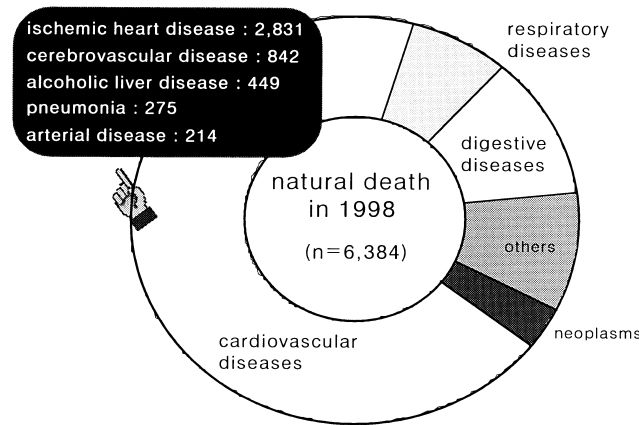


Fig. 2 Breakdown of natural deaths in the medical examiner cases.

within 24 hours after the onset of attack, and reported that IHD was the likely cause of death in 1,342 (44.2%) of those among the 3,179 deaths in the apparently healthy group, and in 6,799 (45.3%) among the 15,010 deaths of individuals with a medical history. Murai² reported that 8,897 deaths (40.0%) among 22,221 pre-hospital deaths were due to IHD.

Sudden death due to IHD includes acute myocardial infarction (AMI), acute coronary syndrome (ACS), arrhythmogenic myocardial scars and other conditions that interfere with confirming the cause of death as IHD, because early myocardial ischemia cannot be pathologically proven. A precise histological examination of the coronary arteries is necessary to identify ruptured atheromatous plaques with thrombosis.

A pathological study of the 83 deaths cases that the authors had determined to be caused by IHD showed that acute myocardial ischemia was suspected in 31 (37.3%), fresh or recent myocardial infarct in 11 and rupture of the atheromatous plaque of the coronary

Table 1 Pathological findings of the heart in the cases of ischemic heart disease

fresh or recent MI rupture		ACS
(-)	(+)	
5 (6.0%)	6 (7.2%)	20 (24.1%)
31 (37.3%)		
old MI	focal fibrosis	unclear
12 (14.5%)	27 (32.5%)	13 (15.7%)
39 (47.0%)		13 (15.7%)

MI: myocardial infarct, ACS: acute coronary syndrome.

Table 2 Comparison of the site of infarct in cardiac rupture between hospital (pathological) and medico-legal autopsies

site of myocardial infarct	hospital cases*	medical examiner cases**
anterior***	21 (75.0%)	150 (46.0%)
lateral	2 (7.2%)	75 (23.0%)
inferior	4 (14.3%)	64 (19.6%)
postero-lateral	1 (3.5%)	17 (5.2%)
massive LV		15 (4.6%)
LV + RV		5 (1.5%)

*Murai,² **Yamaguchi,⁶ ***including antero-septal and antero-apical infarcts.

artery without pathological infarct in 20 cases (Table 1). If this result is applied to the total number of deaths recorded by the TMEO, the estimated incidence of unexpected death due to clinical AMI in Tokyo, including ACS, is 11–12/100,000 population per year.

Clinical studies of circadian variation in the incidence of sudden death due to IHD in Japan and elsewhere have demonstrated a high frequency of sudden death in the morning and a low frequency during the night.^{3,4} However, Matsuo, *et al.* reported a high frequency of sudden death due to IHD during the night.⁵ This discrepancy is explained by the fact that medical examiner cases include patients who had died at night and are often found dead the next morning.

One fatal complication of myocardial infarction is cardiac tamponade due to myocardial rupture. Yamaguchi⁶ stated that the characteristics of cardiac rupture in deaths investigated by the medical examiner are (1) rupture of the free wall of the left ventricle (LV), (2) relatively high frequency in the lateral wall of the LV, (3) limited area of myocardial infarct, and (4) relatively rare coexistence of old myocardial infarct. Table 2 compares the data reported by Yamaguchi to those

from pathological autopsies examined by the authors in a hospital setting. Although cardiac rupture usually occurs 3–10 days after the onset of the myocardial infarction, we occasionally encountered deaths in which cardiac rupture occurred in a much more recent myocardial infarct (Fig. 3).

Most sudden death caused by IHD happens to individuals over the age of 30 with severe coronary artery sclerosis. Among children and or young adults who suddenly die of IHD, such rare coronary lesions are usually sequelae of Kawasaki disease⁷ or due to a congenitally anomalous origin of the left coronary artery.^{8,9} Rupture of an atheromatous plaque with coronary thrombosis is found in most deaths due to AMI as well as ACS (Fig. 4), whereas coronary embolism (Fig. 5),¹⁰ primary coronary dissection¹¹ and coronary involvement in aortic dissection (Fig. 6) are rare causes of myocardial infarction.

