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Influence of perioperative nutritional support on recovery and complications following radical cystectomy and urinary diversion

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Abstract
Radical cystectomy (RC) with pelvic lymph node dissection (PLND) and urinary diversion is the preferred treatment for T_2-T_4a N0M0 muscle-invasive bladder cancer, BCG-refractory, very-high-risk non-muscle-invasive bladder cancer (NMIBC), BCG-relapsing, and BCG-unresponsive NMIBC, and bacillus of Calmette-Guérin (BCG)-responsive NMIBC. Nevertheless, this procedure continues to be categorized by a high incidence of perioperative complications, regardless of whether it is performed using a laparotomic or minimally invasive approach. Overall complications are encountered by up to 64% of RC patients. The preoperative nutritional status of patients is one of the emerging factors that may influence their rehabilitation after this surgery. Patients who are at malnutrition risk are more susceptible to post-surgical complications following major urological surgery. Additionally, adverse overall survival and ninty-day mortality are significantly predicted by nutritional status prior to RC, which is determined by evaluation of preoperative body mass index, serum albumin, and weight loss. To enhance perioperative care, pathways OF enhanced recovery after surgery (ERAS) have been implemented in the field of urology. Specialized immunonutrition (SIM) beverages, which are intended to enhance the immune function of patients, are included in these protocols and have been shown to decrease complications following RC, particularly infections. SIM beverages are composed of standard nutrition preparations that have been supplemented with specific nutrients, involving arginine, omega-3 fatty acids, and glutamine. Even though SIM has been demonstrated to enhance the host immune response, modulate inflammatory response, and enhance protein synthesis following surgery, its function through ERAS pathway following RC remainders uncertain.
This review article aims to highlight effect of perioperative nutritional optimization on post operative complications incidence, particularly wound related complications in cases had RC and ileal conduit urinary diversion.

Keywords: Perioperative, nutritional support, recovery, complications, radical cystectomy, urinary diversion

Introduction
Urothelial carcinoma of the bladder (UCB) is 5th most prevalent cancer overall and 4th most common cancer in men, as per 2019 statistics published by American Cancer Society. In 2019, it is anticipated that there will be about 80,470 new cases suffered from UCB (61,700 in men and 18,770 in women) and 17,670 fatalities from UCB (12,870 in men and 4,800 in women). It is estimated that UCB is accountable for approximately 90% of all bladder malignancies. Patients are diagnosed with non-muscle invasive bladder cancer in the majority of cases; however, approximately 30% of patients develop MIBC, which rises to 40% when they transition from MIBC to NMIBC [1].
In the management of UCB, radical cystectomy (RC) is pivotal. It is a critical component of the management of MIBC, in addition to appropriate lymphadenectomy and perioperative chemotherapy. Additionally, it is relevant for treatment refractory NMIBC and treatment of very high-risk. The RC technique is one of the most challenging surgical procedures in the field of urology. Even though the first records of RC date back to the 1900s, the surgical principles of RC were first described by Whitmore and Marshall in the 1940s. Even though these methods have been enhanced over time, the rates of complications and morbidity that

occur following RC remain high. Although robotic-assisted laparoscopic RC and other minimally invasive techniques have been developed, their effectiveness has not yet been significantly affected [2].

This review article aims to highlight perioperative nutritional optimization effect on postoperative complications incidence, particularly wound associated complications in cases had RC and ileal conduit urinary diversion.

Indications for RC

MIBC, NMIBC, or metastatic UCB (mUCB) can be treated with RC. RC is most frequently administered in the NMIBC setting for high-risk disease, which is distinct as high-grade Ta/T_1 tumors of carcinoma in situ (CIS) that have recurred or persisted following adequate intravesical Bacillus Calmette-Guerin (BCG) therapy. The risk of MIBC progression is significant, and salvage treatment options are generally ineffective. RC is a particularly effective curative intervention. If the recurrence is T_1, "BCG-unresponsive" denotes high-grade recurrences that develop after induction BCG or after induction and one round of maintenance BCG in the case of Ta or CIS. Moreover, any high-grade tumors that recur within 6 months (Ta/T_1) or 12 months (CIS) of the most recent BCG dose, provided that there has been a prior disease-free period. If high-risk NMIBC is unresponsive to BCG, RC is the recommended intervention. RC is also recommended as the initial treatment for very high-risk NMIBC, i.e., in the absence of prior BCG therapy. An extremely high risk of an NMIBC is characterized by lymphovascular invasion presence, extensive invasion into the lamina propria, large high-grade T_1 tumors (>5 cm), variant histology (e.g., sarcomatoid, micropapillary, or plasmacytoid histology), persistent T_1 tumor on re-resection, and disease in prostatic urethra). Neoadjuvant chemotherapy based on cisplatin is the most efficacious treatment for non-metastatic MIBC (T_2-T_4N0M0), which is subsequently after that RC. In certain patients, trimodal therapy (TMT) is an alternative to RC. TMT involves the maximal transurethral resection of bladder tumor and chemoradiation. Additionally, in the event of a bladder tumor recurrence or persistence, the RC is a standard component of TMT protocols (Figure 1). It is crucial to note that approximately half of the cases of non-metastatic MIBC in the United States do not receive any treatment with a therapeutic purpose [3].

