Opinion

Impact of Acute Coronary Syndrome (ACS) on Work-Relatedness Evaluation in Cerebrovascular and Cardiovascular Diseases among Workers

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Globally, Japan, Taiwan, and South Korea are the countries recognizing cardiovascular diseases (CVDs) due to overwork as work-related diseases and compensate those who suffer from them. In Japan CVDs are considered to result from overwork. In addition, the underlying diseases (hypertension, atherosclerosis, and diabetes mellitus) of those who suffer from such diseases are recognized in Japan as being significantly facilitated and aggravated by overwork, especially the accumulation of fatigue from long working hours. Thus, the manifestation of CVDs is considered to be work-related. Initially, South Korea began with criteria for work-related CVDs (WR-CVDs) similar to those developed by the Japanese. However, South Korea has revised certain areas of the criteria many times for administrative and social reasons, without any basis of scientific evidence or support¹⁾.

CVDs are the number one cause of death in the adult population, not only in Korea but globally. Although the patient may survive a stroke or myocardial infarction (MI), it can cause a permanent physical disablement, thus obstructing work ability. This disability can be tragic for the individual and the family, and may be a big loss for the company and the nation that loses a member of a skilled and important workforce.

Due to the dramatic development of medical knowledge over the years, the pathophysiology of CVDs has been determined and new risk factors such as inflammation or stress have been included. In addition, what in the past has been collectively termed ischemic heart diseases has now been differentiated into coronary

artery disease (CAD) and acute coronary syndrome (ACS). Following these clinical developments, there must be a process of verifying whether the many epidemiological studies that have presented scientific evidence for the association between stress and the causal risks of CVDs agree with the new medical knowledge.

Moreover, South Korea is currently greatly influenced by both Japan and the West on the issue of WR-CVDs. There is therefore a need for a definite clarification of the difference between the West's concept of job stress and Japan's focus on overwork and how each factor influences health. Based on recent scientific evidence, the criteria on the work-relatedness of CVDs need to be revised, not only to improve the fairness and decision time for claims regarding work-related diseases, but also to prevent CVDs more effectively. Work-related diseases are preventable by controlling those work-related factors that are involved in the occurrence of such diseases, as well as in the facilitation or aggravation of CVDs. Work-related causal factors should therefore be the subject of scientific investigation.

Accordingly, this paper discusses 1) the differences between CAD and ACS, 2) the differences in how job stress and overwork influence CVDs, 3) the differences between cerebrovascular diseases and CVDs in terms of the etiopathogenesis, and 4) necessary revisions to the method for preventing workers' CVDs and the criteria on the work-relatedness of CVDs.

The Natural History of CAD is Punctuated by Clinical Manifestations of ACS

An understanding of the pathogenesis of CVDs is necessary for the correct assessment of its work-relatedness.

First, CAD, known as the pathological manifestation of atherosclerosis in the coronary artery, is a vascular disease resulting in the narrowing of the arteries due to the accumulation of cholesterol in the inner lining of the coronary artery. The narrowing of the coronary arteries by atherosclerotic plaques is associated with 3 non-modifiable risk factors (age, gender, and family history) and 6 modifiable risk factors (hypertension, diabetes mellitus, hypercholesterolemia, smoking, obesity, and inactivity)²⁾. Furthermore, a recent study reported a relationship between general psychological strain and carotid atherosclerosis³⁾. The first stage of atherosclerosis occurs in childhood while the more harmful second stage, the atheromatous plaque, appears after puberty in boys and much later in girls⁴⁾, and progresses over many years, typically decades. The natural history of CAD is punctuated by clinical manifestations of ACS (unstable angina, acute MI, and ischemic sudden death)⁵⁾.

Without thrombosis, coronary atherosclerosis (CAD) is benign. It is plaque disruption, or fissuring, and subsequent thrombosis that make coronary atherosclerosis

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dangerous. Small ruptures often remain clinically silent, whereas more extensive plaque ruptures may cause clinical manifestations of ACS⁶. Nearly 60–70% of ACS cases evolve from atherosclerotic plaques that are minimally or mildly obstructive of the lumen before the acute event⁷. The risk of plaque disruption depends more on plaque type (composition) than on plaque size and stenosis severity. Both plaque vulnerability (intrinsic disease) and rupture trigger (extrinsic forces) are important for plaque disruption⁶.

Insight into the pathophysiology of ACS can be gained by studying the role of triggering activities, such as heavy physical exertion and episodes of anger, in promoting plaque rupture vulnerability to disruption, which include lipid-rich plaque, a thin fibrous cap, and increased macrophage activity⁸. Cerebral infarction may occur in the same pathophysiology as ACS.

Concerning individual workers, apart from whether risk factors are involved in the progress of latent CAD, work-related factors may act as the triggering factor in the manifestation of ACS. According to studies to date, heavy physical exertion can trigger the onset of acute MI, particularly in people who are habitually sedentary⁹. Aerobic physical activities such as exercise or walking at work seemed to reduce the risk of MI, whereas anaerobic activities such as heavy lifting at work were related to increased risk of MI¹⁰. Emotional stress, anger, or worry has a dominant influence on the severity, frequency, and treatment of angina. When angina is associated with periods of emotional stress or anger, the angina is not usually the result of progressive coronary disease, but rather is due to an increase in oxygen demand¹¹. Besides, low levels of carboxyhemoglobin exacerbate myocardial ischemia during graded exercise in subjects with CAD^{12, 13}.

