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Economic and Radiation Costs of Initial Imaging Approaches After a Child's First Febrile Urinary Tract Infection

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Abstract

Background—The traditional initial imaging approach following pediatric urinary tract infection is the “bottom-up” approach (cystogram and renal ultrasound). Recently, the “top-down” approach (nuclear renal scan followed by cystogram for abnormal scans only) has gained increasing attention. The relative cost and radiation doses of these are unknown

Methods—The authors used a decision model to evaluate these imaging approaches. Cost and effective radiation dose estimates, including sensitivity analyses, were based on one-time imaging only.

Results—Comparing hypothetical cohorts of 100 000 children, the top-down imaging approach cost \$82.9 million versus \$59.2 million for the bottom-up approach. Per-capita effective radiation dose was 0.72 mSv for top-down compared with 0.06 mSv for bottom-up.

Conclusions—Routine use of nuclear renal scans in children following initial urinary tract infection diagnosis would result in increased imaging costs and radiation doses as compared to initial cystogram and ultrasound. Further data are required to clarify the long-term clinical implications of this increase.

Keywords

urinary tract infection; vesicoureteral reflux; imaging; pediatrics

Introduction

The optimal diagnostic imaging approach following a child's initial febrile urinary tract infection (UTI) is controversial. In 1999, the American Academy of Pediatrics (AAP) issued guidelines on the evaluation and management of a child following UTI, recommending that renal ultrasound (RUS) and either a radionuclide or fluoroscopic cystogram be performed to determine the presence of vesicoureteral reflux (VUR).¹ However, these guidelines may not be routinely followed; by one estimate, fewer than 40% of US children receive a cystogram following their first UTI.² To explain this decreased cystogram use, some authors have cited

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the discomfort of urethral catheterization or concerns over ionizing radiation exposure during fluoroscopy as barriers to implementing recommended imaging protocols.³

An alternative to the traditional “bottom-up” approach to post-UTI diagnostic imaging has recently been endorsed by the European Society of Pediatric Radiology.⁴ This “top-down” approach begins with a nuclear renal cortical scan (typically ^{99m}Tc dimercaptosuccinic acid [DMSA]) to evaluate for renal involvement; a cystogram is performed only if renal involvement is identified. Possible benefits of this approach include decreased detection of clinically insignificant VUR, decreased urethral catheterizations and a possible decrease in gonadal radiation.^{3,5} Unfortunately, there is little long-term data on the effectiveness of the top-down approach, and formal comparisons of the cost and radiation implications of the 2 approaches are lacking, as are consensus definitions of “insignificant” VUR.

Our objective was to compare the relative cost and radiation dose of these 2 initial imaging approaches in the context of a child undergoing initial evaluation following a febrile UTI.

Patients and Methods

Model Design

We constructed a nonrecursive decision model to evaluate 2 competing VUR initial imaging approaches: bottom-up imaging (all UTI patients undergoing RUS and cystography) or top-down imaging (all UTI patients undergoing DMSA followed by cystography only if a renal abnormality is detected). Although a recursive model would have been ideal given the biology of UTI and VUR, we were unable to define stable parameter estimates based on the published literature. Rather than pursue an inherently unstable model design to evaluate the entire treatment algorithm, we chose to focus this analysis on initial imaging costs and consequences by using a nonrecursive decision tree. Thus the analysis time horizon was limited to the immediate outcomes of each imaging approach, and the perspective was that of a health care system. The index case was that of a 1-year-old child, recently diagnosed with an initial febrile UTI. For the top-down approach, the index case underwent DMSA and RUS followed by pulsed fluoroscopy voiding cystourethrography (pVCUG) if and only if a renal defect was detected on DMSA. For the bottom-up approach, the index case underwent pVCUG and RUS only.

Parameter Estimates

Probability estimates were based on a systematic review of MEDLINE and EMBASE for English-language articles published prior to September 2009. Reference lists of identified studies were hand-screened for missed studies. Probability estimates were based on pooled results using inverse variance weighting.⁶ All parameter values are detailed in Table 1.

