

# Barrett's esophagus and adenocarcinoma of the lower part of esophagus - the experience of one center

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A - Study Design  
B - Data Collection  
C - Statistical Analysis  
D - Data Interpretation  
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G - Funds Collection

Andrzej Nowicki<sup>1ADE</sup>, Zbigniew Kula<sup>2BDF</sup>, Alicja Świerczyńska<sup>1BF</sup>

<sup>1</sup>Department of Oncology Nursing, Collegium Medicum in Bydgoszcz, Nicolaus Copernicus University in Toruń, Poland; Head: dr. hab. med. Andrzej Nowicki

<sup>2</sup>Department of Endoscopy at Oncology Center in Bydgoszcz, Poland; Head: dr Zbigniew Kula

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**ABSTRACT:** **Objective:** The aim of the study was to evaluate the prevalence and clinical aspects of Barrett's esophagus and adenocarcinoma of the lower part of esophagus in gastroscopy.

**Material and methods:** Retrospective review of 10000 upper gastrointestinal endoscopic examinations were performed at the Department of Oncology Endoscopy in Bydgoszcz from 2004 to 2014 in terms of incidence of Barrett's esophagus and adenocarcinoma in the lower part of esophagus.

**Results:** The medical records of 5378 (53,8%) women and 4622 (46,2%) men were analyzed. The average age of men and women was 62,4 and 62,7, respectively. Barrett's esophagus was diagnosed in 67 patients, including 38 (56,7%) of men where the average age of men and women was 56,9 and 60,2 years, respectively. The most commonly reported symptom was heartburn occurred in 45 (67,2%) of patients. During ten years of follow-up PB examination the adenocarcinomas were detected in 3 (4,47%) cases. Adenocarcinoma was diagnosed in 46 patients, of whom 37 in men. In the case of 27 patients (58,7%), esophageal cancer was treated with the intention of radicalization. The probability of 5-year survival in these patients was 10,2% for women and 9,2% for men.

**Conclusions:** The number of Barrett's esophagus and adenocarcinoma are increasing at 0,67% and 0,46% annually, respectively. The risk of adenocarcinoma developed from Barrett's esophagus during endoscopic follow-up period was 4,47%. Probability of 5-year survival in patients with adenocarcinoma was 9,7%.

**KEYWORDS:** gastroscopy, Barrett's esophagus, adenocarcinoma of esophagus

Barrett's esophagus (Barrett's Esophagus, BE) is the replacement in the esophagus of stratified squamous epithelium by glandular epithelium with the presence of intestinal metaplasia [1, 2]. BE is a complication of gastroesophageal reflux disease (GERD) and occurs in approximately 10% of patients with GERD. It has also been shown that BE is more frequent in obese, smoking people and people with BE or esophageal adenocarcinoma (EAC) [3, 4, 5]. The prevalence of BE in the general population is up to 5.6% and concerns mainly in white males over 50 years of age [6].

Great interest in BE is associated with an increased risk of development of metaplastic carcinoma on the bed of the epithelial tissue. It is assumed that the risk of developing EAC in BE is up to 10 times higher than in the general population, and the progression of adenocarcinoma from metaplasia to low-grade dysplasia, followed by high-grade dysplasia and adenocarcinoma is about 0.38% per year [7].

Diagnosis of BE is clinical-morphological and is based on endoscopic examination of the upper gastrointestinal tract and collecting specimens from areas of the salmon-colored mucosal membrane above the upper border of the stomach folds. A biopsy of 4 quadrants and from different levels of the esophagus every 2 cm is recommended. In most studies, the precondition for microscopic diagnosis of BE is the presence of metaplastic columnar glandular epithelium with the presence of intestinal metaplasia foci [4]. The dynamic development of advanced endoscopic techniques allows a significant improvement in diagnostic efficiency [8]. Depending on the length of the affected area, there is long > 3 cm (classic), 1-3 cm (short) and <1 cm (ultrashort) BE. The Prague classification

introduces additionally endoscopic terms of C (circumferential) and M (maximum), according to which the researcher determines the circular (C) and maximum (M) BE range in endoscopic examination [4, 9, 10].

