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Uroradiological screening for upper and lower urinary tract anomalies in patients with hypospadias: a systematic literature review

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Abstract

Introduction Hypospadias is associated with anomalies of the urinary tract, but the exact prevalence and significance of these anomalies are still controversial.

Objectives To assess the percentage of patients with hypospadias and associated urological anomalies, either requiring or not requiring medical or surgical attention.

Material and methods We searched several databases using the following Mesh terms: hypospadias AND urination, ultrasonography, urinary tract/abnormalities, urinary bladder/radiography, ureteral obstruction, hydronephrosis or vesico-ureteral reflux. Type of uroradiological studies performed, type of urological anomalies, medical or surgical interventions, number of patients available, enrolled and undergoing uroradiological studies and number of patients with abnormal uroradiological exams were recorded.

Results We found 24 studies. Four studies included 100% of available patients. In the other ones, the percentage of patients undergoing uroradiological screening varied from 12 to 82%. Frequency of anomalies varied from 0 to 56%. The most common anomalies were kidney position anomalies, vesico-ureteral reflux and hydronephrosis.

Conclusions The data published about screening patients with hypospadias for associated anomalies of their urinary tract are of poor quality. The clinical significance of the anomalies found is difficult to evaluate. We found no relationship between the severity of the hypospadias and associated anomalies of the upper or lower urinary tract.

Background

Hypospadias is one of the most common congenital malformations of the urogenital tract in male newborns.[1] Several studies have reported a high prevalence of associated anomalies of the upper and/or lower urinary tract malformations in patients with hypospadias, although this is still controversial. Furthermore, to increase confusion, a recent study from a teratology registry in California reported an even less-than-expected frequency of associated anomalies of the upper or lower urinary tract in children with hypospadias compared to the general population.[2] Despite those still unresolved uncertainties, extensive uroradiological investigations are often routinely performed in patients with hypospadias, although this is no longer recommended by several local, national or international guidelines.[3 4] We therefore performed a systematic review and analysis of the literature to answer the following question: in patients with hypospadias, does the prevalence of significant anomalies of their upper or lower urinary tract justify a systematic uroradiological screening to detect such anomalies?

What is already known on this topic

- Patients with hypospadias have been often reported with an increased prevalence of anomalies of their urinary tract, although this is conflictual, especially in the light of the new (and higher) prevalence of vesico-ureteral reflux in the normal paediatric population.
- Uroradiological exams are often requested in children with hypospadias, but the benefit is unknown.

What this study adds

- The studies published so far about the prevalence of associated anomalies of the urinary tract in children with hypospadias are of poor quality.
- The clinical significance of associated anomalies needs to be reassessed in the light of the current practice in paediatric uro-nephrology.
- Overall, we found no relationship between the severity of the hypospadias and the prevalence of associated urological anomalies in the published studies.
- Further studies need to integrate data from prenatal ultrasonography.

Objectives

The primary objective was to assess the prevalence of anomalies of the upper and/or lower urinary tract in patients (children and adults) with hypospadias, detected with ultrasound (US), voiding cystourography (VCUG) or intravenous pyelography (IVP), in published studies. The secondary objective was to assess the clinical significance of those anomalies in terms of surgical correction (vesico-ureteral reflux (VUR), obstruction) or medical attention (antiobiotherapy and antibioprophylaxis), and hence the overall clinical impact of radiological screening for urological anomalies in patients with hypospadias.

