

# The Case for Including Bowel Urgency in Toxicity Reporting After Pelvic Cancer Treatment

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## Abstract

Bowel toxicity is a major complication of cancer treatment, and its accurate reporting is important for assessing outcomes. The NCI's Common Terminology Criteria for Adverse Events (CTCAE) is the preferred method for capturing adverse events after all cancer treatments, particularly within clinical trials. However, the CTCAE version 4 does not include urgency of defecation as an item, despite this being one of the most common and persistent adverse consequences of treatment of pelvic cancers. The importance of bowel urgency to patients is well documented, and this treatment effect has a negative impact on social function and quality of life. Bowel urgency is also important clinically because it may represent significant underlying problems. This article presents the case for including patient reported assessment of bowel urgency as an independent item in cancer treatment adverse event reporting. (*JNCCN* 2013;11:827–833)

The NCI's Common Terminology Criteria for Adverse Events (CTCAE) is the preferred method for capturing adverse events in clinical trials.<sup>1</sup> CTCAE was the first system for recording acute and late treatment effects that was suitable for use with all cancer treatments.<sup>2</sup> Despite widespread use and regular revision, the system still has its limitations, such as for the collection of rectal injuries.<sup>3</sup> Anorectal toxicity items currently include

rectal or anal fistulation, hemorrhage, mucositis, necrosis, pain, stenosis, and ulceration, along with separate items of fecal incontinence and proctitis. Fecal urgency is only listed as part of the definition of grade 3 proctitis in the CTCAE version 4, despite the fact that it is a common and important consequence of cancer treatments in its own right. Proctitis is the inflammation of the rectal mucosa that can cause discomfort and bleeding. Fecal urgency can be a symptom of severe proctitis, but not always.

Furthermore, the CTCAE has no items that relate to patient distress, and the grading system does not record the effect of different individual items on patient distress. This omission is important, because patients with low rectal toxicity scores (ie, grade 0 or 1) have been shown to report high levels of distress associated with their symptoms.<sup>4</sup> Currently, none of the toxicity scoring systems capture the effect of symptoms in terms of distress levels or quality of life. The use of currently available and validated patient-reported outcome (PRO) tools, such as the inflammatory bowel disease questionnaire (IBDQ), Vaizey incontinence questionnaire (VIQ), or CTCAE pelvic symptom questionnaire, as an adjunct to physician-centric toxicity grading in clinical practice and trials, would address this shortfall.

## Bowel Urgency

Urgency of defecation, or the inability to defer defecation, is frequently part of the cluster of symptoms that can develop after pelvic radiotherapy,<sup>3</sup> and affects between 10% and 53% of patients.<sup>5–10</sup> Bowel urgency is not only one of the most common symptoms experienced by patients after pelvic radiotherapy (Figure 1), but is also frequently associated with reduced social

