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Qualification en ENDOCRINOLOGIE – DIABETOLOGIE –

MALADIES METABOLIQUES

SHOULD WE SCREEN FOR CANCER BY IMAGING IN RAPID DETERIORATION OF GLYCEMIC CONTROL IN DIABETIC PATIENTS?

A MONOCENTRIC FRENCH EXPERIENCE.

DOIT-ON DEPISTER PAR L'IMAGERIE UN CANCER CHEZ UN PATIENT DIABETIQUE EN DESEQUILIBRE HYPERGLYCEMIQUE ?

UNE EVALUATION MONOCENTRIQUE FRANÇAISE.

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Sous la direction de Mme le Dr ALLIX Ingrid

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List of abbreviations

95%IC	95% Confidence Interval
BMI	Body Mass Index
CT	Computed Tomography
HbA1c	Glycated Hemoglobin
IQR	Interquartile Range
MRI	Magnetic Resonance Imaging
NEN	Neuroendocrine Neoplasm
OR	Odds Ratio
US	Ultrasound
WHO	World Health Organization

Plan

SHOULD WE SCREEN FOR CANCER BY IMAGING IN RAPID DETERIORATION OF GLYCEMIC CONTROL IN DIABETIC PATIENTS?

A MONOCENTRIC FRENCH EXPERIENCE.

Doit-on dépister par l'imagerie un cancer chez un patient diabétique en déséquilibre hyperglycémique ?

Une évaluation monocentrique française.

ABSTRACT

Context: Epidemiological data suggest that cancer incidence is associated with diabetes mellitus itself, and that metabolic anomalies observed during diabetes may have a critical role in carcinogenesis.

Objective: Describe the occurrence of radiologically detected neoplasm in case of acute hyperglycemic disequilibrium, and describe the predictive factors.

Design: French monocentric retrospective study recruiting patients during a period of 2 years.

Setting: Angers University Hospital, Diabetology department.

Patients: Preexisting or newly diagnosed diabetic patients hospitalized for deterioration of glycemic control. Patients with active malignancy or other main reason for glycemic imbalance (organ failure, sepsis…) were not included.

Intervention: None.

Main Outcome Measure: Assess the subjective criteria leading to radiological exploration for cancer detection, describe the neoplasms found, and identify predictive factors associated with neoplasm.

Results: 683 patients were included. 183 patients (26.8%) were screened with radiological exploration. Screened population was significantly older, had insulinopenia signs (ketosis, weight loss, cardinal syndrome). HbA1c level was higher and their diabetes was more frequently newly diagnosed. Among them, 23 patients (12.6% of screened population and 3.4% of overall population) had neoplasm (7 pancreatic neoplasms, 11 abdominal and 5

thoracic). They were significantly older, had lost more weight and glycemic imbalance was more severe. Multivariate analysis confirms that ketoacidosis is associated with a significant risk to find a neoplasm, with adjusted OR of 5.705 (1.504 – 21.644), p = 0.010.

Conclusion: Uncontrolled diabetes may appear as indicative of neoplasm, not limited to pancreatic cancer. Particular attention should be paid in patients presenting with ketoacidosis. Early neoplasm detection is important and should include stratification model with bio-clinical and anamnestic criteria, and adapted imaging.

INTRODUCTION

Diabetes mellitus and cancer are frequent and heterogeneous diseases with a major impact on the quality of life and life expectancy. Understanding their mechanisms and their reciprocal influence, even minor, is therefore essential.

In 2016, the French Institute for Public Health Surveillance identified 3.3 million diabetic patients in France, regardless of the etiology (1); and the World Diabetes Report in 2014, approximately 422 million (2). They represent respectively 5% of the French population and 9% of the world population with a clear progression over the years. Similarly, French reports show that incidence of cancers have increased considerably in recent decades (3). In 2018, the total number of new cancer cases is estimated at 382,000 in France (4); and worldwide, 18.1 million cases (WHO) (5)

Experimental data suggest that metabolic anomalies observed during diabetes may have a critical role on the initiation and progression of carcinogenesis (6). Hyperglycemia modifies the expression of proliferation, migration and adhesion genes; and could contribute, by generating advanced glycation endproducts, to stimulate by their chronic activation the production of oxidative stress and inflammation. Endogenous hyperinsulinism could provide growth signals, through insulin and IGF1 receptors, and positively stimulate expansion of cancer (7). Chronic, subclinical inflammation, favored by diabetes and obesity promotes the neoplastic process with high levels of oxidative stress, along with abnormal adipokines production and activation of the pro-inflammatory pathways (6).

Epidemiologic evidence suggests that cancer incidence is associated with diabetes mellitus itself, as well as many diabetes risk factors (8–10). The diabetic population being itself heterogeneous, the metabolic or hormonal anomalies can differ according to the type of diabetes but also confounding factors such as age, sex, obesity, metabolic syndrome, or

even antidiabetic drugs. Several meta-analysis, including Vigneri *et al* in 2009 (11), confirm that diabetes is associated with a higher risk of solid (liver, pancreas, kidney, colorectal) or hematological tumor (non-Hodgkin's lymphoma), and a protective factor against prostate cancer. Noto *et al* in 2011 (12) have conducted a review and meta-analysis of the effect of diabetes mellitus on the incidence and mortality attributable to cancer at any anatomic site. The increased risk of cancer from any cause was estimated to 7 to 10% (12,13). For epidemiological reasons, most studies do not distinguish between types of diabetes. A meta-analysis by Sona *et al* in 2018 (14), bringing together nearly two million Type 1 diabetics, found nearly 32,000 cancers, with an increased risk of solid cancer (thyroid, lung, esophagus, stomach, pancreas, liver, ovary, endometrium, kidney) and lower risk of breast cancer.

The strongest association is observed for pancreatic cancer (RR: 1.73 [1.59 – 1.88]), a key organ in carbohydrate metabolism (11,12,15). The risk of undiagnosed pancreatic cancer in case of diabetes justified the suggestion of screening in case of diabetes appearing at a mature age (45-50 years), with no family history of diabetes, and normal weight patient; this association is particularly strong in the first year of diagnosis, decreases in the second year, but remains elevated thereafter (16–19). However, there is no official recommendation in France that imaging should be routinely performed in such cases.

Unlike pancreatic cancer, there is no incitation to screening for other types of cancer in absence of organ-specific sign directing imaging (20). It has been shown that early detection improves the prognosis of resectable cancer, however cancerous patients with diabetes are often treated with less aggressive cancer strategy and have higher mortality (13,21).