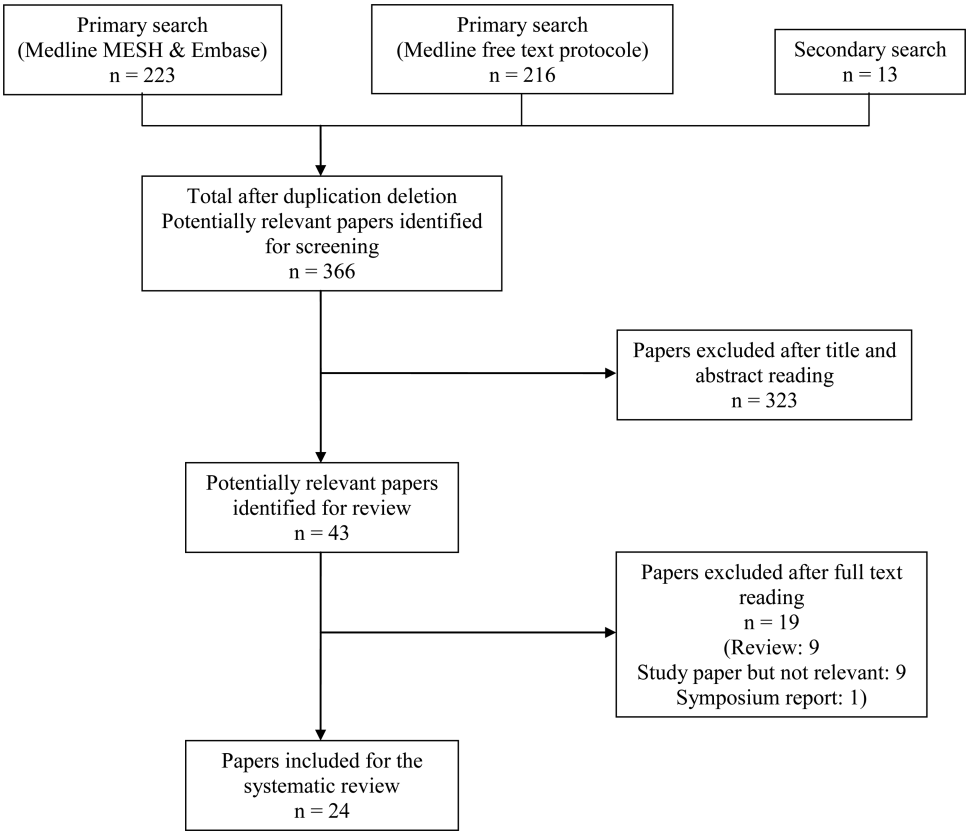

Figure 1 Search strategy.

Search strategy and outcome

Data source

We performed a systematic review of the literature from December 2010 to June 2011 using the following electronic databases: Medline (1951 to June 2011), Embase (1980 to June 2011), CENTRAL (The Cochrane Central Register of Controlled Trials), CINAHL (Cumulative Index of Nursing and Allied Health (1981 to June 2011) and Web of Science (to June 2011). Searches were conducted from the earliest date of titles or abstracts available for each database to the latest titles or abstracts available as of 1 June 2011. Citations in Medline before 1950, retrieved through Medline or OVID Old Medline, were also screened.

Further studies were located through citation searches of major papers and by checking the reference lists in primary and review articles retrieved from the database searches. National and international guidelines and internet medical sites such as ClinicalTrials.gov, ISRCTN register, NICE guidelines, SIGN (Scottish Intercollegiate Guidelines Network), EBM Reviews-Health Technology Assessment, NGC (National Guideline Clearinghouse), Newborn Services Clinical Guidelines and BestBets were searched as well.

Search strategies

The Medline search strategy used both medical subject headings (Mesh) and free-text protocols (figure 1). Specifically, the Mesh search was conducted by combining the following retrieved from the Mesh browser provided by Medline: *hypospadias* AND *urination*, *ultrasonography (US)*, *urinary tract/abnormalities*, *urinary bladder/radiography*, *ureteral obstruction*, *hydronephrosis* OR *VUR*. Subsequently, the results were pooled and the following limits were used: infant, newborn OR infant OR child OR adolescent. Medline search is described below in table 1:

Table 1 Medline search

Search	Most RecentQueries	Time	Result
#24	Search (#22) AND #23	15 : 49 : 54	223
#23	Search (((child, newborn (MeSHTerms)) OR child (MeSHTerms)) OR infant (MeSHTerms)) OR adolescent (MeSHTerms)	15 : 47 : 12	2557392
#22	Search (#20) AND #21	15 : 45 : 11	299
#21	Search ((((((urination (MeSHTerms)) OR ultrasonography(MeSHTerms)) OR urinary tract/abnormalities (MeSHTerms)) OR urinarybladder/radiography (MeSHTerms)) OR ureteral obstruction(MeSHTerms)) OR hydronephrosis(MeSHTerms)) OR vesico-ureteral reflux (MeSHTerms)	15 : 44 : 56	258581
#20	Search hypospadias (MeSHTerms)	15 : 44 : 46	3679

The searches on Embase, CENTRAL, CINHAL, Web of Science, ClinicalTrials.gov, ISRCTN register, NICE, SIGN, EBM Reviews-Health Technology Assessment, NGC, Newborn Services Clinical Guidelines and BestBets were done using only the free-text protocol, with the same keywords, with no time limits.

