

## RESEARCH ARTICLE

# Accuracy of Preoperative Urinary Symptoms, Urinalysis, Computed Tomography and Cystoscopic Findings for the Diagnosis of Urinary Bladder Invasion in Patients with Colorectal Cancer

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### Abstract

**Background:** To determine the accuracy of preoperative urinary symptoms, urinalysis, computed tomography (CT) and cystoscopic findings for the diagnosis of urinary bladder invasion in patients with colorectal cancer. **Materials and Methods:** Records of patients with colorectal cancer and a suspicion of bladder invasion, who underwent tumor resection with partial or total cystectomy between 2002 and 2013 at the Faculty of Medicine Siriraj Hospital, were reviewed. Correlations between preoperative urinary symptoms, urinalysis, cystoscopic finding, CT imaging and final pathological reports were analyzed. **Results:** This study included 90 eligible cases (71% male). The most common site of primary colorectal cancer was the sigmoid colon (44%), followed by the rectum (33%). Final pathological reports showed definite bladder invasion in 53 cases (59%). Significant features for predicting definite tumor invasion were gross hematuria (OR 13.6, sensitivity 39%, specificity 73%), and visible tumor during cystoscopy (OR 5.33, sensitivity 50%, specificity 84%). Predictive signs in CT imaging were gross tumor invasion (OR 7.07, sensitivity 89%, specificity 46%), abnormal enhancing mass at bladder wall (OR 4.09, sensitivity 68%, specificity 66%), irregular bladder mucosa (OR 3.53, sensitivity 70%, specificity 60%), and loss of perivesical fat plane (OR 3.17, sensitivity 81%, specificity 43%). However, urinary analysis and other urinary tract symptoms were poor predictors of bladder involvement. **Conclusions:** The present study demonstrated that the most relevant preoperative predictors of definite bladder invasion in patients with colorectal cancer are gross hematuria, a visible tumor during cystoscopy, and abnormal CT findings.

**Keywords:** Colon cancer - rectal cancer - bladder invasion - preoperative evaluation

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### Introduction

The incidence of colorectal cancer (CRC) is rapidly increasing in Asia (Pourhoseingholi, 2012). The majority of CRC found in Asian populations were more likely to be an advanced stage (Lohsiriwat and Lohsiriwat, 2008; Lohsiriwat et al., 2010; Unal et al., 2013; Wu et al., 2013). Up to 6% of CRC patients were reported to have urinary bladder invasion, especially those with adenocarcinoma of the sigmoid colon and rectum (Kobayashi et al., 2003; Chaleoykitti, 2005). En bloc tumor removal with adequate surgical margin is required to achieve good oncological outcomes. However, a multi-visceral resection could lead to high morbidity and mortality (Park and Lee, 2011; Mohan et al., 2013). Preoperative diagnostic modalities would provide useful information as to whether there is any evidence of CRC extension to the bladder. Accordingly, such information could help physicians educating patients,

optimizing patient's preoperative condition, and planning for appropriate management. The preoperative evaluation of locally advanced CRC including those with a suspicion of bladder invasion has been increasingly important and relevant, especially in the era of minimally invasive surgery for CRC and neoadjuvant chemoradiation for rectal cancer (van de Velde et al., 2014).

Several preoperative investigations are used to determine the extension of CRC to the urinary bladder, including urinalysis, cystoscopy, intravenous pyelography, transabdominal or endorectal ultrasonography, computed tomography (CT), and magnetic resonance imaging (MRI). However, these investigating tools have their own limitations. For example, although CT and MRI are reliable non-invasive modalities, they are costly and may be not widely available. On the contrary, urinalysis is simple and has moderate sensitivity (Chaleoykitti, 2005). Moreover, there are a limited number of studies examining

the accuracy of such investigations (Talamonti et al., 1993; Kobayashi et al., 2003; Chaleoykitti, 2005; Luo et al., 2013), and their results were controversial. The objective of this study was therefore to determine the accuracy of preoperative urinary symptoms, urinalysis, cystoscopic findings, and CT results for the diagnosis of definite bladder invasion in patients with CRC. The authors also aimed to provide an investigation scheme for CRC with a suspicion of bladder involvement.

