

Quality of Life in Patients with Coronary Artery Disease and Panic Disorder: A Comparative Study

Shruti Srivastava^{1*}, Skand Shekhar¹, Manjeet Singh Bhatia¹ and Shridhar Dwivedi^{2,3}

¹Department of Psychiatry, University College of Medical Sciences & Guru Teg Bahadur Hospital, Dilshad Garden, Delhi, India

²Medicine/Preventive Cardiology, University College of Medical Sciences & Guru Teg Bahadur Hospital, Dilshad Garden, Delhi, India

³National Heart Institute, East of Kailash, New Delhi, India

ARTICLE INFO

Article history:

Received: 4 May 2016

Accepted: 22 August 2016

Online:

DOI 10.5001/omj.2017.04

Keywords:

Coronary Artery Disease; Panic Disorder; Quality of Life; Chest Pain; Smoking.

ABSTRACT

Objectives: The quality of life (QOL) of patients with coronary artery disease (CAD) is known to be impaired. Non-cardiac chest pain referrals are often under-diagnosed and untreated, and there are hardly any studies comparing the QOL of CAD and panic disorder related (non-cardiac) chest pain referrals (PDRC). **Methods:** We assessed the psychiatric morbidity and QOL of patients newly diagnosed with CAD (n = 40) at baseline and six weeks post-treatment and compared their QOL with patients with PDRC (n = 40) and age- and gender-matched healthy controls (n = 57). Psychiatric morbidity in the CAD group was assessed using the General Health Questionnaire (GHQ12) item, Hamilton Anxiety Scores (HAM-A), and Hamilton Depression Scores (HAMD). QOL measures were determined by the World Health Organization QOL questionnaire (brief) and Seattle Angina Questionnaire. The CAD group was treated with anti-ischemic drugs (nitrates, betablockers), antiplatelet drugs (acetylsalicylic acid), anticoagulants (low molecular weight heparin, clopidogrel), and managed for risk factors. The PDRC group was treated with selective serotonin reuptake inhibitors and anxiolytics. **Results:** Patients with panic disorder had a worse QOL than those with CAD and healthy controls in the physical domain and psychological domain (PDRC vs. CAD vs. healthy controls, $p < 0.001$). In the CAD group, smoking was associated with change in angina stability ($p = 0.049$) whereas other tobacco products were associated with change in angina frequency ($p = 0.044$). Psychiatric morbidity was present in 40.0% of patients with CAD. In the PDRC group, a significant correlation of HAM-A scores was noted in the physical ($p = 0.000$), psychological ($p = 0.001$), social ($p = 0.006$), and environment ($p = 0.001$) domains of QOL. Patients with panic disorder had a significant improvement in anxiety scores after treatment compared to baseline (HAM-A scores difference 21.0 [16.5–25.6]; $p < 0.001$). **Conclusions:** Patients in the PDRC group had a worse QOL than those in the CAD and healthy control groups. This highlights the need for careful diagnosis and prompt treatment of panic disorder in these patients to improve their QOL. Additionally, smoking, the use of other tobacco products, and hypercholesterolemia were associated with angina symptoms in patients with CAD.

Panic disorder consists of recurrent, unexpected attacks of abrupt onset, intense fear reaching a peak in minutes and are associated with autonomic, psychic symptoms, anticipatory anxiety of future attacks, and avoidance.¹ Panic symptoms in the presence of coronary artery disease (CAD) are often missed since the symptoms of panic attack overlap with the clinical presentation of CAD.² Hence, it becomes imperative to understand the relationship between panic disorder and CAD.

