# Clinical Characteristics and Outcome of Apical Ballooning Syndrome in Auckland, New Zealand

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Background: Apical ballooning syndrome (ABS) mimics myocardial infarction but is characterised by transient left ventricular (LV) dysfunction without significant coronary artery obstruction.

Methods: We prospectively identified 100 consecutive patients presenting in the Auckland region between March 2004 and July 2010 and obtained clinical, laboratory, electrocardiography, echocardiography, coronary angiography and long-term follow-up data.

Results: Chest pain or dyspnoea were the most common presenting symptom, 95% were women (mean age  $65\pm11$  years). An associated stressor was identified in two-thirds of patients, troponin was elevated in all patients, and one-third had ECG ST-elevation. There was a similar range of initial LV ejection fraction (EF), myocardial damage, LV recovery and prognosis in those with and without ST-elevation, and with and without identifiable stressors. One-quarter had a complicated in-hospital course. Lower admission LVEF, but not peak troponin level or ECG ST-elevation, was associated with a complicated in-hospital course. The mean follow-up was  $3.0\pm1.7$  years. One patient died in hospital. Four died late after discharge, all from non-cardiac causes. Seven had recurrent ABS.

Conclusion: In this large, prospective, New Zealand ABS cohort a quarter of patients had a complicated in-hospital course, but almost all recovered, recurrence was infrequent and long-term prognosis dependent on associated non-cardiac disease.

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### Introduction

A pical ballooning syndrome (ABS) (also known as Tako-tsubo cardiomyopathy or stress-induced transient left ventricular dysfunction) is an increasingly recognised subset of the broader group of acute coronary syndromes (ACS) characterised by acute but rapidly reversible left ventricular (LV) dysfunction in the absence of obstructive coronary disease. Prevalence of ABS is reported to be 1–2.5% in patients presenting with acute coronary syndrome (ACS) and 12% of women presenting with anterior ST-elevation myocardial infarction (STEMI) [1,2]. The condition tends to occur in postmenopausal women after a stressful event. The aetiology of ABS is currently poorly understood and likely to be complex but the association with stress and catecholamine surge has

lead many investigators to suspect that this is primarily a neurohormonal phenomenon mediated via coronary vasomotion or directly affecting the LV myocardium [3,4]. Although initially described in Japan, it has subsequently been reported in many countries around the world [5–8].

This study describes the clinical presentation and outcome of patients with ABS in a large New Zealand cohort. We also explored whether any characteristics at admission (e.g. the presence of a precipitating stressor or ST elevation) identified a heterogeneous subgroups of patients with a more complicated in-hospital course.

#### Method

The study population was prospectively identified from the three major public hospitals in the Auckland region (Middlemore Hospital, Auckland City Hospital and North Shore Hospital) between March 2004 and July 2010. The cohort comprised 100 consecutive patients who fulfilled the diagnostic criteria of ABS proposed by the Mayo Clinic group [9]: (1) transient hypokinesis, akinesis, or dyskinesis

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in the left ventricular mid segments with or without apical involvement; regional wall motion abnormalities that extend beyond a single epicardial vascular distribution; and frequently, but not always associated with a stressful trigger; (2) the absence of obstructive coronary disease or angiographic evidence of acute plaque rupture; (3) new ECG abnormalities (ST-segment elevation and/or T-wave inversion) or modest elevation in cardiac troponin; and (4) the absence of phaeochromocytoma and myocarditis. Clinical (age, gender, presentation, coronary risk factors), laboratory, electrocardiographic (ECG), echocardiographic and angiographic data of the study population were obtained at the time of the index admission. Late follow-up data was obtained by reviewing the electronic and paper medical records of each patient. After ABS diagnosis was made, clinical staff made specific enquiry regarding possible stressors. ST-segment elevation was defined as a new >1 mm ST deviation measured 80 ms after the J point in ≥2 contiguous leads and T-wave inversion as negative T waves >3 mm in amplitude in ≥2 contiguous leads not present on previous electrograms. All other ECG changes not fulfilling these criteria were defined as nonspecific ST-T-wave changes. Three different troponin assays were used in the three major public hospitals in Auckland, therefore the results from each were analysed separately. Coronary angiography was performed in all patients during the index hospitalisation. Coronary artery disease was defined as a  $\geq 50\%$  reduction in the luminal diameter of a major coronary artery. Coronary artery spasm was defined as a >50% focal or diffuse narrowing of an epicardial coronary artery not caused by a catheter that resolved after intracoronary nitroglycerin. Standard twodimensional Doppler echocardiography was performed in the acute phase in 92 patients for evaluation of the LV ejection fraction and regional wall motion abnormalities. Left ventriculography in the right anterior oblique projection was performed in 46 patients. Left ventricular function was assessed by reviewing the clinical reports of the echocardiography and left ventriculography performed in the acute phase, and from the reports of follow-up echocardiography and cardiac MRI in the recovery phase.

