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Water-perfused esophageal high-resolution manometry: normal values and validation

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Submitted 19 December 2013; accepted in final form 27 January 2014

Kessing BF, Weijenborg PW, Smout AJ, Hillenius S, Bredenoord AJ. Water-perfused esophageal high-resolution manometry; normal values and validation. Am J Physiol Gastrointest Liver Physiol 306: G491–G495, 2014. First published January 30, 2014; doi:10.1152/ajpgi.00447.2013.—Water-perfused high-resolution manometry (HRM) catheters with 36 unidirectional pressure channels have recently been developed, but normal values are not yet available. Furthermore, the technique has not been validated and compared with solid-state HRM. We therefore aimed to develop normal values for water-perfused HRM and to assess the level of agreement between water-perfused HRM and solid-state HRM. We included 50 healthy volunteers (mean age 35 yr, range 21–64 yr; 15 women, 35 men). Water-perfused HRM and solid-state HRM were performed in a randomized order. Normal values were calculated as 5th and 95th percentile ranges, and agreement between the two systems was assessed with intraclass correlation coefficient (ICC) statistics. The 5th–95th percentile range was 3.0–6.6 cm/s for contractile front velocity, 141.6–3,674 mmHg·s·cm for distal contractile integral (DCI), 6.2–8.7 s for distal contraction latency (DL), and 1.0–18.8 mmHg for integrated relaxation pressure (IRP 4s). Mean (SD) and ICC for water-perfused HRM and solid-state HRM were 4.4 (1.1) vs. 3.9 (0.9) cm/s, ICC: 0.49 for CFV; 1,189 (1,023) vs. 1,092 (1,019) mmHg·s·cm, ICC: 0.90 for DCI; 7.4 (0.8) vs. 6.9 (0.9) s, ICC: 0.50 for DL; and 8.1 (4.8) vs. 7.9 (5.1), ICC: 0.39 for IRP 4s. The normal values presented in this classification have therefore been assessed with intraclass correlation coefficient (ICC) statistics. The 5th–95th percentile range was 3.0–6.6 cm/s for contractile front velocity, 141.6–3,674 mmHg·s·cm for distal contractile integral (DCI), 6.2–8.7 s for distal contraction latency (DL), and 1.0–18.8 mmHg for integrated relaxation pressure (IRP 4s). Mean (SD) and ICC for water-perfused HRM and solid-state HRM were 4.4 (1.1) vs. 3.9 (0.9) cm/s, ICC: 0.49 for CFV; 1,189 (1,023) vs. 1,092 (1,019) mmHg·s·cm, ICC: 0.90 for DCI; 7.4 (0.8) vs. 6.9 (0.9) s, ICC: 0.50 for DL; and 8.1 (4.8) vs. 7.9 (5.1), ICC: 0.39 for IRP 4s. The normal values presented in this classification have therefore been assessed with intraclass correlation coefficient (ICC) statistics. The 5th–95th percentile range was 3.0–6.6 cm/s for contractile front velocity, 141.6–3,674 mmHg·s·cm for distal contractile integral (DCI), 6.2–8.7 s for distal contraction latency (DL), and 1.0–18.8 mmHg for integrated relaxation pressure (IRP 4s). Mean (SD) and ICC for water-perfused HRM and solid-state HRM were 4.4 (1.1) vs. 3.9 (0.9) cm/s, ICC: 0.49 for CFV; 1,189 (1,023) vs. 1,092 (1,019) mmHg·s·cm, ICC: 0.90 for DCI; 7.4 (0.8) vs. 6.9 (0.9) s, ICC: 0.50 for DL; and 8.1 (4.8) vs. 7.9 (5.1), ICC: 0.39 for IRP 4s. The normal values presented in this classification have therefore been assessed with intraclass correlation coefficient (ICC) statistics.