The main hypothesis put forward is that uncontrolled diabetes (at diagnosis or during its evolution) may appear as a symptom of any neoplasm. The suggestion for detection of

pancreatic cancer has influenced professional practices and tends to similar reasoning for detection of other types of cancer. The aim of this real-life clinical study is to assess the professional practices in our Diabetes Center for the radiological detection of cancer in patients hospitalized for rapid deterioration of glycemic control. The aims of this study are to determine the subjective criteria leading to radiological exploration, to analyze the results of imaging and then to identify predictive factors associated with neoplasm in this specific population.

MATERIALS AND METHODS

1. Study population

This study was carried out retrospectively on charts of patients hospitalized in the department of Diabetology in Angers University Hospital, France, between November 2016 and November 2018. Men and women hospitalized for discovery of diabetes mellitus or for decompensated diabetes were included. We classified hospitalization's motivation according to type of diabetes disequilibrium: discovery or pre-existence. For diabetes discovery, diagnosis was made prior to hospitalization in our center, according to the recommendations in force (22): venous fasting blood glucose > 1.26 g/l twice, or non-fasting > 2.0 g/l; and they were hospitalized because of severe hyperglycemia. For those patients, type of diabetes was not specified because sometimes uncertain at the time of admission. Others were classified with preexisting diabetes if mentioned in medical history or treated with glucose-lowering drugs. Patients not included were those with known active malignant neoplasm, with recurrent hypoglycemia, or hospitalized for an obvious main reason likely to cause hyperglycemic imbalance (diabetic foot ulcer, sepsis, organ failure…).

The retrospective data collection was registered to the *Commission Nationale de l'Informatique et des Libertés* (CNIL, n° 2018-046), according to French laws and from Ethics Committee (n° 2020/33).

2. Study measurements

We retrospectively collected data from the computerized medical record.

a. Diabetic-related features

Diabetic related characteristics were collected: severity of glycemic imbalance defined as hyperglycemia, ketosis (capillary ketonemia > 1 mmol/l) or ketoacidosis (blood pH level < 7.38), presence of cardinal syndrome (polyuria-polydipsia syndrome and asthenia) or weight loss (percentage of weight lost compared to usual weight and its duration before hospitalization), glycated hemoglobin level (HbA1c) and its kinetics compared with the most recent measure up to one year back. Type and duration of diabetes were described in case of preexisting diabetes. New Onset Diabetes associates recent discovery of diabetes and preexisting diabetes with duration of 2 years or less. The micro- or macrovascular diabetes complications were defined on one hand by retinopathy, neuropathy or nephropathy, and on the other hand by a history of cardiac or cerebrovascular event or by a distal arteriopathy (mentioned in the report). Glucose-lowering drugs were not collected except for insulin therapy.

b. Covariates

The main demographic characteristics of the patient were specified: age, sex, Body Mass Index (BMI). We recorded also medical history of neoplasm (patients were included only if cancer was considered non active or in remission) and we specified pancreatic illness (acute or chronic calcifying pancreatitis, history of surgery or benign neoplasm). Chronic alcohol misuse (declared as consuming more than 2 drinks per day, or weaned for less than 3 years), tobacco use (active or weaned for less than 3 years) and sedentary behavior (mentioned in record) were collected.

c. Radiological exploration: indication, type and results

The indication for imaging was determined by a team of the diabetologists of the department sharing the same main subjective criteria; such as New Onset Diabetes, signs of

insulinopenia (ketosis or ketoacidosis), seriousness of unexplained weight loss or asthenia, kinetics of hyperglycemia evaluated by the recent changes in HbA1c, and other clinical criteria such as age, BMI or the presence of other risk factors for cancer, or any other anamnestic, clinical or biological sign according to the decision of the practitioners.

All first imaging procedures were performed in the department of Radiology; it comprises ultrasound (US), computed-tomography scan (CT), magnetic resonance imaging (MRI). Others were performed if oriented by organ-specific clinical or biological symptom. Results were given by radiologist's report without double reading.

3. Statistical analysis

The first step consisted of comparing in the overall population those who had or not imaging in search of neoplasm. The second step consisted in splitting the screened subpopulation according to the presence or absence of neoplasm after the radiological exploration.

All quantitative variables were expressed as median with interquartile range [IQR] because variables were mainly skewed as tested with the Shapiro-Wilk test. Continuous variables were compared among groups with the Wilcoxon rank sum test. Categorical data were given as number of patients (percentage) and proportions (n>5) were compared with the Chi-squared test, otherwise Fisher exact test was applied. To explore the risk to find a neoplasm by means of radiological exploration, all the assessed variables were tested through univariate logistic regression. Significant variables were entered in the multivariable logistic regression model, adjusted with age, BMI, sex or other clinically relevant variables, in order to explain that risk. Correlations of the explanatory variables and the standardized

residuals have been checked. The analysis was two-sided and considered statistically significant at 5%. Statistical analysis was performed with SPSS v.24 (IMB corp. USA).

RESULTS

We included 683 patients with diabetes mellitus admitted in the period between 1st November 2016 and 1st November 2018. A total of 183 patients (26.8%) had imaging investigations. Among them, 23 patients (12.6%) were diagnosed with neoplasm through those explorations, representing 3.4% of the overall population.

1. Clinical characteristics of the overall population

Demographic and diabetes-related features of the overall population are presented in **Table I**. Median age was 57 years [44 – 69] from 15.5 to 95.3 years. Men represented 55.2% of patients. Median BMI was 28.6 kg/m² [23.9 – 33.6].

At admission, 26.2% of the population was hospitalized at diagnosis of diabetes, and the others for uncontrolled preexisting diabetes. These were mainly represented by Type 2 diabetes (74.2%) and a smaller proportion by Type 1 diabetes (18.1%); remaining 7.7% were mostly secondary to pancreatopathy (17 patients) or corticosteroid therapy (13 patients). Median duration of evolution was 10 years [4 – 18]. New-onset diabetes represents 39.7% of the population, bringing together 179 new diagnosis and 88 preexisting diabetes for less than 2 years. Insulin therapy concerned 39.9% of patients at admission.

Ketosis and ketoacidosis represented 11.1% and 7.0% of the overall population, respectively. The majority of patients did not meet these criteria and were considered with isolated hyperglycemia (81.8%). Subjective signs of insulinopenia like weight loss were inconstantly found in the medical records (available data in 195 patients, 28.6%). A total of 37.6% of patients declared a cardinal syndrome. The median HbA1c level was 10.7% [9.2 – 12.4]. In cases of uncontrolled diabetes, the degree of variation in HbA1c was available in 338 patients (67.1%), with a median change of 0.8% [-0.1 – 2.4]; 32.0% of patients had a

Table I. Characteristics of overall population.
Analysis of primary outcome: characteristics of patients with or without radiological screening.

