Clinical characteristics of perioperative coronary spasm: reviews of 115 case reports in Japan

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Abstract

Purpose. Factors affecting perioperative development of coronary spasm have not been elucidated. A number of case reports describing perioperative coronary spasm have appeared in Japanese anesthesia journals, mostly published in Japanese. The purpose of this study was to investigate the contributing factors affecting perioperative coronary artery spasm by reviewing the published articles.

Methods. Reports were identified by using Medline database (1968–1998) or by manually searching nonindexed Japanese journals. The clinical characteristics of perioperative coronary spasm were analyzed in 115 patients who developed coronary artery spasm during the perioperative period.

Results. The mean age of the patients was 64 ± 9 years (range, 36 to 87 years). There were 97 men (84%) and 18 women (16%). Preoperative risk factors included hypertension (27%), angina pectoris (27%), cigarette smoking (13%), and diabetes mellitus (11%). The attack was related to inadequate depth of general anesthesia (23%), use of vasopressors (22%), vagal reflex (19%), administration of drugs other than vasopressors (17%), and epidural block (15%). About 85% of patients showed no ischemic abnormality on the preoperative electrocardiogram, whereas 56% had significant coronary stenosis on postoperative coronary arteriography. Coronary spasm tended to occur in patients under inhalation anesthesia combined with epidural block. Nitrates alleviated the episode in the majority of cases, whereas defibrillation and cardiac massage were required in 19% of patients. No deaths were reported.

Conclusion. Perioperative coronary spasm is prevalent in elderly male patients with coronary risk factors who undergo abdominal or thoracic surgery under inhalational anesthesia combined with epidural anesthesia. Instability of the autonomic nervous system and/or vascular hyperreactivity may be the underlying pathogenic mechanisms of perioperative coronary spasm.

Key words Anesthesia · Coronary spasm · Perioperative

Introduction

Coronary artery spasm plays an important role in the pathogenesis of variant angina as well as ischemic heart disease, including acute myocardial infarction and ischemic sudden death [1]. The incidence of variant angina is considered to be relatively high among Japanese compared with Caucasians [2,3], although the morbidity and mortality of coronary arterial disease are much lower in Japanese [4]. A review of the Medline database over the past 30 years has identified over 600 original studies of variant angina, with 30% of these being reported on Japanese patients [4]. With regard to anesthesia-related coronary artery spasm, the majority of case reports were published by Japanese investigators. Searching the Medline database (1968–1998) found more than 30 case reports of anesthesia-related coronary artery spasm in citation-indexed journals [5–33], including more than 60% from Japan. Furthermore, a number of case reports of perioperative coronary artery spasm have been published in nonindexed Japanese anesthetic journals, and were to a large extent authored by Japanese. The individual reports show relatively small numbers of patients with specific conditions and treatment regimens, making it difficult to clearly define which factors affect perioperative coronary artery spasm.

In the present study, we performed a systematic review of 115 cases reported from Japan in a variety of clinical situations to investigate the nature and distribution of the population, the contributing factors inducing the perioperative coronary artery spasm, and the treatment modalities as well as the clinical outcome.

Methods

Reports of perioperative coronary artery spasm were identified by searching Medline (1968–1998) and Japanese journals (1980–1998), including the *Japanese*

Key words for searching in the indexed journals were "perioperative" and "coronary artery spasm" and/or "anesthesia-related." Reports of the perioperative coronary artery spasm in the non-indexed journals were searched by reading articles through the journals.

The selected criteria for perioperative coronary artery spasm included ischemic electrocardiographic changes, as demonstrated typically by ST segment elevation without preceding remarkable changes in determinants of myocardial demand or supply; and occurrence after arrival in the operating room before, during, or following general and/or regional anesthesia. We extracted the following data from each study: the number of patients and their age, sex, preoperative risk factors, preoperative electrocardiography, anesthetic technique, time of onset, possible causes, therapy, and clinical outcome.

Results

A total of 115 case reports were analyzed. Not all case reports, however, described every analyzed factor, but age, sex, and electrocardiographic changes were recorded for all patients.

Age

The mean age of reported patients was 64 ± 9 years (mean ± SD), ranging from 36 to 87 years. The largest number of patients were in the in 60s, followed by the 70s and the 50s (Fig. 1). Patients aged 50 and above accounted for 94% of the total.

Sex

There were 97 men (84%) and 18 women (16%).

