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BRIEF REPORT

Intra-subject Variability in High Resolution Anorectal Manometry Using the London Classification: Diagnostic and Therapeutic Implications

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Abstract

This retrospective pilot study conducted on a community-based cohort of both men and women of various ages and underlying clinical presentations examined the durability and reproducibility of HR-ARM findings influencing their potential impact on clinical decision-making at the point of care (Jameson et al. in Br J Surg 81:1689–1692, 1994). The key finding of our study was that only a minority of patients who underwent repeat anorectal manometry as analyzed by the London Classification had stable manometric findings, raising questions regarding the validity of a single manometric measurement, as currently analyzed, for clinical decision-making.

Keywords London classification · High resolution anorectal manometry · Constipation · Functional anorectal disorders

Introduction

The frequently unappreciated and under-reported symptoms of defecatory straining, incomplete evacuation, constipation, fecal incontinence, in isolation, or in combination with each other, affect quality of life (QoL) in up to 5% of the population [1]. To objectively address any underlying sensorimotor dysfunction, clinicians use anorectal manometry (ARM), the rectal sensory test (RST), and the balloon expulsion test (BET) to better understand the voluntary and involuntary control of the anal canal, the recto-anal coordination and rectal sensation—and make proper management decisions based on such objective measurements [2]. However, over the years, hardware and software developments and protocols have impacted the uniformity of data collection and, as a result, proper diagnosis and subsequent management, based on an individual study [3].

The introduction of high-resolution ARM (HR-ARM) has improved data acquisition and detailed assessment of the pressure profiles and coordination of the anorectal canal. This technology is increasingly used at many centers, frequently together with other diagnostic tools, such as wireless motility capsule testing and magnetic resonance defecography [4]. Recently, an International Anorectal Physiology Working Group (IAPWG) established, standardized and published a consensus on the measurement of anorectal function, using HR-ARM [5]. The so-called London classification provides clinicians with generally accepted parameters of anorectal function, based on which decisions can be made in a hierarchical fashion, highlighting elements of generally accepted significance aiming at prioritization in decision making for patients with symptoms of anorectal dysfunction after exclusion of pertinent structural abnormalities. As the IAPWG acknowledged, further evaluation and reassessment of their initial effort will be needed, and proper re-validation will be forthcoming.

However, the intra-subject variability over time (if any) has not yet been addressed. Recognizing clinical decisions are made based on such anorectal evaluation in practice, intra-subject variability would be important to establish. The availability of such information is scarce, and it would be best addressed in a prospective clinical trial. This retrospective effort tried to collect some early data on such intra-subject variability over time, attempted to clarify the merits of a particular measurement and its potential role in facilitating clinical decisions at the point of care.

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Methods

Study Design

This is a retrospective, pilot study, in which we examined and compared the intra-subject variability of results obtained after patients who had previously undergone HR-ARM were reassessed using the London classification. The study was conducted at the Silicon Valley Neuro-gastroenterology and Motility center, a community-based facility with established referrals for over 15 years. Because of the study's retrospective data review nature, it was IRB exempted.

Inclusion Criteria

All patients in the cohort presented for the assessment and quantification of constipation, disordered rectal evacuation, rectal sensation disorder, possible Hirschsprung's disease, fecal incontinence (alone or in combination with chronic constipation), the identification and quantification of impaired anal sphincter function, functional incoordination and preoperative assessment before partial colectomy, rectopexy, rectocele repair, or before possible biofeedback therapy. All patients gave verbal consent prior to the procedures.

Exclusion Criteria

Patients were excluded from the re-analysis if there was evidence of deviation from the standard protocol described in the London classification paper or technical inadequacies of any of the individual studies conducted as part of patients' clinical care. To preserve accuracy and the clinical implications of the study findings, individual record and tracing review at the point of care was followed by clinical note review over time. Special emphasis was given to exclude patients who had an intervening intervention, such as biofeedback, anal botulinum toxin injection, anorectal surgery, or Secca procedure.

