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Adenocarcinoma and dysplasia in barrett`s esophagus: critical analysis of risk factors and of surveillance protocols

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ADENOCARCINOMA AND DYSPLASIA IN BARRETT`S ESOPHAGUS: CRITICAL ANALYSIS OF RISK FACTORS AND OF SURVEILLANCE PROTOCOLS

Adenocarcinoma e displasia no esôfago de Barrett: análise crítica dos fatores de risco e dos protocolos de vigilância

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ABSTRACT:

BACKGROUND: Identification of epidemiological risk factors in Barrett's esophagus resulting in dysplasia and adenocarcinoma and its impact on prevention and early detection.

AIMS: To evaluate epidemiological risk factors involved in the development of dysplasia and adenocarcinoma from Barrett's esophagus in a specific population. To critically analyze the surveillance period, aiming to individualize follow-up time according to identified risks.

METHODS: A retrospective case-control study in a tertiary center with patients diagnosed and followed up for Barrett's esophagus. Patients with Barrett's esophagus who developed adenocarcinoma and/or dysplasia were compared to those who did not, considering variables such as sex, age, smoking status, Body mass index, ethnicity, and Barrett's extension. Logistic regression was performed to measure the odds ratio between risk factors for the outcome of adenocarcinoma and of dysplasia. The presence of epidemiological risk factors in this population was correlated with the time to develop adenocarcinoma from metaplasia.

RESULTS: There was a statistically significant difference between the variables smoking status, race, sex, Barrett's esophagus extension, and age in the group with adenocarcinoma compared to the group without adenocarcinoma; smokers and former smokers had a 4.309 times higher risk of developing adenocarcinoma; the extension of Barrett's esophagus increased the risk by 1.193 times for each centimeter. In dysplasia group, the variables smoking status, Barrett's extension, and age were statistically significant; the extension of Barrett's esophagus increased the risk of dysplasia by 1.128 times for each centimeter, and age increased the risk by 1.023 times for each year. Patients without risk factors did not develop adenocarcinoma within 12 months, even with prior dysplasia.

CONCLUSIONS: The study confirmed a higher risk of developing dysplasia and adenocarcinoma in specific epidemiological groups, allowing for more cost-effective monitorization in patients with Barrett's esophagus.

Keywords: Barrett’s esophagus. Gastroesophageal reflux diseases. Adenocarcinoma. Epidemiology.

RESUMO

RACIONAL: Identificação de fatores de risco epidemiológicos no esôfago de Barrett resultando em displasia e adenocarcinoma e seu impacto na prevenção e detecção precoce.

OBJETIVOS: Avaliar fatores de risco epidemiológicos envolvidos no desenvolvimento de displasia e adenocarcinoma a partir do Barrett em população específica. Realizar análise crítica do período de vigilância, objetivando individualizar o tempo de seguimento conforme riscos identificados.

MÉTODOS: Estudo caso-controle retrospectivo em centro terciário com pacientes com esôfago de Barrett diagnosticados e seguidos neste centro. Pacientes com Barrett que apresentaram adenocarcinoma e/ou displasia foram comparados aos que não apresentaram, levando em consideração as variáveis sexo, idade, tabagismo, IMC, etnia e extensão do Barrett. Posteriormente, foi realizada regressão logística para mensuração da razão de chances entre fatores de risco para o desfecho adenocarcinoma e desfecho displasia. Foi correlacionada a presença de fatores epidemiológicos de risco nessa população com o tempo de desenvolvimento de adenocarcinoma a partir da metaplasia.

RESULTADOS: Houve diferença estatisticamente significante entre as variáveis tabagismo, raça, sexo, extensão do Barrett e idade no grupo com adenocarcinoma em relação ao sem adenocarcinoma; tabagistas e ex-tabagistas apresentaram risco 4,309 vezes maior de desenvolver adenocarcinoma; a extensão do Barrett aumentou o risco em 1,193 vezes a cada centímetro. No grupo com displasia, as variáveis tabagismo, extensão do Barrett e idade se mostraram significantes estatisticamente; extensão do Barrett aumentou 1,128 vezes a cada centímetro o risco de displasia e idade aumentou 1,023 a cada ano o risco desse desfecho. Pacientes sem fatores de risco não desenvolveram adenocarcinoma em menos de 12 meses, mesmo com displasia anteriormente.

CONCLUSÕES: O estudo confirmou maior risco de desenvolver displasia e adenocarcinoma em grupos epidemiológicos específicos, podendo direcionar o seguimento em pacientes com Esôfago de Barrett de forma mais custo efetiva.

