Incidence of Dysplasia in Patients with Barrett's Esophagus

Thesis

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بسم الله الرحمن الرحيم

﴿وَعَلَّمَكَ مَا لَمْ تَكُنْ تَعْلَمُ وَكَانَ فَضْلُ اللهِ عَلَيْكَ عَظِيمًا﴾

صدق الله العظيم
سورة النساء آية (١١٣)

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Karim Wahid Shawky

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List of Abbreviations

Abb.	Full term
95% CI	95% Confidence interval
AGA	American Gastro-enterological Association
APC	Argon Plasma Coagulation
B	Regression coefficients
BE	Barrett's esophagus
BMI	Body Mass Index
BOBCAT	Benign Barrett's and Cancer Taskforce
BSG	British Society of Gastroenterology
C & M	Circumferential extent and the Maximum extent
CLE	Confocal Laser Endomicroscopy
COX-2	Cyclooxygenase-2
DM	Diabetes mellitus
EMR	Endoscopic Mucosal Resection
EUS	Endoscopic Ultrasonography
GERD	Gastro-esophageal reflux disease
GOJ	Gastro-esophageal junction
HGD	High grade dysplasia
IM	Intestinal Metaplasia
LGD	Low grade dysplasia
LNF	Laparoscopic Nissen Fundoplication
NF	Nissen Fundoplication
NSAIDs	Non steroidal anti-inflammatory drugs
NSE	Neo-squamous Epithelium
OCT	Optical Coherence Tomography
OR	Odds Ratio
OR	Odds ratio
pCLE	Probe-based system Confocal Laser Endomicroscopy

List of Abbreviations Cont...

Abb.	Full term
PDT	Photodynamic Therapy
PGE-2	Prostaglandin E-2
PPI	Proton pump inhibitor
P-value	Probability value
RFA	Radiofrequency Ablation
S.E	Standard error of regression coefficients
SCJ	Squamo-columnar Junction
TFF3	Trefoil Factor-3
TNE	Trans-nasal Endoscopy
VLE	Volumetric Laser Endomicroscopy
Wald	Statistical test
WLE	White Light Endoscopy

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INTRODUCTION

Barrett's esophagus is a condition which predisposes towards development of esophageal adenocarcinoma, a highly lethal tumour which has been increasing in incidence over the past three decades. There have been tremendous advances in the field of Barrett's esophagus, not only in diagnostic modalities, but also in therapeutic strategies available to treat this premalignant disease ***(Tan et al., 2017).***

Barrett's esophagus patients progress through a phenotypic sequence of no dysplasia, low-grade dysplasia, high-grade dysplasia and then into esophageal adenocarcinoma, although the time course is highly variable. Furthermore, some patients may progress directly to cancer without prior detection of dysplasia of any grade. Currently, dysplasia remains the only practical factor useful for identifying patients at increased risk for the development of esophageal adenocarcinoma in clinical practice ***(Gaddam et al., 2013).***

A number of endoscopic, histologic and epidemiologic risk factors identify Barrett's esophagus patients at increased risk for progression to high-grade dysplasia and esophageal adenocarcinoma. Endoscopic factors include segment length, mucosal abnormalities as esophagitis and the 12 to 6 o'clock hemisphere of the esophagus. Epidemiologic risk factors include

aging, male gender, obesity, and smoking. Factors that may protect against the development of adenocarcinoma include a diet rich in fruits and vegetables, and the use of proton pump inhibitors, aspirin/NSAIDs and statins ***(Falk, 2015).***

Aim of this Study

The aim of this study is to evaluate the incidence of dysplasia in patients with Barrett's esophagus in relation to risk factors such as: gender, smoking, obesity, patient's age, duration of reflux, treatment received, associated disease as DM and esophageal histopathology.

