

PANIC DISORDER IN THE EMERGENCY DEPARTMENT
CHEST PAIN POPULATION.

Ellinor Berglund, Psykologi III: Vetenskaplig undersökning, 15 hp.

Handledare: Per Carlbring

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Chest pain (CP) patients in the emergency department (ED) often do not have pain caused by an acute cardiac heart disease. After investigation by physician 35-40 % is diagnosed with “unspecified chest pain”. A Panic attack (PA) can mimic a heart attack, and patients with Panic Disorder (PD) patients often seek medical care from symptoms of the sympathetic nervous system. A hospital quality project investigated the presence of PD in the emergency care units with the aim to find and help patients with PD/PA. The PHQ panic module was used as self-report. This study describes the outcome of nearly 4000 self-reports during 6 years between 2008 and 2013 with the aim of investigating differences in diagnosis and ED-visits in chest pain between patients with and without PD/PA. The result shows that there is a significant difference in diagnosis ($p < 0,000$) and in ED-visits ($p < 0,000$) between patients self-reporting PD, PA and No anxiety. Odds Ratio was calculated and for PD patient the odds of being a frequent ED-Visitor (>4 /year) is shown to be prominent (OR 13.0). The cohort could be used as a matched case-control for long term studies of morbidity and mortality.

People seeking medical care for chest pains in the emergency department (ED) often do not have pain caused by an acute cardiac heart disease. They are thoroughly investigated by a physician, often a cardiologist, with regards to anamnesis, physical exam, electrocardiogram (ECG), biomarkers and traditional risk factors. Patients with a history meeting typical or suspicious characteristics of cardiac events will undergo further examination, and are admitted, to the least over night. The tradition of the emergency cardiac care is to rule out or treat life-threatening events, and admit patients who need further investigation to hospitalization (Stockholms Läns Landsting, 2013). It is of great importance not to miss any cardiac disease and therefore every case of chest pain is checked at least with ECG and biomarkers. If the physician does not find anything fatal, the patient will be let home with reassurance, or with referral to another specialist or general practitioner. From all patients seeking with chest pain and ending up either as outpatient in the ED or as inpatient at the cardiology ward the frequency of unspecified chest pain 35-40 % (Held, 2014). “Unspecified” diagnoses are derived from a symptom and vaguer, meaning

“we did not find anything pathological”.

A thorough investigation of the chest pain patient in the emergency department is of importance. The rate of missed diagnosis of acute myocardial infarction in 10 US emergency wards was investigated by (Pope et al., 2000). They found that 2.1 percent were mistakenly discharged. Patients with normal or non-diagnostic electrocardiograms, and younger women were more likely to have been discharged and the authors discuss if this bias is due to higher rates of atypical symptoms or presentations.

Panic disorder

Panic disorder (PD) is a type of anxiety disorder characterized by recurrent episodes of sudden and unexpected feelings of strong fear of disaster or of losing control in absence of a real danger. Often it is accompanied by prominent physical reactions, including bodily signs such as heart palpitations, chest pain or discomfort, feelings of shortness of breath or choking, dizziness, sweating and flush. These signs arising from the autonomous sympathetic nerve system preparing for fight or flight are in the absence of real and actual fear often mistaken for dangerous symptoms of disease. A panic attack can in that sense mimic a heart attack. For the patient this is a horribly unpleasant experience, which often leads to help seeking in an acute medical setting. PD is relatively common, the 12 months prevalence in the Swedish population was estimated to 2, 2% (Carlbring, Gustafsson, Ekselius, & Andersson, 2002) and life time prevalence in USA is 5, 1% (Grant et al., 2006). In the emergency department as many as 20-25 % of the chest pain population could have PD according to several studies (Fleet et al., 1996; Foldes-Busque et al., 2011; Worthington et al., 1997; Yingling, Wulsin, Arnold, & Rouan, 1993), and among cardiology outpatients and patients with coronary heart disease (CHD) the prevalence is 10-50% (Fleet, Lavoie, & Beitman, 2000). Despite this fact, PD often goes undiagnosed in the emergency department and in cardiology wards.

