Smoking, alcohol consumption and physical activity: associations in acute coronary syndrome

Tabagismo, consumo de álcool e atividade física: associações na síndrome coronariana aguda

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Abstract

Objective: To describe the prevalence of smoking and alcohol consumption; to identify the level of physical activity; the degree of nicotine and alcohol dependence and the association between these risk factors in subjects with acute coronary syndrome.

Methods: Cross-sectional study with 150 patients with acute coronary syndrome. For data collection, interviews, analysis of patients' charts and validated questionnaires on smoking, alcohol consumption and physical activity were used.

Results: 58.7% were smokers (35.2% high dependence), 42% consumed alcohol (65.1% low risk), 36.7% were active. Smoking was significantly correlated to alcohol consumption and high nicotine dependence was associated with sedentary lifestyles.

Conclusion: There was high prevalence of smoking and alcohol consumption. There was a high nicotine dependence and low risk alcohol consumption. Most participants were active. There was a correlation between alcohol consumption and smoking, as well as association of high nicotine dependence with sedentary lifestyles.

Resumo

Objetivo: Descrever a prevalência de tabagismo e consumo de álcool; identificar o nível de atividade física; os graus de dependência de nicotina e álcool e verificar a associação entre esses fatores de risco em indivíduos com síndrome coronariana aguda.

Métodos: Estudo transversal com 150 pacientes com síndrome coronariana aguda. Para coleta de dados, foram utilizadas entrevistas, análise de prontuários e questionários validados sobre tabagismo, consumo de álcool e atividade física.

Resultados: 58.7% eram fumantes (35,2% alta dependência), 42% consumiam álcool (65,1% baixo risco), 36,7% eram ativos. O tabagismo correlacionou-se significativamente ao consumo de álcool e a alta dependência de nicotina associou-se ao sedentarismo.

Conclusão: Houve alta prevalência de tabagismo e consumo de álcool. Observou-se elevada dependência de nicotina e consumo de álcool de baixo risco. A maioria dos entrevistados era ativa. Houve correlação entre consumo de álcool e tabagismo, assim como associação da alta dependência de nicotina com sedentarismo.

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Introduction

The growing prevalence rate of chronic non-communicable diseases in Brazil and in the world is alarming, since they generate disabilities and diminish quality of life due to the debilitation of the individual, keeping them, in many cases, bedridden and under long hospitalizations. In every three deaths, two are caused by non-communicable chronic diseases.[1]

Among these diseases, cardiovascular are the leading cause of mortality in Brazil and worldwide. It is estimated that by 2020, cardiovascular diseases will cause about 25 million deaths, 19 million of them in low- and middle-income countries.[2]

The increased mortality is directly associated with the presence or absence of risk factors and other concomitant diseases, which influence the predisposition of the individual to develop complications and it will generate chronic diseases, which are more healthily compromising.[3] The modification of one or more health risk factors benefits health, significantly reducing morbidity and mortality from heart disease and coronary events. Moreover, it contributes to the improvement of symptoms, general well-being and quality of life.[2-4]

Information about certain groups of risk factors may address the development of intervention programs. Among hypertensive subjects, for example, the prevalence of other cardiovascular risk factors are high. The grouping of some of these factors are associated with the need for greater number of antihypertensive drugs.[5]

Risk factors for cardiovascular disease have received particular attention from governmental organizations, and health systems, providing priority attention to the reduction of chronic diseases.[6] The modifiable risk factors such as smoking, physical inactivity, unhealthy diets and the harmful use of alcohol - we highlight the possibility of being minimized from the pursuit of healthy behaviors acquired by the individual. Some of these factors are shared among individuals with different chronic non-communicable diseases, and might influence the onset of acute coronary syndrome.[4]

Although modifiable, alterations of such risk factors are challenging. A year after coronary artery bypass surgery of 320 individuals, we found that only 9% of smokers had stopped the habit, abdominal obesity had increased 8% and they did not observe changes in eating habits and exercise patterns.[7]

Concerned about the increase of non-communicable chronic diseases, with the impact generated in the country health system and the healthy development of society, the World Health Organization developed a set of targets and indicators that seek, above all, prevention and control of these diseases and their risk factors.[6] This concern is also shared by health professionals, who are urged to seek risk factors in different populations, in order to offer health education and reduce the incidence of these diseases.

