

How common are non-acute coronary syndrome (ACS) diagnoses in patients with suspected ACS investigated with coronary angiography in New Zealand? (ANZACS-QI 58)

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ABSTRACT

BACKGROUND AND AIMS: The last two decades in New Zealand have seen increased availability of primary percutaneous coronary intervention (PCI) for ST-segment elevation myocardial infarction (STEMI) and early invasive coronary angiography (ICA) for other high-risk acute coronary syndrome (ACS) patients. One metric to assess the clinical appropriateness of these invasive strategies is to examine the false-positive rate for the investigation (ie, the rate of non-ACS diagnoses).

METHODS: All patients presenting to New Zealand public hospitals with suspected ACS who underwent ICA between 2015 and 2019 were recorded prospectively in the All New Zealand Acute Coronary Syndrome Quality Improvement registry. The cohort was divided according to clinical impression at presentation: (1) suspected STEMI <24h and (2) other suspected ACS. The final discharge diagnosis for each patient were obtained from the registry.

RESULTS: There were 6,059 (20%) patients with suspected STEMI <24h and 24,258 (80%) with other suspected ACS. Of the suspected STEMIs <24h, 90.6% had a final diagnosis of STEMI, 3.5% non-ST segment elevation ACS (NSTEMI) and only 5.9% had a non-ACS diagnosis. Of those with other suspected ACS, 80.7% had a final ACS diagnosis. Across all New Zealand district health boards (DHBs), the proportion of non-ACS diagnoses was similar for suspected STEMI presentations. However, for other suspected ACS, the proportions were higher in DHBs with rapid access to coronary interventional facilities than in those without (17.6% vs 7.0%, $p < 0.001$).

CONCLUSIONS: False-positive catheter laboratory activations for suspected STEMI patients are low across New Zealand. The differences in the proportion of non-ACS diagnoses according to DHB interventional capability for other suspected ACS requires further investigation.

Over the past two decades, there has been a decline in the incidence of acute coronary syndrome (ACS) and associated mortality worldwide, including in New Zealand.^{1,2} This is in part due to the increased acute reperfusion therapy for ST-elevation myocardial infarction (STEMI) patients presenting within 24 hours of symptom onset, using either primary percutaneous coronary intervention (PCI) or fibrinolysis with early angiography, and a routine invasive approach for those with high risk non-ST elevation ACS (NSTEMI) and other STEMI patients, both of which have been shown to improve patient outcomes.²⁻⁶ However, only 15–30% of patients who present with chest pain have ACS, and with the increase in primary PCI for STEMI and early coronary angiography for NSTEMI, there is potential for inappropriate invasive coronary angiography (ICA) with its associated patient and financial risks.^{7,8} In particular, the out-of-hours activation of catheter laboratories for suspected STEMI has a human cost for the staff involved in the roster, along with financial costs for the institution in maintaining the rosters.

Some studies have reported the rate of false-positive STEMI diagnosis,⁹⁻¹² but no studies have reported specifically on false-positive NSTEMI diagnosis and the appropriateness of ICA in this group of patients, despite NSTEMI comprising 60–70% of ACS presentations.^{3,13}

In this study we aim to identify the incidence and characteristics of false-positive ACS diagnosis and the respective rates of non-ACS conditions in patients presenting with suspected acute STEMI and other suspected ACS.

Method

Data source

Patients were identified from the All New Zealand Acute Coronary Syndrome Quality Improvement registry (ANZACS-QI). This is a nationwide web-based electronic database that captures all patients who present to a New Zealand public hospital with suspected ACS and who are investigated with coronary angiography. It records a mandatory dataset including admission and discharge dates, patient demographics, admission ACS risk stratification, cardiovascular risk factors,

investigations, management, in-hospital outcomes, discharge diagnosis and medications. Details of this registry and data collection have previously been reported. It is audited monthly to ensure more than 99% of patients have complete data entry throughout all New Zealand hospitals, and annual independent audits check the accuracy of data entry.^{14,15}

Study cohort

From the ANZACS-QI registry, consecutive patients 18 years or older presenting with suspected ACS who underwent coronary angiography between January 2015 to January 2019 were included. When patients had more than one suspected ACS admissions during the study period, only the first one was included. Patients who were not New Zealand residents were excluded. The study cohort comprised 30,317 patients. The cohort was divided into two groups according to the clinical impression at the time they entered the catheterisation laboratory:

1. ‘Suspected STEMI <24h’ includes all patients presenting to the catheter laboratory who were suspected of having a STEMI within 24 hours of symptom onset. In New Zealand, as elsewhere, these patients are considered for acute reperfusion therapy—either a primary PCI or fibrinolysis, which is usually followed by early angiography. The choice depends on how quickly patients can access an interventional cardiac catheter laboratory. In larger metropolitan centres most patients are managed with a primary PCI strategy, but for patients living within district health board (DHB) catchments without interventional capability, fibrinolysis is more common.¹⁶ For this analysis the sub-group of those with suspected STEMI <24h who underwent a primary PCI strategy was also identified.
2. ‘Other suspected ACS’ includes all patients with suspected unstable angina (UA), non-ST elevation myocardial infarction (NSTEMI) and those with suspected STEMI studied more than 24 hours after symptom onset.