Data are presented as numbers/available data (%) or median [IQR: interquartile range].
P-value is presented in bold text if significant < 0.05.

	Overall population (n = 683)	No screening (n = 500)	Imagery screening (n = 183)	p-value
Demographic characteristics				
Sex (male), n (%)	377/683 (55.2)	268/500 (53.6)	109/183 (42.4)	0.165
Age (years), median [IQR]	57 [44 – 69]	56 [40 – 67]	63 [52 – 73]	**< 0.001**
BMI (kg/m²), median [IQR]	28.6 [23.9 – 33.6]	28.5 [23.7 – 34.1]	28.7 [24.1 – 32.6]	0.716
Lifestyle				
Alcohol misuse, n (%)	85/639 (13.3)	48/459 (10.0)	37/180 (20.6)	**0.001**
Tobacco use, n (%)	203/653 (31.1)	145/474 (30.1)	58/179 (32.4)	0.656
Sedentary behavior, n (%)	406/544 (74.6)	302/405 (74.6)	104/139 (74.8)	0.953
Medical History				
Pancreatic disease, n (%)	42/683 (6.2)	26/500 (5.2)	16/183 (8.7)	0.088
Neoplasm, n (%)	59/683 (8.6)	38/500 (7.6)	21/183 (11.5)	0.110
Diabetes-related characteristics				
Reason for hospitalization				**0.006**
Diabetes diagnosed on admission, n (%)	179/683 (26.2)	117/500 (23.4)	62/183 (33.9)	
Uncontrolled diabetes, n (%)	504/683 (73.8)	383/500 (76.6)	121/183 (66.1)	
-Type of diabetes				0.079
2	374/504 (74.2)	279/383 (72.8)	95/121 (78.5)	
1	91/504 (18.1)	77/383 (20.1)	14/121 (11.6)	
Other	39/504 (7.7)	27/383 (7.0)	12/121 (9.9)	
-Duration (years), median [IQR]	10 [4 – 18]	10 [4 – 18]	8 [2.5 – 15]	0.063
≤ 2 years, n (%)	88/494 (17.8)	58/374 (15.5)	30/120 (25.0)	**0.018**
New Onset Diabetes, n (%)	267/673 (39.7)	175/491 (35.6)	92/182 (50.5)	**< 0.001**
Diabetes complications				
Microvascular, n (%)	203/683 (29.7)	145/500 (29.0)	58/183 (31.7)	0.495
Macrovascular, n (%)	156/683 (22.8)	115/500 (23.0)	41/183 (22.4)	0.870
Insulin therapy at admission, n (%)	273/683 (39.9)	235/500 (47.0)	38/183 (20.8)	**< 0.001**
Imbalance stage				**0.026**
Hyperglycemic, n (%)	559/683 (81.8)	421/500 (84.2)	138/183 (75.4)	**0.008**
Ketosis, n (%)	76/683 (11.1)	47/500 (9.4)	29/183 (15.8)	**0.018**
Ketoacidosis, n (%)	48/683 (7.0)	32/500 (6.4)	16/183 (8.7)	0.289
Cardinal syndrome, n (%)	257/683 (37.6)	147/500 (29.4)	110/183 (60.1)	**< 0.001**
Patient with weight loss, n (%)	166/195 (85.1)	83/102 (81.3)	83/93 (89.2)	0.123
% of weight loss, median [IQR]	8 [6 – 12] (n = 166)	7 [5 – 10] (n = 83)	9 [6 – 13] (n = 83)	**0.025**
duration (month), median [IQR]	2 [1 – 6]	2 [0.88 – 3]	3 [1 – 6]	**0.006**
0 – 1 month, n (%)	53/152 (34.9)	31/71 (43.7)	22/81 (27.2)	
> 1 – 6 months, n (%)	74/152 (48.7)	34/71 (47.9)	40/81 (49.4)	
> 6 months, n (%)	25/152 (16.4)	6/71 (8.5)	19/81 (23.5)	
HbA1c (%), median [IQR]	10.7 [9.2 – 12.4] (n = 677)	10.3 [9.0 – 12.1] (n = 497)	11.5 [10.2 – 12.8] (n = 180)	**< 0.001**
HbA1c variation (%), median [IQR]	0.8 [-0.1 – 2.4]	0.3 [-0.4 – 1.4]	2.7 [1.2 – 4.7]	**< 0.001**
< 1 %, n (%)	187/338 (55.3)	167/246 (67.9)	20/92 (21.7)	
1 – 1.9 %, n (%)	43/338 (12.7)	30/246 (12.2)	13/92 (14.1)	
2 – 3.9 %, n (%)	59/338 (17.5)	32/246 (13.0)	27/92 (29.3)	
≥ 4 %, n (%)	49/338 (14.5)	17/246 (6.9)	32/92 (34.8)	

≥ 2% increase and 49 patients had an increase ≥ 4% (14.5%), compared with the most recent available value.

2. Factors associated with imaging screening

Subjective analysis of each cases led to the realization of 183 explorations by imaging, which represent 26.8% of the patients. Most of them received at least an abdomino-pelvic or thoraco-abdomino-pelvic CT, 22.4% and 63.4%, respectively. The remaining 14.2% (26/183) did not have a complete abdominal-CT (abdominal US only: 22/183 (12.0%), or CT-colonography, angioMRI, biliary MRI, chest-CT alone).

Participant characteristics according to presence or absence of imaging are described in **Table I**.

Patients who underwent imaging were significantly older (median age: 63 [52 – 73] vs 56 [40 – 67] years, $p < 0.001$) and alcohol misuse was more frequent (20.6% vs 10.0%, $p = 0.001$). Other demographic characteristics, including sex and BMI, were not significantly different.

Imaging was performed more frequently in case of diabetes discovery (33.9% vs 23.4%, $p = 0.006$) or New Onset Diabetes (50.5% vs 35.6%, $p < 0.001$), rather than for uncontrolled preexisting diabetes. There was no significant difference for type, duration and complications. Severity of glycemic imbalance was significantly different ($p = 0.026$), with less isolated non-ketotic hyperglycemia (75.4% vs 84.2%, $p = 0.008$), and more with ketosis (15.8% vs 9.4%, $p = 0.018$). Ketoacidosis was not a significant criterion for radiological exploration ($p = 0.089$).