Considering the high prevalence and associated mortality to worldwide non-communicable chronic diseases, particularly cardiovascular diseases, as well as the objectives established by the World Health Organization for the prevention and control of these diseases and their risk factors, knowledge of the concomitant presence of features that increase the risk of developing acute coronary syndrome is essential at all levels of care.

Based on the above, the objectives of this study were to describe the prevalence of smoking and alcohol consumption; identify the level of physical activity; the degree of nicotine and alcohol dependence and the association between these risk factors in subjects with acute coronary syndrome.

Methods

This is a cross-sectional study conducted in the Cardiologic Intensive Care Unit and Cardiac Inpatient Unit of a large tertiary teaching hospital located in the capital of the state of Sao Paulo, southeastern Brazil.

The sample size was obtained by the Z-test, with normal distribution, with an estimated proportion regarding the population of interest to a significance level of 5% and 90% sample power. The minimum sample size was 138 patients.

Patients aged greater than 18 years and hospitalized for the first time due to acute coronary syndrome were included in the study. Patients with acute pain, dyspnea or symptomatic hypotension at the time of data collection were excluded because of the discomfort they might experience during the interview.

Data were collected between September 2011 to May 2012, through interviews, patients' charts analysis and the use of an instrument developed by the authors composed of three parts: demographic information (gender, age), clinical variables (medical diagnosis) and risk factors related to lifestyle (smoking, alcohol dependence and physical activity).

Risk factors were assessed using internationally validated questionnaires. The nicotine dependence was assessed using the Fagerström Nicotine Dependence Test. This is the most recognized and used test in the detection of nicotine dependence among smokers, composed of six questions. The degree of nicotine dependence is determined by the sum of the responses, with scores ranging from 0-10 points. To assess patients, we used the following categorization: 0-2 points: very low dependence; 3-4 points: low dependence; 5 points: average dependence; 6-7 points: high dependence; 8-10 points: very high dependence.[8]

To assess alcohol consumption, the Alcohol Use Disorders Identification Test developed by the World Health Organization was used to identify the dependence of its consumption and severity in the last year. The questionnaire contains ten questions, each with four alternatives, with scores for each item ranging from zero to four points, totaling zero to 40 points. The patients are classified as: low risk (<7 points); risk (8-15 points); high risk (16-19 points); possible dependence (>20 points).[9]

Physical activity was assessed by the International Physical Activity Questionnaire, long version - developed by the World Health Organization and the Centers for Disease Control and Prevention. This instrument assesses physical activity undertaken by the individual in five different domains related to work, transport, domestic and gardening activities, recreation, sport and leisure time. The absolute intensity of physical activity reflects the rate of energy expenditure during exercise and is expressed in metabolic equivalents (METs), where 1 MET equals the resting metabolic rate of approximately 3.5 mL O_2/kg/min.[10]

We considered the energy expenditure in METs for each activity that composed the five domains. After calculating the energy expenditure of each domain, the values of each individual were summed up, and the results enabled us to stratify the patient as very active, active, irregularly active and sedentary.

Individuals considered very active were those that met the recommendations to achieve a total minimum of 1500 MET-min/week with vigorous activity ≥5 days/week for ≥30 minutes per session or vigorous activity ≥3 days/week for ≥20 minutes associated to moderate activity or walking ≥ 5days/week for ≥30minutes per session. We also considered very active the individuals who had any added activity ≥7 days/week, reaching a minimum total of 3000 MET-min/week.

Individuals considered active were those who fulfilled the recommendations of performing vigorous activity ≥3 days/week for ≥20 minutes per session; moderate activity or walking ≥5 days/week for ≥30minutes per session; or any activity added ≥5days/week, ≥150 minutes/week (walking plus moderate activity plus vigorous activity), reaching a minimum total of 600 MET-min/week.

Individuals considered irregularly active were those who practiced physical activity, however, insufficient to be classified as active, because they did not meet the recommendations regarding the frequency or duration. To perform this classification, we added the frequency and duration of different types of activities (walking plus the moderate and vigorous activities).

Individuals considered sedentary were those who did not perform any physical activity for at least 10 continuous minutes during the week.