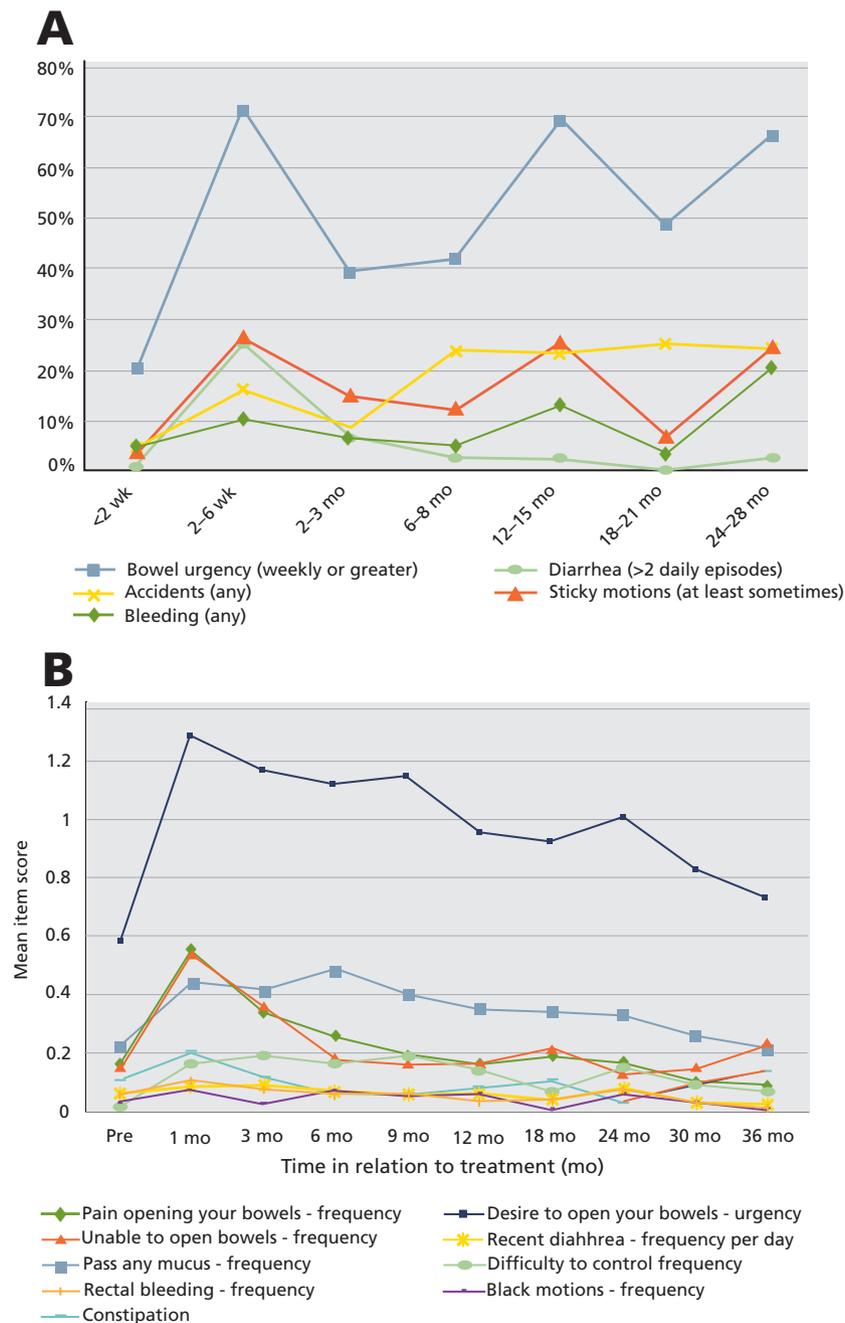
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**Figure 1** Frequency of bowel symptoms over time showing urgency of defecation as the most common and persistent symptom. (A) The change in frequency of bowel-related complications reported after radiotherapy in 327 patients with cervix cancer (Jason Madan, MA, MSc, University of Bristol, and Rachid Rafia, MSc, University of Sheffield, unpublished data). (B) Mean item scores plotted with respect to time after brachytherapy for the rectum/bowel section of Common Terminology Criteria for Adverse Events, version 3, for 368 patients with prostate cancer (Carmel Anandadas, MBChB, MRCP, FRCR, The Christie NHS Foundation Trust, unpublished data).

functioning, reduced quality of life,<sup>11,12</sup> and patient distress.<sup>4</sup> Urgency of defecation can be so debilitating that some patients never leave the house so they can ensure that they are always close to a toilet, or do not eat for many hours before going out to avoid fecal incontinence.<sup>12</sup>

Urgency of defecation is also significant because it may indicate potentially life-threatening underlying problems, such as a recurrent or new malignancy.<sup>7</sup> Multivariate analysis also shows that urgency, along with rectal bleeding and male gender, is an important indicator of chronic radiation proctopathy or

colopathy.<sup>7</sup> In combination, these characteristics have a positive predictive value of 87% for chronic radiation-related gastrointestinal injury.<sup>7</sup> The presence of urgency as a symptom is therefore diagnostically significant. However, one-third of patients with gastrointestinal symptoms have diagnoses unrelated to previous radiotherapy,<sup>7</sup> so other causes of urgency must be identified and excluded in this patient population.

Bowel urgency is an important consequence of not just conventional external-beam pelvic radiotherapy; up to 6.5% and 22% of patients develop bowel urgency after prostate brachytherapy and intensity-modulated radiotherapy, respectively.<sup>11,13–16</sup> It is also a common symptom of other treatment modalities for malignancies of pelvic origin (Table 1). Up to 19% of patients develop bowel urgency after radical prostatectomy<sup>17–21</sup> and up to 73%, 40%, and 59% of patients with rectal cancer develop bowel urgency after surgery, chemoradiotherapy, and a combination of surgery and chemoradiotherapy, respectively.<sup>22–28</sup> Evidence also shows that combining treatment modalities for cervical and prostate cancer can increase gastrointestinal toxicity.<sup>20–29</sup> Urgency of defecation after all modalities of cancer treatment for pelvic malignancies is clearly important in terms of the proportion of patients affected, impact on quality of life, and representation of underlying problems. However, toxicity grading systems do not give this symptom appropriate weighting. A need exists to include urgency of defecation as a separate item in any toxicity scoring system. Table 2 provides a suggested grading system for urgency of defecation as an item in a future revision of the CTCAE.

