Normal values for water-perfused esophageal high-resolution manometry

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ABSTRACT

Background: Normal values for water-perfused esophageal high-resolution manometry have still not been established in our environment, despite its generalized use and the recommendation to determine reference values for each Motility Unit based on their equipment. Normal values established with solid-state high-resolution manometry are currently being used as reference values for water-perfused high-resolution manometry.

Objectives: To obtain normal values for water-perfused esophageal high-resolution manometry, based on the esophageal motility analysis of healthy subjects.

Methods: 16 healthy volunteers without history of digestive complaints or esophageal symptoms were included. 22-channel water-perfused high-resolution manometry was performed.

Results: Normal values were calculated as 5th-95th percentile ranges for the following parameters; upper esophageal sphincter resting pressure (UESRP) (40-195 mmHg), upper esophageal sphincter residual pressure (UESResP) (30-115 mmHg), contractile front velocity (CFV) (2.4-7.1 cm/s), distal contractile integral (DCI) (285-2820 mmHg.s.cm), distal contraction latency (DL) (6.1-10.9 s), intrabolus pressure (IBP) (7-19 mmHg), integrated relaxation pressure (IRP 4s) (2-20 mmHg), lower esophageal sphincter resting pressure (LESRP) (5-54 mmHg), esophageal shortening (Es) (0.3-1.3 cm) and lower esophageal sphincter lift (LESL) (0.1-1.2 cm).

Conclusion: Normal values for the most important parameters (such as IRP 4s, DL and CFV), obtained using a 22-channel water-perfused system resemble previously published data from other perfusion devices. However, there exist small but significant variations compared with values established with solid-state high-resolution manometry. Thus, when using water-perfused catheters, caution is required when normative values are used that were established with solid-state catheters.

Key words: High-resolution manometry. Normal values. Esophagogastric junction. Water-perfused manometry.

BACKGROUND

There exist two types of high-resolution manometry systems: Water-perfused high-resolution manometry (wp-HRM) and solid-state high-resolution manometry (ss-HRM) (1). wp-HRM devices use esophageal catheters fitted with various pressure channels distributed along the catheter, opened to the esophageal lumen through side holes. Each channel is connected to an external transducer that registers pressure changes. A continuous flow of water with constant pressure and speed (determined by the manufacturer of the device) is generated through the catheter by a pneumatic pump. When a catheter orifice becomes occluded by a contraction of the esophageal muscle, the increase of the pressure of the water inside the capillary perfusion is transmitted to the corresponding external transducer (2). The transducer transforms the pressure variations into electrical signals that are processed and converted into a temporospatial image on a computer screen. The combination of HRM and the temporospatial representation of intra-esophageal pressure is known as esophageal pressure topography (3,4). Intraluminal pressure recordings become a continuum in space by interpolation between closely spaced sensors. This allows to measure the esophagogastric junction (EGJ) relaxation with all its components (lower esophageal sphincter, crural diaphragm, intrabolus pressure). The first perfusion catheters to be used had few pressure sensors of large caliber and widely spaced, resulting in inaccurate pressure recordings and difficulties in detecting rapidly changing pressures. Solutions to these limitations were found progressively by adding more channels and reducing the caliber of the recording sensor.

ss-HRM uses catheters with electronic pressure sensors or internal transducers. Current ss-HRM devices consist of 36 circumferential sensors that provide a high response rate and allow for precise studying of the upper esophagogastric junction. Water-perfused high-resolution manometry. Rev Esp Enferm Dig 2015;107:354-358.
geal sphincter (UES) and the EGJ, as well as minor motor abnormalities (5). Normal values established in the Chicago Classification were defined by ss-HRM (6-8). Nevertheless, the cost of ss-HRM devices poses a limitation for its generalized use.

wp-HRM is characterized by its durability and its lower cost. However, perfusion catheters require considerable preparation time before each study and their accuracy is lower than solid-state catheters. 36-channel perfusion catheters have recently been developed, obtaining pressure measurements of a quality comparable to ss-HRM (9).

