- Prévalence RVU de stade III et plus si UTI et EF = 11%
- 4/5ème des RVU de stade III et plus ne sont pas visibles à l'US rénal
- Prévalence RVU de stade III et plus si UTI+ EF selon la PCT =
  - Si US rénal normal
    - PCT > 0,63 ng/ml; RVU III et plus de 15% => faire CUM et prophylaxie.
    - PCT< 0,63 ng/ml; RVU III et plus de 4% => ne pas faire de CUM ni prophylaxie
  - Si dilatation rénale à l'US
    - PCT > 0,17 ng/ml; RVU III et plus de 40% => faire CUM et prophylaxie.
    - PCT< 0,17 ng/ml; RVU III et plus de 0% => ne pas faire de CUM ni prophylaxie

Prediction of Moderate and High Grade Vesicoureteral Reflux After a First Febrile Urinary Tract Infection in Children: Construction and Internal Validation of a Clinical Decision Rule

Sandrine Leroy,*,† Carla Romanello, Vladislav Smolkin, Annick Galetto-Lacour, Bartosz Korczowski, David Tuerlinckx, Carlos Rodrigo, Vincent Gajdos, Florence Moulin, Paolo Pecile, Raphaël Halevy, Alain Gervaix, Barbara Duhl, Thierry Vander Borght, Cristina Prat, Laurence Foix-l'Hélias, Douglas G. Altman, Dominique Gendrel,‡ Gérard Bréart and Martin Chalumeau‡

From the Center for Statistics in Medicine, University of Oxford, Oxford, United Kingdom (SL, DGA); INSERM U953 (SL, GB, MC), Department of Pediatrics, Necker Hospital, AP-HP, Université Paris-Descartes (SL, DG, MC), INSERM U822, University Paris-Sud (VG) and Department of Emergency Medicine, Saint-Vincent-de-Paul Hospital, AP-HP (FM), Paris and Department of Pediatrics, Antoine Béclère Hospital, Clamart (VG, LF-l'H), France; Department of Pediatrics, University of Udine, Udine, Italy (CRom, PP); Department of Pediatrics, Ha'Emek Medical Center, Afula, Israel (VS, RH); Department of Pediatrics, University Hospital of Geneva, Geneva, Switzerland (AG-L, AG); Department of Pediatrics, Regional Hospital No. 2, University of Rzeszow, Rzeszow, Poland (BK); Department of Pediatrics (DT) and Department of Nuclear Medicine (TVB), Cliniques Universitaires de Mont-Godinne, Université Catholique de Louvain, Yvoir, Belgium; and Department of Pediatrics (CRod) and Department of Microbiology (CP), Germans Trias i Pujol Hospital, Autonomous University of Barcelona, Barcelona, Spain

Purpose: Urinary tract infection leads to a diagnosis of moderate or high grade (III or higher) vesicoureteral reflux in approximately 15% of children. Predicting reflux grade III or higher would make it possible to restrict cystography to high risk cases. We aimed to derive a clinical decision rule to predict vesicoureteral reflux grade III or higher in children with a first febrile urinary tract infection.

Materials and Methods: We conducted a secondary analysis of prospective series including all children with a first febrile urinary tract infection from the 8 European participating university hospitals.

Results: A total of 494 patients (197 boys, reflux grade III or higher in 11%) were included. Procalcitonin and ureteral dilatation on ultrasound were significantly associated with reflux grade III or higher and then combined into a prediction model with an ROC AUC of 0.75 (95% CI 0.69–0.81). Given the prespecified constraint of achieving at least 85% sensitivity, our model led to the clinical decision rule, for children with a first febrile urinary tract infection cystography should be performed in cases with ureteral dilatation and serum procalcitonin level 0.17 ng/ml or higher, or without ureteral dilatation (ie ureter not visible) when serum procalcitonin level is 0.63 ng/ml or higher. The rule had 86% sensitivity (95% CI 74–93) with 47% specificity (95% CI 42–51). Internal cross-validation produced 86% sensitivity (95% CI 79–93) and 43% specificity (95% CI 39–47).

Conclusions: A clinical decision rule was derived to enable a selective approach to cystography in children with urinary tract infection. The rule predicts high grade vesicoureteral reflux with approximately 85% sensitivity and avoids half of the cystograms that do not find reflux grade III or higher. Further validation is needed before its widespread use.

Key Words: child, decision support techniques, forecasting, urinary tract infections, vesico-ureteral reflux

Abbreviations and Acronyms

CRP = C-reactive protein
DMSA = dimercapto-succinic acid
PCT = procalcitonin
US = ultrasound
UTI = urinary tract infection
VUR = vesicoureteral reflux

Submitted for publication April 28, 2011.

