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Original

Prevalence of diabetes in a cancer population in a Malaga hospital

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Abstract

Background: **There are multiple risk factors for cancer, including obesity, sedentary lifestyle, diabetes (DM). Hormon Insulin is a growth factor that promotes cellular differentiation.**

Aims: **The aim of our study is to observe impaired glycaemia in cancer population compared with control.**

Methods: **We studied the prevalence of diabetes (DM) and impaired fasting glycaemia (IFG) in 374 patients with different types of cancer before treatment, by medical records in a Malaga hospital (Spain). We compared the prevalence of basal hyperglycaemia in these patients with general population, within an age range and by gender.**

Results and discussion: **The prevalence of diabetes was 32.35% in our cancer patients. The comparison depends of age range, and by gender prevalence was: 45-54 years, DM: 40.91% in men cases, *versus (vs.)* 14.5% in men control (p = 0.005). 55-64 years, IFG: 23.08% in women cases, *vs.* 5.9% in women control (p = 0.001). 65-74 years, DM: 47.13% in men cases, *vs.* 25.4% in men control (p = 0.000), and IFG: 23.81% in women cases, *vs.* 9.5% in women control (p = 0.019). We found a higher prevalence of diabetes in specific types of cancer such as prostate (p < 0.005). Moreover, men had a higher prevalence of diabetes or less diabetes control than women in our cancer sample.**

Conclusions: **We recommend an OGTT (oral glucose tolerance test) for better diagnosis of possible DM in patients with cancer, and an appropriate treatment. It may be an independent risk factor for cancer to have decreased insulin activity, or DM.**

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Key words: *Diabetes. Hypertrophy. Insulin. Oncology.*

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PREVALENCIA DE DIABETES EN UNA POBLACIÓN CON CÁNCER DE UN HOSPITAL DE MÁLAGA

Resumen

Introducción: **Existen múltiples factores de riesgo para que una célula degenere en crecimiento indiferenciado o cáncer. Entre otros factores se ha observado que la obesidad, el sedentarismo y la diabetes aumentan este riesgo. La insulina es un factor de crecimiento que promueve la diferenciación celular.**

Objetivos: **El objetivo de nuestro estudio es observar la glucemia basal en una población con cáncer y comparar con una población control.**

Métodos: **Estudiamos la presencia de diabetes mellitus (DM) y de glucosa alterada en ayunas (GAA) en 374 pacientes de distintos tipos de cáncer mediante sus historiales observando la glucemia basal del ingreso antes de su tratamiento. Comparamos con la glucemia basal en población normal por rangos de edad y sexo.**

Resultados y discusión: **La prevalencia de diabetes en los pacientes con cáncer fue de 32,35%. Comparación por sexo y rangos de edad: observamos que entre 45-54 años, DM: 40,91% en hombres cancerosos *versus (vs)* 14.5% en hombres control (p = 0,005). Entre 55-64 años, GAA: 23,08% en mujeres cancerosas *vs* 5,9% en mujeres control (p = 0001). Entre 65-74 años, DM: 47,13% en hombres cancerosos *vs* 25,4% en hombres control (p = 0,000), y GAA: 23,81% en mujeres cancerosas *vs* 9,5% en mujeres control (p = 0,019). Encontramos una mayor prevalencia de diabetes en unos tipos específicos de cáncer más que en otros, como por ejemplo en el cáncer de próstata (p < 0,005). Así mismo observamos que los hombres tienen una mayor prevalencia de diabetes o un menor control de la enfermedad que las mujeres en nuestra muestra de casos de cáncer.**

Conclusiones: **Recomendamos un diagnóstico sistemático de diabetes en los pacientes con cáncer mediante test de tolerancia oral de glucosa (OGTT) y su conveniente tratamiento. Es posible que la diabetes, o el tener disminuida la actividad insulínica, sea un factor más de riesgo para el cáncer.**

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Palabras clave: *Diabetes. Hipertrofia. Insulina. Oncología.*

