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Article type : Regular Article

**Adolescents with unexplained chest pain reported depression and impaired emotional and social functioning**

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**Short title:** Quality of life with unexplained chest pain

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**This is the author manuscript accepted for publication and has undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the [Version of Record](#). Please cite this article as doi: [10.1111/APA.15144](https://doi.org/10.1111/APA.15144)**

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### **Abstract**

**Aim:** Chest pain is common in adolescence, but there are no established criteria for managing this problem, which is rarely associated with cardiac disease. This study addressed the gaps in the literature by evaluating psychosocial factors that could be associated with medically unexplained chest pain.

**Methods:** We consecutively selected 100 patients (68% girls) aged 13-18 who were diagnosed with unexplained chest pain when they presented to the cardiology outpatient clinics of Tepecik Research Hospital, İzmir, Turkey, between 30 September 2015 and 30 June 2018. The controls were 76 age and sex matched adolescents (69% girls) aged 13-18 who were undergoing routine cardiology assessments before joining sports clubs. We assessed their health-related quality of life and any depression and physical symptoms.

**Results:** Regression analysis showed some adolescents were a number of times more likely to report chest pain. These included those who reported boredom (4.1 times), felt stressed or anxious (2.2) and those who experienced sleep disturbance (2.6), co-morbid headaches (2.0), back pain (3.1) and impaired social functioning (1.2).

**Conclusion:** The results indicated a significant association between unexplained chest pain and physical symptoms, depression and impaired emotional and social functioning. These factors warrant further evaluation.

**Keywords:** Adolescent, chest pain, depression, social functionality, somatic complaints

### **Key notes:**

- We evaluated the psychosocial factors that could be associated with medically unexplained chest pain in 100 adolescents aged 13-18.

- Regression analysis showed that some factors were a number of times more likely to be associated with chest pain: boredom (4.1 times), stress or anxiety (2.2) sleep disturbance (2.6), co-morbid headaches (2.0), back pain (3.1) and impaired social functioning (1.2).
- These factors warrant further evaluation when other causes cannot be explained.

## INTRODUCTION

Chest pain is one of the most common physical complaints in adolescents and can often result in them visiting their family doctor or emergency department or receiving a specialist referral (1,2). It generates significant anxiety for adolescents who may perceive their pain as serious and potentially life threatening (3). Adolescent chest pain can be divided into three forms: cardiac, non-cardiac and psychosomatic. In most cases adolescent chest pain is not caused by heart disease and does not require medical intervention, unlike chest pains in adults (4). Cardiac causes are rare and often the result of congenital structural disease, acquired pericardial, myocardial or coronary artery disease and arrhythmia. Thoracic cage disease, musculoskeletal pain, sickle-cell anaemia, gastrointestinal disease and pulmonary disease are the common causes of non-cardiac adolescent chest pain (5-11).

Chest pain without a significant organic cause has been given various names, such as atypical chest pain, angina-like chest pain, idiopathic chest pain or unexplained chest pain (UCP) (12-14). Age is an important consideration in the differential diagnosis of paediatric chest pain. Younger children are more prone to have a cardio respiratory aetiology, such as asthma, cough, pneumonia or heart disease, while adolescents are more likely to have pain

associated with psychological or emotional distress (12). Children reporting UCP also report higher rates of other physical symptoms that may require medical evaluation and they are high users of medical services (5,11). Accordingly, joint psychosocial evaluation in conjunction with a complete medical assessment is important for thoughtful and comprehensive evaluation and diagnosis of UCP in adolescents.

Despite the fact that UCP is common and associated with significant health care use, the current evidence about the role of UCP and its association with depression in adolescents is limited (5,11,15). Pantell and Goodman reported that 31% of adolescents who presented with chest pain had a history of stressful life events (15). Even less is known about the impact of UCP on functionality or quality of life. The aim of this study was to assess the association between adolescent chest pain and, particularly UCP, on symptoms of depression, reports of other somatic complaints and quality of life. Our hypothesis was that adolescents with UCP would have more symptoms of depression, somatic complaints and a low level of quality of life than controls without UCP.