Untreated PD causes disability and impaired quality of life, were only 20-40 percent of the affected recover, and leads to high societal and health care costs. In a recent report (Statens beredning för medicinsk utvärdering (SBU), 2005) SBU found that the total cost for anxiety disorders in Sweden in 1996 was estimated to 20 billion SEK per year. Physicians in primary care have difficulties to recognize and diagnose anxiety disorders (Bodlund, 1997). Due to neglected diagnosis and treatment patients with anxiety disorders consults different specialties and undergo many investigations which lead to a frequent utilization of health care (Statens beredning för medicinsk utvärdering (SBU), 2005). For this reason, simple standardized instruments such as HADS (Zigmond & Snaith, 1983) and Prime-MD (Spitzer et al., 1994) has been developed for the purpose of finding the patients with depression and anxiety. In a recent report from the Swedish Socialstyrelsen (Socialstyrelsen, 2010a) , it is said to be of high priority to create great availability in the first line health care. They propose a structured assessment by the nurse as being effective from a medical as well as a health economical perspective.

Mental health and Coronary events

Furthermore, the need for assessing *psychosocial distress* in chest pain patients is more important than commonly recognized as it might contribute to a substantial proportion of acute myocardial infarction (Rosengren et al., 2004). Psychosocial distress has almost equal impact on acute myocardial infarction as demographic characteristics and risk markers such as lipids, smoking and obesity indicates data from the large international cohort study INTERHEART (Yusuf et al., 2004). For women the impact of psychosocial distress was larger than smoking, and especially pronounced in younger women <65 years. An association between *anxiety disorders* and cardiovascular morbidity and mortality has been suggested by a number of studies according to a recent review (Thurston, Rewak, & Kubzansky, 2013) but the directionality of the relationship needs to be further assessed. Two large Scandinavian cohort studies have addressed the directionality in retrospective by looking at protocols from psychiatric interviews during conscription. Janszky (Janszky, Ahnve, Lundberg, & Hemmingsson, 2010) found that early onset of anxiety but not depression predicted subsequent coronary events, and in a much larger sample Gale (Gale, Batty, Osborn, Tynelius, & Rasmussen, 2014) demonstrated an increased risk of coronary heart disease for a range of early diagnosed mental disorders.

According to Fleet in a review from 2000 (Fleet et al., 2000), an association between *panic disorder* and coronary artery disease was strongest in patients with atypical chest pain, but the focus of these studies was in the study of non-cardiac chest pain. Gomez-Caminero (Gomez-Caminero, Blumentals, Russo, Brown, & Castilla-Puentes, 2005) found a twofold risk of coronary heart disease for panic patients in a large cohort from IHCIS, (The Impact National Managed Care Benchmark Database) which is representative of the non-elderly, insurance-carrying population in the U.S. In a cohort from GPRD, a large research database from the general practitioners in UK, Walters (Walters, Rait, Petersen, Williams, & Nazareth, 2008) found a significant association between new diagnosis of panic attacks/disorder and increased incidence of coronary heart disease at all ages, and acute myocardial infarction in those <50 years of age, particularly in younger women. Bull Bringager (Bull Bringager, Arnesen, Friis, Husebye, & Dammen, 2008) did not find any association between panic disorder and cardiac morbidity, in a 9-year follow up of a small sample of 199 patients from cardiac out clinics in Oslo. 10 year follow up data from the HUNT 2 study (Gustad, Laugsand, Janszky, Dalen, & Bjerkeset, 2014) showed moderate association between self-reported symptoms of anxiety (HADS) and risk of myocardial infarction, especially if recurrent. Panic disorder has been described as having a twofold excess mortality compared with normal population (SMR 206 %) (Harris & Barraclough, 1998) and is prevalent in coronary artery disease patients (Fleet et al., 2000). In the Swedish Lundby cohort, Gräsbeck, found that circulatory diseases was the largest separate cause of premature death for subjects with panic disorder (Grasbeck, Rorsman, Hagnell, & Isberg, 1996).