## Materials and Methods

After obtaining an approval from our Institutional Review Board, medical records of CRC patients with a suspicion of bladder involvement who underwent CRC resection with partial or total cystectomy between 2002 and 2013 at the Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand was reviewed. Notably choices of preoperative investigation could be varied, and depended on clinical grounds and surgeon's discretion. If appropriated, cystoscopy was performed by well-trained urologists. Meanwhile, all patients were operated on by a team of experienced surgical consultants. All specimens were sent for pathological examination to determine whether there was a definite malignant infiltration to bladder wall by CRC or not.

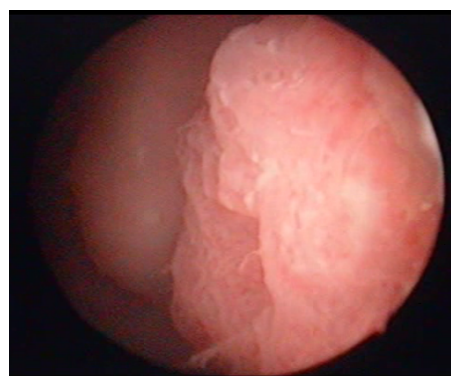
Data collected included patients' demographics, tumor characteristics, preoperative symptoms (gross hematuria, fecaluria, pneumaturia, and lower urinary tract symptoms), urinalysis (red blood cell >3 per high power field, white blood cell >3 per high power field, and positive urine culture for bacteria), cystoscopic findings (visible tumor, external compression, fistula, and bullous edema), and CT findings (gross tumor invasion, enhancing mass at bladder wall, irregular bladder mucosa, and loss of perivesical fat plane).

An odds ratio (OR) was used to determine the association between preoperative urinary symptoms, urinalysis, cystoscopic findings, CT results, and final pathological reports. The sensitivity, specificity, positive predictive value (PPV), and negative predictive value

(NPV) of each investigation were analyzed with 95% Confidence Interval (95% CI) Analysis for Windows (Statistics with Confidence, 2nd Edition, BMJ Books, London 2000).

## Results

This study included 90 eligible cases with an average age of 63 years (range 32-88). Of these, 64 patients (71%) were male. The most common site of primary CRC was the sigmoid colon (n=40, 44%), followed by the rectum (n=30, 33%) and the cecum (n=7, 8%). Final pathological reports showed definite bladder invasion in 53 cases (59%); the others (41%) showed peritumoral inflammatory adhesion to the bladder. Significant features for predicting definite tumor invasion were gross hematuria (OR 13.62,  $p=0.014$ ) and visible tumor during cystoscopy (OR 5.33,  $p=0.016$ ) (Figure 1). Predictive signs in CT scan were gross tumor invasion (OR 7.07,  $p=0.001$ ), abnormal enhancing mass at bladder wall (OR 4.09,  $p=0.003$ ), irregular bladder mucosa (OR 3.53,  $p=0.007$ ), and loss of perivesical fat plane (OR 3.17,  $p=0.022$ ) (Figure 2). Meanwhile, urinary analysis and other urinary tract symptoms were poor predictors of bladder involvement. The odds ratio and accuracy of each diagnostic modality are summarized in Table 1.

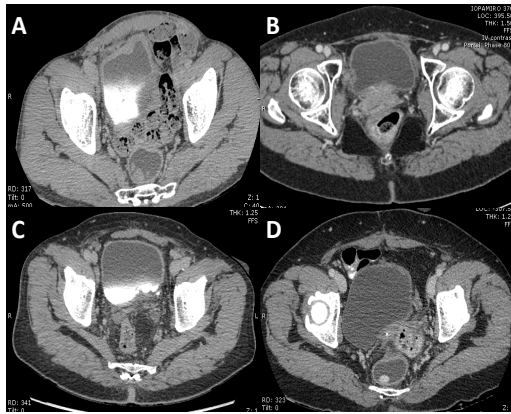


**Figure 1. Visible Colorectal Malignancy During Cystoscopy. Notably this Picture was Correlated with CT imaging in Figure 2A**

