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Clinical Characteristics, Demographics and Prognosis of Transient Left Ventricular Apical Ballooning Syndrome

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***Abstract. Background*: Transient left ventricular apical ballooning syndrome also called Tako-Tsubo cardiomyopathy is defined as a syndrome consisting of stress induced apical ballooning of the left ventricle and normal coronary arteries. The majority of the published reports are case reports or case series with a small number of patients. The goal of this study was to perform statistical analysis of reported cases and case series in the literature in order to study demographic, clinical characteristics and prognosis of this syndrome.**

***Method*: A PubMed search of the terms transient left ventricular apical ballooning, Tako-Tsubo, takotsubo, and apical cardiomyopathy was conducted for this study. All reports that contained information about individual patients were included in the statistical analysis.**

***Results*: The majority of the patients were women (93.5%). Asians were the largest group (57.2%) followed by Caucasians (40%). The presentations mimics an acute myocardial infarction. The most frequent presenting symptom was chest pain (65.9%) followed by dyspnea (16.2%). ST elevation was the most common ECG abnormality (87.5%). Contrary to most reports, this is not a benign disease with complications occurring in 18.9% and death in 3.2%. The most common complication was shock followed by left ventricular thrombus formation and congestive heart failure.**

***Conclusion*: Apical ballooning syndrome occurs most commonly in women and is associated with high complication rate. There are significant differences in presenting symptoms between race and gender which warrant further investigation.**

***Key Words.* apical ballooning, tako-tsubo: stress-induced cardiomyopathy, meta-analysis**

Background

A syndrome consisting of acute onset of chest symptoms, ECG changes with elevated cardiac markers mimicking acute myocardial infarction, left ventricular wall motion abnormalities in the apical region with preserved function of base, and normal coronary arteries was first described by Dote et al. in 1991 [1]. They initially called it Tako-Tsubo due to the afflicted left ventricle resembling a Japanese octopus pot. Other names have been used including apical cardiomyopathy and transient left ventricular apical ballooning syndrome. While initially described in Japan, its occurrence has been documented in multiple countries throughout the world including Belgium, Spain, Germany, Israel, Australia, Italy, and the United States [1–7].

Those affected are typically older women presenting after a stressful trigger, which could be either emotional or physical. Complete recovery is the norm, but complications including death have been reported. While this entity is becoming more recognized, the cause remains unknown, although acute. Acute coronary spasm, dynamic left ventricular outflow tract obstruction, and catecholamine excess have been proposed. However, the majority of the published reports are case reports or series with a small number of patients. The goal of this study was to perform statistical analysis of reported cases and case series in the literature to study demographic, clinical characteristics and prognosis of this syndrome.

Methods

A PubMed search of the terms transient left ventricular apical ballooning, Tako-Tsubo, takotsubo, and apical cardiomyopathy was conducted between 1991 and 2005. All articles published in English or with English translations available were considered for inclusion. All reports containing individual patient information were included. Reports that presented the information as a summary of cases without detailed information for individual cases were excluded. Reports with the same author or from the same institution were cross-referenced so as a case report would not be

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duplicated. Prospective and retrospective case series were included.

Patient's age, gender, race, and symptoms at the time of presentation, precipitating stress (emotional vs. physical vs. none), ECG changes (ST elevations, T wave inversion, or Q waves), cardiac markers (positive or negative), death, and complications were included in the collected data. In this approach, 185 cases were identified and analyzed [2–31]. The purpose was to identify the baseline characteristics in patients with transient apical ballooning syndrome. Comparisons of the characteristics were made based on gender and race. The statistical analysis was performed using SPSS version 13.0 statistical software. Any p value <0.05 was accepted as statistically significant. Continuous variables were analyzed using unpaired t-tests. Binary variables were studied using χ^2 and Fisher's Exact Tests. Quantitative variables were means $\pm$ standard deviation. Odds ratio and their 95% confidence interval were used to indicate the strength of influence.