Today panic disorder is regarded as a simple and treatable disease. Cognitive behavior therapy (CBT) – a well-documented and effective treatment with low costs –is primarily recommended (Socialstyrelsen, 2010b) . An alternative treatment is medication with antidepressant (SSRI). Stockholm Läns Landsting offers Internet mediated CBT at

“internetpsykiatri.se” (Internetpsykiatrienheten M46 SLSO Psykiatri Sydväst) with the aim of treating patients at a large scale.

A quality project conducted at Södersjukhuset

During the years 2008 to 2013 a hospital quality project was conducted at the emergency ward in Södersjukhuset, Stockholm, with the aim to discover and help patients with possible panic disorder seeking care in the emergency ward for acute chest pain. A self-report for signs and symptoms was included in the usual care. The patients, on stating their complaints, were in addition to the usual investigation with ECG and biomarkers asked by the attending staff to fill in a self-report on signs of panic disorder. We used the panic module from PRIME MD (Lowe et al., 2003). The self-report was then handed to the treating physician for guidance in differential diagnosis, in the same sense as other investigations are normally used, for example biomarkers like CRP or glucose. If the screening for panic disorder was positive the physicians were instructed to consider ICD-diagnosis (Socialstyrelsen) F410 “Panic Disorder” and eventual treatment or referral to internetpsykiatri.se, or to a general practitioner. Baseline (year 2007) for the ICD anxiety diagnoses “Panic Disorder” (F 410) and “Unspecified Anxiety” (F 419) was: (n) 60 patients at Södersjukhuset. Since the start of the project in 2008 approximately 4000 screening forms have been gathered.

The PHQ screening

To our experience from the emergency ward, and as mentioned in a systematic review from ESP (Benjamin, Herr, McDuffie, Nagi, & Williams, 2011) a screening instrument for busy medical settings should be feasible and of self-report format, which will not require specialized equipment or trained personnel. The PRIME-MD (Spitzer et al., 1994) was developed for the primary care with the purpose of diagnosing common mental illness. The PRIME-MD is a multi component questionnaire in two stages which takes 5 to 6 minutes for patients without mental illness, and 11-12 minutes if there is a diagnosis. Even this is too long time for a medical setting so the questionnaire was divided in shorter parts and developed to the Patient Health Questionnaire (PHQ) (Spitzer, Kroenke, & Williams, 1999). The PHQ addresses depression, PD and other anxiety disorders, eating disorder and alcohol abuse. The patient completes the self-report and an algorithm helps the physician to a diagnostic decision. In a large meta analysis (Benjamin et al., 2011) ESP concluded that the PHQ is feasible for detecting panic disorder in a primary care setting based on performance and applicability.

The aim of this observational cohort study is to examine the presence of Panic Disorder, diagnosis and frequency of chest pain ED-visits during 6 years between 2008 and 2013. The study group from the population of chest pain ED-visitors at Södersjukhuset, Stockholm has self-reported on panic disorder according to PHQ panic module. Furthermore, subgroups depending on results of self-report are compared for differences in

diagnosis and ED-Visits with chest pain. Age and gender will also be considered.

Research question: *Chest pain patients in a medical emergency setting self-reporting on panic disorder: Is there any difference in seeking behavior and diagnosis?*

Method

From spring 2008 to end of 2013 a total of 4445 self-report forms reached the quality project. Patients having other seeking reason than chest pain (460) were excluded. Other reasons for exclusion were: form not properly filled, missing identity, or answer difficult to interpret. In a total (n 919) self-report forms were excluded. Some patients were asked to self-report two or more times (n 124). A total of 3526 chest pain patients were included in the study group (10 %) during 6 years of intervention.

Compared to the ED chest pain population (2008-2013) the number of woman were slightly higher (51,2%, $\chi^2 = 4,696$, $p < 0.03$) in the study group, and double sided t-test shows that the study group also is significantly younger, mean difference in age was 7 years ($p < 0,05$). During the study period the self-report group has three-fourth ($p < 0,05$) as many ED visits with chest pain compared to the population (Tab 1).

Table 1. Demographics: Chest pain patients 2008-2013 and study group.

	Not self-reported	Self-reported
	N(35502)	n(3248)
Age (mean)	56 _a	49 _b
Gender, Female	49,3%	51,2%
ED-visits CP* (mean)	1,37 _a	2,11 _b
>24	0,0% (12)	0,6% (22)

* Chest Pain.

