Enhanced Recovery after Surgery (ERAS) Protocols versus Standard Care in Perioperative Management of Radical Cystectomy with Urinary Diversion

Thesis

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List of Abbreviations

Abb.	Full term
Ab	*Antibiotic*
AMH	*Asymptomatic Microscopic Hematuria*
AMP	*Antimicrobial Prophylaxis*
ASA	*American Society of Anaesthesiology*
AUS	*Abdominal Ultrasound*
BCG	*Bacillus Calmette-Guérin*
BMI	*Body Mass Index*
BP	*Blood Pressure*
CI	*Carbohydrate Intake*
CIS	*Carcinoma in Situ*
CVP	*Central Venous Pressure*
DVT	*Deep Vein Thrombosis*
EDA	*Epidural Anaesthesia*
EGF	*Epidermal Growth Factor*
EOF	*Early Oral Feeding*
ERAS	*Enhanced Recovery after Surgery*
EUA	*Examination under Anesthesia*
GDFT	*Goal-Directed Fluid Therapy*
HPV	*Human Papilloma Virus*
LMWH	*Low-Molecular Weight*
LOS	*Length of Hospital Stay*
MBP	*Mechanical Bowel Preparation*
MIBC	*Muscle-Invasive Bladder Cancer*
NCI	*National Cancer Institute*
NG	*Nasogastric*
NGT	*Nasogastric Tube*
NMIBC	*Non-Muscle-Invasive Bladder Cancer*

List of Abbreviations (Cont...)

Abb.	Full term
NSAID	*Non-Steroidal Anti-Inflammatory Drugs*
OP	*Outpatient*
PE	*Pulmonary Embolism*
PO	*Per Os (Oral)*
POD	*Postoperative Day*
PONV	*Post-Operative Nausea and Vomiting*
PPI	*Proton Pump Inhibitor*
Rb	*Retinoblastoma*
RC	*Radical Cystectomy*
RCT	*Randomized Controlled Trials*
SCC	*Squamous Cell Carcinoma*
SPSS	*Statistical Package for Social Science*
T9-T11	*Thoracic Vertebra 9–11.*
VAS	*Visual Pain Scale*

ABSTRACT

Background: Bladder cancer is the ninth most common cancer worldwide, with an estimated 430 000 new cases in 2012. Bladder cancer has more than 130,000 deaths per year worldwide, with an estimated male: female ratio of 3.8:1.0.

Aim of the Work: to examine the current evidence for ERAS in preoperative, intraoperative and post-operative setting of care for RC patients, to propose ERAS evidence-based protocol for patients undergoing Radical Cystectomy in Egypt environment and to compare the effectiveness of ERAS versus standard care on perioperative outcomes after cystectomy including Length of Hospital Stay,bowel movement, Complications and Readmission Rate in 30Day.

Patients and Methods: This is a prospective randomized comparative study done at the urology departments of Ain Shams University and Nasser institute for research and treatment in 2018. Forty patients were included in this study who were indicated For Radical Cystectomy. They were recruited and randomized in two groups: Group A: where they followed enhanced recovery after Surgery protocols and Group B: where they followed the the classic pre-operative and post-operative protocols.

Results: We finished to that Enhanced recovery after surgery (ERAS) protocols in radical cystectomy is safe and not associated with any increase in intraoperative and post-operative complications compared to standard protocol. It is associated with reductions in the length of hospital stay, time to return to full diet, time to flatulence, time for defecation and pain post-operative. There is no difference in 30 day readmission rate between ERAS and Standard Care. Our prospective randomized controlled trial covers most of the items recommended for ERAS excluding the use of a laparoscopic or robotic approach, Audit, and use of alvimopan, a peripherally acting μ-opioid antagonist, which is not available in Egypt. Our study reveals many issues that need to be considered when designing a larger more powered study.

Conclusion: Enhanced recovery after surgery (ERAS) protocols in radical cystectomy is safe and not associated with any increase in intraoperative and post-operative complications compared to standard protocol. It is associated with reductions in the length of hospital stay, time to return to full diet, time to flatulence, time for defecation and pain post operative. There is no difference in 30 day readmission rate between ERAS and Standard Care.