Technique

For each of the HR-ARM in our laboratory, we have been using a stabilization period of 2–3 min after catheter insertion, followed by measurements of basal (resting) anal tone over one minute while the patient remains relaxed (maximal anal sphincter basal pressure). The subsequent squeeze period records the anal pressure during voluntary effort to contract the anus/pelvic floor. Three squeezes are then performed each of 5-second duration separated by 30 s. The highest value (maximal anal sphincter squeeze pressure) is then counted. An endurance squeeze follows, with a sustained voluntary effort over 30 s, aiming to assess fatigue over time, followed by a recovery period. Patients are then asked to cough twice with a 30 s recovery period to measure anorectal pressure changes. Again, the greatest increase in rectal pressure is used for analysis. Unfortunately, such measurements are frequently unreliable, particularly in older adults. The Rectal Sensory Test (RST) assesses rectal sensitivity to balloon distension utilizing a rectal balloon placed proximal to the anal canal, recording the volume to first sensation, the volume that induces the need to defecate and the maximum tolerated volume, using gradual inflation of the balloon. This is finally followed by the Balloon Expulsion Test (BET) that measures the ability to expel a 60 ml balloon from the rectum within 60 s [2]. Normal values for our laboratory used over the study period and in this analysis are: maximal anal sphincter basal pressure: 85 mm Hg, maximal anal sphincter squeeze pressure: 245 mmHg, rectal sensation to balloon distention: 10–50 cc. recto-anal inhibitory reflex (RAIR) threshold present and elicited with < 60 cc of balloon distention. For the purposes of this analysis, values outside those ranges were considered abnormal.

Analyses

We used the London classification that hierarchically examines for [1] the presence or absence of RAIR, [2] any disorders of anal tone (maximal anal sphincter basal pressure) and contractility (maximal anal sphincter squeeze pressure, [3] disorders of anorectal coordination and [4] disorders of rectal sensation to balloon distention. BET was also analyzed and reported separately as positive (60 ml balloon expelled in a timely fashion, < 60 s) or negative [6]. The word "directionality" used in the results section below implies that a particular abnormality was noted either at baseline, normalizing upon follow-up, or it was not present at baseline and developed upon follow-up. For example, 8/28 (29%) of patients with recto-anal areflexia were the same, with four patients developing areflexia and four losing (normalizing) it. Similarly, four patients developed anal sphincter hypertonicity and four lost it (normalized it) during follow-up. Anal tone and contractility were also 50% altered from baseline to follow-up.

Results

The study cohort consisted of 28 patients who were identified from our database containing 836 HR-ARM cases performed over the past seven years (3.3% of cases) and had undergone two studies without any intervening therapy (such as pelvic floor physical therapy, surgery, anal botulinum toxin injection, or Secca procedure). An additional 49 patients (5.9%), all with abnormal HR-ARM were

excluded from this analysis because they had undergone an anorectal intervention (pelvic floor physical therapy, surgery or Botox injection) during the interval between the two studies. The study cohort consisted of 10 males and 18 females with mean age of 68 (range 44–96) at the time of re-analysis. Patients were studied at a mean of 32 months apart (range 1–107 months). Eleven patients were studied because of chronic constipation, 10 because of combined chronic constipation and fecal incontinence and 7 because of fecal incontinence only. The severity of their symptoms was not assessed by standardized questionnaires other than the ones used in our clinical practice for each symptom, such as infrequent evacuation, urge for defecation, straining and incomplete evacuation, and fecal incontinence (absent, mild, moderate, and severe). Underlying conditions that could potentially play a role in symptom induction at the time of initial presentation were: chronic depression on tricyclics ($n=2$), chronic visceral and peripheral neuropathy ($n=3$), Parkinson's disease ($n=4$), opioid-induced constipation ($n=1$), constipation-predominant irritable bowel syndrome (IBS-C; $n=3$), sigmoid diverticulosis ($n=1$), idiopathic constipation ($n=10$), chronic intestinal pseudo-obstruction ($n=1$), and hypothyroidism ($n=3$). All medications were discontinued for 24 h prior to HR-ARM except for the patients with Parkinson's disease. Most patients were white ($n=21$), five were Hispanic, and two were Asian.