Preoperative risk factors

Analyses were performed on 94 patients whose preoperative complications and risk factors were clearly documented. A history of hypertension (treated or untreated) was present in 26 patients (28%), followed by angina pectoris, cigarette smoking, diabetes mellitus, and pulmonary dysfunction (Fig. 2). Seventeen patients (18%) were free of any apparent risk factor.
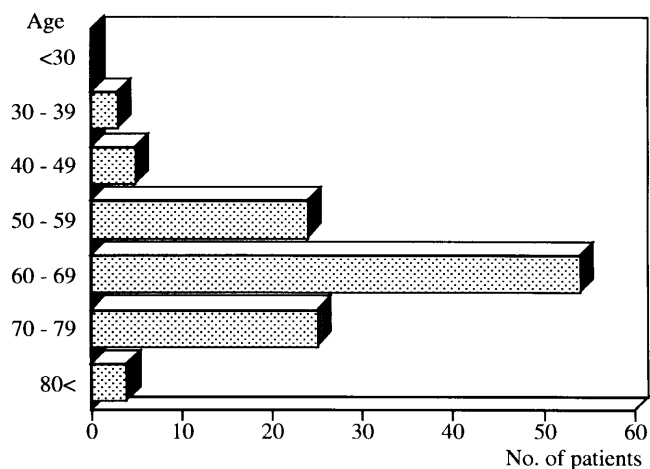

Fig. 1. Age of patients with perioperative coronary spasm. Perioperative coronary spasm occurred in patients older than 30 years, with an average of 60–70 years
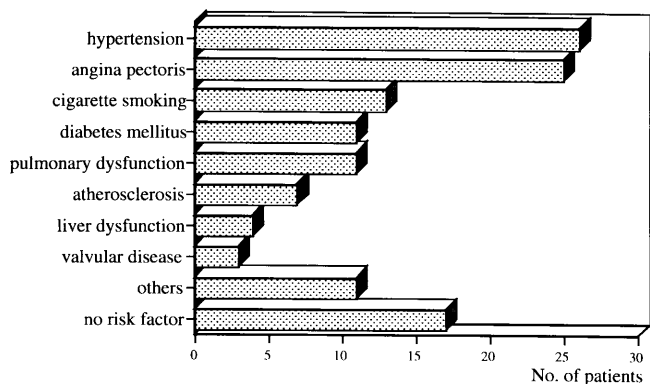

Fig. 2. Preoperative risk factors. Hypertension, angina pectoris, cigarette smoking, and diabetes mellitus were the major risk factors, although 20% of patients were free of all risk factors

Time of onset

The time of onset of coronary artery spasm was clearly documented in 108 patients (Fig. 3). The majority of patients had the episode during surgery.

Anesthetic technique

The anesthetic technique was clearly documented in 111 patients. A combination of inhalation anesthesia and epidural block was most frequently used, followed by inhalation anesthesia alone, total intravenous anesthesia, and inhalation anesthesia plus intravenous anesthesia (Fig. 4).

Site of operation

The site of operation was documented in 110 patients. Upper abdominal operations were performed in 29
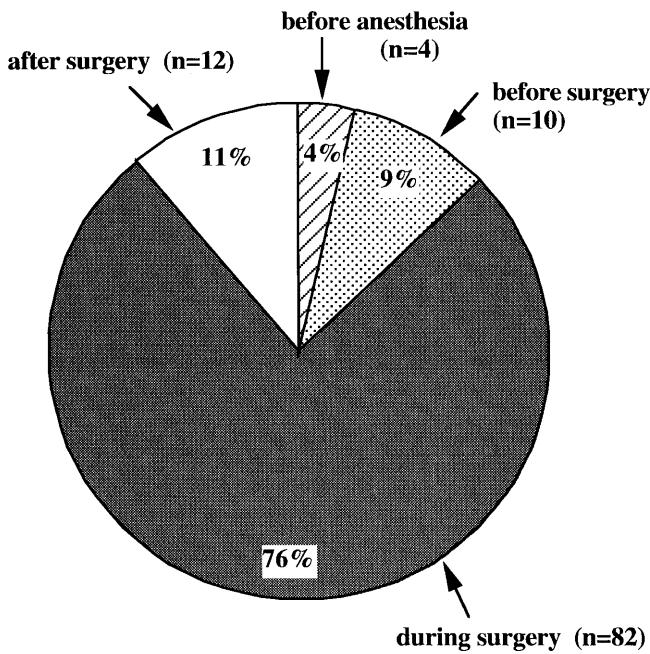
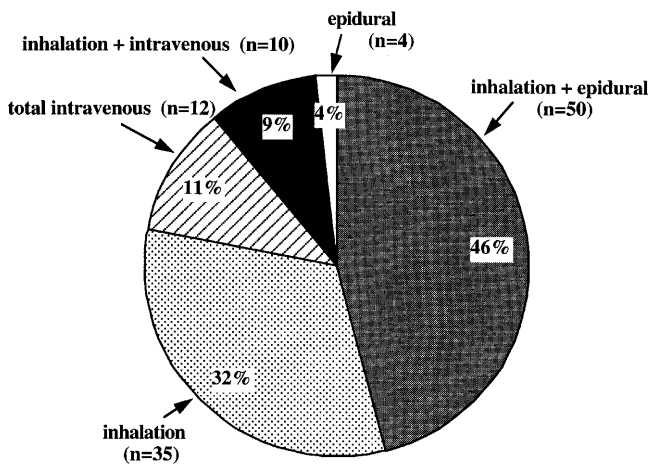**Fig. 3.** Time of onset of perioperative coronary spasm. The most vulnerable time was during surgery