A retrospective analysis of 10,000 gastroscopic examinations for the occurrence of Barrett's esophagus and adenocarcinoma may contribute to a better assessment of these diseases as a growing social problem in developed countries.

## PURPOSE OF WORK

The purpose of the study was to assess the occurrence and selected clinical aspects of Barrett's esophagus and adenocarcinoma of the lower esophagus in the material of the Department of Oncology Endoscopy in Bydgoszcz.

## MATERIAL AND METHODS

A retrospective review of endoscopic examination results of the upper gastrointestinal tract was performed at the Department of Oncology Endoscopy in Bydgoszcz in 2004-2014 in terms of the occurrence of Barrett's esophagus and adenocarcinoma of the lower esophagus. Endoscopic examinations were performed with Olympus cameras (GIF-Q180, GIF-QTH180 and GIF-Q190). White light imaging and Narrow band imaging (NBI) were used. Research photo documentation was recorded in the Olympus endobase system. Initial diagnosis of Barrett's esophagus was based

Tab. I. Annual breakdown of the number of detected Barrett's esophagus.

YEARS	N/%	% OF ALL DETECTED CASES*	FEMALE	MALE N/%**	% FEMALES	% MALES
2004	5/0,65	7,5	3/60	2/40	10,3	5,3
2005	7/1,01	10,4	5/71,4	2/28,6	17,2	5,3
2006	7/0,7	10,4	3/42,9	4/57,1	10,3	10,5
2007	5/0,52	7,5	2/40	3/60	6,9	7,9
2008	5/0,47	7,5	2/40	3/60	6,9	7,9
2009	3/0,29	4,5	2/66,7	1/33,3	6,9	2,6
2010	5/0,47	5/7,5	1/20	4/80	3,4	10,5
2011	6/0,59	9,0	2/33,3	4/66,7	6,0	10,5
2012	9/0,82	13,4	3/33,3	6/66,7	10,3	15,8
2013	10/1,32	14,9	3/30	7/70	10,3	18,4
2014	5/0,87	7,5	4/80	1/20	13,8	2,6
Total	67/0,67	100	29/43,3	38/56,7	100	100

\*p=0,001; \*\*p=0,277

Tab. II. Predominant symptom reported before examination in patients with Barrett's esophagus.

SYMPTOMS	N/%
heartburn	45/67,2
nausea	3/4,5
eructating	11/16,4
epigastric pain	8/11,9
Total	67/100

Tab. III. Histopathological diagnosis in patients with Barrett's esophagus.

DIAGNOSIS	N/%
intestinal metaplasia without dysplasia	35/52,2
intestinal metaplasia with low-grade dysplasia	20/29,9
intestinal metaplasia with medium-grade dysplasia	5/7,5
intestinal metaplasia with moderate-grade dysplasia	3/4,5
intestinal metaplasia with high-grade dysplasia	4/6
Total	67/100,0

Tab. IV. Number of esophageal adenocarcinomas in particular years.

YEARS	N/%	% ALL DETECTED*	FEMALE	MALE N/%**	% FEMALES	% MALES
2004	2/0,26	4,3	0/0	2/100	0,0	5,7
2005	3/0,43	6,5	1/33,3	2/66,7	9,1	5,7
2006	4/0,40	8,7	1/25	3/75	9,1	8,6
2007	3/0,31	6,5	1/33,3	2/66,7	9,1	5,7
2008	2/0,19	4,3	2/100	0/0	18,2	0,0
2009	2/0,20	4,3	0/0	2/100	0,0	5,7
2010	3/0,28	6,5	1/33,3	2/66,7	9,1	5,7
2011	5/0,50	10,9	1/20	4/80	9,1	11,4
2012	8/0,73	17,4	1/12,5	7/87,5	9,1	20,0
2013	7/9,92	15,2	1/14,3	6/85,7	9,1	17,1
2014	7/1,21	15,2	2/28,6	5/71,4	18,2	14,3
Total	46/0,46	100	11/23,9	35/76,1	11/100	35/100

