Is cystoscopy indicated for incidentally identified bladder wall thickening?

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Introduction: *The purpose of this study was to evaluate the yield of cystoscopy in detecting bladder malignancy following incidentally identified bladder wall thickening observed on computed tomography (CT) scans.*
Methods and materials: *Data from 3000 consecutive patients who underwent diagnostic cystoscopy at a single institution from 2006-2009 were collected retrospectively. All prior CT scan reports were reviewed, and patients whose sole indication for cystoscopy was incidentally detected bladder wall thickening were identified. Patients were categorized as diffuse thickening, focal thickening, or focal bladder mass based on the radiologist's report. Collected data included patient age, gender, race, smoking history, history of hematuria, medications for benign prostate hypertrophy or overactive bladder as well as cystoscopy results, pathology results, and follow up.*
Results: *Twenty-two patients (0.7% of cystoscopies) underwent cystoscopy for incidentally identified bladder wall thickening including 11 (50%) with focal bladder wall thickening, 8 (36.4%) with diffuse bladder wall thickening, and 3 (13.6%) with focal bladder mass lesions. Five patients (22.7%) had suspicious lesions on cystoscopy requiring endoscopic surgery with biopsy. Two patients with focal bladder mass lesions were found to have low grade, superficial bladder cancer (66.7% of patients with focal bladder mass lesions and 9.1% of all patients with incidental bladder wall thickening). No patients with diffuse or focal bladder wall thickening had malignancy.*
Conclusions: *Incidental findings of diffuse and focal bladder wall thickening on CT scan were found to have a low yield for the detection of urinary tract malignancy. Incidentally detected focal bladder mass lesions are more likely to have malignant pathology.*

Key Words: urinary bladder, cystoscopy, bladder cancer, incidental finding, computed tomography

Introduction

Computed tomography (CT) is a widely used imaging modality capable of providing high resolution, three dimensional views of virtually all tissue and organ systems. Because of the high sensitivity of this imaging modality, incidental findings representing various degrees of clinical importance are frequently identified.[1] In the urinary system, CT imaging often leads to the incidental identification of renal cysts and other masses for which explicit clinical algorithms have been established.[2] Similarly, incidentally detected findings identified during imaging of the gastrointestinal (GI) tract may require additional work up, and several studies have investigated the significance of truly incidental bowel wall thickening.[3-5]

However, to date, no published studies have investigated the significance of incidentally discovered bladder wall thickening (BWT). Both diffuse[6] and focal BWT can suggest malignancy,[7,8] but several other types of non-neoplastic disease entities can also manifest as BWT on CT.[8,9] Early identification of bladder cancer is an important goal for urologists and their patients, but the risks, costs, and inconvenience of cystoscopic evaluation in asymptomatic patients must be balanced against an evidence-based approach which justifies the procedure.

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Many radiology reports often use language such as "bladder wall thickening… recommend cystoscopy" and our urology division has followed these recommendations for the protection of our patients and for our own medical-legal protection. In addition, with the advent of improved imaging modalities, the number of CT scans has dramatically increased in the past decades, and the finding of incidental BWT is expected to increase as well. Therefore, the goal of our investigation was to provide initial data regarding utility of incidental BWT as an indication for diagnostic cystoscopy.

Methods and materials

This study was approved by the institutional review board of the McGuire Veterans Affairs Hospital. The cystoscopy log book was used to identify 3000 consecutive patients who underwent flexible cystoscopy from January 2006 to September 2009 using Olympus fiberoptic cystoscopes. Cystoscopies were performed by more than 10 rotating urology residents with attending supervision by five board certified urologists. CT scans were interpreted by 10 different attending radiologists. The computerized medical record was reviewed to identify patients whose primary indication for cystoscopy was incidentally identified BWT on CT based upon radiologist impression. Patients were excluded if found on chart review to have a concurrent history of bladder cancer.