There were more patients with cardinal syndrome (60.1% vs 29.4%, $p < 0.001$) and weight loss was deeper (median: 9 [6 – 13] vs 7 [5 – 10] % of weight loss, $p = 0.025$). Median HbA1c was also higher (11.5 [10.2 – 12.8] vs 10.3 [9.0 – 12.1] %, $p < 0.001$), as was its increase (median: 2.7 [1.2 – 4.7] vs 0.3 [-0.4 – 1.4] %, $p < 0.001$).

3. Factors associated with neoplasm diagnosed by imaging

Those radiological explorations led to the diagnosis of 23 cases of neoplasms.

a. Baseline characteristics

Global characteristics are represented in **Table II**, and individual characteristics are detailed in **Table III**. Men represent 60.9% of patients.

Nineteen patients received thoraco-abdomino-pelvic CT. The 4 remaining patients had abdomino-pelvic CT (2 patients), CT-colonography (oriented by iron deficiency anemia) or renal angioMRI (oriented by chronic renal failure and pulmonary edema). Other explorations have been led consecutively to screening results or organ-specific sign. The most represented neoplastic site was the pancreas with 7 patients affected: 4 adenocarcinomas and 3 neuroendocrine neoplasms (NEN), one of each already metastatic to the liver. There were 11 cases of non-pancreatic abdominal neoplasm (liver, kidney, prostate, lower digestive guts, adrenal gland, uterus), and 5 thoracic neoplasms represented by 4 pulmonary cancers (including one NEN) and one esophageal NEN; totalizing 5 neuroendocrine neoplasms.

Nine of all patients were immediately metastatic (39.1%) at diagnosis.

b. Comparisons between patients with or without neoplasm

Patients with neoplasm were significantly older (median: 72 [58 – 80] vs 62 [51 – 71.3] years, p = 0.021). They declared weight loss more frequently (90.9% vs 89.0%, p = 0.009) and had a lower BMI (median: 26.3 [23.5 – 28.4], vs 29.2 [24.3 – 32.8] kg/m², p = 0.041). Most of assessed diabetes characteristics were not significantly different between the subpopulations, such as reason for hospitalization, type and duration of diabetes, cardinal syndrome, HbA1c and HbA1c increase. Four neoplastic patients (17.4%) were admitted for

the recent diagnosis of diabetes mellitus; the other for uncontrolled pre-existing diabetes, with 15 Type 2 (65.2%).

The severity of disequilibrium was significantly different (p = 0.032) with more ketoacidosis (21.7% vs 6.9%, p = 0.018), and less isolated non-ketotic hyperglycemia (56.5% vs 78.1%, p = 0.024).

Table II. Analysis of screened population: characteristics of patients with or without neoplasm.

Data are presented as numbers/available data (%) or median [IQR: interquartile range]. P-value is presented in bold text if significant < 0.05.

	No diagnosis (n = 160)	**Neoplasm diagnosis (n = 23)**	**p-value**
Demographic characteristics			
Sex (male), n (%)	95/160 (59.4)	14/23 (60.9)	0.891
Age (years), median [IQR]	62 [51 – 71.3]	72 [58 – 80]	**0.021**
BMI (kg/m²), median [IQR]	29.2 [24.3 – 32.8]	26.3 [23.5 – 28.4]	**0.041**
Lifestyle			
Alcohol misuse, n (%)	31/157 (19.7)	6/23 (26.0)	0.482
Tobacco use, n (%)	54/156 (34.6)	4/23 (17.4)	0.151
Sedentary behavior, n (%)	91/123 (74.0)	13/16 (81.3)	0.761
Medical History			
Pancreatic disease, n (%)	14/160 (8.8)	2/23 (8.7)	0.999
Neoplasm, n (%)	19/160 (11.9)	2/23 (8.7)	0.999
Diabetes-related characteristics			
Reason for hospitalization			0.099
Diabetes diagnosed on admission, n (%)	58/160 (36.3)	4/23 (17.4)	
Uncontrolled diabetes, n (%)	102/160 (63.8)	19/23 (82.6)	
-Type of diabetes			0.673
2	80/102 (78.4)	15/19 (78.9)	
1	11/102 (10.8)	3/19 (15.8)	
Other	11/102 (10.8)	1/19 (5.3)	
-Duration (years), median [IQR]	7 [2 – 15]	10 [5.5 – 15]	0.374
≤ 2 years, n (%)	26/101 (25.7)	4/19 (21.1)	0.664
New Onset Diabetes, n (%)	84/159 (52.8)	8/23 (34.8)	0.105
Diabetes complications			
Microvascular, n (%)	48/160 (30.0)	10/23 (43.5)	0.194
Macrovascular, n (%)	34/160 (21.3)	7/23 (30.4)	0.323
Insulin therapy at admission, n (%)	33/160 (20.6)	5/23 (21.7)	0.902
Imbalance stage			**0.032**
Hyperglycemic, n (%)	125/160 (78.1)	13/23 (56.5)	**0.024**
Ketosis, n (%)	24/160 (15.0)	5/23 (21.7)	0.408
Ketoacidosis, n (%)	11/160 (6.9)	5/23 (21.7)	**0.018**
Cardinal syndrome, n (%)	99/160 (61.8)	11/23 (47.8)	0.506
Patient with weight loss, n (%)	73/82 (89.0)	10/11 (90.9)	**0.010**
% of weight loss, median [IQR]	9 [6 – 13] (n = 73)	9.5 [6.3 – 13.8] (n = 10)	0.528
duration (month), median [IQR]	2 [1 – 6]	6 [1.6 – 6]	0.782
0 – 1 month, n (%)	20/71 (28.2)	2/10 (20.0)	
> 1 – 6 months, n (%)	34/71 (47.9)	6/10 (60.0)	
> 6 months, n (%)	17/71 (23.9)	2/10 (20.0)	
HbA1c (%), median [IQR]	11.6 [10.4 – 12.8] (n = 157)	10.4 [9.3 – 12.6]	0.164
HbA1c variation (%), median [IQR]	2.8 [1.2 – 4.7]	2.1 [1.3 – 4.7]	0.846
< 1 %, n (%)	18/84 (21.4)	2/8 (25.0)	
1 – 1.9 %, n (%)	12/84 (14.3)	1/8 (12.5)	
2 – 3.9 %, n (%)	25/84 (29.8)	2/8 (25.0)	
≥ 4 %, n (%)	29/84 (34.5)	3/8 (37.5)	

Table III. Neoplasms characteristics.

