Development, Validation and Testing of an Epidemiological Case Definition of Interstitial Cystitis/Painful Bladder Syndrome

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Abbreviations and Acronyms

IC = interstitial cystitis

IC/PBS = IC/painful bladder syndrome

OAB = overactive bladder

RAM = RAND/UCLA Appropriateness Method

RICE = RAND Interstitial Cystitis Epidemiology

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Purpose: No standard case definition exists for interstitial cystitis/painful bladder syndrome for patient screening or epidemiological studies. As part of the RAND Interstitial Cystitis Epidemiology study, we developed a case definition for interstitial cystitis/painful bladder syndrome with known sensitivity and specificity. We compared this definition with others used in interstitial cystitis/painful bladder syndrome epidemiological studies.

Materials and Methods: We reviewed the literature and performed a structured, expert panel process to arrive at an interstitial cystitis/painful bladder syndrome case definition. We developed a questionnaire to assess interstitial cystitis/painful bladder syndrome symptoms using this case definition and others used in the literature. We administered the questionnaire to 599 women with interstitial cystitis/painful bladder syndrome, overactive bladder, endometriosis or vulvodynia. The sensitivity and specificity of each definition was calculated using physician assigned diagnoses as the reference standard.

Results: No single epidemiological definition had high sensitivity and high specificity. Thus, 2 definitions were developed. One had high sensitivity (81%) and low specificity (54%), and the other had the converse (48% sensitivity and 83% specificity). These values were comparable or superior to those of other epidemiological definitions used in interstitial cystitis/painful bladder syndrome prevalence studies.

Conclusions: No single case definition of interstitial cystitis/painful bladder syndrome provides high sensitivity and high specificity to identify the condition. For prevalence studies of interstitial cystitis/painful bladder syndrome the best approach may be to use 2 definitions that would yield a prevalence range. The RAND Interstitial Cystitis Epidemiology interstitial cystitis/painful bladder syndrome case definitions, developed through structured consensus and validation, can be used for this purpose.

Key Words: urinary bladder; cystitis, interstitial; pain; epidemiology; diagnosis

Interstitial cystitis/painful bladder syndrome is a chronic, poorly understood condition. There is no consensus about the cause of the condition, which has prevented identification of an objective marker and development of a clinical diagnostic protocol. As a result, wide variability exists in the ways in which patients are identified for epidemiological studies. Studies have assessed the prevalence of an assigned physician diagnosis of IC/

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PBS. However, such research is limited to patients with access to health care and not all physicians may be familiar enough with IC/PBS to assign the diagnosis. Another method is to ask individuals whether they have ever been diagnosed with IC/PBS. However, this is subject to inaccuracies due to recall bias and selection effects since patients who have the condition may be undiagnosed or diagnosed with another condition.

The most common method to estimate IC/PBS prevalence is to assess symptoms indicating IC/PBS.[1–3] Three epidemiological studies used survey methods to estimate the IC/PBS prevalence in a community population of women. Leppilahti et al used a mailed questionnaire to estimate prevalence[1] using a criterion based on the IC symptom and problem indexes.[4] Clemens et al used mailed questionnaire responses about bladder pain, urgency and frequency to estimate the prevalence of IC symptoms in women sampled from a managed care population.[2] The Boston Area Community Health investigators estimated the prevalence of IC symptoms using questionnaires administered during in person interviews at patient homes.[3] Questions about IC/PBS symptoms were included in the 2004 version of the United States Nurses Health Study, which was administered to women 58 to 83 years old.[5] In this cohort of elderly women the prevalence of IC/PBS symptoms was 2.3%. Prevalence increased with age from 1.7% of those younger than 65 years up to 4.0% in women 80 years old or older. Finally, in 981 women 19 to 89 years old attending a voluntary health screening project in Vienna, Austria, the prevalence of IC/PBS symptoms was 0.3% (306/100,000).[6]

Reported IC prevalence estimates in these various studies vary considerably from less than 1% to 11%. The lack of a standardized method to identify IC/PBS symptoms may be responsible for the different prevalence estimates. Also, to our knowledge no information exists about the ability of various questionnaires to accurately identify women with IC/PBS (sensitivity) or distinguish them from women diagnosed with other similar conditions (specificity).

We report the systematic development and validation of population screening items for use in the RICE study, a national prevalence study of IC/PBS in women. We examined the sensitivity and specificity of this and other epidemiological definitions of IC/PBS used in the literature.

METHODS

Case Definition Panel

We used an adaptation of RAM, a methodology developed to combine the best available scientific evidence with the collective judgment of a group of experts, to yield a statement about the appropriateness of performing a medical procedure. RAM has been used extensively for appropriateness studies worldwide[7] and has been applied to evaluate the appropriateness of diverse medical procedures, such as Crohn's disease therapy,[8,9] coronary angiography and revascularization,[10–14] colonoscopy[15] and spinal manipulation for low back pain.[16,17] It has also been adapted to develop quality of management criteria for noninsulin dependent diabetes mellitus.[18] However, results depend on the quality of the scientific evidence and on expert judgment.

We adapted RAM to determine the appropriateness of various symptom indicators to diagnose IC/PBS compared with indicators of conditions with overlapping symptoms, such as OAB, endometriosis and vulvodynia. We solicited nominations from relevant medical societies, including the American Urological Association, American College of Obstetrics and Gynecology, and American Urogynecologic Society, and from recognized IC/PBS experts. Nine experts were chosen for the final multidisciplinary panel, including 5 in urology, 2 in gynecology, 1 in nursing and 1 in case definition methodology.

We performed a comprehensive literature review of the best scientific evidence about IC/PBS and related conditions with overlapping symptoms, ie OAB, endometriosis and vulvodynia, using the PubMed® database and predefined search terms.[19] The final review included a history of the case definition of each disease and a description of the prevalence of patient reported symptoms within and across diseases. Before the panel meeting we sent to the expert panel members the literature review, a list of 60 possible symptom indicators for the case definition of IC/PBS and related conditions, and symptom rating forms.

Panel members independently rated the extent to which each indicator was evidence for or against a diagnosis of IC/PBS and each related condition, and sent back their ratings. Ratings were analyzed and a report was presented to each individual panel member on meeting day 1. All symptoms were discussed for each condition separately and the moderators focused the group on the areas on which there was substantial disagreement or a spread of ratings. The strength of evidence was discussed as appropriate to determine reasons for disagreement or agreement.

At the end of this discussion panelists completed a second round of ratings. On meeting day 2 panelists were shown the new ratings. After further discussion a consensus case definition was produced.

Validation Study

Measurement. Based on panel results we developed a screening questionnaire including multiple questions on pain, urgency, frequency, nocturia, symptom triggers and alleviators, and quality of life. These items were combined in various ways to yield candidate IC/PBS definitions for testing.

Enrollment. We contacted 42 urologists and gynecologists around the United States, including those in community and academic medical center practices, with recognized expertise in managing IC/PBS, OAB, vulvodynia and endometriosis. We invited the clinicians to refer female patients with these conditions to the investigative team.