Correlation Between New-Onset Atrial Fibrillation and Cancer

[2]Monica Soliman, [1]Carlos Rodríguez Pellicer, [1]Alejandro Herreros-Pomares, [1]Aurelio Quesada Dorador, [1]Francisco Javier Quesada Ocete, [1,3,4]Fernando Vidal-Vanaclocha

[2]George Washington University School of Medicine and Health Sciences, [1]University of Valencia General Hospital, [3]GWU Cancer Center, [4]GWU Department of Biochemistry and Molecular Medicine

INTRODUCTION

An increase in the incidence of new-onset Atrial Fibrillation (AF) has been noticed in patients in acute inflammatory states and with local inflammatory conditions. Cancer, through inflammatory mediators and autonomic dysfunction, may favor the appearance of AF. Some studies have found that cancer patients generally had a 47% higher risk of developing AF than non-cancer patients, and that this risk is increased only in the first 90 days following cancer diagnosis. Furthermore, patients with a first episode of AF could have a higher risk of developing cancer. In fact, AF has been proposed as a marker for occult neoplasia. However, more studies are needed to study the association of AF and cancer, as it is not yet known whether this is a causal association or simply that the two pathologies share the same pathophysiological mechanisms as their etiology. The objective of this study was to analyze the incidence of cancer 2 years after the first episode of AF in patients at the General University Hospital of Valencia, and to search for relevant variables that allow for differentiating patients who will develop cancer from patients who will not.

MATERIALS AND METHODS

- The population sample was obtained from a database in which the encoded anonymized information of 2022 episodes of AF treated in the Emergency Service of the Consortium General University Hospital of Valencia (CHGUV) was collected from 1 January 2010 to December 31, 2015.
- The electrocardiograms associated with the AF episode were reviewed, including only those with a confirmed diagnosis of AF.
- Exclusion criteria included a previous history of AF, previous antiarrhythmic or anticoagulant treatment, previous history of cancer (including non-melanoma skin neoplasms), and an urgent precipitating condition that justified the AF episode (i.e. infections, sepsis, acute coronary syndromes, critically ill patients).
- The final sample was 712 patients.
- Retrospective follow-up of patients for at least 2 years was carried out through the EMR of the hospital to note the development of cancer.
- Student T-test was applied for the comparison of quantitative variables and the Chi-square test for the comparison of qualitative variables of this final sample of cancer vs. non-cancer subjects (95% Confidence Interval).
- Since there was no control group, the results were compared with the incidence of cancer in our environment, which was extracted in 2012 from the Spanish Society of Medical Oncology (SEOM).

RESULTS

- Out of 712 patients with new-onset AF, 35 (4.91%) were found to have a malignancy 2 years after index episode
- Patients without cancer presented more frequently with typical symptoms such as palpitations (32.64%) compared to 14.28% in the cancer group, which is a statistically significant difference (p=0.025).

Table 1. Baseline Characteristics of Cancer-Free and Cancer Patients

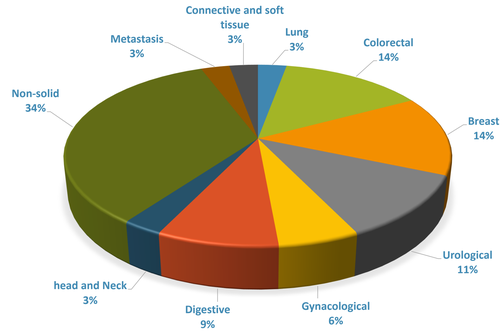
VARIABLE	No cancer (n=677) (95.08%)	With cancer 2 years after index episode (n=35) (4,91%)	p-value
Demographics			
Age	74.14 +/- 12.73	78.68 +/- 12.75	0.039
<65 years	141 (20.82)	4 (11.43)	0.178
65-74 years	158 (23.33)	5 (14.28)	0.213
75-85 years	248 (36.63)	16 (45.71)	0.278
>85 years	130 (19.20)	10 (28.57)	0.173
VARIABLE	No cancer (n=677) (95.08%)	With cancer 2 years after index episode (n=35) (4.91%)	p-value
Sex	F: 418 (61.74) M: 259 (38.26)	F: 23 (65.71) M: 12 (34.28)	0.723
Cardiovascular risk factors			
HTA	523 (77.25)	25 (71.43)	0.414
DM	242 (35.74)	10 (28.57)	0.470
Smoking	74 (10.93)	3 (8.57)	1.000
Obesity	55 (8.12)	2 (5.71)	1.000
Dyslipidemia	279 (41.21)	13 (37.14)	0.633
Alcohol	13 (1.92)	0 (0)	0.408
Comorbidities			
SAHS	21 (3.10)	0 (0)	0.290
COPD	58 (8.56)	4 (11.42)	0.535
Renal Insufficiency	70 (10.33)	1 (2.86)	0.242
Hepatic Insufficiency	7 (1.03)	0 (0)	1.000
Enf. Rheumatic	35 (5.16)	2 (5.71)	0.702
IBD	2 (0.29)	0 (0)	0.747
Cardiovascular history			
Arteriopathy	36 (5.31)	0 (0)	0.249
MI	55 (8.12)	4 (11.42)	0.522
CVA	65 (9.6)	2 (5.71)	0.764
Bleeding	23 (3.57)	2 (5.71)	0.467
LVEF previous cancellation	15 (2.21)	0 (0)	0.373
Cardiopathy	33 (4.87)	3 (8.57)	0.413
IC	100 (14.77)	3 (8.57)	0.459
Mc. Vault. Mitral	60 (8.86)	2 (5.71)	0.760
Mc. Vault. Aortic	49 (7.23)	4 (11.42)	0.321
Mc. Dilated	11 (1.70)	0 (0)	0.447
Mc. Ischemic	47 (6.94)	5 (14.28)	0.169
Hypertrophic Mc.	28 (4.34)	0 (0)	0.219
VARIABLE	No cancer (n=677) (95.08%)	With cancer 2 years after index episode (n=35) (4.91%)	p-value
Mc. Hypertensive	12 (1,86)	0 (0)	0.427
CHA_2DS_2-Vasc	3.61 +/- 1.70	3.49 +/- 1.60	0.672

