Dean of Graduate Studies Al-Quds University



Survival Analysis of the Registered Colorectal Cancer Cases in the Gaza Strip

Murad B. Alrun

MPH Thesis

Jerusalem-Palestine 1438/2017

Survival Analysis of the Registered Colorectal Cancer Cases in the Gaza Strip

Prepared by

Murad Basher Alrun

Bachelor of Nursing, Palestine College of Nursing, Gaza-Palestine

Supervisor: Dr. Khaled Ata Thabet

MD-PhD. Clinical Oncology-Cairo University

A Thesis Submitted in Partial Fulfillment of the Requirement for the Master Degree of Public Health/Health Management- Al-Quds University

Dedication

To my beloved parents who always give us the power, encouragement, and guidance for everything is good.

To my wonderful lovely wife Mona for her endless support, she is a continuous source of motivation, support, love, and hope.

To my amazing son Qais and beautiful daughter Mais who give me bright hope for tomorrow.

To my teachers in school, nursing college, and public health college for their efforts to be active person in our societies.

To my all friend and my all colleagues in the work.

To everyone had help me and contributed to finish this study.

Murad B. Alrun

Declaration
I certify that this thesis submitted for the degree of Master, is the result of my own research, except where otherwise acknowledged, and that this study (or any part of the same) has not been submitted for a higher degree to any other university or institution.
Signed:
Murad Basher Alrun
Date:

Acknowledgment

First and foremost I would like to express my gratitude to Allah -glorified and exalted be He-.

I deeply thank my supervisor Dr. Khaled Thabet who helped, advised, and contributed in each the study steps. Supervision was invaluable and even though he had busy work, he found time to the study.

I am grateful for Dr. Yehia Abed who contributed and extended his valuable assistance in the completion of this study.

My sincere thanks also go to Dr. Bassam Abu Hamad, Dr Khetam Abu Hamad, all academic staff, and employees at the School of Public Health for their help throughout my studying years. Also I would like to thank Dr. Sobhi Skaik for his valuable additions and remarks which enhance the study quality.

I would like to thank the amazing employees in the central archive at ministry of health for their kindly help in data collection process. Also special thanks to Mrs Haya Yaghi head officer of Cancer Registry in Gaza Strip for her kind help.

Also I would like to thank the wonderful staff at European Gaza Hospital, and Al-Shifa Hospital for their kindly help and facilitation.

Special thanks go to my friend Wesam Naser for his kind help along the way of doing my thesis.

I also would like to express my sincere thanks to work management at my work in Red Crescent Society for Gaza Strip for their kind help and encouragement throughout my study.

I would like to extend my special thanks to Dr. Mohammed Alrun for his encouragement and support of me throughout my study.

Last and not least, I express my very profound gratitude to my family and all my friends for providing me with unfailing support and continuous encouragement and through the process of researching and writing this thesis. This accomplishment would not have been possible without them.

Murad B. Alrun

Abstract

Colorectal Cancer (CRC) is the first major common cancer among men in Gaza Strip (GS) and it is considered the second common cancer after breast cancer for both sexes combined. Survival analysis for CRC cases is essential for monitoring and evaluation of health care system effectiveness in managing and fighting CRC. This non-concurrent prospective study was conducted to analyze the survival data for CRC cases who were diagnosed in the period 2008-2010, and to give estimates about overall survival rate, disease free survival rate, progression free survival. Beside exploring main factors may affect on survival rates for CRC in GS.

After some cases were excluded due to various causes, 207 cases were eligible for this study. The main source for data was the medical records for the cases, and data analysis was conducted by using SPSS program version 22. Kaplan-Meier method was used to provide overall survival estimates, survival estimates adjusted to selected prognostic factors and survival curves for subgroups, while the log rank test was used to assess survival differences between the subgroups. Cox regression survival analysis was used to examine the independent effect of study variables on survival data and to estimate the hazard ratio. Statistical significance was defined as P < 0.05. The study findings showed that CRC incidence rate in Gaza Strip (GS) was 14/100000 in the study period (2008-2010).

