Published in final edited form as:

Crit Pathw Cardiol. 2015 September ; 14(3): 97–102. doi:10.1097/HPC.0000000000000050.

Prevalence and Overlap of Noncardiac Conditions in the Evaluation of Low-risk Acute Chest Pain Patients

Mohammad Al-Ani, MD* and David E. Winchester, MD, MS†

*Department of Internal Medicine, University of Florida, Gainesville, FL

†Division of Cardiovascular Medicine, Department of Internal Medicine, University of Florida, Gainesville, FL

Abstract

Background—When patients present to the emergency department with a complaint concerning for heart disease, this often becomes the primary focus of their evaluation. While patients with noncardiac causes of chest pain outnumber those with cardiac causes, noncardiac etiologies are frequently overlooked. We investigated symptoms and noncardiac conditions in a cohort of patients with chest pain at low risk of cardiac disease.

Methods—We analyzed data from a prospective registry of patients who were evaluated in our chest pain evaluation center. Registry participants completed standardized and validated instruments for depression (by Patient Health Questionnaire PHQ-9), anxiety (by Generalized Anxiety Disorder GAD-7), and Gastroesophageal Reflux Disorder (GERD; by GERD Symptom Frequency Questionnaire). Chest pain characteristics were recorded; severity was reported on a 10-point scale.

Results—A total of 195 patients were included in the investigation. Using the instruments noted above, the prevalence of depression was 34%, anxiety was 30%, and GERD was 44%, each of at least moderate severity. 32.5% of patients had 2 or more conditions. The median for the severity of angina was 7/10 and the number of episodes over the preceding week was 2, respectively. Severity of angina was associated with PHQ-9 ($r = 0.238$; $P < 0.001$) and GAD-7 ($r = 0.283$; $P < 0.001$) scores. The number of angina episodes over the prior week correlated with GERD Symptom Frequency Questionnaire ($r = 0.256$; $P < 0.001$) and PHQ-9 ($r = 0.175$; $P = 0.019$) scores. No correlation was observed between any of the scores and body mass index, smoking tobacco, diabetes mellitus, hypertension, or hyperlipidemia.

Conclusion—In our cohort of low-risk acute chest pain patients, depression, anxiety, and GERD were common, substantial overlap was observed. The severity of these noncardiac causes of chest pain causes correlated with the self-reported severity and frequency of angina, but weakly. These conditions should be part of a comprehensive plan of care for chest pain management.

Reprints: David E. Winchester, MD, MS, Division of Cardiovascular Medicine, Department of Internal Medicine, University of Florida, 1600 SW Archer Road, P.O. Box 100277, Gainesville, FL 32610. David.Winchester@medicine.ufl.edu.

Presented at the American College of Cardiology meeting, March 2015, San Diego, CA.

DISCLOSURES

Nothing to declare.

Keywords

noncardiac chest pain; angina; depression; anxiety; gastroesophageal reflux

In the United States, chest pain is the reason for 9%–10% of nontrauma emergency department (ED) visits. About 10% are diagnosed with acute coronary syndrome (ACS)¹ and half of the remaining 90% will receive no explanation for their symptoms after complete inpatient and/or ambulatory evaluation. Numerous other cardiac and noncardiac conditions are associated with chest pain, such as esophageal, pericardial, musculoskeletal, psychosomatic, and neurosensory disorders. Some of the most common disorders are treatable; gastroesophageal reflux disorder (GERD), generalized anxiety disorder (GAD), and major depressive disorder (MDD), each of which is more prevalent than coronary artery disease (CAD).

At our institution, ED patients with low cardiovascular risk are evaluated in a dedicated chest pain evaluation center (CPEC). These patients were invited to participate in a prospective registry of their symptoms and other related conditions. We used these data to investigate the relation between chest pain symptoms and illnesses which have been known to cause noncardiac chest pain (NCCP).

METHODS

Patients presenting to our ED with chest pain underwent an initial evaluation for ACS with electrocardiogram and serum troponin T. Those without ACS and with low cardiovascular risk underwent further evaluation in the CPEC, an 8-bed unit located within the ED. The selection criteria and management within the CPEC has been described previously.² Criteria for exclusion from the CPEC included known CAD, elevated troponin, ischemic ST segment changes, suspected other acute non-ACS diagnoses (pulmonary embolism, pneumonia, heart failure, aortic dissection, or acute drug abuse), pregnancy, and age less than 18 years.