Abbreviations

ADA: American Diabetes Association.
BMP2: Bone morphogenetic protein 2.
CROASA: Andalucian Radio Oncology Centre of Health.
DEN: Diethyl nitrosamine.
DM: Diabetes Mellitus.
DM2: Type-2 Diabetes Mellitus.
Normal G: Normal glycaemia
IFG: Impaired fasting glycaemia.
IGF-1: Growth factor similar to insulin-1.
NADH: Reduced nicotinamide adenine dinucleotide
WHO: World Health Organisation.
OGTT: Oral glucose tolerance test.
STZ: Streptozotocin.
T2DM: Type 2 diabetes mellitus.

Introduction

This study analyses the prevalence of basal hyperglycaemia in cancer patients to observe whether it is greater than in the general population. Insulin favours cellular differentiation, thereby its functional deficiency could imply a greater risk of undifferentiated growth (cancer).

There are numerous studies that have linked diabetes to certain cancers, considering it a risk factor for cancer patients.[1-8]

Other studies have monitored patients with diabetes in order to observe the development of illnesses such as cancer, but these require studying the entire vital period of the patient.[1]

The lack of activity of the insulin hormone results in decreased use of glucose by the body's tissues, increasing glucose levels in the blood. Diabetes Mellitus (DM) is defined as "the set of metabolic diseases of heterogeneous origin and symptoms, characterized by hyperglycaemia resulting from defects in insulin secretion, action (insulin resistance) or both.[9]

The increase of blood glucose displays a deficiency in the activity of insulin that can involve an abnormal glucose tolerance, mainly for digestive sites, an insulin-resistance with compensatory hyperinsulinemia, or less insulin secretion.[10]

In cell growth, two processes must be distinguished, hyperplasia (which maintains the cell number) and hypertrophy which provides differentiation and functionality to the cell. A study on rats demonstrates that differentiation can be induced by hypertrophy with bone morphogenetic protein 2 (BMP2) and insulin.[11]

It has been proved that to obtain mice which develop hepatocarcinogenesis induced by diethyl nitrosamine (DEN), the results are greater if diabetes is also induced in them by injecting streptozotocin (STZ).[12]

The origin of cancer is multi-factorial, and it has been associated with risk factors such as obesity, diabetes, sedentary lifestyle, highly glycaemic foods, etc. It is difficult to know if diabetes is an independent risk factor for cancer.[13,14] Although a recent study indicated that type-2 diabetes (DM2) is associated with endometrial cancer, regardless of whether the rest of the risk factors were present. Diabetes was associated with this type of cancer in women who were slim, overweight and moderately obese.[15] Another study confirms this, and observed that the effective treatment of type 2 diabetes might contribute to endometrial cancer prevention.[16] Therefore, some recent studies support the idea that diabetes could be considered a risk factor for cancer, with independence of the weight of the patient.

It has also been noted that in the early stages of diabetes, normal levels of insulin can be increased to maintain its activity in an attempt to compensate for the insulin resistance that occurs initially in these patients, but the efficiency of their activity is diminished.[17]

Generally, cancer depends on numerous trigger factors (multi-factorial). In tissue that begins to show hyperplasic growth, many changes in different systems have had to occur so that the tissue degenerates into tumour growth.

The diagnosis of diabetes Mellitus and alteration of glucose tolerance is established according to the World Health Organisation (WHO) and the American Diabetes Association (ADA).[18,19] According to the report from the Expert Committee for the diagnosis and classification of diabetes Mellitus, fasting plasma glucose is classified as up to 110 mg/dl (6.1 mmol/l, normal glycaemia), from 110 to 125 mg/dl (impaired fasting glycaemia, IFG) and greater than or equal to 126 mg/dl (diabetes mellitus, DM).[20]

Type 2 diabetes mellitus (T2DM) is the most common type of diabetes (90% of global cases), and it's dependent by age.[21-23].

The objectives of this study are to estimate the prevalence of high basal glycaemia in a population of individuals with cancer from a hospital in Malaga (Spain), and compare with the results of glycaemia obtained in previous studies carried out in healthy individuals by gender and by age.