Quality of life (QOL) as an outcome measure for the treatment CAD has been the focus of recent

research.^{3,4} Several studies conducted globally on patients with CAD revealed that they had a worse QOL compared with healthy controls.^{5–7} A recent study found that anxiety, depression, and QOL are related to CAD severity.⁸ Improvement in health-related quality of life (HRQOL) in CAD patients was found to predict a lower four-year-all-cause-mortality in patients with CAD at three months follow-up using Mac New Heart Disease HRQOL questionnaire scores.⁹ Recent research has also shown that QOL in patients with CAD improves with interventions aimed at mediating psychiatric morbidity.^{10–12}

The Global Burden of Disease study, 2010, found CAD and depressive disorders were the two leading causes of disability-adjusted life years (DALYs).^{13,14} The prevalence of CAD in urban populations in India has been estimated between 5% and 10%,^{14,15} and 3.3% to 7.4% in rural India.^{16,17} According to the 2001–3 census, cardiovascular diseases were the leading cause of mortality accounting for 19% of deaths in India.¹⁸ It is estimated that CAD will reach even higher proportions by 2020, making it a leading cause of mortality and morbidity worldwide in developing and developed countries.¹⁹

Panic disorders in emergency referrals often go unrecognized and untreated.^{20–22} Patients suffering from non-cardiac chest pain referred to the psychiatry department are often associated with impaired QOL.²³

To the best of our knowledge, there are few studies available comparing the QOL in patients newly diagnosed with CAD with those having panic disorder-related chest pain (PDRC). Therefore, our study aimed to investigate the psychiatric morbidity and QOL in patients newly diagnosed with CAD and compare this to patients with PDRC and a healthy control group.

METHODS

Patients were recruited from the Coronary Care Unit and Psychiatry Outpatient Department of Guru Teg Bahadur Hospital, a tertiary care teaching hospital attached to University College of Medical Sciences, Delhi, India. It is a government run hospital providing free consultation, investigations, and treatment.

The diagnosis of CAD was made by the treating physician after taking a thorough history and confirmation by electrocardiography and/or enzyme studies. The diagnosis of CAD was based on the revised definition of myocardial infarction (MI).²⁴ This is characterized by a rise and/or fall of biochemical markers of myocardial necrosis with at least one ischemic symptom, development of pathologic Q waves on the electrocardiogram (ECG), ECG changes indicative of ischemia, imaging evidence of new loss of viable myocardium or new regional wall abnormality. It is also characterized by features of Braunwald's clinical classification of unstable angina/non-ST elevation MI, which includes new onset of severe angina or accelerated

angina, no rest pain (class I), angina at rest within past month but not within 48 hours (class II), and angina at rest within 48 hours (class III).²⁵ Patients who were at least 25 years of age and fulfilled the CAD criteria were included in the study and asked to provide written informed consent. The Institutional Ethics Committee approved the study. Participants were excluded if they had a history of organic mental disorder, epilepsy, or severe mental disorder.

Sixty newly diagnosed CAD patients were evaluated and followed-up weekly for six weeks. Ten patients required stent/bypass procedures and were referred for emergency interventions. Five patients expired during the follow-up period, and assessments not completed. Two patients were lost to follow-up because they traveled a long distance for evaluation, and three withdrew their consent. The final study sample was 40.

Non-cardiac chest pain referrals to the Department of Psychiatry in the absence of a clinical history of cardiac disease, ECG changes or enzyme changes were screened for CAD. Out of 70 referrals during the study period, 40 consecutive diagnosed cases of PDRC (based on the Structured Clinical Interview for Diagnostic and Statistical Manual of Mental Disorders (DSM-IV)) were included. Both the World Health Organization QOL (WHOQOL) and disease severity for anxiety symptoms questionnaires were conducted at baseline and six weeks for the PDRC group.

Fifty-seven age- and gender-matched healthy controls were recruited to compare QOL measures.

We used the WHOQOL Questionnaire brief version (WHOQOL-BREF) to assess QOL. It is one of the most well-known general questionnaires for assessment. It assesses four domains: physical, psychological, social, and environment. It has been used in both healthy populations and various disease groups including CAD²⁶ and panic disorder.²⁷ The WHOQOL-BREF Hindi (standardized) version was completed by all participants in the three groups, and a detailed history of both the patients with CAD and PDRC was taken. The known risk factors for CAD like family history, hypertension, diabetes, dyslipidemia, alcohol consumption, smoking or consumption of other tobacco products and relevant past medical history were also noted.

