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Non-specific chest pain and subsequent serious cardiovascular readmissions

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ABSTRACT

Background: The rates of readmission for serious cardiovascular events among patients admitted with a diagnosis of non-specific chest pain are unknown.
Methods: A national retrospective cohort study in the United States was undertaken to evaluate the rates, trends and predictors of readmission for serious cardiovascular events (acute coronary syndrome (ACS), pulmonary embolism (PE) and aortic dissection (AD)) after an inpatient episode with a primary diagnosis of non-specific chest pain.
Results: Among 1,172,430 patients with an index diagnosis of non-specific chest pain between 2010 and 2014, 2.4% were readmitted with an ACS, 0.4% with a PE and 0.06% with an AD within 6 months of discharge. Predictors of ACS readmissions were diabetes (OR 1.49 95% CI 1.17–1.32), coronary artery disease (OR 2.29 95% CI 2.15–2.44), previous percutaneous coronary intervention (OR 1.65 95% CI 1.56–1.75), previous CABG (OR 1.52 95% CI 1.43–1.61) and discharge against medical advice (OR 1.94 95% CI 1.78–2.12). Female patients (OR 0.82 95% CI 0.78–0.86) and patients in whom a coronary angiogram was undertaken (OR 0.48 95% CI 0.45–0.52) were less likely to be readmitted for ACS. For PE, predictors of readmission were pulmonary circulatory disorder (OR 2.20 95% CI 1.09–4.43), anemia (OR 1.62 95% CI 1.40–1.86) and cancer (OR 4.15 95% CI 3.43–5.02). Peripheral vascular disease (OR 8.63 95% CI 5.47–13.60), renal failure (OR 2.08 95% CI 1.34–3.24) were predictors of AD.
Conclusions: Non-specific chest pain may not be a benign condition as readmissions for serious cardiovascular events occur in 3% of patients within 180 days. Research is needed to define measures that may mitigate readmissions among these patients.

1. Introduction

In the United States, 6 million patients present with chest pain to the emergency department (ED) each year, at an estimated cost of $8 billion [1]. These presentations account for approximately 5% of all ED visits; 65% of patients are subsequently admitted to the hospital, representing a quarter of all emergency medical admissions [2]. An important group of these patients are those diagnosed with non-specific chest pain which was introduced in order to describe the subset of patient not explained by a coronary ischemic etiology [3]. This diagnosis of exclusion accounts for approximately 50% of chest pain related emergency department visits [4].

The primary goal in the evaluation of patients with non-specific chest pain is to accurately identify patients with acute coronary syndrome (ACS) and other serious cardiovascular conditions [5]. Once serious causes of chest pain requiring immediate attention have been ruled out, it is generally safe to discharge patients and investigate those with suspected coronary artery disease as out-patients [4].

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Other potentially life-threatening conditions can also present with symptoms of non-specific chest pain including pulmonary embolism [6] and aortic dissection [7]. However, diagnostic work-ups may not be 100% sensitive or specific, and important diagnoses may have gone undetected on the initial admission. The literature on non-specific chest pain is limited and there are no prior national studies.

The aim of this study is to evaluate the rates of readmission for ACS, pulmonary embolism and aortic dissection among patients in an unselected national cohort previously diagnosed with non-specific chest pain during an admission in the prior 6 months.

2. Methods

The Nationwide Readmissions Database (NRD) contains national hospitalization and rehospitalization data for patients of all ages within the United States, which is produced by the Healthcare Cost and Utilization Project of the Agency for Healthcare Research and Quality. The NRD collects inpatient data and the current analysis does not contain information about emergency department discharges. The NRD contains a de-identified unique patient linkage number, which allows for the determination of readmissions by tracking of patients across hospitals within a calendar year. The annualized nature of NRD means that tracking patients across calendar years is not possible.

We included patients, aged 18 years or older, with a primary diagnosis of non-specific chest pain who were discharged between 2010 and 2014 with at least 180-day follow up. Non-specific chest pain was defined by the International Statistical Classification of Disease and Related Health Problems (ICD) 9 codes 786.50 (CHEST PAIN, UNSPECIFIED), 786.51 (PRECORDIAL PAIN), 786.52 (PLEURITIC PAIN) and 786.59 (OTHER CHEST PAIN). Patients were excluded if they died during index admission, had index admissions with percutaneous coronary intervention (PCI), discharged during the months July to December (thus lacking 180 days of follow up) or had a first readmission that was classified as elective. We collected data on patient demographics, comorbidities, hospital characteristics and tests from codes in the NRD codes, ICD-9 codes and Elixhauser comorbidity codes as described in Supplemental Data 1.

The primary outcome of the study was unplanned readmission within 180 days for a serious cardiovascular event defined by a primary diagnosis of ACS (410.0*–410.9* 411.1*), pulmonary embolus (415.1*) or aortic dissection (441.0*). We also determined the cost of the readmission, length of stay and rate of death during readmission.