In the CPEC, patients were tested with serial serum cardiac markers and electrocardiograms. Before discharge, patients underwent testing for CAD, typically with either exercise treadmill testing or computed tomographic coronary angiography. Those without evidence of obstructive CAD were discharged; otherwise, patients were admitted for continued management.

Patients were asked to participate in a registry which captured demographics, risk factors for CAD, comorbid conditions as well as standardized assessment instruments for MDD, GAD, and GERD; these tools were Patient Health Questionnaire (PHQ-9), Generalized Anxiety Disorder (GAD-7) questionnaire, and GERD Symptom Frequency Questionnaire (GSFQ), respectively. Chest pain pattern, duration, frequency, and associated symptoms were recorded. Severity was assessed on a 10-point scale.

This study was approved by our institutional review board. Written informed consent was sought from all CPEC patients consecutively. Refusal to consent was the only exclusion criterion for the registry. After consent was given, data were collected on paper forms at the

point of care by dedicated nurse practitioners or physician assistants with specific training in both research methodology and the evaluation and management of chest pain. Data from these forms were logged electronically in a custom database using REDcap Software V9 (Vanderbilt University, Nashville TN).^{3,4}

We analyzed data from patients within the registry for whom complete data were available and who were not diagnosed with CAD by noninvasive testing. Independent sample Student's *t* test was utilized to detect any effect of demographics and cardiac risk factors on the 3 obtained scores. Patients who had GAD-7 or PHQ-9 of more than 9 or GSFQ more than 34.5 were considered to be positive for the corresponding diagnosis. These thresholds were associated with moderate to severe disease in prior studies and, in the case of GERD, it correlated with at least grade I esophagitis on endoscopy.⁵⁻⁷ Pain severity was considered moderate if reported to be 5/10 or more and severe if greater than 7/10. Data analysis was performed with SPSS version 22 software (IBM, Armonk, NY).⁸

RESULTS

Patient Baseline Characteristics

Of the patients admitted to CPEC during the period between December 2011 and January 2013, 203 consented to the study. One hundred and ninety-five subjects underwent cardiac testing, of which 7 (3.5%) suggested obstructive CAD or ischemia. Table 1 illustrates the baseline characteristics of our sample and correlations with PHQ-9, GAD-7, and GSFQ scores. No gender differences in any of the scores were observed. Smoking was correlated with all of the scores, while body mass index, diabetes mellitus, hypertension, and hyperlipidemia were not. We did not observe any effect of serum hemoglobin or creatinine on any of the assessed noncardiac conditions. Patients on acid-suppressing medications (16%), antidepressants (16%), or anxiolytics (30%) had higher questionnaire scores than untreated patients. Seventy-four percent of our sample had health insurance, which was associated with GERD symptoms (Table 1).

Effect of Noncardiac Factors on Pain Characteristics

Using Diamond-Forrester criteria, subjects were identified as having typical, atypical, or NCCP. Most patients described typical angina symptoms and 82.8% complained of greater than 4/10 pain severity. The median for the severity of angina and the number of episodes over the preceding week were 7 and 2, respectively. The prevalence of moderate or greater depression, anxiety, and GERD were 34%, 30%, and 44%, respectively. A high degree of overlap of these conditions was observed; 25% of the analyzed sample had both MDD and GAD, whereas 11% tested positive for all three disorders. Overall, 54% had at least 1 NCCP cause and 32.5% had 2 or more (Fig. 1).

We observed a correlation between the severity of angina and PHQ-9 ($r = 0.238$; $P < 0.001$) and GAD-7 ($r = 0.283$; $P < 0.001$); the number of episodes over the prior week correlated with GSFQ ($r = 0.256$; $P < 0.001$) and PHQ-9 ($r = 0.175$; $P = 0.019$) scores (Fig. 2). Subjects who reported only mild pain had lower PHQ-9 and GAD-7 by 44% respectively, and with a *P* value of <0.0001 for both. Patients with GERD often complained from nausea without

other associated symptoms (Table 2). Diaphoresis and nausea are not uncommon anxiety symptoms and were reported more often by patients with higher GAD-7 scores, while depression was associated with diaphoresis only (Fig. 3).

DISCUSSION

In patients from our CPEC without evidence of coronary disease, noncardiac conditions including depression, anxiety, and GERD were common. Each of these conditions was nearly 10 times as common as positive CAD testing in a cohort without history of CAD. Chest pain characteristics (by Diamond-Forrester criteria) were not correlated with these noncardiac conditions. Patients with these disorders reported more severe and frequent pain; however, other characteristics were not different.

