بسم الله الرحمن الرحيم

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تم رفع هذه الرسالة بواسطة / هناء محمد علي

بقسم التوثيق الإلكتروني بمركز الشبكات وتكنولوجيا المعلومات دون أدنى مسئولية عن محتوى هذه الرسالة.

ملاحظات: ....

Local Recurrence of Phyllodes Tumors of the Breast: A Meta-Analysis

Submitted For Partial Fulfilment

of **Master** Degree In General Surgery

By

Ahmed Hamdy Fathy Gafar

M.B., B.Ch.

Faculty of Medicine, Ain Shams University

Under supervision of

Prof. Dr/ Ismail Abd Elhakim Mohammed kotb

Professor of General Surgery

Faculty of Medicine, Ain Shams University

Prof. Dr/ Ahmed Gamal El Din Osman Farag

Assistant Professor of General Surgery

Faculty of Medicine, Ain Shams University

Dr/ MohammedAtef Mohammed El Taib Elazazy

Lecturer of General Surgery

Faculty of Medicine, Ain Shams University

Faculty of Medicine

Ain Shams University

2022

سورة البقرة الآية: ٣٢

ACKNOWLEDGEMENT

First and foremost I feel always indebted to Allah the most beneficent and merciful.

I wish to express my deepest thanks, gratitude and appreciation to **Prof. Dr. Ismail Abd Elhakim Mohammed Kotb**, Professor of General Surgery Faculty of Medicine, Ain Shams University, for his meticulous and generous help.

Special thanks are due to **Prof. Dr. Ahmed Gamal El Din Osman Farag**, Professor of General Surgery Faculty of Medicine, Ain Shams University, for his sincere efforts, fruitful encouragement.

I am deeply thankful to **Dr. Mohammed Atef Mohammed El Taib Elazazy,** lecturer of General Surgery Faculty of Medicine, Ain Shams University, for her great help, outstanding support active participation and guidance.

I would like to express my hearty thanks to all my **Family** for thier support till this work was completed

AHMED HAMDY FATHY GAFAR

CONTENTS

LIST OF ABBREVIATIONS

Abb.		Full term
BCS	**:**	Breast Conserving Surgery
CT	**:**	Computed Tomography
DFS	**:**	Disease Free Survival
DMFS	**:**	Distant Metastasis Free Survival
FNA	**:**	Fine Needle Aspiration
HPF	**:**	High Power Field
HR	**:**	Hazard Ratio
LC	**:**	Local Control
LR	**:**	Local Recurrence
MDE12	**:**	Mediator Complex Subunit 12
MFA	**:**	Malignant Fibrous Histiocytoma
MPTB	**:**	Malignant Phyllodes Tumor of the Breast
MRI	**:**	Magnetic Resonance Imaging
NCCN	**:**	National Comprehensive Cancer Network
PT	**:**	Phyllodes Tumor
PTB	**:**	Phyllodes Tumor of the Breast
RT	**:**	Radiation therapy
SEER	**:**	Surveillance Epidemiology and End Result

List of abbreviations

TM	**:**	Total Mastectomy
UPS	**:**	Undifferentiated Pleomorphic Sarcoma
WHO	**:**	World health Organization
WLE	**:**	Wide Local Excision
RCT	**:**	Randomized Controlled Trial

LIST OF TABLES

LIST OF FIGURES

ABSTRACT

Background: Phyllodes tumors (PTs) are uncommon fibroepithelial breast tumors that are capable of a diverse range of biologic behaviors. In their least aggressive form, phyllodes tumors behave like benign fibroadenomas, although with a propensity to recur locally following excision without wide margins.

Aim of Work: Our study focused on local recurrence and various risk factors of phyllodes tumors of the breast through a meta-analysis.

Patient and Methods: This Review involved case-control studies, case report studies, and retrospective case follow-up evaluating local recurrence (LR) rates of unilateral or bilateral phyllodes tumors. phyllodes tumors of breast and assessing various risk factors for LR.

Results: Forty-eight studies compared the LR risk between Benign / malignant. There was significant higher in Malignant VS Benign regarding rate of local recurrence p-value <0.001. Pooling of data from twenty-three showed significant difference in the LR risk between patients who underwent breast conserving surgery (BCS) and those who had a mastectomy p-value 0.001.

Conclusion: The risk of LR was significantly increased from benign to borderline to malignant PTs, type of surgery, and surgical margin status may be risk factors for LR, while mitoses, tumor border, stromal cellularity, stromal atypia, stromal overgrowth, tumor necrosis had no difference regard increase risk for LR, Different management strategies could be considered for different PT grade.