Since its introduction in the early 1950s, esophageal manometry has contributed to a better understanding of esophageal motor function and is currently a widely performed technique in clinical practice (4). The first manometry systems used a catheter that contained water-perfused channels that opened to the lumen at several points along the catheter. These water-perfused pressure channels were driven by a pneumatic pump and connected to external pressure sensors (4). Water-perfused manometry catheters were hindered by large intervals between the pressure sensors that could result in an inadequate assessment of sphincter pressure and peristaltic abnormalities. This shortcoming was partly overcome by adding a sleeve sensor, which measured the highest pressure exerted along a segment of several centimeters (5). This allowed for a reliable measurement of the esophagogastric junction (EGJ), even though the EGJ moves up and down the catheter during inspiration or during swallowing. However, esophageal pressure was still measured with a low level of detail, and adding more pressure channels would require more water-perfused channels through the catheter and thus a larger diameter of the catheter and a significant amount of water being administered to a patient during the measurement. Furthermore, the response rate of water-perfused manometry is relatively low, which results in difficulties when measuring rapidly changing pressures. Smaller-caliber capillaries have partly overcome these shortcomings, making it now possible to create catheters with many more pressure sensors.

The second type of esophageal manometry system uses a solid-state catheter that has electronic pressure sensors within the catheter itself. With the use of this technique a high-resolution manometry (HRM) catheter was developed that showed a high level of detail at the EGJ and the esophagus by using 36 pressure sensors. The currently available solid-state HRM catheters often use circumferential pressure sensors, and it has been suggested that the latter increase the accuracy of measuring the pressure of the asymmetric EGJ (9). Furthermore, the response rate of solid-state manometry is considerably higher. However, solid-state manometry catheters are relatively expensive and more vulnerable to damage compared with water-perfused manometry.

The solid-state manometry catheter is currently considered as the gold standard for esophageal HRM, and analysis is performed with the Chicago classification (3, 7, 8). The normal values presented in this classification have therefore been developed specifically for the use of solid-state catheters.

Despite the advantages of solid-state HRM, water-perfused HRM systems are still used frequently, and it is estimated that ~400–500 centers worldwide currently use a water-perfused HRM assembly. Their popularity is the result of the relatively low cost of the catheter and the fact that the external pressure transducers result in high durability of the system. These advantages may outweigh the concomitant practical disadvantages of water-perfused systems. These include a longer preparation time of the system before a measurement due to the necessity to perfuse the catheter until all air is removed from

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http://www.ajpgi.org 0193-1857/14 Copyright © 2014 the American Physiological Society G491
the capillaries and the need to sterilize the catheter after use. Recently, a water-perfused HRM catheter has been developed with 36 channels, rendering a pressure measurement resolution equal to that of the solid-state catheters. However, no normal values for this technique are available, which has limited the use of water-perfused HRM in clinical practice so far. Furthermore, the level of agreement between water-perfused HRM and solid-state HRM is currently unknown. The aim of this study was therefore to develop normal values for water-perfused HRM for the parameters defined by the Chicago classification and to assess the level of agreement between water-perfused HRM and solid-state HRM.

METHODS

Subjects. We included 50 healthy volunteers (mean age 35 yr, range 21–64 yr; 15 women, 35 men) without a history of upper gastrointestinal complaints. Subjects who used medication that could affect upper gastrointestinal motility and subjects with a history of upper gastrointestinal surgery were excluded. All subjects provided written informed consent. This study was reviewed by the ethics committee of the Academic Medical Center (internal reference number MEC 2012_017) and was approved on February 19, 2012.

High-resolution manometry. Water-perfused HRM and solid-state HRM were consecutively performed in a randomized order. Subjects reported to the hospital after fasting for a minimum of 3 h. For each manometric study, the manometry catheter was introduced transnasally and positioned to record from hypopharynx to stomach. Subjects were placed in a supine position and received 10 boluses of 5 ml of water with an interval of 20 s.