We used Kuppaswamy's Socio-Economic Status Scale to assess the socio-economic status of the participants.²⁸ It includes three parameters:

education, occupation, and monthly family income (Rupees). Education was further divided into subcategories with scores (professional (7), graduate or postgraduate (6), intermediate or post high school diploma (5), high school certificate (4), middle school certificate (3), primary school certificate (2), illiterate (1)). Occupation was also subdivided and scored (professional (10), semiprofessional (6), clerical/shop owner/farmer (5), skilled worker (4), semiskilled worker (3), unskilled worker (2), unemployed (1)). Monthly income was also graded and scored. Scores from all three parameters were summed and socioeconomic status classified as low, middle, or high income.

The Seattle Angina Questionnaire (SAQ) was used to assess HRQOL at baseline and at six weeks in patients with CAD.²⁹ The questionnaire assessed four parameters: physical limitation, angina frequency, angina stability, and QOL.

Finally, the 12-item General Health Questionnaire (GHQ-12)³⁰ was used to screen for psychiatric morbidity among patients with CAD. Those with significant GHQ scores were evaluated by qualified psychiatrists and were further assessed for depressive symptoms using the Hamilton Rating Scale for Depression–17 item³¹ (HAMD-17), and

the Hamilton Rating Scale for Anxiety (HAM-A)³² for symptoms of anxiety. HAM-A was also used to assess the severity of anxiety symptoms in the PDRC group. A clinical diagnosis of panic disorder was made in patients with CAD by qualified psychiatrists based on the Structured Clinical Interview for DSM-IV Axis I Disorders (SCID-DSM-IV) criteria.

Descriptive statistics were given as mean, standard deviation (SD), absolute frequencies, and percentages. Analysis of variance was used to find differences between the groups in the raw domain mean scores on all QOL measures in patients with CAD, panic disorder, and healthy controls. Pearson correlation was performed to find any association between disease severity and WHOQOL domain scores and the paired *t*-test was performed to determine if any change was significant. Regression analysis was performed between the change in SAQ parameters and risk factors associated with CAD. A *p*-value < 0.050 was considered statistically significant.

RESULTS

Among patients with CAD, the risk factors found were hypertension (50.0%), hypercholesterolemia

Table 1: Demographic data of patients with coronary artery disease (CAD), panic disorder related chest pain (PDRC), and healthy controls (HC).

	CAD (n = 40)	PDRC (n = 40)	HC (n = 57)	<i>p</i> -value
Gender, n (%)				0.002*
Male	33 (82.5)	18 (45.0)	37 (64.9)	
Female	7 (17.5)	22 (55.0)	20 (35.1)	
Age, mean±SD, years	53.9±9.4	47.0±14.0	50.7±10.4	0.004**
Education (score)				0.068
Graduate or higher	6 (15.0)	4 (10.0)	10 (17.5)	
High school or intermediate	7 (17.5)	12 (30.0)	15 (26.3)	
Middle school	16 (40.0)	8 (20.0)	20 (35.1)	
Primary school	7 (17.5)	6 (15.0)	10 (17.5)	
Illiterate	4 (10.0)	10 (25.0)	2 (3.5)	
Socioeconomic class (score)				0.114
Upper income	0 (0.0)	1 (2.5)	4 (7.0)	
Middle income	2 (5.0)	5 (12.5)	10 (17.5)	
Lower income	38 (95.0)	34 (85.0)	43 (75.4)	
Occupation (score)				0.590
Professional	17 (42.5)	13 (32.5)	23 (40.4)	
Worker	22 (55.0)	26 (65.0)	30 (52.6)	
Unemployed	1 (2.5)	1 (2.5)	4 (7.0)	

^sBased on monthly family income. *Bonferroni adjustment for gender in HC vs. PDRC, *p* = 0.153; HC vs. CAD, *p* = 0.162. **Tukey test for age between HC vs. PDRC, *p* = 0.203; HC vs. CAD, *p* = 0.134. Chi-square statistic was used for categorical variables, namely education, income, and occupation.

