Clinical research

Atherosclerotic diseases and lung cancer – a ten-year cross-sectional study in Cyprus

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Abstract

Introduction: The main purpose of this work is to study atherosclerotic diseases and lung cancer in Cyprus during the period 2007–2017 with the aim of finding not only the atherosclerotic diseases with the highest risk but also a possible association between these diseases and lung cancer.

Material and methods: The statistical methods used to extract the results of this work are Student's t-test and one-way analysis of variance (ANOVA), in order to check the statistical significance of atherosclerotic diseases with regard to the characteristics of the patients. Additionally, a multiple logistic regression analysis was used with the aim of finding the disease with the highest risk. Pearson's r was used to find a possible association between atherosclerotic diseases and lung cancer.

Results: As specified by multiple logistic regression analysis, the atherosclerotic diseases with the highest risk of death are intracranial haemorrhage (OR = 17.3), heart failure (OR = 3.29), and stroke (OR = 3.02), with females having higher risk compared to men. Moreover, a statistically significant relation was found between heart failure and cerebral infarction with lung cancer.

Conclusions: The results of this work highlight the statistically significant characteristics of patients with atherosclerotic diseases and identify the risk of death according to the type of the disease. A link between these diseases and cancer was also identified.

Key words: cancer, atherosclerotic diseases, malignant neoplasms.

Introduction

Atherosclerotic diseases are the leading cause of death worldwide, accounting for 17.9 million deaths each year [1]. Some of the processes involved in atherosclerosis are lipid disorders, thrombosis, oxidative stress, and endothelial dysfunction [2]. Risk factors include cigarette smoking, diabetes mellitus, adiposity, hypertension, and blood cholesterol. More specifically, it has been found that smokers are 1.7–5.6 times more likely to be at risk for atherosclerotic diseases than non-smokers [3–5]. Moreover, individuals with diabetes mellitus have twice the risk of mortality, because a 1% increase in haemoglobin A_{1c} (HbA_{1c}) has been shown to increase the risk of atherosclerotic heart disease by 50% [6–9]. Adiposity poses a high risk of atherosclerotic diseases; each 1 kg/m² increase above the level of 25 kg/m² in body mass index (BMI) causes an increase of 8% in atherosclerotic heart disease mortality [10, 11]. Hypertension has been proven to increase the risk of atherosclerotic diseases; any

20 mm Hg increase in usual systolic blood pressure and 10 mm Hg increase in diastolic blood pressure doubles that risk [12–14]. Finally, blood cholesterol plays a key role in the emergence of atherosclerotic heart disease [15–17]. More precisely, there is a strong positive association between non-high-density lipoprotein (non-HDL) cholesterol with atherosclerotic heart disease mortality predominantly in the age group of 50–59 years, while each 38.7 mg/dl decrease in normal total cholesterol is associated with a 42% lower risk of atherosclerotic heart disease mortality [15].

Prior studies identified a strong association between lung cancer and atherosclerotic diseases [18, 19]. Patients with lung cancer have an 89% increased risk of developing atherosclerotic heart disease compared to those not afflicted with cancer. The underlying mechanisms by which atherosclerosis is associated with cancer are chronic inflammation, oxidative stress, altered telomere length, and clonal haematopoiesis [20–22]. It is of the utmost importance to acknowledge the multifaceted interactions that lead to both neoplasia and atherosclerosis, which in turn reflect the responsibility of underlying conditions such as essential (primary) hypertension for the high risk of death from these diseases.

For this purpose, this work studies atherosclerotic diseases in Cyprus during the period 2007–2017 in order to identify which type has the highest death risk, as well as a possible association with lung cancer.

Material and methods

The data used in this work come from the Republic of Cyprus. The target population of the analysis is the 37,628 confirmed cases of patients with atherosclerotic diseases who were hospitalised in Cyprus during 2007–2017.

Statistical analysis

The statistical methods used to extract the results of this work are Student's t-test and one-way analysis of variance (ANOVA) for continuous variables, to check the statistical significance of the characteristics of patients such as gender and age. Factors that ascertain the prevalence of death from atherosclerotic diseases, as well as the severity of each type of disease, were evaluated by using multiple logistic regression analysis. To better estimate the type of disease with the highest risk of death, data from patients with a new diagnosis of an atherosclerotic disease was compared to a matched cohort group of patients who had died from this disease. The data were weighted before analysis. Predictors were presented using the OR and 95% confidence intervals, and $p < 0.05$ was considered as statistically significant. Pearson's r was used for the relationship between atherosclerotic diseases and lung cancer for the years 2007–2017. The statistical analysis of this manuscript was performed by using the software package IBMSPSS 25 for Windows.