Chapter 1

HISTORICAL EVOLUTION OF THE DIAGNOSTIC CRITERIA FOR BARRETT'S ESOPHAGUS

Barrett's esophagus gets its name from the pioneering British surgeon, Norman Barrett who in 1950 published his paper 'Chronic peptic ulcer of the esophagus and esophagitis' where he described the columnar lined esophagus. Over the next four decades, disagreements regarding the distal esophageal histology were prevalent, with some arguing that the ulcers in the distal esophagus were not esophageal, but gastric ulcers within an intra-thoracic stomach in patients with congenital short esophagus ***(Barrett, 1950).***

Fig. (1): Norman Barrett **(https://www.readersdigest.co.uk/health/health-conditions/all-you-need-to-know-about-barretts-oesophagus).**

In 1953, Allison and Johnstone published an influential report rejecting Barrett's hypothesis, and suggesting that the

tubular structure within the distal thorax could not be stomach since it: 1) lacked an outer peritoneal lining; 2) had musculature identical to esophagus; 3) consisted of columnar epithelium interspersed with squamous islands; 4) lacked mucosal oxyntic cells; and 5) had mucosal glands typical of the esophagus ***(Allison and Johnstone, 1953).***

Subsequent re-assessment of these gastric ulcers by Barrett led him to acknowledge his prior misjudgement, and he published a revised report in 1957, redefining this tubular structure as 'Lower esophagus lined by columnar epithelium' ***(Barrett, 1957).***

Between 1960 to the mid-1970s, there were varying histological descriptions of the columnar subtypes in the distal esophagus including junctional (gastric cardiac epithelium), gastric-fundal, and intestinal epithelium with goblet cells ***(Hayward, 1961).***

In the 1980s it was established that chronic gastro-esophageal reflux disease and the presence of a hiatal hernia were risk factors for Barrett's esophagus and it grew to be appreciated that these could distort the anatomic landmarks of the GOJ during endoscopy making a precise diagnosis difficult. To avoid error, diagnostic criteria for Barrett's esophagus were established that a minimum of 3 cm columnar lining is required to diagnose Barrett's esophagus and for enrolment into clinical studies. By the mid-1980s, the association between Barrett's

esophagus and esophageal adenocarcinoma was well established and it became clear that intestinal metaplasia had a mosaic distribution with strong predisposition to dysplasia which led to intestinal metaplasia becoming the defining feature for Barrett's esophagus ***(Hamilton and Smith, 1987).***

In the mid-1990s, Spechler challenged the conventional practice of only performing biopsies on Barrett's esophagus ≥3 cm because he demonstrated that 18% of patients with endoscopically apparent Barrett's esophagus measuring less than 3 cm still contained intestinal metaplasia. These results, coupled with the categorization of Barrett's esophagus into short (≤3 cm) and long segments (≥3 cm) have proved essential in shaping the diagnostic criteria for Barrett's esophagus over the years ***(Spechler et al., 1994).***

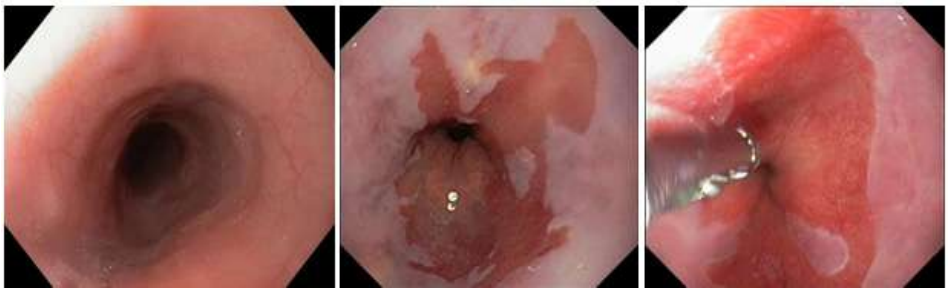

Fig. (2): Normal distal esophagus and examples of Barrett's esophagus. **(http://www.gastromedicine.com.au/barretts-oesophagus/).**