Table 2: Comparison of World Health Organization Quality of Life Questionnaire-brief version (WHOQOL-BREF) domain scores for coronary artery disease (CAD), panic disorder related chest pain (PDRC), and healthy control (HC) groups.

WHOQOL-BREF domains	CAD	HC	PDRC	p-value	Tukey's multiple comparison test		
					CAD vs. HC	CAD vs. PDRC	HC vs. PDRC
Physical	21.1 (3.7)	25.5 (3.6)	18.3 (5.29)	< 0.001	0.000*	0.009*	0.000*
Psychological	20.9 (3.8)	21.6 (3.27)	15.6 (4.1)	< 0.001	0.600	0.000*	0.000*
Social	7.2 (1.1)	10.0 (2.2)	8.4 (2.6)	< 0.001	0.000*	0.019*	0.001*
Environment	26.9 (4.2)	27.1 (4.3)	24.3 (3.9)	0.003	0.953	0.018*	0.004*

Data presented as mean±SD. *p-value < 0.050 (significant).

(42.5%), diabetes (35.0%), family history of CAD (15.0%), alcohol dependence (20.0%), cigarette or bidi (thin Indian cigarette) smoking (67.5%), or current consumption of other tobacco products (27.5%).

Table 1 shows the characteristics of patients in the CAD and PDRC groups. The QOL scores as measured by WHOQOL-BREF are presented in Table 2. All four raw domain scores of physical, psychological, social, and environment in CAD group were lower than those found in healthy controls. Significant differences were noted in only the social and physical domains. There were statistically significant differences in raw scores of QOL in CAD, PDRC, and healthy control groups in all domains. All four WHOQOL-BREF domain scores between the CAD and PDRC groups were statistically significant using Tukey's multiple comparisons. The PDRC group had significantly

lower domain scores than healthy controls in all four domains.

There was statistically significant change in angina stability and frequency after six weeks of treatment in patients with CAD [Table 3]. The pretreatment angina frequency scale score (81.1±16.2) was significantly lower than the post-treatment angina frequency scale score (97.4±11.2). The pretreatment angina stability scale score (0.0 [0.0–25.0]) was significantly lower than the post-treatment angina stability scale score (50.00 [25.0–100.0]), with higher scores indicating less frequent angina post-treatment [Table 3].

GHQ-12 score, an indicator of psychiatric morbidity, was significant in 16 CAD patients (40.0%). HAMD scores in the CAD group were: normal or no depression (0–7) in 24 patients (60.0%), mild depression (8–13) in 12 patients (30.0%) and moderate depression (14–18) in four patients (10.0%). The distribution of HAM-A scores in the CAD group were: no (< 14) or mild anxiety symptom scores (14–17) in 24 patients (60.0%), moderate anxiety (18–24) in eight patients (20.0%), and severe anxiety (25–30) in eight patients (20.0%).

Treatment was initiated after clinical confirmation of psychiatric diagnosis by experienced psychiatrists. Moderate depressive disorder was found in four patients with CAD who were treated with selective serotonin reuptake inhibitors (SSRIs). Eight CAD patients with comorbid panic disorder received anxiolytics along with SSRI in lower doses than those prescribed for depression.

A statistically significant negative association was found between change in angina frequency and other tobacco products consumption ($p = 0.044$) in patients with CAD patients. The negative association

Table 3: Summary scores on Seattle Angina Questionnaire (SAQ) at baseline (pretreatment) and after six weeks follow-up (post-treatment) in patients with coronary artery disease (CAD).

Scale	Pretreatment CAD	Post-treatment CAD	Sig. (two-tailed)
Physical limitation	39.7 (18.4)	41.7 (14.4)	0.421
Angina stability**	0.0 [0.0–25.0]	50.0 [25.0–100.0]	< 0.001*
Angina frequency	81.1 (16.2)	97.4 (11.2)	< 0.001*
Treatment satisfaction	70.4 (9.2)	71.3 (3.7)	0.576
Quality of life	58.8 (12.1)	62.0 (12.9)	0.224

Data presented as mean±SD. * $p < 0.050$ significant. **Wilcoxon signed rank test, median [interquartile range].