Statistical analysis was performed on Stata 14.0 (College Station, TX). Estimated population sizes were determined by using the survey estimation command in Stata (SVY) with the NRD discharge weight (DISCWT). Estimated crude number of admissions for non-specific chest pain and readmission rate for each serious cardiovascular disease was plotted over the years of the study. Time to readmission for serious cardiovascular causes was displayed with histograms. Descriptive statistics are presented according to the presence or absence of readmission for a serious cardiovascular cause and receipt of each group of investigations. Multiple logistic regressions were used to investigate the associations of all the variables previously described to the readmission for each serious cardiovascular disease and the variables described and their association with the receipt of investigation. For the purposes of statistical analyses for the group of patients where investigations were performed, we defined any test as receipt of test for ACS, pulmonary embolism and aortic dissection. The effect of investigations on each serious cardiovascular cause for readmission was explored graphically and subgroup analysis based on receipt of CT thorax and radioisotope scan was performed.

3. Results

There were 2,369,384 patients admitted with an index diagnosis of non-specific chest pain and, after removal of patients according to the exclusion criteria, 1,172,430 patients were included in the analysis (Supplementary Fig. 1). The number of admissions with a primary diagnosis of non-specific chest pain decreased over time from 130,604 in 2010 to 75,906 in 2014 (Fig. 1). During this time there was a modest rise in the proportion of patients receiving in-patient investigation from 20.5% to 21.2% (Fig. 1). The rates of readmissions for acute coronary syndrome, pulmonary embolism and aortic dissection are shown in Supplementary Figure 2.

Among the patients with a diagnosis of non-specific chest pain, 2.4% ($n = 27{,}930$) were readmitted with ACS, 0.4% ($n = 4751$) with a pulmonary embolus and 0.06% ($n = 566$) with an aortic dissection within 6 months of discharge with the time to readmission (up to 180 days) shown in Supplementary Fig. 3. The daily rate of readmission for ACS, pulmonary embolus and aortic dissection was highest during the first few days after discharge with a diagnosis of non-specific chest pain, with a progressive decline in readmissions up to 50 days following discharge.

Patient characteristics according to readmission status are shown in Table 1. Patients readmitted with a serious cardiovascular event were older compared to those not readmitted for serious cardiovascular event (64.4, 61.3 and 64.1 for ACS, pulmonary embolism and aortic dissection, respectively compared to 60.0 years with no readmission). The majority of those who were readmitted with pulmonary embolus were female (55.7%), where the majority of those readmitted for ACS or aortic dissection were male (55.1% and 54.4%, respectively). Medicare coverage was more prevalent among those readmitted for serious cardiovascular events (59.6% for ACS, 55.3% for pulmonary embolism and 56.9% for aortic dissection compared to 42.7% for non-Medicare patients) compared to those not readmitted for a serious cardiovascular cause. The cost for the first index chest pain admission in patients later diagnosed with pulmonary embolism ($6276) and aortic dissection ($6616) was greater than patients with no readmission ($5288) or readmission for ACS ($5299).

The outcomes for patients with serious cause for readmissions are shown in Table 1. The cost of the readmission was $17,708 for ACS, $18,412 for pulmonary embolism and $31,270 for aortic. The length of stay for readmission was 5.4 days, 8.6 days and 8.7 days and the

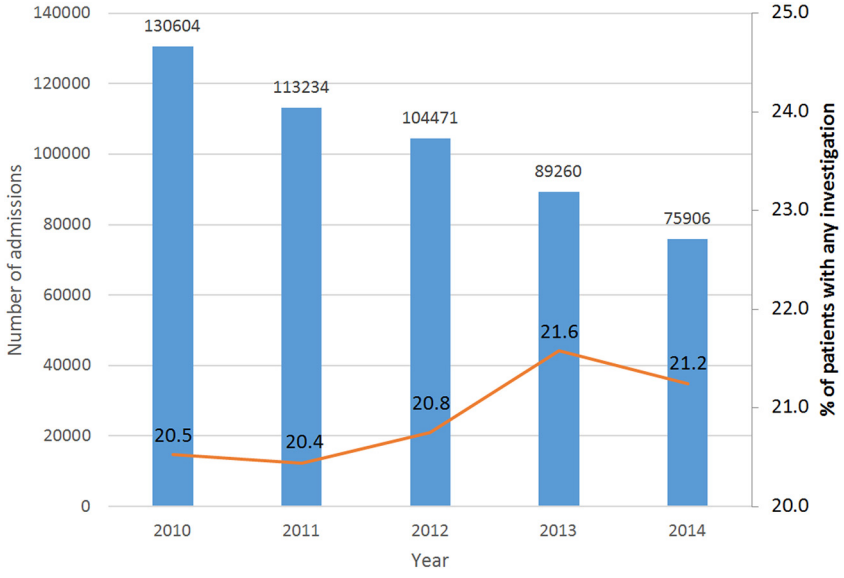

Fig. 1. Rates of chest pain admissions and use of investigations.

