Magnetic Resonance Imaging for Locating Nonpalpable Undescended Testicles: A Meta-analysis

abstract

BACKGROUND AND OBJECTIVE: Preoperative imaging techniques may guide management of nonpalpable, cryptorchid testicles. We evaluated conventional MRI for identifying and locating nonpalpable testicles in prepubescent boys via meta-analysis.

METHODS: Databases including Medline were searched from 1980 to February 2012. Eligible studies included ≥ 10 boys with cryptorchidism/suspected cryptorchidism and reported data on testicular presence/absence and position (abdominal, inguinal, or scrotal) as determined by imaging and surgery. Two investigators independently reviewed studies against inclusion criteria. We captured the number of testicles that were correctly and incorrectly identified and located, relative to surgically verified status, and estimated sensitivity and specificity by using a random-effects model.

RESULTS: Eight unique prospective case series included 171 boys with 193 nonpalpable testicles (22 with bilateral testicles). Surgery identified 158 testicles (81.9%) present and 35 absent. MRI correctly identified testicles with an estimated median sensitivity of 0.62 (95% Bayesian credible interval [BCI]: 0.47–0.77) and a specificity of 1.0 (95% BCI: 0.99–1.0). MRI located intraabdominal testicles with a sensitivity of 0.55 (95% BCI: 0.09–1.0) and inguino-scrotal testicles with a sensitivity of 0.86 (95% BCI: 0.67–1.0). We were not able to obtain estimates for MRI sensitivity or specificity for locating atrophied testicles. The estimated specificity for location-specific testicles reached almost 100%.

CONCLUSIONS: Conventional MRI has low sensitivity for estimating the population sensitivity for identifying the presence of nonpalpable cryptorchid testicles. When testicles are identified, MRI is poor at locating both atrophied and intraabdominal testicles but performs modestly well in locating those in the inguino-scrotal regions. *Pediatrics* 2013;131:e1908–e1916

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KEY WORDS

meta-analysis, cryptorchidism, undescended testicle, sensitivity, specificity, imaging, MRI

ABBREVIATIONS

BCI—Bayesian credible interval

MRA—magnetic resonance angiography

Pr—probability

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Approximately 3% of term male neonates and 30% of premature infants have cryptorchidism, a condition in which 1 or both testicles are not appropriately positioned in the scrotum at birth and cannot be moved into the proper position manually.^{1,2} The etiology of cryptorchidism is not well understood, and the undescended testicles may be palpable or nonpalpable. Undescended testicles may be present in the abdomen, in the groin area, or misplaced in the scrotum and may be viable or atrophied and no longer viable. Finally, in some individuals, no testicle exists at all (anorchia).

Clinical decision-making about treatment is influenced by factors including palpability, whether the condition is present unilaterally or bilaterally, age at presentation, and coexisting medical conditions. Although ~70% of cryptorchid testicles spontaneously descend within the first year of life, the number of boys whose condition persists remains constant at ~1%.^{3,4} Once cryptorchidism is diagnosed, treatment choices may include watchful waiting, hormonal treatment, or surgery. Decisions about which clinical pathway to follow may be guided by results of hormonal stimulation testing and/or imaging, particularly when the testicle is nonpalpable.

Imaging is used to determine the presence of a testicle and, if present, its location to guide treatment. Imaging approaches include ultrasonography, computerized tomography scanning, routine MRI, magnetic resonance angiography (MRA), and magnetic resonance venography, some of which require sedation or anesthesia and are thus not without risks. A previous meta-analysis⁵ on the performance of ultrasound in nonpalpable cryptorchidism concluded that presurgical ultrasound is of no value in localizing nonpalpable testicles, especially intraabdominal testicles. Due to the varied performance of imaging techniques, we meta-analyzed data

from a larger Agency for Healthcare Research and Quality–funded systematic review of evaluation and treatment approaches for cryptorchidism⁶ to assess the performance of a commonly used imaging technique (conventional [T1-, T2-weighted] MRI) for identifying and locating nonpalpable undescended testicles. Information on other evaluation approaches and treatments addressed in the full review, as well as the review protocol, can be found at <http://www.effectivehealthcare.ahrq.gov>.

METHODS

Search Strategy

We searched Medline via the PubMed interface, the Cumulative Index to Nursing and Allied Health Literature, and Embase from 1980 to February 2012 with the use of relevant controlled vocabulary terms and key terms related to cryptorchidism and imaging- and therapy-related terms (eg, cryptorchidism, MRI). We also hand-searched the reference lists of all included articles and of recent

reviews related to cryptorchidism to identify potentially relevant articles.