Palavras-chaves: Esôfago de Barrett. Refluxo Gastroesofágico. Adenocarcinoma. Epidemiologia.

Image

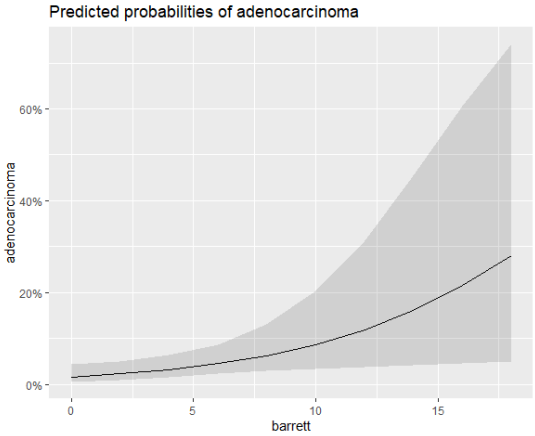

Figure 2. Relation between adenocarcinoma and the extent of Barrett's esophagus

Central message

Patients with a history of smoking, men, whites over 60 years of age and with longer Barrett's esophagus (BE) presented in this specific population study risk factors for the development of esophageal dysplasia and adenocarcinoma. A history of smoking presented a 4.309-fold higher risk of developing adenocarcinoma, and each centimeter of Barrett's esophagus epithelium increased the risk by 1.193 times of developing adenocarcinoma. Patients without risk factors did not develop adenocarcinoma in periods of less than 12 months of follow-up, even when they had dysplasia associated with BE.

Perspectives

The present study showed specific risk factors involved in the progression of Barrett's esophagus to adenocarcinoma and dysplasia in our population. By studying a specific population, there is the prospect of confirming through studies in larger populations and adapting the appropriate endoscopic follow-up period for screening for adenocarcinoma and dysplasia in patients with EB.

INTRODUCTION

Gastroesophageal reflux disease (GERD) is caused by the involuntary and repetitive return of gastric contents into the esophagus [11]. Because of progressive damage from the refluxate, a natural repair process of the esophageal mucosa can occur, resulting in the replacement of the squamous epithelium for a glandular columnar epithelium, accompanied by the appearance of goblet cells in the mucosa, typical of the intestine. This process characterizes intestinal metaplasia, known as Barrett's Esophagus (BE) [28].

It is estimated that the incidence of GERD in Brazil is 12%, which corresponds to about 24 million individuals. However, the actual prevalence of this disease may be even higher, as many individuals access clinical treatment informally [19]. BE occurs in 10 to 15% of patients with GERD, especially in those with a long history of reflux [11]. Thus, BE affects approximately 3 million people in Brazil, and an increase in its incidence has been observed in recent years with changes in the population's dietary patterns and aging [11].

For the definitive diagnosis of BE, upper digestive endoscopy associated with biopsy is necessary to confirm the histopathological presence of goblet cells in the esophageal epithelium [3, 5, 18].

It is important to consider that currently, the follow-up of Barrett's Esophagus aims at the early detection of dysplasia and adenocarcinoma (EAC). This follow-up is standardized by high-definition white-light endoscopy, with random four-quadrant biopsies every 2 cm (or every 1 cm if dysplasia is known or suspected), according to the Seattle protocol [7]. Additionally, biopsies are performed in areas of mucosal irregularities such as nodules, ulcers, or visible lesions [22]. Even in patients who have undergone surgical and endoscopic treatment for BE, the development of adenocarcinoma should be monitored in a standardized manner [4].

The description of Barrett's epithelium should follow the Prague classification, which considers the circumferential extent (C) and the maximum extent (M) of the columnar epithelium with metaplasia [24].

Several risk factors have been identified for the development of Barrett's Esophagus (BE). Endoscopic database studies have reported that the prevalence of BE increases sharply in the fourth and fifth decades of life. Male sex, white race, chronic symptomatic reflux (symptoms more than once a week

for more than 5 years), and central obesity (measured by waist-to-hip ratio or waist circumference) are other associated risk factors [26].

Barrett's esophagus presents a genetically unstable epithelium with risks for dysplasia and adenocarcinoma. Patients with BE have an 11-fold higher relative risk of developing adenocarcinoma, which may result from a metaplasia-dysplasia-carcinoma sequence [18]. The annual risk of esophageal adenocarcinoma from BE without dysplasia is 0.12% (95% CI, 0.09 to 0.15) [12]. In our setting, the current prevalence of AEB development in patients under follow-up is 0.19% [27].