Findings regarding socio-demographic characteristics of study population revealed that the mean of age at diagnosis for cases was 59.6 years, incidence rate among male is slightly higher than female (Male:54.6%, female:45.6%), 16.4% of cases were unmarried at time of diagnosis, while data about education level and work were missed from the majority of medical records. All cases presented with signs and symptoms at time of diagnosis. The common signs and symptoms were bleeding per rectum and abdominal pain 63.3%, 35.3% from all cases respectively. The most common histological type was Nonmucinous adenocarcinomas which accounted 86.7%. More than two third of cases were diagnosed with low grade tumor (grades 1, 2), while more than the half of patients (61.6%) were diagnosed with advanced stages (III, IV). Left-sided colon is the most common site for developing CRC with 52.3% of all cases. It followed with rectal cancer with 25.9%, while right-sided colon accounted only 21.9%. The study revealed that 5-year observed overall survival rate, disease free survival rate, and progression free survival rate probabilities to be 45%, 59% and 19% respectively.

According univariate analysis (log rank test) survival rate was significantly affected by comorbidity status (P-value: 0.040), smoking (P-value: 0.002), stage at diagnosis (P-value< 0.001), tumor grade (P-value=0.41), tumor site (P-value=0.004), and treatment type (P-value=0.001). While the multivariate analysis (Cox regression) showed that only three prognostic factors had statically significant effect which were stage at diagnosis (P-value<0.001, 95%CI 2.673-9.034), Co-morbidity status (P-value=0.031, 95%CI, 0.434-0.962) and tumor site (P-value0.018, 95%CI, 0.373-0.912). Factors such as main treating hospital, diagnostic delay, treatment delay and place, sites of distant metastasis, gender, age, residency, or family history of cancer were found to be without statically significant effect on survival data for CRC cases in GS.

According the current study results, 5-years survival estimates in GS is poorer than the estimates in the developed countries, which were between 60-70% there. However, they are in line with most the estimates in the Arabic countries where the survival rates between 30-50%.

The study concluded that the absence of a national CRC screening program, poor public awareness and official attention, and absences/shortage of many cancer services in GS may be the main causes for poor CRC survival estimates. Decreasing gaps in the last three issues may contribute to enhance the survival data, prevent premature deaths, and promote the quality of life for CRC cases in GS.

Table of content

Dedication	i
Declaration	ii
Acknowledgment	iii
Abstract	iv
Table of content	vi
List of tables	X
List of figures	X
List of Annexes	xi
List of Abbreviation	xii
Chapter (1): Introduction	1
1.1 Background	1
1.2 Research problem	2
1.3 Justification of the study	3
1.4 Study objectives	4
1.5 Research question	4
1.6 Study context	5
1.7 Operational definition	8
Chapter (2) Literature review	10
2.1Conceptual Frame work	10
2.1.1 Patient Related Factors	11
2.1.2 Tumor Related Factors	13
2.1.3 Healthcare Related Factors	14
2.1.3.1 Diagnostic related factors	14
2.1.3.2 Treatment related factors	14
2.1.4 Overall Survival	15
2.1.5 Non-Metastatic Cases	15
2.1.6 Disease free survival (DFS) rate	15
2.1.7 Metastatic Cases	15
2.1.8 Progression free survival rate	15
2.2 Literature review	15
2.2.1 Anatomy of the colon and the rectum	15