Ethical approval was not required in each country, as study was secondary analysis of prospective cohort studies for which ethics committees of each participating center had already approved protocol of initial study.

Supplementary material (including detailed methods and limitations) for this article can be obtained from sandrine.leroy@pasteur.fr.

* Correspondence: Centre for Statistics in Medicine, University of Oxford, Wolfson College Annexe, Linton Rd., Oxford OX2 6UD, United Kingdom (telephone: 44-1865-284422; FAX: 44-1865-284424; e-mail: sandrine.leroy@pasteur.fr).

† Supported by a grant from the French Society of Nephrology, by la Fondation pour la Recherche Médicale and by Assistance Publique-Hôpitaux de Paris (PHRC AOM 05 110).

‡ Supported by unrestricted educational grants for another study, for a total amount lower than €5000, from Brahms AG, the manufacturer of procalcitonin, in 2007 for a 6-month period. The present study started in April 2008 and had no relation with the grant from Brahms. The other coauthors declare that they have no conflict of interest.

See Editorial on page 11.

0022-5347/12/1871-0265/0
THE JOURNAL OF UROLOGY®

Vol. 187, 265-271, January 2012
Printed in U.S.A.
DOI:10.1016/j.juro.2011.09.034

URINARY tract infections are the most common source of bacterial infections among young children with fever. Vesicoureteral reflux is diagnosed in 20% to 30% of children presenting with a first urinary tract infection.[1] The belief that future complications, such as renal scarring, hypertension, eclampsia and rarely end-stage renal failure, can occur has been a major driving force in the impetus to investigate the first occurrence of urinary tract infection in children. In the last decade pediatric societies have recommended that all young children undergo cystography after a first febrile urinary tract infection.[2,3] This approach offers high sensitivity for identifying vesicoureteral reflux but is truly nonselective, so that many children undergo unnecessary cystography, which is painful, irradiating, expensive and associated with a risk of iatrogenic urinary tract infection.[4–7] Moreover, when summarizing the current evidence, no benefit has been shown in treating low grade VUR, and there is a high percentage of spontaneous resolution.[8,9] Thus, this systematic strategy for diagnosing all grade reflux has raised some concerns because there appear to be therapeutic consequences only for children with high grade (III or higher) disease, who account for approximately 15% of those with a first urinary tract infection.[10]

Newer guidelines recommend never performing cystography after a first febrile UTI.[11] However, this strategy presents the risk of delaying diagnosis of high grade VUR, which is associated with recurrent UTI and long-term complications.[1,12] Furthermore, clinicians do not appear ready to change their daily practice after a first UTI so completely from systematic cystography to none at all. Thus, an intermediate evidence-based strategy might be useful to predict high grade VUR and make it possible to avoid cystograms that turn out a posteriori to have no therapeutic consequences while misdiagnosing the fewest cases possible.[10]

Procalcitonin, a sensitive and specific marker of bacterial infections,[13] has been demonstrated and validated as a strong and sensitive predictor of VUR.[14–16] The ability of renal US to predict VUR is largely debated, as revealed by the numerous studies published with conflicting results.[17] Ureteral dilatation appears to be a better renal US criterion to predict VUR but without sufficient sensitivity to be used alone.[17,18] Accordingly it might be clinically relevant to combine renal ultrasound findings with procalcitonin in a clinical decision rule to predict high grade VUR in children with a first febrile UTI. We constructed and performed an internal validation of a clinical decision rule to predict VUR grade III or higher in children with a first UTI.

METHODS

We conducted a secondary analysis of previous single center and multicenter cohort studies.[14,15] All consecutive children 1 month to 4 years old who were hospitalized with a first febrile UTI were considered for inclusion. All patients underwent voiding cystography, which was read by an experienced radiologist blinded to all variables. High grade VUR was defined as grade III or greater.[19] Predictive variables were serum PCT prospectively measured at hospitalization for UTI, findings of renal US performed by an experienced pediatric radiologist (ureteral dilatation, pelvicalyceal dilatation and renal length), family history of uropathy, young age, male gender and serum C-reactive protein at hospitalization.[1,20]

We built a predictive model for high grade VUR using a logistic regression backward elimination modeling technique. To transform the continuous probability of high grade VUR into a binary decision about prescribing cystography, a threshold was chosen based on the area under the ROC area with a prespecified constraint of achieving at least 85% sensitivity with the best specificity and including the best renal US criterion. The performance of this rule was determined in the whole sample set and in the subgroup of children for whom urine was collected by suprapubic aspiration or urethral catheterization. We then performed an internal cross-validation by bootstrapping. We compared the discriminative ability of the decision rule with that of PCT alone and with that of a previous decision rule for high grade VUR proposed by Oostenbrink et al.[20]

RESULTS

Recruitment

Previous data were obtained from 8 prospectively recruited centers (table 1, fig. 1).[14,15] All centers were university hospitals (except Rzeszow, which was a general hospital), and tertiary hospitals (except Afula and Clamart, which were secondary hospitals). Only 2 centers (Geneva and Paris) were exclusively pediatric.