Definitions

'Final ACS' or 'final non-ACS' are defined by the eventual discharge diagnosis, which is based on a combination of angiographic findings, cardiac biomarkers and clinical presentation, at the discretion of the primary medical practitioner. The diagnosis for each patient and their baseline characteristics were obtained from the ANZACS-QI registry. A 'false-positive' diagnosis refers to those who were suspected of having ACS initially but were discharged with a non-ACS diagnosis.

'Myocardial infarction' (MI) was defined according to the contemporary universal definition.¹⁷ UA is diagnosed if one of the following occurred in the absence of biochemical evidence of myocardial necrosis: (1) >20 minutes angina pain at rest, (2) de novo Canadian Cardiovascular Society class II or III angina or (3) recent destabilisation of stable angina with at least CCS class III angina.¹⁸ The final discharge diagnosis for each patient were reported as STEMI, NSTEMI (UA and NSTEMI) or non-ACS condition.

For the purposes of this analysis, DHBs were dichotomised into those with rapid access to a coronary interventional laboratory (Waitematā, Auckland, Counties Manukau, Bay of Plenty, Waikato, Capital and Coast, Hutt Valley, Nelson Marlborough, Canterbury and Southern DHBs) versus those without.

Non-invasive testing recorded prior to ICA included stress testing (exercise treadmill test, exercise stress echocardiogram, dobutamine stress echocardiogram or nuclear stress study) and CT coronary angiogram (CTCA).

'Obstructive coronary disease on ICA' refers to the presence of coronary stenosis 50% or more in any of the major epicardial coronary arteries.

Ethnicity was prioritised using a modified version of New Zealand Standard Ethnicity Data Protocols in the following order: Māori, Pacific, Indian, Other Asian and European/Other.¹⁹

Statistical analysis

Descriptive statistics for categorical data are presented as frequencies and column percentages, and continuous variables as median with interquartile ranges and/or

mean \pm standard deviation. Chi-squared test or Fisher exact test was used for comparison between two groups, and Wilcoxon Mann–Whitney U test or Student's T-test was used for continuous variables where appropriate. All P-values reported were two-tailed and a P-value <0.05 was considered significant. Data were analysed using SAS statistical package, version 9.4 (SAS Institute, Cary, NC).

Results

Between 2015 and 2019, a total of 30,317 patients 18 years of age or older who presented with suspected ACS were identified. This comprised 6,059 patients (20%) with suspected STEMI <24h and 24,258 patients (80%) with other suspected ACS.

Of the 6,059 patients with suspected STEMI <24h, 5,491 (90.6%) had a final diagnosis of STEMI, 212 (3.5%) had NSTEMI (191 NSTEMI and 21 UA) and 356 (5.9%) had non-ACS final diagnoses; 4,072 (67.2%) were managed with a primary PCI strategy, of whom 3,743 (91.9%) had a final diagnosis of STEMI, 61 (1.5%) had a final diagnosis of NSTEMI and 268 (6.6%) had a non-ACS final diagnosis.

Of those with other suspected ACS, 19,597 (80.8%) had a final ACS diagnosis, of which 17,993 (74.2%) were NSTEMI (14,590 NSTEMI and 3,403 UA) and 1,604 (6.6%) were STEMI. There were 4,661 (19.2%) with a non-ACS final diagnosis.

Regional variation in ACS diagnosis

Among patients suspected of having a STEMI, the rate of false-positive diagnoses across New Zealand DHBs was less than 12%. It appears to be independent of the total number of patients, as demonstrated in Figure 1. For the DHBs frequently using a primary PCI strategy, the false-positive rate was low albeit with some variation (Waitematā 9.9%, Auckland 9.1%, Counties Manukau 8.3%, Bay of Plenty 3.6%, Waikato 6.7%, Capital and Coast 2.6%, Hutt Valley 2.9%, Nelson Marlborough 3.9%, Canterbury 9.7% and Southern 7.8%, see Appendix Table 1).

In comparison, there is a wider range in non-ACS final diagnoses for other suspected ACS patients, up to 27.3%. Figure 2 demonstrates a general trend for more non-ACS final diagnoses in DHBs with ready access to

interventional catheter laboratories (17.6% (intervention capable DHBs) vs 7.0% (non-intervention capable DHBs), $p < 0.001$).

Characteristics and investigations in patients presenting with suspected ACS

There were 1,200 patients with non-ACS final diagnoses (78 suspected STEMI <24h and 1,122 other suspected ACS) who only had demographic data available in the registry. They were excluded from the subsequent cohort characteristics comparison, which left 29,117 patients. The demographic characteristics of this reduced cohort were virtually identical to the original cohort.

