Characterizing the Recto-Anal Inhibitory Reflex Parameters in Spinal Cord Injured Subjects Compared to Published Healthy Control Values

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Article

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Abstract

Study Design: Cohort study design

Objectives: (i) Compare Rectoanal Inhibitory Reflex (RAIR) parameters in spinal cord injury (SCI) patients vs. published healthy control (HC) values (ii) Explore correlations and associations between RAIR parameters and SCI duration, location, and AIS levels.

Setting: University of Michigan

Methods: Prospective analysis of SCI participants who underwent High Resolution-Anorectal Manometry (HR-ARM). RAIR was tested by inflating 50 ml into the rectal balloon and immediately deflating. RAIR presence = ≥25% of internal anal sphincter pressure [IAS] (mmHg) amplitude reduction. RAIR parameters included: IAS (mmHg), reflex duration [RD] (seconds), and amplitude reduction [AR] (%). Subjects were categorized by AIS level and completeness of injury.

Results: 30 SCI (cervical= 20; thoracic= 10) subjects underwent HR-ARM. Demographics included: 80.0% male, 90.0% Caucasian, mean age of 48.3 (14.2) (Range:24-75), and mean BMI of 26.6 (7.0) (Range:16.9–41.2). SCI subjects have significant mean differences, RD ($p$=<0.001), and AR ($p$=<0.001), compared to HC (N = 21), but no significant mean differences in IAS pressure. There were no significant correlations between SCI injury duration and IAS ($r$=-.17; $p$=NS), RD ($r$=0.31; $p$=NS) and AR ($r$=-0.09; $p$=NS). No significant mean differences between SCI level and the AIS completeness within RAIR parameters.

Conclusion: Cervical and Thoracic SCI subjects have abnormal RAIR parameters compared to healthy controls. As there is minimal scientific evidence demonstrating digital rectal stimulation [DRS] as an effective method of promoting IAS relaxation for stool evacuation, an altered RAIR response on HR-ARM for SCI subjects provides a scientific basis to determine the use of DRS for bowel evacuation.

Introduction

Spinal cord injury (SCI) is a life-altering event with various consequences. Bowel dysfunction is highly prevalent and occurs in at least 60% of patients because of an SCI. The incidence of SCI ranges from 490 to 526 per million in developed countries. Males are more likely to experience an SCI than females in the United States: male: female ratio of 3.95:1. Age relative to an SCI follows a bimodal distribution – first peak at 15-29 years and second over 65 years of age. Spinal cord lesions affect anal sphincter function which can lead to neurogenic constipation and/or fecal incontinence. Sixty-eight percent of SCI patients experience abnormal defecation and 20% require digital stimulation. A majority of SCI patients report constipation(56% - 80%) and fecal incontinence (42% - 75%).

The International Standards for Neurological Classification of Spinal Cord Injury (ISNCSCI) evaluates global injury severity. The scale assesses the SCI level and grade (A-E), corresponding to the spinal lesion...
level and extent of remaining sensorimotor function. In a meta-analysis from Khorasanizadeh et al., 19,460 SCI subjects were included: Grade A (49.8%), Grade B (15.9%), Grade C (24.6%), and Grade D (9.7%).

Table 1 describes the differences in ASIA Impairment Scale grades. In a study of 142 SCI subjects, there was a more significant association between injury severity and neurogenic bowel dysfunction (NBD). Subjects in the ASIA A group had a 12.8-fold more significant risk of severe NBD than those in the ASIA D group.

Anorectal manometry (ARM) coupled with the Balloon Expulsion Test (BET) is a test that evaluates rectal, anal, and pelvic floor muscle function. ARM assesses the pressure in the anal canal at rest, during voluntary effort (squeeze), and attempted evacuation (simulated defecation). High-resolution manometry pressures in the anal canal and rectum are presented as color-contour plots. The HR-ARM catheter (Diversatek Healthcare, Milwaukee, WI) is 4 mm in diameter of 8 sets of radially and orthogonally arranged pressure sensors spaced 1 cm apart. The HR-ARM catheter configuration consists of five pressure sensors in the anal canal spaced 10 mm apart, two sensors on the distal end used to measure rectum pressure and balloon inflation, and one external reference sensor outside the body to assess atmospheric pressure.