## **PATIENTS AND METHODS**

### **Study setting and population**

This study was carried out between 30 September 2015 and 30 June 2018. The patients were selected from the 144 adolescents (73% girls) aged 13-18 years old who consecutively presented to three different outpatient cardiology clinics of Tepecik Training and Research Hospital and were diagnosed with UCP. We excluded 12 people who were not native Turkish speakers, 11 adolescents with a chronic disease, such as gastroesophageal reflux disease, cardiovascular disease and pulmonary disease, and 21 patients who were not referred to the adolescent medicine outpatient clinic following their initial cardiology visit. During the study period 112 adolescents (82% girls) attended the same hospital for routine cardiovascular screening. In our area of Turkey children who plan to join sports clubs undergo cardiovascular checks to ensure that they are fit enough for competitive sport. We applied the same health and language-related exclusion criteria to this cohort and 76 of the 112 eligible participants agreed to join the control group. The patients and controls were individually matched by age and sex.

### **Data collection**

We focused on the 100 paediatric cardiology patients who received a diagnosis of UCP after they presented to one of the three outpatient cardiology clinics and were then referred to the

adolescent medicine outpatient clinic. This clinic provided further psychosocial evaluation. A structured interview was performed during their first meeting at the adolescent medicine outpatient clinic and this included the first part of the data form. The interview was carried out by an adolescent medicine researcher. The structured form included their sex, age and the HEEADSSSS 3.0 psychosocial interview for adolescents. This acronym stands for: home and environment, education and employment, eating and exercise, activities, drugs and substances, sexuality, suicide and depression and safety (16,17). The depression screening questions in the psychosocial interview were used for this study. We also used additional questions about somatic symptoms during the interview to complement the psychosocial evaluation (17). The questions were related to the previous two-week period and covered boredom, state of stress or anxiety, depressed mood, sleep disturbance and any additional complaints, such as headache, backache, stomach ache or drowsiness (17). The possible responses, which were yes or no, were recorded by the researchers without probing the participants further and used as single items in the study.

After the interview, the participants were asked to fill the Paediatric Quality of Life Inventory (PedsQL) on a paper. The PedsQL is a modular instrument that measures health-related quality of life, as well as physical and psychosocial functioning in children aged 2-18 years. It consists of four subscales including physical, emotional, social, and school functioning. It is a five-point Likert scale, ranging from zero for never to four for almost always. Items are reversed scored and linearly transformed to a 0-100 scale as follows, with higher scores indicating a better quality of life. The PedsQL was used for its strong psychometric properties and the availability, reliability and validity of the Turkish version. The Cronbach's alpha coefficient of the inventory was 0.82 (18).

The data collection process was identical for the 76 controls, but they were interviewed during their outpatients' visit to the paediatric cardiology outpatient clinic.

### **Data analysis**

The number of participants in each group was determined before the study by a power calculation and this found that 75 participants in each group provided 0.05 alpha and 86% power based on Cohen's advice (19). The statistical analyses were performed using SPSS version 21.0 (IBM Corp, New York, USA). Descriptive statistics were used to describe the socio-demographic information of the patient and control groups. As a first step, a univariate binary logistic regression method was performed to compare proportional data, such as the depression symptoms and somatic complaints for each single item or the subscale scores of the PedsQL. By using the Backward-Wald method and, or, any p values of less than 0.1, items

were selected for a multivariate binary logistic regression analysis to determine the effect of subject-related factors on the depression screening, somatic complaints for the risk of exhibiting UCP.

The study protocol was approved by the local ethics committee (30.06.2015/7/24) and informed assent and consent was obtained from the individual participants. Additional consent was obtained from their parent or guardian if they were under the age of 15.

## **RESULTS**

The 100 UCP patients and the 76 controls who took part in this study were aged 13-18 years and were predominantly from low-income families, as defined by the National Income and Living Conditions Survey. The difference in income levels between the patients and controls was not statistically significant (Table 1) (20). There were no statistically significant differences in age or sex between the groups (Table 1). The majority of the participants were girls - 68% of the patients and 69% of the controls – and their mean ages were  $14.5 \pm 1.7$  years for the patients and  $14.9 \pm 2.1$  years for the controls, respectively.