Table 2. Chi-Square for proportions in gender.

Pearson Chi-Square Tests		
		screen
Gender	Chi-sq	4,696
	df	1
	Sig.	,030*
Results are based on nonempty rows and columns in each innermost subtable.		
*. The Chi-square statistic is significant at the,05 level.		
b. More than 20% of cells in this subtable have expected cell counts less than 5. Chi-square results may be invalid.		

The 4445 self-reports from patients seeking care for acute chest pain was collected during a hospital quality project at the emergency room (ER), and in one of the cardiology units at Södersjukhuset, Stockholm. The self-report was handed out by attending staff at the ER to patients in the nurse-based triage or while waiting for the physician, after checking vitals, electrocardiography (ECG) and biomarkers. The staff was instructed to hand out the self-report to all chest pain patients (24 opening hours), except for patients needing immediate attention. Self-reports were also assessed at one of the cardiology units. After the self-report was completed, the screening form was gathered together with the medical record, ECG and other documents. Later on when the patient was discharged from the hospital either from the cardiology unit or from the ER, the medical secretary filed the form to the Quality project for statistics.

We used the panic module from the PHQ (appendix 1). The panic module is a 15 item questionnaire which evaluates the presence of DSM-IV criteria for PD. The first question is “In the last 4 weeks, have you had an anxiety attack – suddenly feeling fear or panic?” If the patient states “no” on this question, the form is completed. If stating “yes” the patient is instructed to fill in the other 14 questions. With the original panic algorithm all the first 4 items must be answered with “yes” and in addition four or more somatic symptoms must be present. With this algorithm the panic module has a sensitivity of 75 % and a specificity of 95 % (Lowe et al., 2003).

Patients were divided in subgroups depending on the answers of the self report. The subgroups were defined as follows:

1. Panic Disorder: If a patient had PD (4 first items positive and at least 4 symptoms) any time during sampling period between spring 2008 and to the end of 2013.
2. Panic Attack: If a patient have had a panic attack (First item (Anxiety yes/no) positive, 0-3 points on item 2, 3 and 4, and at least 4 symptoms positive) at any time during the sampling period between spring 2008 and to the end of 2013. This includes for example patients (n 161) answering “yes” on item 2 (recurrent) and item 3 (unexpected) but not item 4 (discomfort or worry).
3. No anxiety: If a patient only answered the first item (anxiety) with “no” during the whole sampling period.

Unfortunately the indication of date on the self-report was sparse. For this reason, there is no exact date of screening, and the following diagnosis. Data is therefore presented at a large group level. Furthermore, some patients were found to have self-reported two or more times (n 124). ED-visit, main diagnosis and supplemental diagnoses for each visit was added to the screening result. In statistic analysis each patient was a case assigned to a subgroup with (n) ED-visits and following diagnoses.

Data was collected and algorithms were executed in a database (Filemaker Pro 13). The screening result was collected manually and data regarding age, gender and ED visits from the emergency registry database (Akusys version 6.2) was imported via excel files. Diagnose codes were collected from the SKL (Sweden county council and local authority) KPP-database (Kostnad per patient). Statistical analyses were performed with IMB SPSS Statistics, version 22.

Consent was given for a Quality project and a School Report from the head of the Emergency Unit and the Head of the Cardiology unit.

Results

Patients in *PD-group* (*n* 532) tends to be younger, and the number of woman were slightly higher (51, 9). Unspecified Chest Pain, ICD R073-74 (UCP) is the most common diagnosis (61, 5 %), but one third (34, 1 %) received an anxiety diagnosis (19, 4 % ICD F410 and 7,7 % ICD F419). PD-group has the lowest distribution of Acute Myocardial Infarction (AMI) (3, 6 % ICD 121-24). *PA-group* (*n* 637): UCP: 59, 5 %, Anxiety diagnosis: 14,1 % and AMI: 5,2 %. *No Anxiety-group* (*n* 1822) Only 1, 8 % with anxiety diagnosis, and the highest distribution of UCP (64, 8 %), AMI 5,4 %. Pearsons Chi square tests for subgroup variances in diagnosis is significant at the 0,05 level for all tested diagnoses, except for Acute Myocardial Infarction.