The internal anal sphincter is a circular, smooth muscle innervated via the sacral nerves responsible for ensuring the anal canal closure at rest. During the first stage of the evacuation of feces, migrating contractions propel the colonic contents into the rectum. The rectum becomes distended and initiates the rectoanal inhibitory reflex (RAIR), which results in rectal contraction and internal anal sphincter relaxation. The RAIR is manometrically characterized by the relaxation or loss of anal canal pressure during rectal balloon distension and the reflex's lowest anal canal pressure point (residual pressure). Amplitude reduction is the change in pressure from resting to residual pressure. It has been demonstrated that the amplitude reduction and duration of the RAIR are dependent on the frequency and volume of rectal distension. The RAIR response contains various measurement components: the basal internal anal sphincter pressure, excitation latency, amplitude reduction, inhibitory reflex duration, and return toward internal anal sphincter basal pressure. Digital-rectal stimulation (DRS) facilitates defecation in patients with SCI. Data demonstrated that anal dilation stimulates stretch receptors in the internal anal sphincter, causing an increase in rectal pressure mediated by an anorectal reflex. A study of nine SCI subjects illustrated that rectal pressure did not significantly rise with increasing anal distension after a certain threshold, indicating that high pressures may not be necessary to cause bowel evacuation. However, digital stimulation may induce transient rectal pressure relaxation providing compliance for evacuation.

There is little data within the SCI literature defining anorectal function utilizing high-resolution ARM. Mazo et al., assessed a cohort of SCI subjects with neurogenic bowel by ARM and demonstrated lower anal squeeze pressures than controls. Additionally, SCI subjects had significantly lower maximum squeeze pressure than healthy controls. Elevated sensory thresholds for all distension parameters, first
sensation, urgency, maximum tolerated) were reported for SCI subjects compared to healthy volunteers.\textsuperscript{13}

Based on limited studies, SCI subjects tend to have a longer duration of the RAIR reflex and less reduction of the IAS compared to healthy controls.\textsuperscript{13} However, this data does not compare RAIR parameters in SCI subjects undergoing high-resolution anorectal manometry (HR-ARM) compared to healthy control RAIR metrics. Additionally, further investigation of correlations and associations between RAIR parameters and SCI injury duration, location, and AIS levels is required.

**Objectives**

To compare RAIR parameters in SCI subjects vs. published healthy control values. Explore correlations and associations between RAIR parameters and SCI injury duration, SCI location, and AIS levels to provide physiological evidence for using DRS as a tool for bowel evacuation.

**Methods**

A prospective analysis of SCI subjects underwent HR-ARM at the GI Physiology Laboratory at Michigan Medicine from July 2019 to March 2020. The International Anorectal Physiology Working Group (IAPWG) protocol was followed for the HR-ARM.\textsuperscript{15} All patients completed an ARM and BET, performed by experienced GI physiology laboratory technicians per standardized protocol. All included individuals underwent both ARM and BET. ARM was performed by experienced GI physiology technicians per a standardized protocol while using a high-resolution manometry system (Diversatek Healthcare, Milwaukee, WI). The ARM protocol consisted of determining the anal sphincter length (cm), absolute resting and maximum anal sphincter pressures (mmHg), rectoanal inhibitory reflex (RAIR), anal sphincter response during simulated defecation (%), and rectal sensation [ml] (first sensation, urgency, and maximum tolerated). BET was performed to evaluate the ability to pass a 50-cc water-filled rectal balloon, assessed at 60 seconds and 120 seconds. An abnormal BET was the inability to expel a 50-cc water-filled balloon in less than 60 seconds.\textsuperscript{16}