Effective radiation dose estimates (expressed in mil-liSieverts [mSv]) were calculated based on previously published methods.^{7–9} The effective dose represents the overall detrimental biologic effect of a radiation exposure and is calculated by weighting the radiation dose to each organ from a radiation exposure by the radiosensitivity of that organ, allowing for population-level comparisons across different types of radiation exposure.¹⁰

Cost estimates were based on a nationally weighted average of Medicare reimbursements for each diagnostic test, including both technical and professional fees¹¹; these data have been previously noted to closely approximate medical resource costs.^{12,13} All costs were calculated in 2009 US dollars.

Model Outcomes

Model outcomes were the number of patients undergoing each imaging test, the population-level direct medical costs, the average per-patient radiation dose, and the number of patients accurately diagnosed with VUR. All model outcomes and calculations were based on identical cohorts of 100 000 hypothetical patients undergoing each imaging approach. This cohort size was chosen both for mathematical simplicity and to roughly simulate the number of 1-year-old children diagnosed with UTI in the United States annually.

Sensitivity Analyses

There is significant heterogeneity among practitioners regarding UTI and VUR practice patterns, even within the context of the bottom-up or top-down approaches.^{2,14,15} We therefore performed additional analyses using multiple imaging practice patterns for each approach. For bottom-up, we modeled 3 different scenarios for obtaining a DMSA scan following initial RUS and cystogram: first, that a DMSA scan was never obtained; second, that a DMSA would be obtained only if renal scar was noted on RUS; and third, that DMSA would be obtained only if dilating VUR (grades 3–5) was noted on VCUG (Figure 1). For top-down, we modeled 2 scenarios regarding RUS use: either RUS was obtained for all patients or for none (Figure 2).

Because effective radiation dose varies based on body size, we modeled 3 additional age categories (newborns, 5-year-olds, and 10-year-olds) for all simulations along with our index case analysis of a 1-year-old child. Similarly, because both cost and effective dose vary based on the type of cystogram performed, we modeled 2 additional cystogram types (continuous fluoroscopy VCUG [cVCUG] and radionuclide cystography [RNC]) instead of a pVCUG as used with our reference case analysis. Effective dose does not vary based on gender, thus we did not differentiate between boys and girls for this analysis.

One- and 2-way sensitivity analyses were performed for all model parameters (Table 1). All analyses and model simulations were performed using TreeAge Pro Suite 2009 software (TreeAge Software Inc, Williamstown, MA).

Results

Reference Case Analysis

For the index case of a 1-year-old child, the mean per-capita effective radiation dose was 0.06 mSv for the bottom-up regimen. For the top-down index case, this figure was 0.72 mSv. For a hypothetical cohort of 100 000 index children, the total direct medical cost of VUR imaging was \$59.2 million for bottom-up and \$82.9 million for top-down. The number of patients diagnosed with VUR also varied between the 2 approaches. For the bottom-up approach, all 38 700 VUR patients (19 700 with dilating VUR) would have been identified. For the top-down approach, 20 300 of these patients (10 400 with dilating VUR) would have been diagnosed with VUR. For the bottom-up index case, all patients received a cystogram and RUS, whereas none received a DMSA scan. For the top-down index case, all children received a DMSA scan, and 61 900 also received a cystogram (Table 2).

Sensitivity Analyses

Number of tests—On sensitivity analysis, the number and type of tests used per patient were adjusted based on the various possible criteria used for obtaining DMSA and RUS (Table 2). These additional tests affected both the radiation exposure and the costs of each approach (Table 3).

Radiation exposure—Bottom-up was consistently associated with a lower effective dose than top-down. The absolute difference between the 2 approaches ranged from 0.52 to 0.66 mSv depending on the criteria used for obtaining DMSA in the bottom-up approach (Table 3). Similarly, radiation dose varied depending on cystogram method and patient age. Patients undergoing cVCUG had the highest radiation dose, followed by pVCUG and RNC. Bottom-up patients undergoing RNC without supplemental DMSA scan use had the lowest per-capita radiation dose among any cohort studied, ranging from 0.001 to 0.006 mSv depending on patient age. Older patients tended to have a slightly higher imaging-related effective dose, primarily because of the increased amount of radiotracer required for DMSA scans of larger patients. This increase was more pronounced with the top-down approach than with the bottom-up approach.

