



شبكة المعلومات الجامعية  
التوثيق الإلكتروني والميكروفيلم

# بسم الله الرحمن الرحيم



**MONA MAGHRABY**



شبكة المعلومات الجامعية  
التوثيق الإلكتروني والميكروفيلم



## شبكة المعلومات الجامعية التوثيق الإلكتروني والميكروفيلم



**MONA MAGHRABY**



شبكة المعلومات الجامعية  
التوثيق الإلكتروني والميكروفيلم

# جامعة عين شمس التوثيق الإلكتروني والميكروفيلم

## قسم

نقسم بالله العظيم أن المادة التي تم توثيقها وتسجيلها  
علي هذه الأقراص المدمجة قد أعدت دون أية تغييرات



## يجب أن

تحفظ هذه الأقراص المدمجة بعيدا عن الغبار



**MONA MAGHRABY**



# **Correlation between the prostate-specific antigen level and bone metastasis in prostate cancer. (Retrospective study)**

*Thesis*

for fulfillment of master degree in clinical oncology and nuclear medicine

**Presented by**

*Adel Hassan Mohamed*

*(M.B.,B.CH)*

**Supervised by**

**Prof. Dr. Tarek Hussein Kamel**

Professor of Clinical Oncology and Nuclear Medicine

Faculty of Medicine- Ain Shams University

**Assist. Prof. Nesreen Ahmed Mosalam**

Assist. Professor of Clinical Oncology and Nuclear Medicine.

Faculty of Medicine- Ain Shams University

**Dr. Sherif Hassanien Ahmed**

Lecturer of Clinical Oncology and Nuclear Medicine.

Faculty of Medicine- Ain Shams University

**Faculty of Medicine  
Ain Shams University**

**2020**

# Acknowledgment

## Thanks to Allah

*For Accomplishment of this work I wish to express my greatest gratitude to all who helped me to complete this work.*

*First and foremost, my thanks are directed to professor **Dr. Tarek Hussien Kamel** professor of clinical oncology and nuclear medicine. Faculty of medicine. Ain shams university for his unlimited help and continuous insistence on perfection. Without his continuous supervision, this thesis could not have achieved its present form.*

*It is a pleasure to express my deepest regards and gratitude to **DR. Nesreen Ahmed Mosalam**, Assistant professor of clinical oncology and nuclear medicine. Faculty of Medicine -Ain shams University for her sincere continuous help, fruitful suggestion and wise guidance created this thesis.*

*I'm greatly indebted to **Dr. Sherif Hassanien Ahmed** lecturer of clinical oncology and nuclear medicine. Faculty of medicine Ain shams University for his true advise, kind supervision and constant purposeful encouragement which provided me all facilities during the conduction of this work.*

*It is my pleasure to extend my obligation to all the staff of clinical oncology and nuclear medicine department, and to all patients included in this work wishing them a good quality of life.*

*Adel Hassan Mohamed*

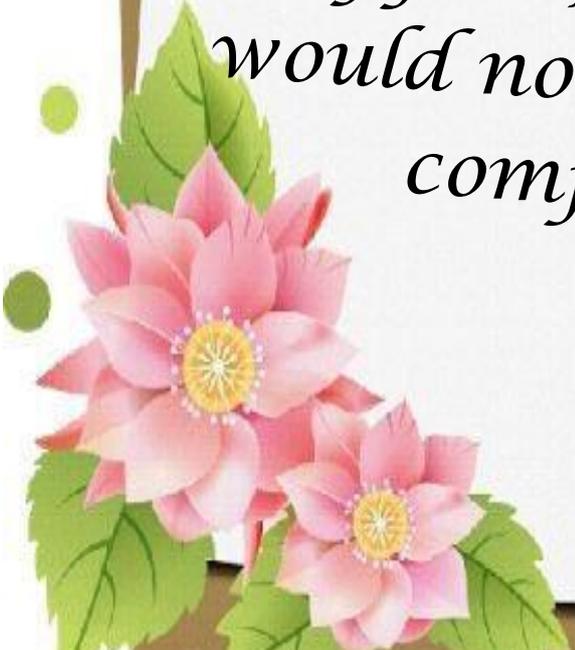
2020



*I would like to dedicate my effort in this  
thesis to:*

*My **parents** and **dear**  
**wife** for their endless  
support, help and  
encouragement.*