Inclusion Criteria

We included all study designs except for single case reports and required that studies include prepubescent males with cryptorchidism or suspected cryptorchidism. We also required that studies evaluate the accuracy with which preoperative MRI identified the presence and location of testicles, with confirmation by surgery. If a study had negative imaging for all subjects, if the imaging techniques were not adequately described, or if relevant data to calculate diagnostic performance were not available, it was excluded. We required that the study reported data on the presence or absence of testicles along with identifying the position of testicles (abdominal, inguinal, or scrotal) as determined by imaging techniques and surgery.

Two investigators independently reviewed each study against the inclusion criteria (Table 1), with disagreements resolved through adjudication by a senior investigator.

TABLE 1 Inclusion and Exclusion Criteria

Category	Criteria
Study population	Prepubescent males presenting with cryptorchidism or suspected cryptorchidism
Time period	Studies published after 1980 due to changes in availability of interventions and imaging approaches around this time
Publication languages	English only
Admissible evidence (study design and other criteria)	Admissible designs: <ul style="list-style-type: none"> • All study designs except for case reports Other criteria: <ul style="list-style-type: none"> • Original research studies that provided sufficient detail regarding methods and results to enable use and adjustment of the data and results • Studies detailing only the prevalence or etiology of cryptorchidism were not included (ie, an intervention for cryptorchidism had to be included) • Studies that included individuals with disorders of sexual development or ambiguous genitalia were not included, even if participants underwent treatment of cryptorchidism, because this treatment was likely to be in concert with treatment of associated conditions that may have compounded the difficulty in drawing meaningful conclusions • Studies must have included at least 1 outcome measure of interest

TABLE 2 Overview of Studies Addressing the Performance of MRI

Characteristic	Conventional MRI
Total studies	8
Study design	
Prospective case series	8
Retrospective case series	0
Confirmatory diagnosis category	
Open surgery	4
Laparoscopy	2
Surgery and/or laparoscopy	2
Included infants	2
Study population	
United States	1
Europe	2
Asia	5
Total no. of participants	171
Total no. of testicles	193

Data Extraction

Two investigators independently extracted data regarding study design, descriptions of the study populations, imaging techniques, and verification method (eg, surgical exploration). Principal outcomes of interest included the presence or absence of testes identified and the number identified and located correctly. For each of 3 status categories (intraabdominal, inguino-scrotal, atrophied), we tallied the number of testes that were correctly (true-positive, true-negative) and incorrectly (false-positive, false-negative) diagnosed, relative to the verified testicle status. For the purposes of the meta-analysis, only studies with surgically located testicles were included, so that sensitivity and specificity could be estimated.

Quality Assessment

We used the QUADAS-2 (Quality Assessment of Diagnostic Accuracy Studies—Revised)⁷ tool to assess studies; the QUADAS-2 includes items on the representativeness of patient spectrum, selection criteria, reference standard, verification bias, timing, and study withdrawals. Two investigators independently assessed each study, with disagreements resolved through discussion. The results of the assessment were then translated to Agency for Health-

care Research and Quality standards of “good,” “fair,” and “poor” quality designations by using a conversion threshold available in the full report.

Statistical Analysis

We evaluated the capability of conventional MRI for identifying the presence or absence of nonpalpable testicles, along with detecting the position and type of testicles, via meta-analysis. Specifically, we estimated the sensitivity and specificity of MRI across studies by using random-effects models in an attempt to generalize its performance. Imaging results were compared with the true state of the testicles, as determined by surgery.

Our estimates of sensitivity and specificity were calculated on the basis of the 4 cell probabilities (Pr) that exhaustively describe the outcomes of imaging diagnoses: true-positive (Pr [testicles detected | testicles present]), false-negative (Pr [testicles not detected | testicles present]), true-negative (Pr [not detected | not present]), and false-positive (Pr [detected | not present]).

We modeled sensitivity and specificity jointly as a function of these probabilities, to account for the dependence among these variables. Following Puggioni et al⁸, we defined random-effects submodels for the following 3 probabilities:

$$\begin{aligned}\text{logit}(Pr(S_i = 1|I_i = 1)) &= \mu_1 + \epsilon_{1i} \\ \text{logit}(Pr(S_i = 1|I_i = 0)) &= \mu_2 + \epsilon_{2i} \\ \text{logit}(Pr(I_i = 1)) &= \mu_3 + \epsilon_{3i}\end{aligned}$$