Table 1. *Patient characteristics*

Characteristics	(%) ($N = 185$)
Mean age (years)	67.7
Female	93.5 (173)
Male	6.5 (12)
Race	
Asian	57.2 (83)
White	40 (58)
Other	2.8 (4)
Not reported	21.5 (40)

Table 2. *Symptoms and Stress at the time of presentation*

Characteristic	(%) ($N = 185$)
Symptom	
Chest Pain	65.9 (122)
Dyspnea	16.2 (30)
Syncope	4.9 (9)
Chest pain and dyspnea	3.2 (6)
Nausea	1.6 (3)
ECG changes	1.6 (3)
CVA	1.1 (2)
Palpitations	1.1 (2)
V-fib	0.5 (1)
Back Pain	0.5 (1)
Fatigue	0.5 (1)
Cardiac Arrest	0.5 (1)
Not Reported	1.1 (2)
Precipitating Stress	
Emotional	47.9 (80)
Physical	29.3 (49)
None	22.8 (38)

Table 3. *ECG findings & cardiac markers*

Characteristic	(%) (N)
ST Elevation	87.5 (136)
T wave inversion	75 (104)
Q Waves	50 (22)
Positive cardiac markers	85.5 (117)
N = number of cases data was reported	

Results

The baseline characteristics are detailed in Table 1. The majority of the reports involved women (93.5%) and older individuals with the mean age of 67.7. Asians made up the largest group (57.2%) with Caucasians being the second most common (40%) of those in whom race was reported.

The patients' presentation frequently mimics an acute myocardial infarction due to the symptoms, ECG findings, and cardiac markers. These characteristics are detailed in Table 2 and 3. The most frequent presenting symptoms, with which prompted patients to seek medical attention were chest pain (65.9%) followed by dyspnea (16.2%). ST elevation was the most common ECG abnormality occurring in 87.5% of the 136 reported cases. T wave inversion occurred at some points during the hospital course in 75% of 104 of reported cases. Q waves were rarely commented on, just 22 out of 185 cases, but were present 50% of the time. Other ECG findings not detailed in this study included prolonged QT interval and arrhythmias. Cardiac markers results, Elevated cardiac markets, either CPK or troponins, were positive in 85.5% of 117 reported cases which were positive in 100 patients (85.5%). These elevations were typically mild relative to the large territory especially when considering the large territory of myocardium thought to be involved based on echocardiograms or left ventriculogram and tended to peak at the time of presentation.

Contrary to most reports this is not a benign disease. While the majority of patients recovered quickly and had uneventful courses, complications did occur in 18.9% of the cases and death in 3.2% (Table 4). The most common complication was shock followed by thrombus formation and congestive heart failure. Other complications included CVA, ventricular tachycardia, left ventricular rupture and ventricular septal defect.

A stressful event typically preceded most cases. This stress could be either emotional or physical. The preceding event was detailed in 167 of 185 reports. An emotional event was responsible 47.9% of the time. The different emotional stressors included learning of someone's death, bad financial

Table 4. *Complications and outcome*

Complication	*N* (%)
Total patients with a complication	35 (18.9)
Shock	12 (6.5)
Thrombus	7 (3.8)
CHF	7 (3.8)
CVA	3 (1.6)
Ventricular tachycardia	3 (1.6)
Atrial fibrillation	2 (1.1)
LV rupture	1 (0.5)
Pneumothorax	1 (0.5)
Ventricular fibrillation	1 (0.5)
Ventricular septal defect	1 (0.5)
Death	6 (3.2)

Table 5. *Gender and characteristics*

Characteristic	Male ($n = 12$)	Female ($n = 173$)	*P* value
Age (years)	64.9	67.9	0.41
Chest pain at presentation	58.3% (7)	69.9% (121)	0.52
ECG findings			
ST elevation	100% (8)	86.7% (111)	0.59
T wave inversion	80% (4)	74.7% (74)	1.00
Positive cardiac marker	88.9 % (8)	85.2% (92)	1.00
Complications	8.3% (1)	19.7% (34)	0.46
Death	0%(0)	3.5% (6)	1.00
Precipitating stress	$N = 10$	$N = 157$	
Emotional	50% (5)	47.8% (75)	1.00
Physical	30% (3)	29.3% (46)	1.00
None	20% (2)	22.9% (36)	1.00
Race	$N = 12$	$N = 133$	
Caucasian	33.3% (4)	40.6% (54)	0.76
Asian	66.7% (8)	56.4% (75)	0.55

news or getting upset after a minor car accident. Physical stress precipitated 29.3% of the episodes. Some examples were undergoing surgery, extreme exercise, and asthma exacerbations. In 22.8% of the cases there was no triggering event and the patients presented spontaneously.