Sex	Age (years)	BMI (kg/m²)	Diabetes at admission	Type	Severity of imbalance	HbA1c (%)	Imagery	Site	Extension
Female	57	26,7	Uncontrolled	2	Hyperglycemic	13,7	TAP-ct	Pancreas, neuroendocrine	Localized
Male	65	33,4	Uncontrolled	2	Ketoacidosis	12	TAP-ct	Pancreas, neuroendocrine	Localized
Male	49	20,2	Uncontrolled	1	Ketoacidosis	11,9	CTAP-ct, ORL endoscopy, OGDs	Liver	Undetermined
Male	82	29,4	Diagnosed	/	Hyperglycemic	13,1	TAP-ct	Pancreas	Localized
Male	81	21,6	Uncontrolled	2	Hyperglycemic	9,5	CTAP-ct	Colon	Metastatic
Female	80	28,7	Uncontrolled	2	Hyperglycemic	11,4	Renal angioMRI	Kidney	Localized
Female	74	36,5	Uncontrolled	2	Hyperglycemic	9,4	TAP-ct	Pancreas	Localized
Male	72	39,1	Uncontrolled	2	Ketosis	14,2	TAP-ct	Pancreas	Locally advanced
Female	56	24,4	Diagnosed	/	Hyperglycemic	6,5	CTAP-ct	Lung, neuroendocrine	Localized
Male	63	26,3	Uncontrolled	2	Hyperglycemic	9,4	TAP-ct	Esophagus, neuroendocrine	Metastatic (lymph nodes)
Female	83	27,9	Uncontrolled	2	Hyperglycemic	10,2	CTAP-ct	Adrenal gland	Localized
Male	48	20,7	Uncontrolled	1	Ketosis	13,2	AP-ct, Echo-endoscopy	Pancreas, neuroendocrine	Metastatic (liver)
Male	52	23,1	Uncontrolled	PC	Hyperglycemic	8,5	TAP-ct, biliary MRI	Liver	Localized
Female	89	24,7	Uncontrolled	2	Hyperglycemic	8,7	ct- colonography	Caecum	Metastatic
Male	75	23,2	Uncontrolled	2	Ketosis	8,7	CTAP-ct	Lung	Metastatic
Male	55	28,1	Uncontrolled	2	Ketosis	9,2	Abdominal US, TAP-ct	Bones, liver, peritoneum, skin: undetermined primary site	Metastatic
Female	80	24,6	Uncontrolled	2	Hyperglycemic	12,6	TAP-ct	Lung	Locally advanced
Male	63	23,7	Diagnosed	/	Ketoacidosis	12,8	TAP-ct, Head-ct	Lung	Metastatic (brain)
Female	59	25,7	Uncontrolled	1	Ketoacidosis	7,4	AP-ct	Uterus	Undetermined
Male	73	28,6	Uncontrolled	2	Ketosis	12,6	TAP-ct, prostatic MRI	Prostate	Metastatic (bones)
Male	77	27,4	Uncontrolled	2	Hyperglycemic	12,6	TAP-ct	Kidney	Localized
Female	62	18,4	Uncontrolled	2	Hyperglycemic	9,4	Abdominal US, TAP-ct	Pancreas	Metastatic (liver)
Male	85	26,4	Diagnosed	/	Ketoacidosis	10,4	Abdominal US, TAP-ct	Colon	Metastatic

Abbreviations:

- CTAP-ct: Cerebro-thoraco-abdomino-pelvic computed tomography
- TAP-ct: Thoraco-abdomino-pelvic computed tomography
- AP-ct: Abdomino-pelvic computed tomography
- OGDs: oesogastroduodenoscopy
- US: ultrasound
- PC: pancreatopathy

c. Univariate and multivariate analysis

Univariate models were conducted, and described in **Table IV**. Among demographic characteristics, age was the only predictor of neoplasm diagnosis, with a 95% CI of 1.040 [1.006 – 1.075], p = 0.020. Regarding diabetes related characteristics: reason for hospitalization, type and duration of diabetes were not significantly associated with the risk of neoplasm diagnosis. Nor were the existence of signs of insulinopenia and HbA1c level and HbA1c increase. However, the severity of the disequilibrium was significant, with, on one hand, isolated hyperglycemia associated with absence of neoplasm (95% CI: 0.364 [0.147 – 0.900]) and, on the other hand, ketoacidosis as a risk factor (95% CI: 3.763 [1.174 – 12.060]). Thus, univariate analysis confirms that age, hyperglycemia and ketoacidosis confer a risk, contrarily to lower BMI and weight loss.

Multivariate logistic regression was performed in order to explain the risk to find a neoplasm, and is presented in **Table IV**. OR were adjusted for potential confounders with the main demographic data: age, sex, BMI. Thus, non-ketotic hyperglycemia confers an adjusted OR of 0.330 (0.125 – 0.870) and ketosis does not confer a significant risk. Moreover, correlations between ketoacidosis and uncontrolled preexisting diabetes – although not associated with increased risk – have been investigated, because it's a main criterion guiding diabetes care. These variables are not correlated with each other, and are therefore accepted together in the multivariate model. This gives ketoacidosis in a known diabetic patient an increased risk to find a neoplasm, with an adjusted OR of 5.705 (1.504 – 21.644), while the risk conferred by age is attenuated (p = 0.070).

Table IV. Risk of neoplasm detection in screened patients, assessed using univariate and multivariate logistic regression adjusted on variables of interest.

Data are presented as numbers/available data (%) or median [IQR: interquartile range].

P-value and OR are presented in bold text if significant.