Fig. 4. Anesthetic technique. Perioperative coronary spasm tended to occur under inhalation anesthesia combined with epidural anesthesia
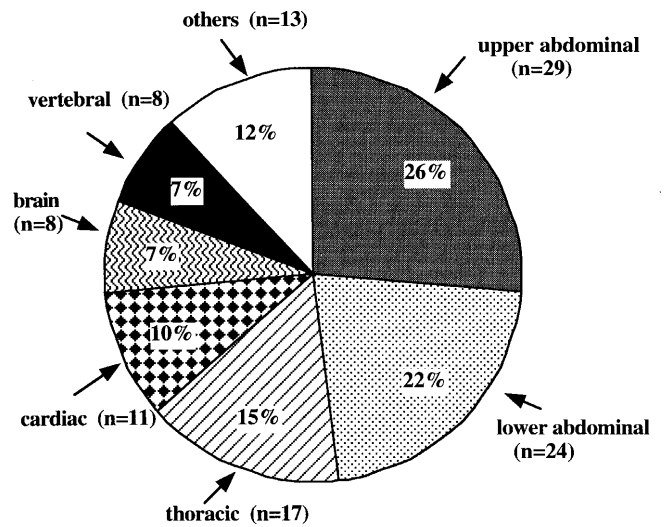

Fig. 5. Site of operation. Perioperative coronary spasm tended to occur during upper and lower abdominal or thoracic surgery
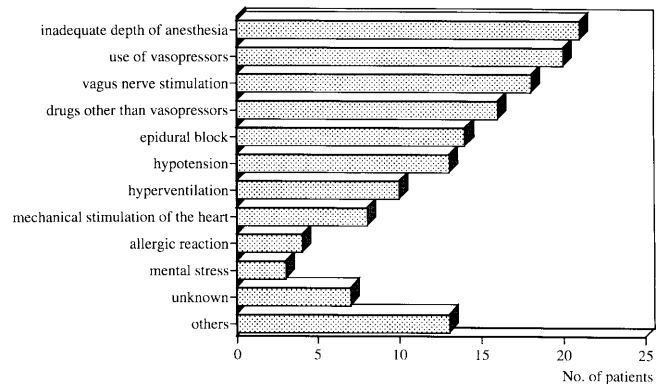

Fig. 6. Contributing factors as possible causes. The major triggering factors included inadequate depth of general anesthesia, use of vasopressors, vagus nerve stimulation, drugs other than vasopressors, epidural block, hypotension, hyperventilation, and mechanical stimulation of the heart

patients (26%), representing the highest frequency (Fig. 5), followed by lower abdominal operation, noncardiac thoracic surgery, cardiac surgery, brain surgery, and vertebral surgery.

Contributing factors as possible causes

The contributing factors that were possible causes were clearly documented in 93 patients. Inadequate depth of general anesthesia was considered as a possible cause in 21 patients (23%), use of vasopressors in 20 patients

(22%), vagus nerve stimulation (vasovagal reflex) in 18 patients (19%), drugs other than vasopressors in 16 patients (17%), epidural block in 14 patients (15%), hypotension in 13 patients (14%), hyperventilation in 10 patients (11%), and mechanical stimulation of the heart in 8 patients (9%) (Fig. 6). Coronary spasm was found to be caused by multiple factors in 41 patients (44%). Drugs other than vasopressors as possible causes included prostaglandin E_1, vecuronuim, doxapram, and trimethaphan.