*Without their  
support, this work  
would not have been  
completed.*



# List of Content

<b>Content</b>	<b>Page</b>
<b>List of Abbreviations</b>	<b>I</b>
<b>List of Tables</b>	<b>II</b>
<b>List of Figures</b>	<b>III</b>
<b>Review of literature</b>	<b>1</b>
<b>Aim of the work</b>	<b>48</b>
<b>Patients And Methods</b>	<b>49</b>
<b>Results</b>	<b>52</b>
<b>Discussion</b>	<b>62</b>
<b>Summary</b>	<b>71</b>
<b>Conclusions</b>	<b>73</b>
<b>References</b>	<b>74</b>
<b>Arabic Summary</b>	

## List of abbreviations

<b>EPE</b>	Extra prostatic extension
<b>ASAP</b>	atypical small acinar proliferation
<b>BS</b>	Bone scan
<b>BM</b>	Bone metastasis
<b>DCE</b>	dynamic contrast-enhanced
<b>DRE</b>	Digital rectal examination
<b>ECE</b>	extracapsular extension
<b>ED</b>	ejaculatory ducts
<b>MRI</b>	magnetic resonance imaging
<b>MDCT</b>	multidetector CT
<b>PET</b>	positron emission tomography
<b>PIN</b>	prostatic intra-epithelial neoplasia
<b>PSA</b>	prostate-specific antigen
<b>PZ</b>	peripheral zone
<b>SV</b>	seminal vesicles
<b>SVI</b>	Seminal vesicle invasion
<b>TRUS</b>	Transrectal ultrasound
<b>TURP</b>	transurethral resection of the prostate
<b>TZ</b>	transition zone
<b>ECE</b>	extracapsular extension
<b>IGF</b>	insulin-like growth factor
<b>PCa</b>	Prostate cancer

## **List of Tables**

<b>No</b>	<b>Tables</b>	<b>Pages</b>
<b>1</b>	Relation between Age and bone metastasis	<b>53</b>
<b>2</b>	Relation between PSA total and bone metastasis	<b>54</b>
<b>3</b>	Relation between Gleason score and bone metastasis	<b>54</b>
<b>4</b>	Relation between two groups A & B	<b>55</b>
<b>5</b>	sensitivity and specificity of PSA cut values	<b>56</b>
<b>6</b>	sensitivity and specificity of PSA total and Gleason score as markers of metastatic PCa to bone.	<b>57</b>
<b>7</b>	the ROC curve for PSA total and Gleason score in the study patients	<b>58</b>
<b>8</b>	Correlation between age , PSA total and Gleason score	<b>61</b>
<b>9</b>	Various Asian studies	<b>64</b>
<b>10</b>	Various Indian studies	<b>66</b>

## List of Figures

No	Figures	Pages
<b>1</b>	Distribution regarding Cases and Deaths of the ten most common cancers for males in 2018	<b>1</b>
<b>2</b>	Global Maps Presenting the Most Common Type of Cancer Incidence in 2018 in Each Country among Men	<b>2</b>
<b>3</b>	Global Maps Presenting the Most Common Type of Cancer Mortality by Country in 2018 among Men	<b>2</b>
<b>4</b>	Number of new cases in 2018 in males of all ages. According to the National Population-Based Registry program of Egypt 2008-2011; incidence of PCa in Egypt is about 4.27%	<b>3</b>
<b>5</b>	Age-adjusted PCa mortality rates worldwide. Rates are age-adjusted for comparisons across countries and are presented per 100,000 in the population.	<b>4</b>
<b>6</b>	Anatomy of PCa	<b>11</b>
<b>7</b>	Simplified endocrinology of the prostate	<b>12</b>
<b>8</b>	Modified Gleason grading based on ISPU 2014	<b>14</b>
<b>9</b>	New grading system based on Gleason score	<b>14</b>
<b>10</b>	Evidence of extra prostatic extension with different magnification powers	<b>16</b>
<b>11</b>	Classical perineural invasion examples	<b>17</b>
<b>12</b>	Digital rectal examination	<b>20</b>
<b>13</b>	Prostate-specific antigen (PSA) density in the diagnostic algorithm of PCa.	<b>22</b>
<b>14</b>	Multiparametric MRI	<b>27</b>
<b>15</b>	Multiparametric MRI	<b>28</b>
<b>16</b>	using mpMRI as triage test	<b>32</b>

<b>No</b>	<b>Figures</b>	<b>Pages</b>
<b>17</b>	Patient 1 (a, b) and Pateint 2 (c, d)	<b>39</b>
<b>18</b>	number of patients with & without bone metastasis	<b>52</b>
<b>19</b>	Clustered column showed the number of patients in Group A and B above and below cut-off value	<b>55</b>
<b>20</b>	Shows ROC curve for PSA total	<b>58</b>
<b>21</b>	Shows ROC curve for gleason score	<b>59</b>
<b>22</b>	Shows ROC curve for both PSA total and gleason score	<b>60</b>