Data were analyzed using SPSS (Statistical Package for Social Sciences) version 19. Descrip-

tive statistics frequencies (absolute and relative) were used for qualitative measurements. Summary statistics of mean, median, standard deviation and percentiles were used for quantitative measurements. The relationship between ordinal and quantitative measures (scores) of smoking, physical activity and alcohol consumption were assessed using the Spearman correlation coefficient. The association between qualitative measures were assessed using the chi square test of Fisher or Pearson. The results were evaluated with a confidence interval of 95%, and the statistical significance established at $p < 0.05$.

The study development followed the national and international standards of ethics in research involving human beings.

Results

One hundred and fifty patients were included in the study, these were hospitalized due to an acute myocardial infarction with ST segment elevation (n=109; 72.7%), unstable angina (n=19; 14.7%) and acute myocardial infarction without ST segment elevation (n=19; 12.7%). The majority were male (72.7%) with mean age of 57.51±11.23 years.

Sixty-three patients (42%) reported alcohol consumption. In most cases, consumption was considered low risk (65.1%) (Table 1). The average consumption score was 7.67±7.07 (low risk), with a minimum of one and maximum of 31.

Eighty-eight patients (58.7%) smoked, of which 35.2% had a high degree of dependence on nicotine and 33% had a very high dependence (Table 1). The dependence average score was 6.29±2.08 (high dependence), with a minimum of one and maximum of ten.

With regard to physical activity, the majority of participants were considered active (36.7%) and only 15.3% were ranked as sedentary people (Table 1).

Among patients who consumed alcohol, there was a weak ($r<0.3$) but significant ($p<0.05$) correlation with smoking. There was no significant correlation between other RF (Table 2).

Table 1. Rate of alcohol consumption, nicotine dependence and physical activity of individuals hospitalized for acute coronary syndrome

Classification	n(%)
Alcohol Consumption	
Low Risk	41(65.1)
Risk	12(19.1)
High Risk	6(9.5)
Probable dependence	4(6.3)
Nicotine Dependence	
Very low	5(5.7)
Low	10(11.4)
Average	13(14.7)
High	31(35.2)
Very High	29(33.0)
Physical activity	
Sedentary	23(15.3)
Irregularly active	40(26.7)
Active	55(36.7)
Very active	32(21.3)

For the classification of alcohol consumption, n=63; for classification of nicotine dependence, n=88; for classification of physical activity, n=150

Table 2. Correlation between smoking, alcohol consumption and frequency of physical activity in individuals hospitalized for acute coronary syndrome

		Physical Activity	Alcohol consumption
Smoking	r	0.088	0.284
	p	0.284	0.024
Physical Activity	r		0.156
	p		0.221

For the classification of alcohol consumption, n=63; for classification of nicotine dependence, n=88; for classification of physical activity, n=150

Weak evidence of an association between nicotine dependence scores and levels of physical activity ($p <0.10$) were found. There was a greater proportion of average nicotine dependence in the very active group (18.8%), and high nicotine dependence in the sedentary group (Table 3).

There was no significant association between the scores of nicotine dependence and alcohol consumption (p=0.620). Levels of physical activity and alcohol consumption were also not significantly associated (p=0.726).

Table 3. Association between the level of nicotine dependence and frequency of physical activity in individuals hospitalized for acute coronary syndrome

Nicotine Dependence	Physical Activity				
	Very active n(%)	Active n(%)	Irregularly active n(%)	Sedentary n(%)	Total n(%)
Does not smoke	13(40.6)	24(43.6)	17(42.5)	7(30.4)	61(40.7)
Very low	1(3.1)	4(7.3)	1(2.5)	0(0)	6(4.0)
Low	0(0)	4(7.3)	5(12.5)	1(4.3)	10(6.7)
Average	6(18.8)	3(5.5)	4(10.0)	0(0)	13(8.7)
High	6(18.8)	13(23.6)	3(7.5)	9(39.1)	31(20.7)
Very high	6(18.8)	7(12.7)	10(25.0)	6(26.1)	29(19.3)
Total	32(100)	55(100)	40(100)	23(100)	150(100)

p=0.056 (Fisher)

Discussion

The results of this study are limited by its cross-sectional design, since no causal relationship between the risk factors can be established. However, important information that differentiates the studied individuals in the general population were revealed.