Results

To test the zero hypotheses that the mean of the patients did not differ in accordance with their characteristics, Student's t-test and one-way analysis of variance (ANOVA) were used. As shown in Table I, there is a statistically significant difference in the number of patients with athero-

Table I. Atherosclerotic diseases: Cyprus 2007–2017. Student t-test

Variable	Males	Females	P-value
Chronic rheumatic heart disease	107	171	< 0.05
Essential (primary) hypertension	480	395	< 0.05
Acute myocardial infarction	5727	1216	< 0.05
Pulmonery embolism	301	439	< 0.05
Conduction disorders and cardiac arrhythmias	6950	5697	< 0.05
Heart failure	4490	2494	< 0.05
Intracranial haemorrhage	676	710	< 0.05
Cerebral infarction	384	340	< 0.05
Stroke, not specified as haemorrhage or infarction	3321	3022	< 0.05
Atherosclerosis	62	53	< 0.05
Arterial embolism and thrombosis	202	121	< 0.05
Overall	22981	14647	< 0.05

Table II. Atherosclerotic diseases by age: Cyprus 2007–2017. One-way ANOVA test

Variable	< 1	1–14	15–44	45–64	≥ 65	P-value
Chronic rheumatic heart disease	0 (0%)	1 (0.4%)	24 (9.7%)	98 (39.5%)	125 (50.4%)	< 0.05
Essential (primary) hypertension	17 (2.1%)	68 (8.4%)	147 (18.1%)	267 (33%)	311 (38.4%)	< 0.05
Acute myocardial infarction	0 (0%)	31 (0.5%)	666 (11.1%)	2948 (49.1%)	2364 (39.3%)	< 0.05
Pulmonery embolism	0 (0%)	12 (1.9%)	103 (16.5%)	178 (28.6%)	330 (53%)	< 0.05
Conduction disorders and cardiac arrhythmias	47 (0.4%)	168 (1.5%)	1041 (9.3%)	3421 (30.4%)	6563 (58.4%)	< 0.05
Heart failure	27 (0.4%)	31 (0.5%)	201 (3.3%)	1432 (23.8%)	4322 (71.9%)	< 0.05
Intracranial haemorrhage	5 (0.3%)	22 (1.5%)	169 (11.8%)	439 (30.7%)	794 (55.6%)	< 0.05
Cerebral infarction	0 (0%)	0 (0%)	30 (5.5%)	121 (22.2%)	393 (72.2%)	< 0.05
Stroke	1 (0%)	29 (0.5%)	303 (5.2%)	1758 (30.1%)	3745 (64.2%)	< 0.05
Atherosclerosis	0 (0%)	2 (1.9%)	9 (8.7%)	29 (28.2%)	63 (61.2%)	< 0.05
Arterial embolism and thrombosis	0 (0%)	1 (0.3%)	24 (7.7%)	100 (32.2%)	186 (59.8%)	< 0.05
Overall	96 (0.4%)	333 (1.3%)	2356 (8.9%)	8802 (33.3%)	14,861 (56.2%)	< 0.05

sclerotic diseases in relation to gender, predominantly in males (61.1%), in the total number of atherosclerotic diseases. More specifically, essential (primary) hypertension (54.9%), acute myocardial infarction (82.5%), conduction disorders and cardiac arrhythmias (55%), heart failure (64.3%), cerebral infarction (53%), stroke that not specified as haemorrhage or infarction (52.4%), atheroscle-

Figure 1. Trends in atherosclerotic diseases and lung cancer during the years 2007–2017 in Cyprus

rosis (53.9%), and arterial embolism and thrombosis (62.5%) prevail mainly in males. While chronic rheumatic heart disease (61.5%), pulmonary embolism (59.3%), and intracranial haemorrhage (42.1%) predominate in females. As shown in Table II, there is a statistically significant difference in the number of patients with atherosclerotic diseases in relation to age, predominantly in the age group of 65 years and over, in all atherosclerotic diseases (56.2%), except for acute myocardial infarction, which was observed mainly in the age group of 45–64 years (49.1%).

Figure 1 represents the trends in all atherosclerotic diseases and lung cancer during the years 2007–2017 in Cyprus. Although there was a decline in the incidence of these diseases in 2011 and 2012, there was an increase in the following years, with conduction disorders and cardiac arrhythmias, heart failure, and acute myocardial infarction occupying the top three in 2017.