Table 1
Characteristics of participants.

Variable	No readmission	Readmission for acute coronary syndrome	Readmission for pulmonary embolus	Readmission for aortic dissection
Age (year)	60.0 ± 14.9	64.4 ± 14.2	61.3 ± 16.2	64.1 ± 15.0
Female	55.1%	44.9%	55.7%	45.6%
Weekend admission	25.0%	26.7%	26.1%	23.4%
Year				
2010	25.5%	24.2%	22.6%	27.4%
2011	22.1%	21.1%	21.6%	14.5%
2012	20.4%	20.3%	19.3%	19.0%
2013	17.4%	18.3%	19.3%	22.2%
2014	14.7%	16.3%	17.2%	16.9%
Primary expected payer				
Medicare	42.7%	59.6%	55.3%	56.9%
Medicaid	16.1%	17.1%	20.4%	19.8%
Private	26.8%	13.7%	14.7%	12.9%
Uninsured	8.7%	5.6%	5.9%	5.2%
No charge	1.1%	0.6%	0.5%	0.4%
Other	4.6%	3.5%	3.2%	4.8%
Median household income (percentile)				
0–25th	33.5%	37.5%	37.3%	36.6%
26–50th	24.7%	24.4%	26.2%	24.0%
51–75th	22.6%	21.2%	21.7%	19.9%
76–100th	19.2%	16.9%	14.8%	19.5%
Smoking	30.3%	34.5%	31.5%	39.1%
Alcohol misuse	4.4%	4.2%	5.8%	4.0%
Dyslipidemia	50.8%	60.4%	46.1%	48.0%
Hypertension	69.5%	80.9%	72.0%	85.5%
Diabetes mellitus	31.0%	48.4%	34.6%	22.6%
Obesity	16.9%	14.9%	21.1%	13.7%
Previous heart failure	0.4%	0.9%	0.9%	0.8%
Coronary artery disease	32.7%	67.1%	37.1%	35.9%
Previous myocardial infarction	10.7%	24.5%	11.9%	12.1%
Previous PCI	13.0%	32.6%	12.9%	12.1%
Previous CABG	7.6%	21.9%	7.5%	11.7%
Valvular heart disease	0.2%	0.4%	0.5%	0.4%
Atrial fibrillation	8.6%	12.7%	11.2%	16.9%
Previous stroke or TIA	7.5%	12.0%	10.9%	12.9%
Peripheral vascular disease	5.0%	11.6%	7.4%	37.5%
Pulmonary circulatory disorder	0.1%	0.2%	0.6%	0%
Peptic ulcer disease	0.03%	0.05%	0%	0%
Chronic lung disease	19.8%	25.7%	28.9%	27.8%
Renal failure	9.5%	23.4%	15.7%	32.3%
Liver disease	2.4%	2.5%	2.9%	3.2%
Hypothyroidism	11.4%	11.7%	12.4%	11.7%
Fluid and electrolyte disorder	11.7%	13.6%	15.9%	14.9%
Anemia	10.2%	17.5%	19.1%	18.6%
Cancer	1.9%	2.4%	9.0%	2.8%
Depression	11.4%	12.4%	14.9%	12.9%
Dementia	3.4%	4.6%	5.6%	4.0%
Charlson comorbidity index	1.1 ± 1.3	1.9 ± 1.6	1.7 ± 1.7	2.0 ± 1.6
Hospital-bed number				
Small	9.1%	9.7%	8.3%	8.1%
Medium	24.6%	25.3%	25.4%	20.2%
Large	66.2%	65.0%	66.3%	71.8%
Urban hospital	7.8%	8.9%	7.9%	4.0%
Teaching hospital	44.7%	44.8%	47.8%	52.4%
Coronary angiogram	17.2%	9.3%	15.9%	10.9%
Echocardiogram	5.8%	5.0%	4.8%	3.2%
Stress test	6.0%	4.3%	3.9%	5.2%
CT thorax	1.5%	1.1%	2.7%	4.0%
MRI	0.02%	0.02%	0%	0%
Pulmonary scan	0.2%	0.2%	0.5%	0.4%
Radioisotope scan	2.7%	2.0%	1.8%	3.6%
Aortogram	1.2%	0.8%	1.0%	1.6%
Length of stay (days)	1.8 ± 2.2	2.1 ± 2.1	2.5 ± 2.4	2.5 ± 2.6
Cost of admission (USD)	$5288 ± 4876	$5299 ± 4303	$6276 ± 4661	$6616 ± 4600
Discharge location				
Home	87.9%	78.3%	75.9%	77.8%
Transfer to other hospital	4.7%	8.1%	9.7%	6.5%
Care home	4.1%	7.4%	9.7%	11.3%
Discharge against medical advice	3.3%	6.2%	4.7%	4.4%
Readmissions outcomes				
Cost of readmission (USD)	–	$17,708 ± 23,137	$18,412 ± 30,815	$31,270 ± 48,377
Readmission length of stay (days)	–	5.4 ± 7.3	8.6 ± 11.4	8.7 ± 12.9
Readmission death	–	5.2%	6.7%	10.9%