Preoperative electrocardiogram

Preoperative electrocardiographic findings were described in 105 patients. No abnormality on electro-
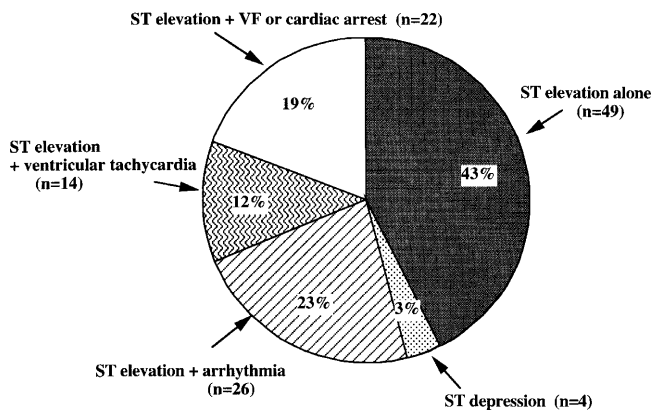
Fig. 7. Electrocardiogram during coronary spasm. ST segment elevation and depression were identified in 97% and 3% of patients, respectively. In about 20% of these patients, these changes were associated with ventricular fibrillation (*VF*) or cardiac arrest

cardiogram was found in the majority of patients (*n* = 74, 71%). Ischemic changes were observed in 16 patients (15%). Conduction abnormalities without ischemic changes were found in 15 patients (14%).

Electrocardiogram during coronary spasm

The electrocardiogram was the means of diagnosis in all 115 patients. ST elevation alone was found in 49 patients, ST depression in 4 patients, ST elevation with arrhythmia in 26 patients, ST elevation with ventricular tachycardia in 14 patients, and ST elevation with ventricular fibrillation or cardiac arrest in 22 patients (Fig. 7).

Therapy and outcome

Therapeutic methods were described in 111 patients. Disappearance of the coronary spasm after the termination of surgery or during observation occurred in 4 patients (4%), and alleviation of the spasm by administration of nitrite products was observed in 70 patients (63%). Nitrates and calcium channel antagonists were mainly used, and vasopressors and lidocaine, an antiarrhythmic agent, were also used. Ephedrine, dopamine, epinephrine, and other vasopressor drugs were used in various combinations. Defibrillation and cardiac massage were conducted in 22 patients (19%). Resuscitation was performed successfully in all patients, and no deaths were reported.

Postoperative coronary arteriography

Postoperative coronary arteriography was performed in 16 patients. Nine of these patients (56%) showed significant stenosis of the coronary arteries, but the other 7 patients (44%) showed no significant stenosis.

Discussion

In the present study, review of the Japanese literature showed that the reported perioperative coronary spasm occurred mostly in elderly men (Fig. 1) who had certain preoperative risk factors, such as hypertension, angina pectoris, cigarette smoking, and diabetes mellitus (Fig. 2). Coronary spasm was not reported in men younger than 30 years, indicating the importance of age in the susceptibility to coronary spasm. Such age and gender effects are compatible with those previously reported for patients with variant angina in both western and Japanese populations [34]. The risk factors identified in this study are also similar to those with variant angina [34], except for cigarette smoking, which has a much higher prevalence (>80%) in variant angina compared with our finding of 13%.

Although approximately 85% of reviewed patients had no ischemic change on the preoperative electrocardiogram, postoperative coronary arteriography, which was performed in only 16 of 115 patients, revealed that approximately half of the patients had significant stenoses of the coronary arteries. These findings indicate that the attack is difficult to predict preoperatively, but the perioperative coronary spasm is somehow related to atherosclerosis or endothelial dysfunction, which may be associated with both aging and coronary risk factors. Previous studies have shown that most of the angiographically normal coronary arteries in subjects aged >30 years exhibit endothelial dysfunction or atherosclerosis in which the proximal segment is more prone to atherosclerosis than the distal segment [35].

Our findings suggested that the major factors that trigger perioperative coronary spasm include inadequate depth of general anesthesia, the use of vasopressors, vagus nerve stimulation, drugs other than vasopressors, and epidural block (Fig. 6). Although the precise mechanism by which coronary spasm occurs remains to be elucidated, several precipitating factors are known, one of which is the impairment of autonomic nervous system [36–38]. In this study, the triggering factors described above may link autonomic imbalance with the pathogenesis of perioperative coronary spasm. Yasue and colleagues [37,38] proposed the presence of a major cholinergic neural constrictor mechanism in human epicardial coronary vessels that may underlie the pathogenesis of either variant angina or episodic coronary artery spasm. The coronary artery responsible for attacks in patients with variant angina is highly sensitive to acetylcholine and constricts abnormally in response to this agent [38]. Employing spectral analysis of

heart rate variability, Yoshio et al. [39] detected an increase in parasympathetic activity 10 min before an episode of spontaneous ST elevation, and a similar increase in sympathetic activity 5 min before the onset of the spasm. However, it has also been shown that vagal withdrawal may often be a component of the mechanisms leading to spontaneous coronary vasospasm [40].