Esophageal shortening may occur during swallowing due to the contraction of the longitudinal muscle fibres of the esophageal body that displaces the EGJ proximally one or two centimeters above the diaphragmatic hiatus. After swallowing, the esophagogastric junction returns to its normal position under the diaphragm due to the intrinsic elasticity of the phrenoesophageal membrane (10). Therefore, there is a balance between the pulling forces that displace the esophagus through the esophageal hiatus and the supporting structures that try to maintain the esophagogastric junction in its normal anatomic position. The length of the esophageal body is measured indirectly through HRM by locating the lower edge of the UES and the upper edge of the lower esophageal sphincter (LES). In this study normal values of the esophageal shortening (Es) and lower esophageal sphincter lift (LESL) are analyzed as well. These are parameters that reflect the contraction of the esophageal longitudinal muscle and may contribute to a more profound understanding of the physiopathology of motility disorders (11-13).

Paradoxically, despite the fact that wp-HRM is being widely used in clinical practice, normal values have not yet been well established. Nowadays, when conducting tests with perfusion devices, normal values for ss-HRM are used as reference values. Several recent studies suggest that data obtained in healthy subjects using water-perfused HRM systems may differ from the reference values established by solid-state HRM. Zavala-Solares et al. determined significantly lower mean values for UESRP, DCI, CFV, LESRP and IRP4s when using a 22-channel perfusion system compared to solid-state sensors (14). Subsequently, Capovilla et al. also found significantly lower values for UESRP, IRP4s, DCI, and CFV using 24-channel water-perfusion devices (15). Recently, Ortiz et al. observed that limit values for IRP 4s that define achalasia should be significantly lower when water-perfused HRM systems are used (16). The most recent attempt to establish reference values for water-perfused HRM was conducted in Amsterdam by Kessing et al., based on the comparative study of the values obtained from both solid-state and 36-channel wp-HRM devices in a healthy population (17,18). The main objective of our study was to establish normal values for the parameters defined by the Chicago Classification for the 22-channel water-perfused HRM, the most widely used system in our environment.

**MATERIALS AND METHODS**

**Subjects**

Sixteen healthy adult volunteers (> 18 years of age) were included. They presented no history of digestive disorders and they completed a specific questionnaire to rule out any possible esophageal symptoms. All subjects voluntarily agreed undergoing a 22-channel water-perfused HRM and provided written informed consent. We proceeded according to the principles of the Declaration of Helsinki.

**Equipment**

A 22-channel water-perfused silicone esophageal catheter of 4 mm in diameter was used. Bi-distilled water circulated through it at a constant flow of 0.6 ml/min. The luminal diameter of each perfusion capillar was 0.4 mm, being them oriented radially, spaced at 1 cm in the areas recording the EGJ and 2 cm in the areas of the esophageal body. Each perfusion capillar acted as a manometric sensor, placing the distal sensors in the gastric lumen during the test. Such an assembly provides a low constant flow with a minimum displaceable nature, detecting any change in pressure of the esophageal lumen by the difference in flow resistance. Pressure changes are transmitted to external transducers that transform the information in electric signals. A computer system amplifies, digitalizes and transforms them in time-space graphs. Data obtained through this system was later analyzed with a specific software (Solar GI HRM - Medical Measurement Systems – MMS) (Enschede, The Netherlands).

**Method**

The catheter was zeroed to atmospheric pressure, then introduced through one of the nostrils and progressed with the assistance of the patient swallowing until the three distal sensors were positioned in the gastric lumen. The manometric signals were recorded with a frequency of 20 Hz. Patients were placed in a supine position and then asked to perform ten fluid swallows of 5 mL of normal saline solution separated by 30-second intervals. Later, the patient remained in forced expiration during 3-5 seconds to record the expiratory resting pressure of the intrinsic LES without the participation of the crural diaphragm. Lastly, a multiple rapid swallowing test was conducted with 100 mL of water, in order to increase the diagnostic sensitivity in LES dysfunctions and other motor abnormalities of the esophageal body.