\*p=0,001; \*\*p=0,129

on the endoscopic image when the Z line was raised > 1 cm from the end of the stomach folds. Ultra-short BE cases were excluded from analysis. The material for histopathological examination was collected from the esophagus below the Z line from four quadrants of esophagus circumference every 2 cm and additionally from the lesions suspected of mucosal dysplasia or neoplastic proliferation. For the purposes of further analysis, patients were included in histopathological examination for the presence of intestinal metaplasia in esophagus and/or adenocarcinoma of the lower part of esophagus. Studies performed in 10,000 people

were analyzed, including 5,378 women and 4,622 men aged 31 to 79 years (median 63). In addition, based on the history of diseases, the most common symptoms with which the patients reported for the study and treatment methods were analyzed.

The descriptive analysis of the results includes tables in which the quantity and percentage were presented. Averages with standard deviations were also calculated. Differences between variables were determined on the basis of the chi-square test for cross tables. Student's t-test for one variable divided into groups was also

**Tab.V.** Symptoms reported before examination in patients with esophageal adenocarcinoma.

OBJAWY	N/%
difficulty swallowing	39/ 84,8
pain during swallowing	1/ 2,2
difficulty swallowing + pain during swallowing	2/ 4,3
difficulty swallowing + epigastric pain	1/ 2,2
difficulty swallowing + epigastric pain + nausea + heartburn	1/ 2,2
difficulty swallowing + heartburn	1/ 2,2
difficulty swallowing + lack of appetite	1/ 2,2
Total	46/100,0

applied. In the data analysis, nonparametric Mann-Whitney U Test was used to evaluate differences in one characteristic between two populations (groups). P value below 0.05 was considered statistically significant. The Kaplan-Meier estimate was used to calculate the probability of survival, and test log-rank survival curves were used for comparison. All calculations and figures were prepared using the Microsoft Excel and Statistica 10.0 spreadsheet.

## RESULTS

### 1. Barrett's esophagus

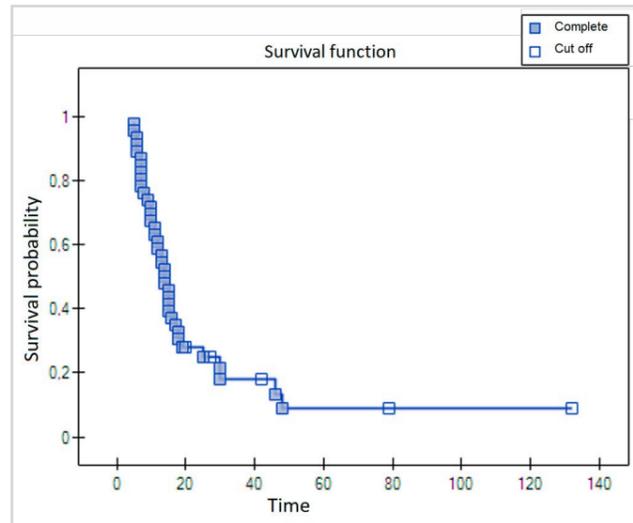
In the period from 2004 to 2014, the endoscopic image of BE was found in 83 (0.83%). In histopathological examination, intestinal metaplasia was not confirmed in 16 patients. In the remaining 63 patients, BE was diagnosed. Most BE - 10 (14.9%) was detected in 2013, the least - 3 (4.5%) in 2009. In particular years, the number of BEs detected ( $R^2 = 0.035$ ) ( $p = 0.001$ ) increased (tab. I). The mean age of all patients with BE was 58.3, with the average female 60.2 and male 56.9 ( $p > 0.05$ ). The most frequently reported complaint was heartburn in 45 (67.2%) people. The fewest people complained of nausea and epigastric pain; 3 (4.5%) and 8 (11.9%) people, respectively (tab. II). In 20 (29.9%) patients, there was intestinal metaplasia with low-grade dysplasia and only 4 (5.9%) patients had intestinal metaplasia with high-grade dysplasia (Tab. III).