GERD and Chest Pain

The literature describes GERD as the single most common cause of NCCP. In their meta-analysis, Wertli et al have found that typical GERD symptoms in chest pain patients have a positive likelihood ratio of 2.7 for the presence of objective evidence of GERD. Also a trial of proton pump inhibitor for 2 weeks had a sensitivity of 0.89 (CI: 0.28–1) and specificity of 0.88 (CI: 0.26–1) for GERD as the cause.^{9,10} In our study, GERD patients presented similarly to other patients apart from experiencing more nausea. Interestingly, only one-third of them were on an acid-suppressant medication. Compared with other conditions, those patients complained of more frequent symptoms for a longer period of time, without increased severity.

Psychosomatic Chest Pain

Although this group of diseases is perceived as less important than heart diseases, they inflict significant morbidity and mortality. Patients with mood disorders tend to have recurrent ambulatory encounters and testing for severe chest pain that manifests in a dramatic fashion under the influence of their mood.¹¹ After an acute chest pain evaluation, many patients do not receive appropriate primary care follow-up.¹² The term cardiophobia has been used to describe a pathological fear from a fatal heart attack; this fear appears to be common (up to 50% prevalence) in the NCCP population.^{13,14}

While causality is difficult to demonstrate, heart disease is associated with psychiatric disease and symptoms of heart disease can contribute to anxiety and depression.¹⁵ This creates the potential for a positive feedback loop between CAD and psychosomatic disorders. Aikens et al¹⁶ demonstrated that fear from cardiopulmonary disease was a strong predictor of a composite index of cardiac complaints intensity in those presenting to the ED with NCCP. In a systematic review focused on NCCP and psychiatric disease, Webster et al¹⁷ observed that quality of life outcomes for NCCP and cardiac patients were similar and poorer than for healthy controls.

In our population, depression and anxiety were present in about a third of patients with less than 20% undergoing treatment. Patients with these conditions reported more severe and frequent pain without major associated symptoms. A systematic review of antidepressants and anxiolytics for NCCP found mixed evidence from few investigations with small sample

size.¹⁸ A Cochrane database review of the efficacy of psychotherapy for chest pain with normal coronary anatomy found 15 randomized controlled trials showing a 32% reduction in chest pain frequency over the first 3 months without effect on severity.¹⁹

Another challenge within the chest pain population is micro-vascular coronary dysfunction or cardiac syndrome X. This condition is thought to be present in up to half of women presenting with chest pain.²⁰ Because definitive testing is difficult, it is frequently not done, leaving the diagnosis one of exclusion or presumption.²¹ Cardiac syndrome X is also associated with anxiety and depression. When patients present with NCCP, it is frequently unclear if symptoms are due to coronary dysfunction, psychiatric disease, or an interplay of both. This may be why cardiac syndrome X sometimes does not respond well to coronary-targeted drugs, but instead improves with psychiatric interventions. Even simple stress coping education and relaxation techniques can be effective.²² Both cardiac syndrome X and mental illnesses should be treated empirically to improve quality of life.

LIMITATIONS

Our study only evaluated low cardiovascular risk patients without known CAD; therefore, our prevalence estimates of NCCP conditions are only applicable to a similarly selected population. Participation in the registry was voluntary; this could result in participation bias, particularly as related to psychiatric disorders. We do not have adequate information on this cohort to describe follow-up with primary care or recidivism to other facilities.

CONCLUSIONS

In our cohort of low-risk acute chest pain patients, depression, anxiety, and GERD were weakly associated with higher self-reported severity of angina and angina frequency. These disorders were each more common than CAD in this population and many patients suffered from more than one disorder. Noncardiac conditions which contribute to or mimic cardiac chest pain should be addressed to best achieve relief for patients seeking acute evaluation of their symptoms.

Acknowledgments

Supported by the Gatorade Trust through funds distributed by the University of Florida, Department of Medicine. Data collection was supported in part by the Clinical and Translational Science Institute (NIH Grants UL1TR0029890; UL1TR000064).

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FIGURE 1.

Overlap between GAD, MDD, and GERD among NCCP patients. Venn diagram representation of the absolute numbers of patients diagnosed with MDD, GAD, and GERD based on validated self-reported questionnaires. Notably, more than two-thirds of patients positive for one condition were positive for least one of the other two disorders.