Cardiovascular Diseases based on Karasek's Job Strain Model are Different from Work-Related Cerebrovascular or Cardiovascular Diseases, or "karoshi" in Japan

The Japanese term "karoshi" represents WR-CVDs due to excessive overwork. This term was first used by Uehata in his presentation of 17 fatal cases caused by overwork at the 51st Annual Conference of the Japan Society of Industrial Health in 1978¹⁴. In the early 1970s, before the term "karoshi" appeared, the Japanese media used expressions such as "sudden death" or "dying at one's post of duty". The media defined this phenomenon as an untimely death of a healthy person after joining a company. Accordingly it can be considered work-related death.

Uehata described "karoshi" as a sociomedical term that refers to fatalities or associated work disability due to cardiovascular attacks (such as strokes, MI or acute cardiac failure) which might occur when hypertensive

arteriosclerotic diseases are aggravated by heavy workload¹⁵. Therefore, "karoshi" can be included as an element of ACS. Furthermore, work-related factors like "an unusual episode clearly evident in time and location of the occurrence prior to the manifestation of a disease" in the Japanese criteria on work-relatedness might be considered to be a trigger factor. Unusual episodes demanding excessive physical activity and anger are not considered common work-related risk factors. Therefore, it is valid to consider them as work-related injuries rather than factors of such work-related diseases.

On the other hand, decision latitude, skill discretion, work speed, work load, conflict situation and others, which Karasek described in his Job Strain Model, are commonly seen as job stressors. According to scientific knowledge, although such job stressors may be considered risk factors of CAD, thus having a chronic influence, they do not act as trigger factors of ACS.

When it is not research focusing on the atheromatous change of the coronary artery or carotid artery as an objective indicator verifying the influence of job stressors, the interpretation of research results might be incorrect. From this perspective, studies supporting Karasek's Job Strain Model that have investigated the association between job stress and CAD, hypertension, and MI may be criticized for not differentiating between CAD and ACS.

In the case of CAD, which begins from adolescence, developing into an atheroma over years or decades until the sudden manifestation of ACS, the individual does not feel any symptoms and is not restricted in the activities of daily life. Therefore, this disease does not inhibit working abilities, although CAD may be identified through a physical examination.

Little is Known about the Etiopathogenesis of Hemorrhagic Strokes Compared to Ischemic Stroke or ACS

Among strokes, cerebral infarction, i.e., an ischemic stroke, is similar to MI in that most of the symptoms are manifested due to the blockage of cerebral blood vessels where atherosclerosis has progressed.

Hemorrhagic strokes include intracerebral hemorrhages (ICH) and subarachnoid hemorrhages (SAH). In many cases of SAH the cause is known as an aneurismal rupture in the subarachnoid arteries due to a trigger factor. Nevertheless, the etiopathogenesis for ICH has not been determined.

Lacunar infarcts and "hypertensive" primary ICH are often collectively referred to as hypertensive small vessel strokes. However, despite their public health importance, their etiopathogenesis remains poorly-understood. Autopsy evidence suggests that the majority of cases are caused by a limited number of cerebral small vessel lesions. A lesion characterized in its acute form by

Table 1. Three different types of Work-relatedness of CVD in the current Japanese criteria

Type	Job stressor action period	Etiopathogenesis of CVD	Work-relatedness
1	Within 24 h, especially within 1 h after the unexpected episode	Manifestation of ACS or cerebral hemorrhage by abrupt overload of circulatory function due to severe emotional stress or physical exertion	Trigger
2	Usually within 1 wk after continuous exposure to extreme overwork	Manifestation of ACS by breakdown of physiological functions (autonomic nerve functions) due to cumulated physical fatigue (*typical <i>karoshi</i>)	Trigger
3	Usually within 6 months after continuous exposure to chronic overwork	Manifestation of ACS by cumulated mental or physical stress due to usually working long hours	?

fibrinoid necrosis on the small vessel atherosclerosis appears to be important in causing both lacunar infarcts and primary intracerebral bleeding¹⁶. Anderson *et al.* showed that moderate to extreme physical exertion was associated with a tripling of the risk of SAH in the subsequent 2 h, compared with periods of light or no activity. They also found that usual levels of activity did not alter this transient risk association. These data suggest that heavy physical activity may trigger SAH¹⁷.

In contrast to the protective effect of mild-to-moderate alcohol use against ischemic strokes, moderate drinking might increase the risk of hemorrhagic strokes. The differential effect of moderate alcohol consumption on hemorrhagic compared to ischemic strokes is mostly attributed to alcohol-and-withdrawal-induced sudden elevations of blood pressure, and coagulation disorders¹⁸.

Recommendations for the Prevention of CVD at Workplaces

Table 1 typifies the risk factors in the current criteria on the work-relatedness of CVDs in Japan and the characteristics of their work-relatedness by each type.

As discussed above, CVDs as CAD do not present any hindrance to the patient's daily life or work ability. CVDs themselves are considered a problem only when ACS is manifested. Besides, as shown in Table 1, job stressors of the three types related to the manifestation of ACS in workers are very limited and work-relatedness itself only functions as a trigger factor.

To remove the work-related triggers of ACS, which are manifested in Table 1, work management is very important. Thus short-term extreme overwork or long-term chronic overwork as well as any work-related stress due to abrupt work change should be avoided. Furthermore, it is suggested that workers identified through regular health monitoring with CAD or a complexity of many risk factors be strictly supervised as subjects of focus for THP (Total Health Promotion) activities at the workplace such as regular physical

exercise, nutrition management, cessation of smoking and blood pressure check-ups in Korea and other countries including Japan with a similar working compensation system.

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