Effects of Chronic Pelvic Pain on Heart Rate Variability in Women

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Purpose: Interstitial cystitis/bladder pain syndrome and myofascial pelvic pain are frequently comorbid chronic pelvic pain disorders. Differences in bladder function between interstitial cystitis/bladder pain syndrome and myofascial pelvic pain suggest that efferent autonomic function may differentiate these syndromes. Heart rate variability, defined as the difference in duration of successive heartbeats, serves as an index of autonomic function by measuring its ability to modify heart rate in response to neurophysiological changes. High frequency heart rate variability was used as a reflection of more rapid vagally mediated (parasympathetic) changes. Low frequency heart rate variability signified slower fluctuations related to the baroreflex and sympathetic outflow.

Materials and Methods: Heart rate variability was derived by autoregressive frequency analysis of the continuous electrocardiogram recording of heart rate with the subject supine for 10 minutes, tilted 70 degrees with the head up for 30 minutes and supine again for 10 minutes. This institutional review board approved study included 105 female subjects, including 32 who were healthy, and 26 with interstitial cystitis/bladder pain syndrome, 12 with myofascial pelvic pain and 35 with interstitial cystitis/bladder pain syndrome plus myofascial pelvic pain.

Results: In all positions healthy controls had higher high frequency heart rate variability than women with interstitial cystitis/bladder pain syndrome and interstitial cystitis/bladder pain syndrome plus myofascial pelvic pain. Subjects with myofascial pelvic pain were similar to controls with greater high frequency heart rate variability at baseline (supine 1) and in upright positions than subjects with interstitial cystitis/bladder pain syndrome. Differences in low frequency heart rate variability were less evident while low-to-high frequency ratio differences appeared to be driven by the high frequency heart rate variability component.

Conclusions: Subjects with interstitial cystitis/bladder pain syndrome had diminished vagal activity and a shift toward sympathetic nervous system dominance. Overall these data support the hypothesis that changes in autonomic function occur in interstitial cystitis/bladder pain syndrome but not in myofascial pelvic pain. These changes may result from interstitial cystitis/bladder pain syndrome or contribute to its pathophysiology through abnormal self-regulatory function.

Key Words: urinary bladder; cystitis, interstitial; myofascial pain syndromes; heart rate; autonomic nervous system

Abbreviations and Acronyms

ANS = autonomic nervous system
BMI = body mass index
CPP = chronic pelvic pain
HF = high frequency
HR = heart rate
HRV = HR variability
IBI = interbeat interval
IC/BPS = interstitial cystitis/bladder pain syndrome
ICEPAC = Interstitial Cystitis: Elucidation of Psychophysiologic and Autonomic Characteristics
LF = low frequency
MPI = Multidimensional Pain Inventory
MPP = myofascial pelvic pain

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Interstitial cystitis/bladder pain syndrome is a common CPP disorder.[1] MPP is commonly comorbid with IC/BPS.[2] Little is known regarding ANS function in CPP, although we recently reported normal ANS structure in women with IC/BPS.[3] Beat-to-beat variation in HR, termed HRV, reflects ANS function, representing the relative sympathetic and parasympathetic contributions to HR control. HF-HRV assesses vagal parasympathetic function and mirrors the integrative system for adaptive self-regulation.[4]

Lutgendorf et al found higher baseline HR in subjects with IC/BPS, compatible with lower HF-HRV (not reported).[5] Additionally, HR and blood pressure increased more than expected during bladder hydrodistention in patients with IC/BPS.[6] Neither of these studies addressed the specificity of these autonomic changes for IC/BPS, particularly since reduced HF-HRV occurs in a variety of chronic pain conditions such as complex regional pain syndrome,[7] fibromyalgia,[8] chronic neck pain,[9] irritable bowel syndrome[10] and headache.[11] Therefore, HF-HRV might be a biomarker for pain related diseases.[12]

We hypothesized that unique ANS changes in IC/BPS absent from other CPP disorders underlie the bladder dysfunction that characterizes IC/BPS. The current study compared autonomic function between women with IC/BPS and those with MPP. Since women with IC/BPS report that stress commonly triggers IC/BPS flares,[13] we investigated whether orthostatic stress might induce an abnormal HF-HRV response. These observations might reflect the underlying neural networks in CPP disorders and aid clinical evaluation with a noninvasive physiological marker. Thus, we expected to find that 1) healthy controls would exhibit higher HF-HRV than each pain group, 2) HF-HRV would be lowest in women with IC/BPS than in the other CPP groups and 3) women with IC/BPS would differ in their response to orthostatic stress.