Figure 1 reveals the percent change between the two individual studies analyzed at baseline and follow-up examination and reveals changes—in either direction—ranging from 0–29% for each of the parameters examined (as described in the legend). The significance of these findings varies depending on their relative importance. For example, recto-anal areflexia is considered a major abnormality while anal hypertension a minor one. Of note, 21% of patients exhibited no changes across all parameters studied, providing assurance of stability of these metrics. In contrast and as compared individually, almost one third of cases of recto-anal areflexia, anal hypertonicity and rectal hyposensitivity were different in a particular patient over time. Further, the BET differed in 25% of studies.

The directionality of change in 8/28 patients with recto-anal areflexia was the same, with four patients developing areflexia and four losing it. Similarly, four patients developed anal sphincter hypertonicity and four lost it during follow-up. Anal tone and contractility were also 50% altered from baseline to follow-up. Ten patients had combined hypotonicity and hypo-contractility at baseline and that was not changed at follow-up. Four patients had anal hypotension and normal contractility at baseline and four had hypotension and normal contractility at follow-up. Anal normotension with hypo-contractility was noted in two patients at baseline and in four patients at follow-up. Eight patients exhibited changes in rectal sensation with equal gains [4] and losses [4] of sensitivity to balloon distention from baseline to follow-up. BET was positive (present) in four patients at baseline and became positive in an additional four; it remained negative (absent or abnormal) in the remaining 20 patients. Analysis of disorders of recto-anal coordination, such as abnormal expulsion with dyssynergia, abnormal expulsion with poor propulsion, and abnormal expulsion

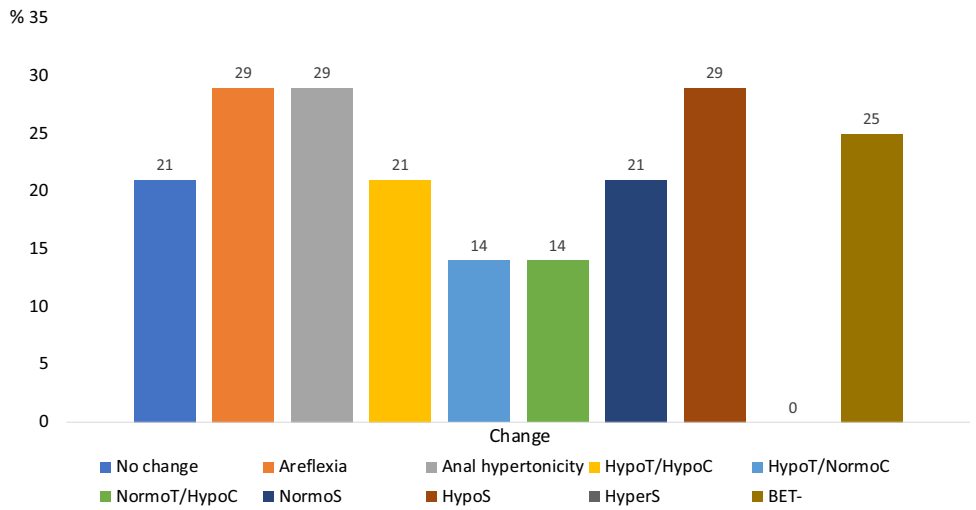

Fig. 1 Depiction of % change between the first (baseline) and the second (follow-up) HR-ARM using the London classification and including the results of balloon expulsion test (BET) in the 28 patients studied. These changes were noted in either direction (from baseline to follow-up study and vice versa). Areflexia: Lack of RAIR; Anal hypertonicity: Increased anal sphincter tone; HypoT/HypoC: Hypotonic/hypocontractile anal sphincter; HypoT/NormoC: Hypotonic/normocontractile anal sphincter; NormoT/HypoC: Normotonic/hypocontractile anal sphincter; NormoS: Normosensitive rectum; HypoS: Hyposensitive rectum; HyperS: Hypersensitive rectum; BET-: Inability to expel 60 ml balloon at 60 s

with poor propulsion and dyssynergia albeit representing minor findings of questionable specificity and validity in this small cohort, revealed that of the 41 studies of abnormal balloon expulsion (both baseline and follow-up), 27 (66%) were attributed to dyssynergia alone, 9 (22%) to poor propulsion, and 4 (10%) to combined poor propulsion and dyssynergia. Of those 41 cases, there were 7 cases that differed between baseline and follow-up study.