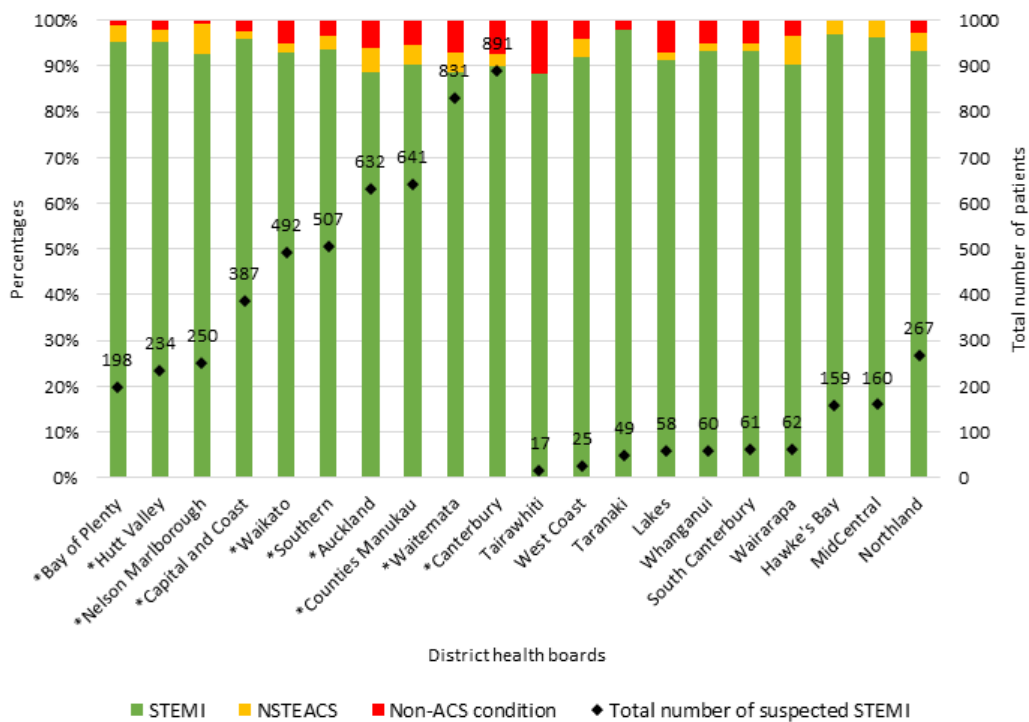
Suspected STEMI <24h: In patients presenting with suspected STEMI, those with non-ACS final diagnoses were likely to be younger (median age of STEMI 63 vs NSTEMI 63 vs non-ACS patients 59, $p < 0.007$) and female (26% vs 29% vs 41%, $p < 0.03$).

Patients with NSTEMI tend to have more cardiovascular comorbidities, including prior history of MI (12.9% vs 24.1% vs 11.5%, $p < 0.001$), congestive heart failure (CHF) (1.5% vs 4.7% vs 1.1%, $p < 0.013$) and diabetes mellitus (DM) (17.4% vs 26.4% vs 11.9%, $p < 0.02$). Conversely, those with non-ACS conditions had the lowest burden of cardiovascular comorbidities and risk factors. Patients with a final diagnosis of STEMI were intermediate among the other two groups. Pacific patients had the highest rate of non-ACS diagnoses compared to other ethnicities (Māori 4.6%, Pacific 8.3%, Indian 5.0%, Other Asian 4.0%, European 4.4%).

The frequency of a stress testing or CT coronary angiography (CTCA) performed prior to undergoing ICA in patients presenting with suspected STEMI was appropriately low (<5%).

Other suspected ACS: Patients who presented with other suspected ACS and

Figure 1: Stacked bar graph demonstrates proportion of final diagnoses in patients presenting to the catheter laboratory with suspected STEMI <24h by DHB (percentages, left-hand y-axis). Scatter plot demonstrates total number of suspected STEMI <24h patients in each DHB (absolute number, right-hand y-axis).



* Rapid intervention capable catheter laboratory available.
STEMI, ST-segment elevation myocardial infarction; NSTEMI, non-ST segment elevation acute coronary syndrome; ACS, acute coronary syndrome.

with non-ACS final diagnoses were also younger (median age of ACS 67 vs non-ACS 62, $p < 0.001$) and more likely to be female (31.6% vs 49.3%, $p < 0.001$). Patients with a final ACS diagnosis had a higher burden of established cardiovascular comorbidities and risk factors (ACS CVD 22.6% vs non-ACS 12.6%, $p < 0.001$). In contrast, those with non-ACS conditions were more likely to have underlying chronic obstructive pulmonary disease (COPD) (9.7% vs 11.5%, $p = 0.001$). The proportion with non-ACS diagnoses was similar across all ethnic groups.

The rate of stress testing was 8% (ACS 6.5% vs non-ACS 15.9%, $p < 0.001$). CTCA was performed in 5.5% (ACS 5.4% vs non-ACS 6.0%, $p = 0.206$).

Angiographic findings

Of the patients with suspected STEMI <24h, the majority of those with non-ACS final diagnoses had no significant