MATERIALS AND METHODS

Subjects

This institutional review board approved study at University Hospitals Case Medical Center, Cleveland, Ohio, was part of the ICEPAC study.[14] All subjects provided informed consent. The study population (accrual between February 2011 and September 2014) consisted of women 18 to 80 years old with and without CPP. IC/BPS was defined according to NIDDK (National Institute of Diabetes and Digestive and Kidney Diseases) criteria.[1] MPP was defined as 3 months or greater of CPP unrelated to bladder state with 2 or more of 5 pelvic floor tender points scoring 4 or greater of 10 on a numerical rating scale from 2 kg pressure. MPI[15] was used to provide an overall pain score and the 1990 fibromyalgia examination[16] was used to assess for fibromyalgia. Subjects stopped autonomically active medications 5 days prior to testing except 3 in the IC/BPS plus MPP group who continued diphenhydramine, amitriptyline or gabapentin plus citalopram.

The control group consisted of women on no medication with no history or manifestation (in the last 5 years) of any disorder commonly comorbid with IC/BPS. All women also met general study exclusions, including pregnancy; active intent or current breastfeeding; hematuria or infection on urinalysis; 3 urinary tract infections in the last 12 months; pelvic or bladder neoplasm; evidence of an unstable medical disorder affecting renal, hepatic, cardiovascular, respiratory or endocrine (HbA1c greater than 6.1) systems; uncontrolled psychiatric illness (untreated depression or psychosis); any central or peripheral nervous system disorder (diabetic neuropathy regardless of HbA1c level, Parkinson disease, Alzheimer disease, multiple sclerosis or stroke); consumption of 10 or more alcoholic beverages per week; or any major surgical intervention with general anesthesia in the 90 days prior to enrollment.

Tilt Table Testing

Testing consisted of 10 minutes with the subject supine at baseline, 30 minutes with a head up tilt at 70 degrees and 10 minutes of supine rest. Data analysis incorporated the last 5 minutes while supine before head up (supine 1), the first 2 consecutive 10-minute segments while upright (upright 1 and upright 2, respectively) and the first 5 minutes supine after reclining (supine 2). The Model 1 Nexfin® Monitor was used to record a continuous electrocardiogram, allowing us to examine not only differences in resting HRV (supine 1) but also differences in reactivity to a physical stressor (upright positions) and recovery from this stressor (supine 2).

Heart Rate Variability Analysis

In each position the time in milliseconds between successive heartbeats, called IBIs, were obtained from electrocardiogram recordings, written in a text file and analyzed using Kubios HRV 2.0[17] in accordance with published guidelines.[18] Artifacts in the R-to-R series were visually detected. We applied an artifact correction level that would differentiate and remove artifacts, differing abnormal IBIs from the mean IBI. Kubios provides time and frequency domain estimates of HRV. Time domain estimates are calculated based only on IBIs and associated variability while frequency domain estimates are derived via a power spectrum density analysis. In the current investigation the primary findings were virtually identical using either method as vagally mediated time and frequency domain estimates of HRV highly correlated (each $r > 0.920$, data not shown).

The current investigation reports power spectrum density results, which allows for the examination of different components (sources) of variability. Specifically autoregressive estimates of HF (0.16 to 0.4 Hz) and LF (0.04 to 0.15 Hz) frequency power bands were obtained from this analysis. HF-HRV reflects vagal activity while LF-HRV in the supine position represents sympathetic baroreflex activity.[19] The LF/HF ratio was used as an