Abstract. – OBJECTIVE: Panic disorder is characterized by the spontaneous and unexpected occurrence of panic attacks. During panic attacks, patients (pts) refer to the Emergency Department (ED). The diagnostic work-up for any panic attack is expensive since symptoms at presentation mimic other diseases such acute coronary syndrome or neurological emergencies.

The aim of the present study was to describe a 10 years cohort of pts diagnosed with panic disorder in the ED in terms of ED visit recurrence.

METHODS: Case-control study, in a tertiary care, involving pts presenting to the ED and diagnosed with panic attack according to the International Classification of Diseases 9th Revision (ICD-9). From January 2001 to Dec 2009 were extracted from the electronic clinical database 469 pts and were divided into “recurrent ED visit” (multiple ED access for panic attack) (N=361) and “no recurrent ED visit” (only one ED access for panic attack in 9 years) (N=108).

RESULTS: At univariate analysis cases and controls differed for male prevalence (p < 0.01), neurological symptoms at presentation (p = 0.02) and history of other psychiatry disorder (p < 0.01).

In multivariate analysis independent predictors were male gender, age under 40 year old, palpitations at presentations, 1 or more cardiovascular risk factors and previous other psychiatry conditions.

CONCLUSIONS: Male under 40 years old with palpitations or cardiovascular risk and other psychiatric diseases, have a higher recurrence of panic attacks. General psychiatric evaluation and treatment with benzodiazepine in ED is not useful to prevent recurrences. Identifying those patients at high risk of panic attack and ED visit recurrence might be useful to establish ad-hoc interventions, improve patients’ morbidity and save precious resources.

Key Words: Panic attack, Anxiety disorder, Psychosomatic symptoms, Emergency Department.

Introduction

Panic disorder (PD) is characterized by the spontaneous and unexpected occurrence of panic attacks, the frequency of which can vary from several attacks per day to only few attacks per year.

Panic attacks have a sudden or out-of-blue cause that lasts shorter with more intense symptoms, as opposed to anxiety attacks. These attacks typically last about ten minutes, but can be as short as 1-5 minutes and last as long as thirty minutes, typically has a peak within 10 minutes and then subside.

Panic attacks can occur in adults, as well as in young people; in this case may be particularly distressing because of less insight about what is happening.

Common symptoms of an attack include chest pain, tachycardia, dizziness, dyspnea, trembling, uncontrollable fear and hyperventilation.

There is no single cause for panic disorder; however, the family environment and genetic predisposition plays a strong role in determining who will get it.

Psychological factors, stressful life events, other psychiatric conditions such as bipolar disorder, alcoholism seems to play a role in the onset of P.D. Often the first attacks are triggered by physical illnesses, major stress, or certain medications.

Patients seek immediate medical care during panic attacks, commonly in the Emergency Department (ED) if they experience severe symptoms or they are not aware of the diagnosis already. Although PD is a benign disease in terms of mortality (but not in morbidity), ED diagnostic work-up for any panic attack is expensive since symptoms at presentation mimic other, less benign, diseases such acute coronary syndrome or neurological emergencies. Therefore, Emergency Medicine research focused on ad-hoc protocols to predict which clinical characteristics are associated with PD among undifferentiated chest pain patients.

How do patients with known PD use the ED, and mostly why, is less investigated. This is not a
trivial question in the overcrowded ED era. Alas, patients with recurrent ED visits for panic attacks and known PD are resource consuming and perhaps suitable for different and more appropriate management.

Some empirical studies have measured the efficacy of treatments for PD patients consulting ED for chest pain\textsuperscript{1-6}. Three studies\textsuperscript{3-5} demonstrated the efficacy of 2 benzodiazepines (aprazolam: 1-10 mg flexible dose 8-week trial; clonazepam: 1-4 mg flexible dose 6-week trial), which reported modest to significant reductions in panic attacks and chest pain episodes. Although these results are encouraging, it is difficult to ascertain whether this type of treatment is appropriate for the maintenance of long-term gains.

Other study\textsuperscript{2} demonstrated that a 1-hour individual psychotherapeutic intervention performed in the ED, consisting of instruction for behavioral exposure, is more efficacious for the reduction of PD symptoms than usual care. A second study offering treatment in the ED\textsuperscript{1} demonstrated the efficacy of paroxetine, 20 mg/d for 4 weeks in reducing PD symptoms, as well as the feasibility of emergency physician initiating the medication. A recently published paper\textsuperscript{6} aimed to assess the efficacy of both a psychological and a pharmacologic intervention for PD initiated and managed directly in the ED, compared with usual care. They conclude that both interventions were efficacious in reducing PD severity, panic attack frequency, and depressive symptoms.

