CE Focused Review

Quality Indicators in the Management of Bladder Cancer

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Abstract

Bladder cancer is predominantly seen in elderly patients. With the aging United States population, the incidence and prevalence of bladder cancer are on the rise, heightening the relevance of this disease as a public health issue. Despite having one of the greatest average cancer treatment costs per patient, improvements in disease-specific survival have been subtle. Clinical guidelines based predominantly on expert opinion and randomized controlled studies offer some guidance, but adherence to these guidelines is lacking. Building awareness of quality indicators to optimize patient care represents an opportunity to improve bladder cancer outcomes. Although quality indicators exist for other disease states, widely accepted quality indicators for the management of bladder cancer have not yet been established. This article proposes an initial set of quality indicators for both non–muscle-invasive and muscle-invasive bladder cancer based on established clinical guidelines and the available literature. (*JNCCN* 2013;11:492–500)

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Learning Objectives

Upon completion of this activity, participants will be able to:

- Identify proposed quality indicators for non–muscle-invasive and muscle-invasive bladder cancer.
- Discuss treatment recommendations and guidelines for non–muscle-invasive and muscle-invasive bladder cancer.

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Driven by third-party payers, patients, and health care providers, increasing interest has been shown in improving treatment outcomes and providing cost-conscience care. These efforts include the development of quality indicators for many disease processes and clinical care scenarios. The National Quality Forum, Agency for Healthcare Research and Quality (AHRQ), Leapfrog Group, and RAND Corporation represent only a few of the public and private entities involved in these endeavors. For a quality measure to be useful in improving patient outcomes, it must be based on high-level clinical evidence and/or expert opinion and be measurable (http://www.qualityforum.org/Home.aspx). An indicator that is difficult to measure lacks impact; a major avenue to improve care is to track and report quality measures to health care providers and patients. The goal of providing this feedback is to effect change that will improve patient outcomes and safety, and to identify barriers to high-quality care.

Despite an incidence of bladder cancer in the United States of more than 73,000 patients per year and a prevalence of more than 500,000 people,[1] a paucity of widely accepted quality indicators exists for this disease. However, guidelines based on level 1 evidence and expert opinion do exist for the treatment of patients with both non–muscle-invasive and muscle-invasive bladder cancer (NMIBC and MIBC, respectively).[2–4] With these guidelines as the accepted urologic standard, an initial set of quality indicators for bladder cancer care can be proposed.

Quality Indicators in the Management of NMIBC

NMIBC is distinguished from invasive disease by its natural history. Left untreated, most patients with bladder cancer invading the muscularis propria will die within 2 years of diagnosis.[5] In contrast, outcomes for patients with NMIBC are more favorable and are influenced heavily by the grade and stage of the disease; high-grade tumors and advancing-stage indicate a greater risk of progression.[6] Once patients are allowed to progress to invasive disease, their chances of survival are no better than that for those who present with muscle-invasive disease at initial diagnosis.[7] Several interventions exist that improve outcomes for patients with NMIBC and can serve as a basis for quality indicators (Table 1).

Appropriate Imaging for Bladder Cancer Staging

Quality care for NMIBC starts with appropriate staging of the disease. Transurethral resection of bladder tumor (TURBT) is a crucial component of staging, because it defines tumor grade, stage, and underlying histology. Imaging should be performed before TURBT. The presence of perivesical stranding and bladder wall thickening suggests invasive (clinical stage T2–T3) disease, whereas hydronephrosis indicates possible clinical T3 disease. TURBT can cause perivesical stranding and bladder wall thickening, lowering the imaging sensitivity for these findings. Cross-sectional imaging with either a CT scan or an MRI evaluates the local disease burden and assesses for nodal and distant metastases. The accuracy of CT and an MRI for staging the local extent of disease varies from 73% to 96% and 55% to 92%, respectively.[8] CT and MRI have similar sensitivity for identifying nodal enlargement suggestive of metastatic disease.[9] In addition, delayed CT or MR urogram phases are essential to assess for upper tract disease. In situations in which patients cannot undergo contrast-enhanced imaging because of allergy or poor renal function, retrograde pyelograms combined with renal ultrasound or noncontrast CT or MRI can rule out concurrent upper tract neoplasm. Chest CT can be performed at the time of abdominal and pelvic components to rule out lung metastases; alternatively, a chest radiograph should be obtained. Bone scan and brain imaging are not routinely indicated unless the patient exhibits specific signs or symptoms, making metastasis to these sites a concern.