The water-perfused HRM assembly consisted of a 36-channel water-perfused catheter (Dentsleeve, Mississauga, ON, Canada). The luminal diameter of each perfusion capillary was 0.4 mm, and the total diameter of the catheter was 4.7 mm. The perfusion pressure during the entire manometric study was maintained at 0.15 ml/min. Pressures were recorded with external pressure transducers (Argon Medical Devices, Plano, TX). The catheter was zeroed to atmospheric pressure before the catheter was introduced. The manometric signals were recorded with a frequency of 20 Hz and were stored on a personal computer.

Solid-state HRM was carried out with a solid-state HRM assembly with 36 circumferential pressure sensors spaced at 1-cm intervals (Given Imaging, Los Angeles, CA). A sampling frequency of 37 Hz was used to record HRM signals with the solid-state catheter. Before the onset of the measurement, the HRM pressure tracings were calibrated at 0 and 300 mmHg.

Data analysis. Water-perfused HRM data were analyzed with dedicated software [Medical Measurements Systems (MMS), Enschede, The Netherlands]. Solid-state HRM data were also analyzed with dedicated software (Given Imaging). Esophageal motility was assessed with the Chicago criteria (3, 7, 8). Assessment of EGJ relaxation pressure, resting pressure, and upper esophageal sphincter (UES) resting pressure and relaxation pressure was automatically performed with dedicated software after manual inspection of the tracings and correct placement of analysis markers during a period of nonswallowing directly following the 10 liquid swallows (QuickView Measurement and analysis software v. 8.23a; MMS). EGJ pressure was referenced to gastric pressure, whereas the esophageal contraction parameters and UES pressures were referenced to atmospheric pressure. Breaks in the esophageal contraction wave were defined as segments within the esophageal contraction wave with an amplitude below the 20-mmHg isobaric contour (6). Average break length was defined as the mean break length during the 10 swallows. Contractile front velocity (CFV) was defined as the slope of the line connecting the points on the 30-mmHg isobaric contour where propagation velocity slows, demarcating the tubular esophagus from the phrenic ampulla (10, 11). The distal contractile integral (DCI) was calculated by multiplying the length of the smooth muscle esophagus by the duration of propagation of the contractile wave front and the mean pressure in the manually placed frame excluding pressures below 20 mmHg (3). Deglutitive relaxation of the EGJ was assessed with the integrated relaxation pressure (IRP), which measured the lowest 4-s cumulative pressure values that occurred during a 10-s postdeglutition time window in the electronically generated e-sleeve signal through the anatomic zone defining the EGJ (3). There is currently no general consensus for the assessment of deglutitive relaxation of the UES; we therefore assessed UES relaxation with the IRP during the lowest 0.2-s and 0.8-s cumulative pressure values that occurred during a 3-s window in the electronically generated e-sleeve signal through the UES. Furthermore, UES relaxation was assessed by calculating the UES residual pressure (intrabolus pressure at the level of the UES during a swallow) automatically through the manually placed marker during UES relaxation. Esophageal intrabolus pressure (IBP) was measured between the peristaltic wave front and the EGJ.

Table 1. Esophageal parameters, EGJ parameters, and UES parameters as measured by water-perfused HRM

