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Research Article

Young Patients with Frequent Attendance to the Emergency Department for Atypical Chest Pain

Win Wah[1]*, Pauline See Joon Seah[2], Huihua Li[3], Susan Yap[1], Qi En Hong[2] and Marcus Eng Hock Ong[1,4]

[1]Department of Emergency Medicine, Singapore General Hospital, Singapore

[2]Yong Loo Lin School of Medicine, National University of Singapore, Singapore

[3]Health Services Research and Biostatistics Unit, Division of Research, Singapore General Hospital, Singapore

[4]Health Services and Systems Research, Duke-NUS Graduate Medical School, Singapore

***Corresponding Author:** Win Wah, Department of Emergency Medicine, Singapore General Hospital, Singapore.

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Abstract

Background: Understanding the characteristics of young frequent attenders (FA) with atypical chest pain to the ED and clinical factors associated with cardiac Troponin T(cTnT) elevation could possibly help to avoid unnecessary hospital admissions for low risk patients.

Objective: This study aimed to describe the characteristics of young FA presenting to the ED with atypical chest pain and identify clinical factors associated with serial cTnT rise.

Methods: This was a retrospective study of patients aged ≤ 50 years with a primary diagnosis of atypical chest pain who attended an urban tertiary ED for 4 or more times in 2010. Based on serial cTnT level (> 0.01 ng/ml), patients and their visits were divided into 2 groups, elevated and normal cTnT. Logistic regression and Generalized Estimating Equations analyses were done to identify factors associated with the risk of elevated cTnT per unique patient and visit.

Results: A total of 149 young FA patients (300 visits) with an attending diagnosis of atypical chest pain were identified, in which 6% had elevated cTnT. All patients with elevated cTnT had at least one or more major cardiovascular risk factors. The most predictive factors for cTnT elevation were renal disease (OR = 33.65, 95% CI = 3.14 - 360.9), diabetes mellitus (OR = 15.79, 95% CI = 2.43 - 102.85) and stroke (OR = 30.39,95% CI = 1.14-811.4). 71.33% of the total visits were independently judged by two reviewers to be inappropriate (Kappa = 0.786).

Conclusion: This study found young FA with atypical chest pain and elevated cTnT had at least one or more major cardiovascular risk factors. Renal disease, diabetes and stroke were highly predictive of cTnT elevation.

Keywords: *Chest Pain; Emergency Department; Troponin T; Emergency Diagnosis*

Introduction

Frequent attenders (FA) are defined as patients who attended the Emergency Department (ED) four times or more in a year [1]. In Singapore, the number of ED visits has increased by 5 - 10% annually at major public hospitals [2]. Atypical chest pain was reported as one of the most frequent diagnosis among patients discharged from the ED [3]. Many clinicians establish the diagnosis of Acute Coronary Syndrome (ACS), angina and myocardial infarct (MI), in the presence of typical clinical features. The typical features of ACS are usually described as left-sided substernal pain, a compressive/strangling sensation worsened by exertion and relieved by rest that radiates to

the left arm [4]. Atypical chest pain is referred to as signs and symptoms that do not fit the typical complaints associated with myocardial ischemia [4]. However, characteristics of chest pain alone are not reliable for acute diagnosis of myocardial ischemia [4].

Cardiac troponins are the cardiac necrosis biomarkers of choice for diagnosing MI [5]. Cardiac troponin T (cTnT) is detected within 4 - 6 hours after onset of myocardial necrosis [5]. One meta-analysis showed serial cTnT had summary sensitivity 93% (95% CI, 85 - 97%) and specificity 85% (95% CI, 76 - 91%) for the diagnosis of MI with serial testing [5]. However, there are several clinical conditions that can lead to serum cTnT elevation other than myocardial necrosis and ischemia [6]. Due to the higher prevalence of ACS in elderly patients, comparatively limited studies have evaluated risk factors associated with cTnT elevation in young FA patients with atypical chest pain, a population which commonly presents to the ED.

Understanding the characteristics of young FA with atypical chest pain to the ED and the clinical factors associated with cTnT elevation could possibly help to avoid unnecessary hospital admissions for low risk patients. This study aimed to describe the characteristics of young FA presenting to the ED with atypical chest pain and to identify significant clinical factors associated with serial cTnT rise.