Dysplasia, characterized by abnormal organization or disordered differentiation of cells or tissue present in an organ, is considered a premalignant lesion. Dysplasia remains the primary biological predictor marker for progression to esophageal adenocarcinoma, despite active research into biological and molecular markers. Efforts should be concentrated on the early detection of dysplasia and adenocarcinoma in BE to avoid diagnosing adenocarcinoma at an advanced stage, which leads to a worse prognosis, with an overall five-year survival rate of approximately 18% [17].

In a meta-analysis conducted by Krishnamoorthi, R., including 74.943 patients, the epidemiological factors involved in the progression of BE to adenocarcinoma were evaluated, finding age (OR 1.47, 95% CI 1.01–1.05), male sex (OR 2.16, 95% CI 1.84–2.53), smoking (OR 1.47, 95% CI 1.09–1.98), and BE segment length (OR 1.25, 95% CI 1.16-1.36) [15].

However, despite the presence of epidemiological risk factors for the progression of BE to esophageal adenocarcinoma, the follow-up recommendations for BE proposed by different international societies (Table 1) considered only the presence or absence of dysplasia and its grade as variables to define the follow-up intervals, without taking into account known epidemiological factors in the literature.

It is necessary to better understand the epidemiological factors associated with the development of dysplasia or EAC in BE in our population and to critically analyze the proposed intervals among international societies, in order to promote personalized screening. This was the motivation behind conducting the present study.

The objective of this study is to evaluate the relationship of epidemiological risk factors for the development of dysplasia/adenocarcinoma from BE in a specific population, as well as to conduct a critical analysis of the BE follow-up period, with the aim of individualizing the follow-up time according to the identified risk factors.

METHODS

Study Design

A retrospective case-control study was conducted in the Esophageal Surgery Service at University Hospital of Faculty of Medicine of Universidade de Sao Paulo, collecting data from patients with Barrett's esophagus followed in this Service. The study was approved by the Ethics Committee of the Institution.

Eligibility Criteria

In this study, patients with a diagnosis of Barrett's esophagus made via endoscopy at the service and who were followed up at this center were included in the analysis, totaling 646 patients attended between 1991 and 2020. Among them, 71 presented with dysplasia and 21 presented with adenocarcinoma.

Variables Studied

- Sex (male and female)
- Age
- Smoking status (current smoker, former smoker, and non-smoker)
- Body Mass Index (BMI)
- Ethnicity (Asian, white, mixed-race, and black)
- Extent of Barrett's esophagus

Studied Outcome

The outcomes studied were adenocarcinoma and dysplasia in patients diagnosed with Barrett's esophagus. Among the patients with confirmed Barrett's esophagus by endoscopy performed at the service, those who presented with adenocarcinoma or dysplasia were compared with those who did not. The incidence of variables was compared between the group that presented with

dysplasia and/or adenocarcinoma and the group that did not present these outcomes.

The variables sex, smoking status, and ethnicity were compared with the presence or absence of dysplasia and adenocarcinoma using the chi-square test, while the variables extent of Barrett's esophagus, BMI, and age were compared between the two groups using the Student's t-test. A significance level (alpha) of 5% was adopted.

The variables that showed a significant difference ($p<0.05$) for the progression of Barrett's esophagus to adenocarcinoma were selected, and the odds ratio (OR) for these outcomes was measured through logistic regression, as demonstrated in the diagram below (Figure 1). In this stage, the ethnicity variable was divided into white and non-white, and the smoking status group was divided into smoker or former smoker and non-smoker. A significance level (alpha) of 5% and a 95% confidence interval were considered. The same process was performed for the variables that showed a significant difference for the progression of BE to dysplasia.

The evaluation of risk factors for patients who progressed from esophageal dysplasia to adenocarcinoma was not performed because all patients with esophageal adenocarcinoma who had variable information also previously presented with dysplasia.

Finally, the follow-up endoscopies of patients who developed dysplasia and/or adenocarcinoma were observed in an intragroup analysis. We analyzed the maximum endoscopy interval capable of identifying 100% of the sought outcomes, comparing this interval between patients who did or did not present the risk factors previously identified by logistic regression.