Cerebrovascular Disorders

Among the cerebrovascular disorders, subarachnoid hemorrhage (SAH) and intracerebral hemorrhage (ICH) are important causes of unexpected death, and fatal cerebral infarction is much rarer in deaths investigated by the medical examiner. SAH and ICH often occur between the ages of 40–70 years. A gender difference is not apparent in SAH, whereas males predominate in ICH.

Sugai and Kono pathologically examined 117 deaths due to SAH and found ruptured aneurysms in 110 of them (94.0%).¹² They reported that the most common site of the ruptured aneurysm was the anterior communicating artery followed by the internal carotid arteries, the middle cerebral arteries and the basilar artery. Aoki, *et al.*¹³ examined autopsy records of SAH and reported that the anterior communicating artery had the highest incidence of ruptured aneurysm, and the middle cerebral arteries had the second highest. Although most of the cerebral aneurysms are of the saccular type that usually occurs in the bifurcations of the cerebral arteries, arteriosclerotic, spindle-shaped and dolichoectatic types were identified by Akimoto.¹⁴ Intracranial dissecting aneurysms have recently attracted attention both clinically and pathologically. Murai, *et al.*¹⁵ reported that about 40% of the vertebral aneurysms with SAH were associated with medial dissection of the arterial wall (Fig. 7).

Though the frequencies of SAH and ICH are similar among deaths investigated by medical examiners, patients with SAH often die more rapidly than those with ICH, which sometimes results in prehospital death. Most ICH is regarded as hypertensive, but this is difficult to prove pathologically without clinical informa-

tion. Concentric hypertrophy of the left ventricle and sclerosis of the arterioles and the small arteries in the kidneys, adrenal glands and in other location are useful for estimating a history of hypertension. Besides ICH due to hypertension, Yasuhara¹⁶ stated that cerebral amyloid angiopathy with cerebral hemorrhage might be significant in the field of forensic medicine.

Aortic Dissection and Aortic Aneurysm

Among the aortic disorders are aortic dissections and ruptured aortic aneurysms important in sudden unexpected death. Aortic dissection has the second highest frequency as a disease of the heart and great vessels in sudden deaths investigated by medical examiners, and Tokudome, *et al.*¹⁷ reported that the frequency of aortic dissection is double that of true aortic aneurysm.

Murai¹⁸ examined the TMEO autopsy records of 1,320 deaths due to aortic dissection and found that most of the sudden death due to this cause occurred during the acute phase of medial dissection and that rupture of a chronic dissecting aneurysm of the aorta is rare in deaths investigated by the medical examiner. The features of sudden death due to aortic dissection are a higher incidence in winter than in summer (Fig. 8), predominance of type II dissection by DeBakey that was considered to be rare in clinical deaths, and male predominance at a gender ratio of 1.53:1. Rupture of the dissected channel was the most frequent cause of death and cardiac tamponade due to a rupture of the ascending aorta was regarded as the cause of death in 86.6% of acute dissections. Some patients with acute dissection died although the aortic wall had not ruptured.¹⁹ Acute myocardial ischemia due to the extension of the medial dissection to the left coronary artery was considered to be a probable cause of such death.^{20,21}

If aortic dissection is found in a child or young adult at autopsy, hereditary connective tissue disorders such as Marfan's syndrome as well as Ehlers-Danlos' syndrome,²² pregnancy,²³ or cardiac anomalies,^{24,25} especially a bicuspid aortic valve, should be suspected as the pathological base of the aortic dissection. Although the etiology and pathogenesis of aortic dissection remain ambiguous, cystic medionecrosis with disruptions of elastic fibers is often present. Furthermore, we found 3 cadavers with significant granulomatous aortitis^{26,27} among 170 deaths due to acute aortic dissection. Hemodynamic factors such as a transient elevation of blood pressure could have triggered medial dissection of the weakened aortic wall.

True aortic aneurysms are usually arteriosclerotic. Syphilitic mesaortitis is scarce among recent deaths due to aortic aneurysm. Takayasu's truncoarteritis, though

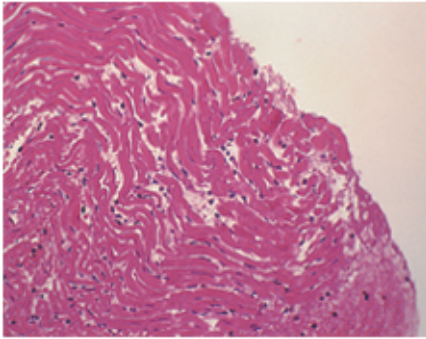


Fig. 3 Fresh myocardial infarct with a rupture. Myocardial necrosis with neutrophilic infiltration is observed, but no granulation tissue is found. (H-E)