Overall 595 patients met the inclusion criteria (fig. 1). Of these patients 46 (8%) were lost to followup before cystography and 5 (1%) had radionuclide cystography results that did not allow analysis of VUR grade. PCT values were unavailable for 15 other patients (3%) and were measured by the PCT-Q® semiquantitative test for 32 patients (5%). Three children (1%) had no renal US available. Thus, the analysis was based on 494 patients (83%).

Mean ± SD patient age was 12.1 ± 11.2 months (median 8.0, IQR 4.0 to 17.0, 95th percentile 36 months). Of the children 197 (40%) were boys. VUR was diagnosed in 126 children (26%) and was grade III or higher in 56 (11%). No adverse event was reported in performing PCT measurement, renal US or cystography.

The 101 excluded children did not differ significantly in their baseline characteristics from those who

Table 1. *Population characteristics*

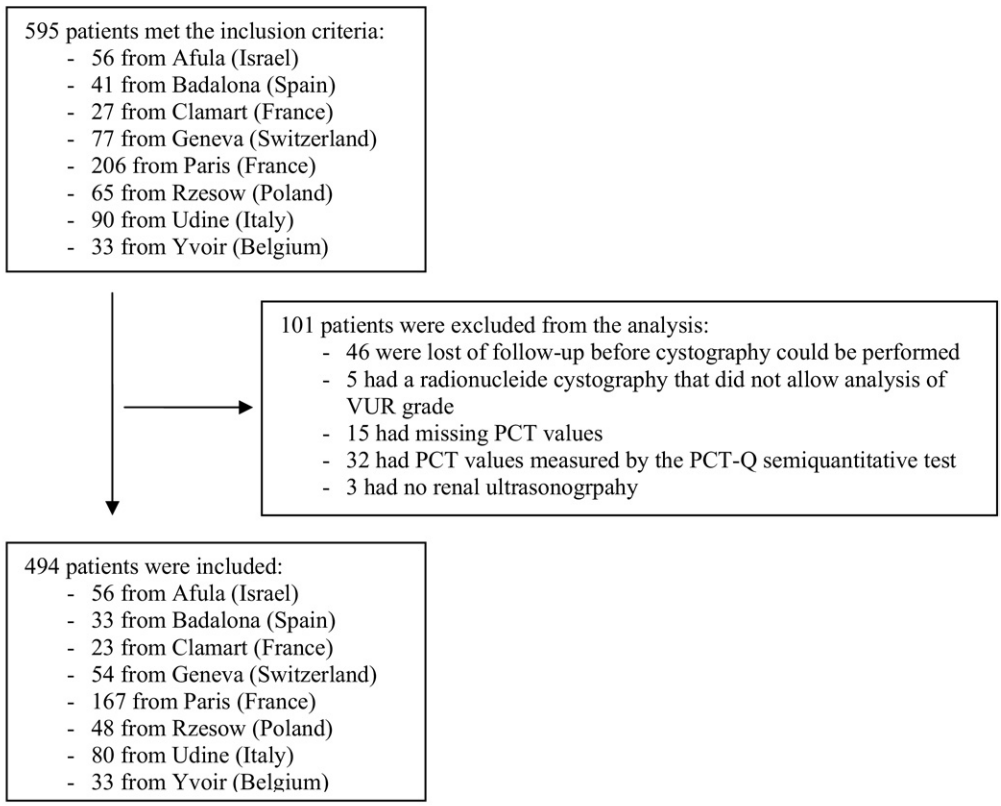
Center*	Urine Collection Techniques (threshold of positive bacteriuria in cfu/ml)	No. Pts	No. Males (%)	No. Pts 1 Yr or Younger (%)	No. All Grade VUR (%)	No. Grade III or Higher VUR (%)
Centers using SA or UC:						
Afula	Suprapubic aspiration (10^1), urethral catheterization (10^3)	56	16 (29)	22 (39)	14 (25)	6 (11)
Badalona	Suprapubic aspiration (10^2), urethral catheterization (10^4), clean voided midstream (10^5)	33	17 (52)	24 (73)	9 (27)	9 (27)
Geneva	Suprapubic aspiration (10^3), urethral catheterization (10^4), clean voided midstream (10^5)	54	17 (31)	29 (54)	19 (35)	9 (17)
Udine	Urethral catheterization (5–10^4), clean voided midstream (10^5)	80	27 (34)	58 (73)	15 (19)	9 (11)
Yvoir	Suprapubic aspiration (10^3), urethral catheterization (5–10^4), clean voided midstream (10^5)	33	9 (27)	15 (45)	7 (21)	4 (12)
Centers using SB:						
Clamart	Sterile bag (10^5)	23	16 (70)	23 (100)	7 (30)	1 (4)
Paris	Sterile bag (10^5), clean voided midstream (10^5)	167	75 (45)	129 (77)	44 (26)	14 (8)
Rzeszow	Sterile bag (10^5), clean voided midstream (10^5)	48	20 (42)	26 (54)	11 (23)	4 (8)
Totals		494	197 (40)	326 (66)	126 (26)	56 (11)