RESULTS

Table 2 shows the relationship between qualitative variables (sex, smoking status, and ethnicity) and adenocarcinoma. There was a statistically significant difference in the incidence of adenocarcinoma among different ethnicities ($p=0.027$), among smokers, non-smokers, and former smokers ($p<0.001$), and between different sexes ($p=0.019$).

The relation between qualitative variables and dysplasia is shown in Table 3. A statistically significant difference in the incidence of dysplasia was observed among smoking statuses ($p=0.04$). There was no statistical difference in dysplasia between different sexes ($p=0.155$) and ethnicities ($p=0.325$).

In Table 4, the relation between quantitative variables (extent of Barrett's, BMI, age) and the incidence of adenocarcinoma is shown. Using the Student's t-test, the variables extent of Barrett's ($p=0.002$) and age ($p=0.044$) were statistically significant, while the BMI variable ($p=0.449$) did not show a statistical difference.

In Table 5, the relation between quantitative variables and the incidence of dysplasia is shown. Using the Student's t-test, the variables extent of Barrett's ($p=0.004$) and age ($p=0.049$) were statistically significant, while the BMI variable ($p=0.240$) did not show a statistical difference.

Thus, the significant variables for the development of adenocarcinoma were smoking status, ethnicity, sex, extent of Barrett's, and age. While the significant variables for the development of dysplasia were smoking status, extent of Barrett's, and age.

In logistic regression (Table 6), smokers or former smokers had a higher incidence of adenocarcinoma, with an odds ratio of 4.309 times higher to develop adenocarcinoma from BE ($p=0.014$). Analyzing the extent of Barrett's, each centimeter increase was associated with an odds ratio of 1.193 times to develop adenocarcinoma ($p=0.017$).

In the analyzed sample, patients with dysplasia had an odds ratio 206 times higher for developing adenocarcinoma compared to patients without dysplasia (Table 6). This aligns with the literature, which identifies dysplasia as the main marker for the progression to esophageal adenocarcinoma.

When analyzing Figure 2 on the predicted probability of adenocarcinoma, it is evident that the increase in the extent of Barrett's esophagus corresponds with an increase in the incidence of adenocarcinoma. Similarly, when analyzing Figure 3, there is a higher incidence of adenocarcinoma among smokers and former smokers.

In the logistic regression to identify the odds ratio for the development of dysplasia from BE, shown in Table 7, age was associated with an odds ratio of 1.023 times higher for developing dysplasia with each year of life (p=0.041). The extent of Barrett's was identified as a significant factor for the progression to dysplasia, increasing the chance by 1.128 times with each centimeter (p=0.008).

When analyzing Figure 4 on the predicted probability of dysplasia, it is evident that the increase in the extent of Barrett's esophagus corresponds with an increase in the incidence of dysplasia. Similarly, when analyzing Figure 5, the incidence of dysplasia increases with the age of the patients.

Considering the period which smokers or former smokers developed EAC from BE (noting that all previously presented dysplasia), we observed that if follow-up were conducted every 6 months, 100% of the patients would have an early diagnosis of adenocarcinoma. On the other hand, for non-smokers, 100% of the diagnoses would be made early if follow-up were conducted every 12 months. Conversely, if smokers were followed every 12 months, only 81.81% of the cases would be diagnosed early.

Considering the period which patients with long-segment Barrett's esophagus developed EAC from BE (noting that all previously presented

dysplasia), we observed that if follow-up were conducted every 6 months, 100% of the patients would have an early diagnosis of adenocarcinoma. For patients with short-segment Barrett's esophagus, 100% of the diagnoses would be made early if follow-up were conducted every 12 months. However, if patients with long-segment Barrett's esophagus were followed every 12 months, only 75% of the cases would be diagnosed early.

If the follow-up of patients aged ≥60 who developed dysplasia from BE were conducted every 6 months, 100% of the patients would have an early diagnosis of adenocarcinoma. For patients under 60 years old, 100% of the diagnoses would be made early if the follow-up were conducted every 12 months. However, if patients aged ≥60 were followed every 12 months, only 92.5% of the cases would be diagnosed early.

When analyzing the progression time from BE to dysplasia between patients with short-segment and long-segment Barrett's esophagus, no difference was observed in the early detection of dysplasia cases between these groups. Thus, if follow-up were conducted every 6 months, 100% of the patients in both groups would be diagnosed early, while if the follow-up were conducted every 12 months, both groups would lose around 7% in the detection rate.