2.2.2 Colorectal cancer definition	16
2.2.3 Clinical manifestation of colorectal cancer	16
2.2.4 Risk factors for colorectal cancer	16
2.2.5 Staging of colorectal cancer	17
2.2.9 Treatment	18
2.2.10 Burden of colorectal cancer	19
2.2.10.1 Global burden of colorectal cancer	19
2.2.10.2 Burden of colorectal in Eastern Mediterranean Region (EMRC)) 19
2.2.10.3 Burden of colorectal in Palestine	20
2.2.11 Colorectal cancer survival	20
2.2.12 Variances in colorectal cancer survival over the world	21
2.2.13 Factors affecting survival rate for colorectal cancer	22
2.2.13.1 Patient Related Factors	23
2.2.13.2 Tumor Related Factors	27
2.2.13.3 Healthcare Related Factors	28
2.2.13.3.1 Diagnostic related factors	28
2.2.13.3.2 Treatment related factors	29
Chapter (3) Methodology	32
3.1 Study design	32
3.2 Study population	32
3.3 Study setting	32
3.4 Study period	33
3.5 Eligibility criteria	33
3.5.1 Inclusion	33
3.5.2 Exclusion	33
3.6 Study instruments	34
3.7 Scientific rigor	34
3.7.1Validity	34
3.7.2 Reliability	35
3.8 Ethical and administration consideration	35
3.9 Pilot study	36
3.10 Data collection	36
3.11 Data entry and analysis	37

3.12 Limitation of the study	38
Chapter (4) Results and Discussion	39
4.1 Descriptive analysis	39
4.1.1 Socio-demographic characteristics of study population	39
4.1.1.1 Age at diagnosis	39
4.1.1.2 Gender	40
4.1.1.3 Marital Status	42
4.1.1.4 Residency	42
4.1.1.5 Work	43
4.1.1.6 Education	43
4.1.2 Patient medical profile	44
4.1.2.1 Co-morbidity	46
4.1.2.2 History of cancer	46
4.1.2.2 Obesity status	46
4.1.2.3 Smoking	47
4.1.3 Tumor characteristics	47
4.1.3.1 Histological type	47
4.1.3.2 Tumor grade	48
4.1.3.3 Stage at diagnosis	48
4.1.3.4 Tumor site	48
4.1.3.5 Distant metastasis status	51
4.1.4 Medical management of colorectal cancer in the Gaza Strip	52
4.1.4.1 Diagnostic process	52
4.1.4.2 Treatment process	55
4.1.4.2.1 Treatment types	55
4.1.5 The overall observed survival rate	57
4.2 Inferential analysis	58
4.2.1 Observed survival estimates by using Kaplan-Meier method	58
4.2.1.1 Overall survival estimates	58
4.2.1.2 Disease Free Survival (DFS) estimates for non-metastatic ca	ses 60
4.2.2 Effect of patient related factors on overall survival rate	62
4.2.2.1 Survival analysis according age group	62
4.2.2.2 Survival analysis according Gender	65

4.2.2.3 Survival analysis according to Marital Status	66
4.2.2.4 Survival analysis according to place of residency for all study cases	67
4.2.2.5 Survival analysis according co-morbidity status of cases.	68
4.2.2.6 Survival analysis according Patient's family history of cancer	69
4.2.2.7 Survival analysis according Body Mass Index-BMI of the cases.	70
4.2.2.8 Survival analysis according smoking status of the cases	72
4.2.3 The effect of tumor related factors on survival estimates	73
4.2.3.1 Survival analysis according stage at diagnosis	73
4.2.3.2 Survival analysis according tumor grade	74
4.2.3.3 Survival analysis according tumor site.	76
4.2.3.4 Survival analysis according distant metastasis sites	77
4.2.4 The effect of healthcare related factors on survival estimates	78
4.2.4.1 Survival analysis according main treating hospital.	78
4.2.4.2 Survival analysis according diagnostic delay.	80
4.2.4.3 Survival analysis according the main treatment type.	82
4.1.4.4 Survival analysis according surgical intervention place	83
4.2.4.5 Survival analysis according surgery delay.	84
4.2.4.6 Survival analysis according chemotherapy place.	85
4.2.4.7 Survival analysis according chemotherapy delay	86
4.2.5 Cox Regression survival analysis	87
Chapter (5) Conclusion and Recommendation	90
5.1 Conclusion	90
5.2 Recommendation	92
5.2.1 The study Recommendation	92
5.2.2 Recommendation for further research	92
References	93
Annex (1): Palestine map	106
Annex (2): Gaza strip map	107