* Classified according to urine collection technique in nontoilet trained children.

were included in the study. Of these patients 46 (46%) were boys (p = 0.4), and mean ± SD age was 12.8 ± 12.9 months (median 8.0, IQR 3.0 to 14.0, p = 1.0).

Construction of Clinical Decision Rule

Because the assumption of linearity for PCT as a continuous variable made by the logistic regression model was not achieved (p <0.001), PCT was transformed into a first degree fractional polynomial function. PCT was statistically significantly associated with high grade VUR, as well as CRP (for which no transformation was needed, as the linearity assumption was verified), pelvicalyceal dilatation and



PCT = Procalcitonin; VUR = vesico-ureteral reflux.

Figure 1. Flow diagram

Table 2. *Crude relationships between vesicoureteral reflux grade III or higher and all variables*

	No. VUR Grade II or Lower (%)	No. VUR Grade III or Higher (%)	OR (95% CI)		p Value	Adjusted OR (95% CI)*		p Value
Gender:					0.5			0.2
M	177 (40)	20 (36)	0.8	(0.5–1.5)		0.6	(0.3–1.2)	
F	261 (60)	36 (64)	1			1		
Age:					0.8			0.3
1 Yr or younger	288 (66)	38 (68)	1.1	(0.6–2.0)		1.5	(0.7–2.8)	
Older than 1 yr	150 (34)	18 (32)	1			1		
Family history of uropathy:†					0.8			0.9
Yes	57 (14)	7 (13)	0.9	(0.4–2.1)		1.0	(0.4–2.1)	
No	354 (86)	48 (87)	1			1		
Ureteral dilatation:					<0.001			0.001
Yes	16 (4)	10 (18)	5.7	(2.5–13.4)		4.6	(1.9–14.4)	
No	422 (96)	46 (82)	1			1		
Pelvicalyceal dilatation:					0.002			0.06
Yes	93 (21)	21 (38)	2.5	(1.4–4.6)		2.0	(0.97–4.0)	
No	345 (79)	35 (62)	1			1		
Abnormal renal length:					0.3			0.9
Yes	31 (7)	6 (11)	1.6	(0.6–4.0)		1.0	(0.3–2.7)	
No	407 (93)	50 (89)	1			1		
CRP as continuous variable‡			0.005	(0.001–0.008)	0.01	−0.0009	(−0.006–0.004)	0.7
PCT as continuous variable (transformed in FP1)‡			−0.14	(−0.19–−0.08)	<0.001	−0.13	(−0.19–−0.07)	<0.001

* Adjusted OR for nonsignificant variables from model during stepwise reduction procedure just before their elimination and from final model for remaining variables.
† Sample size for family history differs from that for other variables because of missing data.
‡ Coefficient for CRP and PCT calculated from logistic regression equation, degree 1 fractional polynomial transformation used for PCT was, $\sqrt{}(100/PCT) - 4.888$.

ureteral dilatation in univariate analysis (table 2). All variables were entered into the model, and after a stepwise reduction procedure PCT and ureteral dilatation remained significantly associated with VUR grade III or higher and made a significant contribution to the prediction according to the maximum likelihood ratio estimation (table 2). The fit of the model was good ($p > 0.2$), and its area under the ROC curve was 0.75 (95% CI 0.69–0.81).

Using the coefficients assigned to each predictor in the logistic regression model, we derived the prediction model, logit (predicted probability of having VUR grade III or higher) = $-1.554 + 1.536 \times$ ureteral dilatation $- 0.129[\sqrt{}(100/PCT) - 4.888]$, where ureteral dilatation was coded (0) if absent and (1) if present, and PCT was the serum measurement. The model led to the rule, cystography should be performed in case of ureteral dilatation on renal US when serum PCT is 0.17 ng/ml or greater, or if there is no ureteral dilatation on renal US but serum PCT level is 0.63 ng/ml or greater (see Appendix). The clinical decision rule was significantly associated with high grade VUR (OR 5.2, 95% CI 2.4–11.3, $p < 0.001$). Sensitivity was 86% (95% CI 74–93), specificity 47% (95% CI 42–51) and negative predictive value 96% (95% CI 93–98) for VUR grade III or higher. The presence of ureteral dilatation correctly identified only 10 of 56 patients with VUR grade III or higher, corresponding to a sensitivity of 18% (95% CI 10–30) and a specificity of 96% (95% CI 94–98). Adding PCT to the decision rule helped to identify correctly 37 other patients with VUR grade III or higher (ie 66% of patients with reflux grade III or higher, fig. 2).