Study selection (inclusion criteria)

Inclusion and exclusion criteria

Eligible studies

Human clinical studies reporting the prevalence of associated upper or lower urinary tract anomalies in patients with hypospadias were considered for review and inclusion. The degree of hypospadias was not taken into account for inclusion. The associated anomalies considered were as follows: VUR (of any degree), mega-ureter, complete or incomplete double ureteral system, ureteropelvic junction obstruction, ureterovesical junction obstruction, ureterocele, posterior urethral valves, bladder diverticulum, multicystic dysplastic kidney, single kidney, kidney dysplasia or hypoplasia, kidney malposition (pelvic kidney and horseshoe kidney), urethral anomalies and prostatic utricle. Prospective or retrospective studies, cohort studies and transversal studies were all included. Case reports, review papers and opinion papers/editorials were excluded. Studies including adults and children with hypospadias were included. The presence of external non-urogenital malformation was not a reason for exclusion. There was no language limitation.

Eligible patients

All patients with hypospadias, regardless of the severity of the hypospadias or their age, were eligible for inclusion.

Eligible investigations

Eligible investigations included: renal/abdominal US, VCUG and IVP.

Eligible study measure

To be eligible, a study should at the very minimum reports the prevalence of associated urological anomalies in patients with hypospadias examined with a least one exam, regardless of the type of radiological exam used or the clinical significance of the findings.

Data extraction

A data collection form for extracting information from eligible studies was developed by adapting the methods recommended by the Cochrane Methods Working Group on Systematic Reviews of Screening and Diagnostic Tests. The following data were recorded from each study:

- Patients' details, including demographic characteristics (age and ethnicity), and medical condition associated with hypospadias (intersex status and other visible external malformations).
- Type of uroradiological studies used: *US/VCUG/IVP.*
- Reported percentage of patients *available*, *included* in the study, and finally *undergoing uroradiological studies*.
- Reported numbers of patients with abnormal uroradiological exams.
- Type of urological anomalies: *VUR/mega-ureter/complete or incomplete double ureteral system/ureteropelvic junction obstruction/ureterovesical junction obstruction/ureterocele/posterior urethral valves/bladder diverticulum/multicystic dysplastic kidney/single kidney/kidney dysplasia or hypoplasia/kidney malposition/urethral anomalie/prostatic utricle.*
- Reported number of patients needing medical or surgical interventions secondary to uroradiological exam findings, and therefore considered by the authors with clinically relevant anomalies.
- Type of medical or surgical interventions: *surgical correction of VUR/surgical correction of obstruction/pyeloplasty/ureteral reimplantation/urethral dilation/kidney removal/kidney surgery (not otherwise specified).*

We calculated the 95% CI with the Wilson method modified for the discrete variable. Two of the authors (FC and VC) reviewed the abstracts and then the full text of the pertinent articles. Data extraction was done in duplicate. Where disagreement continued after discussion between the two reviewers, a third reviewer (PR) was available to help to resolve discrepancies by open discussion. We laid special emphasis on the quality assessment of the studies, the clinical relevance of the findings and the strength of the intervention. The relationship between the severity of the hypospadias and associated urological anomalies was studied using goodness-of-fit or Fisher's exact test, when appropriate.

Data synthesis

All reviewed studies are summarised and reported in table 2.

Methodological quality

The following criteria were used to assess study quality:

- Selection of the study sample: was a consecutive or random selection of cases sampled?
- Subgroups: were subgroups analysed separately? Were they prospectively defined?
- Completeness: how complete was the data set? How many patients were originally considered for inclusion, the number of eligible patients, the number of patients included at the start and the number of patients lost. A low completeness rate could result in bias.

This systematic review was reported according to the PRISMA statement for Reporting Systematic Reviews and Meta-Analyses of Studies That Evaluate Health Care Interventions.[5] This is not a commissioned or funded systematic review.

Results

Search strategy is depicted in figure 1. Primary search retrieved 439 papers. Thirteen additional articles and one thesis were found with secondary sources. After careful independent reading of the titles and abstracts, 43 studies were fully analysed. Twenty-three studies[6–28] and one thesis[29] were finally kept (table 2). The primary measure was the percentage of patients with hypospadias and associated anomalies of their urinary tract. The secondary measure was the percentage of patients with