Variables	Univariate model		Multivariate models					
			Hyperglycemic imbalance		Ketosis imbalance		Ketoacidosis imbalance	
	OR (95% IC)	p-value	OR (95% IC)	p-value	OR (95% IC)	p-value	OR (95% IC)	p-value
Sex (male)	0.940 (0.384 – 2.299)	0.891	1.073 (0.401 – 2.866)	0.889	0.937 (0.358 – 2.447)	0.894	0.991 (0.378 – 2.600)	0.985
Age (years)	**1.040 (1.006 – 1.075)**	**0.020**	**1.039 (1.004 – 1.076)**	**0.029**	**1.039 (1.004 – 1.074)**	**0.028**	1.034 (0.997 – 1.073)	0.070
BMI (kg/m²)	0.930 (0.865 – 1.001)	0.053	0.935 (0.864 – 1.012)	0.097	0.936 (0.865 – 1.013)	0.102	0.927 (0.854 – 1.007)	0.071
Lifestyle								
- Alcohol misuse	1.435 (0.522 – 3.940)	0.484	-	-	-	-	-	-
- Tobacco use	0.398 (0.129 – 1.228)	0.109	-	-	-	-	-	-
- Sedentary behavior	1.524 (0.408 – 5.695)	0.531	-	-	-	-	-	-
Medical History								
- Of pancreatic disease	1.224 (0.529 – 2.832)	0.636	-	-	-	-	-	-
- Of neoplasm	0.959 (0.696 – 1.321)	0.796	-	-	-	-	-	-
Type of Diabetes (Type 2 vs Type 1)	0.688 (0.171 – 2.762)	0.597	-	-	-	-	-	-
Diabetes duration (years)	1.019 (0.978 – 1.062)	0.361	-	-	-	-	-	-
Reason for hospitalization (Uncontrolled diabetes vs Diabetes discovery)	2.701 (0.877 – 8.323)	0.084	-	-	-	-	2.989 (0.876 – 10.197)	0.080
Imbalance mode								
- Hyperglycemic	**0.364 (0.147 – 0.900)**	**0.029**	**0.330 (0.125 – 0.870)**	**0.025**	-	-	-	-
- Ketosis	1.574 (0.534 – 4.643)	0.411	-	-	1.648 (0.525 – 5.172)	0.392	-	-
- Ketoacidosis	**3.763 (1.174 – 12.060)**	**0.018**	-	-	-	-	**5.705 (1.504 – 21.644)**	**0.010**
Cardinal syndrome	0.565 (0.235 – 1.359)	0.202	-	-	-	-	-	-
Weight loss (% of usual weight)	1.007 (0.920 – 1.102)	0.883	-	-	-	-	-	-
Weight loss duration (month)	0.999 (0.928 – 1.075)	0.971	-	-	-	-	-	-
HbA1c (%)	0.830 (0.674 – 1.023)	0.080	-	-	-	-	-	-
HbA1c variation (%)	0.986 (0.750 – 1.297)	0.921	-	-	-	-	-	-

d. Comparisons between patients with pancreatic or non-pancreatic neoplasm

Within the neoplastic subpopulation, we compared in **Table V** the characteristics of pancreatic and non-pancreatic neoplasms. It appeared that HbA1c level was significantly higher for those with pancreatic neoplasm (median: 13.1 [10.7 – 13.5] vs 9.9 [8.7 – 12.1] %, p = 0.030). Other criteria were not different.

Table V. Comparison between patient with or without pancreatic neoplasm.
Data are presented as numbers/available data (%) or median [IQR: interquartile range]. P-value is presented in bold text if significant < 0.05.

	Pancreatic neoplasm (n = 7)	**Other neoplasm (n = 16)**	**p-value**
Demographic characteristics			
Sex (male), n (%)	4/7 (57.1)	10/16 (62.5)	0.999
Age (years), median [IQR]	65 [59.5 – 73]	74 [68.3 – 80.3]	0.442
BMI (kg/m²), median [IQR]	29.4 [23.7 – 35.0]	25.2 [23.6 – 27.5]	0.198
Lifestyle			
Alcohol misuse, n (%)	1/7 (14.3)	5/16 (31.3)	0.621
Tobacco use, n (%)	1/7 (14.3)	3/16 (18.8)	0.999
Sedentary behavior, n (%)	4/6 (66.7)	9/10 (90.0)	0.518
Medical History			
Pancreatic disease, n (%)	0/7	2/16 (12.5)	0.999
Neoplasm, n (%)	0/7	2/16 (12.5)	0.999
Diabetes-related characteristics			
Reason for hospitalization			0.999
Diabetes diagnosed on admission, n (%)	1/7 (14.3)	3/16 (18.8)	
Uncontrolled diabetes, n (%)	6/7 (85.7)	13/16 (81.3)	
-Type of diabetes			0.999
2	5/6 (83.3)	10/13 (76.9)	
1	1/6 (16.7)	2/13 (15.4)	
Other	0/6	1/13 (7.7)	
-Duration (years), median [IQR]	6 [5.3 – 7.5]	15 [10 – 19]	0.086
≤ 2 years, n (%)	2/6 (33.3)	3/13 (23.1)	0.999
New Onset Diabetes	2/7 (28.6)	6/16 (37.5)	0.679
Diabetes complications			
Microvascular, n (%)	2/7 (28.6)	8/16 (50.0)	0.405
Macrovascular, n (%)	0/7	7/16 (43.8)	0.057
Insulin therapy at admission, n (%)	0/7	5/16 (31.3)	0.272
Imbalance stage			0.999
Hyperglycemic, n (%)	4/7 (57.1)	9/16 (56.3)	0.968
Ketosis, n (%)	2/7 (28.6)	3/16 (18.8)	0.599
Ketoacidosis, n (%)	1/7 (14.3)	4/16 (25.0)	0.656
Cardinal syndrome, n (%)	4/7 (57.1)	7/16 (43.8)	0.667
Individuals with weight loss, n (%)	6/6	4/5 (80.0)	0.455
% of decrease, median [IQR]	9.5 [6.8 – 13]	10 [6.8 – 14]	0.914
duration (month), median [IQR]	6 [1.5 – 6.5] (n = 7)	4 [1.6 – 6]	0.628
0 – 1 month, n (%)	1/7 (14.3)	1/4 (25.0)	
> 1 – 6 months, n (%)	4/7 (57.1)	3/4 (75.0)	
> 6 months, n (%)	2/7 (28.6)	0/4	
HbA1c (%), median [IQR]	13.1 [10.7 – 13.5]	9.9 [8.7 – 12.1]	**0.030**
HbA1c variation (%), median [IQR]	2.1 [2 – 4] (n = 5)	0.8 [0.4 – 3.8] (n = 3)	0.393
< 1 %, n (%)	0/5	2/3 (66.7)	
1 – 1.9 %, n (%)	1/5 (20.0)	0/3	
2 – 3.9 %, n (%)	2/5 (40.0)	0/3	
≥ 4 %, n (%)	2/5 (40.0)	1/3 (33.3)	

DISCUSSION AND CONCLUSION

This real-life study is the first dedicated to evaluate, through observation of local clinical practices, if rapid deterioration of glycemic control may appear indicative of neoplasm among patients hospitalized either for discovery of diabetes, or for uncontrolled known diabetes. It was elaborated with two main outcomes: 1/ assess the subjective criteria leading to radiological exploration, 2/ identify predictive factors associated with neoplasm in this specific population.