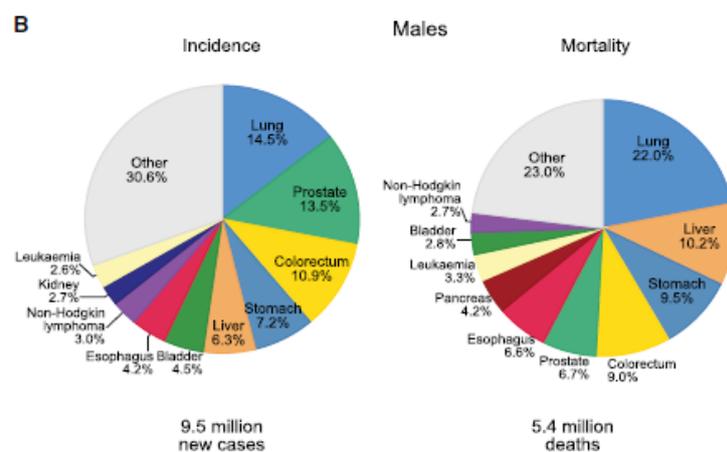
## Chapter 1

### Epidemiology and Risk Factors

Cancer is not one disease, but a heterogeneous cluster of malignancies. Even within one cancer type substantial variations exist, and prostate cancer (PCa) is no special case to that biological observation. Undoubtedly, disease heterogeneity is reflected by the diverse clinical courses of indolent, aggressive and lethal PCa .PCa is the second most commonly diagnosed cancer and the second leading cause of cancer death in males, after lung cancer (*Siegel et al., 2018*).

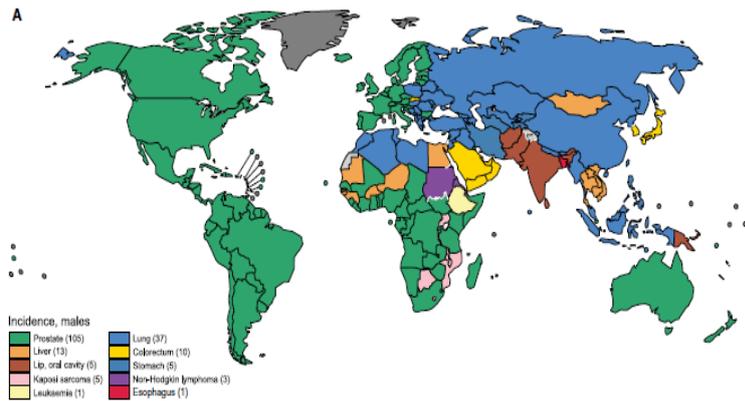
The Incidence of PCa varies greatly worldwide. There are many reasons as the incompletely known risk factors are affected by ethnicity, environment and geography, in addition to lack of proper documentation and registry in some developing countries (*Duggan et al., 2016*).

Bray et al, stated that worldwide the number of new cases diagnosed with PCa is 1,276,106 (7.1%) and the number of cancer deaths is 358,989 (3.8%)(figure 1) (*Bray et al., 2018*).



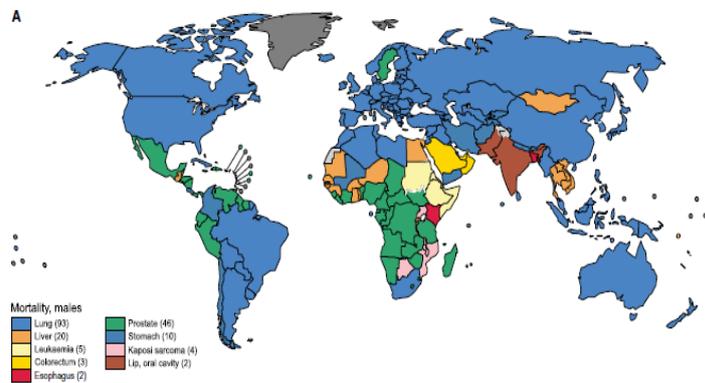
**Figure (1):** Distribution regarding Cases and Deaths of the ten most common cancers for males in 2018 (*Bray et al., 2018*).

PCa is the most common diagnosed cancer in more than 100 countries compared by lung cancer in thirty seven countries, and liver cancer in thirteen countries outstandingly in the Northern and Western Europe, Americas, Australia/New Zealand, and much of Sub-Saharan Africa (Figure 2) (*Bray et al., 2018*).



**Figure (2):** Global Maps Presenting the Most Common Type of Cancer Incidence in 2018 in Each Country among Men (*Bray et al., 2018*).