The aim of the present study was to describe a 10 years cohort of patients diagnosed with PD in the ED in terms of ED visit recurrence. Patients diagnosed with PD and recurrent ED visits might be directed to a specific follow-up if correctly identified at the first episode.

Patients and Methods

Study Design

This study was a case-control study, performed in a tertiary care, university hospital, involving patients presenting to the ED and diagnosed with panic attack according to the ICD-9-CM diagnostic code\textsuperscript{7} at the time of ED disposition. The study considered 9 consecutive years period, from January 1\textsuperscript{st} 2001 through December 31\textsuperscript{st} 2009. Patient’s clinical characteristics were extracted from the electronic clinical database GIPSE(R) (Public Health Agency, Rome, Italy) that was used by ED physicians throughout the study duration and included all clinical patients’ medical records. All charts with primary diagnosis of panic attack were extracted and manually reviewed. Patients were excluded if symptoms at presentation and medical history were not consistent with the diagnosis of panic attack according to the DSM IV criteria\textsuperscript{8}. Two Authors checked for diagnosis accuracy and patients were considered eligible if the two Authors agreed on the panic attack diagnosis. If disagreement existed, a third Author was asked to review the case and make a final decision.

All patients selected (N=469) were searched for other ED visits in the same hospital following the access for panic attack. Those patients having a repeated ED diagnosis of panic attack (in a different ED visit) or symptoms consistent with panic attack according to the DSM IV criteria during the nine years considered, were classified as “recurrent” (N=361). This group was compared to those patients (N=108) whom had a panic attack in 2001 (12 consecutive months) and had no other ED access for the same problem (but had other ED access not related to anxiety disorder, such trauma).

Clinical information for patients enrolled were manually extracted in a dedicated database. Ethical approval was waived because of the epidemiological non-intention to treat design. Demographics, clinical pre-existing conditions, cardiovascular risk factors, symptoms at presentation, history of psychiatry disorder, tests performed in ED to rule out acute coronary syndrome (ECG and serial cardiac enzymes determination), treatment received in ED and psychiatry consult in ED were collected.

The primary end point of this study was to analyze which factors are associated with recurrent ED visits among patients with first diagnosis of panic disorder in the ED itself (and not overall panic attack recurrence).

The diagnosis of PD is based on Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV) criteria\textsuperscript{8}.

Panic attacks must be associated with more than 1 month of subsequent persistent worry about.

Having another attack, consequences of the attack, or significant behavioral changes related to the attack\textsuperscript{7,10}.

Panic attacks are a period of intense fear in which 4 of 13 defined symptoms develop abruptly and peak rapidly less than 10 minutes from symptom onset. To make the diagnosis of panic disorder, panic attacks cannot directly or physiologically result from substance use, medical conditions, or another psychiatric disorder (Table I).
**Statistical Analysis**

Eligible patients were divided into “recurrent ED visit” (multiple ED access for panic attack) and “no recurrent ED visit” (only one ED access for panic attack in 9 years). Patients’ characteristics are described as count and percentage, or median and interquartile range, according to the type of variable. Chi-square test for categorical variables and Mann-Whitney U test for continuous variables were used for univariate analysis.

Binary logistic regression was computed to analyze which factor was independent predictor of recurrent ED visits. Forward likelihood ratio entry method (with 0.10 and 0.05 inclusion and exclusion criteria respectively) was used to limit model inflation and overestimation. For each predictor, the Odd’s ratio (OR) and relative 95% confidential interval was computed. Tolerance was assessed to check for variables’ co linearity.

**Results**

Among the 469 patients included in the analysis, 108 (23.0%) were diagnosed with panic attack in the 2001 and never use again the ED for the same reason in the subsequent 9 years, while 361 (77.0%) had multiple ED visits for panic attacks in the same period of time. Patients’ baseline clinical characteristics are shown in Table II. Prevalence of cardiovascular risk factors was: 18 (16.7%) patients had one risk factor in the control group, while 78 (21.6%) in the cases group ($p = 0.25$). Ten patients (9.4%) had two or more risk factors in the cases group and N 45 (12.5%) in the control group ($p = 0.20$).