Imaging-related costs—Costs varied depending on the criteria used for obtaining DMSA and RUS, as well as on cystogram type (Table 3). For the bottom-up approach, costs varied from \$59.2 to \$72.6 million. For the top-down approach, costs varied from \$82.9 to \$105.5 million. In nearly all scenarios, top-down was more expensive than bottom-up, with the absolute difference in total direct imaging-related costs ranging from \$10.3 to \$46.3 million. However, if RNC was the only cystography method used, if all high-grade VUR patients underwent DMSA, and if no top-down patients underwent RUS, then the imaging-related direct costs of bottom-up exceeded those of top-down by \$9 million (\$95.8 vs \$104.8 million).

Sensitivity on uncertain parameters—One- and 2-way sensitivity analyses of each model parameter did not significantly change model outcomes. Specifically, variation of the probabilities of VUR occurring after UTI, of DMSA-detected renal involvement, of ultrasound-detected renal involvement, of VUR detection among the screened populations did not alter the relative model outcomes. Similarly, varying the absolute cost or effective dose of each imaging modality based on reasonable estimates of error did not change the relative model outcomes. The top-down approach in all scenarios resulted in higher imaging-related costs, fewer VUR diagnoses, and a higher effective dose of radiation.

Discussion

Pediatric imaging following UTI is controversial, in large part because of a lack of long-term clinical outcomes data. Current AAP guidelines for evaluation of febrile UTI form the basis of the bottom-up approach, that is, the initial use of cystography to determine the presence of VUR.¹ More recently, the ESPR has proposed the top-down approach, which focuses on the presence or absence of renal involvement rather than conditions (particularly VUR) that may predispose to renal damage.^{3–5} In the United States, adoption of these approaches has been mixed, with wide variations noted in imaging practices nationally.^{2,14,15}

In this decision analysis model, we explored the immediate economic and radiation-related consequences of 2 approaches to VUR imaging, the top-down and bottom-up approaches. The top-down approach was consistently more expensive than bottom-up; for a population of 1-year-old children, initial costs of the top-down approach would be significantly greater than those of bottom-up (\$59 million vs \$105 million). Top-down also entailed a significantly greater per-capita radiation dose compared with bottom-up (Table 3). In addition, the top-down approach would be expected to result in a missed VUR diagnosis in more than 18 000 children, half of whom would be expected to have dilating VUR. As little long-term data exist regarding the clinical ramifications of these VUR diagnoses, it is unclear whether patients would overall benefit or be harmed by these missed diagnoses. Thus the question facing pediatricians and pediatric specialists becomes: Do the benefits of

the top-down approach (fewer urethral catheterizations and likely fewer diagnoses of clinically insignificant VUR) outweigh its consequences (increased cost, increased radiation exposure, and potentially missed clinically significant VUR diagnoses)?

A critical assumption behind the top-down approach is that VUR in the absence of scintigraphic abnormality does not lead to future renal damage.³ Although initial studies are encouraging, long-term data supporting this assumption are limited.¹⁶ It is therefore difficult to compare the clinical effectiveness of these 2 approaches. What if the damage detected by the top-down approach is alone sufficient to produce untoward long-term renal compromise? On one hand, imaging using the bottom-up approach may discover “clinically insignificant” reflux that does not lead to future episodes of pyelonephritis or renal damage, while exposing a large number of children to an invasive radiographic examination (VCUG). This reflux may then be medically or surgically treated—perhaps unnecessarily. On the other hand, the top-down approach may miss VUR, which could expose children to future episodes of pyelonephritis-induced renal damage. It may also find scintigraphic abnormalities that are either not related to reflux or not amenable to any specific available treatment.

In situations characterized by incomplete data, decision analysis can often highlight what factors are important enough influence decisions and which uncertain factors are unlikely to affect management choices. Even though the long term clinical implications of the top-down and bottom-up approaches are not known, the cost of initial imaging and the differences in radiation exposure for each approach can be compared. Because the precise algorithm for work-up in each of these approaches is not uniform, sensitivity analyses are required to see if variations in diagnostic testing algorithms could equalize costs or radiation exposure. However, despite testing multiple combinations of uncertain parameters an initial imaging based on the top-down approach was still significantly more expensive and delivered more radiation in nearly all situations. This was a constant finding across our extensive sensitivity analyses, including multiple common clinical variations (eg, obtaining a DMSA scan for a patient with high-grade VUR).