In the specific subgroup of children for whom urine was collected by suprapubic aspiration or urethral catheterization the rule yielded 84% sensitivity (95% CI 62–95) and 48% specificity (95% CI 41–54). From the whole population 8 cases (2%) of high grade VUR were misdiagnosed by the rule (fig. 3), of which 7 presented with grade III and 1 with grade IV VUR. Internal cross-validation produced 86% sensitivity (95% CI 79–93) and 43% specificity (95% CI 39–47). If the PCT values included in the rule were rounded to the nearest first digit after the decimal point (0.2 ng/ml and 0.6 ng/ml, respectively), this rounding rule had a sensitivity that did not differ significantly from that of the rule (88%, 95% CI 76–94, difference of 2%, 95% CI −5–9), but its specificity was significantly lower (44%, 95% CI 40–49, difference of 3%, 95% CI 1–4, table 3).

When we compared our model to PCT alone, the areas under the ROC curves were not significantly different (0.75, 95% CI 0.69–0.81 vs 0.73, 95% CI 0.63–0.79, $p = 0.2$). Applying the same prespecified constraints, a rule based on PCT alone was derived and formulated as, cystography should be performed in case of PCT 0.6 ng/ml or greater. This rule had 86% sensitivity (95% CI 74–93) and 45% specificity (95% CI 40–50), neither of which was significantly different from those of the rule (0%, 95% CI −1–1 for sensitivity vs 3%, 95% CI −1–9 for specificity).

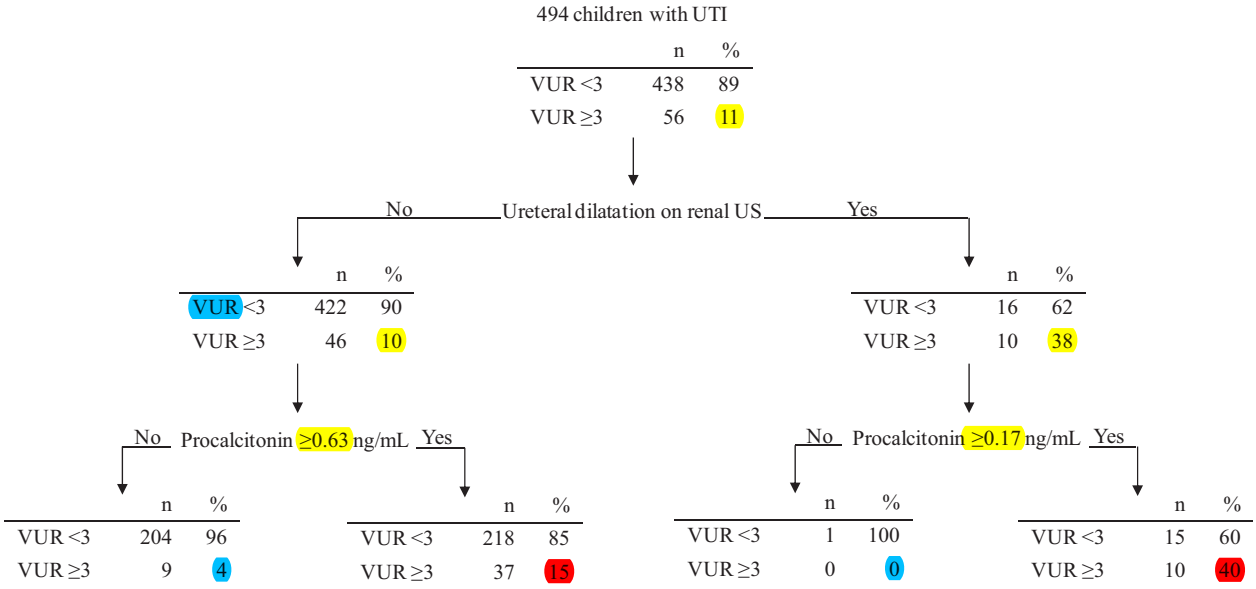


Figure 2. Diagnosis tree and distribution of study population at each step

The Oostenbrink rule yielded a sensitivity of 95% (95% CI 85–98) and a specificity of 17% (95% CI 14–22) for the prediction of VUR grade III or higher. There was no significant difference in sensitivity between the 2 rules (10%, 95% CI −2–20), but our rule had significantly higher specificity (30%, 95% CI 25–35).