When we examined the groups for the cases who had at least one depression symptom, there were 88/100 (88.0%) cases in the chest pain group and 34/76 (44.7%) in the control group. These depression symptoms including boredom, stress or anxiety, depressed mood and sleep disturbance were significantly higher in the UCP group (Table 2). When we examined the groups with regard to somatic complaints, 76.0% of the cases in the UCP group had at least one symptom, while it was 35.5% in the control group. Associated somatic complaints, headache and back pain were significantly higher in adolescents in the UCP group than the control group (Table 2). When we looked at the PedsQL subscales, the emotional and social functionality scores were significantly lower in the UCP group than the controls (Table 3).

Binary logistic regression analysis showed adolescents who were bored were 4.1 times more likely to have be in the UCP group than the control group. Those who felt stressed or anxious were 2.2 times more likely and those with sleep disturbance were 2.6 times. Adolescents presenting with co-morbid headache were 2.0 times more likely to have UCP and those with co-morbid back pain had a 3.1 times greater risk of UCP (Table 2). With regard to the PedsQL subscales, impaired peer functioning increased the risk of UCP 1.2 times and impaired emotional functioning increased it 1.1 times compared to the controls. No other measures on the PedsQL were associated with UCP (Table 3).

## **DISCUSSION**

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As we hypothesised, adolescents with UCP had greater depressive symptoms, worse quality of life and increased somatic co-morbid complaints than the controls. When it came to the depressive symptoms of boredom, stress or anxiety, sleep disturbance, headache and back pain, there was a higher risk for depression and worse mental well-being in adolescents with UCP. Most research in this area has studied both children and adolescents or has studied adolescents with chest pain without discriminating between medical and psychosomatic chest pain. The present study only investigated these factors in a group of adolescents clinically diagnosed with UCP which was not consistent with previous data. The results of this study suggest routine assessment and screening for depression, co-morbid somatic complaints and quality of life are beneficial when evaluating adolescents with UCP.

Adolescence can be challenging from a psychosocial perspective, as the individual asserts their identity and forms their own view of the world and themselves. Increased introspectiveness and sensitivity to bodily symptoms are part of normal adolescent development. As such, somatic symptoms increase during adolescence, both due to an increased perception of physical sensations as well as a manifestation of psychological distress (21-23). This can be a significant reason for healthcare use in this population. In this study, most of the participants were girls. Current evidence suggests that younger children, both boys and girls, face a higher risk for somatoform disorders, with similar ratios between genders (24). As individuals move through adolescence, somatic symptoms are more common in girls (25). The subjects in our study were age and gender matched. Impaired social and economic factors can have an impact on psychosocial factors and can be expected to play a role in developing symptoms of depression in adolescents (26). However, because of the hospital-based design of the current study, both groups came from low-income families and we were restricted to comparing those factors for depression symptoms.

Adolescents with somatic complaints face a greater risk of depression (27). Our study demonstrates that depressive symptoms predicted the occurrence of UCP, which was consistent with previous studies (27). Furthermore, depressive symptoms may influence the emergence of other somatic symptoms and contribute to the development of UCP. Somatisation is strongly and consistently linked to psychological distress and may be a sign of underlying anxiety and, or, depression (28). Given the ratio of somatic complaints and its association with depressive symptoms in this study, a coordinated, joint assessment of physical health and mental health factors when evaluating UCP may be more acceptable to patients and their families. This may also normalise the conversation regarding psychological factors influencing symptom presentation (29). Furthermore, this will expedite the evaluation

and management of psychological and psychiatric co-morbidities and potentially limit unnecessary and invasive medical diagnostic testing and interventions. It will also limit the sense that the patient and family are being handed over to mental health professionals or that the somatic symptoms are all in their head (30). Health professionals frequently encounter patients with somatic complaints that defy effective medical explanations. It is inevitable that somatic complaints may develop into chronic problems, such as stress, considerable distress, disability and healthcare use. Clinicians should understand the mechanism of these conditions to provide better management protocols for medically unexplained symptoms (31). The biopsychosocial model has been used to enhance the knowledge of disease processes and their aetiology, but encouraging clinicians to adopt that approach is essential for better management (32). The current study indicates the importance of biopsychosocial evaluations and the need for a holistic approach to adolescents with UCP. Screening adolescents for psychological health may help to avoid unnecessary investigations and high costs to the healthcare system. Comprehensive diagnostic assessments and the development of new intervention methods are important avenues for future research.

