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SYSTEMATIC REVIEW

Diagnostic accuracy of palpation and ultrasonography for diagnosing infantile hypertrophic pyloric stenosis: a systematic review and meta-analysis

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Objective: Although infantile hypertrophic pyloric stenosis (IHPS) is a well-known disease, there is no systematic review regarding the optimal diagnostic strategy. We conducted a systematic review and meta-analysis to obtain diagnostic accuracy of all methods to diagnose IHPS.
Methods: According to the Preferred Reported Items for Systematic Reviews and Meta-Analysis guidelines, we searched MEDLINE and Embase to identify studies reporting sensitivity and specificity of all methods used to diagnose IHPS. Inclusion criteria were infants with suspicion of/or diagnosed with IHPS who underwent pyloromyotomy or had clinical follow-up. A random-effects model was used to obtain pooled estimates of sensitivity, specificity and area under the receiver operating characteristic curve.
Results: After screening 5364 studies, we included 43 studies with in total 6085 infants (n = 4241 IHPS; n = 1844 controls). The diagnostic sensitivity of palpation ranged from 10.0 to 93.4% and decreased over time. Different parameters for ultrasonography were found. Most used parameters were pyloric muscle thickness (PMT) ≥ 3 mm (pooled sensitivity 97.6% and specificity 98.8%), PMT ≥ 4 mm (pooled sensitivity 94.0% and specificity 98.0%) or a combination of PMT ≥ 4 mm and/or pyloric canal length ≥16 mm (pooled sensitivity 94.0% and specificity 91.7%). The AUC showed high diagnostic accuracy (0.997, 0.966 and 0.981 respectively), but large heterogeneity exists. Due to the large differences in cut-off values no meta-analysis could be conducted for pyloric canal length and pyloric diameter.
Conclusion: Palpation has limited sensitivity in diagnosing IHPS. We showed that ultrasonography has highest diagnostic accuracy to diagnose IHPS and we advise to use PMT ≥ 3 mm as cut-off.
Advances in knowledge: This is the first systematic review and meta-analysis on diagnosing IHPS, which summarizes the available literature and may be used as a guideline.

INTRODUCTION

Infantile hypertrophic pyloric stenosis (IHPS) is a condition which develops in the first weeks of life and requires surgical treatment.[1] Infants with IHPS typically present with projectile vomiting and may suffer from dehydration due to a gastric outlet obstruction. The exact pathophysiology which leads to muscular wall thickening and the inability of the pyloric canal to relax is still unknown, but thought to be multifactorial.[1,2] Well-known risk factors are male sex, prematurity, bottle-feeding and delivery by cesarean section.[3–5]

In children presenting with vomiting, physical examination and imaging are key in the diagnostic process. Before ultrasound made its introduction, medical history and physical examination played a major role in diagnosing infants with IHPS. Important signs suspect for IHPS are non-bilious projectile vomiting, dissatisfaction after feeding and inability to gain weight. Physical examination may consist of careful palpation of the abdomen to search for pyloric thickening ('olive sign') and visualization of peristaltic waves. Although the guideline of the American College of Radiologists still states that in case of new-onset

non-bilious vomiting where a classic 'olive' is palpated, the diagnosis of IHPS can be made clinically, experience has shown that nowadays this sign is often absent.[6,7] Furthermore, test feedings and palpation are invasive and stress enhancing for both infants and parents.

Since Teele and Smith first described the use of ultrasonography to diagnose IHPS in 1977, the incidence of ultrasound diagnosis of IHPS increased.[8] Over the subsequent years, ultrasound has become the diagnostic modality of choice due to its non-invasiveness and the ability to directly observe the pyloric canal and all its assets. Although ultrasound is a common practice in most institutions today, many different parameters are used and the evidence is limited by single studies. Another, historic diagnostic modality for diagnosing obstructive causes of vomiting such as IHPS is an upper gastrointestinal (UGI) studies.[6] However, the use of ionizing radiation makes this test less favorable for young infants.

The aim of this systematic review is to evaluate the evidence base for the diagnostic strategy with respect for physical examination and imaging for IHPS. We have studied the diagnostic accuracy of physical examination and imaging of IHPS and aimed to develop the first evidence-based guideline for diagnosing IHPS in order to ensure highest possible quality of care.

METHODS

Protocol

A systematic review was conducted according to the Preferred Reported Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines on all literature regarding diagnosing IHPS. The protocol was registered at PROSPERO (2021, CRD42021227343).

Literature search

We performed a search in PubMed and EMBASE (Ovid). Keywords were hypertrophic pyloric stenosis, infant, diagnostic imaging, diagnostic techniques, physical examination, radiography, fluoroscopy, ultrasonography, Computed Tomography and Magnetic Resonance Imaging. The detailed search strategy is available in the Supplementary Material 1. The reference lists of the included articles were examined for additional publications. The search was conducted in November 2017 and updated in December 2020 and July 2022.

Eligibility criteria

All original studies reporting on sensitivity and specificity of any method used to diagnose IHPS were considered eligible, with language restriction to English publications. Case reports, reviews, letters, and congress abstracts were excluded. Inclusion criteria were infants (<3 months) with suspicion of or diagnosed with IHPS who underwent open or laparoscopic pyloromyotomy after diagnosis or had clinical follow-up. Studies with no clinical follow-up or surgical treatment to confirm or exclude diagnosis of IHPS and/or studies describing infants with other (congenital) gastrointestinal conditions were excluded from data analysis.

Study selection and methodological quality assessment

Studies were included according to the criteria listed above. Two reviewers (JD, RvR) independently screened title and abstract of the studies retrieved using the search strategy. After first selection, full text was screened for final selection. The methodological quality of the included studies was assessed by using the Quality Assessment of Diagnostic Accuracy Studies v. 2 (QUADAS-2) tool (FvdB, JD and RvR). Inconsistencies were solved by second joint review.

Data extraction and analysis

We systematically extracted the data regarding study design characteristics, patient characteristics and test characteristics from all the included studies and recorded them in a data extraction form. If incomplete, missing data were calculated or, if possible, retrieved by contacting the authors. Surgery, *i.e.* open or laparoscopic pyloromyotomy, was used as the reference standard following positive index test results. Negative index test results were followed by surgery or clinical follow-up.

Statistical analysis

Statistical analysis was performed using Review Manager v. 5.4 and Meta-DiSc v. 1.4. The available data were inserted in 2 × 2 tables to compute sensitivity, specificity, positive-predictive value (PPV) and negative-predictive value (NPV) for each study. A random-effects model was used to obtain pooled estimates of sensitivity and specificity with 95% confidence intervals (95% CIs). Heterogeneity between studies was assessed using the $\chi 2$ and I two statistic. The summary receiver operating characteristic (SROC) curve was used to estimate the area under the curve (AUC) that represented overall diagnostic performance of the index test.

