

Evaluation of Charlson Co-morbidity Index and Radical Cystectomy Outcomes

Thesis

***Submitted for Partial Fulfillment for the Master Degree
In Urology***

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Acknowledgement

*First and foremost, all thanks and gratitude to **GOD**, most gracious and most merciful.*

*I would like to express my deepest gratitude and sincere thanks to **Prof. Dr./Amr Lotfy**, Professor of Urology, Faculty of Medicine, Cairo University, for his continuous guidance and valuable advice for enriching this work. I appreciate his great support for me, which has given me a powerful push helping this work to come to reality.*

*I am extremely grateful to **Dr. / Amr Fayad**, Assistant Professor of Urology, Faculty of Medicine, Cairo University, for his continuous guidance and valuable suggestions, saving no effort or time to make this work better.*

*I would like to express my highest appreciation to **Dr./ Ismail Rady**, Lecturer of Urology, Faculty of Medicine, Cairo University, for his enthusiastic cooperation, assistance and valuable efforts during the whole work without which, it wouldn't have been a reality.*

*My deepest gratitude to **My Parents and My Wife** for their support and encouragement throughout my life and for providing me the environment needed for concentration and progress.*

ABSTRACT

The probable value of CCI and ACCI in assessing overall health before recommending and proceeding with surgery, rather than age alone. Chronological age alone may not always reflect the postoperative outcome of surgery. CCI and ACCI include in their calculation a few co-morbid conditions that we did not encounter in our patients (namely AIDS, lymphoma and leukemia). This might have affected the CCI and ACCI of our patients.

Key words

Charlson _ cystectomy _ outcomes

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List of Abbreviations

ACCI	Age-adjusted Charlson Co-morbidity Index
ACE-27	Adult Co-morbidity Evaluation-27
BC	Bladder Cancer
BCSS	Bladder Cancer Specific Survival
BMI	Body Mass Index
CAD	Coronary Artery Disease
CCI	Charlson Co-morbidity Index
CIRS	Cumulative Illness Rating Scale
COPD	Chronic Obstructive Pulmonary Disease
CRF	Chronic Renal Failure
CTCAE	Common Terminology Criteria for Adverse Events
CUH	Cairo University Hospital
DM	Diabetes Mellitus
EBL	Estimated Blood Loss
EMR	Electronic Medical Records
EPC	Early Post-operative Complication
KFI	Kaplan-Feinstein Index
ICED	Index of Coexistent Disease
IDS	Index of Disease Severity
IPI	Index of Physical Impairment
IT	Information Technology
HTN	Hypertension
LOS	Length of Stay
NCI SEER	National Cancer Institute Surveillance Epidemiology and End Results
NIH	Nasser Institute Hospital
NSQIP	National Surgical Quality Improvement Program
OS	Overall Survival
PVD	Peripheral Vascular Disease
RC	Radical Cystectomy
SCC	Squamous Cell Carcinoma
TCC	Transitional Cell Carcinoma

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Introduction

Bladder cancer (BC) accounts for 3% of all malignancies. In the US, it was the second most common urological cancer with an estimated 68,810 new cases and 14,100 deaths in 2008 (*Jamel et al., 2008*). Fifteen percent to 30% of diagnosed patients will have muscle invasive BC ($\geq T2$) (*Lerner et al., 1992*). Radical cystoprostatectomy in males and anterior exenteration in females, coupled with en bloc pelvic lymphadenectomy remain the standard surgical approaches to muscle-invasive BC in the absence of metastatic disease (*Stein et al., 2001*).

Potential complications of radical cystectomy (RC) include major and minor morbidity as well as mortality. The morbidity associated with RC may be related to the ablative part of the procedure (cystectomy and lymphadenectomy), or complications resulting from use of segments of the gastrointestinal tract for urinary tract reconstruction or diversion after RC (*Skinner and Kaufman, 1980*).

Operative mortality for RC has been shown to be between 1% and 3% in most modern series. The overall complication rate after RC and urinary diversion may be as high as 25% to 35% (*Donat et al., 1999*).

This is a direct result of the fact that BC patients are more likely to present with significant co-morbidity because of

their advanced age at diagnosis and association with cigarette smoking (*Bjerregaard et al., 2006*).

In a SEER database review, researchers showed that 69.9% of bladder cancer patients were 65 years or older (*Yancik, 1997*). Also in a retrospective study, older and sicker patients were more likely to present with extravesical disease at time of RC (*Koppie et al., 2008*).

A number of studies have shown a strong correlation between age or co-morbidity and outcomes of RC namely a significantly lower rate of progression-free survival for older patients and higher co-morbidity. Elderly and sick patients with advanced disease are often not considered for the most aggressive cancer therapies that are very much recommended for their malignancy. Consequently, the significance of objectively and consistently quantifying co-morbidity is being recognized (*Nilesen et al., 2007*). A plethora of co-morbidity illness scales were found useful in patient stratification in relation to aggressive treatment tolerance. However, none of such scales was widely integrated into clinical practice to help making aggressive treatment decisions in this subset of older and sicker patients.