The RAIR response was assessed by inflating a non-latex balloon attached to the distal end of the HR-ARM catheter with 30 ml of air. The inflation and deflation of 30 ml of air into the balloon were performed in less than 5 seconds. If no RAIR response was visualized, the rectal distension was repeated once. A reduction of at least 25% of internal anal sphincter pressure (mmHg) from baseline would indicate a positive RAIR.\textsuperscript{17} HR-ARM data acquisition illustrates spatiotemporal anorectal pressure plots and conventional line-tracings for five channels spaced 1 cm apart, which are positioned proximal to the distal from the anus.\textsuperscript{18} The channel with the most significant amplitude reduction in anal sphincter pressure was selected for analysis. A random quality control verification for an agreement was performed between two evaluators verifying data interpretation accuracy. RAIR parameters included\textsuperscript{12,13}: internal anal sphincter pressure measured in mmHg (IAS), reflex duration measured in seconds (RD), and percentage of amplitude reduction (AR). Excitation latency is the time to return to resting pressure after
maximal stimulation. The reflex duration started at the IAS resting pressure after the excitation latency and ended when the IAS pressure returned to the basal state. Amplitude reduction was measured from resting pressure to the lowest point of the RAIR response. SCI subjects’ RAIR parameters were compared to published HC. SCI subjects were categorized by AIS level (cervical vs. thoracic) and completeness of injury (A-E). Using descriptive statistics, sample demographics, including age, sex, BMI, and race, were depicted.

Statistical analyses included descriptive and frequency calculations for demographic differences between SCI subjects and published healthy controls. A one-sample t-test was used to evaluate mean differences between SCI RAIR parameters, RD, AR, and IAS, and published healthy control RAIR metrics. Pearson correlations were assessed for the relationship between RAIR parameters and SCI injury duration. Correlations were assessed by the following criteria: Weak 0.0 – 0.3 (0.0 to -0.3); Moderate 0.3 – 0.7 (0 to -0.7), and Strong 0.7 – 1.00 (-0.7 to -1.00). Independent t-tests measured the mean difference between RAIR parameters and the SCI injury level (cervical vs. thoracic). A p-value of ≤ 0.05 was considered significant.

Results

Thirty SCI (20 cervical, 10 thoracic) subjects were included. The mean age was 48.3 (14.2) years (Range = 24 – 75). The majority of the SCI subjects were male (80.0%) and Caucasian (90.0%) with a mean BMI of 26.6 (7.0) (Range = 16.9 - 41.2) (Table 1). The mean duration of injury was 16.0 (12.5) years (Range 1.5 - 45.8). AIS grade distribution consisted of: A = 56.7%, B = 20.0%, D = 23.3% (Table 2). All RAIR parameters were compared with previously published data of 21 healthy volunteers (14 female; mean age 35, range 23-48).

SCI subjects had significantly longer RD, M = 17.4 (5.7), than healthy controls, M = 5.0 (3.4), p = <0.001 (Figure 1). Healthy controls had a significantly larger mean AR, M = 76.0% (33.0%), than SCI subjects, M = 56.9% (23.0%), p = <0.001 (Figure 2). No significant mean difference in the resting IAS pressure between the SCI and HC groups. (Figure 3).

The Pearson correlations were weak between the RD, AD, IAS, and duration of SCI injury (Figure 4). A positive weak correlation between SCI duration and RD: r = 0.14, p = 0.459. Conversely, negative weak correlations were depicted between SCI duration and AR (r = -0.23, p = 0.253) and IAS (r = -0.14, p = 0.577).

Table 4 displays AR, RD, and IAS differences between SCI with a cervical vs. thoracic injury. There is no significant mean difference in AR (p = 0.513) and IAS (p = 0.653) between SCI injury levels: cervical vs. thoracic. Cervical SCI subjects exhibited a trend for a longer mean reflex duration, M = 18.9 (5.6) compared to thoracic subjects, M = 14.3 3.9, (p = 0.046).