RESULTS

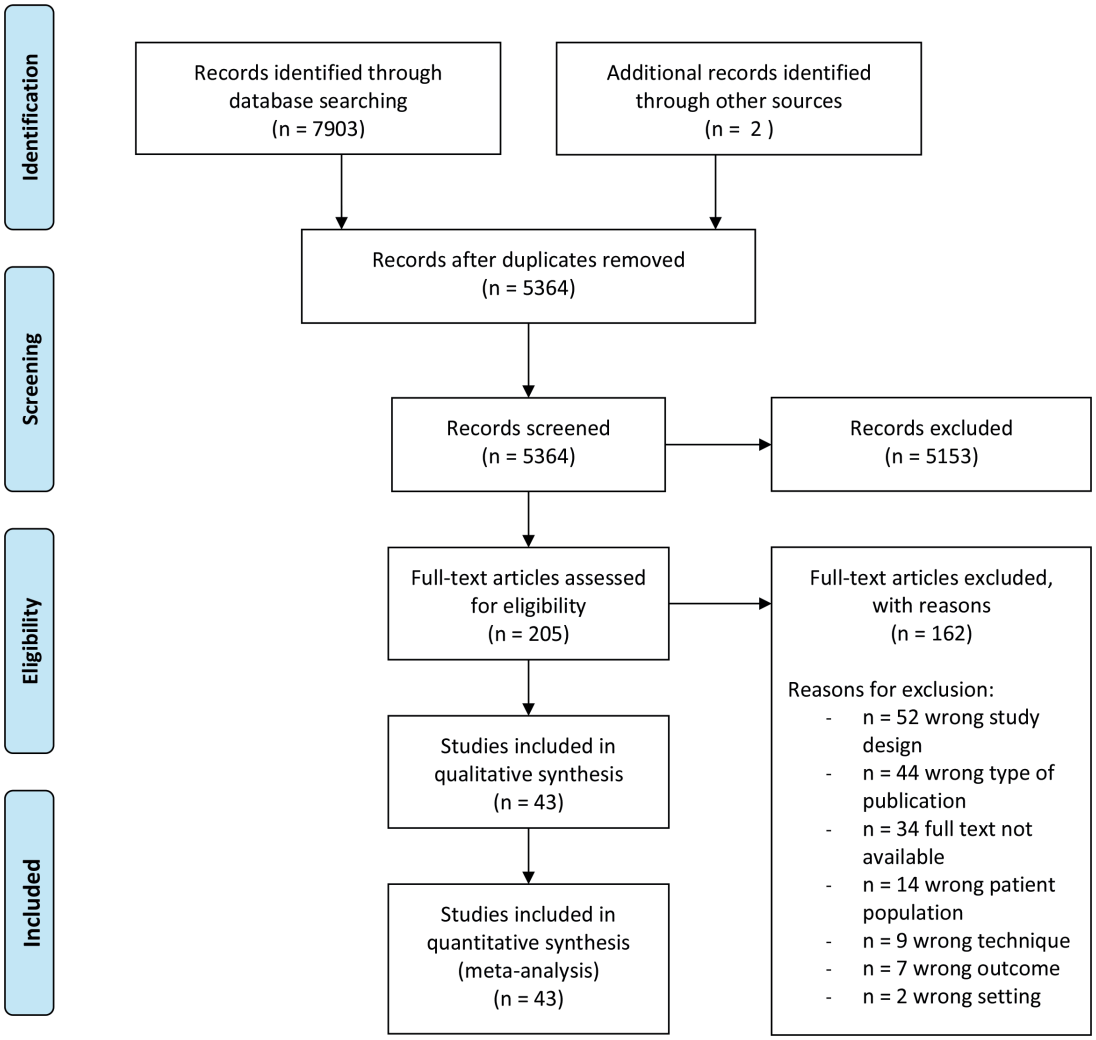
Literature search

The literature search initially provided 7903 potentially suitable studies. Two studies were added after examination of reference lists and hand searching. After exclusion of duplicates, 5364 studies remained, of which 5153 studies were excluded subsequent to first screening. After full text screening, 162 more studies were excluded and 43 were included. See Figure 1 for the detailed PRISMA chart.

Study characteristics

The 43 included studies were published between 1968 and 2021. In total, 6085 infants were included, of which 4241 infants had IHPS and 1844 were controls. The boys–girls ratio of positive cases was described in 25 articles and was 5:1 (boy $n = 2040$ vs. girl $n = 436$). The mean age of infants with IHPS was described in only 14 publications and ranged between 34 and 46 days. 23 studies (n = 3164 infants) investigated the sensitivity of palpation of a pyloric mass[9–31] and 31 studies the sensitivity and specificity of ultrasonography (n = 3685 infants; n = 1914 with IHPS *vs* n = 1771 controls).[12–16,20,23,26,28,30–51] The presence of a pyloric mass was assessed during clinical examination by any doctor. However, information in regard to the performer of physical examination was not available for all studies. Optionally, an additional test feed was conducted to observe for the presence of peristaltic waves. The ultrasound was (if mentioned) performed by a (pediatric) radiologist, ultrasonographer or other doctor.

Figure 1. PRISMA flowchart. PRISMA, Preferred Reported Items for Systematic Reviews and Meta-Analysis.



Measurements performed during ultrasonography included pyloric muscle thickness (PMT), pyloric canal length (PCL), pyloric muscle diameter (PD) and in a few cases pyloric ratio (PR) or pyloric muscle index (PMI). The upper limits of normal of PMT, PCL and PD differed between studies and varied between ≥ 3–4 mm, ≥ 11–17 mm and ≥ 13–20 mm respectively. Some studies used combined measurements to diagnose IHPS.

Methodological quality

Quality assessment by using the QUADAS-2 tool showed a high risk regarding both patient selection and index test in more than half of the studies (Figure 2). Many studies only included patients with IHPS and no control group,[9–12,16–19,22–30,37,44] some excluded infants with a palpable pyloric mass[33,39,42] and others did not describe in- and exclusion criteria.[49,50] In regard to the index test, it was often unknown who performed palpation of the pyloric mass or ultrasound and/ or whether this person had experience with this technique,[9–12,14,15,17,18,21,24–30,40,41] sometimes no pre-determined cut-off values were available in regard to ultrasonography[14,42,51] and some authors documented a learning curve during performing ultrasounds.[23,46] The risk of bias concerning reference test and flow and timing were considered low to moderate. Assessment of bias regarding the overall applicability was considered low.