Comparisons

Gender

As already stated, most of the cases were females (93.5%). The baseline characteristics and data at time of presentation for males and females are listed in Table 5. There was no difference in average age for males and females (64.9 vs. 67.9), respectively. Symptoms at presentation were also similar for chest pain, ECG changes, and cardiac enzymes. Females were twice as likely to have a complication (19.7 vs. 8.3%) though this was not statistically significant ($p = 0.4$). Females were also the only gender to suffer from death as a result of apical ballooning, 6 cases versus 0 for men.

Table 6. *Race and characteristics*

Characteristic	Asian $n = 83$	White $n = 58$	*P* value
Age (years)	70.4	64.3	0.001*
Gender (female)	90.4%	93.1%	0.76
Chest pain	55.4%	81%	0.002*
ECG changes			
ST elevation	97.1% (68)	83.3% (30)	0.027*
T wave inversion	67.3% (52)	95.8% (24)	0.008*
Q waves	50% (8)	25% (8)	0.60
Positive cardiac markers	77.1% (35)	97.6% (41)	0.01*
Complication	18.1%	17.2%	1.00
Death	6%	1.7%	0.40
Precipitating stress	$N = 77$	$N = 47$	
Emotional	28.6%	63.8%	0.0001*
Physical	28.6%	34%	0.55
None	42.9%	2.1%	0.0001*

*Significant finding.

Again this was not a statistically significant. The differences may reflect the few number of men included in the analysis. There was no difference between the genders for the preceding stress that triggered their cases.

Race

Asians and Caucasians were chosen for comparison since they made up the majority of cases whose race was known (97.2%). Multiple differences were found between races (Table 6). Asians tended to be older, 70.4 years versus 64.3 for Caucasians ($p = 0.001$). At the time of presentation Caucasians more frequently suffered from chest pain (81% vs. 51.4%, $p = 0.0002$). With regards to ECG findings, Caucasians more frequently had T wave inversions (95.8% vs. 67.3%, $p = 0.008$) while Asians more frequently had ST elevation (% and *p* value) for Asians, and Asians had ST elevation (97.1% vs. 83.3% for Caucasians, $p = 0.027$). Positive cardiac markers were common in both groups but significantly more common with Caucasians (97.6% vs. 77.1%, $p = 0.01$). While no significant differences were noted for complications, Asians tended to have more deaths than Caucasians (6% vs. 1.7%). Lastly, Caucasians more frequently had an emotional stress as a trigger (63.8% vs. 28.6% $p = 0.000$) while Asians most commonly had no preceding stress (42.9% vs. 2.1% $p = 0.000$). There was no difference between the two races with regard to frequency of physical stress as a trigger.

Preceding Stress

As stated earlier most cases of apical ballooning are preceded by a stressful event, either emotional or physical. Table 7 demonstrates the effects of different stress triggers on presenting symptoms

Table 7. Precipitating stress and characteristics

Characteristic	Emotional	Physical	*P* value
Chest Pain	90% (72)	44.9% (22)	0.0001*
ST elevation	80.4% (41)	85% (34)	0.56
T wave inversion	74.4% (29)	86.7% (26)	0.24
Q wave	66.7% (4)	33.3% (4)	0.32
Positive cardiac marker	78.8% (41)	100% (36)	0.003*
Complication	16.3% (13)	30.6% (15)	0.05*
Mean age	62.7 (80)	71.9 (49)	0.0001*

* Significant finding.

Table 8. Odds ratio complications including death

Variable	RR	95% CI	*P* value
Female vs male	2.89	0.36 – 23.26	0.46
ST elevation	0.17	1.08 – 1.26	0.07
T wave inversion	1.41	1.23 – 1.61	0.02*
Q waves	8.33	0.77 – 90.90	0.14
Caucasian	0.74	0.31 – 1.74	0.53
Asian	1.07	0.47 – 2.45	1.00
Chest pain	0.67	0.31 – 1.42	0.32
Cardiac markers positive	1.87	0.39 – 8.85	0.52
Emotional trigger	0.69	0.31 – 1.51	0.43
Physical trigger	2.61	1.18 – 5.81	0.03*
No trigger	0.42	0.13 – 1.29	0.16

* Significant finding.

such as, ECG changes, cardiac enzymes and complications. Emotional stress triggers presented with chest pain twice as often as physical stress triggers did (90% vs. 44.9%, $p < 0.0001$). Positive cardiac markers were common with both triggers, but much more common with physical triggers, occurring 100% of the time vs 78.8% of time with emotional triggers ($p = 0.001$). Physical stress was also more likely than other triggers to result in complications (30.6% vs. 16.3%) for emotional and 10.5% for no trigger ($p = 0.04$). ECG changes were not effected by the triggering stress. Those who suffered from emotional stress were on average younger compared to those with a physical trigger (62.7 vs. 71.9, $p = 0.0001$).