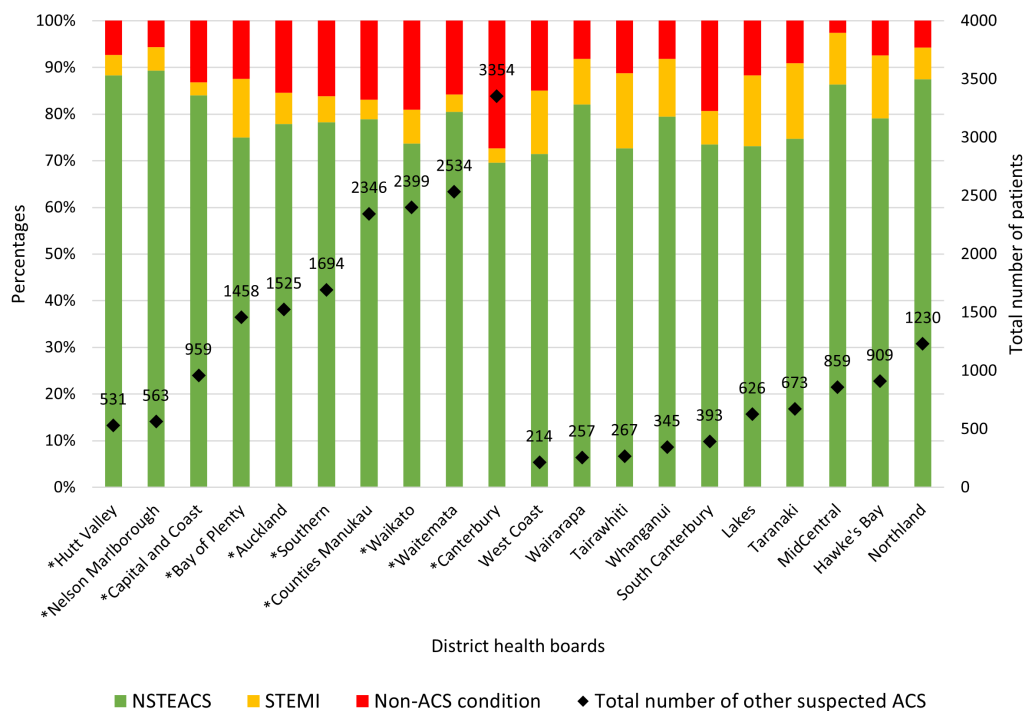
obstructive coronary disease (non-ACS 81.7% vs STEMI 3.5% vs NSTEMACS 13.7%, $p < 0.001$). Findings of significant single- or double-vessel obstructive coronary disease were more common in those with a final diagnosis of STEMI (75.1% vs 57.6% vs 13.3%, $p < 0.001$). Patients with a final diagnosis of NSTEMACS had higher proportion of three-vessel coronary disease or left-main stenosis than other groups (21.4% vs 28.8% vs 5.0%, $p < 0.001$).

A similar trend was demonstrated in patients with other suspected ACS. Among the non-ACS group, 79.6% had no significant obstructive coronary disease.

Non-ACS diagnoses

The non-ACS conditions most likely to raise suspicion for ACS on presentation and undergo ICA included stress cardiomyopathy (11.9%), arrhythmia (10.4%), stable angina (9.3%) and myocarditis (7.9%). In

Figure 2: Stacked bar graph demonstrates proportion of final diagnoses in patients presenting to the catheter laboratory with other suspected ACS by DHB (percentages, left-hand y-axis). Scatter plot demonstrates total number of other suspected ACS patients in each DHB (absolute number, right-hand y-axis).



* Rapid intervention capable catheter laboratory available
 STEMI, ST-segment elevation myocardial infarction; NSTEMACS, non-ST segment elevation acute coronary syndrome; ACS, acute coronary syndrome.

Table 1: Demographics, cohort characteristics and investigations (excludes 1,200 patients without clinical details other than basic demographic information).

	Suspected STEMI <24h (n=5981)						Other suspected ACS (n=23136)		
Final diagnosis	STEMI n=5491 (91.8%)	NSTEACS n=212 (3.5%)	Non-ACS n=278 (4.6%)	p-value, STEMI vs NSTEACS	p-value, STEMI vs non-ACS	p-value, NSTEACS vs non-ACS	ACS n=19597 (84.7%)	Non-ACS n=3539 (15.2%)	p-value
Age (years)									
<65 n (%)	3,125 (56.9)	123 (58.0)	181 (65.1)	0.749	0.007	0.109	9,145 (46.7)	2,117 (59.8)	<.001
≥65 n (%)	2,366 (43.1)	89 (42.0)	97 (34.9)				10,452 (53.3)	1,422 (40.2)	
Median (IQR)	63 (54 to 72)	63 (54 to 71.5)	58.5 (47 to 70)				67 (58 to 74)	62 (53 to 71)	
Sex, n (%)									
Male	4,064 (74.0)	151 (71.2)	164 (59.0)	0.365	<.001	0.005	13,401 (68.4)	1,796 (50.7)	<.001
Female	1427 (26.0)	61 (28.8)	114 (41.0)				6,196 (31.6)	1,743 (49.3)	
Ethnicity, n (%)									
Māori	542 (9.9)	20 (9.4)	27 (9.7)	0.010	0.025	0.956	2,174 (11.1)	452 (12.8)	0.001
Pacific	255 (4.6)	21 (9.9)	25 (9.0)				1,012 (5.2)	210 (5.9)	
Indian	312 (5.7)	14 (6.6)	17 (6.1)				884 (4.5)	136 (3.8)	
Other Asian	247 (4.5)	11 (5.2)	11 (4.0)				592 (3.0)	127 (3.6)	
European/Other	4,135 (75.3)	146 (68.9)	198 (71.2)				14,935 (76.2)	2,614 (73.9)	
Past medical history and risk factors									
History of CVD, n (%)	1,042 (19.0)	67 (31.6)	38 (13.7)	<.001	0.027	<.001	6,874 (35.1)	866 (24.5)	<.001
History of MI, n (%)	711 (12.9)	51 (24.1)	32 (11.5)	<.001	0.485	<.001	4,432 (22.6)	445 (12.6)	<.001
History CHF, n (%)	80 (1.5)	10 (4.7)	3 (1.1)	0.002	0.798	0.013	782 (4.0)	150 (4.2)	0.490
Diabetes, n (%)	955 (17.4)	56 (26.4)	33 (11.9)	0.001	0.017	<.001	4,828 (24.6)	602 (17.0)	<.001
COPD, n (%)	395 (7.2)	16 (7.5)	20 (7.2)	0.845	1.000	0.882	1,906 (9.7)	406 (11.5)	0.001
BMI									
Mean ± SD	28.5 ± 5.6	29.2 ± 5.8	27.7 ± 6.9	0.111	0.012	0.04	29.4 ± 6.0	29.6 ± 6.8	0.418
Total cholesterol (mmol/l)									
Median (IQR)	4.8 (4.0 to 5.7)	4.9 (3.8 to 5.9)	3.9 (3.5 to 4.8)	0.934	0.003	0.004	4.7 (3.8 to 5.7)	4.6 (3.6 to 5.4)	0.079