Methods

Subjects characteristics

A cross-sectional study was performed on a population of 374 patients with cancers in different tissues, from the Hospital Carlos Haya, Hospital Civil and the Andalucian Radio Oncology Centre of Health (CROASA) of Malaga (Spain). Data were obtained from medical records at hospital admission before treatment. These were collected from May 2004 to June 2006. Inclusion criteria were individuals over 18 years of age, diagnosed with cancer, (baseline glycaemia data appeared in the general medical record). Patients whose records lacked any of the required data were excluded (gender, age, fasting glycaemia, type of cancer).

Glycaemia control

The basal glycaemia levels were measured at the moment of admission of the patient diagnosed with cancer. The results were mostly obtained from the clinical laboratory of the Carlos Haya hospital, and were taken by measuring the absorbance due to reduced nicotinamide adenine dinucleotide (NADH) by means of a dichromate endpoint technique (340 and 383 nm). All results were obtained in mg/dl.

Control group

Data about the hyperglycaemia of the healthy population was obtained from previous publication carried out in the population of Gerona, Spain.[23] In this publication baseline glycaemia was analyzed by ten years range and by gender.

Diabetes prevalence is known to increase as people age, thus the correlation of diabetes and cancer without a proper age matched control group is meaningless.

Types of cancer of the sample

The cancers studied were breast, lung, colorectal, bone, liver, pancreas, other gastrointestinal, skin, female reproductive organ, vesical urothelium, prostate and others; with a sample size differently depending on the frequency of each type of cancer.

Statistical analysis

The prevalence of impaired basal glycaemia in patients with cancer was estimated. To compare these results with the prevalence of impaired glycaemia in a baseline healthy population, the exact method based on binomial distribution was used.

In the case of categorical variables the chi-square or Fisher (if more than 20% of expected frequencies were less than 5) tests were applied.

Results

Anthropometric characteristics

The study sample consisted of 54.8% men and 45.2% women. The average age was 61 years with a standard deviation of 13. The median was 64 years. In the sample, 24.6% of individuals were between 55 and 64 years of age, 34.5% of individuals were between 65 and 74, and 12.3% of individuals were over 75 years. Mean basal glycaemia levels were 119.58 mg / dl with a standard deviation of 44.5.

Types of cancer distribution

The 21.4% of individuals of the sample had breast cancer, 18.2% had colorectal cancer, 14.2% had prostate cancer, 13.9% had skin cancer, 13.9% had lung cancer, 5.6% had other digestive cancers, 2.7% had female reproductive organ cancer, 2.4% had vesical urothelium cancer, 1.6% had pancreatic cancer, 0.8% had bone cancer, 0.5% had liver cancer, and 4.8% had other types of cancers. Due to the low frequencies that had bone cancer, liver, pancreas and vesical urothelium, these were regrouped in "other cancers" for further analysis.

Cancer age distribution

Regarding the distribution of the sample by type of cancer and by age range, it was observed that 66% (higher percentage) of individuals with prostate cancer were between 65 and 74 years of age, 34.6% of individuals with lung cancer were between 55 and 64 years of age, 26.9% of individuals with skin cancer were between 65 and 74 years, 45.6% of individuals with colorectal cancer were between 65 and 74 years, 40% of individuals with female reproductive organ cancer were between 55 and 64 years, and 22.5% of individuals with breast cancer were between 45 and 54 years, and with the same percentage, between 55 and 64 years (fig. 1).