Complications

Complications were found to occur in 18.9% of the cases. Baseline characteristics and data at the time of presentation were analyzed for their influence on causing complications (Table 8). T-wave inversion and physical stress trigger were the only two variables found to increase the likelihood of the complication. Gender and race did not affect the complication rate. Neither did the presence of ST elevation, Q waves, positive cardiac markers, or chest pain at time of presentation. Death occurred in 3.2% of the cases. Those who died were on average older than those who survived (77.5 vs. 67.3, $p = 0.04$) (Fig. 1). Using multivariate analysis, we could not found any significant predictors for death or complications.

Discussion

This is the largest study of transient left ventricular apical ballooning, involving 185 cases. It confirms that most cases involved are older women. New aspects were found, including differences between races, the large number of cases without stressful events and high frequency of complications.

While females make up the majority of those affected, there were no differences between females and males for presenting symptoms, precipitating stress and outcomes. The reason for female predominance is not known. Estrogen may play a role. Ueyama et al demonstrated in rats that estradiol diminishes the pathologic changes in heart rate induced by emotional stress [32]. No studies, including the present study, comment on the hormonal status of the female patients, therefore the role of menopause or hormone replacement therapy is unknown in apical ballooning.

There were a number of differences due to race. Most striking was the differences in the preceding stress. Caucasians were more then twice as likely to have emotional stress as the triggering event while Asians were 20 times more likely to have no precipitating stress. The reason for these differences is not known. Asians were also notably older by 8 years.

This is the first study concerning apical ballooning to examine complications in detail. In 6 of the larger studies on apical ballooning,

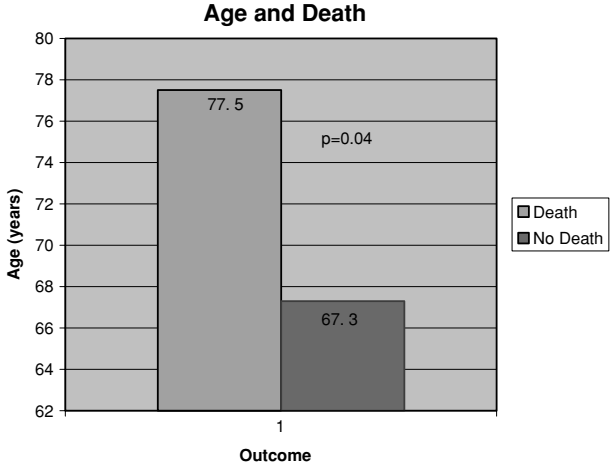

Fig. 1. *Increase risk of death in older patients with apical ballooning syndrome*

those with greater then 15 cases, only one gives more detailed information about complications [8–11,33–35]. This was Tsuchihashi et al's study of 88 patients [33]. In this study complications were detailed and the rates for shock were 15%, pulmonary edema 22%, ventricular tachycardia 9% and death 1% respectively. While this study detailed the rates of different complications, it didn't explore variables that could impact complications. In our study, we showed that T wave inversion and physical stress increased the risk of developing complications. We also showed that those who died were on average older than those who survived. This may impact treatment by identifying those at higher risk. Other variables likely need to be found to help identify those at risk. This could take the form of an echocardiogram. Echocardiogram could identify those with greater amounts of LV involvement, which may precipitate thrombus formation or heart failure and identify the need for mechanical or chemical support.

This study did not examine the cause or predisposing risk factors for apical ballooning syndrome. The cause of apical ballooning remains unknown. Wittstein et al. showed that plasma catecholamines were elevated at the time of presentation [8]. It is unknown if catecholamines caused the syndrome or were increased as a result of the syndrome. This study did show that women and older individuals are more likely to be affected. The left ventricle is smaller in women. This smaller left ventricular size, in the face of excess catecholamines, may predispose to the development of an outflow tract obstruction. The hyper-contractile base can create the outflow tract obstruction, increasing the intraventricular pressure gradient, causing a state of oxygen mismatch for the apex, and the apex ballooning. This would create the symptoms and signs associated with apical ballooning in spite of normal coronary arteries. As the pressure gradient subsides the apex has a chance to recover.