Cases and controls differed at univariate analysis for male prevalence ($p < 0.01$), neurological symptoms at presentation ($p = 0.02$) and history of other psychiatry disorder ($p < 0.01$). Fifty percent of the patients with recurrent panic attacks had 6 or more ED visits. The first ED visit recurrence was within 7 days in 16.6% of the cases and within 30 days in the 29.9%. Figure 1 shows recurrency pattern. Age distribution is shown in Figure 2 and it is comparable to previous publications.

Multivariate logistic regression model with recurrent versus non recurrent groups as dependent variable included the following predictors: demo-

### Table I. Symptoms of panic attack according to DSM-IV.

<table>
<thead>
<tr>
<th>Panic attack is diagnosed if 3 or more of the following symptoms are present (adapted from DSM-IV)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Palpitations, pounding heart, or accelerated heart rate</td>
</tr>
<tr>
<td>Sweating</td>
</tr>
<tr>
<td>Trembling or shaking</td>
</tr>
<tr>
<td>Sense of shortness of breath or smothering</td>
</tr>
<tr>
<td>Feeling of choking</td>
</tr>
<tr>
<td>Chest pain or discomfort</td>
</tr>
<tr>
<td>Nausea or abdominal distress</td>
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<tr>
<td>Feeling dizzy, unsteady, lightheaded, or faint</td>
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<tr>
<td>Derealization or depersonalization (feeling detached from oneself)</td>
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<tr>
<td>Fear of losing control or going crazy</td>
</tr>
<tr>
<td>Fear of dying</td>
</tr>
<tr>
<td>Numbness or tingling sensations</td>
</tr>
<tr>
<td>Chills or hot flashes</td>
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</tbody>
</table>

### Table II. Patients’ clinical characteristics. All numbers represent absolute count (percentage) except age expressed as medina (interquartile range).

<table>
<thead>
<tr>
<th>Cases (recurrent) N = 361</th>
<th>Controls (non recurrent) N = 108</th>
<th>$p$-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age 37 (30-48)</td>
<td>40.5 (31-50)</td>
<td>0.14</td>
</tr>
<tr>
<td>Male gender 148 (41%)</td>
<td>28 (25.9%)</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>Dyspnoea 79 (21.9%)</td>
<td>29 (26.9%)</td>
<td>0.28</td>
</tr>
<tr>
<td>Palpitations 102 (28.3%)</td>
<td>17 (15.3%)</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>Chest pain 46 (12.7%)</td>
<td>10 (9.3%)</td>
<td>0.33</td>
</tr>
<tr>
<td>Neurological symptoms</td>
<td>114 (31.6%)</td>
<td>0.02</td>
</tr>
<tr>
<td>Headache 22 (6.1%)</td>
<td>12 (11.1%)</td>
<td>0.08</td>
</tr>
<tr>
<td>Self-reporting anxiety</td>
<td>186 (51.5%)</td>
<td>0.54</td>
</tr>
<tr>
<td>No cardiovascular risk factors</td>
<td>270 (74.8%)</td>
<td>0.13</td>
</tr>
<tr>
<td>History of psychiatric disorder</td>
<td>175 (48.5%)</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>Cardiac work up 120 (35.7%)</td>
<td>28 (25.9%)</td>
<td>0.06</td>
</tr>
<tr>
<td>Psychiatric evaluation in ED</td>
<td>55 (15.2%)</td>
<td>0.55</td>
</tr>
<tr>
<td>Treatment with benzodiazepines</td>
<td>200 (55.4%)</td>
<td>0.98</td>
</tr>
<tr>
<td>Other drugs 42 (11.6%)</td>
<td>8 (7.4%)</td>
<td>0.21</td>
</tr>
</tbody>
</table>
Recurrent use of the Emergency Department in patients with anxiety disorder

graphics (age and gender), symptoms of presentation (chest pain, dyspnea, palpitation, self-reporting anxiety, headache and paresthesia), cardiovascular risk factors (hypertension, diabetes, smoke, dyslipidemia, coronary artery disease, family history of myocardial infarction before 65 year old), history of psychiatric disorder, cardiac work up performed during the ED visit (ECG and serial cardiac enzymes determination), treatment received in ED (benzodiazepines), psychiatry consult in the ED, and medical/psychiatry follow up recommended at discharge. Table III shows results from the model using forward likelihood ratio entry method. Overall model had p-value < 0.01, with Hosmer and Lemershow test value of 0.74. Independent predictors were gender (male), age under 40 year old, palpitations at presentations, one or more cardiovascular risk factors and previous other psychiatry conditions.