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Mean</th>
<th>SD</th>
<th>Median</th>
<th>5th</th>
<th>95th</th>
<th>95th Chicago</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>EGJ parameters</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Basal pressure (resp min) mmHg</td>
<td>11.6</td>
<td>8.1</td>
<td>9.5</td>
<td>3</td>
<td>29.8</td>
<td>&gt;10, &lt;35</td>
</tr>
<tr>
<td>Basal pressure (mean) mmHg</td>
<td>23.7</td>
<td>12.9</td>
<td>20.5</td>
<td>9.1</td>
<td>54.8</td>
<td>N.A.</td>
</tr>
<tr>
<td>IRP 4s, mmHg</td>
<td>8.1</td>
<td>4.8</td>
<td>7</td>
<td>1</td>
<td>18.8</td>
<td>&lt;15</td>
</tr>
<tr>
<td><strong>UES parameters</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Basal pressure (mean), mmHg</td>
<td>91.8</td>
<td>55.5</td>
<td>76</td>
<td>28.8</td>
<td>199.3</td>
<td>26.3–85.1</td>
</tr>
<tr>
<td>Residual pressure, mmHg</td>
<td>13.0</td>
<td>8.2</td>
<td>11.5</td>
<td>1.7</td>
<td>30.7</td>
<td>N.A.</td>
</tr>
<tr>
<td>IRP 0.2s, mmHg</td>
<td>11.3</td>
<td>7.9</td>
<td>9.5</td>
<td>1.1</td>
<td>28.9</td>
<td>N.A.</td>
</tr>
<tr>
<td>IRP 0.8s, mmHg</td>
<td>24.8</td>
<td>10.5</td>
<td>24.0</td>
<td>8.0</td>
<td>42.6</td>
<td>N.A.</td>
</tr>
<tr>
<td><strong>Esophageal parameters</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CFV, cm/s</td>
<td>4.4</td>
<td>1.1</td>
<td>4.2</td>
<td>3.0</td>
<td>6.6</td>
<td>&lt;7.5</td>
</tr>
<tr>
<td>DCI, mmHg·s·cm</td>
<td>1,189</td>
<td>1,023</td>
<td>970</td>
<td>141.6</td>
<td>3,674</td>
<td>&lt;5,000</td>
</tr>
<tr>
<td>DL, s</td>
<td>7.4</td>
<td>0.8</td>
<td>7.4</td>
<td>6.2</td>
<td>8.7</td>
<td>&gt;4.5 (5th percent)</td>
</tr>
<tr>
<td>IBP, mmHg</td>
<td>5.7</td>
<td>3.5</td>
<td>6.0</td>
<td>0.0</td>
<td>12.0</td>
<td>&lt;15</td>
</tr>
<tr>
<td>Total break length, cm</td>
<td>3.0</td>
<td>2.7</td>
<td>2.3</td>
<td>0.0</td>
<td>9.5</td>
<td>N.A.</td>
</tr>
</tbody>
</table>

EGJ, esophagogastric junction; UES, upper esophageal sphincter; HRM, high-resolution manometry; IRP, integrated relaxation pressure; CFV, contractile front velocity; DCI, distal contractile integral DL, latency; IBP, intrabolus pressure; N.A., not applicable.

AJP-Gastrointest Liver Physiol • doi:10.1152/ajpgi.00447.2013 • www.ajpgi.org
**Table 2. Esophageal parameters, EGJ parameters, and UES parameters as measured by water-perfused HRM and solid-state HRM**

<table>
<thead>
<tr>
<th></th>
<th>Solid-State HRM</th>
<th>Water-Perfused HRM</th>
<th>ICC</th>
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<tbody>
<tr>
<td></td>
<td>Mean (SD)</td>
<td>5th–95th</td>
<td>Mean (SD)</td>
</tr>
<tr>
<td><strong>UES parameters</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Resting pressure, mmHg</td>
<td>75.8 (32.2)</td>
<td>34.6–137.7</td>
<td>91.8 (55.5)</td>
</tr>
<tr>
<td>Residual pressure, mmHg</td>
<td>1.9 (2.6)</td>
<td>0.0–8.5</td>
<td>13.0 (8.2)</td>
</tr>
<tr>
<td><strong>EGJ parameters</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Resting pressure (min), mmHg</td>
<td>14.7 (8.3)</td>
<td>3.0–31.2</td>
<td>11.6 (8.1)</td>
</tr>
<tr>
<td>IRP 4s, mmHg</td>
<td>7.9 (5.1)</td>
<td>2.0–15.5</td>
<td>8.1 (4.8)</td>
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<td></td>
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</tr>
<tr>
<td>DCI, mmHg·s·cm</td>
<td>1.092 (1.019)</td>
<td>178–2,828</td>
<td>1.189 (1.023)</td>
</tr>
<tr>
<td>CFV, cm/s</td>
<td>3.9 (0.9)</td>
<td>2.9–5.9</td>
<td>4.4 (1.1)</td>
</tr>
<tr>
<td>DL, s</td>
<td>6.9 (0.9)</td>
<td>5.4–8.5</td>
<td>7.4 (0.8)</td>
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<tr>
<td>IBP, mmHg</td>
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<td>0.0–7.9</td>
<td>5.7 (3.5)</td>
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<td>IBP, mmHg</td>
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<td>0.0–7.9</td>
<td>5.7 (3.5)</td>
</tr>
</tbody>
</table>