Data collected from each patient's record included age, gender, race, smoking history, history of microscopic or gross hematuria, occupational history and exposures, and history of current indwelling urinary catheter usage. Formulary approved medications for benign prostate hyperplasia (BPH) including finasteride, dutasteride, prazosin, terazosin, doxazosin, tamsulosin or overactive bladder (OAB) including oxybutynin and tolterodine were also recorded. Radiologic data included the name of the attending radiologist who reported the BWT. Cystoscopic findings, bladder biopsy results, and time of follow up from date of cystoscopy to last documented GU or non-GU follow up were also recorded.

Patients were subdivided into types of BWT including diffuse thickening, focal thickening, and focal mass as described in the radiologist's report and confirmed by an outside radiologist blinded to the initial reports. Suspicious findings on cystoscopy were subsequently evaluated with bladder biopsy performed under general or regional anesthesia. Numeric data are reported as means ± SEM. Chi-square tests compared categorical variables and Students t-tests compared continuous variables with $p < 0.05$ considered significant.

Results

Twenty-two of 3000 patients (0.7%) who underwent cystoscopy during the study period were referred for incidentally identified BWT on CT. Patient characteristics are described in Table 1 and demonstrate that 50% had diffuse BWT, 36.4% had focal BWT, and 13.6% had a focal mass. Examples of BWT subtypes including diffuse, focal, and mass are demonstrated in Figure 1. The mean age of the patients was 65.1 ± 2.7 years. The racial makeup was diverse with 45.5% Caucasians and 54.5% patients whose race was described as African-American or other, and the overwhelming majority were males (95.5%). The mean length of follow up (time from cystoscopy to last recorded medical visit) was 892 days ± 83 days with 72.7% alive at last follow up. Of the six patients who died in follow up, none died of bladder cancer, and 63.6% of patients had genitourinary (GU)-specific follow up appointments. There were no differences in age, race, gender, or length of follow up between the groups.

TABLE 1. **Patient characteristics**

	n (%)	**Age (yr)**	**White n (%)**	**Male n (%)**	**Total follow up (days)**	**GU follow up n (%)**	**Alive in follow up n (%)**
Total	22 (100)	65.1 ± 2.7	10 (45.5)	21 (95.5)	892 ± 83	14 (63.6)	16 (72.7)
Diffuse	11 (50.0)	64.6 ±3.9	3 (27.3)	10 (90.9)	775 ± 104	7 (63.6)	9 (81.8)
Focal + mass	11 (50.0)	65.6 ± 4.0	7 (63.6)	11 (100)	1010 ± 123	5 (45.5)	7 (63.6)
Focal	8 (36.4)	63.1 ± 4.9	5 (62.5)	8 (100)	1082 ± 159	4 (50.0)	5 (62.5)
Mass	3 (13.6)	72.3 ± 6.4	2 (66.7)	3 (100)	816 ± 121	3 (100)	2 (66.7)

Total follow up = days from cystoscopy to last documented visit. Continuous data compared to diffuse group using t-tests. Categorical data compared to diffuse group using chi square tests

Figure 1. Examples of contrast-enhanced axial CT images through the pelvis demonstrating **a)** diffuse BWT, **b)** focal BWT and **c)** focal bladder mass from patients in the current study. Bladder is denoted by "BL". Arrows in (b) point to an area of focal BWT, and arrows in (c) point to a focal bladder mass lesion.

A total of five (22.7%) patients were found to have positive cystoscopic findings (suspicious lesions) and were scheduled for endoscopic biopsy in the operating room including one patient in the diffuse group (9.1%), two patients in the focal group (25%), and two patients in the mass group (66.7%), Figure 2a. Of these five patients, a biopsy was not performed in one as no lesions were seen during the operative cystoscopy which occurred 47 days later. Biopsies were performed in four additional patients. Two were found to have "chronic inflammation" and two were found to have low grade superficial transitional cell carcinoma (papillary urothelial neoplasm of low malignant potential) which represents 0.07% of all cystoscopies, Figure 2b. The first patient with malignancy was an 84-year-old Caucasian male non-smoker in the mass group who had documented microscopic hematuria and was not taking medications for BPH or OAB. This patient had a focal bladder mass identified incidentally on CT scan for "failure to thrive." The second patient with malignancy was a 62-year-old Caucasian male smoker with no history of hematuria or use of medications for BPH or OAB. This patient had an incidental focal bladder mass identified during a CT-arteriogram for "severe peripheral vascular disease with rest pain."