This increased ionizing radiation exposure can be translated into a small but measurable increase in long-term risk of radiation-related cancer development.¹⁷ Assuming a linear, nonthreshold model of cancer risk as a result of low-dose ionizing radiation (as recommended by the National Research Council),¹⁸ the risk of contracting a lethal cancer is approximately 1 in 20 000 per mSv for an adult. However, children exposed to radiation are presumed to be at a higher risk than adults because of the higher sensitivity of growing tissues and their longer life expectancy.¹⁹ For the bottom-up index case, the estimated population-level risk of developing a radiation-induced lethal cancer was 0.8 cancers per 100 000 patients. For the top-down index case, the estimated population-level risk was 10.1 cancers per 100 000 patients. In terms of the natural incidence of cancer, this increased risk is tiny; by comparison, 42 000 of the 100 000 children in our cohort would be expected to eventually develop a lethal cancer from other causes.¹⁸ Similarly, it should be noted that although a DMSA scan has more radiation than pVCUG, cVCUG, and RNC, the radiation is focused farther from the gonads, particularly in males. There is unfortunately no perfect way to perfectly quantify gonadal radiation dosage, which is why we have instead focused on the effective radiation dose. It is worth noting, however, that increased gonadal radiation could theoretically lead to infertility or damage to immature gonocytes.

Thus the central question in evaluating post-UTI imaging methods is whether the clinical information gained through use of top-down is great enough to offset its low radiation-related risks, particularly in the context of increased medical radiation use nationwide.^{10,17,20} It should also be noted that the long-term risk of renal damage in the

setting of VUR is low. In the end, the best approach to imaging for VUR will have to be able to identify a modifiable risk factor for future renal compromise while balancing costs and imaging related harm. Without solid evidence to support the clinical benefit of a particular approach, the “as low as reasonably achievable” (ALARA) principle suggests the regimen with a lower radiation exposure should be preferred.^{21,22}

This study’s results should be interpreted in light of its limitations. Perhaps most important, all study parameters were based on a systematic review of the current pediatric literature. As such, any significant biases present in the literature would be echoed in our assumptions. In addition, we considered only the one-time, direct medical costs and radiation dosages of VUR imaging from a health care system perspective. This perspective approximates true economic value rather than the costs to any particular individual or financial entity. Although this approach is recommended by many authorities,²³ the results of such an analysis will clearly differ from those considering another perspective. Other direct medical costs, such as repeat imaging, physician visits, and medical or surgical interventions, were not included in this analysis; nor were the costs of VUR-related morbidity (eg, hypertension or renal insufficiency), which might have been prevented by intervention following an early diagnosis. This limitation is important; if the long-term costs of one approach were markedly higher than the other, our analysis of initial imaging choice would not capture that difference. This short-term focus is a direct result of the significant limitations of the available data. Although a recursive (eg, Markov) model would have been ideal given the biology of UTI and VUR, we were unable to define stable parameter estimates based on the published literature. Rather than pursue an inherently unstable model design to evaluate the entire treatment algorithm, we chose to focus this analysis on initial imaging costs and consequences. Although this approach provides a stable model, it unfortunately limits our ability to comment on events beyond the initial diagnostic imaging, such as recurrent UTI or the costs and biologic consequences of ongoing management of VUR once it is diagnosed.

Similarly, the significant lack of long-term outcomes data for both diagnosed, but untreated, VUR patients, as well as undiagnosed VUR patients limits this study. If future research determines that those patients missed by the top-down approach are not at increased risk of renal damage, then the benefits of top-down imaging might be much higher than our calculations demonstrate. However, any future benefits would need to be balanced against the increased imaging-related economic costs and radiation-related consequences of the top-down approach.

Conclusions

The top-down approach for the initial work-up of pediatric febrile UTI would result in increased initial imaging costs and increased radiation dose compared with the bottom-up approach. However, the clinical importance of these increases is unclear, as long-term outcomes data from each approach are lacking. Further research should be directed toward the association between the VUR identified by these 2 initial imaging approaches and long-term renal damage, as this association is key to determining the safest, most cost-effective imaging method in children with UTI.

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Figure 1.

Schematic diagram of the bottom-up approach

Abbreviations: UTI, urinary tract infection; VCUG, voiding cystourethrography; US, ultrasound; DMSA, ^{99m}Tc dimercaptosuccinic acid.