Table 3. Distribution of diagnoses a) Acute Myocardial Infarction (ICD I 21-24), b) Panic Disorder (ICD F 410) c) Anxiety Unspecified (ICD F 419) and d) Chest Pain Unspecified (ICD R 073-74) in self-report subgroups Panic Disorder, Panic Attack and No Anxiety.

		Panic disorder (n 532)	Panic attack (n 637)	No anxiety (n 1822)
Age	(mean)	44 _a	47 _b	51 _c
Gender, Female	(n(%))	276 (51,9)	330 (51,8)	921(50,5)
a) AMI	(n(%))	19 (3,6)	33 (5,2)	98(5,4)
b) PD		103 (19,4)	49 (7,7)	11(0,6)
c) Anx UNS		78 (14,7)	41(6,4)	21(1,2)
d) CP UNS		327 (61,5)	379 (59,5)	1180 (64,8)
ED-visits CP	(mean)	2,92 _a	1,97 _b	1,79 _b
ED-Visit Frequency	CP			
	1-3/yr	522 (98,1)	633 (99,4)	1818 (99,8)
	>4/yr	10 (1,9)	4 (0,6)	4 (0,2)

Note: Values in the same row and subtable not sharing the same subscript are significantly different at $p < .05$ in the two-sided test of equality for column means. Cells with no subscript are not included in the test. Tests assume equal variances.¹

1. Tests are adjusted for all pairwise comparisons within a row of each innermost subtable using the Bonferroni correction.

Table 4. Pearsons Chi square tests for subgroup variance in diagnosis.

		SubGroup	
Gender	Chi-square		0,475
	df		2
	Sig.		0,789
AMI	Chi-square		2,87
	df		2
	Sig.		0,238
PD	Chi-square		289,06
	df		2
	Sig.		,000 ^a
Anx UNS	Chi-square		174,019
	df		2
	Sig.		,000 ^a
CP UNS	Chi-square		6,321
	df		2
	Sig.		,042 ^a
ED-Visit >4/yr	CP	Chi-square	18,982
		df	2
		Sig.	,000 ^{a,b}
Results are based on nonempty rows and columns in each innermost subtable.			
*. The Chi-square statistic is significant at the ,05 level.			

During the study period the Anxiety diagnoses (F410 and F419) have doubled from less than 1 % (2007) to approximately 2 %. Self-reported Panic Disorder and Panic Attacks were given an Anxiety Diagnosis in 34, 1 % and 13, 8 % respectively which significantly varies with the No Anxiety group. The main finding is the difference in ED visit frequency for the Panic Disorder group ($p < 0,000$). Unfortunately this dataset has no baseline for this.

Logistic regression (Table 5.) with outcome 4 or more chest pain ED-visits/year shows that patients self reporting Panic Disorder have a far greater risk (OR 13) than No Anxiety group of having 4 or more ED- visits with chest pain per year during the sampling period. Even self report Panic Attack shows higher risk (OR 3, 69).

Table 5. Logistic regression with outcome 24 visits or more.

Variables in the Equation		95% C.I.for EXP(B)		
		OR	Lower	Upper
Step 1 ^a	Age	1,051	1,023	1,081
	Sex	0,382	0,141	1,039
	No Anxiety			
	Panic Disorder	13,033	3,966	42,825
	Panic attack	3,687	0,911	14,927
	Constant	0		

a. Variable(s) entered on step 1: Age, Sex, SubGroup.

Discussion

The main finding in this study is the self report of Panic Disorder high odds ratio of being a frequent ED-visitor compared to the No anxiety group. This is consistent with 2005 report from SBU where patients with anxiety disorders were found to consult different specialties and undergo many investigations which lead to a frequent utilization of health care (Statens beredning för medicinsk utvärdering (SBU), 2005). On the other hand (Dyckman, Rosenbaum, Hartmeyer, & Walter, 1999) found that support with a brochure from the emergency department to the panic patient increased the number of ED visits. The present study cannot answer if the self-report itself have had any effect on the frequency of ED visits since we lack baseline data for this.