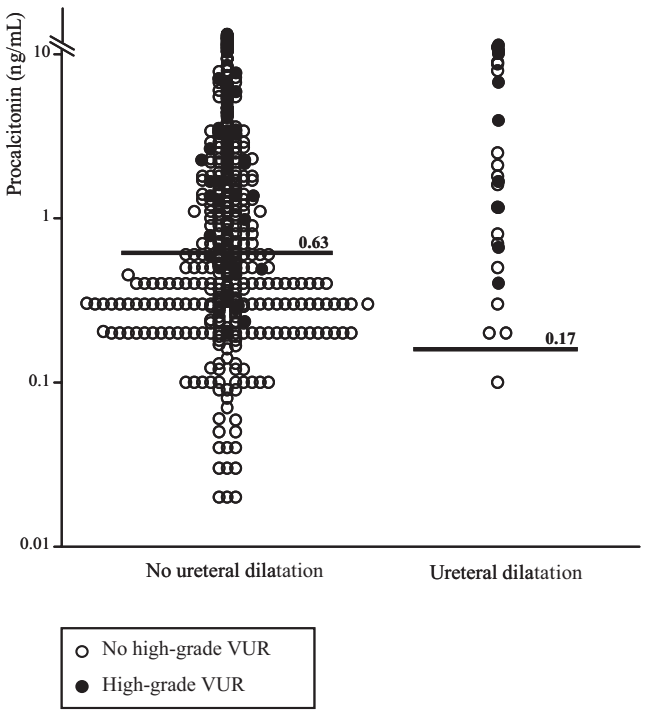


Figure 3. Distribution of PCT values according to presence of ureteral dilatation on renal ultrasound. Horizontal lines represent dichotomization threshold in each group.

DISCUSSION

We formulated a clinical decision rule derived from a small number of easily observed additional testing factors that might permit a more selective approach to cystography in children younger than 4 years with UTI (see Appendix). For children with a first febrile UTI cystography should be performed in the presence of ureteral dilatation and serum PCT level 0.17 ng/ml or greater, or without ureteral dilatation when the serum PCT level is 0.63 ng/ml or greater. This rule predicted moderate or high grade (above grade III) VUR with approximately 85% sensitivity and would make it possible to avoid nearly half of the cystograms that have no therapeutic consequences. Negative predictive value was high, thereby indicating that less than 5% of cases with a negative result from the rule would have been misdiagnosed when they actually were mostly grade III VUR. Moreover, because only patients with a positive test (ie 56% of sample set) would undergo cystography, half of the cystograms would be avoided. The rule included PCT, a twice validated predictor of VUR,[15,16] and ureteral dilatation, which was shown to be the renal US criterion with the best diagnostic accuracy for VUR.[17]

In addition to its significant association to high grade VUR, including a renal US criterion in such a decision rule appears to be clinically important in terms of clinician habits and beliefs.[21] Despite the high specificity of ureteral dilatation, its contribution to the model was less important compared to PCT. However, most of the predictive ability of a model depends on 1 major predictor, and that is the case with PCT. Moreover, as renal US is systemat-

Table 3. *Performance of different rules for moderate and high grade vesicoureteral reflux*

	Rule OR (95% CI)	Rounding Rule OR (95% CI)	Rule Based on PCT Alone OR (95% CI)	Oostenbrink's Rule OR (95% CI)
Sensitivity	86 (74–93)	86 (76–94)	86 (74–93)	95 (85–98)
Specificity	47 (42–51)	44 (40–49)	45 (40–50)	17 (14–22)
Pos predictive value	17 (13–22)	17 (13–21)	17 (13–21)	13 (10–17)
Neg predictive value	96 (93–98)	97 (93–98)	96 (93–98)	96 (89–99)
Pos likelihood ratio	1.6 (1.4–1.8)	1.6 (1.4–1.8)	1.6 (1.4–1.8)	1.2 (1.1–1.2)
Neg likelihood ratio	0.3 (0.2–0.6)	0.3 (0.1–0.6)	0.3 (0.2–0.6)	0.3 (0.1–1.0)

ically performed in children with UTI, regardless of the overall lack of evidence and the ongoing debates about renal US diagnostic accuracy,[22] including such a criterion in the rule did not have any supplementary cost in the management. Nonetheless, ureteral dilatation was kept in the rule in view of its significant association to high grade VUR, its clinical relevance and clinician beliefs.

