Serous acute pyelonephritis: a predictive score for evaluation of deterioration of treatment based clinical and radiologic findings using CT

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Purpose

Acute pyelonephritis (APN) is an infection of the renal parenchyma and collecting system. The diagnosis is mainly based on a combination of typical clinical symptoms and laboratory findings, such as loin pain, high temperature and dysuria accompanying pyuria on urinalysis. Patients with a quick response to antibiotic treatment do not necessarily require radiological evaluation, as this is generally reserved for patients who have unusual severe symptoms and no response to antibiotic therapy within 72 hr. Computed tomography (CT) is superior for detecting parenchyma and collecting system abnormalities, and for defining disease extent despite the radiation hazard.

APN is a common disease, but the diagnostic approach, and deterioration into systemic inflammatory response syndrome (SIRS) with severe symptomatic and laboratory findings, and indications for aggressive treatment are still problems. In serious APN, the only reliable investigation for diagnosing treatment deterioration is symptomatic and laboratory findings. This type of investigation accompanying a radiological evaluation is probably helpful for a prognosis of this serious condition. These observations prompted us to develop a simple tool for diagnosing treatment deterioration in patients with serious APN. The purpose of this study was to develop and validate a predictive score to evaluate treatment deterioration in patients with serious APN based on clinical and CT findings.
Methods and Materials

Patient Population

Our study was approved by the institutional review board, with waiver of informed consent. We reviewed the medical records, and pertinent images of consecutive CT examinations performed on 305 patients with APN (197 women and 108 men; median age, 48.5 years; range, 20.4-85.2 years) undergoing subsequent hospitalization for treatment deterioration between March 1, 2008 and March 1, 2010. All patients had typical clinical findings (e.g., loin pain, loin tenderness, dysuria, pyuria, fever, nausea, and vomiting), and CT was performed within 72 hours after initiating treatment.

Exclusion criteria included immunocompromised status (n=35), vesicoureteral reflux (n=28), neurogenic bladder (n=25) or a ureteral obstruction from benign prostate hyperplasia (n=24) diagnosed previously. Imaging was performed at an immediate stage in immunocompromised patients such as those with HIV, transplant recipients on immunosuppressant therapy, and patients receiving cytotoxic chemotherapy, or in those with underlying disease entities such as vesicoureteral reflux, neurogenic bladder, or a ureteral obstruction by benign prostate hyperplasia. Therefore, our final analysis included data from clinical and CT examinations conducted in 193 patients. CT in children or pregnant women with possible APN was not considered due to the ionizing radiation hazard.

The score was developed in a retrospective derivation cohort of 193 consecutive patients between March 1, 2008 and March 1, 2010. We prospectively included 40 consecutive patients between March 1, 2010 and December 31, 2010 for the validation study.

CT Technique

Because each CT scan was performed at different times over a period of 3 years, helical CT of various types was performed in all patients using either 16, 64, or 128-channel multi-detector row scanners (Siemens Medical Systems, Erlangen, Germany). All patients underwent three-phase helical CT, which included unenhanced, corticomedullary, and early excretory phases. Intravenous contrast material was administrated in an anticubital vein with an injector at a dose of 1.5 mL/kg body weight at a rate of 3 mL/sec to a maximum of 120 mL. Corticomedullary phase scans were started 30-50 sec after contrast injection and at 90-120 sec for the early excretory phase.

Variables of Interest

Our investigation was limited to those patients who had serious APN with treatment deterioration. Initial clinical data were collected by reviewing the medical records, and two radiologists reviewed the CT findings by consensus. A standardized form was used to collect the prospective cohort data. Old age (>60 years), diabetes, tachycardia (>90 beats
per minute) or hypotension (systolic pressure < 90 mmHg), persistent fever or pyuria, and intensity of loin pain (worsening) were recorded.

Because of its superiority in depicting abnormalities and the full extent of the disease, CT was evaluated using the following patterns during the early excretory phase. A striated or wedge shaped nephrogram (low density from papilla in the medulla to cortex, unifocal or multifocal), focal or global renal enlargement, obliteration of perinephric fat, thickening of Gerota's fascia, obliteration of the renal sinus, pelvicalyceal wall thickening and enhancement, focal or globally poor excretion of contrast, urinary tract stones, pelvicalyceal air, abscess, and pyonephrosis (with or without stone) were reviewed.

The reference standard for serious APN with treatment deterioration was the gradual progress into SIRS (e.g., heart rate > 90 beats per minute, respiratory rate > 20 breaths per minute), white blood cell count > 12,000, < 4,000, or > 10% band forms), body temperature (<36 °C or >38 °C), Urine white blood cells (>5 per high power field)].

Statistical Analysis

Patients with and without criteria applicable to our investigation were compared using Pearson's $x^2$ test for qualitative variables and Student's $t$-test for quantitative variables. Ordinal and continuous variables that yielded P-values < 0.05 in the univariate analysis were dichotomized based on the area under the receiver operating characteristic (ROC) curve (AUROC) and used in a predictive model. We calculated sensitivity, specificity, the positive likelihood ratio (Lr+), and the negative likelihood ratio (Lr-) for each variable with a significant association.