Restaging TURBT

Detrusor muscle in the pathologic specimen indicates completeness of resection and decreases the likelihood of understaging.[10] In the presence of bulky, high-grade Ta disease, any T1 bladder cancer (even with muscle in the specimen), or an incomplete initial resection, current guidelines recommend a restaging transurethral resection 2 to 6 weeks after the initial resection.[4] Approximately 30% of patients with T1 bladder cancer are understaged in the absence of a restaging TURBT, resulting in potential undertreatment.[11,12] Accordingly, restaging TURBT should be considered an important quality indicator. Unfortunately, as few as 4.9% of eligible patients undergo this procedure within 60 days of initial resection.[13]

Table 1 Proposed Quality Indicators for Non–Muscle-Invasive Bladder Cancer

Proposed Quality Measure	Support Data	Population Impacted	What Is Measured?	Reporting Mechanism	Proposed Benchmark	Behavior Change
Imaging before initial tumor resection	EAU/AUA guidelines	All patients with newly diagnosed bladder cancer	Percentage of patients undergoing appropriate imaging before initial tumor resection[a]	Institutional tracking and reporting to clinicians quarterly (dashboard)	80% (based on institutional data)	Create checklist for operative scheduling requiring preoperative imaging
Initial transurethral resection of bladder tumor checklist Examination under anesthesia (EUA) Report adequacy of tumor resection Report whether muscle obtained	NCCN Clinical Practice Guidelines in Oncology for Bladder Cancer[14]	All patients with newly diagnosed bladder cancer	Percentage of patients undergoing EUA and documenting completeness of tumor resection (Y/N) and impression of depth of resection	Institutional tracking and reporting to clinicians quarterly (dashboard)	90% (based on institutional data)	Create operative note templates requiring this information to complete report
Restaging TURBT for bulky high-grade Ta, all T1 and incomplete resection	EAU/AUA guidelines	All patients with high-grade bulky Ta, all T1 patients, and any patient with an incompletely resected tumor within 2–6 wk after prior resection	Percentage of appropriate patients undergoing restaging TURBT within 6 wk of prior resection	Institutional tracking and reporting to clinicians quarterly (dashboard)	90%	Incorporate guidelines into pathology report for all patients with NMIBC meeting patient population criteria
Use of perioperative intravesical chemotherapy	Sylvester et al,[16] EAU, AUA	Low-grade Ta/low-volume bladder cancer	Percentage of patients receiving mitomycin within 24 h of TURBT	Link operative data to institutional pharmacy data to identify patients and report to clinicians quarterly; they can screen for why patients did not receive	30%	Reviewing of quarterly information will require clinician to consider whether appropriate patients were missed
BCG	Meta-analysis	High-risk NMIBC	Percentage of patients initiating intravesical BCG with high-risk NMIBC	Link pathology data to pharmacy data to identify patients receiving or not receiving BCG	60%	
Maintenance BCG	Lamm et al[20] (EAU/AUA)	Complete response to induction BCG	Percentage of patients completing 1 y of maintenance BCG after complete response to induction BCG	Use pharmacy data to identify patients receiving prescribed time frame of BCG	90% (expected that tolerance of induction would allow maintenance)	Report data to clinician to review cases in which patients did not receive maintenance and provide feedback

Abbreviations: AUA, American Urologic Association; BCG, bacillus Calmette-Guérin; EAU, European Association of Urology; NMIBC, non–muscle-invasive bladder cancer; TURBT, transurethral resection of bladder tumor.