Methods

Setting and Design

Singapore is a modern city state with a population of 5.1 million in 2011 [7]. Singapore General Hospital (SGH) is Singapore's flagship tertiary hospital. Each year the SGH Department of Emergency Medicine sees more than 135,000 patients in the emergency care setting.

This was a retrospective study of young adult patients with a primary International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM) diagnosis of atypical chest pain treated at the SGH ED in 2010. Institutional Review Board approval was obtained to conduct this study.

Data Collection and Analysis

This study included patients aged 50 years or younger with a primary diagnosis of atypical chest pain who attended the SGH ED for 4 or more times in 2010. The conventional fourth-generation assay was used to measure the cTnT levels. The lower detection limit of the conventional assay was 0.01 ng/ml [6,8]. Studies showed that even minimally increased cTnT (> 0.01 ng/ml) may represent subclinical cardiac injury and have important clinical implications [8]. Patients were divided into 2 groups based on serial cTnT level: normal/undetectable (< 0.01 ng/ml) and elevated (> 0.01 ng/ml). In cases where there was an elevated baseline level, patients were only considered to have elevated cTnT if there was a serial rise (3 consecutive readings, each 3 hours apart) in cTnT. Electronic case records of each patient's visit were reviewed. Details of each visit were captured in electronic case record forms (Research Electronic Data Capture- REDCap Consortium).

All analyses were done using STATA 11 (STATA Corporation, College Station, TX USA). Univariate and multivariate stepwise logistic regression analyses were done to identify factors associated with the risk of elevated cTnT per unique patient. Univariate Generalized Estimating Equations (GEE) analyses were performed to evaluate factors associated with the risk of elevated cTnT per unique visit. Finally, a multivariate model was built starting with all possible important factors identified by univariate GEE.

Results

The selection process of cases for the study is displayed in figure 1. Patients with a primary diagnosis of atypical chest pain contributed around 5.5% of all patients who visited the ED in 2010. 498 unique patients attended to the ED for 4 or more times with at least 1 attending diagnosis of atypical chest pain and represented around 0.5% of all patients and 8.6% of atypical chest pain patients. Within that group, 149 unique patients (29.9%) were aged 50 years old or younger contributed to 300 ED visits with an attending diagnosis of atypical chest pain.