**Data analysis**

Water-perfused HRM data was analyzed according to the algorithm recommended by the Chicago Classification. Manometric parameters of the UES (upper esophageal sphincter resting pressure, upper esophageal sphincter residual pressure), of the esophagus (contractile front velocity, distal contractile integral, distal contraction latency, intrabolus pressure) and of the EGJ (lower esophageal sphincter resting pressure, 4-second integrated relaxation pressure, esophageal shortening, lower esophageal sphincter lift) were deter-
mained. The upper esophageal sphincter resting pressure (UESRP) and the upper esophageal sphincter residual pressure (UESResP) were automatically recorded after the placement of specific software markers on the UES outline during a period of no swallowing and during relaxation at the beginning of the swallowing, respectively. The contractile front velocity (CFV) was defined as the slope of the best-fit tangent to the 30 mmHg isobaric contour between the proximal pressure trough (P) and the contractile deceleration point (CDP). The CDP was taken as the inflection point along the 30 mmHg isobaric contour where propagation velocity slows, demarcating the phrenic ampulla. The distal contraction latency (DL) was defined as the interval of time between the deglutitive UES relaxation and the CDP. The distal contractile integral (DCI) was calculated by multiplying the amplitude by the duration by the length of the distal esophageal contraction from P until the distal pressure trough (D), excluding pressures below 20 mmHg. The lower esophageal sphincter resting pressure (LESRP) was automatically determined by placing the specific marker over the EGJ outline during a period of no swallowing. The 4-s integrated relaxation pressure (IRP 4s) was defined as the mean EGJ relaxation pressure during 4 s, contiguous and/or separated, during a 10 second period following the relaxation of the UES. Esophageal intrabolus pressure (IBP) was measured between the edge of the contraction of the distal esophageal body segment and the esophagogastric junction. This parameter allows the assessment of whether a certain degree of functional obstruction exists at the level of the esophagogastric junction. As the contractile wavefront approaches the esophagogastric junction, the magnitude of the IBP approximates the integrated EGJ relaxation pressure. Esophageal shortening (Es) was defined as the maximum reduction of the length of the esophageal body during swallowing. The difference between the maximum length of the esophageal body (in basal conditions) and the minimum length (generally during swallowing) was measured. Lower esophageal sphincter lift (LESL) refers to the proximal displacement of the LES as a consequence of esophageal shortening. This was measured as the maximum difference between the distance from the nostrils to the lower border of the LES, in rest and during esophageal shortening.

Statistical analysis

The mean value ± SD, the median (P50) and the 5th, 25th, 75th and 95th percentiles were calculated for each parameter. Reference values were established as the interval between the 5th and 95th percentiles of values.

RESULTS

Subjects

Water-perfused HRM was performed on 16 healthy volunteers (mean age 39 ± 11.6 yrs., 56% women, 44% men) without incidents. Two of the subjects (13%) had peristaltic defects: One of them weak peristalsis with large peristaltic defects and the other one weak peristalsis with small peristaltic defects. Both were included in the data analysis because there are multiple studies that demonstrate that non-specific peristaltic defects may exist in a healthy population without any pathological significance (19-23). The recent 3.0 version of the Chicago Classification (8) establishes that only peristaltic defects exceeding 5 cm (present in up to 14% subjects with dysphagia and in only 4% of asymptomatic subjects) must be taken into account. The remaining fourteen subjects (87%) presented intact peristalsis. One subject (6%) met the manometric criteria for EGJ outflow obstruction and was included in the statistical analysis given the absence of upper digestive symptoms. Other studies also found healthy subjects that met manometric criteria for EGJ outflow obstruction. No peristaltic abnormalities were recorded in any of the subjects in the multiple rapid swallowing tests.