[a]A percentage of patients are diagnosed incidentally during transurethral resection of bladder tumor for emergent bleeding, and therefore imaging may not have been performed before.

Examination Under Anesthesia

NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines) for Bladder Cancer recommend bimanual palpation of the bladder with the patient under anesthesia for a more thorough staging,[14] and this should be performed at TURBT (to view the most recent version of these guidelines, visit NCCN.org). Presence of a palpable mass suggests T2–T3 disease, whereas the presence of a fixed bladder or invasion into the vagina or rectum indicates T4 disease. Again, the importance of accurate clinical staging cannot be overstated, because level 1 evidence exists for the use of platinum-based neoadjuvant chemotherapy for patients with T2–T4 localized bladder cancer followed by radical cystectomy to optimize disease outcomes.[15]

Perioperative Intravesical Chemotherapy

Studies dating back to the early 1990s evaluated the use of immediate-dose (within 24 hours) intravesical chemotherapy after TURBT with the goal of preventing disease recurrence. The 2 most commonly studied of these medications are epirubicin and mitomycin. In 2004, Sylvester et al[16] published a meta-analysis of 1400 patients who received a single dose of intravesical therapy, confirming a resultant reduced risk of recurrence. Patients with single or multiple tumors benefited, with reduced odds of recurrence of 0.66 for single tumors and 0.44 for multiple tumors. However, tumors of higher grade and stage were more likely to recur, suggesting that this approach is indicated for a select group of patients with low-volume, low-grade Ta bladder cancer. These data serve as the driving force behind both the European Association of Urology (EAU) and American Urological Association (AUA) guidelines recommending a single perioperative dose of intravesical therapy after TURBT for low-grade Ta bladder cancer.

Despite the data and guidelines, some evidence suggests that this approach is infrequently implemented, with only 0.3% of Medicare patients receiving immediate intravesical therapy.[17] However, this may not represent current practice. Recent data from the Urological Surgery Quality Collaborative suggest that the percentage of appropriate patients receiving a single dose of intravesical therapy after TURBT is higher, ranging from 20% to 50% of patients treated in large academic or community urology practices.[18] The primary contraindication to giving this therapy, is deep resection. Allergic cystitis has been reported in up to 10% of patients undergoing immediate intravesical therapy, with the most severe cases ultimately requiring cystectomy.[19] Other barriers to the use of mitomycin include a drug shortage, a belief that this therapy is not effective, or that giving the medication presents too great a risk. Continued provider education efforts and improved systems for delivering the medication are needed to expand the use of this therapy.

Use of Bacillus Calmette-Guérin in NMIBC

Bacillus Calmette-Guérin (BCG) is the most effective intravesical agent for the management of high-risk NMIBC, and its use is advocated by both AUA and EAU guidelines. BCG has been shown to reduce the risk of recurrence, and increasing data show that it may also reduce the risk of disease progression.[20] A complete resection is essential to optimize the response to BCG, especially for T1 disease, because BCG does not penetrate beyond the bladder mucosa basement membrane. An estimated 50% to 55% of patients with high-risk NMIBC experience a complete response to intravesical BCG. Response rates are as high as 70% in patients with carcinoma in situ alone.[21] Shelley et al[22] performed a meta-analysis of 6 randomized controlled studies including 585 patients with Ta and T1 disease undergoing TURBT with or without subsequent BCG. This study showed a 70% lower likelihood of recurrence at 1 year in patients receiving BCG. However, BCG complications are not inconsequential, with up to 71% of patients experiencing urinary frequency, 67% cystitis, 25% fever, and 23% hematuria. Serious local and systemic infections from BCG occur and may require antituberculosis therapy and even hospitalization. Although the use of BCG should be considered a quality indicator for this patient population, there are reasons why BCG may not be given or may not be effective.[23–26]