Gastroscopy examination was performed between 1 and 5 years after diagnosis in 51 (75%) patients. 32 (25%) people did not report for follow-up examinations. During the 10th year of BE monitoring, 3 (4.5%) glandular cancers and 2 (2.4%) cases of high grade dysplasia were detected.

### 2. Adenocarcinoma of the lower part of the esophagus

46 esophageal gland carcinomas were diagnosed including 3 during endoscopic surveillance of BE. Cancers occurred mainly in men - 35 (76.1%) (Tab. IV). The average age of esophageal adenocarcinoma patients was 62.4 years and was similar for women and men ( $p > 0.05$ ). The main symptom in 39 (84.8%) patients was difficulty with swallowing (Tab. V).

In the case of 27 patients (58.7%) treatment with the intention of radicalization was used, while in 19 patients (41.3%) palliative treatment. The most frequently used treatment with the intention of radicalization was partial or complete excision of the esophagus in 12 (44.4%) patients, while in other patients radical radiochemo-

**Fig. 1.** Survival probability in patients with esophageal adenocarcinoma.

rapy was applied. The most commonly used palliative treatment was radiotherapy, which was applied in 9 patients (47.4%) and in 7 patients (36.8%) chemotherapy was performed. In 3 (15.8%) patients, an esophageal self-expandable stent was placed. 32 (69.6%) patients reported for regular check-ups, 25 (54.3%) of them were subject to control gastroscopy.

### 3. Probability of survival of patients with glandular cancer of the lower esophagus

Approx. 38 (82.6%) patients died of esophageal cancer in the years 2004 to 2014. The probability of five-year survival was 9.7% (Fig. 1). The probability of survival of women and men was similar, and amounted to 10.2% and 9.2%, respectively ( $p = 0.797$ ); it was not dependent on age ( $p = 0.405$ ).

## DISCUSSION

In the last 10 years in the Oncology Center in Bydgoszcz, Barrett's esophagus was diagnosed more often in men than in women. Studies carried out in other centers also indicate a more frequent occurrence of BE in men [11, 12].

All patients diagnosed with BE reported dyspeptic symptoms, mainly in the form of heartburn. Other studies indicate that people who have been diagnosed with BE also complain of ailments associated with reflux disease of the esophagus [13]. Of 10,000 gastroscopies, Barrett's esophagus was diagnosed in several dozen patients. Intestinal metaplasia without properties of dysplasia was found in almost half of them and in a few, high-grade dysplasia was found. Regular examinations including endoscopic examination were performed more than half of the patients. EAC was diagnosed during endoscopic surveillance in 3 patients.

The time intervals of repeated endoscopic examinations depend on the length of the BE segment. The European Society of Gastrointestinal Endoscopy (ESGE) recommends that in the case of BE  $\geq 1$  cm and  $< 3$  cm, examination is recommended every 5 years, and for BE  $\geq 3$  cm and  $< 10$ , every 3 years, whereas in patients with BE  $\geq 10$  cm, examination in expert centers is recommended [14, 15].

The risk of adenocarcinoma in the ultrashort esophagus is very low and endoscopic and histopathological surveillance is not recommended. However, it should be considered in people with long-term symptoms of GERD ( $> 5$  years) and with multiple risk factors (age  $> 50$  years, white race, male gender, obesity, BE or ECA in first-degree relatives) [14, 15].