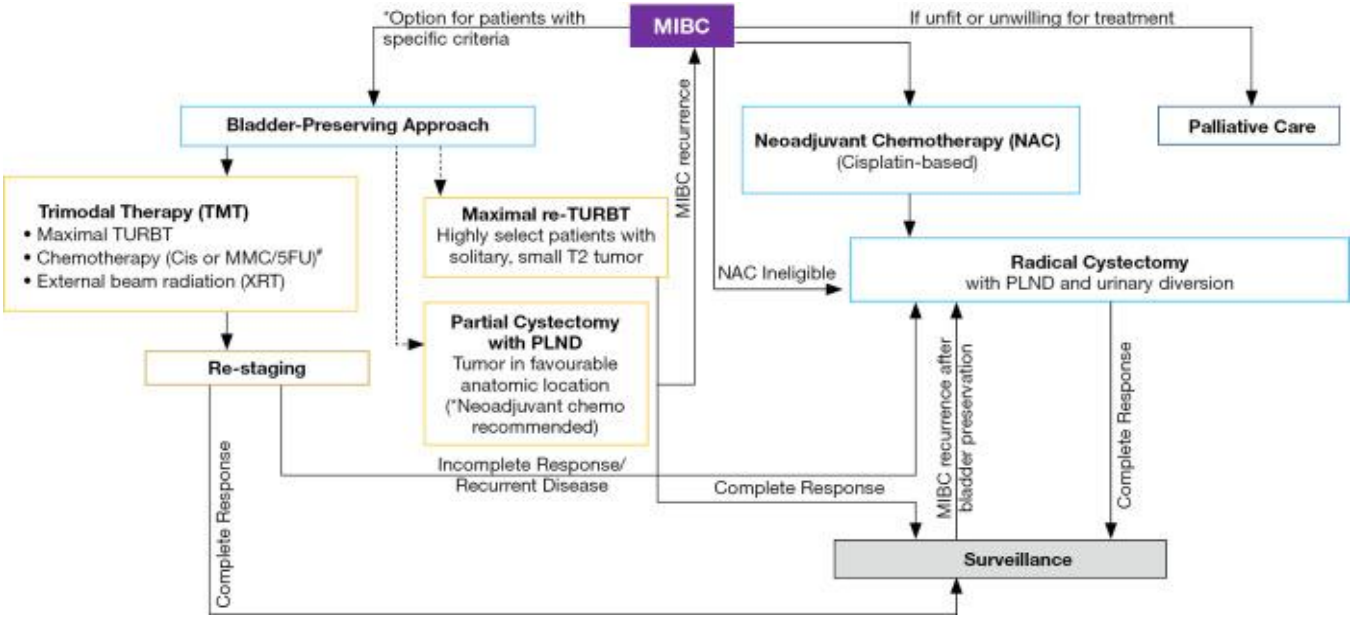

Fig 1: Upon diagnosis of non-metastatic, muscle-invasive bladder cancer, the recommendation is for patients to undergo neo-adjuvant chemotherapy (NAC) followed by radical cystectomy (RC) and pelvic lymph node dissection (PLND). Surgery alone is offered to patients ineligible for or declining NAC, RC (with possible adjuvant chemotherapy). Trimodal therapy (TMT), as part of a bladder-preserving approach, is another option for select patients. However, if TMT fails, RC remains an option for salvage therapy. This figure has been adapted from the AUA guidelines for MIBC therapy [4]

In a systematic review by Williams and colleagues (2019) [2], The utilization of RC as a therapeutic approach was observed in 6% of cases across all age categories, with 19-21% of patients had ≤ sixty-six years old. Increasing patients' number who receive treatment with therapeutic intent, whether it be RC or TMT, will be a critical initiative in future.

In locally advanced or mUCB, RC serves a restricted role. Patients with unresectable local disease, which is diagnosed as clinical stage T_4b or N1-3, are treated primarily with chemotherapy. Administration of RC is initiated when a favorable response is observed. The survival rates of patients who underwent RC after a significant response to chemotherapy (but with residual disease) were found to be comparable to those of patients who had a complete response to chemotherapy (without residual disease). The morbidity of surgery and the limited life expectancy of patients with mUCB make palliative RC a rare choice for the management of hemorrhage and local symptoms. This could potentially change in the future if novel treatment options, such as immune checkpoint blockade, are established [4].