Maintenance BCG

Level 1 evidence shows improved recurrence- and progression-free survivals in patients undergoing maintenance BCG therapy after a complete response to an induction course. Lamm et al[20] reported on a cohort of 384 patients who received induction BCG and then were randomized to surveillance versus maintenance BCG given each week for 3 weeks at 3, 6, 12, 18, 24, 30, and 36 months after the initial induction course. The median recurrence-free survival

was 80 months for patients receiving maintenance therapy versus 36 months for those undergoing surveillance alone. In addition, patients on maintenance were found to have improved progression-free survival. One notable limitation of this study is that only 17% of patients completed the full maintenance course.[20] Although current EAU guidelines recommend at least 1 year of maintenance BCG therapy, and AUA guidelines "suggest that maintenance BCG be administered," NCCN Guidelines list maintenance BCG as "optional," and uncertainty exists regarding optimal dosing and length of duration of therapy.[14]

Quality Indicators in the Management of MIBC

Widely accepted quality indicators for the treatment of MIBC have not been established. Although some efforts have been made to adapt practices from other surgical specialties, patients with bladder cancer pose unique challenges for pre-, intra-, and postoperative care that deserve disease-state–specific quality measures. Patients with MIBC tend to be older, with multiple comorbidities. In addition, these comorbidities, including coronary, vascular, and pulmonary disease, are often more severe in this population. Although other treatment options are available and should be considered on an individual basis, most patients with MIBC undergo cystectomy with urinary diversion. Cystectomy is a major surgery requiring significant patient convalescence and adjustment postoperatively. Quality indicators for the management of MIBC will promote improved outcomes for these patients (Table 2).

Multidisciplinary Care

Once MIBC is diagnosed, patients must be educated regarding treatment options so that they may make an informed treatment decision. Given the complexity of this disease and patient characteristics, a multidisciplinary approach is preferred, involving medical and radiation oncologists when appropriate. This may be in the form of a multidisciplinary bladder cancer clinic, coordinated consultations, or the presentation of individual cases to an institutional tumor board. With this, patients receive a more thorough evaluation, including input from multiple providers with unique treatment perspectives. As seen in studies examining the use of neoadjuvant chemotherapy[27] and the combination of tumor resection, chemotherapy, and radiation therapy,[28] multidisciplinary therapy for MIBC is often associated with optimal disease outcomes for individual patients.

Neoadjuvant Chemotherapy

The 5-year survival rate after cystectomy for MIBC is only approximately 50%.[8] To improve these poor outcomes, platinum-based neoadjuvant chemotherapy should be considered for all patients with T2 or greater disease. Some advantages of platinum-based neoadjuvant chemotherapy is that drug is delivered early in the treatment course when the volume of micrometastatic disease is at its lowest, the delivery of systemic therapy is not delayed because of patient recovery after cystectomy, and negative node and margin status may be more attainable at cystectomy after chemotherapy. Platinum-based neoadjuvant chemotherapy followed by cystectomy has been shown to improve patient median survival from 46 to 77 months compared with surgery alone.[27,29] Multiple meta-analyses of randomized neoadjuvant chemotherapy trials show survival advantages of approximately 5% at 5 years after treatment.[8] These superior disease outcomes are achieved without significant differences in perioperative complications between patients who undergo neoadjuvant chemotherapy and those who do not. Unfortunately, the use of neoadjuvant chemotherapy in patients undergoing cystectomy is limited, with as few as 17% of patients with T2 or greater disease receiving treatment, even at academic centers.[30,31] These low rates of use can be partially explained by patient comorbidity, especially renal insufficiency, and poor performance status. Some experts advocate for early cystectomy in patients who are unable to tolerate platinum-based chemotherapy regimens, although this remains an area of controversy. Despite this, missed opportunities occur to provide patients with MIBC with best possible care supported by randomized prospective data.