PCI = percutaneous coronary intervention, CABG = coronary artery bypass graft, CT = computed tomography, MRI = magnetic resonance imaging, USD = US dollar.

mortality rate was 5.2%, 6.7% and 10.9% for ACS, pulmonary embolism and aortic dissection, respectively.

The multivariable adjusted predictors of readmission for serious cardiovascular events are shown in Table 2. Predictors of ACS readmissions included diabetes (OR 1.49 95% CI 1.17–1.32), coronary artery disease (OR 2.29 95% CI 2.15–2.44), previous PCI (OR 1.65 95% CI 1.56–1.75), previous CABG (OR 1.52 95% CI 1.43–1.61) and discharge against medical advice (OR 1.94 95% CI 1.78–2.12). Female patients (OR 0.82 95% CI 0.78–0.86) and patients who received a coronary angiogram (OR 0.48 95% CI 0.45–0.52) were least likely to be readmitted for ACS. For pulmonary embolus, independent predictors of readmission were pulmonary circulatory disorder (OR 2.20 95% CI 1.09–4.43), anemia (OR 1.62 95% CI 1.40–1.86) and cancer (OR 4.15 95% CI 3.43–5.02). Peripheral vascular disease (OR 8.63 95% CI 5.47–13.61) and renal failure (OR 2.08

Table 2
Predictors of readmission for acute coronary syndrome, pulmonary embolism and aortic dissection.

Variable	Odds ratio for readmission with acute coronary syndrome (95% CI)	Odds ratio for readmission with pulmonary embolus (95% CI)	Odds ratio for readmission with aortic dissection (95% CI)
Age (year)	NS	0.99 (0.99–1.00)	NS
Female	0.82 (0.78–0.86)	NS	NS
Weekend admission	1.07 (1.02–1.12)	NS	NS
Year vs 2010			
2011	NS	NS	0.55 (0.32–0.95)
2012	NS	NS	NS
2013	NS	NS	NS
2014	NS	NS	NS
Primary expected payer vs Medicare			
Medicaid	NS	NS	NS
Private	0.66 (0.61–0.71)	0.48 (0.40–0.57)	0.52 (0.29–0.94)
Uninsured	0.71 (0.64–0.79)	0.56 (0.44–0.72)	NS
No charge	0.65 (0.51–0.84)	0.30 (0.16–0.57)	NS
Other	0.79 (0.70–0.89)	0.54 (0.40–0.72)	NS
Median household income (percentile) vs 0–25th			
26–50th	0.88 (0.83–0.93)	NS	NS
51–75th	0.86 (0.81–0.92)	NS	NS
76–100th	0.87 (0.81–0.93)	0.82 (0.69–0.96)	NS
Smoking	1.11 (1.06–1.17)	NS	NS
Alcohol misuse	NS	1.38 (1.11–1.71)	NS
Dyslipidemia	NS	0.86 (0.77–0.95)	0.62 (0.43–0.90)
Hypertension	1.25 (1.17–1.32)	NS	1.90 (1.18–3.04)
Diabetes mellitus	1.49 (1.43–1.57)	NS	0.44 (0.29–0.65)
Obesity	0.87 (0.82–0.93)	1.31 (1.15–1.49)	NS
Previous heart failure	NS	NS	NS
Coronary artery disease	2.29 (2.15–2.44)	NS	NS
Previous myocardial infarction	1.25 (1.19–1.32)	NS	NS
Previous PCI	1.65 (1.56–1.75)	NS	NS
Previous CABG	1.52 (1.43–1.61)	NS	NS
Valvular heart disease	NS	NS	NS
Atrial fibrillation	NS	NS	NS
Previous stroke or TIA	1.07 (1.00–1.15)	NS	NS
Peripheral vascular disease	1.36 (1.26–1.46)	1.23 (1.00–1.51)	8.63 (5.47–13.61)
Pulmonary circulatory disorder	NS	2.20 (1.09–4.43)	NS
Peptic ulcer disease	NS	NS	NS
Chronic lung disease	1.12 (1.06–1.18)	1.28 (1.14–1.43)	NS
Renal failure	1.65 (1.56–1.75)	NS	2.08 (1.34–3.24)
Liver disease	NS	NS	NS
Hypothyroidism	NS	NS	NS
Fluid and electrolyte disorder	NS	NS	NS
Anemia	1.24 (1.17–1.32)	1.62 (1.40–1.86)	NS
Cancer	NS	4.15 (3.43–5.02)	NS
Depression	NS	1.20 (1.04–1.40)	NS
Dementia	0.90 (0.80–1.00)	NS	NS
Hospital-bed number vs small			
Medium	NS	1.26 (1.02–1.55)	NS
Large	0.86 (0.80–0.93)	1.31 (1.09–1.59)	NS
Urban hospital	1.14 (1.05–1.01)	NS	0.48 (0.23–1.00)
Teaching hospital	NS	1.14 (1.02–1.27)	NS
Coronary angiogram	0.48 (0.45–0.52)	NS	NS
Echocardiogram	NS	0.79 (0.63–0.99)	0.43 (0.21–0.87)
Stress test	0.85 (0.75–0.96)	NS	NS
CT thorax	0.81 (0.68–0.98)	1.73 (1.30–2.31)	2.45 (1.22–4.92)
MRI	NS	NS	NS
Pulmonary scan	NS	NS	NS
Radioisotope scan	NS	NS	NS
Aortogram	NS	NS	NS
Discharge location vs home			
Transfer to other hospital	1.34 (1.23–1.46)	1.85 (1.52–2.24)	NS
Care home	1.29 (1.18–1.40)	1.96 (1.62–2.36)	1.98 (1.10–3.56)
Discharge against medical advice	1.94 (1.78–2.12)	1.56 (1.21–2.01)	NS