The results described above are illustrated in the Figure 6 below:

DISCUSSION

Given that most EACs arise in the presence of BE, it is necessary to establish a well-defined surveillance system, as early detection of BE through endoscopic surveillance would detect the progression to dysplasia/EAC in its early stages, allowing for endoscopic or surgical treatment with higher success rates [14]. This scenario was demonstrated in a cohort study of 30,000 patients with BE followed for 5 years, where patients diagnosed with EAC during surveillance were detected at an earlier stage (stage 0 to 1: 74.7% versus 56.2%; $p<0.001$), survived longer (median 3.2 versus 2.3 years; $p<0.001$), and had lower cancer-related mortality (34.0% versus 54.0%; $p<0.0001$) compared to those not under surveillance [8].

However, it is important to note that the approach to follow-up and surveillance of patients with BE is still controversial in the literature and in various international guidelines for Barrett's esophagus, as presented in the introduction

of this study. Considering the conditions and limitations of the Brazilian public health system and the difficulty in increasing the number of endoscopy exams for screening [21], it is important to conduct a detailed study on risk factors for the development of dysplasia and adenocarcinoma that can be practically evaluated in our population. This aims to adapt the surveillance criteria to our reality in a more cost-effective manner.

In this context, risk stratification of patients with Barrett's esophagus based on demographic data, clinical information, and diagnostic or predictive biomarkers of disease progression can facilitate more targeted screening, subsequent surveillance, and early-stage treatment, thus increasing survival rates with optimized resources [16].

The data found in our study suggest that smoking or former smoking, as well as the extent of Barrett's esophagus (in centimeters), were risk factors for the development of adenocarcinoma, similar to the findings in the meta-analysis by Krishnamoorthi, R., which included 74,943 patients [15]. In this meta-analysis, the authors also highlighted age and male sex as risk factors. However, these variables did not present as risk factors in the logistic regression conducted in this study, although they were statistically significant in the group analysis.

When analyzing patients who developed only dysplasia, it was identified that age, as well as the extent of Barrett's esophagus (in centimeters), were risk factors for the development of dysplasia. As observed in the literature [20], in the population analyzed in this study, dysplasia remains the strongest marker for progression to adenocarcinoma, with a 206-fold higher risk of this outcome compared to patients who did not present dysplasia.

In the analyzed population, the BMI variable did not show a statistically significant difference between the group that developed adenocarcinoma and the group that did not. However, it is important to note that the average BMI of the patients is above 25, suggesting that patients who did not develop adenocarcinoma were also overweight, complicating the analysis of BMI's influence on the higher incidence of this outcome [13, 25].

After analyzing the studied population, we can identify the risk factors associated with the development of dysplasia and adenocarcinoma. By observing the performed endoscopies, it becomes possible to evaluate the maximum follow-up period capable of early detection of patients with adenocarcinoma and

dysplasia. Thus, a critical analysis of the proposals from international societies for EB surveillance against our data becomes essential, as we do not have guidelines customized to the national context.

In our population, non-smoking patients with dysplasia did not develop adenocarcinoma within 12 months, similar to patients with short-segment BE. In contrast, both smoking patients and patients with long-segment Barrett's developed adenocarcinoma in less than 12 months. These findings suggest that the follow-up of patients in these specific groups (non-smokers or short-segment Barrett's) could be conducted over a longer period, contrary to the main international recommendations [9].

This analysis of a small cohort from a single service shows the relevance of associating epidemiological and clinical data (smoking status and extent of BE) with dysplasia (the main risk factor considered in international follow-up guidelines) to optimize and tailor follow-up to the reality of each region, considering cost-effectiveness.

Being a retrospective study, one of its limitations was the inability to evaluate the total sample of 646 patients for all variables, as some information was not present in the records. Continuation of this study, seeking a larger sample size and association with multicentric data, should be encouraged to obtain increasingly reliable data and to propose follow-up guidelines for BE based on the characteristics of our population.

CONCLUSIONS

The follow-up suggested for our population by international guidelines was appropriate for patients with risk factors for the development of adenocarcinoma (smoking and long-segment Barrett's). However, patients without risk factors could have their follow-up extended to 12 months, even with a prior diagnosis of dysplasia.