Multiple logistic regression analysis was then used to select the best model for diagnosing APN applicable to our investigation. Variables yielding P-values < 0.05 in the univariate analysis were entered into the logistic regression model. A forward stepwise procedure using the jackknife method was performed to obtain the best combination of variables independently associated with our investigation at a P threshold < 0.05. The jackknife procedure was used to estimate the bias and standard error of the statistical variance. Therefore, we applied our method to a prediction rule with ordinal and continuous predictor variables for APN applicable to our investigation, and showed that our method for dichotomizing continuous regressor variables is a valid and useful tool to create probability tables.

The scores applicable to our investigation were based on items significant in the multivariate logistic regression analysis and found to be stable using the jackknife procedure. The number of points contributed by each score item was obtained by rounding up coefficient values of the logistic regression to generate a simple scale, and the AUROC of the score was then compared with the AUROC of the logistic regression to check that the two values were not significantly different from each other. Sensitivity and specificity were calculated for each score value in the derivation cohort to assess the probability that APN was applicable to our investigation. Risk groups were then
constructed to maximize classification rates, by considering that the probability should be $< 5\%$ in the low-risk group and $> 70\%$ in the high-risk group.

A score was calculated and correlated with the final diagnosis for each patient in the validation cohort.
Results

We included 193 patients in the retrospective derivation cohort, and 40 patients in the validation cohort. The rate of APN applicable to our investigation was not significantly different between the two cohorts (23.5 and 18.1%, respectively; \( P = 0.49 \)), and the main characteristics were comparable (data not shown).

**Derivation Cohort**

The diagnostic performance of the variables associated with our investigation in the univariate analysis is shown in Table 1. APN applicable to our investigation was significantly associated with tachycardia or hypotension, persistent fever or pyuria, and diabetes, and CT findings for discriminating between the two groups were global renal enlargement, obliteration of the renal sinus, poor global excretion of contrast, pelvicalyceal air, abscess, and pyonephrosis with or without stone (Fig. 1).

Nine variables independently predicted the APN diagnosis by multiple logistic regression analysis. The adjusted odds ratios (ORs) are reported. The AUROC was 0.90 [95% confidence interval (95% CI), 0.84-0.95]. The jackknife procedure showed that the logistic model was stable. The APN score applicable to our investigation was given by the following equation:

\[
\text{Score} = \text{abscess}, +20; \text{pyonephrosis with or without stone}, +20; \text{pelvicalyceal air}, +15; \text{poor global excretion of contrast}, +10; \text{tachycardia or hypotension}, +10; \text{obliteration of the renal sinus}, +10; \text{persistent fever or pyuria}, +10; \text{diabetes}, +10; \text{and global renal enlargement}, +5. \]

The probability that APN was applicable to our investigation was estimated using an appropriate logistic transformation such as: \( P = 1/[1 + \exp(0.098* \text{score} - 6.42)] \). The ROC curve with the score values is shown in Fig. 2.

The low-risk group comprised patients with scores \# 40, whose probability of investigation was 3.5% (95% CI, 0-7.5), and the high-risk group comprised patients with scores > 60, whose probability was 67% (95% CI, 51-83).

**Validation Cohort**

The diagnostic performance characteristics and the probability that APN was applicable to our investigation at each probability-level group are listed. With a cut-off of 40, the sensitivity and specificity were 72% (95% CI, 51-84) and 100% (95% CI, 60-100) and the \( Lr^- \) was zero. A cut-off of 60 produced low sensitivity (50%, 95% CI, 19-81) and high specificity (94%, 95% CI, 90-100) and \( Lr^+ >16 \), indicating that patients with at least four
to six of the nine independent criteria had a high probability of APN applicable to our investigation
Fig. 1: A 36-year-old woman with acute pyelonephritis (APN), fever, and pyuria over 5 days. Early excretory phase computed tomography (CT) scan through the right kidney shows wedge shaped hypoattenuation, global enlargement of the kidney, obliteration of perinephric fat, obliteration of the renal sinus, and a small focal abscess.

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Fig. 2: A 44-year-old woman with APN and underlying diabetes. Early excretory phase CT scan through the left kidney shows global enlargement of the kidney, obliteration of perinephric fat, pelvicalyceal wall thickening and enhancement, pyonephrosis, and relatively decreased enhancement compared to that in the normal right kidney.

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Fig. 3: Receiver operating characteristic (ROC) curve for the acute pyelonephritis (APN) score.

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Conclusion

we developed a simple diagnostic score based on nine reproducible criteria to assist in triaging patients with APN who deteriorate with treatment. This easy-to-calculate score may prove useful for diagnosing patients with serious APN who deteriorate with treatment.
References