Normal values for 22-channel water-perfused HRM

The values observed for each of the UES parameters, the esophageal body parameters and the EGJ parameters are shown in table I. The 5th and 95th percentile range for UESRP resting pressure was 40-195 mmHg and 30-115 mmHg for UESResP. The 5th and 95th percentile range for CFV was 2.4-7.1 cm/s, 285-2,820 mmHg.s.cm for DCI and 6.1-10.9 s for DL. The 5th and 95th percentile range for IRP 4s was 2-20 mmHg and 5-54 mmHg for LESRP. The 5th and 95th percentile range for Es was 0.3-1.3 cm and 0.1-1.2 cm for LESL.

DISCUSSION

This study provides reference values for 22-channel water-perfused HRM for the first time in Spain. Due to the amount of population attended in our centre, the limited resources and the lack of financing, only 16 subjects were used as sample. Normal values were defined as 5th and 95th percentile ranges. Table II compares the values obtained in different studies for the most relevant parameters.

In EGJ analysis, the upper limit obtained for IRP 4s was 20 mmHg, a similar value to the 18.8 mmHg observed by Kessing et al. (17) through the 36-channel water-perfused HRM and significantly higher than the 15 mmHg established by the Chicago Classification (6). The range of values observed for LESRP was wider than other recently published studies, with the 95th percentile being 54 mmHg.

When referring to esophageal parameters, the normal values observed for DCI were remarkably lower than the reference criteria used up to date. This fact had already been observed in other studies in which wp-HRM was performed (14-16) and also in the comparative study of wp-HRM and ss-HRMs conducted by Kessing et al. (17). Experience gained from these studies suggest that part of the differences among these measurements could be attributed to regional, intradividual and even, interindividual variability, depending on when the procedure
was performed (25,26). The values obtained for CFV and DL were practically equivalent to those published in other wp-HRM studies (14-16). When comparing them with the Chicago Classification, the upper limit of CFV was similar (7.1 cm/s vs. 7.5 cm/s in Chicago), but the lower limit of DL was significantly higher (6.1 s vs. 4.5 in Chicago).

The ranges observed for UES parameters do not match the most recent studies. The normality range of the UESRP was narrower (40-195 mmHg) than the last published value, whereas the UESResP was strikingly higher, both for the upper and lower limit. Part of these differences could be explained by the fact that the 22-channel-sensor is less sensible than the 36-channel one when studying the UES. Also, the considerable variability of these results in the different series conducted with equivalent devices must be taken into account. As the availability of the 36-channel water-perfused and solid-state HRM continue to increase, further studies should be conducted to define the reference values of the UES parameters more accurately.

Additionally, normal values of Es and LESL were determined for the first time, due to the increasing importance they are acquiring when outlining some motility disorders. Further studies are necessary to measure both parameters within each specific disorder, with the purpose of establishing their role in the diagnosis of esophageal pathology.

### Table I. Esophageal parameters, EGJ parameters, and UES parameters as measured by 22-channel water-perfused HRM

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Mean</th>
<th>SD</th>
<th>Median (P50)</th>
<th>5th</th>
<th>95th</th>
<th>Kessing et al. ** (17)</th>
</tr>
</thead>
<tbody>
<tr>
<td>UESRP (mmHg)</td>
<td>102.6</td>
<td>50.3</td>
<td>97</td>
<td>40</td>
<td>195</td>
<td>28.8-199.3</td>
</tr>
<tr>
<td>UESResP residual pressure (mmHg)</td>
<td>60.6</td>
<td>27.2</td>
<td>54</td>
<td>30</td>
<td>115</td>
<td>1.7-30.7</td>
</tr>
<tr>
<td>CFV (cm/s)</td>
<td>4.2</td>
<td>1.4</td>
<td>4.1</td>
<td>2.4</td>
<td>7.1</td>
<td>3.0-6.6</td>
</tr>
<tr>
<td>DCI (mmHg.s.cm)</td>
<td>972.4</td>
<td>598.9</td>
<td>841</td>
<td>285</td>
<td>2.820</td>
<td>142-3.674</td>
</tr>
<tr>
<td>DL (s)</td>
<td>7.1</td>
<td>1.3</td>
<td>7.5</td>
<td>6.1</td>
<td>10.9</td>
<td>6.2-8.7</td>
</tr>
<tr>
<td>IBP (mmHg)</td>
<td>10.6</td>
<td>3.7</td>
<td>10</td>
<td>7</td>
<td>19</td>
<td>0.0-12</td>
</tr>
<tr>
<td>LESRP (mmHg)</td>
<td>27.4</td>
<td>10.3</td>
<td>27.5</td>
<td>5</td>
<td>54</td>
<td>3.0-29.8</td>
</tr>
<tr>
<td>IRP 4s (mmHg)</td>
<td>9.6</td>
<td>5.2</td>
<td>9</td>
<td>2</td>
<td>20</td>
<td>1.0-18.8</td>
</tr>
<tr>
<td>Es (cm)</td>
<td>0.7</td>
<td>0.3</td>
<td>0.7</td>
<td>0.3</td>
<td>1.3</td>
<td>N.A.</td>
</tr>
<tr>
<td>LESL (cm)</td>
<td>0.3</td>
<td>0.3</td>
<td>0.6</td>
<td>0.1</td>
<td>1.2</td>
<td>N.A.</td>
</tr>
</tbody>
</table>