where S_i is the surgery outcome (0 = absent, 1 = present) from study i , I_i is the imaging outcome from study i , μ_k is the population mean (on the logit scale) for probability k , and ϵ_{ki} is the random effect for probability k in study i . These probabilities were defined for each of the intraabdominal, inguino-scrotal, and atrophied testicles. Random effects, in each case, are modeled as simple, independent, normally distributed random variables with zero mean as follows:

$$\epsilon_{ki} \sim N(0, \sigma_k^2)$$

Note that each of the 3 probabilities gets its own random-effect variance, σ_k^2 . The probabilities above uniquely determine the sensitivity and specificity rates, via Bayes' formula, as follows:

$$\begin{aligned}\text{sensitivity}_i &= Pr(I_i = 1|S_i = 1) \propto Pr \\ &\quad (S_i = 1|I_i = 1) Pr(I_i = 1) \\ \text{specificity}_i &= Pr(I_i = 0|S_i = 0) \\ &\quad \propto (1 - Pr(S_i = 1|I_i = 0)) \\ &\quad (1 - Pr(I_i = 1))\end{aligned}$$

The data likelihoods for the observed true-positive and true-negative counts were then modeled as binomial draws from the sum of true-positive and false-negative counts and true-negative and false-positive counts, respectively.

To represent the lack of previous information, vague priors were placed on all stochastic parameters in the model. Namely, the population means for the cell probabilities (μ_k) were given $N(0, 100)$ priors, which are relatively flat on the probability (inverse-logit) scale, and the random-effects SDs were given uniform priors on the (0, 1000) interval (Gelman et al⁹). Models for all possible combinations of MRI and testicular position or type (intraabdominal, inguino-scrotal, or atrophied) were fit via Markov chain Monte Carlo methods (Gamerman et al¹⁰) by using PyMC 2.1¹¹. Models were run for 500 000 iterations, with

TABLE 3 Studies Assessing MRI (Conventional) for Identifying and Locating Nonpalpable Undescended Testicles

Study (Ref No.)	N (No. of Testicles)	Study Quality	Reference Standard	Presence of Testicles		Absence of Testicles		Surgery (TP)		
				Surgery	TP	TN	IA Testicles	IS Testicles	Atrophied Testicles	
Al-Shareef et al (12)	19 (24)	Fair	Laparoscopy	21	7	3	16 (6)	0 (NA)	5 (1)	
Kanemoto et al (13)	40 (47)	Poor	Surgical exploration/ laparoscopy	38	24	5	2 (2)	26 (22)	10 (0)	
Kier et al (14)	14 (15)	Poor	Laparoscopy/surgical exploration	8	5	6	1 (0)	7 (5)	0 (NA)	
Lam et al (15)	14 (17)	Fair	Surgical exploration	17	14	0	3 (3)	11 (11)	3 (0)	
Maghnie et al (16)	17 (21)	Poor	Surgical exploration	16	11	5	4 (4)	6 (6)	6 (1)	
Miyano et al (17)	17 (17)	Poor	Surgical exploration	11	9	6	1 (1)	10 (8)	0 (NA)	
Siemer et al (18)	29 (29)	Poor	Surgical exploration	25	17	4	8 (7)	17 (10)	0 (NA)	
Yeung et al (19)	21 (23)	Poor	Laparoscopy/surgical exploration	22	9	1	4 (1)	10 (8)	8 (0)	
Total	171 (193)			158	96	30	39 (24)	87 (70)	32 (2)	

IA, intraabdominal; IS, inguino-scrotal; NA, not applicable; TP, true-positive; TN, true-negative.

the first 400 000 discarded as a precaution to avoid problems with lack of convergence, and the remaining sample was thinned by a factor of 10, yielding 10 000 samples for inference.

RESULTS

The original literature search, conducted for the broader review of evaluation and

treatment approaches, identified 3448 citations. Eighteen unique studies met our inclusion criteria (Table 1) and addressed the performance of imaging techniques in identifying and locating nonpalpable undescended testicles in prepubescent boys. Of these, 8 unique studies, all prospective case series addressing the performance of MRI

before surgery in identifying and locating nonpalpable undescended testicles, were selected for the meta-analysis.^{12–19} All studies were conducted in the hospital setting with more studies conducted in Asia ($n = 5$) than in the United States ($n = 1$) or in Europe ($n = 2$). The number of participants in each study ranged from 14 to 40; the

FIGURE 1

Estimated sensitivity of MRI in the identification of nonpalpable undescended testicles by study, including the overall random-effects mean, with associated credible intervals. The thinner lines represent the 95% BCI, the thicker lines represent the interquartile range, and the dots represent the median.