The characteristics and associations investigated in this study contribute to the expansion of knowledge about the differential grouping of risk factors for cardiovascular disease. Since nurses are placed in the context of health education, such information also supports the planning of interventions directed at the main risk factor, smoking. When implemented such interventions, it is expected that there is also a positive impact of harmful alcohol consumption and physical activity level.

Alcohol dependence in the Brazilian population is increasing. Research conducted with more than 200,000 inhabitants in 107 Brazilian cities in 2001 and 2005 show that alcohol consumption in the general population increased from 11.2% to 12.3%.[11] In the present study, the prevalence of alcohol consumption was 3.4 times higher than that of the general population. However, most patients had low risk of dependence, suggesting that this risk factor may not have significantly contributed to the acute coronary syndrome.

In fact, when consumed daily in low to moderate doses (15g of ethanol for women and 15 to 30g of ethanol for men) it is associated with cardio-protection.[12] However, one of the factors associated with reduced chance of smoking cessation is current consumption of alcohol. In a prospective cohort of 4832 individuals, those who consumed four or more drinks once or more per week (considered heavy consumption) had lower rates of smoking cessation compared to the other participants.[13]

The results of the current research show a positive correlation between smoking and alcohol consumption, especially in subjects with high nicotine dependence and moderate consumption of alcohol. These results corroborate previous findings that, even in the absence of alcohol dependence, there is a strong positive linear relationship between greater alcohol involvement and increased chance of progression of smoking as a sporadic practice into a daily habit and nicotine addiction.[14]

Most patients with cardiovascular disease continues to smoke after acute myocardial infarction, exposing themselves to a 50.0% increased risk of recurrent coronary events among nonsmokers.[15] In Brazil, the population of smokers is 14.8%, with a higher prevalence among men.[16] Among the individuals evaluated in this study, the prevalence of smoking was almost four times higher than that of the general population, with a predominance of high and very high dependence, suggesting that RF may have played a crucial role in the development of acute coronary syndrome.

Sedentarism was the most prevalent risk factor (86.8%) among 152 patients with acute coronary syndrome treated in an emergency department.[17] Regular physical activity is recommended in both primary prevention and secondary prevention of coronary artery disease. A program of aerobic exercise three times a week involving treadmill, bike or walking exercise lasting 45 minutes for six weeks significantly reduced the inflammatory status of 52 patients with coronary artery disease and was associated with improved body mass index.[18]

However, among the patients in our sample, more than 50.0% were considered active. This result approximates to that of the general population of the state capitals of Brazil, where 76% of the adult population is active in at least one of the domains of physical activity (leisure, work, domestic and gardening activities or transport).[19]

Although most have been considered active, it may be suggested, based on the assessment of the existence of associations between the risk factors, the greater nicotine intake leads to sedentary lifestyle, or sedentary lifestyle leads to increased nicotine dependence. Approximately 60.0% of patients who had an acute myocardial infarction or other coronary event are at high risk for developing a new event. The presence of risk factors increase susceptibility. Thus, it was demonstrated that smoking cessation, consumption of fruits and vegetables and exercise regimes together may decrease the relative risk of acute myocardial infarction in up to 80.0%.[20]

Changes in risk factors for cardiovascular disease may have global impact. From 1991 to 2005, there was a significant reduction in deaths from coronary heart disease in the world. It is noteworthy that 54.0% of the decline in mortality were attributed to changes in risk factors, especially the reduction of the concentration of total cholesterol and an increase in physical activity. Blood pressure levels decreased in females, which explained the decrease in mortality in 29.0% and about 15.0% of the decline in mortality rate was attributed to the reduction of smoking in males.[21]

Despite the high risk for cardiovascular disease is present in only 10.0% of the population, there is a group of people from intermediate and low risk factors who are more prone to cardiovascular events. As a result, 90.0% or more cardiovascular events occur in people with one or more risk factors. This population would not qualify for intensive and invasive procedures, but they would benefit from the reduction of risk factors through changes in lifestyle and consequent reduction in risk of cardiovascular events. Therefore, we understand as keystones for the lower rates of morbidity,

for the maintenance of life and the reduction of comorbidities, the urgent implementation of educational measures.[22]