Uncontrolled diabetes as a revealing cause of cancer, although present in the diabetologist minds, has never been supported by a clinical study. This hypothesis was led by two proven facts: diabetes increases the risk of many cancer (11,12,14), and some patients should be screened for pancreatic cancer (19); and by the description of pathophysiological mechanisms (6,7).

First of all, our results confirm part of the untold criteria for carrying out radiological investigations. Through 2 years of data collection and different diabetologists in the same department, results remain consistent. It corresponds with New Onset Diabetes, risk factors of cancer (older patients, alcohol misuse), signs of insulinopenia (ketosis, cardinal syndrome, higher HbA1c and rapid deterioration of glycemic control), or both (larger and longer weight loss). Unexpectedly, ketoacidosis does not appear as a leading criterion; p-value could have been drawn toward non significance because ketoacidosis was more frequent among Type 1 and these patients were less likely to have an exploration from this criterion. Indeed, ketoacidosis is classically associated with uncontrolled Type 1 diabetes mellitus because of poor insulin management or insulinopenia; thus, radiological explorations are rarely conducted. It has been increasingly recognized that it may also occur in Type 2 diabetes

mellitus (23). We cannot compare our population to this study because patients with potential precipitating factors (organ failure, sepsis…) were not included.

Early cancer detection among diabetic patients needs further explorations. Indeed, prevalence and incidence of diabetes are too high and increasing, so that screening all diabetic patients is not cost-effective.

Some studies limit screening to pancreatic cancer among diabetics. While a lot suggests that New Onset Diabetes aged over 50 require routinely pancreatic imaging (24), others tend to develop less irradiating and less expensive methods, studying several potential biomarkers, like Plasma Free Amino Acid profile. Further large prospective study is ongoing in USA (NOD Study) (25). The aims of NOD Study (cohort of 10,000 subjects aged over 50 with New Onset Diabetes) are to estimate the 3 years probability to develop a pancreatic adenocarcinoma, to determine biomarkers for its identification, and then to define screening algorithms.

Sharma *et al* in 2018 (16) described a model to determine pancreatic cancer risk among patients within 3 years New Onset Diabetes (END-PAC model). The overall population is estimated with 1% risk of pancreatic cancer, enhanced or decreased according to 3 supplemental factors: change in weight, change in blood glucose and age at onset of diabetes. Risk increased to 3.6% in high-risk group, requiring explorations and close follow-up; intermediate stratification might need complementary analysis like biomarkers under study. While this study seems promising, false positive appeared in case of steroid use or different malignancy, highlighting the need for overall cancer screening.

It echoes with searching for multi-analyte blood test. CancerSEEK (26) is designed for detection of early stage of eight cancers, common in western populations (ovary, liver, pancreas, colorectum, lung, breast, esophagus, stomach), combining assays for genetic

alterations and protein biomarkers. Further prospective studies are required to establish the clinical utility.

Secondly, among screened patients, those with neoplasms were older, and they declared weight loss most frequently, which is consistent with lower BMI – although still classified in overweight category. We found that ketoacidosis was more frequent. Univariate analysis confirmed that age, isolated hyperglycemia and ketoacidosis confer a significant risk (decreased or increased), unlike BMI and weight loss. Multivariate model showed that adjusted with potential confounders (age, BMI and sex), age impact on neoplastic risk is attenuated. Very interestingly, ketoacidosis, which have not led to carry out radiological explorations, confers on its own a significant adjusted OR of 5.705 in preexisting diabetes.

Ketoacidosis is a marker of insulin deficiency and a potentially lethal complication of diabetes mellitus. It is known to occur in patients with Type 1 but there is now increasing recognition of its occurrence in type 2 or newly diagnosed diabetes (27). In Type 2 diabetes, ketoacidosis is often associated with conditions of extreme stress (infection, intercurrent illness) or poor compliance to therapy. But precipitant factor is not always found, and psychological stress is then considered. Pathophysiological hypothesis link ketoacidosis with Type 2 diabetes mainly through insulinopenia (others include elevation of counter regulatory stress hormones and increase of free fatty acids) (23).

Ketoacidosis is rarely an initial presenting symptom of neoplasm. It has been described in rare endocrine tumors (pancreatic: glucagon-secreting islet cell neoplasm (28), somatostatinoma (29); non pancreatic: acromegaly (30), pheochromocytoma (31), adrenocortical adenoma (32)). Only a few case-reports documented it in pancreatic adenocarcinomas (33–36). Then, diabetes could be newly diagnosed; ancient and neglected;

or ancient with recent change in diabetes pattern. No case-report or clinical study had described other neoplasm and occurrence of ketoacidosis.

In our study, none of the patient with pancreatic adenocarcinomas had ketoacidosis, but it was the case with 5 other patients. Two of them were Type 1 diabetes and were diagnosed with liver and uterine neoplasm, but their extension was undetermined upon hospitalization and need further follow-up. For them, ketoacidosis might be linked with Type 1 rather than neoplasm. One was found with a localized pancreatic NEN currently under surveillance. His diabetes was preexisting and ancient. The last two had ketoacidosis as a presenting symptom of both metastatic lung or colon cancer, and of newly diagnosed diabetes. According to data collection, there was no other precipitating factor.

To our knowledge, they are the first cases to be documented. Further studies are needed to understand the relation between ketoacidosis and neoplasm. Thus, these results may suggest changes in our professional practices, with paying special attention to neoplastic risk of diabetic patients admitted for ketoacidosis.

Reference imaging is different according to the type of cancer (US for endometrial, renal and gallbladder cancer; mammography for breast cancer; CT-colonoscopy for colon cancer; endoscopic US for pancreatic and esophageal cancer; US, CT or MRI for hepatocellular cancer). None of these specific procedures – although improved by technical advances – is suited for overall cancer screening. Plus, associated factors like obesity or impaired renal function might challenge radiologists and result in suboptimal examination (20). The choice of screening method must be considered with cost-effectiveness balance and be as complete and large as possible.

Moreover, cancer screening rate is significantly lower in people with diabetes than in people without diabetes (37,38). All diabetic patients should undergo recommended age- and sex-appropriate cancer screenings to promote primary prevention and early detection.

In our study, all type of imaging was identified. The screening method frequently comprised abdominal imaging (abdomino-pelvic CT), but we showed several thoracic neoplasms (esophageal and pulmonary) that were not looked for in those who did not have chest imaging. Therefore, we think that thoraco-abdomino-pelvic CT should be the preferred screening imaging. Other investigations should be performed if clinical, biological or anamnestic signs point to a specific organ.

There were some methodological strengths and weakness to this study.