The incidence of PCa as well as the mortality rate from PCa in Middle East and North Africa region is likely expected to increase from more than 29 thousands in 2012 to more than 38 thousands in 2020 and from about 15 thousands in 2012 to about 20 thousands in 2020 respectively (Figure 3) (*Hilal et al., 2015*).

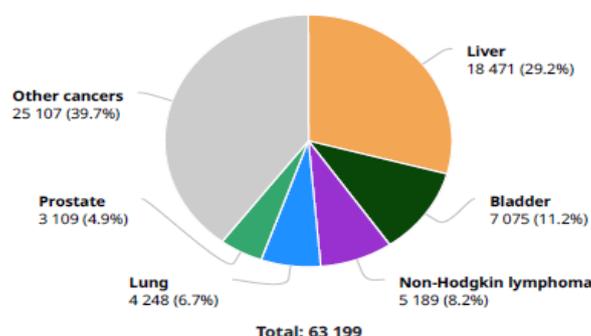


**Figure (3):** Global Maps Presenting the Most Common Type of Cancer Mortality by Country in 2018 among Men (*Bray et al., 2018*).

The different levels of awareness about PCa and prostate specific antigen (PSA) testing with urbanization and sedentary life are the main reasons for higher PCa mortality rates in developing countries (*Banerjee and Aaron, 2016*).

According to (*Globocan 2018*), incidence of PCa in Egypt in 2018 is 3109 (2.67%) that makes PCa the ninth between all cancers in Egypt. Also the number of patients who died from PCa is roughly 1237 patients (1.58%), and the 5-year prevalence among all ages is 6485 (12.91%) (*Bray et al., 2018*).

Although incidence rates are high in Northern and Western Europe (eg, Norway, Sweden, Ireland), Australia/ New Zealand, and North America (particularly in the United States), death rates distribution is different from those of incidence, with death rates elevated in the Sub-Saharan Africa regions (eg, Benin, Zambia, South Africa, and Zimbabwe) as well as the Caribbean (Jamaica, Barbados, and Haiti)(*Figure 4*) (*Siegel et al., 2018*)



**Figure (4):** Number of new cases in 2018 in males of all ages.

According to the National Population-Based Registry program of Egypt 2008-2011; incidence of PCa in Egypt is about 4.27% (*Ibrahim et al., 2014*).

Although PCa is a very common disease, its etiology is still not totally known. Ethnic and genetic predisposition somehow plays a role as

increasing the incidence of PCa among African men in the Caribbean and The United States (*Harris, 2015*).

### **Risk factors for PCa:**

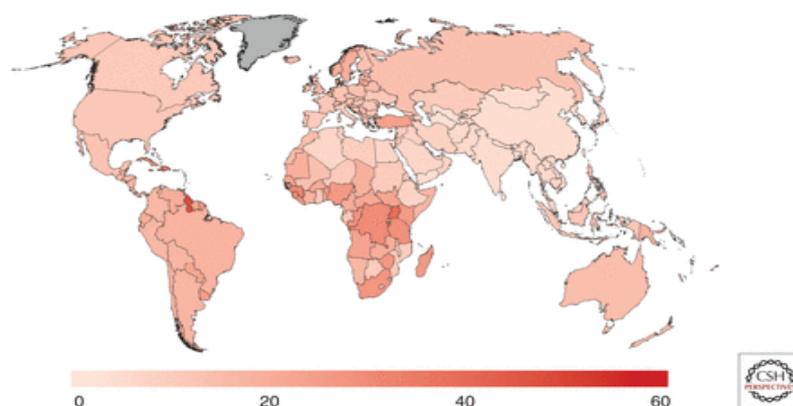
- **Old age.**

Age is one of the strongest associations with increased risk of PCa. It is uncommon for males younger than 40 years old to have PCa. Also, there is dramatic increase of PCa incidence rate after the age of 55 years old (*Torre et al., 2015*).

However, after the implantation of screening for PSA in developed countries, diagnosis of PCa is shifted to an earlier age with average of 66 years old (Figure 5) (*Tosoian et al., 2016*).

Besides that, early onset PCa has a different clinical phenotype and etiology (*Salinas et al., 2014*).

The practice of PSA screening results in a lead time of ~10 years because of detection of PCa before symptom onset. Following the implementation of PSA screening in the United States, the average age at PCa diagnosis shifted earlier and is currently 66 years of age (*Howlader et al. 2016*).



**Figure (5):** Age-adjusted PCa mortality rates worldwide. Rates are age-adjusted for comparisons across countries and are presented per 100,000 in the population. Gray, no data available. (*Globocan 2012*)