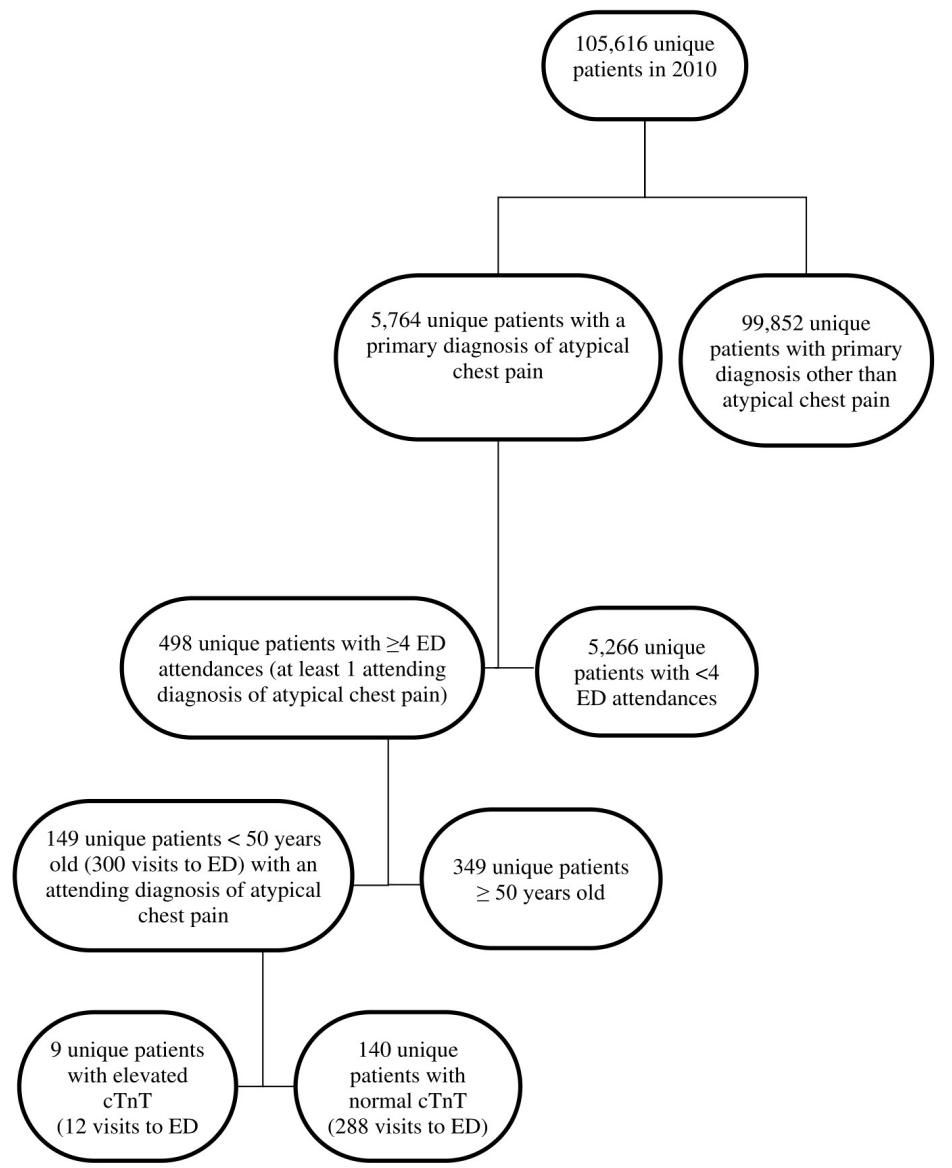

Figure 1: *Flow diagram for selection of cases.*

9 patients (6%) (12 visits) were identified with elevated cTnT levels. Of these 9 patients, 7 (10 visits) were admitted to hospital with suspected acute coronary syndrome. All were subsequently discharged in stable condition and had follow up treatment. The other 2 patients who were not admitted were referred to the specialist outpatient clinic. Of these 9 patients, one patient was re-admitted and died 17 days after the last hospital discharge due to ventricular fibrillation complicating non-segment ST elevation myocardial infarction. Two other patients died within a year after discharge although we were not able to obtain the cause of death.

Table 1 shows the univariate analysis of factors associated with cTnT elevation in young FA patients with atypical chest pain. The majority of patients were male and Chinese. Age > 30 years, heart disease, diabetes, hypertension, hyperlipidemia, stroke, renal disease and unemployment were the strongest univariate predictors of cTnT elevation. In the multivariate analysis, the most predictive risk factors for cTnT elevation were renal disease, diabetes mellitus and stroke (Table 2). The proportions of patients with no and 1 or more major cardiovascular risk factors were 62.4% and 37.6% respectively. All patients with elevated cTnT had at least one or more major cardiovascular risk factors. The proportion of patients with no and 1 or more social risk factors were 44.3% and 55.7% respectively. Patients with 2 or more social risk factors were significantly more likely to develop risk of cTnT elevation.