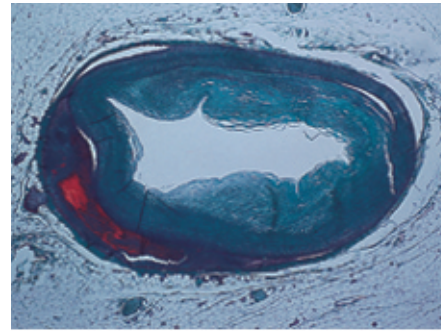


Fig. 6 Medial dissection of the left coronary artery as a complication of aortic dissection. (Elastica Masson stain)

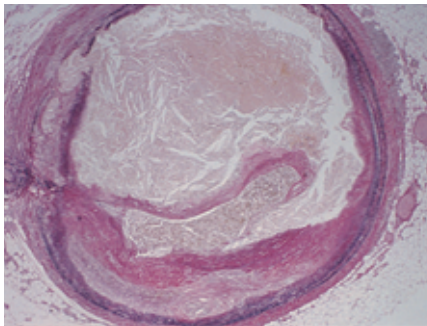


Fig. 4 Rupture of an atheromatous plaque and thrombosis of the coronary artery. (Elastica van Gieson stain)

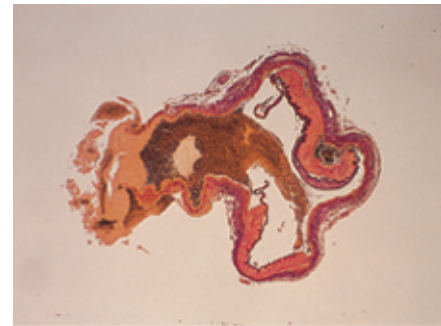
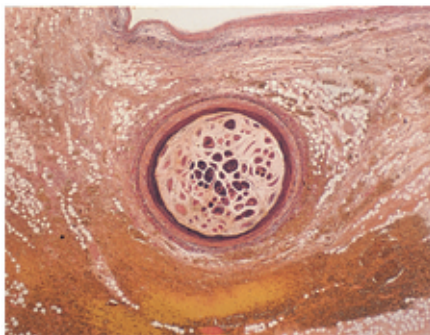
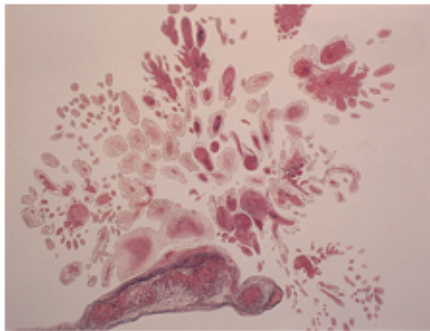


Fig. 7 Dissecting aneurysm of the vertebral artery with a rupture resulting in SAH. (Elastica HE stain)



(a)



(b)

Fig. 5 Tumor embolism in the coronary artery. (a) Embolization of a tumor tissue in the right coronary artery resulting in myocardial infarction. (b) The tumor (papillary fibroelastoma) originated from the aortic valve. (Elastica van Gieson stain)

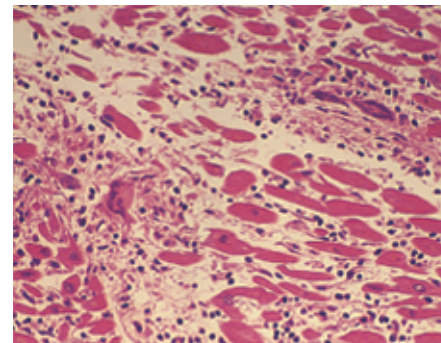


Fig. 9 Severe myocarditis with multinucleated giant cells (giant cell myocarditis). Differential diagnosis with myocardial sarcoidosis is necessary for this finding. (H-E)

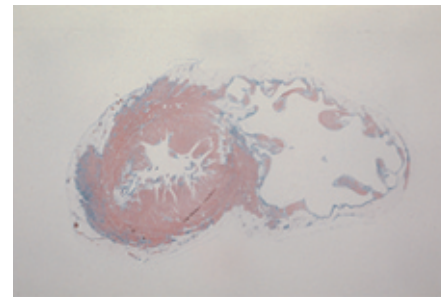


Fig. 10 Marked fibrofatty replacement of the right ventricular myocardium in ARVC/D. The outer layer of the left ventricle also shows an irregular and fibrofatty substitution of the myocardium. (Masson's trichrome stain)