IC: Cardiac Insufficiency; CVA: Cerebrovascular Accident; Mc: Cardiomyopathy; SAHS: Sleep Apnea/Hypopnea Syndrome

The average age of cancer patients in the study period (78.68 ± 12.75) was higher than that presented by those who did not develop cancer (74.14 ± 12.73), this difference being statistically significant (p=0.039). Looking at patients over 65 years of age, this group represented 88.57% of cancer patients, while in patients without cancer it represented 79.17%. The rest of the variables analyzed, including cardiovascular risk factors, a history of smoking or alcohol, or inflammation-sensitive labs (troponin, leukocytes, CRP) did not present significant differences.

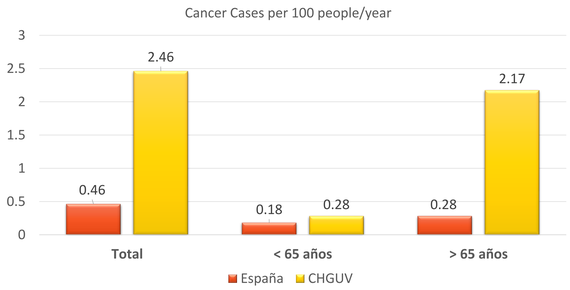
RESULTS (Cont.)

Graph 1. Proportion of each type of cancer to the total number of patients diagnosed with cancer in the 2 years following the debut of AF



The number of neoplasms diagnosed in the study period was 2.45 cases per 100 people/year. When compared with the incidence of cancer in Spain in 2012 (0.46 cases per 100 people/year) as notified by the SEOM, the difference is found to be statistically significant. Non-solid neoplasms comprised the largest type of frequency, representing 34.28% of the total. Colorectal and breast neoplasia were shown to be the second in frequency, but with a markedly lower percentage than the former (both with 14.28%).

Graph 2. Incidence of cancer by age in Spain in 2012 and in the two years after the debut of AF in our study. CHGUV: Consortium General University Hospital of Valencia



There was a higher incidence of cancer in patients with AF over 65 years of age compared to those under this age (2.17 versus 0.28 cases per 100 people/year). When compared by age groups, it was observed that there is a higher incidence of cancer in our sample in comparison to the general population both in individuals under 65 years of age (0.28% vs 0.18%) and those over 65 years of age (2.17% vs 0.28%).

CONCLUSION

This study detected an unusually high incidence of cancer in patients with a first diagnosis of AF. Specifically, the annual incidence of 2.45 cases per 100 people/year after the debut of AF is 6.1 times more than the risk in the general Spanish population, being especially higher in those over 65 years of age. Although other studies had also come to a similar conclusion, this study differs in that it used stricter exclusion criteria to avoid confounding bias, and it relied on an electrocardiographic diagnosis of AF, which is essential to ensure the correct diagnosis of the arrhythmia. A major limitation to this study was the absence of a control group to compare the incidence of cancer to. Univariate and multivariate analysis did not detect a relevant variable that allows for differentiating patients who will present with cancer from patients who will not. However, with the results of this study, surveillance of cancer should be considered in patients presenting with new-onset AF, especially in those over 65 years of age with atypical symptoms. Further studies are needed to explore the relationship between these two pathologies as it is still unknown whether there is a causal relationship between both conditions or if both simply share the same pathophysiological mechanism involved in their genesis.

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