

## AN ONCOLOGIC APPROACH TO ULCERATIVE INTERSTITIAL CYSTITIS: DEFINING COMPLETE REMISSION

### Hypothesis / aims of study

Ulcerative Interstitial Cystitis (UIC) with bladder ulcers or Hunner lesions (HL) represents a distinct entity which is unrelated to Bladder Pain Syndrome (BPS). It occurs in a different patient population, has a different prognosis, and differing response to various treatments. Unfortunately, for the past twenty-five years, the conditions have for the most part been lumped together in basic science and clinical research. This has greatly hindered our understanding of UIC which is a serious, challenging, but potentially solvable problem.

For the past five years, the author has developed an “oncologic” approach to IC with a goal of critically evaluating treatment response and ultimately resolving the disease completely when possible.[1] This depends on a combination of surgical, pharmacologic, and behavioural therapies. Herein is presented one logical construct that will facilitate the study of UIC. The approach is described, outcome measures defined, and results presented.

### Study design, materials and methods

A retrospective chart review of patients undergoing endoscopic evaluation/treatment for chronic bladder pain was performed beginning in July 2014 when the author started a new practice and continuing to present. Surgical findings, symptom scores, bladder diaries, and clinic notes were included in the database.

Endoscopic surgery is essential to both evaluation and treatment of UIC. The diagnosis of UIC is made by typical cystoscopic appearance of HL, severe inflammation on biopsy, and no carcinoma in situ or other specific pathology seen on biopsy and bladder wash cytology. Surgical staging includes the location and size of HL, the approximate percentage of the bladder involved, and the capacity under anesthesia. Bladder capacity is assessed at 80cm H<sub>2</sub>O with the urethra manually compressed around the cystoscope. Capacity is classified as:

- Normal >600cc
- Reduced 300-600cc
- Contracted bladder <300cc

With surgical treatment every effort is made to cauterize the entirety of the ulcerative disease, even when a large portion of the bladder is involved.

The patient is typically first evaluated 4-6 weeks after surgery. The following definitions are employed:

- Complete remission (CR): no pain (0 scores for pain questions on O’Leary-Sant symptom and problem indices) AND no pain medication (including urinary analgesics) AND normal bladder function (no incontinence and functional capacity  $\geq$  400cc AND no functional limitations related to UIC (no food sensitivities, dyspareunia, etc.)
- Partial remission (PR): no pain AND no pain medication but does not meet other criteria for CR (typically has low functional capacity).
- Improved: >50% decrease in combined pain scores and pleased with outcome (currently using moderately or markedly improved on Global Response Assessment)
- Failure:  $\leq$ 50% reduction in pain AND all patients with incomplete follow-up data

For patients who have not achieved a CR with surgery an individualized treatment plan is developed with regular assessment by bladder diary and symptoms. This begins with simple bladder training to improve capacity supplemented as needed with urinary analgesics. All other standard treatments used in BPS/UIC may be considered based on the patient’s history and preferences but cyclosporine is often used in more severe/aggressive cases.

Time to relapse (recurrent pain) and time to failure (repeat endoscopic therapy) has not been precisely defined but is clinically considered in treatment planning as a surrogate for “oncologic” Grade of disease—a measure of aggressiveness of the underlying UIC.

### Results

A total of 23 procedures were performed in 20 patients. Two patients had BPS, not UIC, and are excluded from further analysis. This leaves 18 unique subjects comprising the study group. 16 had one endoscopic procedure, 1 each had 2 and 3 procedures. The surgical staging and post-operative results are shown in Table following:

	Gender	Age at Surgery	Anesthetic capacity	Outcome	Comment
1	F	72.5	375	Failure	Bladder perforation. Resolved with 3 wks catheter. Improved but unknown degree
4	F	65.3	690	Failure	Minimal improvement in pain, remained in urinary retention
2	F	50.8	300	Failure*	< 50% reduction in pain but $\downarrow\downarrow$ meds and pleased. Retreated at 9 months
3	M	53.2	425	Failure*	Clinically all symptoms resolved but did not complete follow-up

5	F	74.2	480	Failure*	Clinically all symptoms resolved but did not complete follow-up
6	F	66.2	400	Failure*	Less than 50% pain improvement but ↓↓ in pain meds at 3 months
7	F	61.0	240	Improved	6 months, marked reduction in pain and medication
8	M	74.8	500	Improved	Retreated x 2 at 6 months; no adjuvant therapy due to intercurrent medical problems
9	F	53.8	480	Improved	↓↓ pain meds at 6 months
10	F	65.9	220	Improved	Decreasing capacity at 4 months, still largely pain free at 9 months
11	M	71.4	610	Improved	Non-zero pain scores, ↓↓ meds at 1 month, unknown after
12	N	70.4	340	Improved	Initial pain 0/0 on amitriptyline, stable mild symptoms at 18 months
13	M	45.4	325	PR	Early CR for symptoms but functional capacity < 400cc
14	F	67.7	260	PR	Early CR for symptoms but functional capacity < 400cc
15	F	54.9	450	PR	Recurrent pain at 4 months, starting medical therapy
16	F	78.2	260	PR	Recurrent pain at 4 months, now near CR at 18 months on cyclosporine
17	F	68.0	380	CR	Recurrent pain after 12 months, starting cyclosporine
18	F	47.0	350	CR	Asymptomatic off meds at 8 months

#### Interpretation of results

Published results of surgical treatment for UIC nearly all report excellent outcomes but have not used structured evaluation tools. In this series almost all patients (88%) were very pleased with their results; many were completely uninterested in additional treatment. Yet, stringent objective analysis within an “oncologic” framework shows that only 33% were actually asymptomatic and only 11% achieved a strict CR. Nevertheless, CR is possible—at least for some patients. This presents an opportunity for research aimed at optimizing care for this select group by identifying and classifying candidates for early adjuvant therapy.

#### Concluding message

Patients with UIC present a special challenge which has largely been ignored in both clinical and basic research. Their unique pathophysiology and clinical features are lost when combined into the large group of BPS patients. An “oncologic” framework is proposed which can both facilitate communication about these patients and the research necessary to optimize their care.

#### References

1. Payne CK. A New Approach to Urologic Chronic Pelvic Pain Syndromes: Applying Oncologic Principles to “Benign” Conditions. *Current Bladder Dysfunction Reports*. March 2015;10(1), pp 81-86.

#### Disclosures

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