*5th-95th percentile range of 16 subjects determined with 22-channel water-perfused high-resolution manometry. **5th-95th percentile range of 50 subjects determined with 36-channel water-perfused high-resolution manometry. EGJ: Esophagogastric junction; UES: Upper esophageal sphincter; IRP: Integrated relaxation pressure; CFV: Contractile front velocity; DCI: Distal contractile integral; DL: Distal latency; IBP: Intrabolus pressure; Es: Esophageal shortening; LESL: Lower esophageal sphincter lift; N.A.: Not applicable.

### Table II. Normal values of the most relevant parameters obtained with perfusion devices in recent studies

<table>
<thead>
<tr>
<th></th>
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</thead>
<tbody>
<tr>
<td>Catheter</td>
<td>MMS 22-channel water-perfused (Solar GI HRM)</td>
<td>EB neuro 24-channel water-perfused (EB Neuro)</td>
<td>MMS 36-channel water-perfused (Dentsleeve)</td>
<td>Solid-state</td>
</tr>
<tr>
<td>CFV (cm/s)</td>
<td>&lt; 7.1</td>
<td>&lt; 7.2</td>
<td>&lt; 6.6</td>
<td>&lt; 7.5</td>
</tr>
<tr>
<td>DCI (mmHg.s.cm)</td>
<td>285-2,280</td>
<td>557-1,726</td>
<td>142-3,674</td>
<td>&lt; 5,000</td>
</tr>
<tr>
<td>DL (s)</td>
<td>&gt; 6.1</td>
<td>&gt; 7.0</td>
<td>&gt; 6.2</td>
<td>&gt; 4.5</td>
</tr>
<tr>
<td>IBP (mmHg)</td>
<td>&lt; 19</td>
<td>NA</td>
<td>&lt; 12</td>
<td>&lt; 15</td>
</tr>
<tr>
<td>LESRP (mmHg)</td>
<td>&lt; 54</td>
<td>NA</td>
<td>&lt; 29.8</td>
<td>&lt; 35</td>
</tr>
<tr>
<td>IRP 4s (mmHg)</td>
<td>&lt; 20</td>
<td>&lt; 8.8</td>
<td>&lt; 18.8</td>
<td>&lt; 15</td>
</tr>
</tbody>
</table>

*5th percentile is shown for DL, 5th-95th for DCI and 95th percentile for the rest. *Burgos-Santamaría et al.; 5th-95th percentile range of 16 subjects determined with 22-channel water-perfused high-resolution manometry. **Capovilla et al.; 5th-95th percentile range of 20 subjects determined with 24-channel water-perfused high-resolution manometry. ***Kessing et al.; 5th-95th percentile range of 50 subjects determined with 36-channel water-perfused high-resolution manometry.
the higher variability of the rest of parameters, supports the recommendation that each Motility Unit establishes normal values adapted to the reality of their devices and the population they assist.

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