Table 2 Summary of literature search findings

Citation (author/year)	Study type	Study group/age/ country	Indications for imaging clearly defined*	Type of imaging studies with number of patients and % from initial study group	Description of uroradiological abnormalities clearly defined†	Description of significance of abnormalities clearly defined‡	Key results/comments
Moore (1990)[6]	P	All children, <2 years, Saudi Arabia	Yes, all patients	VCUG: 153/153 (100%) IVP: 153/153 (100%)	Yes	No	36 patients had abnormal investigations. IVP abnormal in 21(14%) (6 patients hydronephrosis (4%)), VCUG abnormal in 30 (20%) (20 VUR, grade not stated (13%)). 7 and 11 patients required surgery for hydronephrosis or VUR, respectively, clear surgical indication not stated. Other malformations (horseshoe kidneys or SK) did not require intervention
Gupta *et al* (2010)[7]	P	All children, 1–14 years, India	Yes for US No for VCUG	US: 65/65 (100%) VCUG 5/65 (8%)	Yes	No	12 patients (18.5%) had abnormal US findings (1 single kidney, 1 dysplastic kidney, 1 epididymal cyst, 5 cystitis and 4 hydronephrosis (6%)). 3 patients had VUR (1 grade II and 2 grade IV). 3 patients had VUR correction, 1 PUV fulguration and 1 urethral diverticulum excision
Friedman *et al* (2008)[8]	R	163/400+ patients included, 1 month–20 years, Israel	No	VCUG: 68/? IVP: 65/? US: 98/? Combination of exam: 69/?	No	No	34 patients had some type of abnormalities. 9 patients had abnormal VCUG (6 with grade II-III VUR), 18 patients had abnormal IVP (no major hydronephrosis), 13 patients had abnormal US (no major hydronephrosis). Need for medical or surgical attention not mentioned
Wu *et al* (2002)[9]	R	45/356, 2 months—15 years, Taiwan, China	No	US: 45/356 (13%) VCUG: unclear	Yes	Yes	1 and 1 patient with grade II VUR and single renal cyst, respectively. Need for medical or surgical attention not mentioned.
Albers *et al* (1997)[10]	R	48 patients with severe hypospadias, 1–18 years, Germany	No	US: 33/48 (69%) VCUG: 15/48 (31%)	No	No	Only severe peno-scrotal hypospadias included. 2 patients with dilated (degree?) renal pelvis. No VUR. Need for medical or surgical attention not mentioned
Kulkarni *et al* (1991)[11]	R	130 patients, 1–11 years, India	No	IVP: 130/130 (100%) VCUG: unclear	No	No	14 and 14 patients with abnormal IVP and VCUG, respectively. 7 patients with VUR (3 of them with UTI). Need for medical or surgical attention not mentioned
Davenport and MacKinnon (1988)[12]	R	111 patients, age not mentioned, UK	No	US: 82/111 (74%)	No	No	7 abnormal US exams, including 1 double system with grade II VUR, 1 SK. Need for medical or surgical attention not mentioned
Cerasaro *et al* (1986)[13]	R	301 patients, age not mentioned, USA	No	IVP: 168/301 (56%) US: 65/301 (22%) Total exam: 233/301 (77%)	No	No	1 patient each with obstructive megaureter, UPJO, grade I hydronephrosis, pelvic kidney. Need for medical or surgical attention not mentioned

Shelton and Noe (1985)[14]	R	304 patients, birth–30 years, USA	No	169/304 with some form of investigation (IVP ±VCUG±US)	No	Yes	*Asymptomatic patients*: 102 screened: 27 patients with abnormalities: 1 pelvic kidney, 1 SK, 1 UPJO, 1 grade III VUR (no surgery needed in that group). *Symptomatic patients*: 47 screened: 14 patients with abnormalities: 2 grade III VUR, 2 PUV, 1 horseshoe kidney, 1 SK, 1 dysplastic kidney. Need for medical or surgical attention not mentioned. *Intersex group*: 15 patients screened: 2 VUR (needing surgery), 1 VUR and 1 hypoplastic kidney. *Multiple abnormalities group*: 4 screened: 1 horseshoe kidney. Need for medical or surgical attention not mentioned. *Sibling with VUR group*: 1 screened
Kelly *et al* (1984)[15]	R	55 patients, age not mentioned, USA	No	IVP: 45/55 (82%)	No	Yes	10 abnormalities: 1 mild hydronephrosis and 1 ureterocele. No surgical intervention required
Caione *et al* (1982)[16]	R	853 patients, age not mentioned, Italy	No	IVP: 106/853 (12%) VCUG: 106/853 (12%)	No	No	5 patients with upper urinary tract anomalies including 2 SK, 1 UPJO, 1 double system and 1 horseshoe kidney. 9 patients with lower urinary tract anomalies, including VUR, bladder diverticulum and prostatic utricle. Need for medical or surgical attention not mentioned
Shafir *et al* (1982)[17]	R	305 patients, 0–13 years, USA	No	VCUG: 245/305 (80%)	Yes	No	37 patients with VUR out of 218 patients (3 grade III and 2 grade IV). 6 patients underwent surgery. 21 VUR patients discovered after correction of hypospadias with VUR. 2 underwent surgical correction
Khuri *et al* (1981)[18]	R	1076 patients, age not mentioned, USA	No	IVP: 452/1076 (42%)	Yes	No	48 patient with abnormalities (10 SK, 8 UPJO, 18 grade II-III VUR, 4 horseshoe kidneys, 3 pelvic kidneys, and 1 each of Wilm's tumour, kidney cystic disease, dysplasia, hydronephrosis and ectopia. 14 patients required surgery
Rozenman and Hertz (1979)[19]	R	110 patients, 1 week–45 years, USA	No	IVP: 110/110 (100%) VCUG: 110/110 (100%)	No	No	50 patients with abnormal IVP, including 32 malrotation, 4 ectopic kidney, 11 UPJO/hydronephrosis (10%) and 3 double collecting system. 57 patients with abnormal VCUG, including 31 meatal stenosis, 14 VUR, 11 utriculus prostaticus and 1 urethral stricture. Need for medical or surgical attention not mentioned
Shima *et al* (1979)[20]	R	272 patients, 2–36 years, USA	No	IVP: 194/272 (71%) VCUG: 196/272 (72%)	No	No	11 patients with abnormal IVP, including 6 UPJO, 3 duplication and 2 horseshoe kidney. 40 patients with abnormal VCUG, including 4 VUR (grade not stated), 32 utriculus masculinus, 1 mega-urethra and 3 meatal stenosis. Need for medical or surgical attention not mentioned
	R		No	IVP: 87/121 (72%)	No	Yes	