Discussion

This retrospective pilot study conducted on a community-based cohort of both men and women of various ages and underlying clinical presentations examined the durability and reproducibility of HR-ARM findings influencing their potential impact on clinical decision making at the point of care [7]. The key finding of our study was that only a minority of patients who underwent repeat anorectal manometry as analyzed by the London Classification had stable manometric findings, raising questions regarding the validity of a single manometric measurement, as currently analyzed, for clinical decision making.

In their recent article, the IAPWG emphasizes that what is not normal on HR-ARM is not necessarily a reflection of disease and we will need more outcome studies that will be linked to clinical presentations to overcome existing disagreements. The group recommends a comprehensive pelvic floor evaluation to assess structure and function, such as endoanal ultrasound, defecography, rectal barostat or even the emerging Functional Lumen Imagine Probe (FLIP). Further, the IAPWG does not recommend specific, quantitative reference limits but they describe findings in accordance with the upper and lower limits of "normal", as we did in our study. The IAPWG also acknowledges that female sex, advanced age, and parity may have a deleterious effect on anorectal motor and sensory dysfunction, and this may have played a role in our study exhibiting long inter-study intervals (mean of 32 months) [8]. In a similar fashion to the Chicago Classification for esophageal high-resolution esophageal manometry that, after being a research tool, was accepted into clinical practice because of better diagnostic yield and accuracy, we will continue to observe improved diagnostic accuracy of HR-ARM and novel functional metrics in addition to clarity and importance of various observations recognized and reported thus far [9, 10].

Given the poor relationship between subjective symptoms and objective anorectal findings, anorectal function testing has been used for many years as a guide in clinical decision making [11]. The recent consensus of the IAPWG has been long awaited and is of significant impact in current and future decisions for patients with functional anorectal symptoms as a guide and a new standard to be followed among clinicians and investigators around the world. Further, the hierarchical separation of the London classification into major abnormalities only seen in disease, minor and potentially of significance in symptomatic patients, or inconclusive, would objectively facilitate characterization and individualize treatment of chronic constipation, fecal incontinence and/or both, and hopefully lead to better outcomes. We think that this early study provides another dimension, that of time, on the usefulness of the London classification in decision making since there is a significant probability of natural change or spontaneous alteration of the HR-ARM results.

The key strength of our study is its community-based nature, derived from a stable cohort of patients followed by one clinician able to obtain high degree of granularity in the changes with associated clinical follow-up. The findings suggest that one should not make clinical decisions based on HR-ARM results alone, but instead use them in context. Indeed, this could be viewed as natural history study of untreated patients with functional anorectal symptoms, since no patients, either at baseline or follow-up, had structural abnormalities. More work will be needed to demonstrate the value of such measurements as surrogate markers of clinical response or as a response to a given pharmacologic, endoscopic, or surgical intervention. Key weaknesses of our work are the small study sample that will require further validation and confirmation prospectively on more patients undergoing HR-ARM, using well-validated clinical questionnaires for both chronic constipation and fecal incontinence that would link the frequency and severity of clinical presentation to HR-ARM findings. Such study should also be multi-institutional and involving patients with a wider spectrum of indications and symptom intensity. The patients in this cohort had more severe and refractory anorectal symptoms that had not responded to medical therapy, mostly comprised of various osmotic and stimulant laxatives, sometimes combined with enemas and/or suppositories. Because of the refractoriness of their symptoms, alternative decisions needed to be considered, hence the second HR-ARM that was performed at variable time intervals after the first study. Obviously, the long duration of follow-up in between studies (mean 32 months) could by itself be altered by the natural history of disease in evolution and not related to a test re-test phenomena that would need to be measured at a short-time frame (1–2 months). This approach would have been more suitable in the assessment of technical elements in the execution of the studies.

In summary, this early, retrospective, and limited study raises some provocative questions about the temporal instability of HR-ARM parameters that will need to be addressed in a larger prospective trial before we can depend on the specificity of these parameters in clinical decision making in patients with functional anorectal symptoms.

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