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ORIGINAL PAPER

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Heavy Smoking is Associated with Low Depression and Stress: a Smokers' Paradox in Cardiovascular Disease?

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ABSTRACT

Introduction: Smoking, anxiety and depression constitute predisposing factors of coronary artery disease. **Aim:** The aim of this study was to investigate the degree of nicotine dependence in coronary patients and its relationship to anxiety and depression. **Methods:** The study population consisted of 208 coronary patients, 131 men and 77 women, who were hospitalized in a hospital in Attica and were all smokers. The degree of nicotine dependence was measured by the Fagerstrom scale, while depression and anxiety intensity were assessed with the Zung SDS and SAS scales respectively. **Results:** 158 participants (75.9%) were moderately to highly dependent on nicotine, 108 participants (51.9%) reported moderate to severe depression intensity levels while 91 participants (43.8%) reported moderate to severe anxiety intensity levels. The degree of dependence on nicotine was negatively related to the intensity of anxiety and depression experienced by coronary patients. Additionally, the degree of nicotine dependence, anxiety and depression was associated with various sociodemographic and clinical factors such as educational level, social support, and information on their condition and treatment. **Conclusion:** Overall, the findings of this study point to an inverse relationship of nicotine dependence, depression and anxiety. However, this paradoxical association could be a product of shared risk factors or confounding. Nonetheless, the development of individualized educational and supportive interventions to quit smoking in coronary patients should primarily focus on the assessment of depression and stress.

Keywords: Nicotine Dependence, coronary heart disease, Depression, Anxiety.

1. INTRODUCTION

Smoking constitutes the most important modifiable risk factor for coronary heart disease and a leading cause of death worldwide (1). Despite the strong association of smoking to atherosclerotic disease, its prevalence in patients hospitalized for an acute cardiac condition is two times higher compared to that of the general population (2). Cardiac patients who quit smoking have markedly lower rates of major cardiac events and mortality compared to those who continue smoking (2-4). Nonetheless, more than one third of smokers who suffer an acute coronary event continue to smoke after hospitalization (3-4). Moreover, some studies report an unexpected survival benefit of smokers with acute coronary syndrome, a phenomenon which is known as the "smoker's paradox" (5-6).

Most studies referring to the smoker's paradox focus on the biochemical effect of smoking, namely its pre-thrombolytic and thrombolytic effect or on unmeasured confounding factors (5). Nonetheless, it is cited by patients as an argument against smoking cessation and therefore caution is needed to prevent damaging misperceptions. Furthermore, arguments against quitting smoking in cardiovascular disease are contradicted by other robust trials (6).

Other important risk factors for acute cardiovascular disease are related to the psychological health of patients. Type A personality, anxiety and depression have been implicated as predisposing conditions to the development of coronary artery disease (7-8). Biological factors and behavior interact in a continuous dialogue and continuous feedback and affect the state of health (9-11). Depressive symptoms such as futility, fatigue and feelings of frustration are

inherent in the progression of the disease. Behavioral, biological and pathophysiological factors associate depression with cardiovascular risk factors such as hypertension, smoking, physical inertia, age, sex, hyperlipidemia, inflammatory process and platelet aggregation (7-9). Several pathophysiological features of depression may increase the risk of coronary artery disease, such as arrhythmias (7). People who experience such psychosocial difficulties as depression are more likely to be physically inactive, which is also a risk factor for coronary artery disease (5).

As far as anxiety symptomatology is concerned, chronic anxiety can increase the risk of developing coronary heart disease by influencing health behaviors, promoting atherosclerotic plaque, increasing the risk of hypertension and triggering deadly coronary events through arrhythmia, plaque rupture, coronary spasm or thrombosis (8,10). Finally, some behaviors and social characteristics in people with depression may also contribute to the development and progression of coronary artery disease. These include diet, exercise, adherence to medication, as well as social isolation and chronic stress, as well as extensive use of tobacco (8-10).

Nonetheless, although the effect of smoking, depression and anxiety on coronary heart disease has been adequately studied, there are not enough studies to investigate nicotine dependence and its relation to anxiety and depression in coronary artery disease patients (7). Some studies investigate how affective states influence the smoking cessation process but these studies are focused mainly on specific interventions addressing motivation to quit and self-efficacy or symptoms of depression and anxiety (12-13).

This study is timely because there appears to be an emerging international interest in the association between smoking and levels of depression and anxiety in hospitalized coronary heart disease patients; Moreover, this is the first study conducted in Greece in relation to this topic.

2. AIM

The aims of the study were threefold: a) to investigate the level of nicotine dependence in patients hospitalized for cardiovascular disease; b) to examine levels of depression and anxiety in these patients and c) to explore the relationship between nicotine dependence, depression and anxiety.