	Suspected STEMI <24h (n=5981)						Other suspected ACS (n=23136)		
LDL (mmol/l)									
Median (IQR)	2.9 (2.2 to 3.6)	2.8 (2.0 to 3.6)	2.4 (1.8 to 3.1)	0.335	<.001	<.001	2.7 (2.0 to 3.6)	2.7 (2.0 to 3.5)	0.211
Smoking status n (%)									
Non-smoker	2,364 (43.1)	98 (46.2)	145 (52.2)	0.233	0.011	0.183	8,475 (43.2)	1,891 (53.4)	<.001
Ex-smoker	1,426 (26.0)	60 (28.3)	59 (21.2)				6,914 (35.3)	1,042 (29.4)	
Current smoker	1,701 (31.0)	54 (25.5)	74 (26.6)				4,208 (21.5)	6,06 (17.1)	
Clinical presentation									
Killip Class									
I	4,943 (90.0)	192 (90.6)	260 (93.5)	<.001	0.055	0.225	17,838 (91.0)	3,213 (90.8)	0.652
II-IV	548 (10.0)	20 (9.4)	18 (6.5)				1,759 (9.0)	326 (9.2)	
Admission systolic BP (mmHg)									
Median (IQR)	133 (116 to 151)	135 (129 to 150)	130 (114 to 150)	0.565	0.352	0.274	141 (126 to 160)	138 (122 to 155)	<.001
Investigations									
Stress test done, n (%)	46 (0.9)	2 (0.9)	5 (1.8)	0.699	0.097	0.704	1,276 (6.5)	561 (15.9)	<.001
CTCA done, n (%)	224 (4.1)	11 (5.2)	8 (2.9)	0.425	0.320	0.189	1,065 (5.4)	211 (6.0)	0.206
LVEF*									
Normal (≥50%)	2,087 (38.0)	92 (43.4)		<.001	-	-	9,543 (48.7)		-
Mild (40 to 49%)	1,409 (25.7)	35 (16.5)	-				2,496 (12.7)		
Moderate or severe (<40%)	1,139 (20.7)	32 (15.1)					2,182 (11.1)		
No EF documented	856 (15.6)	53 (25)					5,376 (27.4)		
Revascularisation*	5,045 (91.9)	146 (67.9)	-	<.001	-	-	12,935 (66.0)	-	-
CABG	239 (4.4)	30 (14.2)	-	<.001	-	-	2,788 (14.2)	-	-
PCI	4,806 (87.5)	116 (54.7)	-	<.001	-	-	10,147 (51.8)	-	-

	Suspected STEMI <24h (n=5981)						Other suspected ACS (n=23136)		
Acute reperfusion strategy*									
Primary PCI	3,880 (70.7)	-	-	-	-	-	-	-	-
Thrombolysis	1,174 (21.4)	-	-	-	-	-	-	-	-
None	437 (8.0)	-	-	-	-	-	-	-	-
Angiographic findings									
CAD >50% stenosis on angiogram, n (%)									
No obstructive disease	192 (3.5)	29 (13.7)	227 (81.7)				3,025 (15.5)	2,811 (79.6)	
Single/double vessel disease	4,123 (75.1)	122 (57.6)	37 (13.3)	<.001	<.001	<.001	10,438 (53.4)	519 (14.7)	<.001
Three vessel disease and/or LMS >50%	1,172 (21.4)	61 (28.8)	14 (5.0)				6,087 (31.1)	203 (5.8)	
Time from admission to angiogram (days)									
n	5487	212	278				19,550	3,533	
Mean ± SD	0.24 ± 0.86	0.75 ± 1.35	0.19 ± 0.78	<.001	0.058	<.001	2.66 ± 2.36	2.66 ± 3.05	0.090

STEMI, ST-segment elevation myocardial infarction; NSTEMI, non ST elevation acute coronary syndrome; CVD, cardiovascular disease; MI, myocardial infarction; CHF, congestive heart failure; COPD, chronic obstructive pulmonary disease; BMI, body mass index; LDL, low density lipoprotein cholesterol; BP, blood pressure ;CTCA, CT coronary angiogram; LVEF, left ventricular ejection fraction; CABG, coronary artery bypass grafting; PCI, percutaneous coronary intervention; CAD, coronary artery disease; LMS, left main stem.

*Data regarding LVEF and revascularization are not collected for non-ACS patients in the ANZACS-QI registry.

patients suspected of STEMI <24h, stress cardiomyopathy (23%), myocarditis (13.3%) and pericarditis (14.4%) were most common, whereas stress cardiomyopathy (11.1%), arrhythmia (10.7%) and stable angina (10%) were more common in those suspected of having other ACS (see Appendix Table 2 for a detailed breakdown).