PCI = percutaneous coronary intervention, CABG = coronary artery bypass graft, CT = computed tomography, MRI = magnetic resonance imaging, NS = not statistically significant $p > 0.05$.

95% CI 1.34–3.24) were independently associated with aortic dissection. Patients who had received a CT thorax had significantly greater odds of readmissions for pulmonary embolus (OR 1.78 95% CI 1.39–2.29) and aortic dissection (OR 2.45 95% CI 1.22–4.92) compared to patients who did not receive a CT thorax.

Differences in characteristics according to receipt of coronary angiography at index admission was greater among smokers (36.1% vs 29.2%), patients with dyslipidemia (60.7% vs 49.0%) and patients a prior diagnosis of coronary artery disease (44.9% vs 31.2%) (Supplementary Table 1). Among patients with coronary angiogram 53.9% were women while the proportion of women was 55.1% among those without coronary angiogram. Tests for pulmonary embolism were more commonly undertaken in patients at teaching hospitals (62.0% vs 44.0%) while tests for aortic dissection were more commonly performed in patients with peripheral vascular disease (10.3% vs 5.0%) admitted to teaching hospitals (56.5% vs 44.4%).

Independent predictors for coronary angiography at index admission included a previous diagnosis of coronary artery disease (OR 2.40 95% CI 2.31–2.48) and large hospital-bed number (OR 2.01 95% CI 1.75–2.31) (Table 3). Other factors associated with a coronary angiogram included a history of smoking (OR 1.28 95% CI 1.24–1.31), dyslipidemia (OR 1.45 95% CI 1.41–1.48), obesity (1.42 95% CI 1.38–1.46) and private healthcare insurance (OR 1.20 95% CI 1.16–1.24). Patients from the highest income group were more likely to receive tests for pulmonary embolus and aortic dissection, (OR 2.63 95% CI 2.20–3.16 and OR 1.53 95% CI 1.31–1.80, respectively) as were patients admitted to large hospital-bed number (OR 1.42 95% CI 1.05–1.91 and OR 1.57 95% CI 1.26–1.95, respectively) and teaching hospitals (OR 1.94 95% CI 1.58–2.38 and OR 1.57 95% CI 1.36–1.83, respectively). Patients with peripheral vascular disease and cancer were more likely to receive tests for pulmonary embolus and aortic dissection (OR 1.32 95% CI 1.22–1.43 and OR 2.64 95% CI 2.44–2.87 and OR 1.34 95% CI 1.20–1.49 and OR 1.52 95% CI 1.34–1.73, respectively).

The rate of readmission for ACS in patients who received a coronary angiogram during index admission was 1.34% compared to 2.64% among patients who did not receive an angiogram during their index admission (Supplementary Fig. 4). Patients who were tested for pulmonary embolism had a similar rate of readmission

Table 3
Predictors of receiving investigation for acute coronary syndrome, pulmonary embolism and aortic dissection.