Palpation

23 papers reporting on the sensitivity of palpation of the 'olive' were found (Table 1). The diagnostic sensitivity ranged widely from 10.0 to 93.4%. It is of interest to note that over the years, the sensitivity of palpation seems to drop. Only six studies included infants without IHPS, of which four studies reported one or more false-positive cases, leading to a specificity ranging from 0.0 to 100.0%.[12–14,20,21,26] No meta-analysis could be conducted due to lack of control patients in most studies.

Ultrasonography

Of the 31 included studies on ultrasonography, 16 papers described the diagnostic accuracy of pyloric muscle thickness (PMT) (Table 2), 12 the pyloric channel length (PCL) and 6 the pyloric diameter (PD, Table 3) as unique parameters. Furthermore, 15 articles described sensitivity and specificity of ultrasonography in the diagnosis of hypertrophic pyloric stenosis based on combined measurements. (Table 4). The included studies used varying types of ultrasound systems. In

Figure 2. Quality assessment.

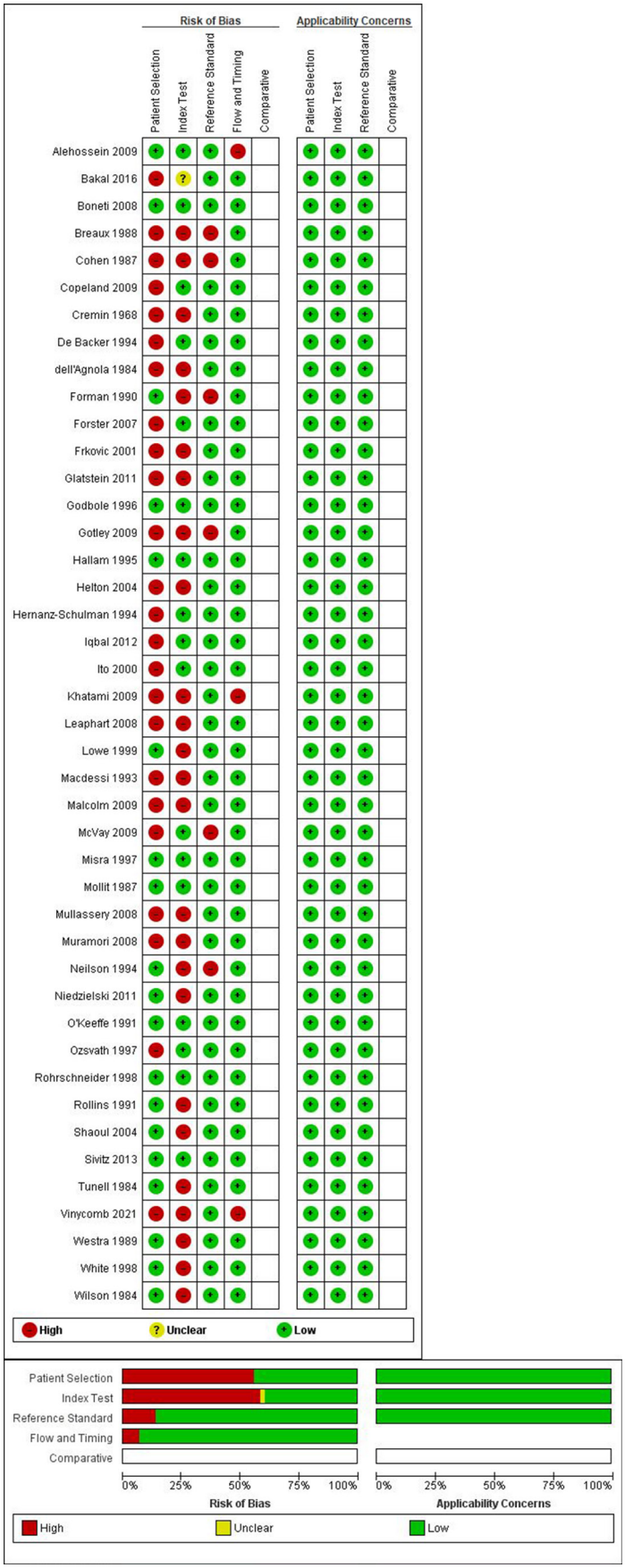


Table 1. Percentage of 'olives' palpated

Author	Year[a]	Cases[b]	Proportion IHPS	Sensitivity (95% CI)	Specificity (95% CI)
Cremin[9]	1956–1967	165	1.0	0.84 [0.77–0.89]	n/e
Macdessi[10]	1974–1977 and 1988–1991	402	1.0	0.90 [0.86–0.92]	n/e
Breaux[11]	1980–1984	363	1.0	0.85 [0.80–0.88]	n/e
dell'Agnola[12]	1981–1982	17	0.82	0.15 [0.02–0.45]	1.00 [0.29–1.00]
Mollitt[13]	1983–1986	101	0.57	0.47 [0.33–0.60]	0.98 [0.88–1.00]
Forman[14]	1985–1988	101	0.77	0.77 [0.66–0.86]	1.00 [0.29–1.00]
Rollins[15]	1986–1988	100	0.44	0.86 [0.73–0.95]	n/e
De Backer[16]	1986–1991	63	1.0	0.60 [0.47–0.72]	n/e
Muramori[17]	1986–1996	103	1.0	0.79 [0.69–0.86]	n/e
Shaoul[18]	1990–2000	70	1.0	0.50 [0.38–0.62]	n/e
Ozsvath[19]	1991–1995	60	1.0	0.33 [0.22/0.47	n/e
Godbole[20]	1993–1995	116	0.65	0.80 [0.69–0.88]	0.98 [0.87–1.00]
White[21]	1994–1996	234	0.64	0.74 [0.66–0.81]	0.99 [0.94–1.00]
Gotley[22]	1994–2004	329	1.0	0.44 [0.39–0.50]	n/e
Frkovic[23]	1995–1999	14	1.0	0.15 [0.02–0.45]	n/e
Bakal[24]	1996–2015	56	1.0	0.54 [0.40–0.67]	n/e
Helton[25]	2000–2002	175	1.0	0.32 [0.25–0.39]	n/e
Mullassery[26]	2000–2004	343	1.0	0.94 [0.89–0.96]	0.00 [0.00–0.97]
Leaphart[27]	2001–2006	314	1.0	0.63 [0.57–0.68]	n/e
Khatami[28]	2001–2008	84	1.0	0.15 [0.09–0.25]	n/e
Glatstein[29]	2006–2008	118	1.0	0.13 [0.07/0.20]	n/e
Malcolm[30]	n/a (published in 2009)	8	1.0	0.25 [0.03–0.65]	n/e
Sivitz[31]	2009–2012	67	0.15	0.10 [0.00–0.45]	n/e

IHPS, Infantile hypertrophic pyloric stenosis.
[a]Range of data collection
[b]Total number of cases included in the study. n/e means not estimable, 95% CI means 95% confidence interval

most cases, a linear transducer was used with a frequency of 5 or 7.5 MHz, but other transducers and frequencies were described as well. Eight studies did not describe the type of transducer at all. In Figure 3, we have shown a schematic drawing and an ultrasound image of the pylorus illustrating the different measurements. Only two articles described the exact cursor placement for the measurement of PMT and PCL.[33,38] PMT measures included the thickness of one muscle layer and excluded the mucosa and lumen and PCL was measured from the base of the duodenal cap to the gastric antrum.

