

Won Sik Dho¹, Kyeong Jae Lee¹, Mu Su Kim¹, Sungchul Huh^{1,2*}Department of Rehabilitation Medicine, Pusan National University Yangsan Hospital¹
Department of Rehabilitation Medicine, Pusan National University School of Medicine²

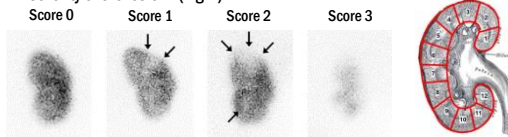
Introduction

- Renal scarring not only deteriorates renal function, but also increases the risk of proteinuria, hypertension, and cardiovascular disease¹ (CVD).
- Early detection of renal scar could reduce the risk of such complications.
- In scarred kidney, hyper filtration of remnant nephrons affects selective permeability, leading to renal disease and segmental ischemia with increased renin secretion result in hypertension².
- Aim of this study is to identify the factors of risk and severity of renal scarring in spinal cord injury (SCI) patients and to assess whether cystatin C can be a useful marker for detecting renal scar in SCI patients.

Method

- Imaging studies

- The gold standard for evaluating renal parenchymal involvement is 99m Tc-dimercaptosuccinic acid³ (DMSA).
- DMSA grading system of Ziessman and Majd was used to quantify the severity of the lesion⁴ (Fig. 1).

Figure 1. DMSA grading system of Ziessman and Majd⁴

- Voiding cystourethrography (VCUG) was conducted to identify vesicoureteral reflux and bladder trabeculation.

- Variables

- Urodynamic study was conducted to identify the urodynamic parameters, such as detrusor overactivity (DO), detrusor function during voiding phase, types of DO, detrusor external sphincter dyssynergia (DESD), bladder compliance, maximum cystometric capacity (MCC), maximum detrusor pressure (MDP) and detrusor leak point pressure (DLPP).
- UTI frequency was counted according to McGeer's criteria⁵.
- Onset to scar refers to the time from onset to confirmation of renal scars by DMSA scan.

- Statistical analyses

- Student's t-test was done for continuous variables with a normal distribution, Mann-Whitney U tests for continuous variables with a skewed distribution, and Pearson's chi-squared test for categorical variables to assess the differences and correlations between groups.
- Renal scarring risk factors were evaluated by forward selection multivariate regression analysis.
- Odds ratio (OR) was determined for analysis of renal scarring risk factor, with 95% confidence interval (CI).
- A receiver operating characteristic (ROC) / area under the curve (AUC) was drawn by plotting the sensitivity versus the specificity and Youden's J statistic was used to determine the cut-off value of serum cystatin C for the renal scar prediction.

Result

- Frequency of UTI, DO, MDP and bladder compliance were significantly higher in patients with renal scar than in patients without renal scar ($p < 0.05$).
- Four variables were included in multivariate regression analysis; UTI frequency, DO, MDP and bladder compliance.
- After adjustment by multivariate analysis, UTI frequency [OR=2.14, 95% CI 1.51-3.20, $p < 0.001$] found to be the strongest risk factor.
- UTI frequency was the only factor that showed a significant difference between subgroups categorized by the severity of scarring.
- At a cut-off value of 1.05 mg/l, the ROC/AUC analysis demonstrated a sensitivity of 46 % and specificity of 69 % (AUC=0.594).

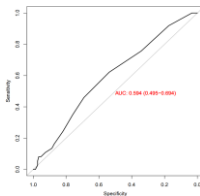


Figure 2. ROC curve showing the sensitivity and specificity of serum cystatin C for diagnosing renal scar at cut-off value of 1.05 mg/l

Table 1. Comparison of patients with and without renal parenchymal scarring

| | Renal scar (+) (n=37) | Renal scar (-) (n=149) | p-value |
|------------------------------------|-----------------------|------------------------|---------|
| UTI frequency | 1.00 [0.0-3.0] | 0.00 [0.0-1.0] | 0.001 |
| VUR | | | 0.498 |
| Normal | 37 (100.00%) | 94 (63.10%) | |
| Grade 1 | 0 (0.00%) | 29 (19.46%) | |
| Grade 2 | 0 (0.00%) | 18 (12.08%) | |
| Grade 3 | 0 (0.00%) | 8 (5.36%) | |
| DO | | | 0.047 |
| Normal | 21 (56.76%) | 110 (73.83%) | |
| DO (+) | 16 (43.24%) | 39 (26.17%) | |
| DO type | | | 0.084† |
| Normal | 21 (56.76%) | 110 (73.83%) | |
| Phasic DO | 10 (27.03%) | 16 (10.74%) | |
| Terminal DO | 4 (10.81%) | 10 (6.71%) | |
| Sustained DO | 2 (5.41%) | 12 (8.05%) | |
| Compound DO | 0 (0.0%) | 1 (0.67%) | |
| Compliance (ml/cmH ₂ O) | 135.00 [14.7-380.0] | 270.00 [22.60-500.0] | 0.044 |
| MCC (ml) | 420.00 [230.0-500.0] | 470.00 [300.00-600.0] | 0.133 |
| Detrusor function | | | 0.280† |
| Normal | 3 (8.11%) | 4 (2.68%) | |
| Underactive detrusor | 10 (27.03%) | 40 (26.85%) | |
| Acontractile detrusor | 24 (64.86%) | 105 (70.47%) | |
| DESD | | | 0.477 |
| Normal | 24 (64.86%) | 108 (72.48%) | |
| DESD (+) | 13 (35.14%) | 41 (27.52%) | |
| Maximum detrusor pressure | 17.00 [6.0-36.0] | 9.00 [2.0-27.0] | 0.046 |
| DLPP | 18.00 [15.0-42.0] | 34.00 [25.5-40.0] | 0.231 |
| Onset to test (months) | 7.00 [2.0-48.0] | 5.00 [2.0-57.0] | 0.626 |
| Trabeculation | | | 0.249 |
| Normal | 21 (56.76%) | 102 (68.46%) | |
| Trabeculation (+) | 16 (43.24%) | 47 (31.54%) | |
| Voiding method | | | 0.092 |
| Self-voiding | 8 (21.62%) | 60 (40.27%) | |
| Indwelling catheter | 17 (45.95%) | 57 (38.26%) | |
| CIC | 12 (32.43%) | 32 (21.48%) | |