FIGURE 2.

Correlation between chest pain severity and frequency and the studied noncardiac causes of chest pain. The severity of chest pain (A) correlated best with anxiety and depression, whereas the frequency (B) correlated with all 3 scores with strongest relation to GERD. The R^2 linear, or coefficient of determination, is included with both plots.

FIGURE 3.

Interaction between duration of symptoms and associated complaints and the studied noncardiac causes of chest pain. Interaction between noncardiac factors and the pain duration and associated symptoms. Graph (A) demonstrates that most patients with higher scores had symptoms for greater than 1 week and GERD patients had significantly more nausea as well (B).

TABLE 1

Traditional Cardiac Risk Factors and Their Effect on Depression, Anxiety, and Acid Reflux Scores

Characteristic	n (%)	PHQ-9*	GAD-7*	GSFQ*
Male gender	59 (33)	-0.64 ($P=0.6$)	0.71 ($P=0.60$)	-1.01 ($P=0.25$)
Diabetes mellitus	17 (10)	2.55 ($P=0.095$)	1.16 ($P=0.08$)	-3.024 ($P=0.77$)
Hypertension	62 (35)	0.47 ($P=0.65$)	-0.64 ($P=0.49$)	2.96 ($P=0.39$)
Hyperlipidemia	30 (17)	0.48 ($P=0.72$)	0.59 ($P=0.64$)	-1.1 ($P=0.80$)
Current smoking	41 (23)	3.41 ($P=0.004$)	4.57 ($P<0.001$)	10.21 ($P=0.009$)
Health insurance	54 (27)	-0.08 ($P=0.28$)	0.12 ($P=0.11$)	0.24 ($P<0.001$)
On acid-suppressant	22 (12)	1.64 ($P=0.28$)	1.42 ($P=0.86$)	22.58 ($P<0.001$)
On antidepressants	20 (11)	3.51 ($P=0.047$)	2.49 ($P=0.09$)	-3.81 ($P=0.47$)
On anxiolytics	16 (9)	4.47 ($P=0.010$)	4.54 ($P=0.005$)	3.17 ($P=0.59$)

Smoking showed strong association with all scores. Patients who were on medical treatment for depression, anxiety, or gastroesophageal reflux had significantly higher scores indicating poor symptomatic relief of their respectively associated disorders. Statistically significant results are in bold.

* Correlations are listed as mean difference (P value) obtained using independent sample Student's t test.

TABLE 2
Effect of Different Chest Pain Characteristics on PHQ-9, GAD-7, and GSFQ scores

Pain Characteristic	n (%)	PHQ-9		GAD-7		GSFQ	
		Σ	P	σ	P	σ	P
Diamond-Forrester class							
Typical	29 (16)	7.59	0.603	6.82	0.895	22.74	0.77
Atypical	42 (24)	7.62		7.53		24.72	
Noncardiac	106 (60)	8.64		7.28		26.07	
Severity *							
Mild	31 (19)	4.50	0.001	2.74	<0.001	19.79	0.247
Moderate	64 (38)	8.68		8.09		28.06	
Severe	69 (43)	9.77		8.59		26.65	
Duration of current episode							
0–15 min	65 (37)	8.09	0.878	6.42	0.202	26.08	0.647
15–60 min	20 (11)	7.68		6.35		21.00	
>60 min	91 (52)	8.47		8.09		25.85	
Duration of chest pain symptom							
<24 hours	83 (46)	7.40	0.261	6.57	0.144	21.22	0.019
1–2 days	31 (17)	8.70		8.06		24.22	
<7 days	31 (17)	7.90		6.23		24.89	
7 days	36 (20)	10.03		9.06		25.22	
Angina during the prior week							
once	77 (46)	7.19	0.092	6.92	0.632	20.89	0.039
>once	87 (54)	8.94		7.39		28.04	
Associated symptoms							
Diaphoresis	36 (20)	9.97	0.083	8.71	0.118	27.88	0.388
Nausea	69 (38)	9.03	0.186	8.19	0.109	32.49	0.001
Dizziness	78 (43)	7.7	0.369	7.39	0.782	26.45	0.461
Dyspnea	99 (55)	8.29	0.822	7.97	0.083	26.35	0.392
None	36 (20)	7.36	0.407	6.00	0.188	20.31	0.016

Statistically significant results are in bold.

* Severity was classified on a scale of 0–10 with mild being 1–4, moderate 5–7, and severe 8–10 out of 10.

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