Variable	Coronary angiogram	Test for pulmonary embolus	Test for aortic dissection
Age (year)	0.99 (0.99–0.99)	1.01 (1.00–1.01)	0.99 (0.99–1.00)
Female	NS	1.06 (1.03–1.10)	NS
Weekend admission	0.81 (0.79–0.83)	NS	NS
Year vs 2010			
2011	NS	NS	NS
2012	NS	NS	NS
2013	NS	NS	NS
2014	NS	NS	NS
Primary expected payer vs Medicare			
Medicaid	0.59 (0.56–0.61)	1.35 (1.25–1.47)	NS
Private	1.20 (1.16–1.24)	1.16 (1.09–1.23)	NS
Uninsured	0.76 (0.72–0.81)	0.81 (0.72–0.91)	0.72 (0.65–0.80)
No charge	0.69 (0.59–0.80)	NS	0.70 (0.51–0.95)
Other	NS	1.24 (1.05–1.46)	NS
Median household income (percentile) vs 0–25th			
26–50th	NS	1.25 (1.12–1.38)	NS
51–75th	0.88 (0.83–0.93)	1.60 (1.41–1.82)	NS
76–100th	0.74 (0.68–0.80)	2.63 (2.20–3.16)	1.53 (1.31–1.80)
Smoking	1.28 (1.24–1.31)	NS	NS
Alcohol misuse	0.65 (0.62–0.69)	NS	0.78 (0.70–0.88)
Dyslipidemia	1.45 (1.41–1.48)	NS	NS
Hypertension	1.03 (1.01–1.05)	NS	NS
Diabetes mellitus	0.88 (0.86–0.90)	1.05 (1.01–1.10)	0.89 (0.84–0.93)
Obesity	1.42 (1.38–1.46)	1.15 (1.09–1.21)	1.13 (1.06–1.20)
Previous heart failure	0.43 (0.35–0.52)	NS	NS
Coronary artery disease	2.40 (2.31–2.48)	0.75 (0.70–0.80)	1.31 (1.22–1.41)
Previous myocardial infarction	0.68 (0.66–0.71)	1.10 (1.04–1.17)	0.78 (0.72–0.85)
Previous PCI	NS	0.86 (0.80–0.91)	0.70 (0.64–0.76)
Previous CABG	0.48 (0.45–0.50)	0.90 (0.84–0.97)	0.83 (0.76–0.91)
Valvular heart disease	0.66 (0.51–0.86)	NS	NS
Atrial fibrillation	0.96 (0.92–0.99)	0.85 (0.80–0.91)	0.91 (0.84–0.99)
Previous stroke or TIA	0.87 (0.84–0.90)	NS	NS
Peripheral vascular disease	1.13 (1.08–1.17)	1.32 (1.22–1.43)	2.64 (2.44–2.87)
Pulmonary circulatory disorder	0.62 (0.42–0.92)	NS	NS
Peptic ulcer disease	NS	NS	NS
Chronic lung disease	NS	NS	1.06 (1.01–1.12)
Renal failure	0.72 (0.69–0.75)	NS	0.59 (0.54–0.65)
Liver disease	NS	1.27 (1.15–1.40)	1.19 (1.05–1.34)
Hypothyroidism	1.11 (1.07–1.14)	0.93 (0.88–0.98)	NS
Fluid and electrolyte disorder	0.91 (0.88–0.94)	0.89 (0.83–0.94)	NS
Anemia	0.82 (0.79–0.85)	1.09 (1.03–1.16)	0.90 (0.83–0.97)
Cancer	0.57 (0.52–0.62)	1.34 (1.20–1.49)	1.52 (1.34–1.73)
Depression	NS	0.88 (0.83–0.93)	0.91 (0.85–0.98)
Dementia	0.37 (0.34–0.41)	0.79 (0.71–0.88)	0.71 (0.62–0.83)
Hospital-bed number vs small			
Medium	1.59 (1.37–1.85)	NS	NS
Large	2.01 (1.75–2.31)	1.42 (1.05–1.91)	1.57 (1.26–1.95)
Urban hospital	0.67 (1.37–1.84)	0.57 (0.43–0.76)	NS
Teaching hospital	1.13 (1.04–1.22)	1.94 (1.58–2.38)	1.57 (1.36–1.83)

for pulmonary embolism compared to those who were not tested (0.43% vs 0.41%). There were slightly more readmissions for aortic dissection among patients who had a test for aortic dissection (0.09% vs 0.05%) compared to no test. The effect of investigations during index admission on the timing of readmissions for serious cardiovascular causes is shown in Supplementary Fig. 5. Receipt of any investigation significantly reduced events at all time points after discharge. Patients who received CT thorax and radioisotope scans had fewer readmission for ACS but more readmissions for aortic dissection (Supplementary Table 2). Patients with CT thorax had greater rate of readmission for pulmonary embolism but there were fewer readmissions for pulmonary embolism among patients with radioisotope scans.