Discussion
The RAIR findings, RD, AR, and mean IAS support DRS use for stool evacuation for cervical and thoracic SCI subjects. SCI subjects had longer RD significantly compared to HC. This RAIR parameter proves that the IAS requires more time to return to basal pressure following rectal distention. The increased time for RD supports DRS utilization in SCI subjects because the IAS will be relaxed longer, allowing the passage of stool. SCI subjects had a significantly reduced RAIR amplitude compared with healthy controls. This finding differs from previous data showing SCI subjects had a significantly increased RAIR amplitude.\textsuperscript{19} There was no significant difference in mean IAS pressure between SCI subjects and HC, suggesting that the injury may not affect the basal innervation of the IAS.\textsuperscript{20} Our study results differ from a study done on 24 supraconal SCI subjects (5 cervical [3 complete injuries], 17 thoracic [13 complete injuries], and two complete lumbar injuries) in which anal resting pressures were significantly decreased compared to healthy controls.\textsuperscript{19} No correlations were found between injury duration and RD, AR, or mean IAS resting pressure. The blunted IAS relaxation in SCI participants compared to published HC measurements supports evidence from previous data demonstrating that SCI subjects require greater anal distention to increase rectal pressure compared to HC.\textsuperscript{11} Therefore, our data provide additional evidence for using digital stimulation within a spinal cord injured patient population to induce internal anal sphincter stretch receptors to stimulate evacuation.\textsuperscript{11}

Injuries above the conus medullaris result in hyper-reflexic bowel, characterized by increased colonic and anal sphincter tone. Hypo/areflexic bowel results from injury at the conus medullaris or cauda equina and is characterized by slow bowel transit and an atonic external anal sphincter.\textsuperscript{5} Subjects deemed to have hypo/areflexic injury (lumbar, sacral, conus) were excluded from this project. There were no significant differences in AR for thoracic and cervical SCI subjects, suggesting the IAS relaxes similarly regardless of injury location. The RD was longer for cervical subjects than thoracic subjects. Like previously published data, our data demonstrated greater AR with rectal balloon distension in spinal cord injured participants than healthy controls. RAIR parameters have been impacted in participants experiencing fecal incontinence and chronic constipation. Heterogeneous chronic constipation patient with symptoms for at least three months expressing only one bowel movement every four days and/or at 25% of bowel movements were associated with excessive straining has shown to elicit longer recovery duration related to rectal distension compared to controls and neuropathic fecal incontinence participants with unintentional leakage of liquid stool without internal or external sphincter defects evaluated using magnetic resonance image.\textsuperscript{21,22} Recently, Ng et al. (2005) demonstrated that participants with a cervical spinal cord injury have a higher likelihood of experiencing chronic constipation (OR= 5.6, p=0.02) compared to lumbar lesions.\textsuperscript{23} Therefore, our data suggest that an extended AR in cervical participants compared to thoracic participants may experience greater chronic constipation severity relative to a number of bowel movements and excessive straining.

**Conclusion**
Cervical and thoracic SCI subjects elicit abnormal RAIR parameters, longer reflex duration, and amplitude reduction compared to healthy controls. Despite standard clinical recommendations for bowel management, there is minimal scientific evidence demonstrating the use of digital-rectal stimulation (DRS) as an effective method of promoting internal anal sphincter (IAS) pressure relaxation. Findings of altered RAIR response on HR-ARM for SCI subjects provide a scientific basis for using DRS for bowel evacuation with cervical and thoracic lesions. HR-ARM may be used to determine the most effective protocol for DRS in bowel management.