Variables	Elevated cTnT (%) 9 (6)	Normal cTnT (%) 140 (94)	*p* value	OR (95% CI)
Gender (%)				
Male	7 (77.8)	101 (72.1)	0.715	1.35 (0.27-6.79)
Ethnicity (%)				
Chinese	6 (66.7)	58 (41.4)	0.411	1.77 (0.45-6.87)
Malay	1 (11.1)	23 (16.4)	0.676	0.64 (0.08-5.33)
Indian	2 (22.2)	43 (30.7)	0.593	0.64 (0.13-3.23)
Age (%)				
> 30 years old	8 (88.9)	68 (48.6)	0.047	8.47 (1.03-69.53)
Medical History (%)				
Heart Disease	4 (44.4)	21 (15.0)	0.034*	4.53 (1.12-18.28)
Diabetes	6 (66.7)	16 (11.4)	<0.001*	15.5 (3.53-68.12)
Hypertension	7 (77.8)	26 (18.6)	0.001*	15.35 (3.01-78.18)
Hyperlipidemia	4 (44.4)	23 (16.4)	0.048*	4.07 (1.01-16.32)
Stroke	2 (22.2)	1 (0.7)	0.004*	39.71 (3.2-492.44)
Renal Disease	4 (44.4)	2 (1.4)	<0.001*	55.2 (8.11-375.62)
Cancer	0 (0)	4 (2.9)	-	
Asthma	0 (0)	40 (29)	-	
COPD	0 (0)	1 (0.7)	-	
Mental disorder	2 (22.2)	26 (18.6)	0.786	1.25 (0.25-6.38)
Alimentary disease	2 (22.2)	26 (18.6)	0.786	1.25 (0.25-6.38)
Epilepsy	1 (11.1)	2 (1.4)	0.092	8.62 (0.71-105.5)
Others	5 (55.6)	51 (36.4)	0.261	2.18 (0.56-8.49)
Major cardiovascular risk factors				
No	0 (0)	93 (66.4)	-	
1 or more	9 (100)	47 (33.6)	-	
Social History (%)				
Smoker	6 (66.7)	57 (40.7)	0.142	2.91 (0.7-12.12)
Heavy Drinker	2 (22.2)	8 (5.7)	0.078	4.71 (0.84-26.48)
Previously known to MSW	1 (11.1)	4 (2.9)	0.218	4.25 (0.42-42.58)
Known substance abuser	0 (0.0)	6 (4.3)	-	
Unemployed	3 (33.3)	6 (4.3)	0.003*	11.17 (2.23-55.82)
Lives alone	0 (0.0)	4 (2.9)	-	
Bad Debtor	3 (33.3)	23 (16.4)	0.209	2.54 (0.59-10.91)
Social risk factors				
No	1 (11.1)	65 (46.4)	Reference group	
1	2 (22.2)	57 (40.7)	0.505	2.28 (0.2-25.82)
2 or more	6 (66.7)	18 (12.9)	0.006*	21.67 (2.45-191.75)

Table 1: *Univariate analysis of factors associated with cardiac Troponin T elevation among young frequent attenders with atypical chest pain.*

*FA: Frequent Attender; cTnT: Cardiac Troponin T; OR: Odds Ratio; 95% CI: 95% Confidence Interval; COPD: Chronic Obstructive Pulmonary Disease; MSW: Medical Social Wor; *: Statistically Significant (p < 0.05)*

Variables	p value	OR (95% CI)
Age > 30 years old	0.841	1.35 (0.07 - 25.31)
Diabetes Mellitus	0.004*	15.79 (2.43 - 102.85)
Stroke	0.042*	30.39 (1.14 - 811.4)
Renal disease	0.004*	33.65 (3.14 - 360.9)
Heart disease	0.674	1.64 (0.16 - 16.31)
Hypertension	0.260	4.55 (0.33 - 63.7)
Hyperlipidemia	0.154	9.94 (0.42 - 234.59)
Unemployed	0.224	4.96 (0.38 - 65.46)

Table 2: *Multivariate analysis of factors associated with cardiac Troponin T elevation among young frequent attenders with atypical chest pain.*

*OR: Odds Ratio; 95% CI: 95% Confidence Interval; *: Statistically Significant (p < 0.05)*

Table 3 shows the clinical characteristics of each visit associated with cTnT elevation. Radiating chest pain and pain associated with reduced effort tolerance was non-significantly associated with increased risk of cTnT elevation at each visit. Those visits with elevated cTnT had significantly shorter ED length of stay and lower number of visits with Priority 3 status. Table 4 shows the substantial level of agreement (kappa = 0.786) between 2 clinical reviewers regarding the patient's medical status [9]. 71.33% of the total visits were independently judged by 2 reviewers to be inappropriate.