Continued

Table 2 Continued

Citation (author/year)	Study type	Study group/age/ country	Indications for imaging clearly defined*	Type of imaging studies with number of patients and % from initial study group	Description of uroradiological abnormalities clearly defined†	Description of significance of abnormalities clearly defined‡	Key results/comments
Lutzker *et al* (1977)[21]		121 patients, 6 weeks–22 years, USA					16 patients with abnormal IVP, including 11 ureteral duplication, 1 malrotation, 1 horseshoe kidney, 2 ureteral ectasia and 1 UPJO. 1 patient only needed surgery (UPJO)
Fallon *et al* (1976)[22]	R	200 patients, 1–37 years, USA	No	IVP: 160/200 (80%) VCUG: unclear	No	No	16 patients with abnormal IVP, including 3 duplications, 2 SK, 1 retrocaval ureter, 7 VUR and 3 UPJO. 10 patients needed surgery (UPJO)
McArdle and Lebowitz (1975)[23]	R	355 patients, age not mentioned, USA	No	IVP: 200/355 (56%)	Yes	No	6 patients with abnormal IVP, including 2 horseshoe kidney, 2 duplex system, 1 SK and 1 pelvic kidney. No patient needed treatment/surgery
Willis *et al* (1967)[24]	R	181 patients, age not mentioned, USA	No	IVP: 96/181 (53%)	No	No	14 patients with abnormalities, including 3 SK, 2 ectopic kidneys, 2 hydronephrosis, 2 duplicated ureters and 1 polycystic kidney. Need for medical or surgical attention not mentioned
Neyman and Schirmer (1965)[25]	R	105 patients, age not mentioned, USA	No	IVP: 37/105 (35%) VCUG: unclear	No	No	9 patients with abnormalities, including 2 UPJO, 2 ectopic kidneys, 1 dysplastic kidney, 1 PUV and 1 VUR. Need for medical or surgical attention not mentioned
Kennedy (1961)[26]	R	489 patients, age not mentioned, USA	No	Unclear	No	No	Unclear how anomalies were discovered. Reported renal anomalies include 10 bladder neck obstruction and VUR, 3 duplication of collecting system, 2 pelvic ectopia, 2 horseshoe kidney, 1 hypoplastic kidney, 2 UPJO, 1 SK, 1 multicystic kidney, 1 neurogenic bladder with VUR, 1 hydronephrosis and 1 bladder diverticulum. Need for medical or surgical attention not mentioned
Felton (1959)[27]	R	142 patients, age not mentioned, USA	No	IVP: 53/142 (37%)	No	No	6 patients with abnormal IVP, including 3 grade I-II hydronephrosis, 1 double system and 2 abnormal pyelogram with no further description. Surgery reported for 2 hydronephrosis
Smyth *et al* (1959)[28]	R	75 patients, 2–14 years, USA	No	IVP: 60/75 (80%) VCUG: 60/75 (80%)	No	No	15 patients with anomalies, including 2 PUV (surgery), 4 prostatic utricle, 1 hydro-ureter, 1 bladder neck obstruction (surgery), 5 VUR (grade not reported), 1 short urethra and 1 double system
Boissonnat (1952)[29]	R	60 patients, 2–51 years, France	No	IVP: 59/? VCUG: 58/?	Yes	No	24 patients with hydronephrosis on IVP, 5 ureteral duplication, 3 malrotation and 2 VUR, 1 PUV. Need for medical or surgical attention not mentioned