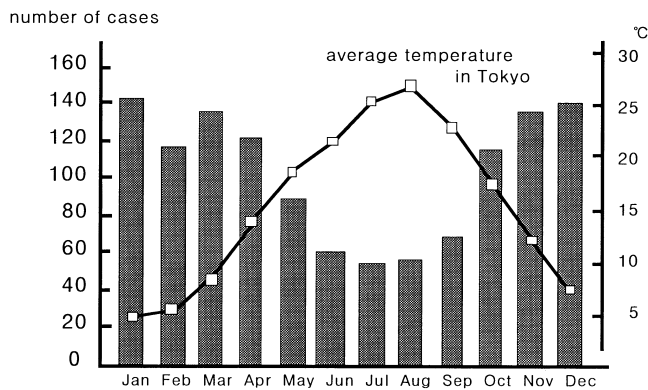


Fig. 8 Monthly distribution of sudden death by aortic dissection. (Tokyo Medical Examiner's Office)

rare even in Japan, might have caused sudden death in individuals with aortic regurgitation.

Acute Myocarditis

Several to tens of deaths due to acute myocarditis (viral or Fiedler's isolated myocarditis) each year are identified at autopsy by the TMEO. Sudden death is caused by this disease independently of age and gender. Murai, *et al.*²⁸ examined 58 autopsies according to the criteria for acute myocarditis (Dallas),²⁹ which include myocardial necrosis and/or degeneration in addition to interstitial infiltration of mononuclear cells.³⁰ The infiltrated cells consisted mainly of lymphocytes, but marked infiltration of eosinophils and/or granulomatous inflammation with multinucleated giant cells was sometimes evident (Fig. 9). Under such circumstances, the participation of a drug allergy should also be considered. Sudden death due to acute myocarditis occurs frequently in winter, and incidence of death due to this cause temporally and spatially accumulates, which are features of death due to infectious diseases.

Murai, *et al.*²⁸ revealed a socio-medical problem associated with sudden death caused by acute myocarditis. About half of the patients who presented with fever and/or chest pain had been sent home by a doctor due to misdiagnosis. Under such circumstances, trouble arising between the family of the deceased and the medical institution can develop into a civil action.

Cardiomyopathies

Cardiomyopathies account for 0.4% of the deaths investigated by the Tokyo Medical Examiners. Most of these consisted of the hypertrophic (HCM) and dilated types (DCM). The number of deaths due to HCM and DCM are similar, but the ratios of a clinical

history of cardiomyopathy differ. A clinical diagnosis of cardiomyopathy was correct in under 50% of those with HCM, and in 80% of those with DCM.³¹ Sudden death in children and in young adults is often attributed to HCM. Patients with HCM should be carefully monitored at school, because fatal attacks often occur during or after physical exertion. The heart of a patient with HCM usually shows asymmetrical septal hypertrophy as well as bizarre myocardial hypertrophy with fiber disarray, but the weight of the heart is not always increased in younger patients.³²

Arrhythmogenic right ventricular cardiomyopathy/dysplasia (ARVC/D) is not so frequent, but it is important as a cause of death in young adults.³³ Myocardial cells of the right ventricular wall are replaced by fibrofatty tissue in ARVC/D (Fig. 10) and the left ventricular myocardium, though not to the same extent as the right, is also affected.³⁴

The secondary, or specific, cardiomyopathies that are significant in medico-legal autopsy consist of fatal myocardial sarcoidosis (FMD)³⁵ and cardiac lesions in myotonic dystrophy (MyD).³⁶ FMD or MyD are not usually diagnosed until autopsy. Arrhythmia based on lesions of the atrio-ventricular conducting system leads to sudden death in FMD and MyD.

Autopsy reports of DCM-like cardiac lesions in "ocult" progressive muscular dystrophy of the Becker type³⁷ and eosinophilic heart disease³⁸ are rare.

Pulmonary Thromboembolism

Although pulmonary thromboembolism (PTE) was rare in Japan, the frequency of sudden death due to massive PTE has significantly increased in the medical examiner investigations in Tokyo.³⁹ About 20–30 deaths per year are diagnosed as being caused by PTE at autopsy by the TMEO, but these numbers remain much lower than those of IHD and SAH/ICH.

Obesity is a risk factor for PTE and one third of the cadavers found to have died due to this cause have a body mass index (BMI) of over 24, whereas cases of almost the same number were associated with a BMI of under 20. With respect to medical histories, 26 (15.6%) of 167 deaths caused by PTE had psychosis (schizophrenia, circulatory psychosis, and others). The reason why PTE occurs so frequently in the psychotic patients remains unknown, but the hypokinetic state of a patient with psychosis and the acceleration of the thrombogenesis by antipsychotics may be risk factors. Unlike patients with thromboembolism elsewhere, the factor V Leiden mutation and the prothrombin G20210A mutation have not been found in Japanese patients with this condition.⁴⁰ Differences in genetic background and lifestyles between Japan and other countries might account for the lower incidence of PTE in Japan.

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