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Table 1. International Society Guidelines for Barrett's Esophagus Surveillance

-	AGA[1]	ACG[23]	ASGE[2]	BSG[6,10]	ESGE[29]	Australian[30]
Barrett's Esophagus without Dysplasia (BEWD)	Surveillance every 3-5 years	Surveillance every 3-5 years.	Surveillance every 3-5 years.	Surveillance every 3-5 years. If length <3 cm without intestinal metaplasia/dysplasia → repeat EGD. If repeat EGD is negative → discontinue surveillance. If repeat EGD is positive for intestinal metaplasia → surveillance every 3-5 years. If length is ⩾3 cm → surveillance every 2-3 years.	<1 cm → no surveillance, ⩾1 cm and <3 cm: surveillance every 5 years ⩾3 cm and <10 cm: surveillance every 3 years ⩾10 cm: consult a BE specialist center. Continue surveillance until at least 75 years old.	Short segment (<3 cm): repeat EGD in 3-5 years. Long segment (⩾3 cm): repeat EGD in 2–3 years.
Barrett's Esophagus with Indefinite Dysplasia (IND)	No information	Repeat EGD after PPI therapy for 3-6 months. If the repeat EGD shows indefinite, then surveillance	Additional pathological review, increased dose of PPI therapy, and repeat EGD with biopsy	Repeat EGD after PPI therapy for 6 months. If it indicates Barrett's Esophagus without Dysplasia again, follow this BEWD protocol .	Repeat EGD after PPI therapy for 6 months. If it shows IND or BEWD, follow the BEWD protocol.	Repeat EGD after PPI therapy for 6 months. If it shows BEWD / LGD / HGD / EAC, follow the respective protocols. If it shows IND,

		every 12 months				repeat EGD in 6 months.
Barrett's Esophagus with Low-Grade Dysplasia (LGD)	Surveillance every 6–12 months	Endoscopic eradication therapy is recommended for confirmed LGD without life-limiting comorbidities or, alternatively, surveillance every 12 months	Repeat EGD in 6 months to confirm the diagnosis. Subsequently, perform annual surveillance EGD in selected patients	Repeat EGD in 6 months. If LGD persists EET is recommended or, alternatively, surveillance every 6 months.	Repeat EGD in 6 months. If shows complete eradication of dysplasia (BEWD), then perform EGD annually until two consecutive results show BEWD. Then, follow the BEWD protocol. If LGD persists, then EET is recommended	Repeat EGD every 6 months until two consecutive results show BEWD. Then, follow a less frequent surveillance schedule.
Barrett's Esophagus with High-Grade Dysplasia (HGD)	EET or alternatively, surveillance every 3 months	EET for HGD confirmed without life-limiting comorbidities	EET, or, alternatively, surveillance every 3 months	EET.	EET. If biopsies show BEWD repeat EGD in 3 months.	EET, or, alternatively, surveillance every 3 months.

EAC=Esophagus adenocarcinoma ; PPI=Proton-pump inhibitor ; EGD=Esophagogastroduodenoscopy ; EET=Endoscopic eradication therapy ; BEWD=Barrett's Esophagus without Dysplasia ; IND=Barrett's Esophagus with Indefinite Dysplasia ; LGD=Barrett's Esophagus with Low-Grade Dysplasia ; HGD=Barrett's Esophagus with High-Grade Dysplasia ; ACG=American College of Gastroenterology ; AGA=American Gastroenterological Association ; ASGE=American Society for Gastrointestinal Endoscopy; BSG=British Society of Gastroenterology ; ESGE=European Society of Gastrointestinal Endoscopy ; Australian

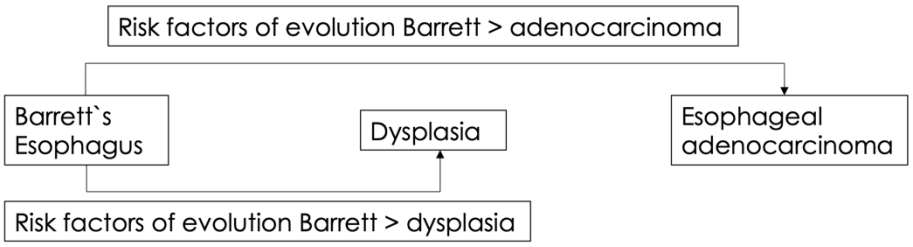

Figure 1. Flowchart of the progression of Barrett's esophagus to adenocarcinoma and dysplasia

Table 2. Comparison of qualitative variables between groups with and without adenocarcinoma.