Surgical techniques

Regional lymph nodes, adjacent organs, and the bladder are all removed during RC. To optimize oncologic outcomes, seminal vesicles and prostate are removed in males, while reproductive organs (fallopian tubes, anterior vagina, uterus,

and ovaries) may also be removed in females. RC is differentiated from simple cystectomy by fact that simple cystectomy is prostate-sparing or supra trigonal, and trigone urothelium and pelvic lymph nodes are frequently left behind during bladder removal. In patients with persistent symptoms, simple cystectomies are frequently implemented; however, they aren't implemented for the purpose of controlling cancer [5].

Open versus robot assisted RC

Even in the most experienced hands at high-volume institutions, open RC continues to have high rates of perioperative complication and mortality, despite advancements in technology and patient care. The minimally invasive approach is deemed to be the superior choice for a variety of abdominal surgeries, as it does not impact cancer-free rates and minimizes perioperative morbidity and postoperative recovery. The introduction of robotic assisted surgery has potential to enhance dexterity and precision of surgeons, while simultaneously decreasing their fatigue. There have been a multitude of studies conducted to determine whether robot-assisted RC (RARC) can enhance outcomes of this highly deleterious surgery.

Bochner and colleagues [6] The study informed on a randomized controlled trial that than RARC and ORC. At the scheduled interim analysis, the trial was prematurely terminated due to realization that additional patient enrollment would not result in a significant improvement in ninety-day rate of grade 2-5 complications with RARC. The trial demonstrated a reducing in blood loss and an increase in duration of the surgery. Nevertheless, the length of the stay and the results of the pathology were comparable, and RARC was significantly more cost-effective.

A Cochrane review was recently conducted to evaluate the outcomes of five randomized controlled trials, which were overseen by ORC and RARC and involved a total of 541 participants. Time until recurrence and severe complications (Clavien grade 3 to 5) were the primary outcomes. This review determined that the treatment of MIBC by RARC and ORC resulted in minimal or no variation in oncological outcomes or the likelihood of significant complications. Extracorporeal urinary diversion was implemented, which seems to be primary factor contributing to postoperative complications. It is yet to be determined whether intracorporeal diversion, which is gaining popularity, will alter this equilibrium. Furthermore, robotic platform has potential to facilitate future technological advancements, like reduction of uretero-enteric strictures using indocyanine green. This could result in more significant advances in future outcomes [7].

Pelvic lymph node dissection (PLND)

PLND has been demonstrated to enhance survival and has become a well-established component of RC for UCB. However, the optimal level of PLND for attaining the highest level of oncologic control remains a topic of ongoing debate. According to a meta-analysis conducted by Ku and colleagues [8], Metastatic deposits were present in the regional lymph nodes in up to 25% of organ limited MIBC. Despite the potential to eradicate this metastatic disease through an extended PLND, the implementation of an extended template may result in increased costs and perioperative complications. Nodal templates are described using a variety of nomenclature in various studies. The lateral border of a limited template is defined as the external iliac vein, while medial border is defined as the obturator nerve. This template comprises nodes in obturator fossa and perivesical space. "standard" lymphadenectomy is proximately restricted by bifurcation of common iliac artery, which encompasses the genitofemoral nerve laterally, bladder and internal iliac vessels medially, and the circumflex iliac vein distally. In extended PLND, which extends cephalad to aortic bifurcation (and occasionally above to inferior mesentery artery), the pre-sciatic and presacral nodes are included [4].

Urinary diversion

RC necessitates urinary diversion. Incontinent and continent diversion are the two primary categories of diversion. As a result of their technical simplicity and their ease of management by the elderly, fragile RC population, incontinent diversions are more widespread. The cutaneous ureterostomy is the most accessible diversion; however, it has declined in popularity because of increased risk of stricture at ostomy sites. This approach offers a significant advantage in that it mitigates complications risk, particularly in patients who may be marginal candidates for RC, by avoiding a colon anastomosis. Consequently, cutaneous ureterostomy is occasionally still accomplished in vulnerable patients at specific centers. In same vein, ureterosigmoidostomy was a straightforward approach to urinary diversion; however, The potential for pyelonephritis and adenocarcinoma at the site of ureteral implantation into the colon has also contributed to its decline in fame [9].

Prior to the introduction of continent diversions, ileal conduits were standard for urinary diversion and continue to be the preferred method, particularly in patients with significant comorbidities and those who are elderly. Among complications associated with ileal conduits are stomal complications, renal insufficiency, including stomal stenosis, parastomal hernias, stone formation, urinary tract infections, and ureteral obstruction. The reported complication rates range from 45% at 5 years to 94% at 15.

Furthermore, the continent diversion is subdivided into orthotopic neobladder and continent cutaneous diversion. Significant inflammatory bowel disease, severe hepatic dysfunction, and feeble renal function are absolute contraindications to continent diversion. The rate of metabolic complications is higher in continent diversions due to waste products reabsorption. Mental impairment and prior pelvic and abdominal radiation are relative contraindications. neobladder is contraindicated in of urethra malignant involvement presence necessitating recurrent urethral strictures and urethrectomy; however, continent cutaneous diversion isn't [10].