The advantage of ureteral dilatation compared to pelvicalyceal dilatation (for example) is that there is no need for a threshold definition, which is especially useful given the lack of consensus for such a definition for pelvicalyceal dilatation, and that its predictive ability is the highest.[17] When normal, the ureter is an invisible anatomical structure on renal US in a child. Thus, its visibility on renal US is synonymous with dilatation, and its interobserver variability might be lower than that of other renal US criteria, thereby improving its reproducibility and transportability. Furthermore, as most of the predictive ability of the rule is based on PCT, the variability due to this renal US criterion may affect the rule only slightly. Although developed with complex mathematical modeling techniques, the rule was finally clinically reasonable and easy to use formulated as a list of items. These 2 characteristics appear important for a decision rule designed to assist clinicians in making diagnostic decisions. Interestingly our rule had higher specificity than that of Oostenbrink et al,[20] and its sensitivity did not differ significantly. This finding confirms the lack of reproducibility of this rule, as previously demonstrated by us,[23] and Venhola et al.[24]

Briefly limitations must be addressed, such as the presence of classification biases, selection bias (due to the urine collection techniques used, or the loss of patients to followup) and choices in the statistical analysis. However, none of these limitations appeared to have significantly modified our results.

We propose an evidence-based strategy intermediate between the systematic cystography recommended in the past decade,[2,3] and the wait and see policy for recurrent UTI proposed in the National Institute for Health and Clinical Excellence guidelines.[11] The clinical decision rule could misdiagnose a small number of children with VUR grade III or higher, who could undergo cystography at the second UTI. Considering that even high grade VUR can spontaneously resolve in some patients,[9] and that most clinicians do not make any decision about surgery to treat VUR grade III or higher after the first UTI,[1] little renal damage is likely before the second UTI.

Our clinical decision rule focuses only on VUR grade III or higher, meaning that cystography should not be performed to diagnose low grade VUR. Indeed, diagnosis of low grade VUR serves no therapeutic purpose, given that its antibiotic prophylaxis has been observed to be equivalent to no treatment.[8] The cost of voiding cystography ($150) is 10 times that of PCT ($15). PCT makes it possible to avert 42% of the routine cystograms. Thus, a PCT based strategy vs a systematic approach reduces costs by 30%.

We propose a predictive rule to identify children at high risk for VUR grade III or higher and selectively perform cystography for these patients. We did not consider the use of DMSA scan, which, when negative, reportedly is useful to rule out grade III or higher VUR in children with febrile UTIs.[25] Although the frequency of VUR grade III or higher is increased in children with renal damage,[25] DMSA scan is not the gold standard examination for VUR. However, a top-down approach based on early DMSA scan to diagnose acute pyelonephritis first followed by application of our rule to decide on prescribing cystography would be valuable. The possible limitations of such an approach are 1) DMSA scans are not available at all centers, even university centers, 2) children are often sedated for the examination and 3) DMSA scans expose patients to some radiation even if less than cystography. All of these questions complicate the issue of which examination should be prescribed after UTI.

CONCLUSIONS

We derived a clinical decision rule that could permit a more selective approach to cystography in children younger than 4 years with UTI. This rule predicts VUR grade III or higher with approximately 85% sensitivity and would make it possible to avoid nearly half of the cystograms that are a posteriori without any therapeutic consequences. Although

ureteral dilatation was incorporated into the rule because of its significant association to high grade VUR, its clinical relevance and clinician beliefs, ureteral dilatation did not significantly improve the predictability of the VUR grade III or higher compared to procalcitonin alone.

ACKNOWLEDGMENTS

Drs. Serena Ellero (Department of Pediatrics, University of Udine) and Elizabeth Marc (Department of Emergency Medicine, Saint-Vincent-de-Paul Hospital) recruited patients. Prof. Jean-Marc Tréluyer and Mélanie Annoussamy (URC, Cochin Hospital, Paris) provided administrative support. Dr. S. Fargue (Department of Human Biology, University College London) participated in helpful discussions.

APPENDIX

Clinical decision rule to predict moderate and high grade vesicoureteral reflux

A cystography should be performed in children aged 1 month to 4 years with a first febrile urinary tract infection:

- in case of ureteral dilation on renal ultrasonography (defined by its visibility on the examination) when serum procalcitonin (measured at the time of UTI diagnosis) is greater than or equal to 0.17 ng/mL,
- or if there is no ureteral dilation (ie ureter non visible on the examination) on renal ultrasonography, when serum procalcitonin level is greater than or equal to 0.63 ng/mL.