The Charlson Co-morbidity Index (CCI) was developed in 1987 based on 1-year mortality data from internal medicine

patients admitted to a New York Hospital and was initially validated within a cohort of breast cancer patients. The aim was to evaluate prognosis based on age and co-morbid conditions. It encompasses 19 medical conditions weighted 1–6 with total scores ranging from 0–37 with additional points added for age. With each increased level of the co-morbidity index the cumulative mortality attributable to co-morbid disease increased in a step-wise fashion (*Hall et al., 2004*).

Aim of Work

We aim to recognize the impact of age and co-morbidity on early outcome of RC patients, using the CCI to quantify preoperative co-morbidity. We also aim at identifying an association between clinicopathologic and treatment characteristics of RC patients with different CCI risk subgroups.

Bladder Cancer

BC constitutes about 4% of all cancers in west. It is the second most common malignancy in the urinary tract. It is the fourth most common cancer in men as it accounts for about 6.5% of all men cancer. In women it is the ninth most common cancer accounting for about 2.5% of women cancer (**Greenlee et al., 2000 and Jemal et al., 2005**).

In Egypt, bladder cancer accounted for up to 33% of malignant tumors registered in 1980 at the registry of the National Cancer Institute in Cairo. According to **Ibrahim and Elsebai (1983)**, it is the most frequent malignancy in males (46% of male malignancy), and ranks after breast cancer in females (16% of female malignancy) (**Ibrahim and Elsebai, 1983**).

Bladder cancer is generally a disease of middle-aged and elderly people as it is less common in persons younger than the age of 50 (**Lynch and Cohen, 1995**).

Bladder cancer has a more aggressive variant in elderly people, being relatively at an advanced stage at diagnosis (for both social reasons [patient and medical provider driven] and biologic reasons [such as impaired host defenses in the elderly]). Also it appears that less aggressive therapies are not offered to elderly patients due to a combination of the above

factors (**Linn et al, 1998**), Nevertheless, younger patients appear to have a more favorable prognosis because they present more frequently with superficial, low-grade tumors; however, the risk for disease progression is the same, grade-for-grade, in younger patients as in older ones (**Wan and Grossman, 1989**).

Bladder cancer has different histological patterns, where in the US about 90% is transitional cell carcinoma (TCC) (**Epstein et al, 1998**).

But there is a considerable variation in the pathological patterns noted in different parts of the world. For instance, squamous cell carcinoma (SCC) accounts to as many as 75% in Egypt's bladder cancer statistics (**El-Bolkainy et al., 1981**), compared to U.S. incidence which is less common as it ranged between 3% to 7% (**Hamid et al., 2003**).

About 80% of SCCs in Egypt are associated with chronic infection with *schistosoma haematobium*. These cancers occur in patients who are, on the average, 10 to 20 years younger than patients with TCC (**Ghoneim and Awad, 1980**).

There are also rare variants of bladder cancer as adenocarcinoma (less than 2% of primary bladder cancers) and urachal carcinoma (**Lynch & Cohen, 1995 and Mostofi, 1954**).

Radical Cystectomy

RC is the standard and most definitive form of therapy for high-grade, invasive BC. Improvement in anesthesia and postoperative management greatly enhanced the outcomes of RC. Also, lower urinary tract reconstruction, particularly orthotopic diversion, has been a major component in enhancing the quality of life of patients requiring cystectomy. The first cystectomy was performed in the late 1800s, but in 1926 Young and Davis indicated a high mortality rate and poor success made cystectomy unjustified. In 1939 a mortality rate of 34.5% was reported by Hinman (**Hinman, 1939**).

An early series of 250 cystectomy patients demonstrated high incidence of local invasion, prompting aggressive surgical therapy in those patients who underwent cystectomy. Anterior exenteration with vaginectomy and salpingo-oophrectomy was common. Improvements in surgical anesthetic techniques as well as perioperative care have reduced the mortality rate of radical cystectomy to 1% to 3% in most contemporary series. The complications of cystectomy range from 25% to 35%, including a wound complication rate of 10% in the form of infection or dehiscence (**Hendery, 1986**).

RC is a major surgery and with it significant morbidity may happen. Urologists should be familiar with the prevention, presentation and treatment of the major causes of morbidity and mortality associated with RC and lower urinary tract reconstruction. Complications can be minimized with strict devotion to proper surgical technique and attention to detail in the perioperative period. Thus, the procedure is complex with the potential for both short and long-term complications.

There is abundant evidence that RC for bladder malignancies and pelvic exenteration for primary rectal cancer and cervical cancer can lead to meaningful long-term survival. The success of RC or pelvic exenteration is highly dependent on good patient selection where an en-bloc resection may result in prolonged disease-free survival. In recent times the morbidity and mortality of this operation has decreased so that palliative exenteration has a role to help improve quality of life for this difficult group of patients (*Buscarini M et al, 2007*).

Complications of Radical Cystectomy [Table1]:

The potential complications of RC include major and minor morbidity as well as mortality (*Skinner and Kaufman, 1980*).

Complications are directly related to the type of urinary diversion, patient age, tumor stage and previous morbidity. The