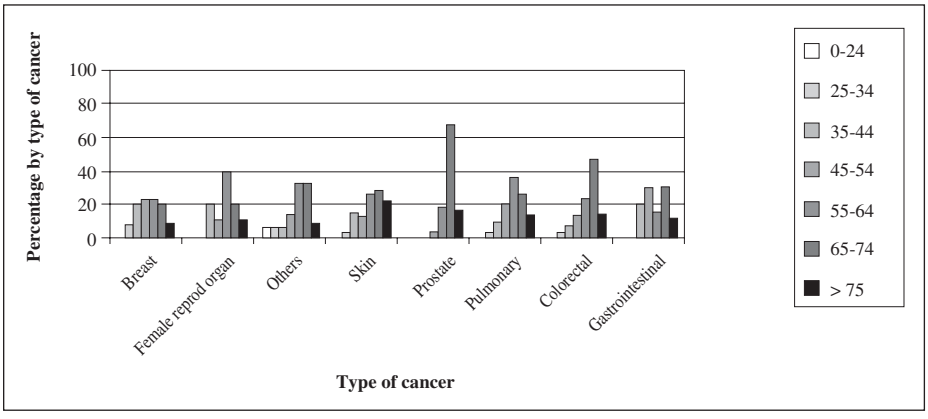

Fig. 1.—Age distribution by type of cancer.

Table I
Distribution of IFG and DM in the sample by type of cancer in a Malaga hospital

	n < 6.1	*Nº subjects with IFG*	*Nº subjects with DM*	*Total*	*Prevalence of IFG*	*p*	*Prevalence of DM*	*p*
Breast	44	17	19	80	21.25	0.34	23.75	0.00**
Pulmonary	31	8	13	52	15.38	0.97	25	0.02*
Colorectal	27	15	26	68	22.06	0.31	38.24	0.31
Bone	2	0	1	3				
Liver	1	0	1	2				
Pancreatic	2	2	2	6				
Gastrointestinal	15	3	3	21	14.29	0.80	14.29	0.01*
Skin	25	8	19	52	15.38	0.97	36.54	0.08
Female reproductive organ	5	3	2	10	30.00	0.39	20	0.18
vesical urothelium	4	1	4	9				
Prostate	20	7	26	53	13.21	1	49.06	1
Others	12	1	5	18	5.56	0.65	27.78	0.19
All	188	65	121	374	17.38		32.35	

*p < 0.05 *versus* breast cancer.
**p < 0.005 *versus* breast cancer.

Diabetes prevalence in cancer patients

The prevalence of diabetes was 32.35%, establishing a cut-off point of 126 mg/dl baseline glycaemia in individuals with cancer over 18 years in a hospital in Malaga (table I).

The prevalence of DM in individuals with prostate cancer differs significantly from the prevalence of DM in breast cancer ($P < 0.005$), the prevalence of DM in lung cancer ($P = 0.02$), and the prevalence DM in individuals with other gastrointestinal cancers ($P = 0.01$) (table I).

In figure 2, it is noted that some types of cancer are associated with diabetes more than others: 49.06% of individuals with prostate cancer, 38.24% with colorectal cancer, 36.54% with skin cancer, 25% with lung cancer, 23.75% with breast cancer, 20% with female reproductive organ cancer, and 14.29% of other gastrointestinal cancers. Therefore it is demonstrated that the presence of diabetes is associated with the type of cancer ($P < 0.03$).

The prevalence of diabetes (bearing in mind the cut-off point of 126 mg/dl) is 7.69% in a population of individuals with cancer between 35 and 44 years of age, 25.45% between 45 and 54 years of age, 32.61% between 55 and 64 years of age, 42.69% between 65 and 74 years old, and 41.30% older than 75 years (table II).

On introducing a gender perspective in the analysis, it was observed that the prevalence of diabetes was 40.91% in the population of men with cancer between 45 and 54 years of age, 32.08% between 55 and 64 years, 47.13% between 65 and 74 years, and 42.31% in men more than 75 years old (table II).

In women cancers, the prevalence of diabetes was 15.15% between 45 and 54 years, 33.33% between 55 and 64 years, 33.33% between 65 and 74 years and 40% in women more than 75 years old (table II). The prevalence of diabetes is 38.54% in men with cancer and 24.85% in women. In the bivariate analysis, it was observed that the level of glycaemia above 126 mg/dl and the gender variable are related ($P = 0.005$).