**Statistical analysis.** Normal values were defined as the interval between the 5th and 95th percentiles of values. The levels of agreement between the two systems were assessed with intraclass correlation coefficient (ICC) statistics. Data are presented as means ± SD, medians, and 5th and 95th percentiles.

**RESULTS**

**Subjects.** Measurements were successfully performed in all subjects, and none of the subjects met the criteria for achalasia or esophageal spasm.

**Normal values for water-perfused HRM.** EGJ, esophageal, and UES parameters are shown in Table 1. The 5th–95th percentile range for the IRP 4s was 1.0–18.8 mmHg. For the basal pressure of the EGJ (respiratory minimum) the 5th–95th percentile range was 3.0–29.8 mmHg. The 5th–95th percentile range was 3.0–6.6 cm/s for CFV, 141.6–3,674 mmHg·s·cm for DCI, and 6.2–8.7 s for DL. Total break length in the esophageal contraction length was 3.0 cm, and its 5th–95th percentile range was 0.0–9.5 cm. The 5th–95th percentile range was 28.8–199.3 mmHg for basal pressure of the UES (mean), 1.7–30.7 mmHg for UES residual pressure, and 1.1–28.9 mmHg for the UES IRP 0.2s.

**Agreement between solid-state HRM and water-perfused HRM.** The levels of agreement between water-perfused HRM and solid-state HRM are shown in Table 2. Fair agreement between the two measurement techniques was observed for the IRP 4s values (ICC = 0.39), with a slightly higher 95th percentile of 18.8 mmHg measured with water-perfused HRM compared with 15.5 mmHg measured with solid-state HRM. The Bland-Altman plot did not demonstrate a consistent trend (increased or decreased value) between the techniques for these measures (Fig. 2). No agreement (ICC = −0.07) was observed between the IBP values as measured by the two techniques.

There was no agreement in UES resting pressure as measured with the two techniques (ICC = −0.11). In general, a markedly higher 95th percentile was observed for water-per-
fused HRM compared with solid-state HRM (199.3 vs. 137.7 mmHg). A consistent trend (increased or decreased value) in resting UES pressure differences between the two techniques was not identified with the Bland-Altman plots (Fig. 3A). Slight agreement between the two techniques was observed for UES residual pressures (ICC = 0.15). The 95th percentile of UES residual pressure was 30.7 mmHg with water-perfused HRM compared with 8.5 mmHg with solid-state HRM. Moreover, the Bland-Altman plot demonstrated that the residual UES pressure measured with the solid-state catheter is consistently lower compared with that measured with the water-perfused catheter (Fig. 3B).

DISCUSSION

This study provides normal values for water-perfused HRM of the esophagus. The normal values for the most important parameters, DL, CFV, and IRP 4s, acquired by a water-perfused catheter are comparable to previously published described criteria, and a moderate to good agreement was observed compared with solid-state HRM performed in the same subject on the same day. Furthermore, even though the normal values for DCI appear to be markedly lower compared with previously published criteria, an almost perfect ICC was observed between water-perfused HRM and solid-state HRM. Basal pressure of the EGI and UES appear to be markedly different between water-perfused HRM and solid-state HRM, a finding that is also reflected by a poor ICC. However, the latter two parameters do not form part of the Chicago classification, the relevance of these observations for clinical practice is considered limited, and parameters expressing relaxation of the sphincters are much more important.