PMT

Cut-off levels used for PMT were 3 and 4 mm. One article described a cut-off of PMT ≥ 3.5 mm.[51] Based on PMT only, the sensitivity ranged from 76 to 100% and the specificity from 85–100%, depending on both the patient population and the cut off level chosen (Table 2). PPV and NPV ranged from 88.1 to 100% and 85.7 to 100% respectively with an accuracy ranging from 87.2 to 100%. Five studies were excluded from meta-analysis because the diagnostic or reference test results could not be extracted, calculated or obtained from the authors.[30,36,37,42,44] The pooled sensitivity of PMT ≥ 3 mm was 97.6% (95% CI 95.8–98.7%; $\chi2 = 23.01$, $p < 0.001$; $I^2 = 73.9\%$) and the pooled specificity was 98.8% (95% CI 98.0–99.4%; $\chi2 = 31.12$, $p < 0.001$; $I^2 = 81.9\%$) (Figure 4a). The AUC of the SROC was 0.997 (Figure 5a). The pooled sensitivity of PMT ≥ 4 mm was 94.0% (95% CI 92.0–96.0%; $\chi2 = 3.25$, p 0.517; $I^2 = 0.0\%$) and the pooled specificity was 98.0% (95% CI 97.0–99.0%; $\chi2 = 36.80$, $p < 0.001$; $I^2 = 89.1\%$) (Figure 4b). The AUC of the SROC was 0.966 (Figure 5b).

PCL

Cut-off levels used for PCL ranged widely from >13 mm to ≥20 mm (Table 3). Based on PCL only, the sensitivity ranged from 54.5 to 100% and the specificity from 76.9 to 100%, this also depended on both the patient population and the cut-off level chosen. PPV and NPV could be determined in a limited number of studies and ranged from 89.0 to 100% and 71.4 to 99.1% respectively with an accuracy ranging from 78.7 to 98.3%.[34–36,39,40,43,51] Due to the large differences in cut-off values, no meta-analysis could be conducted.

PD

Cut-off levels used for PD were ranging widely from ≥11 mm to ≥15 mm (Table 3). Based on PCL only, the sensitivity ranged from

Table 2. Sensitivity and specificity of ultrasonography in the diagnosis of infantile hypertrophic pyloric stenosis based on PMT ≥ 3 mm and PMT ≥ 4 mm

Author	Year[a]	Cases[b]	Proportion IHPS	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)
O'Keeffe[32]	1991	145	0.29	95.2	100	100	98.1	98.6
Hernanz-Schulman[33]	1994	150	0.44	100	100	100	100	100
Hallam[34]	1995	47	0.45	81	92.3	89.5	85.7	87.2
Rohrschneider[35]	1998	169	0.5	100	100	100	100	100
Lowe[36]	1999	84	0.41	100	100	n/e	n/e	n/e
Forster[37]	2007	187	0.47	91.9	85.1	n/e	n/e	n/e
Alehossein[38]	2009	444	0.17	100	100	100	100	100
Malcom[30]	2009	8	1	100	n/e	n/e	n/e	n/e
Iqbal[39]	2012	304	0.22	95.5	99.2	97	99.7	98.4
Vinycomb[51]	2021	284	0.5	97.8	94	94.6	97.7	96
Tunell[40]	1984	91	0.44	92.5	90.2	88.1	93.9	91.2
Wilson[41]	1984	50	0.58	93.1	90.5	93.1	90.5	92
Cohen[42]	1987	156	0.08	100	n/e	n/e	n/e	n/e
Westra[43]	1989	47	0.47	95.5	100	100	96.2	97.2
Ito[4444]	2000	57	1	93	n/e	n/e	n/e	n/e
Mullassery[2626]	2008	343	99.1	95.2	0	99.1	0	94.4
Alehossein[3838]	2009	444	0.17	96	100	100	99.2	99.3

IHPS, infantile hypertrophic pyloric stenosis; NPV, negative-predictive value;PMT, pyloric muscle thickness; PPV, positive-predictive value.

[a]Year published

[b]Total number of cases included in the study. N/e means not estimable, because there was lack of sufficient data to calculate value and/or value was not reported in publication.

Table 3. Sensitivity and specificity of ultrasonography in the diagnosis of infantile hypertrophic pyloric stenosis based on (A) PCL and (B) PD

A									
Author	**Year[a]**	**Cases[b]**	**Proportion IHPS**	**Cut-off value**	**Sensitivity (%)**	**Specificity (%)**	**PPV (%)**	**NPV (%)**	**Accuracy (%)**
Hallam[34]	1995	47	0.45	PCL>13 mm.	57.1	96.2	92.3	73.5	78.7
Mullassery[36]	2008	343	1	PCL≥14 mm.	99.6	0	98.7	0	98.3
Rohrschneider[35]	1998	169	0.5	PCL≥15 mm.	91.8	98.8	98.7	92.2	95.3
Malcolm[30]	2009	8	1	PCL≥15 mm.	100	n/e	n/e	n/e	n/e
Iqbal[39]	2012	304	0.22	PCL≥15 mm.	97	97	89	99.1	96.7
Lowe[36]	1999	84	0.4	PCL≥14 mm	84	100	n/e	n/e	n/e
				PCL≥15 mm	92	97	n/e	n/e	n/e
				PCL≥16 mm.	98	97	n/e	n/e	n/e
				PCL≥17 mm	100	84.9	n/e	n/e	n/e
Vinycomb[51]	2021	284	0.5	PCL≥15 mm	95.8	90.4	91.9	95	93.3
				PCL≥17 mm	76.7	98.4	98.2	78.8	86.9
Forster[37]	2007	87	0.47	PCL≥16 mm.	85.1	76.9	n/e	n/e	n/e
				PCL>17 mm.	75.8	84.6	n/e	n/e	n/e
Ito[44]	2000	57	1	PCL≥18 mm.	98	n/e	n/e	n/e	n/e
Tunell[40]	1984	91	0.44	PCL>19 mm.	95	100	100	96.2	97.8
Westra[43]	1989	47	0.47	PCL≥19 mm.	54.5	100	100	71.4	78.7
Cohen[42]	1987	156	0.07	PCL≥20 mm.	64	n/e	n/e	n/e	n/e