Table 4: Comparison of the change in mean five summary scales scores of the Seattle Angina Questionnaire(SAQ) with risk factors for coronary artery disease (CAD).

Change in SAQ scales	Diabetes	Hypercholesterolemia	Alcohol	Smoking	Other tobacco products
Physical limitation	0.600	0.168	0.468	0.273	0.229
Angina stability	0.354	0.086	0.333	0.049*	0.209
Angina frequency	0.196		0.645	0.331	0.044*
Treatment satisfaction	0.238	0.991	0.778	0.281	0.227
Quality of life	0.372	0.723	0.537	0.177	0.275

*statistically significant.

between change in angina stability and smoking ($p = 0.049$) was also significant [Table 4]. Multiple linear regression analysis with change in angina frequency as a dependent variable in the CAD group revealed a statistically significant ($p < 0.050$) association between hypercholesterolemia ($p = 0.033$) and nicotine consumption ($p = 0.020$). Non-tobacco users had a greater mean change in angina frequency and angina stability scale scores compared to tobacco users in the CAD group after six weeks.

A statistically significant negative correlation was found in all four QOL domain scores in the PDRC group ($n = 40$) with HAM-A scores at six weeks follow-up [physical ($r = -0.541$; $p < 0.001$), psychological ($r = -0.494$; $p = 0.001$), social ($r = -0.427$; $p = 0.006$), environment ($r = -0.511$; $p = 0.001$)]. Patients in the PDRC group showed reduced anxiety scores and had increased WHOQOL scores (in all four domains) at six weeks follow-up compared to baseline. Patients with panic disorder had a significant improvement in anxiety scores post treatment compared to baseline (HAM-A scores difference 21.03 [16.5–25.6]; $p < 0.001$).

DISCUSSION

This is one of the few studies to compared QOL in patients with these two disorders; the comparative data is sparse. One of our prominent was that patients with PDRC had a worse QOL than patients with CAD.

A study by Candilis et al³³ revealed that the patients with panic disorder are often more distressed than those with cardiac disease and reported poorer role functioning than patients with congestive heart failure. One possible explanation given was that the pathway of care to a psychiatrist was long after multiple visits to physicians, cardiologists, and gastroenterologists, resulting in a negative effect on

both mental and physical health.³³ Another more recent study concluded that panic disorders have a negative impact on both global adjustment and QOL, which could further exacerbate the course of cardiac disease.³⁴ Our study also revealed that treatment with anxiolytics and specific agents had a positive impact on the QOL, which was also reported by Agbrignani et al.³⁴

Psychiatric morbidity was present in 40.0% CAD patients, a similar finding to a study by Fleet et al,³⁵ which reported panic disorder in 34% CAD patients. Although several studies using rating scales reported depression and anxiety symptoms in CAD patients,^{36,37} the need for actual treatment initiation in liaison with psychiatrists has not been highlighted. A study by Stafford, Beck and Johnson,³⁸ found that tobacco smoking at the time of index cardiac event was associated with depression and poor QOL in CAD patients. Smoking and other tobacco products associated with impaired QOL in CAD patients. This was similar to a previous study wherein 46.9% patients were reported to use nicotine.³⁹

We observed psychiatric morbidity in a high proportion of patients with CAD, similar to another study that found the majority of the patients had either depression or anxiety.³⁹

Non-angina chest pain referrals are consistently associated with panic disorder.²⁰ An interesting finding among PDRC referrals compared to healthy controls and patients with CAD was that those with PDRC had a worse QOL. This finding is supported by other studies.^{20,40} All four domains of QOL scores in patients with panic disorder improved significantly at six weeks follow-up after treatment with SSRIs. There were positive correlations that reflected improvement in QOL scores at six weeks compared to baseline pretreatment physical, psychological, social, and environment domain scores. Improvement in WHOQOL domain scores

and reduction in anxiety scores (as measured by HAM-A) at six weeks post-treatment showed negative association.