REFERENCES

1. Williams G, Fletcher JT, Alexander SI et al: Vesicoureteral reflux. J Am Soc Nephrol 2008; **19:** 847.
2. Practice parameter: the diagnosis, treatment, and evaluation of the initial urinary tract infection in febrile infants and young children. American Academy of Pediatrics. Committee on Quality Improvement. Subcommittee on Urinary Tract Infection. Pediatrics 1999; **103:** 843.
3. Jodal U and Lindberg U: Guidelines for management of children with urinary tract infection and vesico-ureteric reflux. Recommendations from a Swedish state-of-the-art conference. Swedish Medical Research Council. Acta Paediatr 1999; **88:** 87.
4. Hägglöf B: Psychological reaction by children of various ages to hospital care and invasive procedures. Acta Paediatr Suppl 1999; **88:** 72.
5. Fotakis M, Molyvda Athanasopoulou E, Psarrakos K et al: Radiation doses to paediatric patients up to 5 years of age undergoing micturating cystourethrography examinations and its dependence on patient age: a Monte Carlo study. Br J Radiol 2003; **76:** 812.
6. Nicklasson L and Hogard S: Cost-analysis of management strategies for children with vesico-ureteric reflux. Acta Paediatr 1999; **88:** 79.
7. Guignard JP: Urinary infection after micturating cystography. Lancet 1979; **1:** 103.
8. Mattoo TK: Evidence for and against urinary prophylaxis in vesicoureteral reflux. Pediatr Nephrol 2010; **25:** 2379.
9. Silva JM, Diniz JS, Lima EM et al: Predictive factors of resolution of primary vesico-ureteric reflux: a multivariate analysis. BJU Int 2006; **97:** 1063.
10. Jodal U: Selective approach to diagnostic imaging of children after urinary tract infection. Acta Paediatr 2000; **89:** 767.
11. Mori R, Lakhanpaul M and Verrier-Jones K: Diagnosis and management of urinary tract infection in children: summary of NICE guidance. BMJ 2007; **335:** 395.
12. Coulthard MG: NICE on childhood UTI: nasty processes produce nasty guidelines. BMJ 2007; **335:** 463.
13. Simon L, Gauvin F, Amre DK et al: Serum procalcitonin and C-reactive protein levels as markers of bacterial infection: a systematic review and meta-analysis. Clin Infect Dis 2004; **39:** 206.
14. Leroy S, Adamsbaum C, Marc E et al: Procalcitonin as a predictor of vesicoureteral reflux in children with a first febrile urinary tract infection. Pediatrics 2005; **115:** e706.
15. Leroy S, Romanello C, Galetto-Lacour A et al: Procalcitonin to reduce the number of unnecessary cystographies in children with a urinary tract infection: a European validation study. J Pediatr 2007; **150:** 89.
16. Leroy S, Romanello C, Galetto-Lacour A et al: Procalcitonin is a predictor for high-grade vesicoureteral reflux in children: meta-analysis of individual patient data. J Pediatr 2011; **159:** 644.
17. Leroy S, Friedman J, Mourdi N et al: Renal ultrasonography to predict vesico-ureteral reflux after urinary tract infection in childhood: systematic review and meta-analysis. Pediatr Nephrol 2008; **23:** 1702.
18. Leroy S, Vantalon S, Larakeb A et al: Vesicoureteral reflux in children with urinary tract infection: comparison of diagnostic accuracy of renal US criteria. Radiology 2010; **255:** 890.
19. Hoberman A, Charron M, Hickey RW et al: Imaging studies after a first febrile urinary tract infection in young children. N Engl J Med 2003; **348:** 195.
20. Oostenbrink R, van der Heijden AJ, Moons KG et al: Prediction of vesico-ureteric reflux in childhood urinary tract infection: a multivariate approach. Acta Paediatr 2000; **89:** 806.
21. McGinn TG, Guyatt GH, Wyer PC et al: Users' guides to the medical literature: XXII: How to use articles about clinical decision rules. Evidence-Based Medicine Working Group. JAMA 2000; **284:** 79.
22. Whiting P, Westwood M, Bojke L et al: Clinical effectiveness and cost-effectiveness of tests for the diagnosis and investigation of urinary tract infection in children: a systematic review and economic model. Health Technol Assess 2006; **10:** 1.
23. Leroy S, Marc E, Adamsbaum C et al: Prediction of vesicoureteral reflux after a first febrile urinary tract infection in children: validation of a clinical decision rule. Arch Dis Child 2006; **91:** 241.
24. Venhola M, Huttunen NP, Renko M et al: Practice guidelines for imaging studies in children after the first urinary tract infection. J Urol 2010; **184:** 325.
25. Preda I, Jodal U, Sixt R et al: Normal dimercaptosuccinic acid scintigraphy makes voiding cystourethrography unnecessary after urinary tract infection. J Pediatr 2007; **151:** 581