Keywords: Phyllodes Tumors, Local Recurrence, breast tumors

INTRODUCTION

Phyllodes tumors of the breast are typically large, rapidly growing tumors that account for up to 1% of all breast neoplasms. The World Health Organization classifies phyllodes tumors into three histologic subtypes: benign, borderline, and malignant, based on stromal cellularity, stromal cell mitotic activity, stromal nuclear atypia, stromal overgrowth and type of borders (infiltrating or pushing) (Chao *et al*., 2019).

The term "phyllodes," which means leaf-like, describes the typical papillary projections that are seen on pathologic examination. Although they were originally called "cystosarcoma phyllodes" by Johannes Müller in 1838 (**Calhoun *et al*., 2014**).

Phyllodes tumors only occasionally have cystic components and are not true sarcomas by either cellular origin or biologic behavior. The terminology has since evolved, with over 60 synonyms having been applied to this entity before the term "phyllodes tumors" was adopted by the World Health Organization (**Tavassoli and Devilee, 2013**).

AIM OF THE WORK

This review focuses on local recurrence and various risk factors of phyllodes tumors of the breast through a meta-analysis.

REVIEW OF LITERATURE

❖ Pathophysiology of phyllodes tumer

- EPIDEMIOLOGY AND RISK FACTORS

Phyllodes tumors account for less than 1 percent of all breast neoplasms (**Geisler *et al*., 2011**). Given their rarity, epidemiologic data are scant. In a study from Los Angeles county over a 17-year period, the average annual incidence rate of malignant phyllodes tumors was 2.1 per million women, and the incidence was higher in Latina whites than in non-Latina whites, Asians, and African Americans (**Bernstein *et al*., 2011**).

The vast majority of phyllodes tumors occur in women, with a median age of presentation of 42 to 45 years (range 10 to 82 years). Higher-grade tumors are more common in older patients. In men, phyllodes tumors usually occur in association with gynecomastia (**Karim *et al*., 2019**).

Phyllodes tumors have been associated with Li-Fraumeni syndrome, a rare autosomal dominant condition that is characterized by the development of multiple tumors (**Birch *et al*., 2011**).

Pathophysiology of phyllodes tumer

Phyllodes tumor has a smooth, sharply demarcated texture and typically is freely movable. It is a relatively large tumor, with an average size of 5 cm (though lesions larger than 30 cm have been reported). The etiology of phyllodes tumors is unknown (**Parker et al., 2011**).

Because of limited data, the relative percentages of benign and malignant phyllodes tumors are not well defined. Reports have suggested, however, that about 85-90% of phyllodes tumors are benign and that approximately 10-15% are malignant (**Jones *et al*., 2015**).

Although benign phyllodes tumors do not metastasize, they have a tendency to grow aggressively and can recur locally. Like other sarcomas, malignant phyllodes tumors metastasize hematogenously. Unfortunately, the pathologic appearance of a phyllodes tumor does not always predict the neoplasm's clinical behavior; in some cases, therefore, there is a degree of uncertainty about the lesion's classification (**Parker et al., 2011**).

The characteristics of a malignant phyllodes tumor include the following:

- Recurrent malignant tumors seem to be more aggressive than the original tumor.
- The lungs are the most common metastatic site, followed by the skeleton, heart, and liver.
- Symptoms of metastatic involvement can arise from as early as a few months to as late as 12 years after the initial therapy.

- Most patients with metastases die within 3 years of the initial treatment.
- No cures for systemic metastases exist.
- Roughly 30% of patients with malignant phyllodes tumors die of the disease. **(Abe *et al*., 2011)**.

Although most phyllodes tumors are benign, it is nonetheless important not to underestimate the potential of these lesions for malignancy. Moreover, some juvenile fibroadenomas in teenagers can look like phyllodes tumors on histologic examination; however, they behave in a benign fashion similar to that of other fibroadenomas. The difficulty of distinguishing among fibroadenomas, benign phyllodes tumors, and malignant phyllodes tumors may be vexing for even the most experienced pathologist **(Yohe *et al*., 2012)**.

• CLASSIFICATION

World Health Organization divided phyllodes tumor into benign, borderline, and malignant categories based on the degree of stromal cellular atypia, mitotic activity per 10 high power fields, degree of stromal overgrowth (these three are main), tumor necrosis, and margin appearance (Tables 1, 2) **(Yohe *et al*., 2012)**.