## The Importance of PROs

The incidences of bowel urgency in the studies summarized earlier were assessed using PRO measures. Toxicity reporting in both clinical and research settings is highly variable. Clinician-rated toxicity scores are often based on passive data collection relying on retrospective review and interpretation of case notes. This assumes that no report of toxicity equates to no toxicity, rather than the fact that the right questions may not have been asked or that the recording or interpretation of the patient's response may have been inaccurate. Many clinician-scored tools, including those in the CTCAE version 4, are very coarse tools arbitrarily reducing toxicity to an

ordinal score ranging from 1 (mild or asymptomatic) to 5 (death). Problems particularly exist with accurate detection of toxicity at the lower end of the spectrum. Information about symptoms that have required significant intervention or hospitalization (ie, CTCAE grades 3 or 4) are easier to capture, but those considered “mild” or requiring “localized treatment” (ie, CTCAE grades 1 or 2) may not be recorded in hospital notes. Significant limitations clearly exist with ordinal scales and the process of assigning arbitrary values or numbers to symptoms in terms of accuracy and clinical relevance. Additionally, although many scores require categorization of toxicity symptoms according to severity, no published data exist on which to base this stratification. This represents an important area for future research based on prospective cohorts of patient-reported data.

Underreporting of symptoms by patients also affects the ability to accurately identify and manage consequences of cancer treatment. Patients are often reluctant to disclose symptoms either because of embarrassment,<sup>30</sup> not wanting to appear ungrateful about the treatment they have been given,<sup>30</sup> thinking that symptoms are inevitable consequences and that nothing can be done about them,<sup>31</sup> and wanting to use the time available to discuss issues specifically related to their cancer.<sup>32</sup> Patients also do not always report symptoms because of the measures they have taken to avoid them (eg, not leaving the house to avoid urgency-related fecal incontinence).<sup>33</sup>

Increasing evidence shows that PROs can complement survival outcome measures in patients with cancer<sup>34</sup> to fully assess the impact of the disease and treatment on the physical, psychological, and social functioning of the patient.<sup>35</sup> PROs and health-related quality-of-life measures, which assess not only symptom frequency but also severity and impact on a patients' life, can play an invaluable role in cancer intervention assessment and decision-making.<sup>36</sup>

Routine use of PROs would address the problem of underreporting of toxicity symptoms and would standardize toxicity documentation. PROs are a form of active data collection and do not rely on the correct questions being asked by the clinician, the answer being recorded appropriately, or the answer being recorded in a way that accurately reflects the patient's experience. Several PROs have been used to “measure” toxicity, but caution must be exercised to avoid their inappropriate use. PROs should be used in the

**Table 1 The Incidence of Bowel Urgency for Different Treatment Modalities for Various Tumor Sites**

Tumor Site	Treatment Modality	Method for Identifying Bowel Urgency	Percentage	References
Anus	EBRT and brachytherapy	Symptom questionnaire <sup>a</sup>	50%	44
Cervix	EBRT	Symptom questionnaire <sup>a</sup>	33%	45
Cervix & uterus	EBRT	Symptom questionnaire <sup>a</sup>	67%	46
Gynecologic	EBRT +/- surgery	Symptom questionnaire <sup>a</sup>	29%	47
Prostate	EBRT	UCLA prostate cancer index	30%	17
		PCOS survey	29%	20
		Symptom questionnaire <sup>a</sup>	36%	48
		Symptom questionnaire <sup>a</sup>	13%	49
		LENT SOMA	Grade 1: 13% Grade 2: 7% Grade 3: 8% Grade 4: 7%	8
Prostate	Whole pelvis radiotherapy	RTOG/EORTC	Grade 2: 3%	15
		Expanded prostate cancer index composite	15%	8
Prostate	Prostate only radiotherapy	Expanded prostate cancer index composite	3%	8
Prostate	IMRT	RTOG <sup>b</sup>	Grade 1: 11% Grade 2: 3%	11
		RILIT	Grade 1: 21% Grade 2: 1%	13
Prostate	Radical prostatectomy	UCLA prostate cancer index symptom questionnaire	2%–19%	17–21
		Expanded prostate cancer index composite		
		Modified Kelly questionnaire		
Prostate	Radical prostatectomy and EBRT	Symptom questionnaire <sup>a</sup>	53%	18
Prostate	Brachytherapy	RTOG/EORTC, <sup>b</sup> CTCAE v3 <sup>c</sup>	Grade 0: 100% Grade 1: 7%	15 16
Rectum	Surgery alone	History of urgency; symptom quest <sup>a</sup> ; structured interview	4%–73%	22–24
Rectum	Surgery with preoperative CRT	Modified AMS fecal incontinence questionnaire	40%	26
Rectum	Surgery with postoperative CRT	Anorectal function questionnaire	36%	27
Rectum	Surgery with EBRT	Symptom questionnaire <sup>a</sup>	53%	50
Rectum	Intersphincteric resection +/- CRT	Symptom questionnaire <sup>a</sup>	59%	28
Rectum	Intersphincteric resection +/- preoperative EBRT	Modified AMS fecal incontinence questionnaire	19%–32%	51,52
		Symptom questionnaire <sup>a</sup>		
Rectum	CRT	Symptom questionnaire <sup>a</sup>	40%	25
Mixed pelvic tumor sites	EBRT	Symptom questionnaire <sup>a</sup>	53%	10