Variables	Elevated cTnT(%) 12 (4)	Normal cTnT (%) 288 (96)	OR (95% CI)	p-value
Location of chest pain (%)				
Central only	4 (33.3)	86 (29.9)	reference	
Left-sided	2 (16.7)	112 (38.9)	0.31 (0.07, 1.46)	0.139
Right-sided	1 (8.3)	37 (12.8)	0.63 (0.09, 4.23)	0.634
Others	5 (41.7)	53 (18.4)	1.82 (0.71, 4.67)	0.216
Character/Quality of Chest pain (%)				
Pressure/squeezing	2 (16.7)	67 (23.3)	0.54 (0.08, 3.75)	0.534
Stabbing/sharp	5 (41.7)	91 (31.6)	1.49 (0.38, 5.78)	0.567
Pulling	1 (8.3)	28 (9.7)	1.10 (0.21, 5.65)	0.909
Others	5 (41.7)	112 (38.9)	1.24 (0.39, 3.96)	0.717
Radiation (%)				
No Radiation	2 (16.7)	83 (28.8)	0.53 (0.15, 1.87)	0.322
Neck and left arm	2 (16.7)	19 (6.6)	2.39 (0.66, 8.65)	0.184
Back	3 (25.0)	31 (10.8)	3.12 (0.99, 9.86)	0.052
Others	6 (50.0)	160 (55.6)	0.79 (0.27, 2.26)	0.658
Associated Symptoms (%)				
Shortness of Breath	6 (50.0)	140 (48.6)	1.21 (0.35, 4.15)	0.762
Nausea and vomiting	2 (16.7)	16 (5.6)	2.47 (0.49, 12.48)	0.275
Diaphoresis	4 (33.3)	56 (19.4)	2.17 (0.78, 6.02)	0.138
Palpitations	1 (8.3)	25 (8.7)	1.14 (0.19, 6.96)	0.887
Reduced effort tolerance	2 (16.7)	15 (5.2)	3.68 (0.94, 14.38)	0.06
None of the above	4 (33.3)	124 (43.1)	0.61 (0.25, 1.50)	0.281
Triage Class (%)				
P1	2 (16.7)	9 (3.1)	reference	
P2	9 (75.0)	204 (70.8)	0.19 (0.03, 1.12)	0.067
P3	1 (8.3)	75 (26.0)	0.07 (0.01, 0.78)	0.031*
Mode of Arrival (%)				
Ambulance	1 (8.3)	12 (4.1)	reference	
Self	11 (91.7)	276 (95.8)	0.67 (0.16, 2.89)	0.591
Time spent in ED (%)				
Mean hours (SD)	2.83 (1.57)	4.93 (5.62)	0.83 (0.74, 0.93)	0.002*

Table 3: *Clinical characteristics of each visit associated with cardiac Troponin T elevation.*

cTnT: Cardiac Troponin T; OR: Odds Ratio; P1: Resuscitation and Critically-ill Patients; P2: Major Emergencies (Non-Ambulant); P3: Minor Emergencies (Ambulant),

*ED: Emergency Department; SD: Standard Deviation; *: Statistically Significant (p < 0.0.5)*

Medical Status (%)	Reviewer 2		Total (%)
Reviewer 1	Appropriate	Inappropriate	300 (100.0)
Appropriate	62 (75.6)	4 (1.8)	66
Inappropriate	20 (24.4)	214 (98.2)	234 (78%)
Total (%)	82	218 (72.6)	300
Kappa = 0.786			

Table 4: *Medical status agreement between 2 reviewers.*

Discussion

In this study, the diagnosis of atypical chest pain was made after excluding ACS with typical symptoms. The majority of young FA patients with atypical chest pain was Chinese, male and had a history of hypertension. More than one-third of those patients had one or more major cardiovascular risk factors which suggested risk for ACS. In the patients free of major cardiovascular risk factors, we did not find any patients with elevated cTnT. This study found young FA patients with atypical chest pain and elevated cTnT had at least one or more major cardiovascular risk factors. Renal disease, diabetes and stroke were highly predictive of cTnT elevation. The results of this study suggest that young FA with atypical chest pain and no major cardiovascular risk factors are a low-risk group and can possibly be discharged without extensive investigations. Conversely, those with risk factors warrant further investigation. Further studies are needed to validate these findings. This study finding is consistent with previous studies showing an association between elevated cTnT levels and high comorbidity and cardiovascular risk factors [8,10]. Those risk factors associated with cTnT elevation reflected the factors related to MI risk in the literature [11-14]. Poor life-style habits, socio-economic problems and lack of awareness of their own health might have contributed to ill health.