3. METHODS

Participants

Questionnaires were distributed to 208 patients with chronic coronary artery disease or acute coronary syndrome who were hospitalized in the ICU or cardiology clinic in a public hospital of Attica. Study inclusion criteria for participants were: to be literate in Greek language, presence of CCAD or acute Coronary syndrome, absence of mental illness, presence of smoking habits.

Procedure and ethical considerations

The Ethical Committee of University of Kapodistrian University approved of the study protocol. Additionally, the study was conducted after review and written approval by the Administrational and Scientific Society of a public hospital in Athens. The researcher informed each participant about the purpose of the study. Furthermore,

all participants were informed of their rights to refuse or to discontinue their participation, according to the ethical standards of the Helsinki Declaration of 1983. Participation in the study was contingent on individual verbal consent.

Measures

The study questionnaire included three validated measurement instruments: The Fagerström Test for Nicotine Dependence, The Zung Self-Rating Depression Scale (SDS), The Zung Self-Rating Anxiety Scale (SAS) and a set of questions on demographic and clinical characteristics.

The Fagerström Test for Nicotine Dependence (FTND) is widely used to assess the patient's intensity of physical addiction to nicotine. The test consists of 6 questions, which evaluate the quantity of cigarette consumption, the compulsion to use, and dependence. Items Yes/No are scored from 0 to 1, the multiple-choice items are scored from 0 to 3. The items are summed to total score 0-10. The higher the total Fagerström score, the more intense is the patient's physical dependence on nicotine. The scores are classified in 5 intensity categories: very low (0 to 2 points); low (3 to 4 points); moderate (5 points); high (6 to 7 points); and very high (8 to 10 points).

The Zung Self-Rating Depression Scale (SDS) evaluates emotional, psychological and somatic symptoms associated with depression. The SDS consists of 20 questions; items are scored on a Likert scale ranging from 1 to 4, with 4 representing the most unfavorable answer. A total score comes from summing the individual item scores and ranges from 20 to 80. As regards the interpretation of the SDS scores, lower than 50 scores is within normal range, 50-59 scores suggests minimal to mild depression, 60-69 refers to moderate to severe depression while more than 70 relates to severe depression. In addition, the scale is a simple tool for recording changes in the severity of depression over time. The Greek version of SDS has been proved to demonstrate high reliability and internal validity (15).

Self-rating Anxiety Scale (SAS), introduced by Zung, is widely used for the detection of anxiety. SAS consists of 20 items rated on a 1-4 likert type scale from "none of the time" to "most of the time". There are 20 questions with 15 increasing anxiety level questions and 5 decreasing anxiety questions. The total SAS score varies from 20 (no anxiety at all) to 80 (severe anxiety). The clinical interpretation of the anxiety level comes in four categories as following: 20-44 refers to normal range, 45-59 to mild to moderate anxiety levels, 60-74 marked to severe anxiety levels and above 75 refers to extreme anxiety levels. The SAS Greek version presents sufficient psychometric properties regarding its reliability and validity (16).

Demographic and social characteristics, patient opinion on information regarding their current health condition, smoking habits, were collected through 21 item questionnaire which was specially designed for the purposes of the study. Patient clinical data such as diagnosis was obtained from patients' files.

Statistical analysis

A descriptive analysis was used to identify samples' characteristics. T-tests were calculated to determine significant differences in means, and Pearson's Chi-square or Fisher's exact tests of correlations were computed to determine the

strength and relations between variables. Student’s t-test was used in comparison between two groups of quantitative variables. The Bonferroni correction was used to control Type I error. In multiple comparisons, significance level of 0.05 / κ (κ = number of comparisons) was set. All statistical analyses were performed using the Statistical Package for Social Sciences, Version 22.0 for Windows.

4. RESULTS

Demographic and Clinical Characteristics

Questionnaires were distributed to 208 patients with chronic or acute coronary disease with mean age 70.7 ±10.4 years. 131 participants were men (63%) and 123 participants were married (59.4%). One hundred of all participants (48.1%) had completed primary education and 48 (23.1%) were working in private sector. 161 participants (89.9%) had children over 18 years of age and lived predominantly (60.6%) with spouse (Table 1).

Out of 62 participants (29.8%) were hospitalized with the diagnosis of heart failure. Other diagnoses were “myocardial infraction” (56 participants), “unstable angina” (48 participants), “atrial fibrillation” (27 participants) and “by-pass” (15 participants). For half of the participants the cardiac problem had occurred during the last year. Additionally, 59.4% suffered from a concomitant illness. Still, 87 participants (42.4%) were only briefly informed of the problem for which they were being hospitalized while 28 participants reported that they had not been informed at all. Furthermore, 89 participants (43.2%) were only briefly informed of the treatment they were being offered (Table 1).