In-hospital complications including death, cardiogenic shock, requirement for intra-aortic balloon pump insertion, endotracheal intubation and ventilation, radiological pulmonary oedema, ventricular arrhythmias and use of inotropes were recorded. A "complicated in-hospital course" was defined as the patient having one or more of these complications. Post discharge mortality and rehospitalisation for recurrence of ABS were also recorded. Recurrent ABS was defined using the Mayo criteria, except that in most cases the coronary angiography was not repeated. The incidence of ABS in patients presenting with ABS in those admitted with suspected ACS is reported for the Middlemore Hospital catchment. At Middlemore Hospital all patients with suspected ACS admitted to CCU are captured in the Acute Predict registry [10]. This registry provides the denominator for estimating the incidence of ABS in those with suspected ACS.

The study was approved by the Northern Regional Ethics committee as a clinical audit (NTX/11/EXP/288).

**Table 1.** *Patient Clinical Characteristics.* 

	Total Population
n	100
Gender, n (%)	
Female	95 (95)
Age (years)	
$Mean \pm SD$	$65\pm11$
Ethnicity, n (%)	
European	75 (75)
NZ Maori	11 (11)
Pacific Islanders	8 (8)
Asians	5 (1)
Middle Eastern	1 (1)
Hypertension (%)	35 (35)
Diabetes (%)	11 (11)
Dyslipidaemia (%)	29 (29)
Current smoker (%)	
Current smoker	16 (16)
Admission medication	
Aspirin	36
Warfarin	3
Statins	25
Beta-blockers	17
Calcium channel blockers	13
ACE inhibitors	27

The descriptive data was presented as mean ± standard deviation, or median (interquartile range). The unadjusted survival was estimated for different outcomes (death or first recurrence of ABS) using the Kaplan–Meier method. Survival was measured from hospital admission to time of death or first recurrence. Data were analysed using SAS statistical package, version 9.2 (SAS Institute, Cary, NC).

#### Results

One hundred consecutive patients with ABS (95 females, 5 males) were included in the study. The clinical characteristics of all patients are presented in Table 1. The mean age at presentation was  $65\pm11$  years (median 66) and 95% were women. Seventy-five patients were European. Thirty-five patients had hypertension and 17 patients were on  $\beta$ -blockers before admission.

#### Incidence of ABS

In the Middlemore Hospital cohort, between November 2004 and February 2010, 36 patients had ABS. Of these, 33 were female. Over this period 957 females and 2176 males were admitted to CCU with a suspected ACS. The incidence of ABS in those with suspected ACS was therefore 3.4% for women and 0.1% for men.

#### *Symptoms and Precipitants*

Clinical presentation is presented in Table 2. The most common presenting symptoms were chest pain and or dyspnoea. Fourteen patients presented with pulmonary oedema. Five patients presented with a ventricular arrhythmia: three patients presented with ventricular fibrillation arrest and two patients had ventricular tachycardia. Seven patients presented with new atrial arrhythmia. Precipitating factors considered possible triggers for ABS are listed in Table 3. A stressful trigger

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