Keywords: *Enhanced Recovery after Surgery - Radical Cystectomy - Standard Care*

INTRODUCTION

Bladder cancer is the ninth most common cancer worldwide, with an estimated 430,000 new cases in 2012 ***(Antoni et al., 2017).***

Bladder cancer has more than 130,000 deaths per year worldwide, with an estimated male: female ratio of 3.8: 1.0 ***(Ploeg et al., 2009).***

At the initial diagnosis of bladder cancer, 70% of cases are diagnosed as non-muscle-invasive bladder cancer (NMIBC) and approximately 30% as muscle-invasive bladder cancer (MIBC). 57% of Patients treated with radical cystectomy (RC) had muscle invasion at presentation while 43% had been initially diagnosed with NMIBC that progressed to invasive disease ***(Vaidya et al., 2001).***

In Egypt, bladder cancer has been the most common cancer during the past 50 years. In 2002, Egypt's world-standardized bladder cancer incidence was 37/ 100,000, representing approximately 30,000 new cases each year. Data from the National Cancer Institute (NCI) in Cairo showed that patients diagnosed in 2005 had six fold higher odds of developing transitional cell carcinoma compared with patients diagnosed in 1980. The first half of the study period at the NCI-Cairo was dominated by squamous cell carcinoma (SCC), (proportion of tumors that were Squamous cell carcinoma:

78%, 83% and 55% for 1980, 1983 and 1990 respectively). Subsequently, TCC replaced squamous cell carcinoma as the more prevalent histopathological type. In 1994, 2001, and 2005 SCC represented 39%, 42%, and 27% of all diagnosed bladder tumors, respectively. Declining SCC rates and rising TCC rates suggest possible changes in exposures related to bladder cancer induction; with reductions in schistosomal infection and increases in cigarette smoking and chemical exposures related to occupation ***(Felix et al., 2008).***

Despite improvements in surgical technique, anesthesia and perioperative care, radical cystectomy is still associated with greater morbidity and prolonged in-patient stay after surgery than other urological procedures. Overall complication rates have been reported as high as 64% at 90 days, with an average in-patient stay of 17.4 days ***(Novotny et al., 2007).***

In recent years, a shift has occurred in the perioperative management of patients undergoing cystectomy with urinary diversion. The previous tradition-based, non-standardized components of perioperative care, which included different forms of bowel preparation, preoperative fasting routines, gastrointestinal decompression, and postoperative bowel rest, have evolved in the past decades into clinical pathways that attempt to minimize variation in care. Commonly referred to as enhanced recovery after surgery (ERAS) pathways, these steps can accelerate postoperative convalescence, decrease costs, and maintain quality ***(Geltzeiler et al., 2014).***

ERAS programs are evidence-based protocols designated to standardize medical care, improve outcomes and lower healthcare costs. In 2002, Kehlet and Wilmore introduced the concept of accelerated post-operative convalescence of patients using new fast track approaches ***(Kehlet et al., 2002).***

ERAS protocols aim to relieve the surgical stress response and to minimize end-organ dysfunction through integrated preoperative, intra-operative and post-operative pathways. The ERAS society has established several protocols for major colorectal and pelvic surgeries. The use of ERAS pathways has proven to reduce care time by more than 30% and post-operative complications by up to 50 % ***(Varadhan et al., 2010).***

AIM OF THE WORK

Radical cystectomy is an extremely morbid operation. Thus, there appears to be a high potential for reducing morbidity associated with the procedure. Decreasing surgical stress by utilization of ERAS provides a reasonable avenue for achieving this goal. The majority of recommendations for RC ERAS protocols are based on extrapolation from colorectal surgery protocols. Currently, low level of evidence exists directly from RC studies ***(Cerantola et al., 2013).***

So I aim from this thesis to examine the current evidence for ERAS in preoperative, intraoperative and post-operative setting of care for Radical Cystectomy patients, to propose ERAS evidence-based protocol for patients undergoing Radical Cystectomy in Egypt environment and to compare the effectiveness of ERAS versus standard care on perioperative outcomes after cystectomy including Length of Hospital Stay, bowel movement, Complications and Readmission Rate in 30Day.

Chapter 1

ANATOMY OF THE URINARY BLADDER

Anatomic Relationships

When filled, the bladder has a capacity of approximately 500 mL and assumes an ovoid shape. The empty bladder is tetrahedral and is described as having a superior surface with an apex at the urachus, two inferolateral surfaces, and a posteroinferior surface or base with the bladder neck at the lowest point ***(Brooks et al., 2007).***

The urachus anchors the bladder to the anterior abdominal wall. There is a relative paucity of bladder wall muscle at the point of attachment of the urachus, predisposing to formation of diverticula. The urachus is composed of longitudinal smooth muscle bundles derived from the bladder wall. Near the umbilicus, it becomes more fibrous and usually fuses with one of the obliterated umbilical arteries. Urachal vessels run longitudinally, and the ends of the urachus must be ligated when it is divided. An epithelium-lined lumen usually persists throughout life and uncommonly gives rise to aggressive urachal adenocarcinomas ***(Begg, 1930).*** In rare instances, luminal continuity with the bladder serves as a bacterial reservoir or results in an umbilical urinary fistula ***(Brooks et al., 2007).***