Tables III and IV represent the multiple logistic regression analysis and odds ratios in order to find the atherosclerotic diseases with the highest death risk. Based on multiple logistic regression, the risk of death from intracranial haemorrhage is the highest (OR = 17.3), with no statistical difference between the two genders. The risk of death is three times higher in heart failure (OR = 3.29) and stroke (OR = 3.02) not specified as haemorrhage or infarction, with females having higher risk than males. Conduction disorders and cardiac arrhythmias (OR = 3.13) also have a three-times higher risk of death, with no statistical difference between the two genders. Subsequently, in pulmonary embolism (OR = 2.72) the risk of death
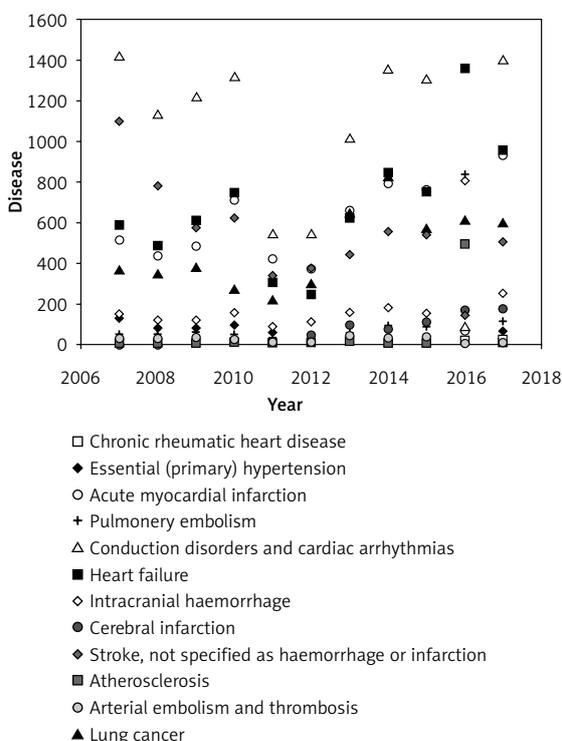
Table III. Atherosclerotic diseases: Cyprus 2007–2017. Multivariate logistic regression.

Variable	Alive	Dead	Odds ratio (95% CI)	P-value
Chronic rheumatic heart disease:				> 0.05
Female	165	2	1.0 (0.2–4.4)	
Male	104	3	1.0 (ref.)	
Essential (primary) hypertension:				< 0.05
Female	385	2	14.6 (14.4–15.9)	
Male	469	0	1.0 (ref.)	
Acute myocardial infarction:				< 0.05
Female	1.086	114	4.0 (3.1–5.2)	
Male	5.501	141	1.0 (ref.)	
Pulmonery embolism:				> 0.05
Female	399	5	1.1 (0.6–2.0)	
Male	277	22	1.0 (ref.)	
Conduction disorders and cardiac arrhythmias:				> 0.05
Female	5.084	503	0.9 (0.8–1.2)	
Male	6.205	630	1.0 (ref.)	
Heart failure:				< 0.05
Female	2.153	284	1.4 (1.2–1.6)	
Male	4.036	370	1.0 (ref.)	
Intracranial haemorrhage:				> 0.05
Female	591	115	1.0 (0.7–1.3)	
Male	817	155	1.0 (ref.)	
Cerebral infarction:				> 0.05
Female	321	17	1.0 (0.5–1.9)	
Male	364	19	1.0 (ref.)	
Stroke, not specified as haemorrhage or infarction:				< 0.05
Female	2.674	324	1.6 (1.3–1.9)	
Male	3.066	233	1.0 (ref.)	
Atherosclerosis:				> 0.05
Female	50	3	3.7 (0.3–36.2)	
Male	61	1	1.0 (ref.)	
Arterial embolism and thrombosis:				> 0.05
Female	115	5	1.7 (0.5–6.0)	
Male	197	5	1.0 (ref.)	

is two times higher, with no statistical difference between the two genders. In cerebral infraction, acute myocardial infarction, atherosclerosis, arterial embolism and thrombosis, and chronic rheumatic heart disease there is no statistically significant risk of death compared to other atherosclerotic diseases. Comparing the two genders, the risk of death in the acute myocardial infarction is four times higher in females (OR = 4.0). Finally, in essential (primary) hypertension (OR = 0.07) the risk of death is lower than the other atherosclerotic diseases and occurs mainly in females.