In this study, those visits with elevated cTnT had higher prevalence of radiating chest pain and reduced effort tolerance. This is clinically useful and consistent with previous literature [15]. Counter-intuitively, those visits with elevated cTnT level spent shorter hours in the ED. This is due to the fact that visits with elevated cTnT would have been admitted quickly for in-patient management while those with uncertain diagnosis (normal cTnT) were usually kept for 8 hours for further cardiac investigations in the ED.

Atypical chest pain can be caused by a wide range of etiologies, such as pulmonary, musculoskeletal, gastrointestinal, dermatologic, psychiatric and cardiovascular problems, including ACS and non-ACS [16-18]. Studies have shown that patients with atypical chest pain have a higher prevalence of psychiatric problems such as depression and anxiety and they are more likely to seek continued treatment at the ED or with a General Practitioner (GP) [16-18]. This study also showed patients with elevated cTnT had relatively high rates of mental disorders.

In Singapore, MI in the younger population (aged less than 50 years) represented only 11.1% of overall disease burden compared to 88.8% in patients over 50 years of age [19]. Nevertheless, the risk of MI in the young population should not be overlooked. Chest pain patients often present a diagnostic dilemma to the ED and it is important to differentiate ACS diagnosis from non-ACS.

This study found a small proportion (6%) of young FA patients with atypical chest pain developed cTnT elevation. One cohort study in the ED showed that fewer than half of patients with chest pain had a diagnosis of acute MI or unstable angina and over half of those patients did not necessarily need hospital admissions [20]. Studies have described inappropriate use of the ED as being non-emergency, non-urgent, due to minor illness and those cases that could have been handled by GP [21]. In this study, more than 70% of visits were categorized as inappropriate by 2 reviewers. This inefficient use of the health care system has enormous economic implications [22]. The use of prospectively validated chest pain protocols could improve clinical diagnostic accuracy. There is also a need for recognition of low risk patients to limit unnecessary hospital admissions and investigations [23].

One limitation of this study is that while elevated troponins are well accepted to reflect myocardial necrosis,24 troponin elevations can occur in clinical conditions other than ACS [25].

As this study was purely a retrospective chart review, we did not recall any patients to confirm if those with elevated cTnT were due to an episode of ACS or had falsely elevated cTnT. Although we were able to track subsequent mortality through the hospital electronic medical records, those who died at home or did not return to the same hospital might have been missed. Another limitation for this study was that patients' ECGs were not reviewed because they were not available for extraction at the time of the study.

There are several clinical conditions including complications from diabetes mellitus, hypertension, stroke, renal disease and other causes of myocardial necrosis (eg acute heart failure or myocarditis) which could elevate troponin level rather than ACS [25]. Additionally, elevated cTnT levels has shown to be an important prognostic indicator of poor health [26,27] as in our study. This study highlights a need to follow up long term prognosis outcomes among young patients with elevated cTnT.

Current guidelines recommended cTnT levels > 0.03 ng/ml as abnormal but this study used a serial rise of levels of cTnT above 0.01 ng/ml as being elevated [24]. Although cTnT can be used to detect myocardial necrosis with a high degree of sensitivity, single normal cardiac biomarker level cannot be used to rule out ACS [28]. This study did not account for the potential influence of false positive cTnT values [29].

This was a single center study and limited to young FA with chest pain. The results would not be generalizable to other populations. Prospective validation of these preliminary data in a large cohort is needed to confirm the findings. Other limitations of this study include a relatively small sample size and retrospective study design. Currently, there is no consensus opinion on what exactly defines atypical chest pain [30]. In the literature, approximately 20 different synonyms have described atypical chest pain due to its heterogeneous nature [30]. Whether chest pain is typical or not depends on one's perception, culture, gender, ethnicity and language. It also depends on the clinician's skills and the time spent evaluating the patient.

Conclusion

This study found young FA with atypical chest pain and elevated cTnT had at least one or more major cardiovascular risk factors. Renal disease, diabetes and stroke were highly predictive of cTnT elevation. Conversely, young patients with no major risk factors are at low risk and likely do not need extensive investigation. Further studies are needed to validate these findings.

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