Discussion

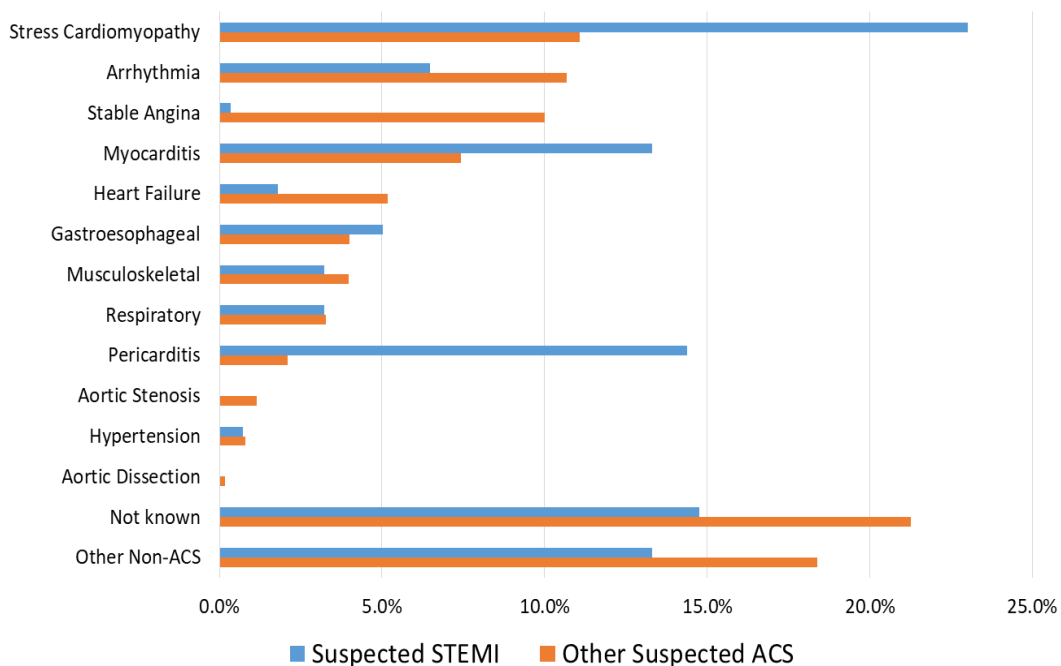
This nationwide ANZACS-QI study demonstrates one in twenty patients undergoing ICA for a suspected acute STEMI <24h had a non-ACS diagnosis. Of the sub-group managed with a primary PCI strategy, the proportion was similar. Of patients with other suspected ACS, one in five had a non-ACS final diagnosis. Half of non-ACS final presentations were for other cardiac-related conditions. For patients investigated with other suspected ACS, the rate of non-ACS diagnosis was greater in DHBs with interventional capability, but for those with suspected STEMI the rate was similarly low across all DHBs.

Suspected STEMI <24h

It is reassuring that the rate of non-ACS diagnosis across the DHBs was low,

suggesting that current guidelines are generally working well for selecting the appropriate patients for acute coronary angiography. However, even in the high-volume centers, there was some variability, with false-positive rates approaching 10% in the metropolitan Auckland and Waikato DHBs compared to 3% in the Wellington region. We are unable to determine from this study whether this DHB variation is because the criteria and processes to activate the catheter laboratories are too restrictive, resulting in some patients who should be studied early being missed, or too liberal, resulting in unnecessary activations with the associated patient risks and staff impacts. Our false-positive rate is relatively low, however, compared to those reported in other series, which can range from 5% to 40%.^{9-12,20,21} The wide variability in reported rates can be partially explained by the different criteria used to define a false-positive diagnosis of STEMI. In some studies, it is based on the absence of angiographically identifiable lesions and/or absence of myocardial necrosis biomarkers. In others, combinations of angiographic and clinical data or a discharge diagnosis other than STEMI have been used.^{9,10,12} We defined

Figure 3: Proportion of non-ACS diagnoses according to suspected ACS sub-types.



'false-positive' as a discharge diagnosis of non-ACS condition. Of the 'true positives', the majority were STEMI, with a very small proportion (less than 5%) of other NSTEMI diagnoses. Although these NSTEMI cases also have a high rate of revascularisation, they would not necessarily require this performed on as urgently.

The National Cardiac Network and New Zealand ambulance services have recently developed the National Out-of-Hospital STEMI Pathway to improve STEMI care.²² This pathway stipulates time frames for reperfusion and recommends criteria for entering the primary PCI pathway. Ongoing audit of false-positive cases will be important to ensure that patients are not harmed by inappropriate referrals for urgent angiography.

The non-ACS conditions most likely to mimic a STEMI on presentation, and therefore to be considered during the acute clinical assessment, included stress cardiomyopathy (23%), myocarditis (13.3%) and pericarditis (14.4%). ICA is appropriately performed as a diagnostic tool for these conditions that are associated with marked ECG changes and symptoms that can mimic potentially life-threatening STEMI.

Other suspected ACS

In contrast, there is a paucity of prior data on false-positive rates in other suspected ACS presentations. We have previously reported the overall rate of coronary angiography for ACS in New Zealand to be lower in comparison to similar European countries.¹⁻³ This is even more pronounced in non-interventional DHBs.²³ Although at 19.2% the non-ACS rate for suspected other ACS in our study is higher than for suspected STEMI, it is still much lower than the proportion of patients presenting with chest pain who have a final diagnosis of ACS. This is consistent with the use of diagnostic pathways to select those more likely to have ACS for invasive angiography. These patients have less well defined ECG changes and more cardiovascular comorbidities, in particular pre-existing history of MI and diabetes mellitus, which may lower the threshold for ICA in equivocal presentations. Because of its role as a non-urgent diagnostic test, a higher false-positive rate is appropriate for this group of patients. The reasons for the observed lower proportion

of non-ACS diagnoses in DHBs without rapid access to coronary intervention requires further investigation, but possible reasons include variation in referral practice and greater use of non-invasive investigations for case selection. Although the use of non-invasive investigation was low in this study, the registry does not capture patients who had a non-invasive test and were not referred for angiography.