**Table 1. Sensitivity, Specificity, Positive Predictive Value (PPV), Negative Predictive Value (NPV), and Odds Ratio (OR) with 95% Confidence Interval (95% CI) of Each Feature for Predicting Invasion of Colorectal Cancer to the Urinary Bladder**

		Sensitivity (95% CI)	Specificity (95% CI)	PPV (95% CI)	NPV (95% CI)	OR (95% CI)	p value
Symptoms	Gross hematuria	28 (17-41)	97 (86-99)	93 (70-99)	49 (38-61)	13.62 (1.70-109.03)	0.014*
	Fecaluria/ pneumaturia	26 (16-39)	89 (75-96)	77 (43-90)	47 (35-58)	2.82 (0.84-9.50)	0.09
	Lower urinary tract symptoms	39 (27-53)	73 (57-85)	67 (49-81)	47 (34-59)	1.74 (0.70-4.36)	0.24
Urinalysis	Red blood cell > 3 HPF	48 (35-61)	67 (52-81)	69 (53-82)	47 (34-61)	2.02 (0.82-4.96)	0.13
	White blood cell > 3 HPF	67 (54-79)	46 (31-62)	65 (52-76)	49 (33-65)	1.73 (0.72-4.18)	0.22
	Positive urine culture	38 (24-55)	69 (51-83)	60 (39-77)	49 (34-66)	1.38 (0.48-3.92)	0.55
Cystoscopy	Visible tumor during cystoscopy	50 (36-64)	84 (62-95)	89 (72-96)	40 (26-55)	5.33 (1.37-20.71)	0.016*
	External compression	13 (6-25)	90 (69-97)	75 (41-93)	29 (19-41)	1.21 (0.22-6.62)	0.82
	Fistula	8 (3-20)	90 (67-97)	67 (30-90)	28 (18-40)	0.77 (0.13-4.62)	0.78
CT Findings	Bullous edema	44 (31-58)	47 (27-68)	68 (50-81)	25 (14-41)	0.7 (0.24-2.03)	0.51
	Gross tumor invasion	89 (77-95)	46 (31-62)	69 (56-80)	76 (55-89)	7.07 (2.26-22.14)	0.001*
	Enhancing mass at bladder wall	68 (54-80)	66 (49-79)	73 (58-84)	61 (45-74)	4.09 (1.62-10.35)	0.003*
	Irregular bladder mucosa	70 (56-81)	60 (44-74)	70 (56-81)	60 (44-74)	3.53 (1.41-8.89)	0.007*
	Loss of perivesical fat plane	81 (68-90)	43 (28-59)	66 (53-76)	63 (43-79)	3.17 (1.18-8.51)	0.022*

\* $P<0.05$



**Figure 2. Predictive Signs in CT Scan for Bladder Invasion in Patients with Colorectal Cancer; Gross Tumor Invasion A), Abnormal Enhancing Mass at Bladder wall B), Irregular Bladder Mucosa C) and Loss of Perivesical Fat Plane D)**

## Discussion

Although the precise staging of CRC is based on pathological report, reliable preoperative investigations in locally advanced CRC with a suspicion of bladder involvement would help surgeons to differentiate between direct tumor invasion and peritumoral inflammatory reaction. Moreover, a careful preoperative assessment in CRC patients could minimise unexpected findings of urinary tract involvement during an operation (McNamara et al., 2003). Accordingly, proper preoperative counseling to patient, appropriate preoperative preparation and well-planned intraoperative management could be achieved. The present study demonstrated that significant predictors of definite bladder invasion in CRC patients were gross hematuria, visible tumor during cystoscopy, and abnormal CT findings.