FIGURE 2

Estimated specificity of MRI in the identification of nonpalpable undescended testicles by study, including the overall random-effects mean, with associated credible intervals. The thinner lines represent the 95% BCI, the thicker lines represent the interquartile range, and the dots represent the median.

number of nonpalpable testicles to be located ranged from 15 to 47. Participants' ages were between 10 months and 16 years, with 2 studies that included infants. Six of the 8 studies (75%) assessed bilateral undescended testicles (Table 2). Only 2 studies^{12,15} adequately described selection criteria for the participants, and none provided the time interval between imaging technique and surgery. Two studies were of fair quality^{12,15} and the rest of poor quality. None of the studies reported any complication attributable to the imaging procedures. Pediatric urologists¹³ or pediatric surgeons¹⁹ or physicians¹⁶ were reported to have conducted the preoperative physical examination in these included studies, although 63% did not note who completed the examination.

Our meta-analyses showed no evidence of lack of convergence, except for the atrophy model, which did not converge even after 500 000 additional iterations. Posterior predictive checks conducted on the converged intraabdominal and inguino-scrotal models revealed a good fit to the data in both cases.

Identification of Nonpalpable Testicles

The 8 studies evaluating the accuracy of MRI for identifying nonpalpable testicles included a total of 171 boys with 193 testicles (22 boys with bilateral testicles). Surgery identified 158 testicles (81.9%) as present and 35 as absent, whereas MRI identified 101 testicles (52.3%) as present and 92 (47.7%) as absent in the pooled sample of studies (Table 3). The random-effects model

revealed that MRI correctly identified testicles in the included studies, with a sensitivity ranging from 0.42 to 0.75 and a specificity from 0.61 to 0.99 (Figs 1 and 2), with a posterior expected median sensitivity of 0.62 (95% Bayesian credible interval [BCI]: 0.47–0.77) and a specificity of 1.0 (95% BCI: 0.99–1.0).

Location and Type of Testicles

Among the studies evaluating the performance of MRI for locating testicles, surgery confirmed the location of 39 testicles in the intraabdominal region, 87 inguino-scrotal testicles, and 32 atrophied testicles in the pooled sample of studies. MRI correctly located 25% to 97% of the intraabdominal testicles across all 8 studies as shown by posterior median estimates (Fig 3; Table 4), whereas 64% to 93% of the testicles in

FIGURE 3

Estimated sensitivity of MRI in locating intraabdominal testicles by study, including the overall random-effects mean, with associated credible intervals. The thinner lines represent the 95% BCI, the thicker lines represent the interquartile range, and the dots represent the median.

inguinal or scrotal regions were correctly located in 7 studies (Fig 4). Only 5 studies could be used to evaluate the performance of MRI for locating atrophied testicles, and the posterior estimates of median sensitivity ranged from 0% to 14%.

MRI was able to locate intraabdominal testicles with a posterior expected median sensitivity of 0.55 (95% BCI: 0.09–1.0). The performance of MRI was very poor when locating atrophied testicles, and its sensitivity and specificity

could not be estimated. MRI was effective for locating inguino-scrotal testicles, with a median expected sensitivity of 0.86 (95% BCI: 0.67–1.0). The estimated specificity to correctly locate absent testicles at different sites reached almost 100%.

DISCUSSION

Cryptorchidism is a common anomaly that often warrants early surgical management. Preoperative identification and location of testicles can help to

determine the optimal type of procedure and allow for appropriate advance planning. On the basis of the imaging findings, the surgeon can appropriately counsel the patient and alter the operative approach as needed. In the case of absent or vanishing testicles, imaging findings could obviate the need for surgical exploration altogether.

Various imaging techniques have been suggested for use in identifying and locating nonpalpable testicles preoperatively in young boys, with varying limitations including expense, invasiveness, technical difficulty, radiation risk, need for contrast medium, effectiveness in particular groups of subjects, and need for sedation. Because ultrasound, which is the least expensive and frequently used technique of all

TABLE 4 Estimates of Expected Sensitivity and Specificity in Locating the Position of Functioning Testicles

Imaging Technique	Testicular Position	Sensitivity Median (95% BCI)	Specificity Median (95% BCI)
MRI (7 studies)	Inguino-scrotal	0.855 (0.672–1)	1 (0.999–1)
MRI (8 studies)	Intraabdominal	0.549 (0.094–1)	1 (0.999–1)

Median, posterior median.