A recent prospective study examined patients admitted to the ICU with echocardiogram and found apical ballooning occurring in 28% of the cases [36]. This study is limited by not confirming the absence of obstructive coronary artery disease. However, it suggests that this syndrome is most likely under recognized.

Limitations

This study is a retrospective summary of reported cases limiting the study. It is possible that uncomplicated cases are under reported leading to overestimation of complications. The data were not uniform limiting our study.

Conclusion

Apical ballooning syndrome occurs in the majority of cases apical ballooning syndrome occurs in women and is associated with a high complication rate. There are significant differences in presenting symptoms between race and gender which warrant further investigation.

References

1. Dote K, Sato H, Tateishi H, et al. Myocardial stunning due to simultaneous multivessel coronary spasm: A review of 5 cases. *J Cardiol* 1991;21:203–214.
2. Desmet WJ, Adriaenssens BF, Dens JA. Apical ballooning of the left ventricle: First series in white patients. *Heart* 2003;89(9):1027–1031.
3. Marcu CB, Andresen KM, Donohue TJ. Transient apical ballooning of the left ventricle. *Med J Aust* 2004;181(10):572.
4. Ibanez B, Navarro F, Farre J, et al. A, Cordoba M. Takotsubo syndrome associated with a long course of the left anterior descending coronary artery along the apical diaphragmatic surface of the left ventricle. *Rev Esp Cardiol* 2004;57(3):209–216.
5. Lupi G. Transient ballooning of the left ventricle: A case report. *Ital Heart J* 2004;5(8):635–637.
6. Osherov A, Matetzky S, Beinart R, et al. Transient left ventricular apical ballooning (Tako-tsubo): The syndrome that mimics acute myocardial infarction. *Isr Med Assoc J* 2004;6(9):550–552.
7. Glockner D, Dissmann M, Behrens S. Atypical acute myocardial ischemia syndrome with reversible left ventricular (LV) wall motion abnormalities ("apical ballooning") without significant coronary artery disease. *Z Kardiol* 2004;93(2):156–161.
8. Wittstein IS, Thiemann DR, Lima JA, et al. Neurohumoral features of myocardial stunning due to sudden emotional stress. *N Engl J Med* 2005;352(6):539–548.
9. Sharkey SW, Lesser JR, Zenovich AG, et al. Acute and reversible cardiomyopathy provoked by stress in women from the United States. *Circulation* 2005;111(4):472–479.
10. Bybee KA, Prasad A, Barsness GW, et al. Clinical characteristics and thrombolysis in myocardial infarction frame counts in women with transient left ventricular apical ballooning syndrome. *Am J Cardiol* 2004;94(3):343–346.
11. Kurisu S, Sato H, Kawagoe T, et al. Tako-tsubo-like left ventricular dysfunction with ST-segment elevation: A novel cardiac syndrome mimicking acute myocardial infarction. *Am Heart J* 2002;143(3):448–455.
12. Fritz J, Wittstein IS, Lima JA, et al. Transient left ventricular apical ballooning: magnetic resonance imaging evaluation. *J Comput Assist Tomogr* 2005;29(1):34–36.
13. Nishikawa S, Ito K, Adachi Y, et al. Ampulla ('takotsubo') cardiomyopathy of both ventricles: Evaluation of microcirculation disturbance using 99mTc-tetrofosmin myocardial single photon emission computed tomography and doppler guide wire. *Circ J* 2004;68(11):1076–1080
14. Ito K, Sugihara H, Katoh S, et al. Nakagawa M. Assessment of takotsubo (ampulla) cardiomyopathy using 99mTc-tetrofosmin myocardial SPECT–comparison with acute coronary syndrome. *Ann Nucl Med* 2003;17(2):115–122.