In cases of dysplasia of the mucus membrane, treatment depends on its severity. In patients with low-grade dysplasia or undifferentiated dysplasia, a re-evaluation in a reference center is recommended, and examination should be repeated after 6 months. Patients with high-grade dysplasia require confirmation by a second pathologist in the reference center. All visible abnormalities should be removed by endoscopic methods [14]. In our material, high-grade dysplasia was found in 4 cases. Three patients were treated with endoscopic mucosectomy, one patient was not eligible for treatment due to many comorbidities. In the case of EAC T1a endoscopic resection is the method of choice. In our material, all diagnosed esophageal carcinomas were of a degree that prevented treatment with advanced endoscopic techniques. However, we believe that in the coming years, an accurate technique of testing and application of new generation endoscopes should contribute to an increase in the frequency of detection in patients with BE dysplasia and early adenocarcinoma. An accurate assessment is recommended using a cap that is applied to the gastroscope, NBI system and acetic acid, and an appropriate examination time of about 1 minute per cm in the BE segment [8,15].

Recent studies indicate that the risk of BE-based adenocarcinoma with endoscopic surveillance in screening is low. Endoscopic surveillance of patients with BE is not associated with a significantly reduced risk of death from cancer. This is especially true for patients with BE without dysplasia [16]. Also, a meta-analysis of 19 examinations involving 7,930 patients with BE showed that EAC was the cause of death in only 7% (cardiovascular disease in 35%) [5]. In Polish studies based on National Barrett's Oesophagus Registry, the risk of EAC was estimated at  $< 0.1\%$  per year, and the risk of developing cancer in case of low-grade dysplasia was 3.7/1000/year [17].

In the last dozen or so years, changes have been observed in the epidemiology of glandular adenocarcinoma. We demonstrated the presence of adenocarcinoma in 0.46% of people/year with BE among 10,000 gastroscopies performed, mainly in men with an average age of 62 years. The available data confirm that esophageal adenocarcinoma is more frequent in men and occurs most frequently after the age of 65, with a basis of BE with dysplasia [18].

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In our patients, the main reason for reporting to the doctor was difficulty in swallowing. Late reporting to a physician of patients with dysphagia is probably related to low awareness and socioeconomic status of these patients. The vast majority were patients without endoscopic surveillance, who never had endoscopic examinations performed. In more than half of patients with diagnosed glandular cancer, surgery and chemoradiation were used with the intention of radicalization. The basic method of radical treatment is surgery through the chest or esophageal hiatus.

Almost half of the patients diagnosed with glandular cancer were treated palliatively. Radio- and chemotherapy was the most commonly used procedure. Individual cases were subject to esophageal stent implantation or brachytherapy. During surgical endoscopy, in order to provide nutrition, it is possible to destroy the intra-esophageal part of the tumor with a laser or argon coagulation, expand the narrowing and/or place a self-expandable stent into the esophageal clearance.

Despite the different treatment methods used, adenocarcinoma of the esophagus is burdened with high mortality. Our study showed that the vast majority of patients diagnosed with esophageal adenocarcinoma have died. In addition, the study also demonstrated that the probability of five-year survival decreased with time and only every 10th patient was saved. Similar results were obtained by other authors. According to them, the 5-year survival of patients with EAC is around 10%, which means that for the majority the disease is incurable [18].

There is no doubt that unfavorable results of esophageal cancer treatment are an indication for the search for new diagnostic and therapeutic methods. Early diagnosis, treatment and endoscopic-histopathological monitoring in BE can improve the effectiveness of adenocarcinoma treatment of the lower esophagus.

## CONCLUSIONS

- The percentage of Barrett's esophagus and glandular adenocarcinoma of the lower esophagus increases at a level of 0.67%/year and 0.46%/year, respectively.
- The risk of adenocarcinoma on the basis of Barrett's esophagus during endoscopic surveillance is 4.47%.
- The probability of 5-year survival in adenocarcinoma of the lower esophagus, regardless of its severity, is 9.7%.

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Corresponding author: Andrzej Nowicki Associate Prof. UMK, Department of Oncology Nursing, Collegium Medicum in Bydgoszcz, Nicolaus Copernicus University in Toruń, ul. Łukasiewicza 1, 85-801 Bydgoszcz, Poland, e-mail: [anow1\\_xl@wp.pl](mailto:anow1_xl@wp.pl)

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