FIGURE 4

Estimated sensitivity of MRI in locating inguino-scrotal testicles by study, including the overall random-effects mean, with associated credible intervals. The thinner lines represent the 95% BCI, the thicker lines represent the interquartile range, and the dots represent the median.

imaging tools, had been shown to have low sensitivity in identifying nonpalpable testicles preoperatively in a recent meta-analysis,⁵ we undertook this analysis to see if the next most commonly used imaging technique, namely MRI, could stand alone and perform better in identifying and locating cryptorchid testicles. Even though MRI is more expensive than either ultrasound or computed tomographic scan, it may be clinically preferable to ultrasound because it allows global, multiplanar depiction of the anatomy of the structures and can distinguish testicles from lymph nodes by using specific orientation and sequences in axial or coronal plane films.²⁰

In our review of these 8 studies assessing the performance of conventional MRI to

identify the presence or absence of testicles, we found the overall accuracy rate to range from 42% to 88%. The high false-negative rate (39%) associated with this technique in identifying the presence of a viable testes makes it unlikely that MRI can reliably replace surgical exploration. In addition, conventional MRI seems to confuse lymph nodes with viable testicular tissue, leading to a false-positive rate of 14% (5 of 35 cases) (see full report in ref 6).

The meta-analysis of the included studies reveals that MRI has a fairly low sensitivity for identifying the presence of nonpalpable cryptorchid testicles (sensitivity of 62%). When testicles are identified, MRI is poor at locating both atrophied and intraabdominal testicles but performs modestly well (expected

sensitivity of 86%) in locating those in the inguino-scrotal regions. Our meta-analysis used a random-effects model, accounting for the stochastic dependence between specificity and sensitivity by modeling them jointly as a function of individual cell probabilities. Our approach was an efficient use of the information from each study, because the model borrowed strengths from each study in estimating population means, while still allowing each study an independent random effect. For studies in which the sample size was small, the corresponding estimates of sensitivity and specificity were shrunk toward the population mean, whereas larger studies were influenced less by shrinkage to the mean.

The sensitivity for intraabdominal testes was extremely variable across

studies, resulting in considerable posterior uncertainty in the random-effects mean (Fig 3). A pure random-effects process may not be warranted in this case, and it is likely that there are unmeasured covariates that resulted in large differences in sensitivity among studies. We did not report estimates of likelihood ratios because the likelihood ratio—positive values were numerically unstable in our models. In the intra-abdominal model, the credible interval spanned 6 orders of magnitude, due to the extremely high estimates of specificity, whereas for the inguino-scrotal model it spanned 2 orders of magnitude.

To our knowledge, this is the first study to meta-analyze the performance of conventional MRI in identifying and locating nonpalpable undescended testicles. Lack of information on study characteristics, selection criteria, the timing interval between imaging and surgery, and nonblinding of radiologists could have influenced the performance of this technique. In addition, considering atrophied testicles separately in our analyses, along with exclusion of

studies with <10 subjects with nonpalpable testicles, could have affected our degree of confidence in establishing a rate of prediction for identifying and locating nonpalpable testicles.

In our full systematic review of imaging techniques for identifying and locating cryptorchid testicles, we observed that the overall accuracy rate (using surgery as a reference standard) at identifying testicles using ultrasound ranged from 21% to 76% across the studies, compared with 42% to 92% for any type of MRI and 60% in the 1 study on computed tomographic scan. MRI performed much better at locating intraabdominal testicles than ultrasound, and both ultrasound and MRI demonstrated poor accuracy at locating atrophied testicles compared with higher accuracy for MRA and magnetic resonance venography. When the testicles were located in the inguino-scrotal area, however, ultrasound demonstrated a 92% accuracy rate compared with 83% for MRI.⁶ MRI in combination with fat-suppressed T2-weighted images^{6,20} and diffusion-weighted imaging^{6,20–21} has been shown to improve not only the overall accuracy

rate of prediction up to 98.4% but also perform effectively with a high sensitivity rate of 100% for locating intraabdominal testicles.^{6,20}

CONCLUSIONS

Conventional MRI is moderately specific in identifying absent testicles but poorly sensitive in identifying the presence of nonpalpable testicles. MRI appears to be less efficient in locating intraabdominal functioning testicles and shows limited sensitivity in locating inguino-scrotal testicles, but it fails to locate most of the atrophied testicles, which makes MRI a less reliable technique in providing guidance to differentiate those children needing surgery from those who do not. To increase the preoperative sensitivity in identifying nonpalpable cryptorchid testicles, conventional MRI alone may not be beneficial. Additional study is needed to determine if other forms of MRI such as fat-suppressed T2-weighted MRI, diffusion-weighted MRI, or MRA may improve false-negative rates in order to make this form of imaging more useful in assessing boys with cryptorchidism.

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