15. Kawabata M, Kubo I, Suzuki K, et al. Tako-tsubo cardiomyopathy' associated with syndrome malin: Reversible left ventricular dysfunction. *Circ J* 2003;67(8):721–724.
16. Kyuma M, Tsuchihashi K, Shinshi Y, et al. Effect of intravenous propranolol on left ventricular apical ballooning without coronary artery stenosis (ampulla cardiomyopathy): Three cases. *Circ J* 2002;66(12):1181–1184.
17. Kurisu S, Inoue I, Kawagoe T, et al. Left ventricular apical thrombus formation in a patient with suspected tako-tsubo-like left ventricular dysfunction. *Circ J* 2003;67(6):556–558.
18. Witzke C, Lowe HC, Waldman H, et al. Images in cardiovascular medicine. Transient left ventricular apical ballooning. *Circulation* 2003;108(16):2014
19. Pison L, De Vusser P, Mullens W. Apical ballooning in relatives. *Heart* 2004;90(12):e67.
20. Nyui N, Yamanaka O, Nakayama R, et al. 'Tako-Tsubo' transient ventricular dysfunction: a case report *Jpn Circ J* 2000;64(9):715–719.
21. Connelly KA, MacIsaac AI, Jelinek VM. Stress, myocardial infarction, and the "tako-tsubo" phenomenon. *Heart* 2004;90(9):e52.
22. Peraira Moral JR, Segovia Cubero J, Oteo Dominguez JF, et al. A case of transient left ventricular apical ballooning with an unusual complication. *Rev Esp Cardiol* 2002;55(12):1328–1332.
23. Barriales Villa R, Bilbao Quesada R, Iglesias Rio E, et al. Transient left ventricular apical ballooning without coronary stenoses syndrome: importance of the intraventricular pressure gradient. *Rev Esp Cardiol* 2004;57(1):85–88.
24. Gallego Page JC, Lafuente Gormaz C, Dominguez Rodriguez P, et al. Rudilla M, Fuentes Manso R, Aguilera Saldana M. Transient ventricular dysfunction after emotional stress. *Rev Esp Cardiol* 2004;57(11):1124–1127.
25. Miyazaki S, Kamiishi T, Hosokawa N, et al. Reversible left ventricular dysfunction "takotsubo" cardiomyopathy associated with hyperthyroidism. *Jpn Heart J* 2004;45(5):889–894.
26. Yasuga Y, Inoue M, Takeda Y, et al. Tako-tsubo-like transient left ventricular dysfunction with apical thrombus formation: a case report. *J Cardiol* 2004;43(2):75–80.
27. Matsuoka K, Nakayama S, Okubo S, et al. Transient cerebral ischemic attack induced by transient left ventricular apical ballooning. *Eur J Intern Med* 2004;15(6):393–395.
28. Sasaki N, Kinugawa T, Yamawaki M, et al. Transient left ventricular apical ballooning in a patient with bicuspid aortic valve created a left ventricular thrombus leading to acute renal infarction. *Circ J* 2004;68(11):1081–1083.
29. Amaya K, Shirai T, Kodama T, et al. Ampulla cardiomyopathy with delayed recovery of microvascular stunning: A case report J Cardiol. 2003;42(4):183–188.
30. Kai R, Yasu T, Fujii M, et al. Apical ballooning by transient left ventricular dysfunction (so-called "ampulla" cardiomyopathy) associated with therapy for acute pulmonary thromboembolism: a case report. *J Cardiol* 2001;38(1):41–46
31. Ishikawa K. "Takotsubo" cardiomyopathy A syndrome characterized by transient left ventricular apical ballooning that mimics the shape of a bottle used for trapping octopus in Japan. *Intern Med* 2004;43(4):275–276.
32. Ueyama T, Hano T, Kasamatsu K, et al. Estrogren attenuates the emotional stress-induced cardiac responses in the animal model of Tako-tsubo. *J Cardiovascular Pharmacol* 2003;42 Suppl.
33. Tsuchihashi K, Ueshima K, Uchida T, et al. Transient left ventricular apical ballooning without coronary artery stenosis: a novel heart syndrome mimicking acute myocardial infarction. *J Am Coll Cardiol* 2001;38:11–18.
34. Abe Y, Kondo M, Matsuoka R, et al. Assessment of clinical features in transient left ventricular apical ballooning. *J Am Coll Cardiol* 2003;41:737–742.
35. Tsuchihashi K, Ueshima K, Uchida T, Oh-mura N, Kimura K, Owa M, Yoshiyama M, Miyazaki S, Haze K, Ogawa H, Honda T, Hase M, Kai R, Morii I. Angina pectoris-myocardial infarction investigations in japan. Transient left ventricular apical ballooning without coronary artery stenosis: a novel heart syndrome mimicking acute myocardial infarction. Angina pectoris-myocardial infarction investigations in Japan. *J Am Coll Cardiol* 2001;38(1):11–18.
36. Park JH, Kang SJ, Song JK, et al. Left ventricular apical ballooning due to severe physical stress in patients admitted to the medical ICU. *Chest* 2005;128(1):296–302.