Intermittent self-catheterization is a lifelong commitment for patients had a continent cutaneous diversion. Approximately 90% to 98% of patients report a high quality of life because of this reconstruction procedure, with documented daytime and nighttime continence rates. Stone formation and stomal stenosis, which necessitates reoperation in up to 21% of patients, are potential complications. This method is now utilized less frequently due to the introduction of orthotopic urinary diversion. The external sphincter is relaxed along with the Valsalva maneuver to achieve the voiding of the orthotopic neobladder. In high-volume facilities, daytime continence rates exceed 85%; however, they can range from 47% to 100%, contingent upon continence definition and

follow-up duration. The of physiological storage reflexes loss is cause of nocturnal incontinence in up to 50% of patients. The use of Valsalva voiding may result in increased rates of ventral hernias following neobladder construction. In approximately 4% to 25% of patients, intermittent self-catheterization is necessary because of incomplete bladder emptying following neobladder surgery. This condition is significantly more prevalent in females.

The selection of appropriate diversion and reconstruction method is contingent upon several factors, like patient's comorbidities and cancer control, in addition to surgical suitability, postoperative ability to achieve, and diversion care patient preference. Rarely have formal studies been conducted that have documented a distinction in total life quality between continent and incontinent urinary diversion. However, the reason for this is that the patient typically has already chosen their preferred diversion method. The quality of life was not demonstrated to be superior by any of the urinary diversion techniques in a systematic review of health-related life quality [11].

Complications of RC

Despite advancements in surgical techniques and perioperative care, RC is related to a relatively high rate of perioperative mortality and morbidity. A 30-70 percent complications incidence has been described following surgery. The complications associated with RC can be classified as early and late, as evidenced by a significant number of single-center studies. Late complications are those that occur between 30 and 90 days after operation, while early complications occur within the first 30 days. The postoperative mortality rate is variable, ranging from 0.8% to as high as 3%. Even though the patient population at high-volume academic institutions is enriched with individuals who have a greater number of co-morbidities, mortality seems to be lower. Ventral hernia (17%), ureteroenteric strictures (14%), parastomal hernias (8%), and calcification formation (16%) were identified as the most prevalent late complications. Additionally, the authors discovered that more elderly patients were susceptible to vitamin B12 deficiency and kidney function loss than their younger counterparts. At least fifty percent of patients aged seventy and older experienced. Additionally, 26% of patients over the age of 70 encountered a decline in renal function for 5 years follow-up, while only 7% of patients below 70 years old experienced this phenomenon. This systematic report of post-RC complications is one of the first to employ a standardized Clavien-Dindo classification. Their findings indicated that complications were experienced by 64% of patients within 90 days of their surgery. The preponderance of these were classified as "minor" and were graded 1 to 2. Within the initial 30 days following surgery, most patients experienced one or more complications. This pattern varied from the early to late stages of the conditions, with infectious, wound-related, cardiac, gastrointestinal, and genitourinary complications being most prevalent. gastrointestinal, wound-related, and infectious complications were the most prevalent of early all-grade complications. In the late phase, this underwent a transition to genitourinary, infectious, and gastrointestinal [12].

Genitourinary complications were the most prevalent in both the early and late phases, it is important to acknowledge. Similar discoveries were made in an additional extensive series. Implementation of Enhanced Recovery after Surgery (ERAS) pathways has been a significant advancement in our endeavors to mitigate perioperative complications and enhance postoperative quality of life. These pathways establish a variety of evidence-based standard interventions that must be adhered to, including preoperative education, intraoperative fluid management, and postoperative nutrition. There is significant evidence that the consolidation of elements reduces the frequency of complications and shortens hospital stays, even though the impact of any single element is frequently uncertain. From this point forward, it is imperative to implement a unified reporting system for cystectomy-related complications. Individual patients' preoperative risk for post-cystectomy complications can be assessed using this data. If the risk of an operation is too high, patients may be offered alternative management methods or optimized prior to surgery. A successful operation necessitates meticulous patient selection [13].