*Has the need for uroradiological study been clearly defined before starting the study, in the protocol or under the method section?
†Has the description of the associated anomalies been clearly defined before starting the study, in the protocol or under the method section, or at least during completion of the study?
‡Is the significance of reported anomalies clearly defined before starting the study, or at least during completion of the study? IVP, intravenous pyelography; P, prospective, PUV, posterior urethral valve; R, retrospective; SK, single kidney; UPJO, ureteropelvic junction obstruction; US, ultrasound; UTI, urinary tract infection; VCUG, voiding cystourography; VUR, vesico-ureteral reflux.

associated anomalies requiring medical or surgical attention.

There were only two prospective studies.[6 7] These prospective studies[6 7] and two retrospective studies[11 19] were the only ones in which 100% of enrolled patients underwent uroradiological screening, regardless of the severity of the hypospadias. Seven studies (1132 patients) reported exclusively children[6 7 9–11 17 28]. In all other studies, the published data did not allow us to calculate the percentage of adults versus children.[8 12–16 18–27 29]

Moore[6] studied prospectively 153 infants with VCUG and IVP. Fourteen and 20% of patients had an abnormal IVP and VCUG, respectively. Seven and 11 patients needed surgery for hydronephrosis and VUR, respectively, which represents 5% and 7% of enrolled patients, respectively. Definition or clinical significance of urological anomalies was not defined in the protocol. The grades of hydronephrosis or VUR and indications for surgery were not clearly reported.

Gupta *et al*[7] prospectively enrolled 65 children, and all of them had an ultrasonographic evaluation of their urinary tract. The authors found 12 patients (19%) with abnormal US findings, including five patients with cystitis. Three patients had endoscopic correction of a VUR. None of the patients with hydronephrosis (and no VUR) had surgical intervention. The need for antibiotherapy/antibioprophylaxis was not mentioned.

Kulkarni *et al*[11] studied 130 patients with IVP: 14 (11%) had urological anomalies, including five hydronephrosis. Seven patients had VUR. The need for medical or surgical need was not mentioned.

Rozenman and Hertz[19] studied 110 patients with VCUG and IVP. Fifty patients (46%) had an abnormal IVP, including 36 position anomalies, 3 double-collecting systems and 11 hydronephrosis. Forty-nine patients had an abnormal VCUG (including 31 meatal stenosis, 14 VUR (grade not stated), 11 utriculus prostaticus and one urethral stricture. One patient required surgery, but the need for surgical attention was poorly reported.

These four studies are the only ones in which 100% of enrolled patients underwent a systematic uroradiological screening, with renal US, VCUG or IVP. Altogether, 65, 263 and 393 patients had a renal US, VCUG or IVP performed systematically: 12 renal US exam[7] (19% of enrolled patients), 87 VCUG[6 19] (33% of enrolled patients) and 85 IVP[6 11 19] (22% of enrolled patients) were considered as abnormal. But a clear description of medical or surgical requirements was lacking in all four studies, which makes the evaluation of the clinical significance of these anomalies impossible to evaluate.

All the other studies[8–10 12–18 20–29] were retrospective, and none included 100% of available patients in their uroradiological screening. In those studies, the percentage of patients with hypospadias in whom at least one uroradiological exam (VCUG or IVP or US) was performed varied from 12%[16] to 82%.[15] No study except for two prospective ones[6 7] reported clear indication for uroradiological screening. This might have introduced severe bias in the evaluation of the incidence of anomalies of the upper and lower urinary tract in children with hypospadias.

We also found extreme variations in the percentage of abnormal results (US, VCUG or IVP), or reported as such, varying from 0%[10] to 56%[29] (calculated from the number of patients having had the exam) (figure 2). Given the fact that the description of the anomalies was too often poor and incomplete (degree of VUR or hydronephrosis not stated), this again makes the interpretation of the percentage of anomalies very difficult (figure 2).