Abbreviations: AMS, American Medical Systems; CRT, chemoradiation; CTCAE, Common Terminology Criteria for Adverse Events; EBRT, external-beam radiotherapy; EORTC, European Organisation for Research and Treatment of Cancer; IMRT, intensity-modulated radiotherapy; LENT SOMA, Late Effects of Normal Tissue—Subjective, Objective, Management, Analytic scale; PCOS, Prostate Cancer Outcomes Study; RILIT, Radiotherapy-Induced Lower Intestinal Toxicity score (adapted from RTOG); RTOG, Radiation Therapy Oncology Group Score; UCLA, University of California, Los Angeles.

<sup>a</sup>Refers to locally developed in-house symptom-based questionnaire to identify gastrointestinal symptoms delivered as either a questionnaire or interview. Urgency is mainly scored as either absent or present, but sometimes in terms of how common the symptom is to the individual participant. This table reports any urgency as an overall percentage for in-house questionnaires.

<sup>b</sup>Modified to include urgency of defecation.

<sup>c</sup>Modified to include urgency of defecation under "gastrointestinal – other."

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**Table 2 Suggested Grading for Urgency of Defecation as an Item in Common Terminology Criteria for Adverse Events**

Adverse Event	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5
Urgency of defecation <sup>a</sup>	Intermittent urgency of defecation (1 episode in the last month or less) No associated fecal incontinence or soiling No impact on ADL	Frequent urgency of defecation (1 episode in the last week or more) with no associated fecal incontinence or soiling but limiting ability to complete all desired activities	Daily urgency of defecation with or without fecal incontinence with or without the need to wear pads or take constipating medication Limitation of ADL	Constant urgency of defecation with regular fecal incontinence or soiling with or without the need to wear pads or take constipating medication Significant limitation of ADL or inability to leave the house	-

Abbreviation: ADL, activities of daily living.

<sup>a</sup>Defined as a disorder characterized by the inability to defer defecation by 15 minutes, which is often associated with fear of or actual fecal incontinence.

context in which they were validated. In terms of gastrointestinal toxicity, IBDQ, VIQ, and CTCAE pelvic symptom questionnaires are all validated. Quality-of-life questionnaires, however, are frequently misused as a surrogate measure of toxicity outcomes for cancer treatments despite the fact that they are not designed to detect toxicity and have not been validated for this indication. Numerous factors affect quality of life other than symptoms, including personal and environmental factors and having a diagnosis of cancer,<sup>37</sup> and therefore using these tools to assess toxicity constitutes a significant methodologic error.

## The Future of Toxicity Measurement

Accurate and consistent identification and measurement of the consequences of cancer treatment are essential to ensure the safety of current and emerging interventions and facilitate the provision of gold-standard aftercare. Assessment tools need to be refined to ensure that they are asking the right questions to detect toxicity, and the way toxicity is measured and compared must be improved. Widely accepted tools must be available to allow comparison between trials and within clinical practice, and those comparisons must be statistically meaningful. Toxicity must be measured at consistent time points, and routine use of validated PROs must be seriously considered. Several groups are working to develop PROs for this patient group, including the NCI PRO program and the Patient Reported Outcome Measurement Information System (PROMIS).

Despite increasing recognition that routine measurement of PROs can potentially improve planning, monitoring, and management of cancer care,<sup>38–42</sup> several barriers remain to their adoption in clinical practice, including concerns regarding confidentiality, doubts that they are a valuable tool to guide patient care, and concerns regarding the time and resources required for their implementation in routine practice.<sup>34</sup> These issues are beginning to be addressed with the development of electronic versions of PROs, which have been shown to be as feasible as paper forms,<sup>43</sup> and work to statistically change the scoring system from an ordinal to a linear score and to simplify it and facilitate its use in the clinic setting.

## Conclusions

The purpose of oncology follow-up is early detection of disease recurrence, metastatic spread, or treatment-related morbidity. In terms of detecting toxicity after cancer treatment, the tools must fit this purpose, and be practical to use in a clinical setting and comprehensive in reporting important symptoms experienced by patients. Having the right tools will ensure adequate identification of symptoms to facilitate appropriate intervention and specialist referral. In the context of pelvic malignancies, current scoring systems should be revised to include bowel urgency,<sup>3</sup> and toxicity recording should include suitable validated PROs to complement physician-reported measures.

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