Urinary Diversion Teaching

Managing urinary diversion after cystectomy has a significant effect on a patient's lifestyle. Patients must be thoroughly educated regarding their preferred urinary diversion before surgery. For patients opting for an ileal conduit, meeting with an enterostomal therapist trained to educate stoma patients is important.[32] The enterostomal therapist should

Table 2 Proposed Quality Indicators for Muscle-Invasive Bladder Cancer

Proposed Quality Measure	Support Data	Population Impacted	What Is Measured?	Reporting Mechanism	Proposed Benchmark	Behavior Change
Multidisciplinary care	EAU guidelines	All patients with ≥T2 disease	Percentage of patients referred to a medical oncologist before surgery	Institutional tracking and reporting to clinicians quarterly (dashboard)	80%	Develop a multidisciplinary case review process
Neoadjuvant chemotherapy	EAU guidelines	All patients with ≥T2 disease	Percentage of patients receiving neoadjuvant chemotherapy	Institutional tracking and reporting to clinicians quarterly (dashboard)	60% of chemotherapy-appropriate patients	≥T2 status generates an automatic referral to medical oncology
Urinary diversion teaching	AUA/WOCN guidelines	All patients undergoing cystectomy	Percentage of patients evaluated with stoma site marked by entero-stomal therapist or equivalent	Institutional tracking and reporting to clinicians quarterly (dashboard)	90%	Establish institutional guidelines for booking cystectomy patients for surgery
Prophylactic antibiotics	AUA guidelines	All patients undergoing cystectomy	Percentage of patients receiving appropriate prophylactic antibiotics within 60 min of incision	Link anesthesia and pharmacy data to measure compliance	90%	Assure appropriate antibiotics given during pre-incision "Time Out"
Thrombosis prophylaxis	AUA best practice statement	All patients undergoing cystectomy	Percentage of patients receiving appropriate thrombosis prophylaxis at cystectomy	Link nursing and pharmacy data to measure compliance	90%	Establish institutional guidelines for thrombosis prevention
Lymphadenectomy	EAU guidelines	All patients undergoing cystectomy for bladder cancer	Percentage of appropriate patients who receive at least a standard lymph node dissection at cystectomy	Review operative notes documenting extent of lymph node dissection	80%	Establish institutional standard of care guidelines
Monitoring complications	EAU guidelines	All patients undergoing cystectomy	Percentage of patients with 90-day morbidity and mortality data	Prospectively monitor for patient complication and death	80%	Establish prospective complication database

Abbreviations: AUA, American Urologic Association; EAU, European Association of Urology; WOCN, Wound, Ostomy and Continence Nurses Society.

evaluate the patient's abdomen and mark the optimal site for the stoma before surgery. Even patients who choose a neobladder or continent catheterizable urinary diversion should be marked for a stoma if, intraoperatively, an ileal conduit is the best option because of anatomic limitations or disease extent. It is also important to ensure that patients with a neobladder and continent catheterizable urinary diversion possess sufficient manual dexterity and are willing to catheterize their diversion postoperatively. It is often also helpful to have patients meet with an enterostomal therapist several times after surgery to reinforce teaching and troubleshoot any difficulties. If a specialized enterostomal therapist is not available, a nurse or physician with considerable experience managing urinary diversions can provide the necessary teaching.

Perioperative Antibiotics

One well-established quality indicator applied to open abdominal surgery is the appropriate use of perioperative prophylactic antibiotics to prevent surgical site infections. Despite the strength of evidence supporting this practice, studies indicate that timely antibiotic administration does not occur in upwards of 54% of cases.[33] General recommendations include administering perioperative antibiotics in an adequate dose based on patient weight within 60 minutes of the surgical incision, and discontinuing them 24 hours after surgery.[34] In addition, intraoperative redosing should occur after 2 antibiotic half-lives to ensure sufficient antimicrobial serum levels until the incision is closed. With entry into the urinary tract and creation of the urinary diversion from intestine, using a second- or third-generation cephalosporin as first-line antibiotic prophylaxis is recommended for cystectomy.[35]