The primary and secondary prevention should be a priority in assistance to individuals with risk factors for the development of acute coronary syndrome, and other chronic non-communicable diseases.[22] One of the key challenges facing public health professionals are the difficulties we face when developing intervention programs that address multiple risk factors, since there are infinite combinations of RF that each patient can have.[23]

Three studies (EUROpean Action on Secondary Prevention through Intervention to Reduce Events - EUROASPIRE I, II , III) investigated the temporal trends of cardiovascular risk factors in patients previously hospitalized for coronary artery disease, they demonstrated that the recommendations for the control of cardiovascular risk factors have not been implemented in clinical practice and show the urgent need to strengthen prevention strategies in patients with coronary artery disease.[24]

Behavioral modification should have similar priority to drug therapy immediately after acute coronary syndrome. A population study followed 18809 patients from 41 countries up to 6 months after hospitalization for acute coronary syndrome. Patients who reported continuing smoking and lack of adherence to diet and exercise had a 3.8 times greater chance of myocardial infarction, stroke or death compared to non-smokers who modified their diet and exercise pattern within six months.[25]

Many studies have important results for patients in secondary prevention who receive educational interventions. Among 1510 patients hospitalized for acute coronary syndrome followed for six months, there was a mean reduction in body mass index, waist circumference and increased regular physical activity in the group that received an intervention.[21] In Italy, an implemented educational program by nurses for hypertensive patients significantly improved obesity, low fruit consumption, uncontrolled hypertension, LDL and total cholesterol.[26]

Conclusion

There was a high prevalence of smoking and alcohol consumption, nicotine dependence was high, alcohol consumption was low risk. Most individuals were active. There was a significant correlation between alcohol dependence and smoking. The high nicotine dependence was significantly associated with sedentary lifestyles.

Acknowledgements

Collaborations

Brunori EHFR contributed to project design, analysis and interpretation of data and writing the paper. AMRZ Cavalcante and Lopes CT contributed to the analysis and interpretation of data and writing of the paper. Lopes JL and Barros ALBL participated in the project design, analysis and interpretation of data, critical review of the relevant intellectual content and final approval of the version to be published.

References

1. Beaglehole R, Bonita R, Horton R, Adams C, Alleyne G, Asaria P, et al. Priority actions for the non-communicable disease crisis. Lancet. 2011; 377:1438–47.

2. Servinc S, Akyol AD. Cardiac risk factors and quality of life in patients with coronary artery disease. J Clin Nurs. 2010;19(9-10):1315–25.

3. Chan CW, Perry L. Lifestyle health promotion interventions for the nursing workforce: a systematic review. J Clin Nurs. 2012; 21(15-16):2247-61.

4. Marrero SL, Bloom DE, Adashi EY. Noncommunicable diseases. A global health crisis in a new world order. J Am Med Assoc. 2012; 307(19): 2037-8.

5. Ohta Y, Tsuchihashi T, Onaka U, Hasegawa E. Clustering of cardiovascular risk factors and blood pressure control status in hypertensive patients. Intern Med. 2010; 49(15):1483-7.

6. World Health Organization. Reducing risks and preventing disease: population-wide interventions. [Internet]. 2011[cited 2013 Jun 17]. Available from: http://www.who.int/nmh/publications/ncd_report_chapter4.pdf.

7. Pomeshkina S, Borovik IV, Barbarash OL. Adherence to non-medication treatment in patients undergoing coronary artery bypass surgery. Eur Heart J. 2013;34 (Suppl 1):1213-8.

8. Pérez-Ríos M, Santiago-Pérez MI, Alonso B, Malvar A, Hervada X, Leon J. Fagerstrom test for nicotine dependence vs heavy smoking index in a general population survey. BMC Public Health. 2009;9:493-7.

9. Jomar RT, Paixão LA, Abreu AM. Alcohol Use Disorders Identification Test (AUDIT) e sua aplicabilidade na atenção primária à saúde. Rev APS. 2012;15(1):113-7.

10. Lee PH, Macfarlane DJ, Lam TH, Stewart SM. Validity of the international physical activity questionnaire short form (IPAQ-SF): A systematic review. Int J Behav Nutrit Physical Activity. 2011;8:115-26.

11. Fonseca AM, Galduroz JC, Noto AR, Carlini EL. Comparison between two household surveys on psychotropic drug use in Brazil: 2001 and 2004. Ciênc Saúde Coletiva. 2010;15(3): 663-70.