Discussion

Panic attack is an appropriate reason to seek care in the ED since symptoms at presentation mimic other life threatening conditions such myocardial infarction. In fact, the goal of the ED visit is to rule out such conditions and address the patient to the right follow up and treatment. Research focused on clinical signs, symptoms and protocols able to discriminate patients with organic diseases to those with psychosomatic or psychiatry symptoms.

Figure 1. First recurrent ED visit (days).

Figure 2. Age distribution of the Cohort.
But, few evidences (if not at all) exist that investigate clinical factors predicting recurrent ED visits for patients with anxiety disorder. In our cohort one out of three patients present to the ED for the same symptoms within 1 week after receiving a diagnosis of panic attack. Most of the times, patients were screened again for cardiac conditions perhaps for the perception of the emergency physician to have missed the diagnosis in the first (and recent) patient’s encounter, perhaps for the symptoms themselves that required further tests. The bottom line is that no emergency physicians want to miss a diagnosis of acute coronary syndrome, even if often in time a previous anxiety disorder diagnosis is known.

Identifying those patients at high risk of panic attack and ED visit recurrence might be useful to establish ad-hoc interventions, improve patients’ morbidity and save precious resources. Such interventions were already demonstrated to be effective in undifferentiated disorder anxiety populations18-20).

Multivariate logistic regression indicated that male gender, especially male under 40 years old, have a higher recurrence even if the prevalence of panic attacks in the general population is higher in women than men21,22.

Short acting drugs administration in the ED (i.e. benzodiazepine) is interestingly not associated with ED visit recurrence, indicating that patients seek care not for medications rather than to rule out “organic” dysfunctions. Moreover, general ED psychiatric consultations seemed not to prevent ED recurrent visit.

We acknowledge important possible bias in this study. First, cohort was a prospective collection of data but originally not created for the purpose of this study. Second, we cannot rule out that patients with no ED recurrence visited another ED elsewhere (although we tried to minimize such bias looking at a relative long period of time such 10 years). Third, the diagnosis of “panic attack” was reviewed blindly by two Authors to reduce the possible bias to include misdiagnosed patients in the cohort along with all hospital admission after the panic attack diagnosis, but we cannot rule out that few patients had medical conditions worsening the panic attack (i.e. subclinical hyperthyroidism). Therefore, the criteria presented here require further prospective evaluation to be used as predictors. However, our aim was rather to describe that a certain category of patients use recursively the ED.

Manifestations of overcrowding include boarding of patients in the ED, increased risk of medical errors, reduced reliability of the emergency care system, etc.

General psychiatric evaluation and treatment with benzodiazepine in ED is not useful to prevent recurrences. Perhaps these kind of patients need different treatment23.

PD often coexists with mood disorders. Many medical conditions apparently have in common significant comorbidity with PD. These conditions include cardiovascular disorders (e.g., mitral valve prolapse, hypertension, cardiomyopathy) and other disorders (e.g., chronic obstructive pulmonary disorder, irritable bowel syndrome, migraine headache)24.

The prevalence is higher in women than men and its incidence has a bimodal distribution, it means highest incidence in late adolescence and a second peak in early adulthood25, but not everyone who experiences panic attacks will develop panic disorder. Many people have just one attack and never have another. The tendency to develop panic attacks appears to be inherited26. Diagnosis is not simple because there are not specific laboratory parameters and specific imaging studies for PD. It is necessary to exclude any possible differential diagnosis.

History and mental status examination are the only things you can use to diagnose it.

In ED most chest pain patients do not have symptoms due to a clear cardiac cause27.
A good percentage of patients who arrive in ED has symptoms included in diagnostic criteria for PD28. Six of the 13 diagnostic symptoms of a panic attack are in common with cardiovascular diseases: chest pain, palpitations, sweating, shortness of breath, sensation of choking, and hot flushes29,30.

PD patients are underestimated and not followed by a clinical point of view if they don’t have a real cardiovascular disease. There is not a real screening for that kind of patients in emergency. When PD is identified and treated early the outcome is good11, instead untreated PD causes a chronic disabling disease32-35.

Untreated PD patients have high rate of recurrences and it is cause of ED overcrowding because patients with PD use frequently ED and health care resources36.

The only psychiatric examination in ED did not reduce the recurrences but outpatient psychiatric treatment should be started, in fact a cross-sectional study shows that if ED doctor don’t fail diagnoses of PD, patients with clinical criteria of PD should be willing to receive psychiatric care or psychological treatment.

Conclusions

Recognize diagnostic criteria for PD in ED and use specific protocol will improve patients’ care and reduce ED overcrowding due to PD patients.

References