No significant differences were observed between the socioeconomic strata, occupation, and educational status of patients in the CAD, healthy control, and PDRC groups as our hospital is the largest government-run tertiary care hospital of east Delhi and provides free medicines and consultations, largely catering to the needs of the lower socioeconomic strata of society.

We found a negative association between smoking, change in angina stability score, and other tobacco products with change in angina frequency. Non-tobacco users had better angina stability and angina frequency scores. These findings emphasize that both smoked and smokeless forms of tobacco are not the only risk factors for CAD, but also lead to worsening of angina symptoms. Complete abstinence from the use of any nicotine was practiced by our hospitalized patients with CAD, which contributed to improvement in angina symptoms. Dietary modification was advised routinely to all patients with CAD as per their individual requirement by a qualified dietician. A previous study by Khunti et al,⁴¹ demonstrated that interventions for smoking cessation, blood pressure management, cholesterol reduction, and prescription of secondary CAD prevention drugs (lipid lowering drugs, aspirin, beta-blockers, inhibitors of the renin-angiotensin-aldosterone system) were associated with improved QOL scores and SAQ scores at one-year follow-up.

CONCLUSION

The focus on psychiatric aspects of medical disease has been on the increase in the past few decades. Likewise, a psychiatrist should also be aware of the various comorbid medical illnesses that could occur commonly with psychiatric disorders. Both physicians and psychiatrists need to focus on the interrelation between various anxiety disorders and CAD. Patients with PDRC had a worse QOL than those with CAD and healthy controls. This highlights the need for careful diagnosis and prompt treatment to improve the QOL in these patients. Complete abstinence from the use of any smoked or smokeless tobacco products in patients with CAD patients should be encouraged to improve their QOL and control angina symptoms. Hypercholesterolemia

also needs to be tackled to improve angina symptoms in patients with CAD.

Disclosure

The authors declared no conflicts of interest. No funding was received for this study.