As for suspected STEMI patients, around half of the non-ACS diagnoses were cardiac related—stress cardiomyopathy (11.1%), arrhythmia (10.7%) and stable angina (10%) were the common non-ACS diagnoses.

A third of patients with a final NSTEMI diagnosis who had angiography did not require revascularisation. There are recent studies assessing the utility of non-invasive imaging in reducing unnecessary invasive tests. The use of CTCA demonstrated a high diagnostic accuracy to rule out significant coronary artery disease in patients with NSTEMI in the VERDICT trial.²⁴ Likewise, initial cardiac MRI or CTCA appears to reduce unnecessary invasive coronary angiography in CARMEN.²⁵ However, the RAPID-CTCA trial was unable to show any benefit in early CTCA utilisation when hard end-points such as death and myocardial infarction were assessed.²⁶ Non-invasive imaging as a routine diagnostic tool in suspected ACS is likely to evolve in the near future.

Demographic considerations

We found that women suspected of having a STEMI or other ACS were more likely to have a non-ACS diagnosis,^{9,10,12} which is similar to the findings reported in other studies. This may reflect the known greater difficulty in making ACS diagnoses due to atypical and equivocal symptoms more often observed in women.^{5,18} Moreover, stress cardiomyopathy, the most common non-ACS diagnosis in our study (suspected STEMI 23%, other suspected ACS 11.1%), occurs predominantly in women, which may contribute to the gender differences.^{5,17,18} Non-ACS diagnoses were also more common in younger patients. This may represent their lower prevalence of atherosclerotic disease relative to other conditions. It is also possible that clinicians are more likely to refer these patients when the presentation is equivocal.

Ethnic differences in false-positive STEMI diagnoses in non-Europeans have been reported on internationally, such as higher rates of false-positive STEMI in African Americans in the Activate-SF Registry.¹⁰ In our study, Pacific patients appear to have a higher rate of false-positive diagnosis in comparison to other ethnicities when presenting with a suspected STEMI, but not in suspected other ACS. A recent study by Grey et al demonstrated that ischaemic heart disease (IHD) mortality for Māori and Pacific people remains twice that for Europeans in New Zealand, despite an overall declining trend in IHD deaths and hospitalisations across all ethnic groups—albeit this decline was smaller among Pacific people.²⁷ It is therefore conceivable that the diagnostic threshold for interpreting an equivocal presentation or ECG as a STEMI in Pacific patients may be lower. However, it is unclear why this was not observed in Māori patients and suspected other ACS patients in our study. This highlights a perspective for future studies to assess diagnostic differences between ethnic groups in ACS.

Limitations

The study cohort was patients with suspected ACS who were referred and underwent ICA. We have no information regarding how many patients with ACS might have been missed due to the condition not being suspected and/or not being

referred for ICA. All MIs have been included as final ACS diagnoses for this study. There is a small proportion of NSTEMI cases (6%) recorded as Type II MI in the cohort. Whilst reallocation of Type II MIs to the non-ACS group would increase the false-positive rate, this may be misleading because the cases clinically selected for invasive coronary angiography often requires it to make the diagnosis and a third of these patients received revascularisation for stable coronary artery disease. Although the final ACS and broad non-ACS diagnoses were available and reported for all patients, the more detailed non-ACS diagnoses and other data were not captured. This occurred in a small number of DHBs, making systematic bias unlikely.

Conclusions

Patients who present with suspected ACS and have a final non-ACS diagnosis were more likely to be younger, female and have fewer cardiovascular comorbidities. False-positive catheter laboratory activations for suspected STEMI <24h patients are generally low across New Zealand. The difference in the proportion of non-ACS diagnosis in other suspected ACS presentations between DHBs with and without rapid access to coronary interventional facilities requires further investigation.

Competing interests:

Nil.

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REFERENCES

1. Wang TKM, Grey C, Jiang Y, et al. Trends in cardiovascular outcomes after acute coronary syndrome in New Zealand 2006–2016. *Heart*. 2020.
2. Timmis A, Townsend N, Gale CP, et al. European Society of Cardiology: Cardiovascular Disease Statistics 2019. *European Heart Journal*. 2019; 41:12-85.
3. Benjamin EJ, Muntner P, Alonso A, et al. Heart Disease and Stroke Statistics-2019 Update: A Report From the American Heart Association. *Circulation*. 2019; 139:e56-e528.
4. Wang TKM, Grey C, Jiang Y, Jackson R, Kerr A. Epidemiology of acute coronary syndrome by subtype in New Zealand 2006–2016: an ANZACS-QI nationwide linkage study of hospitalisation, procedures and case fatality. *European Heart Journal*. 2019; 40.
5. Ibanez B, James S, Agewall S, et al. 2017 ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation: The Task Force for the management of acute myocardial infarction in patients presenting with ST-segment elevation of the European Society of Cardiology (ESC). *European Heart Journal*. 2017; 39:119-77.
6. ST-elevation myocardial infarction: New Zealand Management Guidelines, 2013. *New Zealand Medical Journal*. 2013; 126:127-64.
7. Launbjerg J, Fruergaard P, Hesse B, Jorgensen F, Elsborg L, Petri A. Long-term risk of death, cardiac events and recurrent chest pain in patients with acute chest pain of different origin. *Cardiology*. 1996; 87:60-6.
8. Lindsell CJ, Anantharaman V, Fau - Diercks D, Diercks D, Fau - Han JH, et al. The Internet Tracking Registry of Acute Coronary Syndromes (i*trACS): a multicenter registry of patients with suspicion of acute coronary syndromes reported using the standardized reporting guidelines for emergency department chest pain studies. *Annals of Emergency Medicine*.
9. Regueiro A, Fernandez-Rodriguez D, Freixa X, et al. False Positive STEMI Activations in a Regional Network: Comprehensive Analysis and Clinical Impact. Results From the Catalan Codi Infart Network. *Rev Esp Cardiol (Engl Ed)*. 2018; 71:243-9.
10. McCabe JM, Armstrong EJ, Kulkarni A, et al. Prevalence and factors associated with false-positive ST-segment elevation myocardial