Fagerström Test (FTND)

All subjects in the sample smoked. According to the Fagerström Test (FTND), 97 participants (46.6%) were moderately dependent on nicotine while 50 (24%) and 61 (29.3%) participants reported low and high dependence on nicotine respectively. 130 participants (54.3%) smoked the first cigarette of their day 6-30 minutes after waking up. 55 participants (26.4%) found it hard not to smoke in smoke-free places, and 70.2% have difficulty not smoking the first cigarette of the day. The majority of participants (158) smoked 10 or more cigarettes a day. 162 participants (77.9%) smoked more in the morning than in the afternoon. 49 participants (23.6%) smoked even when a disease forced them to stay in bed.

Self-rating Depression Scale (ZSDS)

Depression levels resulting from SDS analysis showed the mean score for the sample to be 47,8±8,7 (lowest 30 and highest 68). Forty patients (19.2%) had severe depression intensity with moderate intensity presented in 68 (32.7%) followed by low-moderate intensity in 58 (27.9%). Forty-two (20.2%) patients were within normal range of depression intensity. Patients with “high nicotine dependence” had statistically significant lower anxiety intensity (FTND = 47,8±8,7, p<0.0001).

Self-rating Anxiety Scale (SAS)

Anxiety levels resulting from SAS analysis showed the mean score for the sample to be 44.7±7.9 (lowest 27 and highest 63). Thirteen patients (6.3%) had severe anxiety intensity with moderate intensity presented in 78 (37.5%) followed by low-moderate intensity in 55 (26.4%). Sixty-

Socio – Demographic & Clinical characteristics		n	%
Sex	Male	131	63.0
	Female	77	37.0
Age	Mean (±SD)	70,7(±10,4)	
	<66	56	26.9
	66-75	64	30.8
	>75	88	42.3
Marital status	Married	123	59.4
	Single	15	7.2
	Divorced/ Separated	23	11.1
	Widow/er	42	20.3
	Living together	4	1.9
Education level	Illiterate	26	12.5
	Primary	100	48.1
	Secondary	59	28.4
	University	21	10.1
	Postgraduate	2	1.0
Employment	Unemployed	4	1.9
	State employee	21	10.1
	Private employee	48	23.1
	Free licensed	44	21.2
	Domestic	40	19.2
	Other	51	24.5
Number of children	0	29	13.9
	1	37	17.8
	2	76	36.5
	>2	66	31.7
Children's age	<18	18	10
	>18	161	90
Live with	None	58	27.9
	Husband/wife	126	60.6
	Children/other	24	11.5
Diagnosis	Myocardial infraction	56	26.9
	Unstable angina	48	23.1
	Heart failure	62	29.8
	By-pass	15	7.2
	Atrial fibrillation	27	13.0
Cardiac problem occurrence	< 1 year	103	50.0
	2-5 years	69	33.5
	6-10 years	30	14.6
	11-15 years	3	1.5
Concomitant illness	Yes	123	59.4
	No	84	40.6
Type of concomitant illness	Diabetes	62	50.04
	Anaemia	12	8.09
	Renal failure	6	4.9
	Dyslipidemia	12	9.2
	Hypertension	32	2.6
Informed on their condition	Very much	14	6.8
	Adequately	75	36.6
	A little	87	42.4
	Not at all	28	14.1
Informed on treatment received	Very much	16	7.8
	Adequately	73	35.4
	A little	89	43.2
	Not at all	28	13.6

Table 1. Demographic and Clinical Characteristics of the Sample (N = 208)

two (29.8%) patients were within normal range of anxiety intensity. Patients with “high nicotine dependence” had statistically significant lower anxiety intensity (FTND = 40.9 ± 7.4 , $p < 0.0001$).

Dependence, depression, anxiety and sociodemographic characteristics

Many significant differences were found in comparisons of the sociodemographic characteristics between highly dependent, depressed and distressed individuals and the rest of participants. Nicotine dependence was found to be significantly heavier among men ($p < 0.038$), below the age of 66 ($p < 0.001$), who were highly educated ($p < 0.001$), freelancers ($p < 0.001$), and lived alone ($p < 0.001$). As far as depression and psychologically distressed participants are concerned, the results were similar, i.e. serious depression and anxiety was experienced by people over the age of 75 ($p < 0.001$), lonely people ($p < 0.001$), people with a low educational level ($p < 0.001$), the unemployed ($p < 0.001$), childless people ($p < 0.001$), people whose children were over 18 ($p < 0.001$), and those who did not live with their partners ($p < 0.001$). Moreover, participants who reported to be adequately informed about their condition and the treatment they were receiving reported at the same time lower nicotine dependence, depression and anxiety levels ($p < 0.001$).