List of tables

Table (3.1) Distribution of medical records for all study cases according their Location $\dots 37$
Figure (4.1): Distribution of colorectal cancer cases according age at diagnosis group in GS (2008-2010)
Table (4.1): Socio-demographic characteristics of study population
Table (4.2): Incidence rate for study population according Gaza Governorates
Table (4.3): Distribution of the study cases according selected medical profile items 45
Table (4.4) Distribution of the study cases according selected tumor characteristics 50
Table (4.5) Distribution of CRC cases (2008-2010) according distant metastasis status 52
Table (4.6) : Distribution of the study cases according signs and symptoms at diagnosis. $.53$
Table (4.7): Distribution of the study cases according treatment process
Table (4.8) Calculation of observed overall survival rate for the entire study population 57
Table (4.9): Kaplan-Meier survival analysis for all study cases/observed survival rate 59
4.2.1.3 Progression Free Survival (PFS) estimates for metastatic cases
Table (4.11): Kaplan-Meier survival analysis according selected tumor related factors 74
Table (4.12): Kaplan-Meier survival analysis according healthcare related factors 79
Table (4.13): Cox regression survival analysis of colorectal cancer in the Gaza Strip (2008-2010)
List of figures
Figure (2.1) Conceptual Framework - Self Developed
Figure (2.1) Conceptual Framework - Self Developed
Figure (2.1) Conceptual Framework - Self Developed
Figure (2.1) Conceptual Framework - Self Developed
Figure (2.1) Conceptual Framework - Self Developed
Figure (2.1) Conceptual Framework - Self Developed
Figure (2.1) Conceptual Framework - Self Developed
Figure (2.1) Conceptual Framework - Self Developed

Figure (4.11): Kaplan-Meier survival curves by Body Mass Index-BMI7
Figure (4.12): Kaplan-Meier survival curves by smoking status
Figure (4.13): Kaplan-Meier survival curve according satge at diagnosis
Figure (4.14): Kaplan-Meier survival curves according tumor grade
Figure (4.15): Kaplan-Meier survival curves according tumor site
Figure (4.16): Kaplan-Meier survival curves according distant metastasis sites
Figure (4.17): Kaplan-Meier survival curve according main treating hospital for cases 80
Figure (4.18): Kaplan-Meier survival curves for cases according diagnostic delay 82
Figure (4.19): Kaplan-Meier survival curves for study cases by treatment type
Figure (4.20): Kaplan-Meier survival curves for cases according surgical intervention place.
Figure (4.21): Kaplan-Meier survival curves for cases according surgery delay 8.
Figure (4.22): Kaplan-Meier survival curves for cases according chemotherapy place 8
Figure (4.23): Kaplan-Meier survival curves for cases according chemo-therapy delay 8
List of Annoyos
List of Annexes
Annex (1): Palestine map

List of Abbreviation

ACS American Cancer Society

CBC Complete Blood Cell

CRC Colorectal Cancer

CT Computed Tomography

CEA Carcinoembryonic Antigen

DFS Disease Free Survival

DRE Digital Rectal Examination

EGH European Gaza Hospital

FAP Familial Adenomatous Polyposis

GG Gaza Governorates

GS Gaza Strip

HNPCC Hereditary Non-Polyposis Colorectal Cancer

IARC International Agency for Research on Cancer

MOH Ministry of Health

MRI Magnetic Resonance Imaging

NCI National Cancer Institute (American)

NGOs Non Governmental Organizations

NIH National Institutes of Health (American)

OS Overall Survival

OECD Organisation for Economic Co-operation and Development

PCR Palestinian Cancer Registry

PFS Progression Free Survival

PHIS Palestinian Health Information System

RSPH Rantesi Specialist Pediatric Hospital

SoP State of Palestine

TNM Tumor size, Lymph node, Metastasis

UK United Kingdom

United Nations Relief and Works Agency for the Refugee of Palestine in the Near East. UNRWA

USA United States of America

Palestine News & Information Agency West Bank WAFA

WB West bank

World Health Organization WHO