REFERENCES

1. American Psychiatric Association. The Diagnostic and Statistical Manual of Mental Disorders DSM-V. Washington, D.C.: American Psychiatric Association; 2013.
2. Tully PJ. A good time to panic? Premorbid and postmorbid panic disorder in heart failure affects cardiac and psychiatric cause admissions. *Australas Psychiatry* 2015 Apr;23(2):124-127.
3. Sipötz J, Friedrich O, Höfer S, Benzer W, Chatsakos T, Gaul G; PRODES-Austria Investigators. Health related quality of life and mental distress after PCI: restoring a state of equilibrium. *Health Qual Life Outcomes* 2013 Aug;11:144.
4. Yang LX, Zhou YJ, Wang ZJ, Li YP, Chai M. Impact of invasive treatment strategy on health-related quality of life six months after non-ST-elevation acute coronary syndrome. *J Geriatr Cardiol* 2014 Sep;11(3):206-211.
5. Seo J, Lee Y, Kang S, Chun H, Pyun WB, Park SH, et al. Poor health-related quality of life and proactive primary control strategy may act as risk factors for acute coronary syndrome. *Korean Circ J* 2015 Mar;45(2):117-124.
6. Unsar S, Sut N, Durna Z. Health-related quality of life in patients with coronary artery disease. *J Cardiovasc Nurs* 2007 Nov-Dec;22(6):501-507.
7. Westin L, Carlsson R, Israelsson B, Willenheimer R, Cline C, McNeil TF. Quality of life in patients with ischaemic heart disease: a prospective controlled study. *J Intern Med* 1997 Sep;242(3):239-247.
8. Ekici B, Ercan EA, Cehreli S, Töre HF. The effect of emotional status and health-related quality of life on the severity of coronary artery disease. *Kardiol Pol* 2014;72(7):617-623.
9. Höfer S, Benzer W, Oldridge N. Change in health-related quality of life in patients with coronary artery disease predicts 4-year mortality. *Int J Cardiol* 2014 Jun;174(1):7-12.
10. Colquhoun DM, Bunker SJ, Clarke DM, Glozier N, Hare DL, Hickie IB, et al. Screening, referral and treatment for depression in patients with coronary heart disease. *Med J Aust* 2013 May;198(9):483-484.
11. Jespersen L, Abildstrøm SZ, Hvelplund A, Prescott E. Persistent angina: highly prevalent and associated with long-term anxiety, depression, low physical functioning, and quality of life in stable angina pectoris. *Clin Res Cardiol* 2013 Aug;102(8):571-581.
12. Höfer S, Benzer W, Alber H, Ruttman E, Kopp M, Schüssler G, et al. Determinants of health-related quality of life in coronary artery disease patients: a prospective study generating a structural equation model. *Psychosomatics* 2005 May-Jun;46(3):212-223.
13. Ferrari AJ, Charlson FJ, Norman RE, Patten SB, Freedman G, Murray CJ, et al. Burden of depressive disorders by country, sex, age, and year: findings from the global burden of disease study 2010. *PLoS Med* 2013 Nov;10(11):e1001547.
14. Murray CJ, Vos T, Lozano R, Naghavi M, Flaxman AD, Michaud C, et al. Disability-adjusted life years (DALYs) for 291 diseases and injuries in 21 regions, 1990-2010: a systematic analysis for the Global Burden of Disease Study 2010. *Lancet* 2012 Dec;380(9859):2197-2223.
15. Gupta R, Gupta VP, Sarna M, Bhatnagar S, Thanvi J, Sharma V, et al. Prevalence of coronary heart disease and risk factors in an urban Indian population: Jaipur Heart Watch-2. *Indian Heart J* 2002 Jan-Feb;54(1):59-66.