Nutrition and radical cystectomy

Malnutrition

The term "malnutrition" denotes the imbalance, excess, or deficiency of nutrients that adversely affect body composition, clinical outcomes, and health. Malnutrition is defined by the Academy of Nutrition and Dietetics and the American Society for Parenteral and Enteral Nutrition as the reflection of nutrient status in body composition and function. Malnutrition necessitates the presence of at least two of the following characteristics: inadequate energy intake, muscle mass loss, subcutaneous fat loss, unintentional weight loss, fluid accumulation, or impaired muscle function. While different organizations may define malnutrition by varying parameters, these organizations require the diagnosis of at least two of the following characteristics: insufficient energy intake, loss of muscle mass, accumulation of fluids, or diminished muscle function. Surgical outcomes and patient recovery are significantly enhanced by nutritional support. In the medical literature, the role of nutritional support, which includes oral supplements, enteral nutrition, and parenteral nutrition, in promoting wound healing, reducing infections risk, and enhancing immune function is well-documented. Obesity (BMI >30 kg/m2) appears to increase the risk of developing venous thromboembolism and deleterious outcomes after RC, while low albuminemia tends to rise mortality risk and overall complications. Mortality risk and complications following RC has not been linked to any other factor. To optimize perioperative care, ERAS pathways have been included in the field of urology. Specialist immunonutrition (SIM) beverages, which are intended to enhance the immune function of patients, are included in these protocols and have been shown to decrease complications following RC, particularly infections. Specific nutrients, including omega-3 fatty acids, arginine,and glutamine, are incorporated into standard nutrition preparations to create SIM beverages [14].

Although SIM has been shown to regulate inflammatory response, improve host immune response, and increase protein synthesis after surgery, its role in an ERAS pathway following RC is still ambiguous. There is no correlation between SIM and decreased rates of postoperative complications in RC candidates. Additionally, the SIM group exhibited a higher incidence of documented

infections. Infections were more prevalent among patients who had undergone surgery for ileus. A study by Gregg *et al*. [15] like our results, indicating that patients undergoing RC experienced a rise in 90-day and overall mortality because of low albumin and a 5% weight loss prior to surgery. A higher risk of cancer-specific mortality and a reduced survival rate are associated with sarcopenia, a condition that is closely associated with malnutrition and is characterized by a reduction in muscle mass and function. Additionally, sarcopenia is postoperative complications risk factor in RC and is frequently disregarded, suggesting an unmet need that could potentially affect surgical outcomes. In the preoperative period, the significance of customized nutritional interventions has been emphasized by recent developments in clinical nutrition. There is potential for immune-modulating diets, which are high in omega-3 fatty acids, nucleotides, and arginine, to enhance recovery rates and reduce postoperative complications [16].

The catabolic effects of RC further exacerbate the poor nutritional status of many MIBC patients at the conclusion of neoadjuvant chemotherapy. Within two weeks of the procedure, RC surgery induces a 5% decrease in body weight and a 7-17% decrease in muscle mass. Prior to RC, malnutrition was identified in 21-55% of patients using the Nutritional Risk Screening (NRS2002) instrument. Significant nutritional challenges may be present for those in whom bladder cancer has been diagnosed. Additionally, older individuals are more susceptible to malnutrition than their younger counterparts. The discrepancy can be attributed to the presence of other health conditions, the limited availability of nutritious food, and the decreased desire for and amount of food consumed. A variety of factors, including the catabolic impact of tumors, due to tumor-induced appetite suppression, inadequate food intake, diminished appetite as a result of chemotherapy or radiotherapy's adverse consequences, and diminished intake due to pain, anxiety, or depression, may result in malnourishment and a reduction in body weight in the context of cancer. There is a 22% increase in complications rate among malnourished cases who undergo cystectomy. Additionally, up to 15% of these patients develop infections because of nutritional deficiencies [17].

Previous studies on RC have documented elevated rates of mortality and morbidity among malnourished individuals. An individual who was previously in outstanding nutritional condition may become susceptible to malnutrition because of a significant physiological response to stress caused by surgery. The elderly and malnourished cases had inadequate preoperative functional reserve can be severely affected by a series of reactions, including immunity, metabolism, and inflammation, which are a result of surgical stress. Insulin resistance, elevated blood glucose, increased glycogenolysis, increased gluconeogenesis, protein and fat degradation are all potential consequences of surgical stress in the body. In the past, strict fasting was enforced for several hours prior to surgery in order to prevent reflux or aspiration during anesthesia. However, this practice restricted the intake of nutrition. The surgical stress response will be exacerbated, insulin resistance will be exacerbated, glycogen and protein degradation will be increased, and gastrointestinal function will be compromised by perioperative fasting. Therefore, it seems that it would be advantageous to implement a nutritional support strategy during the perioperative period [18].

Nutritional considerations in radical cystectomy

A perioperative approach Effective nutritional management is critical for patients undergoing RC, given the high metabolic stress and risk of malnutrition. Organizing nutrition by perioperative phases helps tailor interve ntions to each stage of care, thereby optimizing recovery and reducing complications [19].

Preoperative nutrition

The aim of the preoperative nutrition is to assess and optimize the patient's nutritional status before surgery, prevent muscle loss and improve immune function and minimize the catabolic impact of surgery [20]. It involves the following strategies

1. Nutritional screening and prehabilitation

Early nutritional assessment (e.g., using tools like NRS-2002) identifies patients at risk for malnutrition. Interventions such as a high-protein, high-calorie diet are recommended to build nutritional reserves and support the stress response. Immunonutrition: Research has demonstrated that supplements containing immune-nutrients (e.g., omega-3 fatty acids, arginine) can decrease the risk of infection and enhance postoperative outcomes [21].