Regarding preoperative symptoms, we found that only gross hematuria was a good predictor for bladder invasion whereas fecaluria, pneumaturia and lower urinary tract symptoms were less accurate. Although fecaluria and pneumaturia are suggestive of colovesical fistula, this condition is uncommon in CRC (Garcea et al., 2006). Whilst the lower urinary tract symptoms were non-specific, gross hematuria could indicate direct tumor infiltration in a more meaningful way since advanced CRC is likely to bleed (Smith et al., 2006), especially when the bladder is contracted. Interestingly, it was recent evidence that even microscopic hematuria can be used as a screening test to detect urinary bladder mucosal infiltration of cervical cancer (Chuttiangtum et al., 2012).

The present study also showed that urinalysis and urine culture for bacteria were poor predictors for direct tumor infiltration to bladder. In the literature, only a few studies have been published on the value of urinalysis and urine culture in locally advanced CRC with a suspicion of bladder involvement. In 2005, Chaleoykitti from Thailand reported 59% sensitivity of abnormal urinalysis for predicting bladder invasion (Chaleoykitti, 2005), whereas several investigators from Japan did not recommend urine examination for screening of bladder involvement (Kobayashi et al., 2003). However, in the

future a better qualitative and quantitative urinalysis, including urine cytology, urine biomarker and metabolite analysis (Ghafouri-Fard et al., 2014), may be a non-invasive test that helps diagnosing of CRC and detecting bladder involvement by CRC (Kim, 2013).

Cystoscopy has been used by many physicians to determine bladder invasion and to evaluate the anatomical extension of the tumor (Kobayashi et al., 2003; McNamara et al., 2003; Chaleoykitti, 2005). Our study revealed that the most reliable sign for determining direct tumor infiltration was visible tumor during cystoscopy. Meanwhile, other abnormal cystoscopic findings such as external compression, fistula and bullous edema were not good predictors for malignant infiltration. A possible explanation for these findings is that external compression and bullous edema did not provide direct evidence of definite tumor infiltration; on the other hand visible tumor with proven histology from a biopsy did. Meanwhile, colovesical fistula could be strongly suggestive of tumor involvement, but the incidence of colovesical fistula in CRC patients with bladder involvement was uncommon especially in female patients (Pollard et al., 1987). Moreover, the visibility of fistula during cystoscopy was not highly sensitive (Garcea et al., 2006).

The present study demonstrated that several findings in CT scan were good predictive signs of definite malignant infiltration to bladder. These signs were gross tumor invasion, abnormal enhancing mass at bladder wall, irregular bladder mucosa and loss of perivesical fat plane. Our results are similar to other previous reports (Kim et al., 1992; Kobayashi et al., 2003; Chaleoykitti, 2005), thus confirming the reliability of CT scan to determine bladder involvement in locally advanced CRC. Apart from its non-invasiveness and high availability, CT scan provides both local staging and distant metastasis evaluation. Therefore, CT scan could be a useful non-invasive tool for screening bladder involvement in locally advanced CRC and for determining preoperative CRC staging. However, high-resolution MRI and positron emission tomography (PET)-CT could be of better predictive value in CRC patients receiving preoperative chemoradiation (Heo et al., 2014).

In conclusion, our results indicate that the symptom of gross hematuria, visible tumor during cystoscopy, and abnormal CT findings (gross tumor invasion, abnormal enhancing mass at bladder wall, irregular bladder mucosa and loss of perivesical fat plane) are good predictors for definite bladder invasion in CRC patients. Considering the nature of each investigation and its clinical application, CT scan of abdomen and pelvis could be an initial investigation for CRC patients with a suspicion of bladder involvement. Meanwhile, cystoscopy is reserved in case of abnormal CT findings of the bladder aiming to confirm definite tumor infiltration and to evaluate the anatomical extension of the tumor. Urinalysis and urine culture can be omitted except in case of urosepsis.