The strength of this study was the number of participants with a total of 683 patients. The large number of patients allowed us to obtain interesting significant results in light of the current literature. However, due to the retrospective design, some data of interest were unavailable from some medical records, such as weight loss and the kinetics of HbA1c, not allowing these parameters to be forced in the multivariate model. In addition, HbA1c might not be an optimal criterion to assess long-term glycemic control. Other like glycemic variability, through SD-HbA1c (intrapersonal mean and standard deviation of all recorded glycemic control measurements), may increase risk of cancer (39). Saito *et al* followed 2640 patients; cancer occurred in 12.5% of patients with a median follow-up of 4.1 years. Glycemic variability was significantly associated with malignancy, while mean HbA1c and diabetes duration were not. In our study, variability was not collected and HbA1c kinetic was incomplete.

Data about anti-diabetic drugs were not collected although it has been proven that it could confer an increased risk (insulin, insulin-secretagogues) or a protection (metformin)

against cancer (13,40–43). This study was not intended to assess their impact, but these treatments are potential confounding factors here.

It is a monocentric study, collecting patient data over 2 years. A larger population could have highlighted other criteria described in the literature. In particular, New Onset Diabetes corresponds to a period favorable to the diagnosis of cancer, which is not the case for our screened population even in patients with pancreatic neoplasm.

Our concern about cancer screening for diabetic patients may have led to a bias in modifying practices, through the prescription of more CT-scans, and particularly thoraco-abdomino-pelvic CT. Moreover, the accessibility of imaging (especially CT-scans) has improved in recent years.

Our findings suggest that cancer screening should not be limited to pancreas, and require specific attention in case of ketoacidosis. Other evaluations could result from our study, focusing in particular on the fate of the overall population and the occurrence of neoplasm in those who were not screened and those for whom imaging did not reveal neoplasm.

Thus, associating a stratification model based on bio-clinical and anamnestic criteria, with cancer-specific biomarkers, and adapted, large and complete imaging may be the key to allow an earlier detection and a better prognosis in a growing diabetic population.

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VAILLANT Charly

Doit-on dépister par l'imagerie un cancer chez un patient diabétique en déséquilibre hyperglycémique ? Une évaluation monocentrique française.

RÉSUMÉ

Contexte : Les données épidémiologiques suggèrent que l'incidence du cancer est associée au diabète et que les anomalies métaboliques observées au cours du diabète pourraient avoir un rôle critique sur la carcinogenèse.
But de l'étude : Décrire les modalités de dépistage radiologique de néoplasie en cas de déséquilibre hyperglycémique aigu et en décrire les facteurs prédictifs.
Protocole : Etude rétrospective monocentrique française recrutant des patients sur 2 ans.
Lieu de l'étude : Service de Diabétologie, Centre Hospitalier Universitaire d'Angers, France.
Malades : Diabétiques connus ou nouvellement diagnostiqués hospitalisés pour déséquilibre hyperglycémique. Les patients présentant une néoplasie maligne active ou une autre cause principale de déséquilibre glycémique (insuffisance d'organe, sepsis…) n'ont pas été inclus.
Intervention : Aucune.
Critère de jugement principal : Évaluer les critères subjectifs menant à l'exploration radiologique pour la détection du cancer, décrire les néoplasies retrouvées et identifier les facteurs prédictifs associés.
Résultats : 683 patients ont été inclus. 183 patients (26.8%) ont bénéficié d'une exploration radiologique. La population dépistée était significativement plus âgée, présentait des signes d'insulinopénie (déséquilibre cétosique, perte de poids, syndrome cardinal). Le taux d'HbA1c était plus élevé et leur diabète était plus souvent de découverte récente. Parmi eux, 23 patients (12.6% des patients dépistés et 3.4% de la population totale) présentaient une néoplasie (7 néoplasies pancréatiques, 11 abdominales et 5 thoraciques). Ces patients étaient significativement plus âgés, avaient perdus plus de poids et présentaient un diabète plus déséquilibré. L'analyse multivariée confirme que l'acidocétose est associée à un risque significatif de retrouver une néoplasie, avec un OR ajusté de 5.705 (1.504 – 21.644), p = 0.010.
Conclusion : Un déséquilibre de diabète pourrait apparaître comme un signe évocateur d'un cancer, d'origine pancréatique ou autre. Une attention particulière doit leur être portée en cas d'acidocétose. Le dépistage précoce de ces néoplasies est important et devrait inclure un modèle de stratification avec des critères bio-cliniques et anamnestiques, et une imagerie adaptée.

Mots-clés : Diabète, Cancer, Dépistage, Acidocétose, Tomodensitométrie

Should we screen for cancer by imaging in rapid deterioration of glycemic control in diabetic patients? A monocentric French experience.

ABSTRACT

Context: Epidemiological data suggest that cancer incidence is associated with diabetes mellitus itself, and that metabolic anomalies observed during diabetes may have a critical role in carcinogenesis.
Objective: Describe the occurrence of radiologically detected neoplasm in case of acute hyperglycemic disequilibrium, and describe the predictive factors.
Design: French monocentric retrospective study recruiting patients during a period of 2 years.
Setting: Angers University Hospital, Diabetology department.
Patients: Preexisting or newly diagnosed diabetic patients hospitalized for deterioration of glycemic control. Patients with active malignancy or other main reason for glycemic imbalance (organ failure, sepsis…) were not included.
Intervention: None.
Main Outcome Measure: Assess the subjective criteria leading to radiological exploration for cancer detection, describe the neoplasms found, and identify predictive factors associated with neoplasm.
Results: 683 patients were included. 183 patients (26.8%) were screened with radiological exploration. Screened population was significantly older, had insulinopenia signs (ketosis, weight loss, cardinal syndrome). HbA1c level was higher and their diabetes was more frequently newly diagnosed. Among them, 23 patients (12.6% of screened population and 3.4% of overall population) had neoplasm (7 pancreatic neoplasms, 11 abdominal and 5 thoracic). They were significantly older, had lost more weight and had a more decompensated diabetes. Multivariate analysis confirms that ketoacidosis is associated with a significant risk to find a neoplasm, with adjusted OR of 5.705 (1.504 – 21.644), p = 0.010.
Conclusion: Uncontrolled diabetes may appear as indicative of neoplasm, not limited to pancreatic cancer. Particular attention should be paid in patients presenting with ketoacidosis. Early neoplasm detection is important and should include stratification model with bio-clinical and anamnestic criteria, and adapted imaging.

Keywords: Diabetes Mellitus, Neoplasm, Screening, Ketoacidosis, Computed Tomography

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