UTI: urinary tract infection, VUR: vesicoureteral reflux, DO: detrusor overactivity, MCC: maximum cystometric capacity, DESD: detrusor external sphincter dyssynergia, CIC: clean intermittent catheterization, DLPP: detrusor leak point pressure, Values are given as median [Range]. †: Fisher's exact test

Table 2. Comparison of patients with renal parenchymal scarring according to the scar grade

| | Mild scar (n=15) | Moderate scar (n=38) | Severe scar (n=12) | p-value |
|------------------------------------|------------------|----------------------|--------------------|---------|
| UTI frequency | 0.60 ± 0.91 | 1.27 ± 1.62 | 1.51 ± 1.73 | 0.001 |
| DO | | | | 0.104† |
| Normal | 8 (53.33%) | 9 (81.82%) | 4 (36.36%) | |
| DO (+) | 7 (46.67%) | 2 (18.18%) | 7 (63.64%) | |
| DO type | | | | 0.211† |
| Normal | 8 (53.33%) | 9 (81.82%) | 4 (36.36%) | |
| Phasic DO | 4 (26.67%) | 1 (9.09%) | 5 (45.45%) | |
| Terminal DO | 1 (6.67%) | 1 (9.09%) | 2 (18.18%) | |
| Sustained DO | 2 (13.33%) | 0 (0.0%) | 0 (0.0%) | |
| Compliance (ml/cmH ₂ O) | 21 [12-345] | 210 [80-465] | 135 [19-257] | 0.135 |
| MCC (ml) | 310 [250-460] | 500 [365-590] | 420 [180-500] | 0.162 |
| Detrusor function | | | | 0.065† |
| Normal | 2 (13.33%) | 1 (9.09%) | 0 (0.0%) | |
| Underactive detrusor | 1 (6.67%) | 3 (27.27%) | 6 (54.55%) | |
| Acontractile detrusor | 12 (80.00%) | 7 (63.64%) | 5 (45.45%) | |
| DESD | | | | 0.123† |
| Normal | 8 (53.33%) | 10 (90.91%) | 6 (54.55%) | |
| DESD (+) | 7 (46.67%) | 1 (9.09%) | 5 (45.45%) | |
| Maximum detrusor pressure | 18.0 [13.5-30.5] | 10.0 [6.0-24.5] | 21.0 [8.5-45.0] | 0.417 |
| DLPP | 22.0 ± 12.0 | 36.5 ± 13.1 | 29.2 ± 18.7 | 0.301 |
| Onset to test (months) | 7.0 [1.5-36.5] | 2.0 [1.5-6.0] | 25.0 [5.5-113.0] | 0.155 |
| Trabeculation | | | | 0.086† |
| Normal | 5 (33.33%) | 8 (72.73%) | 8 (72.73%) | |
| Trabeculation (+) | 10 (66.67%) | 3 (27.27%) | 3 (27.27%) | |
| Voiding method | | | | 0.619† |
| Self-voiding | 4 (26.67%) | 1 (9.09%) | 3 (27.27%) | |
| Indwelling catheter | 5 (33.33%) | 7 (63.64%) | 5 (45.45%) | |
| CIC | 6 (40.00%) | 3 (27.27%) | 3 (27.27%) | |

UTI: urinary tract infection, DO: detrusor overactivity, MCC: maximum cystometric capacity, DESD: detrusor external sphincter dyssynergia, CIC: clean intermittent catheterization, DLPP: detrusor leak point pressure, Values are given as mean ± SD (standard deviation) and median [Range]. †: Fisher's exact test

Conclusion

- Frequency of UTI, MDP, DO and bladder compliance are important factors for renal scarring, with UTI being the riskiest factor among them.
- Routine monitoring of urodynamic parameters and early detection of UTI history may provide us with an opportunity to prevent the renal scar which may result in kidney function deterioration, hypertension, and CVD.
- However, the exact threshold of UTI frequency, MDP and bladder compliance leading to renal scarring has not been confirmed.

References

- Nakaya Hooman, The prevalence of hypertension and cardiovascular risks in children with renal scars secondary to urinary tract infection, Paediatrica Croatica, 2015
- Young Seo Park, Renal scar formation after urinary tract infection in children. Korean J Pediatr, 2012
- Hains DS. Etiopathogenesis of renal scars in children with vesicoureteral reflux: a pilot study. Kidney Int Rep, 2017
- Tej K. Intraobserver Variability for Interpretation of DMSA Scans in the RIVUR Trial. J Pediatr Urol, 2017
- T Anne, Diagnosis and Management of Urinary Tract Infection in Older Adults, Infect Dis Clin North Am, 2014