In addition, this study highlights the association between UCP and quality of life. The emotional and social quality of life subscale scores were significantly lower in the UCP group than the control group. Past studies have shown that adolescent somatisation originates from negative emotions, maladaptive coping, poor emotion regulation, ineffective interpersonal skills and limited social support (33). Our study identifies the importance of healthy peer relationships and social support, in line with past studies. These findings underscore the important role that peer relations play in adolescent well-being among those with UCP (34,35). On the other hand, the physical functioning scores of the PedsQL were not statistically impaired in the UCP group. In the literature, there was only one study about the restricted physical activities of adolescents with chest pain. However, the study group consisted of organic and somatic causes at the same time (15). In the present study, the participants with chest pain were all medically unexplained and it was suggested that the adolescents did not accept they had cardiac issues and they did not feel any need to restrict any physical activities. In addition, the school functioning scores of the PedsQL were not statistically different. This dimension is related to perceived academic performance and school adjustment. The possible reason for this surprising finding can be another confounding variable that can affect school functioning, like temperament, character or family factors that we did not evaluate in this study.



This study had several important limitations. It obtained the quality of life scores based on self-report questionnaires, which may be subject to bias due to the subjects' self-concepts and perceptions. However, the value of quality of life is largely related to the perception of individuals and therefore this limitation should not have any impact on the findings. The cross-sectional nature of the study may have prevented our ability to detect direct causal relationships between the variables. The lack of detailed demographic information, such as the marital status of the parents and co-morbidities limited the discussion on the participants' characteristics. In addition, the investigators were not blinded to group membership during the structured interview of depressive symptoms and somatic complaints that were used in HEEADSSS (16). They were not validated questions. However, investigators had considerable experience in the subject area and were able to ask direct questions about symptoms during the interview. The decision to not blind the investigators was made to give the investigator the ability to obtain a more accurate history of the adolescents' depressive symptoms by using their clinical judgment. This is also what is typically done in practice and allows the study findings to be more applicable to real-life settings.

## **CONCLUSION**

Our findings suggest that there is an association between UCP and adolescent depressive symptoms. Furthermore, adolescents with UCP appeared to have impaired emotional and social functioning. This was one of the few studies in the literature to evaluate adolescent depression and quality of life in relation to UCP. The results of the study affirm the importance of early mental health and psychosocial assessments and screening in this population, as well as the value of joint mental health and physical health evaluations in managing UCP. An evaluation of associated co-morbid factors is helpful in developing comprehensive holistic formulation. This study should promote greater awareness of the psychological and psychiatric factors that have an impact on the evaluation and management of adolescents presenting with chest pain. We hope that this will limit both the low yield and the number of unnecessary diagnostic studies or interventions, as well as provide a coordinated approach that involves both mental health and physical health professionals.

## **Abbreviations**

PedsQL, Paediatric quality of life inventory; UCP, Unexplained chest pain.

## **FUNDING**

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This study did not receive any specific funding.

## CONFLICTS OF INTEREST

The authors have no conflicts of interest to declare.

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**Table 1.** Participant socio-demographics

	UCP group (n=100)	Control group (n=76)	<i>p</i> value
<i>Age (y)</i>	14.5 ± 1.7	14.9 ± 2.1	**0.114
<i>Gender</i>			
Girls (n, %)	68 (68%)	53 (69%)	*0.806
Boys (n, %)	32 (32%)	23 (31%)	
<i>Household income</i>	1041 ± 112 TL	829 ± 136 TL	**0.221

UCP, unexplained chest pain, TL, Turkish Lira \*chi-square test, \*\*independent sample t-test,

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**Table 2.** Univariate and multivariate analyses showing factors independently associated with chest pain, with individual binary logistic regression values for each symptom included in the screening for depression and somatic complaints