The values obtained with the water-perfused HRM catheter in the present study were slightly different from the solid-state HRM performed on the same day and also slightly different from the normal values measured with solid-state HRM previously in Chicago (3, 7–9). However, it should be mentioned that the solid-state HRM values we measured in the present study with the same catheter as used in Chicago were also slightly different from those historic values measured in Chicago with that type of catheter. It is likely that part of the differences found cannot be attributed to the system used but are the result of the large variability within subjects and groups. Although we performed the measurements consecutively and in a randomized order, we cannot exclude the presence of a considerable intraindividual variability, as was also demonstrated in a recent study by Bogte et al. (1). It is likely that this is responsible for a large part of the differences between the two consecutive measurements in the same subject and only smaller differences can be accounted by differences in measurement technique (1).

The water-perfused catheter used in this study incorporates unilateral pressure sensors, in contrast to the circumferential pressure sensors of the solid-state catheter used in previous publications (3, 7, 8). Since the EGI is asymmetric, the latter could explain the poor agreement between water-perfused HRM and solid-state HRM for measuring pressure in the sphincter. However, a recent study that also incorporated
use water-perfused HRM catheters in clinical practice and help
4s, i.e., for measurements performed on the same day in the
and solid-state HRM was observed for CFV, DL, DCI, and IRP
agreement between measurements with water-perfused HRM
obtained normal values, and a moderate to high level of
CFV.
less clear for other parameters such as break size, DCI, and
seems clear for well-studied parameters such as IRP, it is much
future studies evaluate the effect of larger sensor spacing on
values for EGJ measurement. However, we advise caution when these
Water-perfused catheters with a high-resolution segment
only at the position of the EGJ are also available. These
catheters measure pressure at the EGJ similarly to the catheter
used in our study but have a larger spacing between the sensors
positioned at the level of the esophageal lumen. We therefore
propose that centers that use these catheters adopt our proposed
values for EGJ measurement. However, we advise caution in
using our proposed criteria for esophageal parameters until
future studies evaluate the effect of larger sensor spacing on
HRM parameters defined by the Chicago classification.
The present normal values for water-perfused manometry
and the moderate to good agreement between water-perfused
and solid-state manometry for the most relevant HRM param-
eters suggest the uncomplicated use of this technique in the
diagnostic assessment of patients with dysphagia. However,
the usefulness of normal values is always determined by the
likelihood that an abnormal value can indeed be considered
pathological and responsible for symptoms, and while this
seems clear for well-studied parameters such as IRP, it is much
less clear for other parameters such as break size, DCI, and
CFV.
In conclusion, in this study we have established normal
values for a water-perfused HRM system. The normal values
that we propose are only slightly different from previously
obtained normal values, and a moderate to high level of
agreement between measurements with water-perfused HRM
and solid-state HRM was observed for CFV, DL, DCI, and IRP
4s, i.e., for measurements performed on the same day in the
same subject. The presented normal values allow physicians to
use water-perfused HRM catheters in clinical practice and help
to define normal and abnormal. However, the results of our
study also confirm that differences in measurement outcome
exist between different manometric systems and that normal
values must be determined for each different manometric
system.
GRANTS
This study was financially supported by an unrestricted grant from Medical
is supported by The Netherlands Organization for Scientific Research (NWO).
DISCLOSURES
A. J. Bredenoord has been a consultant and honoraria recipient for AstraZeneca
and has received grant funding from Shire and payment for development of
educational presentations from Medical Measurements Systems (MMS).
A. J. P. M. Smout has been a consultant and honoraria recipient for AstraZeneca
AUTHOR CONTRIBUTIONS
Author contributions: B.F.K., A.J.S., and A.J.B. conception and design of
research; B.F.K. and S.H. performed experiments; B.F.K., P.W.W., and S.H.
analyzed data; B.F.K., P.W.W., A.J.S., and A.J.B. interpreted results of
experiments; B.F.K. prepared figures; B.F.K. drafted manuscript; B.F.K.,
P.W.W., A.J.S., S.H., and A.J.B. edited and revised manuscript; B.F.K.,
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