In our study cohort, we estimate that there were approximately 5586 ACS admissions, 950 pulmonary embolism admissions and 113 aortic dissection admissions between the years of 2010 and 2014 following a diagnosis of non-specific chest pain during the index admission representing approximately $99 million, $17 million and $3.5 million dollars of healthcare expenditure respectively.

4. Discussion

Our outcome analysis of a national cohort of patients with a diagnosis of nonspecific chest pain is not benign as readmission for serious cardiovascular events occur in up to 1 in 30 of patients (primarily due to ACS) within a period of 6 months. The daily readmissions for serious cardiovascular events appear to be greatest shortly after discharge, peaking at 4 days for ACS and pulmonary embolism and 6 days for aortic dissection. This suggests that some of these diagnoses may have been responsible for the initial admission. While receipt of an investigation as an inpatient, particularly a coronary angiogram, is associated with fewer readmissions, patients still return with serious cardiovascular events. The mortality rate for readmissions for ACS, pulmonary embolus and aortic dissection was 5.2%, 6.7% and 10.9%, respectively and the estimated cost of $120 million between 2010 and 2014 (ACS $17,708, PE $18,412 and aortic dissection is $31,270 per readmission). Strong predictors of ACS readmissions were diabetes, coronary artery disease, previous PCI, previous CABG and discharge against medical advice. For pulmonary embolus these included pulmonary circulatory disorder, anemia, cancer and receipt of CT thorax. Peripheral vascular disease, renal failure and receipt of a CT thorax were strong predictors of aortic dissection. Furthermore, we observed clear differences in utilization of investigations, particularly at the institutional level, with differences observed by teaching hospital status and hospital-bed number. Our findings suggest that clinicians should be aware that the diagnosis of non-specific chest pain is not always benign and that “rule-out” strategies for this diagnosis may not be 100% robust, as potentially preventable readmissions for serious cardiovascular events may still occur.

The ANMCO-SIMEU consensus document published by the European Society of Cardiology provided the most recent guidance on in-hospital management of patients with chest pain [9]. The document proposes an in-hospital diagnostic pathway that aims to identify patients with a high probability of ACS, identify other diseases of non-coronary origin requiring emergency or urgent treatment and assess the likelihood of ACS in patients with chest pain with no clear cause and non-diagnostic ECG. It suggests nurse led triage with an ECG, physical examination and assessment of vital parameters. This is followed by emergency room physical examination, blood tests including troponin, blood gas analysis if applicable, and further investigations such as bedside ultrasound and radiological studies including chest X-ray, chest angiogram CT or multi-slice coronary CT depending on the clinical history. The main focus is to identify coronary ischemia and life-threatening causes of chest pain but there is limited guidance on what should be done once these serious causes have been excluded.

The American Heart Association published a scientific statement about testing of low-risk patients presenting to the ED with chest pain [10]. They suggest that low-risk patients are increasingly being managed in chest pain units with accelerated diagnostic protocols including serial electrocardiograms and cardiac biomarkers. Patients with negative findings usually complete a confirmatory test to exclude ischemia such as an exercise treadmill test or cardiac imaging study (rest myocardial perfusion imaging or computed tomography coronary angiogram). A negative diagnostic protocol facilitates discharge while a positive finding results in admission. While this approach is safe, accurate and cost-effective in low-risk patients with chest pain there is no further guidance for patients that are admitted.

Our study builds on the limited outcomes data for patients diagnosed with non-specific chest pain following an inpatient admission. A previous literature review of 12 studies incorporating 24,829 patients found that patients with non-specific chest pain are heterogeneous and co-existing coronary heart disease was present in nearly 40% of patients [3]. In the current study, 33.5% of patients had known coronary artery disease, 11.1% had previous myocardial infarction, 13.5% had previous PCI and 8.0% had previous CABG. Ruddox et al. further suggests that the prognosis among these patients is not necessarily benign as mortality at 1 year was 3.2% and was highest among patients with pre-existing coronary artery disease. Readmissions up to 1 year ranged from 14% to 40%. Unfortunately, there are no studies of non-specific chest pain which specifically consider ACS, pulmonary embolism or aortic dissection. Our evaluation of serious cardiovascular causes for readmissions supports the finding that non-specific chest pain remains a condition that may not be benign as 2.8% return with ACS, pulmonary embolism or aortic dissection at 6 months.