In examining factors potentially associated with BWT, 32% of patients had a history of hematuria, 9% used indwelling catheters for voiding dysfunction, 54% were smokers, 23% used medications for BPH or OAB, and 54.5% had non-bladder cancer related GU issues requiring separate GU follow up (i.e. prostate cancer, renal cell cancer, neurogenic bladder,

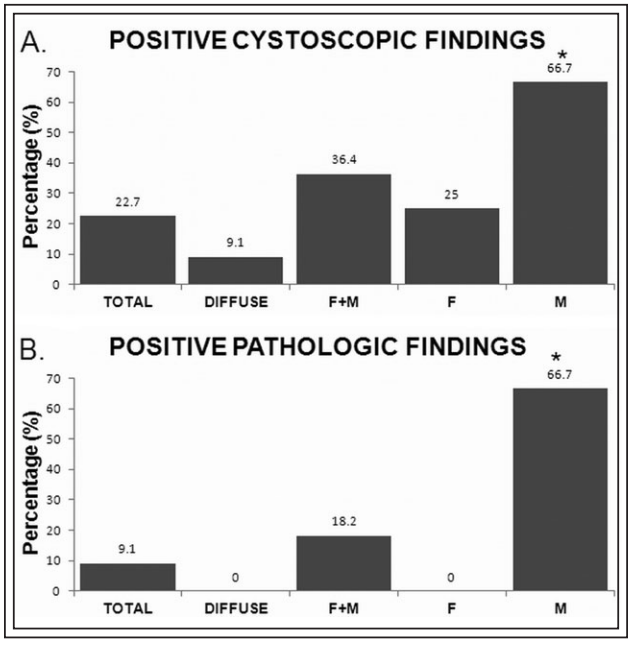

Figure 2. a) Patients with positive cystoscopic findings requiring subsequent operative endoscopic biopsy grouped according to subtype of BWT. **b)** Patients with positive pathologic findings (bladder malignancy) grouped according to subtype of BWT.
F = focal; M = mass.
*$p < 0.05$ when compared to the "Diffuse" group.

TABLE 2. **Factors associated with bladder wall thickening**

	n (%)	Heme n (%)	Cath n (%)	Smoke n (%)	Meds n (%)	GU n (%)
Total	22 (100)	7 (31.8)	2 (9.1)	12 (54.5)	5 (22.7)	12 (54.5)
Diffuse	11 (50.0)	6 (54.5)	2 (18.2)	6 (54.5)	5 (45.5)	8 (72.7)
Focal + mass	11 (50.0)	1 (9.1)*	0 (0)	6 (54.5)	0 (0)*	5 (45.5)
Focal	8 (36.4)	0 (0)*	0 (0)	4 (50.0)	0 (0)*	3 (37.5)
Mass	3 (13.6)	1 (33.3)	0 (0)	2 (66.7)	0 (0)	1 (33.3)

heme = history of any hematuria; cath = use of indwelling urinary catheter; smoke= active smoker; meds = active use of meds for BPH or OAB; GU = followed for unrelated GU issues.
*$p < 0.05$ (compared to the diffuse group)

renal calculi, BPH), Table 2. Only the presence of incidentally indentified focal bladder mass lesions were found to be associated with positive cystoscopic or pathologic findings ($p < 0.05$, Figure 2). Surprisingly, patients with focal BWT had significantly lower rates of hematuria (0% versus 54.5%, $p < 0.05$) and lower rates of medication use for OAB and BPH (0% versus 45.5%) than those with diffuse BWT. There were no differences in the rates of smoking, indwelling catheter use, non-bladder cancer related GU issues, or occupation between the groups.