2. Carbohydrate loading

Allowing intake of carbohydrate-rich fluids up to two hours before surgery may help reduce insulin resistance and limit protein catabolism during the fasting period. Carbohydrate intake of 50 g in the form of a beverage (8-10 oz) two hours prior to surgery can mitigate postoperative insulin resistance and hyperglycemia. It is possible that this is due to the fact that the body's catabolism is the dominant process during typical fasting conditions, whereas anabolic pathways are the dominant process when carbohydrates are consumed. This results in increased insulin secretion, increased glucose assimilation by the liver and muscle, and a reduction in protein catabolism [22].

3. Modern guidelines for preoperative fasting

Usually, it is superfluous to fast overnight prior to surgery. According to ESPEN guidelines, patients hadn’t high risk of aspiration are permitted to consume clean liquids two hours prior to surgery and significant foods for a period exceeding six hours prior to anesthesia. The clean liquids are ejected from stomach through 60-90 minutes, and the clean fluid ingested 2 hours prior to anesthesia induction will decrease gastric volume, thereby reducing the risk of aspiration [23].

Intraoperative nutrition

The aim of the intraoperative nutrition is to maintain metabolic homeostasis during surgery and to prevent exacerbation of the catabolic state while the patient is fasting [24]. It involves the following strategies:

1. Goal-directed fluid therapy

Although direct nutritional intake is not provided during surgery, careful management of fluids and electrolytes is crucial. This approach helps maintain normoglycemia and proper tissue perfusion, reducing the stress response [25].

2. Minimizing fasting effects
Maintaining a short fasting period preoperatively and optimizing anesthesia management can help reduce the duration and severity of the catabolic state [26].

Postoperative nutrition
The aim of the intraoperative nutrition is to prevent postoperative fatigue and delayed recovery by avoiding prolonged fasting, support increased metabolic demands during the hypermetabolic and inflammatory state, preserve skeletal muscle and prevent protein catabolism, reduce risk of postoperative infections and complications, and to improve wound healing, immune response, and shorten hospital stay [27]. It involves the following strategies:

1. Early enteral feeding
Initiating enteral nutrition through 24 hours after surgery is a cornerstone of ERAS protocols. Early feeding helps stimulate gut function, reduce the incidence of postoperative ileus, and lower infection rates [27].

2. Protein supplementation
Aiming for a protein intake of 1.5-2.0 g/kg/day is recommended to support wound healing, tissue repair, and to prevent muscle catabolism by addressing elevated amino acid requirements post-surgery [27].

3. Avoiding routine use of total parenteral nutrition
Total parenteral nutrition increases infection risk and cost and should be avoided unless enteral route is contraindicated. It is linked to a variety of complications that impede the recovery of the patient. Nutrient assimilation can be improved, and patient recovery can be facilitated by complementing enteral nutrition [17].

4. Immunonutrition (IMN)
Utilization of glutamine, nucleotides, omega-3 fatty acids, and arginine enhances immune response and has been associated to compact postoperative complications, including infection rates and hospital stay length in major abdominal surgery. Despite the significant amount of data available on the efficacy of perioperative IMN in patients undergoing surgery for gastric, colorectal, and pancreatic cancer, available studies small sample size prevents data availability on benefits of perioperative IMN in patients with urological cancer who had surgical interventions. Furthermore, IMN role in improved recovery pathways is ambiguous due to fact that meta-analyses on this subject were conducted prior to implementation of ERAS protocols [28].

5. Micronutrient monitoring
Monitoring and supplementing essential micronutrients such as vitamin B12, especially in cases had ileal conduit diversions are important to prevent deficiencies and support overall recovery [29].

Nutritional optimization on the surgical outcomes of patients undergoing radical cystectomy and urinary diversion
Nutritional optimization plays a crucial role in improving surgical outcomes, as highlighted by several key studies. The ESPEN guidelines emphasize the importance of preoperative nutritional screening and intervention, particularly for malnourished patients, recommending immunonutrition (arginine, omega-3, and nucleotides) to reduce postoperative infections. Similarly, ERAS protocols advocate for carbohydrate loading before surgery to minimize insulin resistance and encourage early oral feeding postoperatively to enhance recovery. Research supported perioperative immunonutrition, demonstrating its benefits in reducing infection rates and hospital stays, particularly in gastrointestinal and oncologic surgeries. In critically ill surgical patients, it has been found that delayed parenteral nutrition reduces complications compared to early initiation, reinforcing the preference for early enteral feeding. Moreover, it has been highlighted the detrimental effects of sarcopenia on surgical outcomes, stressing the need for prehabilitation strategies combining exercise and nutritional support. Collectively, these studies underscore the necessity of integrating nutritional screening, preoperative carbohydrate loading, perioperative immunonutrition, and early enteral feeding into surgical protocols to optimize patient recovery and reduce complications. More specifically, perioperative nutrition interventions efficacy for cases had RC, particularly those with MIBC has higher of malnutrition risk, has been assessed in a restricted number of clinical trials [30].