In addition to the role of the autonomic nervous system, smooth muscle hyperresponsiveness to constrictor stimuli is suggested as the pathogenic mechanism of coronary spasm [4,36]. It is proposed that coronary spasm involves postreceptor smooth muscle hyperreactivity of a coronary segment, because it can be induced by several pharmacologic stimuli acting on different receptors [3,4]. This is consistent with our findings that vasopressors, such as dopamine, ephedrine, and epinephrine, as well as other agents, such as prostaglandins, trimethaphan, and doxapram, were thought to have potentiated the occurrence of perioperative coronary spasm. Dopamine has been shown to provoke coronary spasm in patients with active variant angina [41]. Anaphylactoid reaction was also considered as the trigger of perioperative coronary spasm in this study, and as the cause of coronary spasm in general [42], where chemical mediators such as histamine may induce coronary spasm. Elevated plasma histamine levels have been observed in many patients with variant angina, and coronary spasm can be provoked by histamine [43]. Hyperventilation was also found to relate to perioperative coronary spasm in 11% of the patients reviewed in our study. Coronary spasm can also be induced by hyperventilation with respiratory alkalosis [36,44,45], which probably enhances the Na-H exchanger followed by the Na-Ca exchanger, resulting in increased intracellular Ca concentration [36].

Perioperative coronary spasm occurred most frequently under inhalation anesthesia combined with epidural anesthesia (46%), followed by inhalational anesthesia alone (32%) (Fig. 4). Coronary spasm was reported to occur in a minority of patients during epidural anesthesia alone (3%). Spasm tended to occur frequently during surgery (78%), in comparison with before anesthetic induction (5%) and prior to surgery after anesthetic induction (12%) and postsurgery (5%) in patients who had undergone upper (26%) and lower (22%) abdominal or thoracic surgery (16%) (Fig. 5). One reason for the prevalence of the spasm in elderly patients undergoing abdominal or thoracic surgery under inhalational anesthesia combined with epidural anesthesia may be autonomic instability and hemodynamic changes, which may enhance inadequate anesthesia and the use of vasopressors.

The diagnosis of coronary artery spasm can be made with a reasonable degree of certainty when ST segment elevation on the electrocardiogram is documented during an anginal episode that occurs at the level of cardiac work below that which is usually tolerated without any signs or symptoms of myocardial ischemia [2]. Our analysis also showed that the diagnosis of perioperative coronary artery spasm was dependent on the identification of ischemic electrocardiographic changes without preceding changes in the determinants of myocardial demand or supply. ST segment elevation was found in 97% of patients and ST segment depression in only 3% of patients (Fig. 7). Severe classic coronary spasm causes ST segment elevation because of transmural ischemia, although a moderate degree of coronary spasm may depress the ST segment as a result of subendocardial ischemia [12]. ST segment elevation was accompanied by ventricular tachycardia in 12% of patients and by ventricular fibrillation or cardiac arrest in 19% of patients, suggesting that perioperative coronary spasm can be associated with life-threatening ventricular dysrhythmias in approximately one-third of patients (Fig. 7). It has been reported that ventricular dysrhythmias are commonly provoked by coronary artery spasm [46]. The dysrhythmias are often observed at the time of ST segment elevation, but they are even more frequently seen as the ST-segment returns to the baseline [46]. We could not, however, delineate this point because of the lack of information.

The management of coronary artery spasm consists of administration of nitrates and calcium antagonists [47]. The dilating effect on large coronary arteries is the principal mechanism of action of nitrates in vasospastic angina [48]. Alleviation of perioperative coronary spasm was observed in 63% of patients treated by nitroglycerin or isosorbide dinitrate. Defibrillation and cardiac massage were required in 19% of patients. Interestingly, resuscitation was performed successfully in all patients and no deaths were reported, suggesting that the outcome of perioperative coronary spasm is relatively good.

Although there are no systematic studies comparing the incidence of coronary spasm between countries, it is believed that this disorder is more prevalent in Japanese than in Caucasians [4]. A review of the Medline database over the past 30 years has identified over 600 original studies of variant angina, with 30% of these being performed on Japanese patients [4]. A prospective comparative study of coronary spasm across racial groups, which compared the incidence of inducible spasm in Japanese and Italian patients 7 to 10 days after myocardial infarction, revealed a marked difference in vasomotor reactivity between these two groups, with 80% of the Japanese and 37% of the Caucasian patients showing inducible coronary spasm [49]. Regarding the perioperative coronary artery spasm, the Medline database (1968–1998) identified 34 case reports of anesthesia-related coronary artery spasm, with more

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