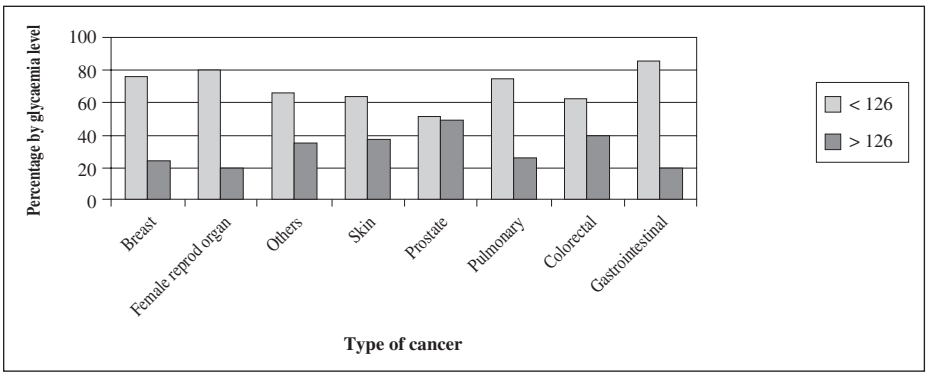

Fig. 2.—Percentage of diabetics and non-diabetics throughout the sample by type of cancer.

Table II
Prevalence of diabetes in individuals with cancer by age and gender in a Malaga hospital

	Total			*Men*			*Women*		
	Normal G n (%)	*IFG n (%)*	*DM n (%)*	*Normal G n (%)*	*IFG n (%)*	*DM n (%)*	*Normal G n (%)*	*IFG n (%)*	*DM n (%)*
0-24	2 (100)			2 (100)					
25-34	11(100)			2 (100)			9 (100)		
35-44	29 (74.36)	7 (17.95)	3 (7.69)	10 (76.92)	2 (15.38)	1 (7.69)	19 (73.08)	5 (19.23)	2 (7.69)
45-54	34 (61.82)	7 (12.73)	14 (25.45)	11 (50)	2 (9.09)	9 (40.91)	23 (69.70)	5 (15.15)	5 (15.15)
55-64	44 (47.83)	18 (19.57)	30 (32.61)	27 (50.94)	9 (16.98)	17 (32.08)	17 (43.59)	9 (23.08)	13 (33.33)
65-74	52 (40.31)	22 (17.05)	55 (42.64)	34 (39.08)	12 (13.79)	41 (47.13)	18 (42.86)	10 (23.81)	14 (33.33)
>75	16 (34.78)	11 (23.91)	19 (41.30)	9 (34.62)	6 (23.08)	11 (42.31)	7 (35)	5 (25)	8 (40)
All	188 (50.27)	65 (17.38)	121 (32.35)	95 (46.34)	31 (15.12)	79 (38.54)	93 (55.03)	34 (20.12)	42 (24.85)

Comparison with control group

45-54 years: In men cases DM: 40.91% (9/22) versus 14.5% in controls (P = 0.005). In men cases IFG: 9.09% (2/22) *versus* 15% in controls (P = 0.676). In women cases DM: 15.15% (5/33) *versus* 8% in controls (P = 0.299). In women cases IFG: 15.5% (5/33) *versus* 7.5% in controls (P = 0.246).

55-64 years: In men cases DM: 32.08% (17/53) versus 23% in controls (P = 0.241). In men cases IFG: 16.98% (9/53) *versus* 16.4% in controls (P = 0.914). In women cases DM: 33.33% (13/39) *versus* 18.6% in controls (P = 0.059). In women cases IFG: 23.08% (9/39) *versus* 5.9% in controls (P = 0.001)

65-74 years: In men cases DM: 47.13% (41/87) *versus* 25.4 % in controls (P = 0.000). In men cases IFG: 13.79% (12/87) *versus* 12.4 % in controls (P = 0.897). In women cases DM: 33.33% (14/42) *versus* 24.1% in controls (P = 0.297). In women cases IFG: 23.81% (10/42) *versus* 9.5% in controls (P = 0.019). Using as a control group the results obtained from the study in Gerona, table 1, in the general population.[23]

Between 45 and 64 years old, some types of cancers were associated with an increased risk of presenting DM with respect to the control group,[23] breast cancer in women [RR = 3.23 CI = (2.23-4.69)], prostate cancer in men [RR = 3.30 CI = (1.64 – 6.65)]. The same occurs with IFG for breast cancer in women [RR = 3.89 CI = (2.56-5.93)] and for prostate cancer in men [RR = 2.54 CI = (1.05-6.14)], (fig. 3).