To our knowledge, the studies evaluated perioperative nutritional optimization impact on surgical outcomes of cases had RC and urinary diversion are scarce. Despite well-established role of nutritional optimization in surgical outcomes, there remains a significant gap in research specifically addressing RC and urinary diversion. While extensive studies have explored perioperative nutrition in gastrointestinal and general surgical contexts, the application of these principles to RC, a highly morbid procedure with significant nutritional implications, remains under-investigated. RC is related to perioperative complications risk, like infections, electrolyte disturbances, and delayed gastrointestinal recovery, all of which are influenced by nutritional status. Existing guidelines for perioperative nutrition often rely on evidence from colorectal or general surgical populations, despite the distinct metabolic demands and prolonged surgical time associated with RC. Given that malnutrition is predominant in bladder cancer patients and is linked to worse postoperative outcomes, tailored nutritional strategies, including preoperative screening, immunonutrition, and enhanced postoperative feeding protocols, are critically needed. These observations underscore the urgent need for tailored nutritional strategies specific to RC, including preoperative nutritional risk screening, perioperative immunonutrition, and early postoperative feeding protocols. To address this gap in evidence, our current study evaluates the impact of structured perioperative nutritional optimization, including the direct involvement of a dedicated clinical nutritionist, on surgical outcomes in cases had RC. The goal is to contribute to development of evidence-based nutritional protocols that improve recovery and reduce complications in this high-risk surgical population [31].

To optimize their nutritional status, the current AUA guidelines for MIBC recommend that all RC patients at high risk for malnutrition undertake nutrition counseling in preparation for surgery. To assist clinicians in identifying high-risk patients, a significant number of validated nutrition screening and/or assessment instruments are

available. The Patient Generated Subjective Global Assessment (PG-SGA) is a validated instrument that is utilized in the outpatient oncology setting. It was expressly developed for cancer patients. It has the potential to identify malnutrition with high positive and negative predictive values. The PG-SGA evaluates muscle, adipose stores, and fluid balance by monitoring weight change, metabolic stressors, gastrointestinal symptoms, physical exam findings, dietary intake, and functional status. Although the Nutrition Risk Screening (NRS-2002) and Malnutrition Universal Screening Tool (MUST) have been validated in the surgical setting, their predictive value in the context of bladder cancer is not well established. In the context of cancer, there is evidence that these tools may also be restricted, as nutritional risk is a multifaceted concept that is influenced by biochemical and immunological factors, as well as taste/smell alterations, vertigo, and dysphagia. The PG-SGA is the preferable treatment for patients undergoing RC, as evidenced by its more comprehensive evaluation, according to the authors of this review. More recently, the Controlling Nutritional Status (CONUT) score, a test that assesses the outcomes of patients with MIBC following RC, has exhibited potential. This examination is predicated on the total cholesterol concentration, lymphocyte count, and serum albumin. The retrospective evaluation of 347 patients who underwent RS revealed a significant correlation between a high preoperative CONUT score and the following: older age, advanced T-stage, higher grade, node-positive disease, protracted median length of stay, and a 30-day readmission rate. Independently, the CONUT score predicts progression-free survival and unfavorable cancer-specific mortality [32].

The assessment of sarcopenia in RC candidates is increasingly supported by a growing body of evidence, as evidenced by established associations between adverse outcomes and sarcopenia. Perioperative infection, ileus, and overall complications subsequent to RC are independently predicted by a variation in skeletal muscle mass following NAC. Rawls *et al*., [33] A correlation was found between the density of the erector spinae muscle and an increased incidence of complications following RC. During a multicenter investigation conducted by Mayr *et al*., [34], Over duration of five years, patients with sarcopenia experienced significantly worse cancer-specific survival and overall survival. Strong consistency and validity have been demonstrated in the identification of patients at risk for sarcopenia by the Strength, Assistance with walking, Rise from a chair, climb stairs, and Falls screening tool. In addition, it is easily implemented in the clinic [35].