Table IV. Atherosclerotic diseases: Cyprus 2007–2017. Multivariate logistic regression

Variable	Alive	Dead	Odds ratio (95% CI)	P-value
Chronic rheumatic heart disease	269	5	0.92 (0.36–2.38)	> 0.05
Essential (primary) hypertension	854	2	0.07 (0.01–0.33)	< 0.05
Acute myocardial infarction	6.587	255	1.20 (0.63–2.29)	> 0.05
Pulmonery embolism	676	27	2.72 (1.37–5.39)	< 0.05
Conduction disorders and cardiac arrhythmias	11.289	1.133	3.13 (1.66-5.89)	< 0.05
Heart failure	6.189	654	3.29 (1.74–6.22)	< 0.05
Intracranial haemorrhage	1.408	270	17.3 (18.0–19.2)	< 0.05
Cerebral infarction	685	36	1.64 (0.80–3.34)	> 0.05
Stroke, not specified as haemorrhage or infarction	5740	557	3.02 (1.60-5.71)	< 0.05
Atherosclerosis	111	4	1.12 (0.34–3.65)	> 0.05
Arterial embolism and thrombosis	312	10	1.0 (ref.)	> 0.05

Table V. Pearson's correlation coefficient

Variable	Lung cancer	
	Pearson's correlation r	P-value
Lung cancer	1	
Chronic rheumatic heart disease	0.08	> 0.05
Essential (primary) hypertension	−0.18	> 0.05
Acute myocardial infarction	0.34	> 0.05
Pulmonery embolism	0.32	> 0.05
Conduction disorders and cardiac arrhythmias	0.15	> 0.05
Heart failure	0.64	< 0.05
Intracranial haemorrhage	0.37	> 0.05
Cerebral infarction	0.68	< 0.05
Stroke, not specified as haemorrhage or infarction	−0.20	> 0.05
Atherosclerosis	0.25	> 0.05
Arterial embolism and thrombosis	0.16	> 0.05

Table V represents the Pearson's r among the total number of atherosclerotic diseases and lung cancer patients for the years 2007 to 2017. As shown in Table V, the incidence of lung cancer is statistically significant with heart failure and cerebral infarction ($p < 0.05$). Pearson's r between the total cases of lung cancer patients and cerebral infarction as well as heart failure patients is 0.68 and 0.64, respectively, which indicates a link between these diseases and lung cancer.

Figure 2 shows the odds ratios for the risk of death from atherosclerotic diseases. As can be seen, intracranial haemorrhage ranks first, followed by heart failure, conduction disorders and cardiac arrhythmias, stroke, not specified as haemorrhage or infarction, and pulmonary embolism.

Discussion

It is worth highlighting that although atherosclerotic diseases occur predominantly in males (61.1%) over 65 years of age, except acute myocardial infarction, which occurs in the age group of 45–64 years, females proved to have a higher risk of death than males. This is due to the rela-
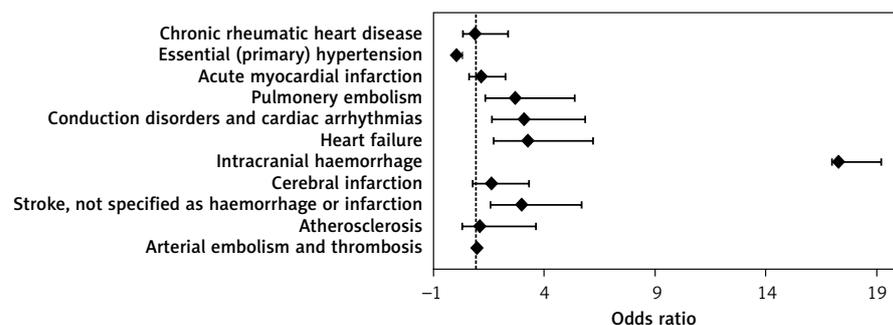

Figure 2. Odds ratios in death risk from atherosclerotic diseases using multiple logistic regression

tionship between atherosclerosis and not only hypertension in females but also autoimmune diseases such as systemic lupus erythematosus, rheumatoid arthritis, and systemic sclerosis [23–25]. Infections that have been proven to induce rheumatoid arthritis are involved in the pathogenesis of rheumatic autoimmune diseases and atherosclerotic diseases [24]. Another reason may be the misdiagnosis of atherosclerosis and therefore the subsequent treatment in women [26].

It is also worth noting that atherosclerotic diseases have been linked to lung cancer. The connecting link between cancer and atherosclerosis is the common molecular pathway and processes such as oxidative stress, inflammation, abnormal apoptosis, uncontrolled cell proliferation, and vasodilation, which are shared by these two multifactorial diseases. More specifically, degradation of cell proliferation, which is exacerbated by oxidative stress, allows not only the development of atherosclerotic plaque but also various types of cancer [27, 28].

In conclusion, the importance of this study lies in the emergence of the statistical significance characteristics of patients with atherosclerotic diseases as well as the atherosclerotic disease with the highest risk of death. It has been also identified a link between heart failure as well as cerebral infarction and lung cancer.

This study is not without limitations. A significant value of Pearson's *r* does not imply causality between the variables, a fact that reflects the need for further studies in order to clarify the relationship between atherosclerotic diseases and lung cancer.

Conflict of interest

The author declare no conflict of interest.

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