	Smoke			Ethnicity				Sex	
	Yes	No	Ex	Asian	White	Birracial	Black	Male	Female
Adenocarcinoma	8	5	4	2	15	2	0	17	4
No adenocarcinoma	52	221	36	7	409	28	14	345	280
P-Value	P<0,001			P=0,027				P=0,019	

Ex = Ex-smoker

Table 3. Comparison of qualitative variables between groups with and without dysplasia. Ex = Ex-smoker

	Smoke			Ethnicity				Sex	
	Yes	No	Ex	Asian	White	Birracial	Black	Male	Female
Dysplasia	17	33	6	3	58	5	3	46	25
No Dysplasia	43	193	34	6	366	25	11	316	259
P-Value	P=0,04			P=0,325				P=0,155	

In Table 4, the relation between quantitative variables (extent of Barrett's, BMI, age) and the incidence of adenocarcinoma is shown. Using the Student's t-test, the variables extent of Barrett's (p=0.002) and age (p=0.044) were statistically significant, while the BMI variable (p=0.449) did not show a statistical difference.

Table 4: Comparison of quantitative variables between groups with and without adenocarcinoma.

	Extent of Barrett`s				BMI				Age			
-	Mean	Std. Deviation	Max	Min	Mean	Std. Deviation	Max	Min	Mean	Std. Deviation	Max	Min
Adenocarcinoma	5.325	3.221	12	1	26.600	4.913	36.707	18.326	62.000	14.843	88	29
No Adenocarcinoma	3.296	2.859	18	0.3	27.706	5.161	53.250	11.157	55.256	14.733	92	14
P-Value	P=0.002				P=0.449				P=0.044			

Std. = Standard; BMI = Body Mass Index; Max = Maximum; Min = Minimum

Table 5: Comparison of quantitative variables between groups with and without dysplasia.

	Extent of Barrett`s				BMI				Age			
-	Mean	Std. Deviation	Max	Min	Mean	Std. Deviation	Max	Min	Mean	Std. Deviation	Max	Min
Dysplasia	4.294	3.139	14	0.5	26.925	5.066	41.913	18.326	58.743	13.918	88	22
No Dysplasia	3.243	2.839	18	0.3	27.814	5.161	53.250	11.157	55.063	14.835	92	14
P-Value	P=0.004				P=0.240				P=0.049			

Std. = Standard; BMI = Body Mass Index; Max = Maximum; Min = Minimum

Table 6: Logistic regression for the outcome of adenocarcinoma.

	Odds Ratio	p
Intercept	0.001	<0.001
Ethnicity (not white)	2.079	0.266
Sex (male)	1.834	0.387
Age	1.029	0.163
Extent of Barrett`s	1.193	0.017
Smoke (Yes or Ex)	4.309	0.014
Dysplasia	206.020	<0.001