In individuals between 65 and 74 years of age, were associated with an increased risk of DM, skin [RR =

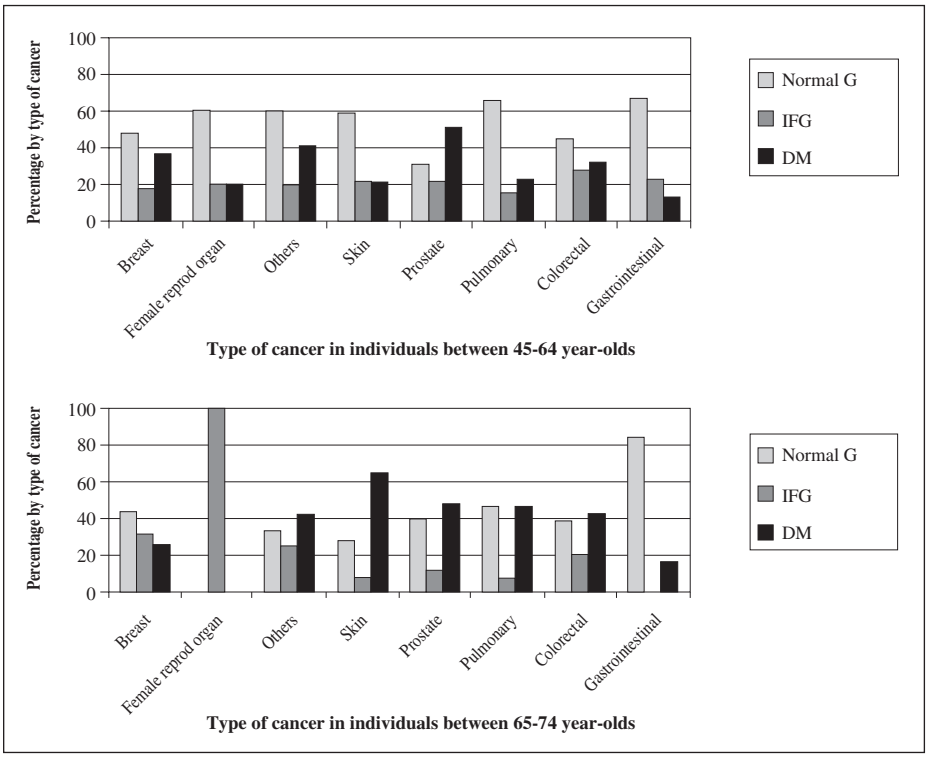

Fig. 3.—Graph of IFG-DM by type of cancer among 45-64 and 65-74 year-olds.

2.81 CI = 1.62-4.90)], lung [RR = 2.03 CI = (1.14-3.61)], colorectal [RR = 2.11 CI = (1.41-3.17)], and prostate [RR = 2.17 CI = (1.48-3.18)]. In the same age range, were associated with an increased risk of IFG with respect to the controls, colorectal [RR = 3.01 CI = (1.87-4.84)]; prostate in men [RR = 1.80 CI = (1.11-2.92)], breast cancer in women [RR = 4.31 CI = (2.39-7.75)] (fig. 3).

Discussion

Between 18 and 40 years of age there are less cancer patients, likewise T2DM is more frequent in adults so the comparison of the percentage of diabetics in our sample with the normal population focuses on ten-year age ranges from 45 years. In addition, the percentage of diabetics increases with age, which was taken into account in the different age ranges.