B									
Author	**Year[a]**	**Cases[b]**	**Proportion HPS**	**Cut- off value**	**Sensitivity (%)**	**Specificity (%)**	**PPV (%)**	**NPV (%)**	**Accuracy (%)**
Rohrschneider[35]	1998	169	0.5	PD≥11 mm.	n/e	n/e	n/e	n/e	92
Tunell[40]	1984	91	0.44	PD>13 mm.	80	96.1	94.1	86	89
Westra[43]	1989	47	0.47	PD≥13 mm.	90.9	100	100	92.6	95.7
Wilson[41]	1984	50	0.58	PD≥15 mm.	51.7	100	100	60	72
Cohen[42]	1987	156	0.07	PD≥15 mm.	55	n/e	n/e	n/e	n/e
Ito[44]	2000	57	1	PD≥15 mm.	93	n/e	n/e	n/e	n/e

IHPS, infantile hypertrophic pyloric stenosis; NPV, negative-predictive value;PCL, pyloric canal length; PD, pyloric diameter; PPV, positive-predictive value.

[a]Year published.

[b]Total number of cases included in the study. N/e means not estimable, because there was lack of sufficient data to calculate value and/or value was not reported in publication.

Table 4. Sensitivity and specificity of ultrasonography in the diagnosis of infantile hypertrophic pyloric stenosis based on combined measurements

Author	Year[a]	Cases[b]	Proportion IHPS	Cut-off value	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)
Neilson[45]	1994	147	0.46	PMT > 2.5 mm or PCL>15 mm or PD>11 mm	97.1	98.7	98.5	97.5	98.0
Vinycomb[51]	2021	284	0.50	PMT ≥ 3 mm and PCL≥14.5 mm PMT ≥ 3 mm and PCL≥15 mm	93.1 94.4	99.1 99.1	99.4 99.3	90.6 93.5	95.5 96.5
Khatami[28]	2009	84	1.00	PMT > 3 mm and PCL>15 mm	87.7	n/e	n/e	n/e	n/e
Sivitz[31]	2013	67	0.85	PMT > 3 mm and PCL>17 mm	100.0	100.00	100.0	100.0	100.0
Niedzielski[46]	2011	115	0.83	PMT ≥ 3 mm and/or PCL≥17 mm	97.9	100.0	100.0	90.5	98.3
Frkovic[23]	2001	9	1.00	PMT ≥ 3 mm, PCL≥17 mm and PD≥13 mm with pyloric canal closed	88.9	n/e	n/e	n/e	n/e
dell'Agnola[12]	1984	17	0.82	PMT > 4 mm or PCL>13 mm or PD>9.9 mm	100.0	100.00	100.0	100.0	100.0
Rollins[15]	1991	100	0.49	PMT ≥ 4 mm and/or PD≥15 mm	100.0	100.0	100.0	100.0	100.0
Misra[47]	1997	65	0.95	PMT > 4 mm and PCL > 16 mm	87.1	0.00	94.7	0.00	83.1
De Backer[16]	1994	63	1.00	PMT > 4 mm and/or PCL>16 mm	60.3	n/e	100.0	n/e	n/e
Forman[14]	1990	44	0.50	PMT > 4 mm. and/ or PCL>16 mm	88.9	100.0	100.0	90.0	94.4
Boneti[48]	2008	30	0.93	PMT ≥ 4 mm and/or PCL>16 mm.	100.0	100.0	100.0	100.0	100.0
Copeland[49]	2009	32	0.78	PMT ≥ 4 mm and/or PCL≥16 mm	100.0	100.0	100.0	100.0	100.0
McVay[50]	2009	71	0.92	PMT ≥ 4 mm and/or PCL≥16 mm	100.0	100.0	100.0	100.0	100.0
Mollitt[13]	1987	54	0.58	PMT > 4 mm MWT and/or PCL>17 mm and/or PD>13 mm	100.0	100.0	100.0	100.0	100.0

IHPS, infantile hypertrophic pyloric stenosis; NPV, negative-predictive value; PCL, pyloric canal length; PD, pyloric diameter; PMT, pyloric muscle thickness; PPV, positive-predictive value.
[a]Year published
[b]Total number of cases included in the study. PMT stands for pyloric muscle thickness, PCL pyloric canal length and PD pyloric diameter. N/e means not estimable, because there was lack of sufficient data to calculate value and/or value was not reported in publication.

Figure 3. Schematic drawing of the pylorus illustrating the different sonographic measurements (a) and ultrasound images of PMT (b) or PCL (c) measurement. PCL, pyloric canal length; PD, pyloric diameter; PMT, pyloric muscle thickness; PR, pyloric ratio.