- infarction diagnoses at primary percutaneous coronary intervention-capable centers: a report from the Activate-SF registry. *Arch Intern Med*. 2012; 172:864-71.
11. Lu J, Bagai A, Buller C, et al. Incidence and characteristics of inappropriate and false-positive cardiac catheterization laboratory activations in a regional primary percutaneous coronary intervention program. *Am Heart J*. 2016; 173:126-33.
 12. Larson DM, Menssen KM, Sharkey SW, et al. "False-Positive" Cardiac Catheterization Laboratory Activation Among Patients With Suspected ST-Segment Elevation Myocardial Infarction. *JAMA*. 2007; 298:2754-60.
 13. Townsend N, Wilson L, Bhatnagar P, Wickramasinghe K, Rayner M, Nichols M. Cardiovascular disease in Europe: epidemiological update 2016. *Eur Heart J*. 2016; 37:3232-45.
 14. Kerr A, Williams MJ, White H, et al. The All New Zealand Acute Coronary Syndrome Quality Improvement Programme: Implementation, Methodology and Cohorts (ANZACS-QI 9). *New Zealand Medical Journal*.
 15. Kerr AJ, Lee M, Jiang Y, et al. High level of capture of coronary intervention and associated acute coronary syndromes in the all New Zealand acute coronary syndrome quality improvement cardiac registry and excellent agreement with national administrative datasets (ANZACS-QI 25). *New Zealand Medical Journal*. 2019; 132:19-29.
 16. Kerr A, Lee M, Grey C, et al. Acute reperfusion for ST-elevation myocardial infarction in New Zealand (2015-2017): patient and system delay (ANZACS-QI 29). *The New Zealand medical journal*. 2019; 132:41-59.
 17. Thygesen K, Alpert JS, Jaffe AS, et al. Fourth universal definition of myocardial infarction (2018). *European Heart Journal*. 2018; 40:237-69.
 18. Roffi M, Patrono C, Collet J-P, et al. 2015 ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation: Task Force for the Management of Acute Coronary Syndromes in Patients Presenting without Persistent ST-Segment Elevation of the European Society of Cardiology (ESC). *European Heart Journal*. 2016; 37:267-315.
 19. Health Mo. HISO 10001:2017 Ethnicity Data Protocols. Wellington: Ministry of Health., 2017.
 20. Lange DC, Rokos IC, Garvey JL, Larson DM, Henry TD. False Activations for ST-Segment Elevation Myocardial Infarction. *Interv Cardiol Clin*. 2016; 5:451-69.
 21. Lange DC, Conte S, Pappas-Block E, et al. Cancellation of the Cardiac Catheterization Lab After Activation for ST-Segment-Elevation Myocardial Infarction. *Circ Cardiovasc Qual Outcomes*. 2018; 11:e004464.
 22. New Zealand National Out-of-Hospital STEMI Pathway. New Zealand National Cardiac Network, 2018.
 23. Williams MJA, Harding SA, Devlin G, et al. National variation in coronary angiography rates and timing after an acute coronary syndrome in New Zealand (ANZACS-QI 6). *New Zealand Medical Journal*. 2016; 129:66-78,6.
 24. Linde JJ, Kelbæk H, Hansen TF, et al. Coronary CT Angiography in Patients With Non-ST-Segment Elevation Acute Coronary Syndrome. *J Am Coll Cardiol*. 2020; 75:453-63.
 25. Smulders MW, Kietselaer B, Wildberger JE, et al. Initial Imaging-Guided Strategy Versus Routine Care in Patients With Non-ST-Segment Elevation Myocardial Infarction. *J Am Coll Cardiol*. 2019; 74:2466-77.
 26. Gray AJ, Roobottom C, Smith JE, et al. The RAPID-CTCA trial (Rapid Assessment of Potential Ischaemic Heart Disease with CTCA) - a multicentre parallel-group randomised trial to compare early computerised tomography coronary angiography versus standard care in patients presenting with suspected or confirmed acute coronary syndrome: study protocol for a randomised controlled trial. *Trials*. 2016; 17:579.
 27. Grey C, Jackson R, Wells S, et al. Trends in ischaemic heart disease: patterns of hospitalisation and mortality rates differ by ethnicity (ANZACS-QI 21). *New Zealand Medical Journal*. 2018; 131:21-31.