Finally and most importantly, the clinical consequences of these anomalies remain also extremely difficult to evaluate. Most of the studies[8–16 19–20 24–27 29] did not mentioned the need for medical or surgical attention at all, or in a very poorly manner. In the other studies, criteria for medical or surgical attention (antibioprophylaxis and surgery) are often incomplete. Moore[6] reports 7 and 11 patients who required surgery for hydronephrosis and VUR, respectively, but grade of hydronephrosis and kidney function was not mentioned. Gupta *et al*[7] performed three Deflux injection for VUR, one posterior urethral valves fulguration, and one urethral diverticulum excision. Shafir *et al*[17] reports 5 patients who underwent surgical correction of their VUR (out of 18 patients), with no details as to the degree of VUR, the number of (breakthrough) infections or the renal function. Khuri *et al*[18] reports 14 patients needing surgery, with no pertaining clinical details. Lutzker *et al*,[21] Fallon *et al*,[22] McArdle and Lebowitz[23] and Smyth and Forsythe[28] also report 1, 10, 0 and 3 patients who required surgery, respectively, but without clear documentation. Overall, we found only six[6 15 18 21 22 27] and two studies[6 17] that reported surgical or medical requirement for all patients with two well-defined conditions: hydronephrosis (as assessed by IVP) and VUR (as assessed by VCUG). 2.8 and 3.8% of all investigated patients had surgery for obstruction and VUR, respectively. These figures drop to 1.5 and 3.2%, respectively, if all primarily enrolled (and not screened) patients are considered.

We found no significant association between the severity of the hypospadias (glanular, coronal/penile/peno-scrotal and perineal) and VUR[9 20] (299 patients, p=0.096), hydronephrosis[6 7 15 20] (465 patients, p=0.64), kidney malposition[7 15 23] (311 patients, p=0.056) or the presence of a SK[6 7 23] (397 patients, p=1) (goodness-of-fit or Fisher's exact test). Six patients had surgery for PUV. Fifteen studies did not report the need for medical or surgical treatment.

Although renal scarring or globally diminished renal function is the ultimate and most important long-term consequences of urological anomalies, we found no study reporting nuclear exam or glomerular filtration rate evaluation.

We found an extremely important risk of sequence generation within and across studies. Except for two prospective studies[6 7] and two retrospective studies,[11 19] none of the studies had clear indication for performing uroradiological studies in patients with hypospadias. Furthermore, the type of uroradiological exam varied between studies as well, making comparisons difficult.

Discussion

Overall prevalence of associated anomalies

Our literature review reveals a wide range of prevalence of associated anomalies of the urinary tract in children with hypospadias, ranging from 0%[10] to 56%.[29] This