5. DISCUSSION

The aim of the present study was to investigate the association between smoking and levels of depression and anxiety in hospitalized coronary heart disease patients. Findings suggest that the majority of participants were moderately to highly dependent on nicotine while the degree of dependence on nicotine was inversely related to the intensity of anxiety and depression experienced by coronary patients. Additionally, the degree of nicotine dependence, anxiety and depression was found to be associated with various sociodemographic and clinical factors such as educational level, social support and information on their condition and treatment.

Overall, the results of the present study point to an inverse relationship between smoking, depression and anxiety. The negative relationship of dependence to levels of depression and stress is contrary to the well-established self-medication hypothesis according to which smoking is the result of an effort to reduce the negative effects of depressive and anxiety symptoms (17). A possible explanation could be that the reduction of negative feeling and stress, weight control, better concentration and the positive energy that nicotine gives -i.e. the satisfaction derived from smoking and alleviation of withdrawal symptoms- may account for this apparently paradoxical result. In other words, smokers may misattribute the relief of withdrawal symptoms as reflecting a genuine antidepressant and anxiolytic effect of nicotine dependence (17-19). Indeed, nicotine has to some extent antidepressant activity which is explained by the fact that the long-term antidepressant activity of any drug appears to depend on its ability to modulate changes in the dopamine, norepinephrine and serotonin. Furthermore, as a major psychoactive component of tobacco nicotine produces both anxiolytic and antidepressant like effects in both humans and animals (18-19). However, co-occurring

depressive symptoms and smoking do not appear to synergistically convey risk for cardiovascular disease (7). Additionally, the relationship between nicotine dependence, anxiety and depression may be bidirectional with smoking initially used to alleviate symptoms but in fact worsening them over time as it dysregulates the hypothalamic-pituitary-adrenal system and results in hypersecretion of cortisol which in turn influences reactions to environmental stressors (17-19).

Another important result of the present study was that participants who reported to be adequately informed about their condition and the treatment they were receiving reported at the same time lower nicotine dependence, depression and anxiety levels. This finding is similar to those of previous research which shows that attendance at cardiovascular rehabilitation is inversely related to smoking behavior (2) and that individuals with depression and psychological distress are less likely to quit smoking (4). Smoking is a bad habit and breaking it needs perseverance; furthermore, it might be that changing this habit is difficult for depressed or distressed patients after an acute coronary syndrome. It appears that smokers with depression and/or anxiety have greater interest in quitting but more frequently fail cessation attempts while they exhibit low confidence in their ability to quit in the future (20). Therefore, designing programs that take into consideration patients' motivational stage of change in an effort to enhance their motivation to discontinue high-risk behaviors while supporting them to achieve their goals can be useful (4). Educational programs could be conducted immediately after hospitalization since health adversities constitute “teachable moments” and opportunities to change patients' views about the role of lifestyle on their health status. Participation of such patients in timely rehabilitation programs and a combined focus on addiction, depression and anxiety symptoms may be necessary to have them break their undesired habits (4,20).

Nonetheless, certain limitations of the study warrant consideration. The main limitation of the study was the selection of the sample. Patients with cardiovascular disease were hospitalized in a specific public hospital and thus the observed results may not be representative for the Greece as a whole. Second, we did not correct for potential confounders in the association between smoking, depression and anxiety while there was no weighting on key sociodemographic and clinical factors such as educational level, social support, and information on patient's condition and treatment. The development of a model including all potential confounders of the relation between smoking and mental health could further expand the analysis of the association of nicotine dependence, depression and anxiety. Multilevel analysis with a 3-level structure (smoking-depression and anxiety-motivation to quit smoking) could illuminate the smoking paradox and the complex mechanisms underlying the relationship of nicotine dependence to depression and anxiety in cardiac patients.

6. CONCLUSION

Overall, the findings of this study point to an inverse relationship of nicotine dependence, depression and anxiety.

However, this paradoxical association could be a product of shared risk factors or confounding. Nonetheless, the results point to a pressing need for the development of educational and supportive interventions tailored specifically to support patients with depressive and anxiety symptoms to quit smoking. Assessment of depression, stress, patients' motivational stage of change and perceptions regarding smoking cessation are necessary in the challenging task of supporting them to achieve self-motivation and successful change.

- **Declaration of patient consent:** The authors certify that they have obtained all appropriate patient consent forms
- **Author's contribution:** A.P. and E.M. gave substantial contributions to the conception or design of the work in acquisition, analysis, or interpretation of data for the work. A.P., A.K., and E.M. had a part in article preparing for drafting or revising it critically for important intellectual content. A.P., A.K., and E.M. gave final approval of the version to be published and agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.
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