We have observed a major decline in non-specific chest pain diagnoses among inpatients over time and a modest increase in the use of investigations. One explanation for the decline may be the rise of the chest pain or observation units in the emergency department. These units which were first developed in the United States have been shown to be safe and cost effective [11]. They have accelerated diagnostic protocols that allow for rapid discharge or admission with suspected ACS [12]. In addition, in the absence of such units, the greater use of observation status rather than hospital admission is increasingly common. Another explanation may be the introduction of the high-sensitivity troponin assays which have facilitated early diagnosis to rule out of myocardial infarction, risk stratification in acute cardiac conditions and assist therapeutic monitoring [13]. Regular troponins may be negative and patients may be diagnosed with non-specific chest pain while high-sensitivity troponin would detect very low levels of troponin and myonecrosis so patients are more likely to receive a diagnosis of ACS. This is likely the main reason because the increase in number of investigations in the current study is small in absolute terms while the decrease in non-cardiac chest pain patients is more significant. However, on the hospital level, availability of the chest pain units and investigations are an important consideration as receiving a test may change the primary diagnosis and affect readmission rates. For ACS readmissions, we observe that large hospitals were associated with reduced odds of readmission and that these hospitals were more likely to undertake coronary angiography and other investigations in this group of patients. However, we show that even if tests are performed, the patients may still present within 6 months with a serious cardiovascular event.

The predictors of readmission for a serious cardiovascular event provide potential insight into risk stratification of patients assumed to have non-specific chest pain. Patients who appear to have more readmissions for ACS have diabetes and existing coronary heart disease. Other variables we identified included anemia, cancer and known pulmonary circulatory disorders which were independently associated with pulmonary embolism readmission and peripheral vascular disease and hypertension were predictors of aortic dissection. Cancer is associated with a hypercoagulable state [14] that is known to increase the risk of pulmonary embolism [15]. Hypertension is an established risk factor for aortic dissections [16]. These non-modifiable variables should

be integrated into assessments and risk stratification for patients with non-specific chest pain.

We recently published work showing that 1 in 12 patients with a diagnosis of non-specific chest pain have an unplanned readmission within 30-days [17]. This study also found that nearly three-quarters of patients who were readmitted was for noncardiac reasons (73.4%) and the 3 most common reasons for readmission were neuropsychiatric, gastrointestinal and infections [17]. Furthermore, patients who received tests had significantly lower unplanned readmission rates (6.1% vs 9.3%) [17]. We have built on the findings of our previous study by including a longer follow up and including the serious and potentially life-threatening causes which should ideally be identified as early as possible and treated as urgently. We show that the peak rates for these serious complications within one week of discharge and the impact is significant as the mortality rate and cost burden is high. We also demonstrate that use of tests has value in reducing the proportion of patients that are readmitted for these serious causes but they are not 100% reliable.

The exact reason why 1.34% of patients who received a coronary angiogram were still readmitted with acute coronary syndrome is unclear. One reason may be that patients had coronary disease which the operator decided to treat medically and they believed that the disease was not significant enough to cause the patient symptoms. This could have progressed and developed ACS. The other issue is that no test is 100% perfect and patients may have received the test but there is no indicator of the quality of the test. For example, if patients had a coronary angiogram and the vessels were poorly visualized or a small diagonal or obtuse marginal branch may have been missed.

Our study has several limitations. The nature of the NRD dataset is such that there is no possible linkage between years as the data is composed of five unique datasets corresponding to the years 2010 to 2014. We had to apply exclusion criteria of patients discharged in the last 6 months of year in order to ensure that patients had 6 months of follow up and seasonal effects could not be explored. The current analysis is limited because we do not have survival information post discharge and it is possible that patients may have died out of hospital and not be captured for readmissions. Another important limitation is that our study lacks data on results from investigations such as calcium score from CT coronary angiography and both troponin and d-dimer levels from blood results. Also, non-specific chest pain, a diagnosis of exclusion has no formal definition, so we expect heterogeneity in the care received and receipt of investigations for patients leading up to the final diagnosis and discharge. In addition, we lack data in the current dataset about medication use and follow up plans for patients once discharged. A major limitation of the current study is that we do not have information on emergency department discharges as patients may have presented with chest pain and directly discharged without admission to hospital. Therefore, the findings on this study are generalizable to the population with an eventual inpatient primary diagnosis of non-specific chest pain. Furthermore, regional difference could not be explored and out of hospital deaths could not be captured. Finally, we are not able to consider patients who were directly discharged from the emergency department with chest pain that were not admitted to hospital.

5. Conclusions

In conclusion, non-specific chest pain as a primary diagnosis for hospital admission may not be a benign condition as readmissions for serious cardiovascular events occur in 3% of these patients. In our study cohort, we estimate that there are approximately 5586 ACS admissions, 950 pulmonary embolism admissions and 113 aortic dissection admissions after admission for non-specific chest pain accounting for approximately $120 million dollars of healthcare expenditure. Clinicians should be careful to risk stratify and tailor services to better manage patients with non-specific chest pain.

Author statement

All authors take responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.

Contributors

CSK and MAM designed the study and concept. CSK performed the data analysis and CSK and MAMA wrote the first draft of the manuscript. All authors contributed to the writing of the paper.

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Conflict of interest

None.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ijcard.2019.04.001.

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