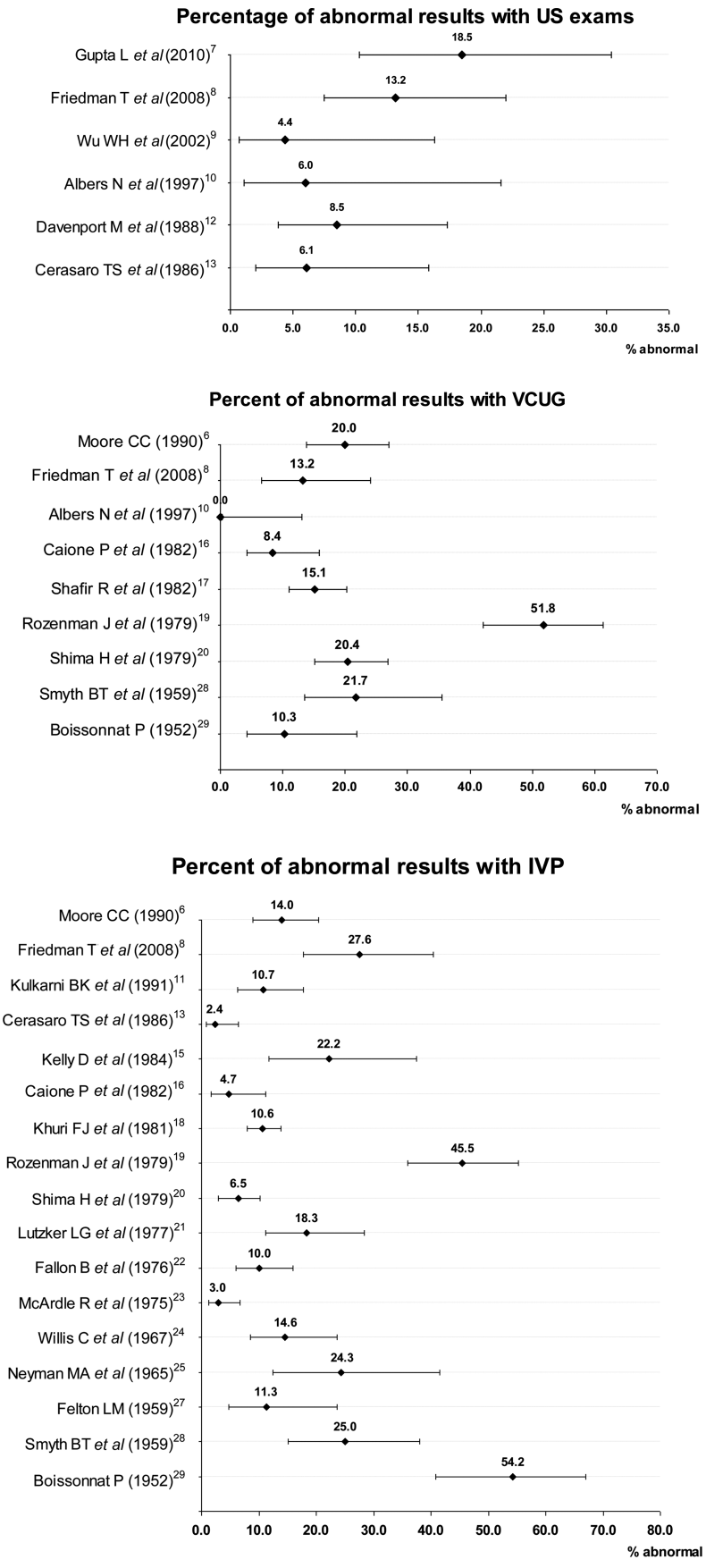

Figure 2 Prevalence in the literature, with their CI, of associated urinary anomalies in children with hypospadias, according to different radiological methods.

wide range is most likely secondary to a major difference in the percentage of patients having the exam. There were only four studies[6 7 11 19] in which all available patients underwent uroradiological screening. In all other studies, the percentage of patients from the initial group that finally had at least one uroradiological exam varied from 12%[16] to 82%.[15] The lack of clear indications for uroradiological screening in children with hypospadias might have introduced major bias in the patient selection, therefore making the interpretation and the comparison of the results extremely hazardous.

Significance of associated anomalies

A screening test is only useful if a treatment is available and potentially improves outcome. We feel that the most commonly reported anomalies of the upper and lower urinary tract in children with hypospadias were mild-to-moderate VUR, mild-to-moderate hydronephrosis (uretero-pelvic junction obstruction) and minor anomalies of the position of the kidney (malrotation and pelvic kidney). Obviously, anomalies of the position of the kidney most often do not require medical attention. Signification of mild-to-moderate VUR or hydronephrosis is more difficult to evaluate, because of its continous evolving management. Recently, it has been shown that the benefice of treating low-grade VUR with continuous antibiotics is fairly low,[30 31] making uroradiological screening obsolete in many cases, but not all.[32–35] This is further emphasised by the fact that the true prevalence of VUR in the normal population might be much higher than what has been reported.[36] This would again lower the utility of screening for associated urological anomalies in children with hypospadias, at least for VUR.

Prenatal ultrasonography

No study integrated information of prenatal US, if available. Given the high sensitivity of prenatal US to detect anomalies of the urinary tract, this would probably lower the likelihood ratio of postnatal screening to detect major and significant anomalies in children with hypospadias, not detected previously by prenatal US screening.

Limitations

For the vast majority of studies, there was no clear indication for the performance of uroradiological studies in patients with hypospadias (differential selection of patients for uroradiological investigations, differential surveillance for outcome and differential management of anomalies). Furthermore, the type of radiological studies changed over the years. Finally, and most importantly, the clinical significance of associated anomalies also changed drastically over the last few years, making comparisons between older and the most recent studies impossible.

Conclusions

Implications for healthcare

The data published so far about screening children with hypospadias for associated anomalies of their urinary tract are of poor methodological quality. The clinical significance of the anomalies found is often not stated, or at best difficult to evaluate. None of the studies took advantage of the prenatal ultrasonographic data.

Based on the current literature analysis (very low quality of evidence), we suggest not performing uroradiological exams in patients with hypospadias and no other anomaly (grade of evidence: weak).

Recommendations for research

The goal of screening children with hypospadias for associated anomalies of their urinary tract is to decrease recurrent urinary tract infections (favored by severe VUR), severe obstruction and ultimately chronic kidney disease. New studies should concentrate on these specific long-term outcomes and integrate the data of prenatal ultrasonography (which now detects most if not all anomalies of the fetal urinary tract).

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Competing interests None.

Provenance and peer review Not commissioned; externally peer reviewed.

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