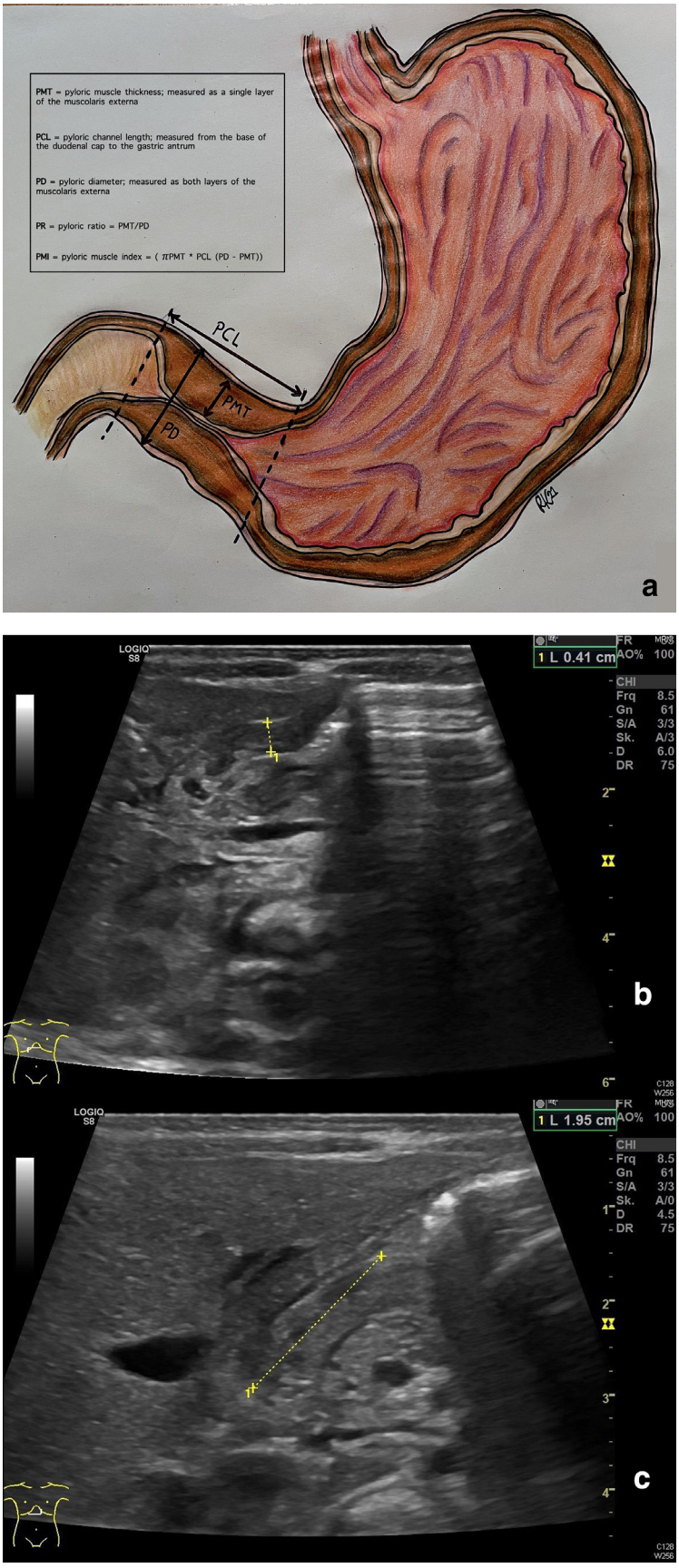
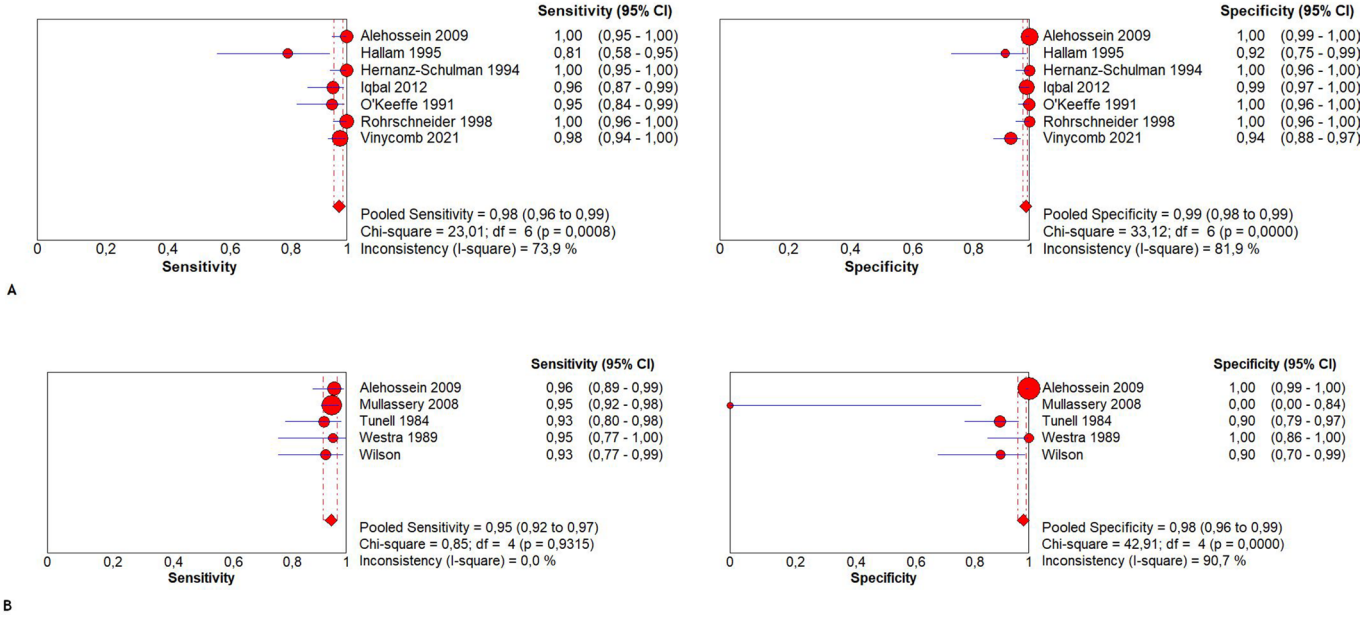


Figure 4. Pooled sensitivity and specificity forest plots including the 95% CI of (A) PMT ≥ 3 mm and (B) PMT ≥ 4 mm. CI, confidence interval; PMT, pyloric muscle thickness.



51.7 to 93.0% and the specificity from 96.1 to 100%, depending on both patient population and cut- off level chosen. PPV and NPV ranged from 94.1 to 100% and 60.0 to 92.6% respectively with an accuracy ranging from 72.0 to 95.7%. Due to the large differences in cut-off values, no meta-analysis could be conducted.

Combined measurements

Table 4 shows the studies which used combined measurements. Those studies combined different cut-off values of PMT, PCL and/or PD. Dependent of patient population, combination and chosen cut-off levels, the sensitivity ranged from 60.3 to 100% and the specificity from 0.0 to 100%. PPV and NPV ranged from 94.7 to 100% and 0.0 to 100% respectively with an accuracy ranging from 83.1 to 100%. Most often used combined measurement was PMT > 4 mm and/or PCL > 16 mm.[14,16,47–50] Therefore, we conducted a meta-analysis of this combination. Two studies were excluded because the diagnostic or reference test results could not be extracted, calculated or obtained from the authors. The pooled sensitivity of PMT > 4 mm and/or PCL > 16 mm was 94.0% (95% CI 89.8–96.9%; $\chi 2 = 15.85$, p 0.003; $I^2 = 74.8\%$) and the pooled specificity was 91.7% (95% CI 77.5–98.2%; $\chi 2 = 20.65$, $p < 0.001$; $I^2 = 80.6\%$) (Figure 6). The AUC of the SROC was 0.981 (Figure 7).

Pyloric ratio and pyloric muscle index

Only one paper used the pyloric ratio (PR), which is calculated by the PMT divided by PD.[36] They compared different cut-offs varying from 0.26 to 0.29 and suggested to use a cut-off of ≥0.27 (sensitivity of 96.0% and specificity of 93.9%). Another paper used the pyloric muscle index as described by Carver et al (πPMT*PCL (PD-PMT) with a cut-off value of>0.46 and found a sensitivity of 98.7% and specificity of 100.0%.[20,52]

Figure 5. Summary receiver operating characteristic curve of (A) PMT ≥ 3 mm and (B) PMT ≥ 4 mm. PMT, pyloric muscle thickness.