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## References

- Chaleoykitti B (2005). Preoperative diagnosis of urinary bladder involvement in adenocarcinoma of colon and rectum. *J Med Assoc Thai*, **88**, 1816-20.
- Chuttiantum A, Udomthavornsuk B, Chumworathayi B (2012). Hematuria screening test for urinary bladder mucosal infiltration in cervical cancer. *Asian Pac J Cancer Prev*, **13**, 4931-3.
- Garcea G, Majid I, Sutton CD, Pattenden CJ, Thomas WM (2006). Diagnosis and management of colovesical fistulae; six-year experience of 90 consecutive cases. *Colorectal Dis*, **8**, 347-52.
- Ghafari-Fard S, Nekooesh L, Motevaseli E (2014). Bladder cancer biomarkers: review and update. *Asian Pac J Cancer Prev*, **15**, 2395-403.
- Heo SH, Kim JW, Shin SS, Jeong YY, Kang HK (2014). Multimodal imaging evaluation in staging of rectal cancer. *World J Gastroenterol*, **20**, 4244-55.
- Kim KH (2013). More than the significance of conventional urinalysis. *Int Neurourol J*, **17**, 153-4.
- Kim SH, Na DG, Choi BI, Han JK, Han MC (1992). Direct invasion of urinary bladder from sigmoid colon cancer: CT findings. *J Comput Assist Tomogr*, **16**, 709-12.
- Kobayashi T, Kamoto T, Sugino Y, et al (2003). High incidence of urinary bladder involvement in carcinomas of the sigmoid and rectum: a retrospective review of 580 patients with colorectal carcinoma. *J Surg Oncol*, **84**, 209-14.
- Lohsiriwat V, Lohsiriwat D (2008). Comparison of immediate surgical outcomes between posterior pelvic exenteration and standard resection for primary rectal cancer: a matched case-control study. *World J Gastroenterol*, **14**, 2414-7.
- Lohsiriwat V, Pongsanguansuk W, Lertakyamanee N, Lohsiriwat D (2010). Impact of metabolic syndrome on the short-term outcomes of colorectal cancer surgery. *Dis Colon Rectum*, **53**, 186-91.
- Luo HL, Tsai KL, Lin SE, Chiang PH (2013). Outcome of urinary bladder recurrence after partial cystectomy for en bloc urinary bladder adherent colorectal cancer resection. *Int J Colorectal Dis*, **28**, 631-5.
- McNamara DA, Fitzpatrick JM, O'Connell PR (2003). Urinary tract involvement by colorectal cancer. *Dis Colon Rectum*, **46**, 1266-76.
- Mohan HM, Evans MD, Larkin JO, Beynon J, Winter DC (2013). Multivisceral resection in colorectal cancer: a systematic review. *Ann Surg Oncol*, **20**, 2929-36.
- Park S, Lee YS (2011). Analysis of the prognostic effectiveness of a multivisceral resection for locally advanced colorectal cancer. *J Korean Soc Coloproctol*, **27**, 21-6.
- Pollard SG, Macfarlane R, Greatorex R, Everett WG, Hartfall WG (1987). Colovesical fistula. *Ann R Coll Surg Engl*, **69**, 163-5.
- Pourhoseingholi MA (2012). Increased burden of colorectal cancer in Asia. *World J Gastrointest Oncol*, **4**, 68-70.
- Smith D, Ballal M, Hodder R, et al (2006). Symptomatic presentation of early colorectal cancer. *Ann R Coll Surg Engl*, **88**, 185-90.
- Talamonti MS, Shumate CR, Carlson GW, Curley SA (1993). Locally advanced carcinoma of the colon and rectum involving the urinary bladder. *Surg Gynecol Obstet*, **177**, 481-7.
- Unal HU, Demiralay E, Tepeoglu M, Fidan C, Kilickap S (2013). Lack of relationships between FGF19 staining pattern, lymph node metastasis and locally invasive characteristics of the tumor in colorectal cancers. *Asian Pac J Cancer Prev*, **14**, 3151-4.
- van de Velde CJ, Boelens PG, Tanis PJ, et al (2014). Experts reviews of the multidisciplinary consensus conference colon and rectal cancer 2012: science, opinions and experiences from the experts of surgery. *Eur J Surg Oncol*, **40**, 454-68.
- Wu HW, Gao LD, Wei GH (2013). hMSH2 and nm23 expression in sporadic colorectal cancer and its clinical significance. *Asian Pac J Cancer Prev*, **14**, 1995-8.