12. Ronksley PE, Brien SE, Turner BJ, Mukamal KJ, Ghali WA. Association of alcohol consumption with selected cardiovascular disease outcomes: a systematic review and meta-analysis. BMJ. 2011;342:d671-83.

13. Kahler CW, Borland R, Hyland A, McKee SA, Thompson ME, Cummings KM. Alcohol consumption and quitting smoking in the International Tobacco Control (ITC) Four Country Survey. Drug Alcohol Depend. 2009;100(3):214–20.

14. Kahler CW, Strong DR, Papandonatos GD, Colby SM, Clark MA, Boergers J, et al. Cigarette smoking and the lifetime alcohol involvement continuum. Drug Alcohol Depend. 2008; 93(1-2):111–20.

15. Kim HE, Song YM, Kim BK, Park YS, Kim MH. Factors associated with persistent smoking after the diagnosis of cardiovascular disease. Korean J Fam Med. 2013;34(3):160-8.

16. Brasil. Ministério da Saúde, Secretaria de Vigilância em Saúde, Secretaria de Gestão Estratégia e Participativa. [Vigitel Brazil 2010: Monitoring System of Risk and Protective Factors for Non Communicable Chronic Diseases by Telephone Survey]. Ministério da Saúde, Brasília [Internet]. 2011. [cited 2013 Dec 12] Available from: http://bvsms.saude.gov.br/bvs/publicacoes/vigitel_2010.pdf. Portuguese.

17. Lemos KF, Davis R, Moraes MA, Azzolin K. [Prevalence of risk factors for acute coronary syndrome in patients treated in an emergency]. Rev Gaúcha Enferm. 2010; 31(1):129-35. Portuguese.

18. Ranković G, Miličić B, Savić T, Đinđić B, Mančev Z, Pešić G Effects of physical exercise on inflammatory parameters and risk for repeated acute coronary syndrome in patients with ischemic heart disease. Vojnosanit Pregl. 2009;66(1):44-8.

19. Florindo AA, Hallal PC, Moura EC, Malta DC. Practice of physical activities and associated factors in adults, Brazil, 2006. Rev Saúde Pública. 2009;43(Supl 2):65-73.

20. Kâner A, Nilsson S, Jaarsma T, Andersson A, Wiréhn A-B, Wodlin P, et al. The effect of problem-based learning in patient education after an event of CORONARY heart disease- a randomized study in PRIMARY health care: design and methodology of the COR-PRIM study. BMC Fam Pract. 2012;13:110-8.

21. Muñiz J, Doblas GJJ, Pérez SMI, Goya LI, Eizagaetxebarría MN, Galván TE, et al. The effect of post-discharge educational intervention on patients in achieving objectives in modifiable risk factors six months after discharge following an episode of acute coronary syndrome (CAM-2 Project): a randomized controlled trial. Health Qual Life Outcom. 2010; 8:137-45.

22. Kones R. Primary prevention of coronary heart disease integration of new data, evolving views, revised goal, and role of rosuvastatin in management. A comprehensive survey. Drug Des Devel Ther. 2011;5: 325-80.

23. Leventhal AM, Huh J, Dunton GF. Clustering of modifiable biobehavioral risk factors for chronic disease in US adults: a latent class analysis. Perspect Public Health. [Internet]. 2013[cited 2013 Dec 02]. Available from: http://rsh.sagepub.com/content/early/2013/08/02/1757913913495780.long.

24. Prugger C, Heidrich J, Wellmann J, Dittrich R, Brand SM, Telgmann R, et al. Trends in cardiovascular risk factors among patients with coronary heart disease. Dtsch Arztebl Int. 2012;109(17):303-10.

25. Chow CK, Jolly S, Rao-Melacini P, Fox KA, Anand AA, Yusuf S. Association of diet, exercise, and smoking modification with risk of early cardiovascular events after acute coronary syndromes. Circulation. 2010;121(6):750-8.

26. Cicolini G, Simonetti V, Comparcini D, Celiberti I, Di Nicola M, Capasso LM, et al. Efficacy of a nurse-led email reminder program for cardiovascular prevention risk reduction in hypertensive patients: A randomized controlled trial. Int J Nurs Stud. 2013 Oct 25. pii: S0020-7489(13)00302-7.