Figure 2.

Schematic diagram of the top-down approach

Abbreviations: UTI, urinary tract infection; DMSA, ^{99m}Tc dimercaptosuccinic acid; US, ultrasound; VCUG, voiding cystourethrography.

Table 1**Model Parameter Values**

Parameter	Value	Sensitivity Analysis Range	Source
Probabilities ^a (%)			
Probability of VUR in a child after febrile UTI	38.7	0–100	5,24–34
Probability of dilating VUR, given VUR	50.8	0–100	
Probability of DMSA lesion, given VUR	52.4	0–100	
Probability of DMSA lesion, given no VUR	32.7	0–100	
Probability of ultrasound-detected lesion, given VUR	11.2	0–100	
Effective dose ^b (mSv)			
RUS	0	0	7,9
cVCUG	0.6	0.1–1.0	
pVCUG	0.06	0.01–0.1	
RNC	0.003	0.001–0.01	
DMSA	0.7	0.1–1.0	
Costs (in 2009 US\$)			
RUS	226	100–1000	11
VCUG	366	100–1000	
RNC	687	100–1000	
DMSA	681	100–1000	

Abbreviations: VUR, vesicoureteral reflux; UTI, urinary tract infection; DMSA, ^{99m}Tc dimercaptosuccinic acid; RUS, renal ultrasound; cVCUG, continuous fluoroscopy voiding cystourethrography; pVCUG, pulsed fluoroscopy voiding cystourethrography; RNC, radionuclide cystography.

^a All probabilities were derived from the authors' systematic review of the literature.

^b All listed parameter estimates are for a 1-year-old child.

Table 2

Comparison of Top-Down and Bottom-Up Approaches, by Number of Diagnostic Procedures Performed and Number of VUR Patients Diagnosed or Missed (per 100 000 Patients)

	Bottom-Up Without DMSA for Any Patient	Bottom-Up With DMSA Obtained Only for Renal Scar on RUS	Bottom-Up With DMSA Obtained Only for Dilating VUR	Top-Down With RUS Obtained for All Patients	Top-Down Without RUS for Any Patient
Cystograms performed; n (% total)	100 000 (100)	100 000 (100)	100 000 (100)	61 900 (62)	61 900 (62)
DMSA scans performed; n (% total)	0 (0)	4600 (5)	19 700 (20)	100 000 (100)	100 000 (100)
RUS performed; n (% total)	100 000 (100)	100 000 (100)	100 000 (100)	100 000 (100)	0 (0)
Any VUR (grades 1–5); n (% total)					
Cases in population; n (% total)	38 700 (39)	38 700 (39)	38 700 (39)	38 700 (39)	38 700 (39)
Cases diagnosed; n (% diagnosed)	38 700 (100)	38 700 (100)	38 700 (100)	20 300 (52)	20 300 (52)
Dilating VUR (grades 3–5); n (%)					
Cases in population; n (% total)	19 700 (20)	19 700 (20)	19 700 (20)	19 700 (20)	19 700 (20)
Cases diagnosed; n (% diagnosed)	19 700 (100)	19 700 (100)	19 700 (100)	10 400 (53)	10 400 (53)

Abbreviations: VUR, vesicoureteral reflux; DMSA, ^{99m}Tc dimercaptosuccinic acid; RUS, renal ultrasound.

Table 3

Comparison of Top-Down and Bottom-Up Approaches in Terms of Cost and Effective Radiation Dose, Using Pulsed Fluoroscopy VCUG

	Direct Imaging-Related Costs, per 100 000 Patients (2009 US\$)	Effective Radiation Dose, per Patient (mSv)
Bottom-up without DMSA for any patient	59 221 000	0.06
Bottom-up with DMSA obtained only for renal scar on RUS	62 400 000	0.09
Bottom-up with DMSA obtained only for dilating VUR	72 600 000	0.20
Top-down with RUS obtained for all patients	105 500 000	0.72
Top-down without RUS for any patient	82 900 000	0.72

Abbreviations: VCUG, voiding cystourethrography; DMSA, ^{99m}Tc dimercaptosuccinic acid; RUS, renal ultrasound; VUR, vesicoureteral reflux.