The highest percentage of individuals diagnosed with cancer that comprise our sample are in the range of 65 to 74 years of age, and the higher incidence of diabetes in individuals with cancer are in the same range, as this is the age range of highest risk for both diseases.

Some cancers are associated more with diabetes and IFG than others, and analyzing by age groups an increase in DM is observed in prostate cancer, in 'others', breast and colorectal in patients between 45 and 64 years old, a general increase in IFG is also noticed except in 'others', where precisely the DM is greatly increased. Between 65 and 74 years of age, there is a large percentage of DM in skin, prostate, lung and colorectal cancer, but a large increase of IFG was observed in female cancers (breast and reproductive organ). IFG indicates an alteration of the insulin activity, demonstrating greater association with the early stages or with more monitoring of the illness. Some studies have observed a difference in healthy behavior between women and men in Spain, both in preventive health care and in food hygiene. A 2006 study indicates that the percentage of women using health service doctors in Spain is greater.[24] This implies a higher registration of chronic diseases, but also more monitoring of them, in Spanish women.

Sometimes the location of a cancer is not clearly defined, and includes various tissues at a time. Some cancers are less common, constituting a smaller sample size (in "others").

It has been shown that there are cases of malnutrition in patients with advanced cancer[25]. However, our patients were not under treatment as their biochemical data were obtained at hospital admission, before treatment.

Likewise, a large proportion of patients with DM2 are obese. In obesity, there is more energy input than output. The intake of rich and excessive food associated with a sedentary lifestyle, in our current society may be increasing the risk of diabetes, and according to other studies, the risk of cancer. An increase of DM2 in children is currently being observed.[26,27] This study[27] highlights the importance of preventing the metabolic disorders associated with diabetes (higher intake - less exercise), and the need to promote physical activity from childhood, and for the ages at risk from DM2. However, a recent paper reveals that even so, there is an alarming increase of obesity and overweight on school children population in Spain.[28]

Other authors analyze the diseases that may occur more frequently in diabetics, but they require almost the entire vital period of the patient to establish them[1]. This study analyzes directly what happens in the same cancer patients with their glycaemia levels. Our study, carried out at the time of diagnosis, deals with the cause and not the effects of any particular treatment. The possible confounding effect introduced by reoccurring cancers was monitored during the collection of data gathered at the time of the first diagnosis of cancer.

A limitation of our study is to use the general population data obtained in previous studies as a control group. It is not therefore possible, from this type of analysis, to reach conclusions at the individual level based on general population, as we are comparing cancer with non-cancerous.

Spanish anthropometric studies confirm a high prevalence of overweight in general population over 45 years[29] and inclusive in a younger range of age.[30] Furthermore, this authors[30] state that the situation is worse than a few years ago. Moreover, other European studies reveal changes in body mass index of patients with cancer, showing a prevalence of overweight related to some types of cancer and age ranges.[31,32] Some authors[31] have performed a report of nutritional status of cancer patients 48 hours after the hospital admission, concluding that a prevalence of overweight is observed in population over 45 years, in both healthy subjects and those with cancer. However, in our paper Diabetes Mellitus has shown to be significantly more notorious in cancer patients than in healthy population.

The possible selection bias introduced by false negatives due to a poor intake, i.e. diabetics whose glycaemia test can give negatives during fasting, could be avoided by applying a glucose tolerance test (OGTT). This has already been suggested in some studies, noting the increased prevalence of diabetes in patients treated for prostate cancer,[33] which leads us to propose a complementary diagnosis of DM in cancer patients by OGTT.

Diabetes can be a risk factor for many diseases. Our work looks at the prevalence of DM in the cancer patient, but it would be interesting to note its presence in the entry of other illness.

In conclusion, there is an association between cancer and diabetes, which shows that Diabetes should be considered one more factor among many that affect cancer. For prospective studies, there may be the need to investigate in more detail the highest correlation with particular types of cancer.

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We confirm that neither the manuscript submitted nor any part of it has been published or is being considered for publication elsewhere.

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