Ex = Ex-smoker

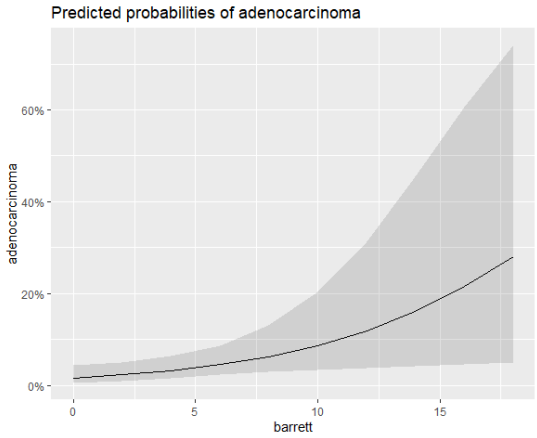

Figure 2. Relation between adenocarcinoma and the extent of Barrett's esophagus

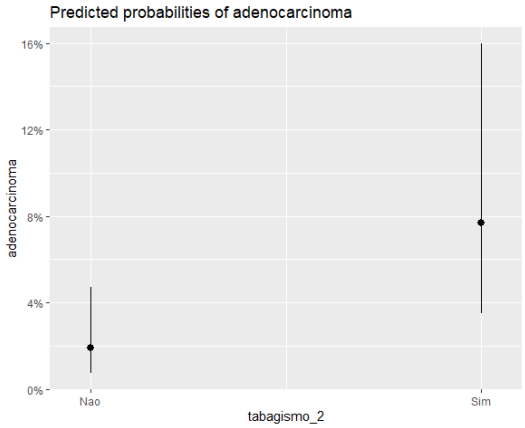

Figure 3. Relation between adenocarcinoma and smoking status

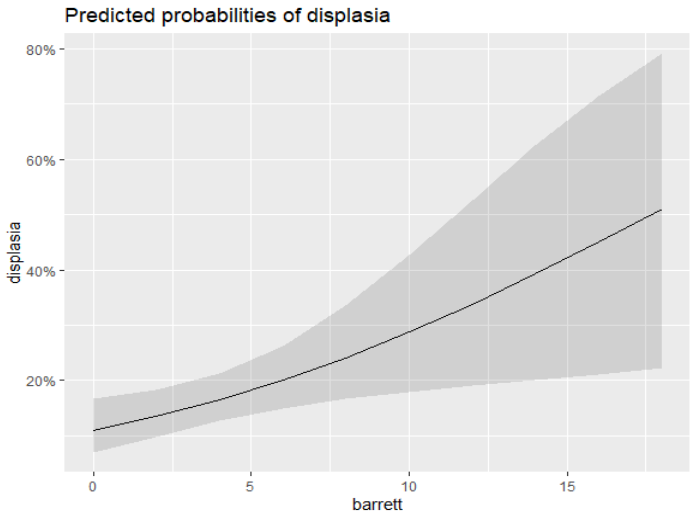

Figure 4. Relation between dysplasia and the extent of Barrett's esophagus

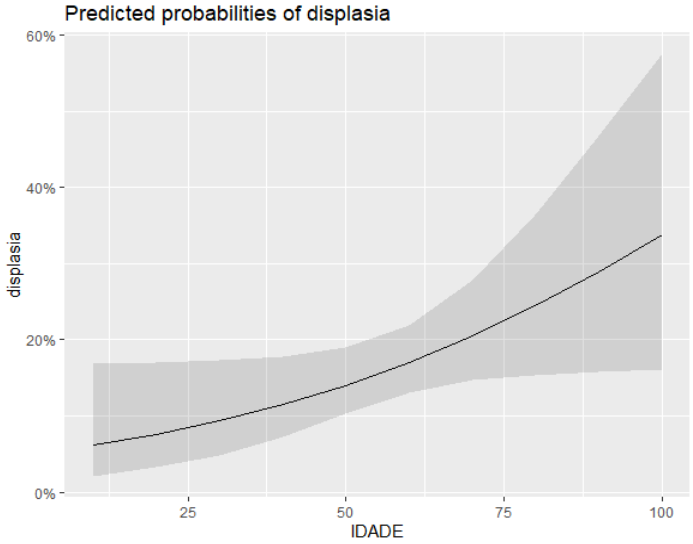

Figure 5. Relation between dysplasia and age

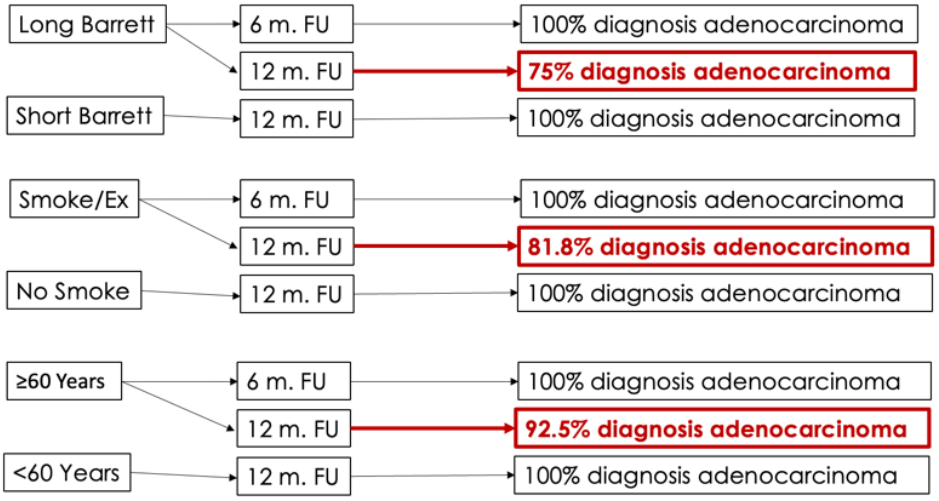

Figure 6. Relation between the follow-up time of individuals with risk factors identified in logistic regression and the percentage of early adenocarcinoma diagnoses. Legend: FU = follow-up; m. = months; Ex = ex-smoker

Table 7. Logistic regression for the outcome of dysplasia

	Odds Ratio	p
Intercept	0.030	<0.001
Smoke (Yes or Ex)	1.538	0.167
Extent of Barrett`s	1.128	0.008
Age	1.023	0.041

Ex = Ex-smoker

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