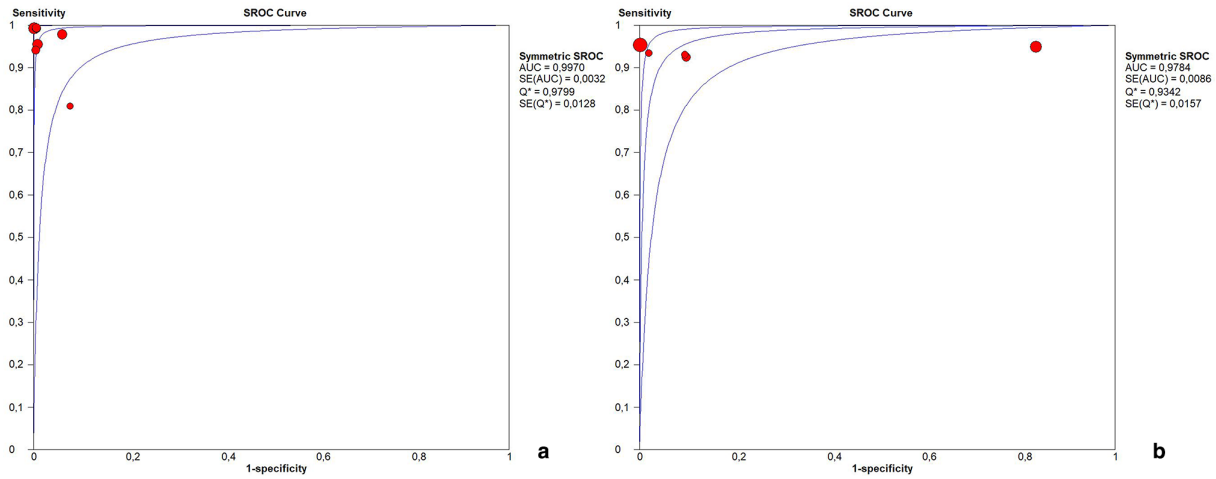
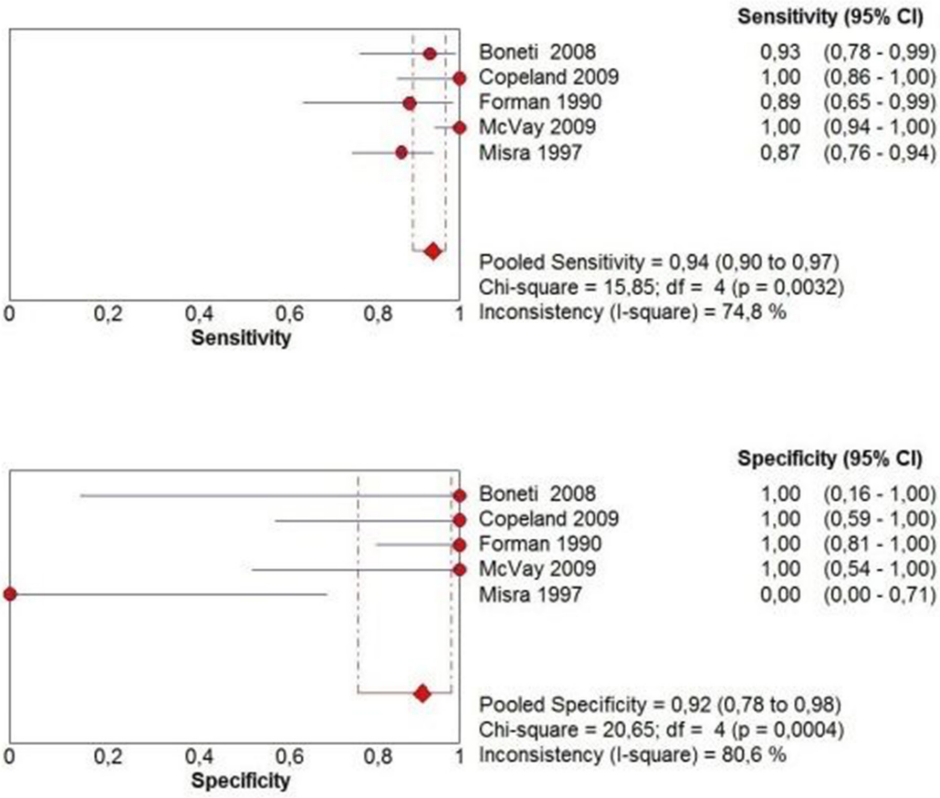


Figure 6. Pooled sensitivity and specificity forest plots including the 95% CI of a combination of PMT ≥ 4 mm and/or PCL ≥ 16 mm. CI, confidence interval; PCL, pyloric canal length; PMT, pyloric muscle thickness.



DISCUSSION

We performed this systematic review to evaluate the accuracy of diagnostic strategies for diagnosing IHPS and to develop an evidence-based guideline for diagnosing IHPS to improve quality of care. In this study, we found a wide range in sensitivity of palpation of the hypertrophied pyloric muscle or 'olive' (10%–93%). An important finding was that the sensitivity seems to decrease over the years. This is in line with the results of Vinycomb et al who performed a trend analysis on the number of palpated tumors observed between 2005 and 2015 and found a significant trend. [53] It is thought that this decrease is caused by earlier presentation and/ or less experience of the medical staff.[18] Furthermore, we found different parameters and corresponding cut-off values for ultrasonography which could be used for diagnosing IHPS. Most used parameters were PMT (≥3 mm or ≥4 mm) or a combination of PMT (≥4 mm) and/or PCL (≥16 mm). Pooled sensitivity and specificity for both PMT solely or in combination with PCL were high. However, PMT ≥ 3 mm is just a little more accurate than PMT ≥ 4 mm or the combination of PMT ≥ 4 mm and/or PCL ≥ 16 mm and is therefore preferable. Although, the results should be interpreted with caution due to high heterogeneity. Unfortunately, we could not obtain pooled data for PCL solely or PD because cut-off values differed largely between the included studies. Future studies to investigate the diagnostic accuracy of these parameters are therefore recommended. Likewise, new combinations of parameters could be studied to aim for maximum accuracy. In literature, ancillary findings as antral nipple sign or double track sign are described as well, but insufficient evidence was found to evaluate the usability and accuracy.[42,54]