Between groups analysis for Panic Disorder, Panic Attacks and No Anxiety groups shows a significant variance in diagnosis. This could be a positive effect of the self-report quality project, and even give support to the accuracy of the diagnostic instrument PHQ. Data from large scale epidemiological surveys suggest that panic disorder is more common in women than in men. This material tends to support those findings.

The self-report most probably did not have any large effect on the overall anxiety ICD diagnosis. There could be several reasons for this, and the most plausible explanation is that physicians in busy emergency settings set their focus in ruling out acute and fatal events.

The significant variation in age and gender between the study group and the population is a sign of weaker external validity. One reason for this could be the lack of high priority

patients in the sample group, but probably there also was a selection bias from the clinically experienced staff due to their ability to discern from various grades of serious and urgent medical conditions. Implementation of quality projects in busy medical settings is likely influenced by for example the work load, and also the altering of staff from day to day. We can therefore not generalize the frequency of panic disorder in the chest pain population. An appropriate randomized controlled study should verify the actual grade of patients with PD presenting in the emergency ward. Another problem was that the indication of screening date was sparse. However 58% of self-report patients (n: 2073) had only one visit during the period and thus a self-report date traceable in the emergency registry database.

Further studies

Though this material has faults and inadequacies relating to the character of a quality project without strict control, it could still serve as a base for a longitudinal study of Panic Disorder as risk factor to later cardiac events. One could assume that the PQT algorithm is safe, since several studies have supported its high specificity (95 %). Taken together there is 1169 cases of Panic Disorder/Panic Attacks which could be matched with the No anxiety group over time as an estimate in differences in ischemic heart disease and mortality. Several well-controlled epidemiological studies have demonstrated an increased risk of later coronary disease in association with early presence of neuroticism and anxiety disorders. The psychological measures in these studies are based on interviews to recall stress and feelings of depression one year before myocardial infarction (Rosengren et al., 2004), interviews from a psychiatrist during military conscription ((Gale et al., 2014) (Janszky et al., 2010)), HADS reports (Hospital Anxiety and Depression Scale) to the Norwegian HUNT study (Gustad et al., 2014) and by ICD diagnostics (International Classification of Diagnoses) from the general practitioner (Walters et al., 2008). The present self-report material from 2008-2013 is from patients presenting with chest pain in an ED setting, which could possibly have a greater impact on the patient overall health status. The material is also constricted to a specific type of anxiety disorder, i.e. panic disorder, on which fewer studies are conducted.

Self-help (as opposed to *guided* self-help) was in a Cochrane report (Mayo-Wilson & Montgomery, 2013) defined as: “a therapeutic intervention administered through text-audiotape, videotape, or computer text, or through group meetings or individual exercises [...] and designed to be conducted predominantly independently of professional contact”. (Marchand et al., 2012) has shown signs of evidence for a lasting therapeutic effect of panic severity from minimal psychological resources from the emergency department, and patients improved even in supportive care group. According to SBU alert report (Statens beredning för medicinsk utvärdering (SBU), 2013), there are not enough studies carried out investigating Internet mediated CBT without advanced support, or the effects of Internet mediated CBT on health seeking behavior.

Since the physicians are preoccupied in ruling out acute and fatal events in the emergency setting, the nurses could possibly be of better help in guiding the Panic patient to proper care. A future study could examine if a brief intervention of health support character carried out by a nurse trained to a protocol in an ED setting, with referral to internet based

cognitive behavior therapy, or to CBT self-help can be beneficial for the panic/chest pain patient. The work should include modifying or developing a tool/manual for a brief intervention in a medical emergency setting, and testing in a randomized controlled trial.

Conclusion:

Patients with Panic Disorder and Panic Attacks have higher odds of being frequent ED-visitors, and it is possible use the PHQ panic module to increase the diagnoses of Panic Disorder in an ED setting. The cohort is probably large enough to be case-control matched (Panic Disorder/No anxiety) by propensity score for longitudinal studies of morbidity and mortality over time. To further help Panic patients in the ED, a nurse based intervention could be tested in a randomized trial.

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