**Limitations**

Our study has a few limitations. Published healthy control values were used to compare data from the SCI subjects. Differences may exist in methodologies such as infusion rate of balloon distension and catheter configuration between the data acquisition for the published healthy controls and SCI subjects. We used high-resolution anorectal manometry, while the HC data was acquired using conventional manometry. The International Anorectal Physiology Working Group (IAPWG) was utilized to collect SCI subjects’ data.\(^{15}\) For the HC data, if RAIR was not present using 50 ml of air to inflate, the balloon inflation volume was increased to 100 ml.\(^{13}\) For our protocol, we used the IAPWG suggested RAIR inflation volume of 30 ml. Thus, the differences in balloon distension volumes may impact RAIR parameters. Additionally, two different researchers were performing the HR-ARM procedure. Lastly, the distribution between cervical and thoracic participants was unequal. Equalizing the sample for both SCI groups may be helpful in determining if there is an actual difference between the cervical and thoracic SCI participants relative to RAIR parameters.

**Declarations**

**Data Availability**

The datasets generated and/or analyzed during the current study are not publicly available due to the confidentiality of data but are available from the corresponding author upon reasonable request.

**Author Contributions**

MA contributed to the manuscript design, manuscript preparation, review, and approval of the final manuscript. JB contributed to the manuscript design, manuscript preparation, review, and approval of the final manuscript. WC contributed to the manuscript design, manuscript preparation, review, and approval of the final manuscript. RS contributed to the data review. EW contributed to the data collection and organization. SM contributed to the manuscript design, manuscript preparation, review, and approval of the final manuscript. LW contributed to data collection. GE contributed to the data collection. GR contributed to the manuscript design, manuscript preparation, review, and approval of the final manuscript.
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Competing Interest

The authors declare no competing interest.

Ethical Approval

The study was approved by the University of Michigan Institutional Review Board (HUM00129060).

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Authors’ Approval: All authors have approved the final version of the manuscript submitted.

Conflicts of Interest: All authors declare no conflicts of interest with this study.

ClinicalTrials.Gov: Non-applicable

References


**Tables**

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<thead>
<tr>
<th>Demographic Variables</th>
<th>SCI N = 30</th>
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<tbody>
<tr>
<td>Mean Age (Range)</td>
<td>48.3 (14.2) (24–75)</td>
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<tr>
<td>Sex (%)</td>
<td></td>
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<tr>
<td>Male</td>
<td>80%</td>
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<tr>
<td>Female</td>
<td>20%</td>
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<td>Mean Body Mass Index (Range)</td>
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<td>Race</td>
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<td>Middle Eastern</td>
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Table 2

<table>
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<tr>
<th>ASIA Grade (%)</th>
<th>Overall Sample (n = 30)</th>
<th>Cervical Injury (n = 20)</th>
<th>Thoracic Injury (n = 10)</th>
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<tbody>
<tr>
<td>A</td>
<td>55.2%</td>
<td>40.0% (n = 8)</td>
<td>40.0% (n = 8)</td>
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<tr>
<td>B</td>
<td>20.7%</td>
<td>30.0% (n = 6)</td>
<td>0.0% (n = 0)</td>
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<tr>
<td>C</td>
<td>0.0%</td>
<td>0.0% (n = 0)</td>
<td>0.0% (n = 0)</td>
</tr>
<tr>
<td>D</td>
<td>24.1%</td>
<td>30.0% (n = 6)</td>
<td>11.1% (n = 1)</td>
</tr>
<tr>
<td>E</td>
<td>0.0%</td>
<td>0.0% (n = 0)</td>
<td>0.0% (n = 0)</td>
</tr>
</tbody>
</table>

*1 missing ASIA Grade for the Thoracic Injury Group.

Figures

Figure 1
Mean RAIR Reflex Duration of Published Healthy Controls Compared to SCI Subjects
* $p < 0.001$

**Figure 2**

*Mean Amplitude Reduction of Published Healthy Controls Compared to SCI Subjects*

* $p < 0.001$
Figure 3

Mean Internal Anal Sphincter (IAS) Resting Pressure of Published Healthy Controls Compared to SCI Subjects
Figure 4

Pearson Correlations for Spinal Cord Injury Duration and Reflex Duration (RD), Amplitude Reduction (AR), Internal Anal Sphincter (IAS)

Note. No significant correlations were found between spinal cord injury duration and reflex duration (A), amplitude reduction (B), or internal anal sphincter pressure (C).