	Univariate analysis			Multivariate analysis <sup>a</sup>					
	UCP group	Control group	<i>P</i> value*	OR (95%CI)	B	S.E.	Wald	<i>P</i> *	OR (95%CI)
<b>Depression screening</b>									
Boredom	63/100 (63%)	18/76 (23.6%)	< <b>0.001</b>	5.486 (2.817-10.686)	1.500	0.382	15.436	< <b>0.001</b>	4.481 (2.120-9.469)
Stress or anxiety	59/100 (59%)	23/76 (30.2%)	< <b>0.001</b>	3.316 (1.764-6.233)	0.856	0.366	5.488	<b>0.019</b>	2.355 (1.150-4.820)
Depressed mood	33/100 (38%)	17/76 (22.3%)	<b>0.027</b>	2.217(1.084- 4.173)					
Sleep disturbance	53/100 (53%)	18/76 (23.6%)	< <b>0.001</b>	3.634 (1.880-7.021)	0.958	0.368	6.791	<b>0.009</b>	2.607 (1.268-5.360)
<b>Somatic complaints</b>									
	Univariate analysis			Multivariate analysis <sup>b</sup>					
Headache	65/100 (65%)	35/76 (46%)	<b>0.012</b>	2.176(1.182- 4.005)	0.708	0.332	4.530	<b>0.033</b>	2.029 (1.058-3.893)
Back pain	31/100 (31%)	9/76 (11.8%)	<b>0.003</b>	3.345(1.481-7.554)	1.131	0.424	7.111	<b>0.008</b>	3.098 (1.349-7.113)
Abdominal pain	19/100 (19%)	9/76 (11.8%)	0.198	1.746(0.741-4.113)					
Drowsiness	18/100 (18%)	11/76 (14.4%)	0.532	1.297(0.573-2.938)					

<sup>a</sup> When all predictors for depression screening were entered included in binary logistic regression. Dependent variable: unexplained chest pain. Independent variables: boredom, stress or anxiety, depressed mood or, sleep disturbance. Omnibus test: chi-square = 42.5,  $p = <0.001$ . Hosmer and Lemeshow test: chi-square = 4.231,  $p = 0.753$ . Cox & Snell R Square: 0.215. Nagelkerke's R Square: 0.288. Omnibus tests of model coefficients: 78.6% of the cases were correctly classified from the full model.

<sup>b</sup> When using the predictors of psychosomatic symptomatology in binary logistic regression. Dependent variable: unexplained chest pain. Independent variables: headache, back pain, abdominal pain and drowsiness. Omnibus test: chi-square = 15.01,  $p = 0.005$ . Hosmer and Lemeshow test: chi-square = 3.101,  $p = 0.684$ . Cox & Snell R Square: 0.082. Nagelkerke's R Square: 0.110. Omnibus tests of model coefficients: 56.8% of the cases were correctly classified from the full model.

\* Binary logistic regression., UCP, unexplained chest pain.

PedsQL subscales	Univariate analysis			Multivariate analysis <sup>a</sup>					
	Chest pain group (mean ± SD)	Control group (mean ± SD)	<i>P</i> value	OR (95%CI)	B	S.E.	Wald	<i>P</i> value	OR (95%CI)
Physical functionality	68.72 ±21.09	74.74 ±17.52	0.052	1.051 (0.999-1.1006)					
Emotional functionality	63.87 ±23.66	73.54 ±17.33	<b>0.005</b>	1.119 (1.034-1.211)	0.074	0.044	2.881	0.090	1.077 (0.989-1.173)
Social functionality	87.73 ±20.03	95.00 ±7.37	<b>0.009</b>	1.225 (1.053-1.4269)	0.166	0.081	4.245	<b>0.039</b>	1.181 (1.008-1.383)
School functionality	62.53 ±24.26	68.40 ±18.68	<b>0.088</b>	1.064 (0.991-1.144)					

**Table 3.** Univariate and multivariate analysis for PedsQL: factors independently associated with chest pain

<sup>a</sup>When all predictors of PedsQL were included in the binary logistic regression. Dependent variable: unexplained chest pain. Independent variables: physical functionality, emotional functionality, social functionality and school functionality. Omnibus test: chi-square = 13.516, *p* = 0.009. Hosmer and Lemeshow test: chi-square = 22.316, *p* = 0.004. Cox & Snell R Square: 0.080. Nagelkerke's R Square: 0.107.

PedsQL: Paediatric Life Quality Inventory Scale