Discussion

The purpose of this study was to investigate the significance of incidentally identified BWT, particularly with regard to the diagnosis of malignancy. No studies have been performed on this subject, and our aim in this initial investigation was to lay the groundwork for continued exploration. Previous studies have investigated the significance of CT detected incidental pulmonary nodules[10] and renal masses[2] and have helped in the formation of evidence-based algorithms to guide clinical management. However, the significance of incidentally detected gastrointestinal wall thickening on CT imaging is still being explored.[3,4,11]

In the current study, only one of the 11 patients (9%) with diffuse BWT had abnormal cystoscopic findings, and no patients were found to have malignancy. One explanation was the high prevalence of BPH in the male Veterans above the age of 60 that were included in this study. Among the diffuse group, 45.5% were taking medication for BPH/OAB versus 0% in the focal or mass groups, which could potentially explain some of the observed CT findings. Furthermore, two patients in the diffuse group required indwelling catheters for chronic urinary retention. High rates of catheter use and BPH could also explain the higher-than-expected rate of hematuria in the diffuse group (54.5%) as compared to the focal group (0%).

Among the patients in the mass group, the data demonstrate a 66.7% positive predictive value for the detection of low grade papillary transitional cell carcinoma. While this type of pathology is considered to be of low malignant potential, it often recurs and can progress to more aggressive pathologies.[12] It is reassuring that no patients in the diffuse or focal groups were found to have bladder malignancies but concerning that three patients categorized as having diffuse or focal BWT underwent unnecessary trips to the operating room for bladder biopsy.

One additional issue in the evaluation of incidentally detected BWT is the variability induced by different scanners, differing protocols, and differing radiologic interpretations. As an example, in a study by Olcott and colleagues,[13] the authors described the appearance of pseudolesions in the bladder during the performance of standard contrasted-enhanced CT scans. In the current investigation, the use and specific protocols for contrast-enhancement were extremely variable and heightened awareness of potential pitfalls such as pseudolesions could improve the diagnostic yield of BWT.

Evidence-based management algorithms have been developed for incidental CT findings in the lungs[10] and kidneys.[2] However, retrospective studies,[3,4,11] demonstrate a low likelihood of finding malignancy on endoscopic evaluation for incidental bowel wall thickening. However, on follow up endoscopic evaluations, many patients with bowel wall thickening received new diagnoses of both malignancy and non-neoplastic diseases. Based on these results, the authors suggested that the finding of incidental bowel wall thickening should warrant continued endoscopic follow up.

This study is limited by the small number of patients with true incidental BWT, and additional studies with larger patient numbers will be necessary to more accurately assess the yield of cystoscopy. Furthermore, BWT was not objectively categorized as there are no standardized criteria for CT-based evaluation of bladder wall lesions analogous to those for renal cysts[14] and renal masses.[15] Future investigations evaluating the long term outcomes of patients who undergo cystoscopy for incidentally detected BWT will be necessary to establish meaningful evidence-based clinical guidelines.

Conclusions

Currently, no studies have investigated the significance of incidentally identified BWT, and our study aims to lay the groundwork for further investigation of this finding. Our study found that no patients with incidentally identified diffuse BWT or focal BWT on CT scans had malignancy when evaluated by cystoscopy, but 66.7% of patients with focal mass lesions were found to have low grade, superficial transitional cell carcinoma. Because of our small sample size and the limits of the current investigation, we recommend that diagnostic cystoscopy continue to be performed for incidental BWT after an informed discussion of these initial results as well as the risks and benefits of the procedure with patients. Further research is required with additional patient numbers prior to the establishment of definitive guidelines for the management of patients with incidentally identified bladder wall thickening on CT scans. □

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