There are currently no well-established methods of targeting sarcopenia that have a significant impact on the outcomes of patients who are undergoing major oncologic surgery, such as RT. To further regulate the inflammatory response and reduce muscle catabolism following RC, additional calories and protein may be added. However, research conducted by Ritch *et al*. and Hamilton-Reeves *et al*. suggests that this approach may help mitigate muscle atrophy after surgery. In addition, the consumption of fish oil as part of a perioperative nutrition intervention may facilitate this process. To initiate nutrition counseling, a registered dietitian may recommend specific foods, oral supplementation, or other targeted medical nutrition therapies after identifying high-risk patients and evaluating their ability to tolerate oral ingestion. Elderly individuals are susceptible to malnutrition and inadequate intake due to a variety of factors, including infirmity, constipation, cognitive decline, oral dysphagia, and polypharmacy. To offer patients guidance regarding MIBC, our institution, in partnership with the Bladder Cancer Advocacy Network, developed patient education videos that concentrated on bladder cancer and nutrition. To preserve lean muscle mass and expedite the healing and restoration process after surgery, it is recommended that MIBC patients who are undergoing RC ingest an adequate amount of protein and calories both prior to and following the procedure. Additionally, routine follow-up consultations are the most effective time to re-screen and re-assess nutritional imbalances that may affect this population, including renal impairment, B12 deficiency, and electrolyte abnormalities [36].

Bertrand *et al*., [37] Distinguished between the number of RC cases who had been administered three daily doses of an arginine-containing formula in the seven days prior to surgery and those who didn't obtain any supplement. Patients who received SIM experienced an overall postoperative complication rate of 40%, as opposed to 76.7% for those who did not receive supplement. Postoperative infections and paralytic ileus were found to have fallen significantly. Hamilton-Reeves *et al*., [38] The year 2016 saw the implementation of a prospective RCT. Those who underwent RC were compared to patients who received a nutritional supplement that did not contain arginine. Although there were insignificantly differences in overall complication rates through 30 days of surgery, patients who received an arginine-containing nutritional supplement experienced a 39% reduction in late postoperative infection rate. At the time of RC, balance of Th1 to Th2 cells was preserved in this cohort. The control group did not exhibit a comparable phenomenon. Additionally, patients who received Specialized immunonutrition (SIM) exhibited a significantly lower plasma concentration of IL6. Lastly, the nutritional supplement containing arginine resulted in a reduction in the number of myeloid-derived suppressor cells in patients. SIM use for RC candidates did not demonstrate any advantages in numerous other reports.

Lyon *et al*., [39] showed a cohort of 104 prospectively identified non-supplemented RC patients was compared to 40 patients who ingested four high-arginine immunonutrient beverages per day for five days prior to RC. The data was then reported. There was no correlation between preoperative supplementation and reduced postoperative infectious complications, even though it was well-tolerated and secure. In a study by Maffezzini *et al*, [40] shown that complication rates were not reduced, and recovery of gastrointestinal function, postoperative albumin depletion, and lymphocyte counts was not influenced by postoperative enteral administration of Impact through a jejunostomy.

Pathologic and clinical outcomes of RC patients are disproportionately influenced by the presence of multiple comorbidities. Comorbidities and age were identified as LOS Predictors, likely readmissions, and non-home-based discharges. However, complications were not predicted independently by age and CCI. It is not uncommon to observe gastrointestinal dysfunction following RC, and it continues to be the most frequent cause of delayed discharge and enteral nutrition. To manage and reverse malnutrition, total parenteral nutrition administered postoperatively may

appear to be the most effective approach. Nevertheless, no prior studies have provided any evidence of an advantage in use of TPN to reverse or regulate weight loss in cases had. Additionally, hyperglycemia and immune system impairment have been previously linked to elevated rates of postoperative infections following RC in the context of TPN. The observations that were previously mentioned were not corroborated by the results. Conversely, postoperative ileus, the most prevalent gastrointestinal complication following RC, has been observed to be linked to documented infection higher prevalence. Consequently, the findings indicate that ileus, which is occasionally accompanied by other complications, may be infections source rather than TPN itself. NAC use has been the subject of numerous concerns regarding the potential for an elevated risk of perioperative mortality and morbidity. In particular, adverse hematologic or gastrointestinal effects are experienced by minimum a third of cases who are cured by cisplatin-based NAC [41].

Conclusion

The postoperative outcomes of RC and urinary diversion are significantly influenced by perioperative nutritional support. The metabolic stress and catabolic burden that patients experience because of the extensive urological procedures they undertake are related to a high risk of malnutrition, sarcopenia, and impaired wound healing. Hospital stay duration, infectious complications, and readmission rates can be significantly reduced by the early identification of nutritional risk, in conjunction with individualized nutritional optimization-particularly through multimodal prehabilitation, immunonutrition, and early enteral feeding-as indicated by current evidence. Structured perioperative nutritional optimization can significantly improve postoperative recovery in patients undergoing RC. This is accomplished through individualized assessment and immunoenhancing supplementation.

The heterogeneity of study designs and nutritional protocols impedes facility to draw definitive conclusions, despite growing body of evidence that supports these interventions. The most effective perioperative nutritional strategies in terms of timing, composition, and duration must be determined through the conduct of future randomized controlled trials of high quality. Consequently, it is essential. The integration of standardized nutritional assessment and intervention into ERAS pathways may be a pragmatic and evidence-based approach to improving Long- and short-term results of patients who undergo RC and urinary diversion.

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