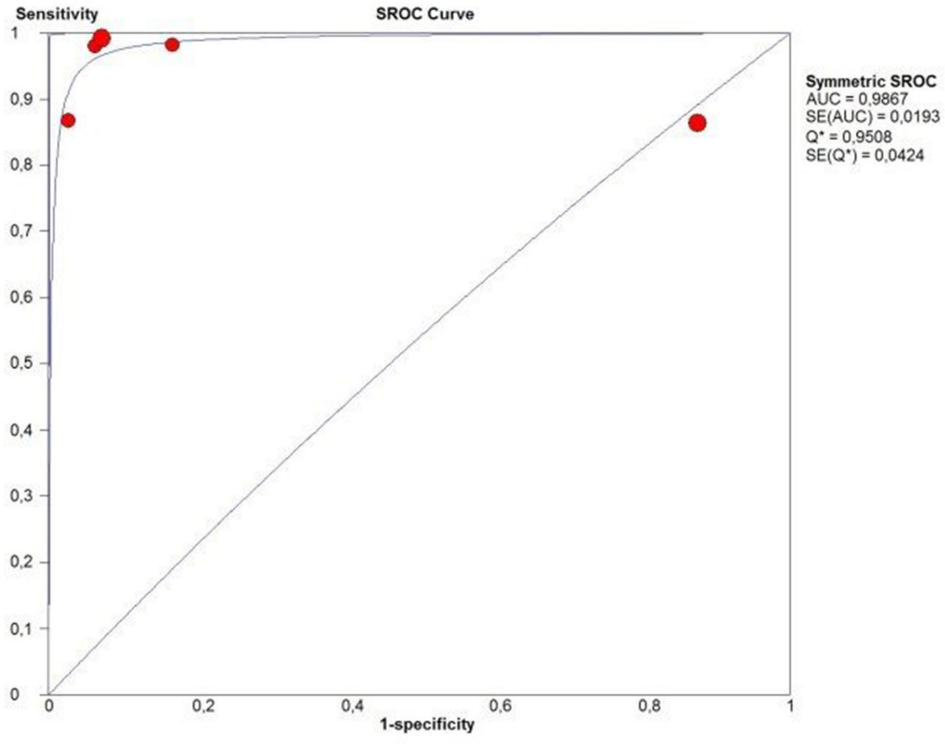
Only two studies mentioned the placement of the cursor during ultrasonography. They both stated to use the standard manner, which included one muscle layer without submucosa and lumen for PMT measurement and the base of the duodenal cap to the gastric antrum for PCL measurement. It seems possible that others authors considered cursor placement as standard practice and therefore did not elucidate cursor placement. However, a recent study showed that in more than half of patient scans, the placement of the internal cursor during PMT measurements included components of the pylorus up to the submucosa, muscularis mucosa, mucosa and in a few instances even the luminal mucosal folds.[55] Furthermore, they found a moderate interobserver agreement of 66% between two pediatric radiologists, indicating operator variability for placement of the internal cursor. We advise to standardize cursor placement at least at an institutional level. It has become common practice in most institutions to use the hypoechoic muscularis externa (single layer) as a sonographical landmark for PMT measurement, the base of the duodenal cap and the gastric antrum for PCL measurement and both layers of the muscularis externa for PD measurement. We suggest to include this practice into local protocols

not only to meet the high diagnostic standards in pediatric radiology but also to ensure comparability of future research on this topic. Since, a deviation of a millimeter may have major consequences we suggest to conduct 2–3 measurements and take the average. Furthermore, the cut-off values used to determine if the infant is diagnosed with pyloric stenosis are mostly based on the term born infant. Some authors demonstrated that sonographic measurements correlated with the weight and age of infants, suggesting that small and premature infants may not fulfill the criteria while having IHPS.[27,56] However, others state that measurements are not affected by weight at presentation and corrected gestational age or that although age, weight and pyloric thickness are associated they do not have impact on the diagnostic criteria for IHPS.[39,57] We think that it should be borne in mind that infants with low (birth)weight and age might not meet the diagnostic criteria and suggest in these cases repeated sonography after a couple of days.

In this review, we primarily focused on palpation and ultrasonography. The use of abdominal radiographs is only described in historic literature and nowadays, there is general consensus that the use of abdominal radiographs should be considered as obsolete in the diagnosis of patients presenting with acute abdominal complaints.[58] Except one study of 14 infants, we did not find any publications of sufficient quality presenting adequate data to calculate sensitivity and/or specificity of an upper gastrointestinal (UGI) study for the diagnosis of IHPS.[47] Although the ACR guideline mentions that contrast UGI studies are excellent for diagnosing obstructive causes of vomiting in young infants, they also note the limitation of the use of ionizing radiation.[6] It is potentially harmful for the infant and obsolete in the light of a radiation free alternative meeting the diagnostic standards needed. Therefore, fluoroscopy should only be considered in those patients where ultrasound is non-diagnostic. No relevant publications related to the use of CT or MRI in the diagnosis of IHPS were found. In our clinical experience, these advanced imaging techniques should have no role in the diagnostic process of patients suspected of IHPS.

The recommendations arising from this systematic review of the literature are subject to some limitations. The level of evidence of the included studies was low to moderate. It is in the nature of case–control studies that the results of the individual studies included are influenced by a certain degree of bias. The ultrasound technology may have been evolved over the years, but we were unable to analyze the potential relation between technical advances and diagnostic accuracy. Furthermore, the author's main concern is the assumption that false-positive imaging results may be underreported. The gold-standard for positive imaging in IHPS is the intraoperative judgement by the surgeon during the laparoscopy or laparotomy for suspected IHPS. The binary classification of IHPS ("yes or no") represents a highly subjective measure and must be regarded as a major source of bias for our results. It is not clear from most series what happened to the patients that were intraoperatively regarded as having "no IHPS" or "early IHPS". Certainly, every pediatric surgeon pursues the

Figure 7. SROC of a combination of PMT ≥ 4 mm and/ or PCL ≥ 16 mm. PCL, pyloric canal length; PMT, pyloric muscle thickness; SROC, summary receiver operating characteristic curve.



intention to avoid re-operations which may have influenced the numbers of pyloromyotomy.

Based on this literature study, we support the current approach and have shown that ultrasonography by an experienced ultrasonographer or (pediatric) radiologist is a valid method to diagnose IHPS. We advise to use PMT ≥ 3 mm to confirm the diagnosis of IHPS. If ultrasound is positive for IHPS in infants with non-bilious, projectile vomiting, the patient should be sent to the operating theatre. In case of a negative ultrasound, further work-up should be done to exclude other causes of IHPS. Further work-up may consist of clinical follow-up or repeated ultrasonography. Optionally contrast UGI series could be considered. However, in this review no sufficient evidence was found to substantiate this. Furthermore, pediatricians and pediatric surgeons should be aware that palpation of a pyloric 'olive' has limited sensitivity and that this appears to be worsening over time.

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