16. Zachariah G, Harikrishnan S, Krishnan MN, Mohanan PP, Sanjay G, Venugopal K, et al; Cardiological Society of India Kerala Chapter Coronary Artery Disease and Its Risk Factors Prevalence (CSI Kerala CRP) Study Investigators. Prevalence of coronary artery disease and coronary risk factors in Kerala, South India: a population survey - design and methods. *Indian Heart J* 2013 May-Jun;65(3):243-249.
17. Singh RB, Sharma JP, Rastogi V, Raghuvanshi RS, Moshiri M, Verma SP, et al. Prevalence of coronary artery disease and coronary risk factors in rural and urban populations of north India. *Eur Heart J* 1997 Nov;18(11):1728-1735.
18. Summary report on causes of Death: 2001-03 in India [cited 2015 June]. Available from: http://censusindia.gov.in/Vital_Statistics/Summary_Report_Death_01_03.pdf.
19. Murray CJ, Lopez AD. Alternative projections of mortality and disability by cause 1990-2020: Global Burden of Disease Study. *Lancet* 1997 May;349(9064):1498-1504.
20. Katerndahl DA. The association between panic disorder and coronary artery disease among primary care patients presenting with chest pain: an updated literature review. *Prim Care Companion J Clin Psychiatry* 2008;10(4):276-285.
21. Campbell SG, Abbass AA. Chest pain—consider panic disorder. *Can Fam Physician* 2007 May;53(5):807-808, author reply 808.
22. Dammen T, Bringager CB, Arnesen H, Ekeberg O, Friis S. A 1-year follow-up study of chest-pain patients with and without panic disorder. *Gen Hosp Psychiatry* 2006 Nov-Dec;28(6):516-524.
23. Hadlandsmyth K, White KS, Krone RJ. Quality of life in patients with non-CAD chest pain: associations to fear of pain and psychiatric disorder severity. *J Clin Psychol Med Settings* 2013 Sep;20(3):284-293.
24. Mendis S, Thygesen K, Kuulasmaa K, Giampaoli S, Mähönen M, Ngu Blackett K, et al; Writing group on behalf of the participating experts of the WHO consultation for revision of WHO definition of myocardial infarction. World Health Organization definition of myocardial infarction: 2008-09 revision. *Int J Epidemiol* 2011 Feb;40(1):139-146.
25. Hamm CW, Braunwald E. A classification of unstable angina revisited. *Circulation* 2000 Jul;102(1):118-122.
26. Najafi M, Sheikhatvan M, Montazeri A, Sheikhatollahi M. Factor Structure of the World Health Organization's Quality of Life Questionnaire-BREF in Patients with Coronary Artery Disease. *Int J Prev Med* 2013 Sep;4(9):1052-1058.
27. De Melo-Neto VL, Valenca AM, Nascimento I, Lopes FL, Nardi AE. Quality of life assessment by WHOQOL-BREF in panic disorder patients during treatment. *Rev Psiquiatr Clin (Santiago)* 2008;35(2):49-54.
28. Kumar BP, Dudala SR, Rao AR. Kuppuswamy's socio-economic status scale—a revision of economic parameter for 2012. *Int J Res Dev Health* 2013;1(1):2-4.
29. Spertus JA, Winder JA, Dewhurst TA, Deyo RA, Prodzinski J, McDonnell M, et al. Development and evaluation of the Seattle Angina Questionnaire: a new functional status measure for coronary artery disease. *J Am Coll Cardiol* 1995 Feb;25(2):333-341.
30. Goldberg DP, Blackwell B. Psychiatric illness in general practice. A detailed study using a new method of case identification. *Br Med J* 1970 May;1(5707):439-443.
31. Hamilton M. A rating scale for depression. *J Neurol Neurosurg Psychiatry* 1960 Feb;23:56-62.
32. Hamilton M. The assessment of anxiety states by rating. *Br J Med Psychol* 1959;32(1):50-55.
33. Candilis PJ, McLean RY, Otto MW, Manfro GG, Worthington JJIII, Penava SJ, et al. Quality of life in patients with panic disorder. *J Nerv Ment Dis* 1999 Jul;187(7):429-434.
34. Abrignani MG, Renda N, Abrignani V, Raffa A, Novo S, Baido RL. Panic disorder, anxiety, cardiovascular diseases. *Clin Neuropsychiatry* 2014;11(5):130-144.
35. Fleet RP, Dupuis G, Marchand A, Kaczorowski J, Burelle D, Arsenault A, et al. Panic disorder in coronary artery disease patients with noncardiac chest pain. *J Psychosom Res* 1998 Jan;44(1):81-90.
36. Staniute M, Brozaitiene J, Burkauskas J, Kazukauskienė N, Mickuviene N, Bunevicius R. Type D personality, mental distress, social support and health-related quality of life in coronary artery disease patients with heart failure: a longitudinal observational study. *Health Qual Life Outcomes* 2015 Jan;13(1):1.
37. Moattari M, Adib F, Kojuri J, Tabatabaee SH. Angina self-management plan and quality of life, anxiety and depression in post coronary angioplasty patients. *Iran Red Crescent Med J* 2014 Nov;16(11):e16981.
38. Stafford L, Berk M, Jackson HJ. Tobacco smoking predicts depression and poorer quality of life in heart disease. *BMC Cardiovasc Disord* 2013 May;13:35.
39. John S. Prevalence and pattern of psychiatric morbidity and health related quality of life in patients with ischemic heart disease in a tertiary care hospital. *Indian J Psychiatry* 2013 Oct;55(4):353-359.
40. Christoph M, Christoph A, Dannemann S, Poitz D, Pfluecke C, Strasser RH, et al. Mental symptoms in patients with cardiac symptoms and normal coronary arteries. *Open Heart* 2014 Oct;1(1):e000093.
41. Khunti K, Stone M, Paul S, Baines J, Gisborne L, Farooqi A, et al. Disease management programme for secondary prevention of coronary heart disease and heart failure in primary care: a cluster randomised controlled trial. *Heart* 2007 Nov;93(11):1398-1405.