Thrombosis Prophylaxis

Given the presence of neoplasm, extent of comorbidities, and older patient age, patients who undergo cystectomy are at high risk for the development of deep vein thrombosis and subsequent pulmonary embolism, collectively representing up to 8% of all cystectomy perioperative complications.[36] This rate is an underestimate because of missed diagnosis of subclinical events. Because this represents an opportunity to prevent significant morbidity and mortality, deep vein thrombosis prophylaxis is a marker of high-quality patient care.[37] Prophylaxis can include mechanical (eg, early ambulation, compression stockings, intermittent pneumatic compression devices) and pharmacologic (eg, low-dose unfractionated heparin, low-molecular-weight heparin) measures.[37] For patients undergoing cystectomy, it is recommended that at least intermittent lower-extremity pneumatic compression devices are placed at the time of anesthesia induction and continued in the postoperative period until the patient is freely ambulating. A more aggressive regimen, including subcutaneous heparin given at the time of surgery, should be considered.[37] Both of these measures, combined with early ambulation, should then be continued during the postoperative admission as long as the patient has no contraindications to this treatment.

Lymphadenectomy

The extent of lymph node dissection needed during radical cystectomy for MIBC is controversial.[8] Data show that a more extensive lymph node dissection may lead to a survival benefit.[38] A more limited node dissection is associated with suboptimal staging, and also worse disease outcomes for patients with node-positive and node-negative disease.[8] Accurate pathologic staging is essential to determine the need for adjuvant therapy and to anticipate disease recurrence. For this reason, at least a standard node dissection, including the common iliac nodes lateral to the ureters, external iliac, obturator, and internal iliac lymph nodes, should be performed if possible during cystectomy.[8]

Monitoring Complications

To improve outcomes and evaluate the quality of care provided to patients undergoing cystectomy, it is important to have a standard and reproducible system for defining and tracking complications.[39] The Clavien-Dindo system of evaluating postoperative complications has gained favor in the urologic community. This method classifies events from I to V, with a higher number indicating a more severe complication requiring more significant intervention.[40] With this system, complications of the same grade can be grouped for ease of communication, whether in a publication or a quality-of-care report. In addition, a standard means of categorizing postcystectomy mortality is important. Several publications report 90-day mortality, because these mortalities are likely attributable to the procedure.

Future Considerations

The goal of this article is to propose a set of quality indicators for NMIBC and MIBC. All of these represent explicit data points that can be tracked longitudinally to generate a bladder cancer quality-of-care profile. This is not an exhaustive list, however. Several additional components of bladder cancer management deserve mention as possible quality-of-care indicators. For MIBC, clear guidelines could help indicate when patients require cystectomy for failed intravesical therapy to reduce the probability of disease progression. For NMIBC, having patients consult with medical subspecialists for preoperative optimization; meeting with a certified nutritionist preoperatively and in the immediate postoperative period to optimize patient nutrition; using postoperative inpatient care pathways to reduce variability in care; and using stage-specific postoperative disease surveillance protocols to reduce excessive testing and imaging are measures that could be incorporated in the future as additional quality indicators.

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Instructions for Completion

To participate in this journal CE activity: 1) review the learning objectives and author disclosures; 2) study the education content; 3) take the posttest with a 70% minimum passing score and complete the evaluation at **http://education.nccn.org/node/17316;** and 4) view/print certificate. After reading the article, you should be able to answer the following multiple-choice questions. Credit cannot be obtained for tests completed on paper. You must be a registered user on NCCN.org. If you are not registered on NCCN.org, click on "New Member? Sign up here" link on the left hand side of the Web site to register. Only one answer is correct for each question. Once you successfully answer all posttest questions you will be able to view and/or print your certificate. Software requirements: Internet.

Posttest Questions

1. Transurethral resection of bladder tumor (TURBT) is a component of staging for non–muscle-invasive bladder cancer that defines _____ of the tumor.
   a. Grade
   b. Stage
   c. Underlying histology
   d. All of the above
2. True or False: Fewer than 5% of eligible patients undergo TURBT restaging within 60 days of initial resection.
3. True or False: Platinum-based neoadjuvant chemotherapy should be considered for all patients with T2 or greater muscle-invasive bladder cancer.