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Development of upper tract stones in patients with congenital neurogenic bladder

Heidi A. Stephany*, Douglass B. Clayton, Stacy T. Tanaka, John C. Thomas, John C. Pope IV, John W. Brock III, Mark C. Adams

Division of Pediatric Urology, Monroe Carell Jr. Children's Hospital at Vanderbilt, 4102 Doctors' Office Tower, 2200 Children's Way, Nashville, TN 37232-9820, USA

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Abstract *Objective:* Patients with neurogenic bladder are at increased risk of developing upper tract stones. We hypothesized that patients with lower urinary tract stone disease are at greater risk of developing upper tract stones.
Methods: We performed a 10-year retrospective case—control study of patients with neurogenic bladder to determine the association between bladder and upper tract stones. Independent risk factors for upper tract stones were assessed. Cases and controls were matched 1:1. Univariable analysis was performed by Fisher's exact test and the Mann—Whitney *U* test. Multivariable logistic regression was performed.
Results: 52 cases and controls were identified. Cases were significantly more likely to be non-ambulatory, have bowel—urinary tract interposition, thoracic level dysraphism, and history of bladder stones. On multivariable analysis, independent predictors of stone formation were male sex (OR 2.82; $p = 0.02$), dysraphism involving the thoracic spine (OR 3.37; $p = 0.014$) bowel—urinary tract interposition (OR 2.611; $p = 0.038$), and a history of bladder stones (OR 3.57; $p = 0.015$).
Conclusion: Patients with neurogenic bladder are at increased risk for upper tract stones. The presence of bladder stones may herald the development of upper tract stones. The predictors of stone disease identified should guide prospective studies to better understand the natural history of upper tract stone development in this population.

Abbreviations: LUTR, Lower urinary tract reconstruction; SD, Synthetic Derivative; PCNL, Percutaneous nephrolithotomy.

* Corresponding author. Tel.: +1 615 936 1060; fax: +1 615 936 1061.
E-mail addresses: heidi.stephany@gmail.com (H.A. Stephany), douglass.b.clayton@vanderbilt.edu (D.B. Clayton), stacy.tanaka@vanderbilt.edu (S.T. Tanaka), john.thomas@vanderbilt.edu (J.C. Thomas), john.pope@vanderbilt.edu (J.C. Pope), john.brock@vanderbilt.edu (J.W. Brock), mark.adams@vanderbilt.edu (M.C. Adams).

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Introduction

Patients with congenital neurogenic bladder, from disorders including spina bifida and caudal regression, are high risk for urologic disease. The main urologic objectives for all patients with neurogenic bladder are to protect bladder health and compliance, preserve renal function, and achieve urinary continence, when appropriate. Lower urinary tract reconstruction (LUTR) utilizing various bowel segments has played an important role in protecting the upper urinary tracts and improving bladder continence in these patients [1,2]. LUTR does not come without recognized risks, including metabolic imbalances, augment perforation, tumor formation, and bladder calculi [3].

The incidence of bladder calculi in patients with an augmented bladder varies greatly between studies with reported rates as high as 50% in the early 1990s and between 10% and 15% in more recent analyses [3–6]. Anecdotally, we noted that patients with congenital neurogenic bladder and a history of bladder calculi seemed to have a greater propensity for upper tract stones than those without. We hypothesized that the presence of bladder calculi increases the risk of developing upper urinary tract stones in these patients. Our primary study endpoint was to determine if bladder calculi independently predict upper urinary tract stone development. The secondary study endpoint was twofold: 1) to identify overall risk factors associated with upper urinary tract stone development and; 2) characterize the stone burden seen in patients with congenital neurogenic bladder.

Materials and methods

Following Institutional Review Board approval, a retrospective case–control study was performed. A unique institution-specific database, Synthetic Derivative (SD), was used to identify a population of interest and potential study subjects. The SD is a de-identified image of the Vanderbilt electronic medical record and is fully compliant with the administrative, physical, and technical provisions of the HIPAA Security and Privacy Rules [7]. The SD contains ~2 million total records and incorporates data from multiple sources and includes diagnostic and procedure codes (ICD-9 and CPT), basic demographics (age, gender, race), and text from clinical care. All clinical data are updated regularly, thus providing a suitable resource for mining information relative to disease progression over time. Identification of patients with spina bifida or caudal regression was accomplished searching the SD using 11 unique ICD-9 codes for myelomeningocele (741–741.93) combined with the keyword "stone". Search results were restricted to the years 2001 through 2011. The population of interest was narrowed to the initial data set using the following inclusion criteria: 1) confirmed diagnosis of spina bifida or caudal regression; 2) outpatient urology visits or in-patient urology consultation in the last 10 years; 3) >24 months of urology-specific follow-up; and 4) age >5 years at last urology visit. Cases were selected from the initial data set and were defined as patients with upper urinary tract stones confirmed radiographically by reviewing reports of computed tomography, renal ultrasound, plain film radiography and/or intravenous pyelogram. Review of actual radiologic imaging was not possible using the SD. Controls were selected from the initial data set randomly and matched in a 1:1 fashion with cases using age at last urologic follow-up as the sole selection criteria. A 1:2 case to control matching was attempted but resulted in significant differences in age at last follow-up. Therefore, an upper limit of age was not set and the 1:1 matching strategy allowed length of follow-up and patient age at last visit to be nearly identical in cases and controls.

Data collection included date of birth, sex, race, level of dysraphism according to radiographic studies and/or neurosurgical clinical documents, ambulatory status at last follow-up, ambulatory status at the time of stone development, and ventriculoperionteal shunt status. Ambulatory status was dichotomized as either non-ambulatory (including wheelchair bound or bedridden) or ambulatory (including walking unassisted or walking with an assist device). Clinical rehabilitation notes were primarily used to make this distinction. Bladder stone formation was defined as a previous documented history of bladder stones and/or a confirmed bladder stone at our center by radiography or cystoscopy. Bladder management was determined at last follow-up in cases and controls and also at the time of stone development in cases. Care was taken to determine the management strategy according to the status of the lower urinary tract (i.e. native unreconstructed bladders vs. bowel–urinary tract interposition versus non-bowel urinary diversion).

Stone burden was characterized by collecting information about stone events in the 52 cases. A stone event was defined as a clinically separate stone(s) requiring evaluation and/or treatment. Stone burden variables included age at first upper tract stone at Vanderbilt, maximal single diameter of entire stone burden at the time of the event, bilaterality of stone disease, and surgical interventions required.

Study data were collected and managed using REDCap electronic data capture tools hosted at Vanderbilt University. REDCap (Research Electronic Data Capture) is a secure, web-based application designed to support data capture for research studies providing: 1) an intuitive interface for validated data entry; 2) audit trails for tracking data manipulation and export procedures; 3) automated export procedures for seamless data downloads to common statistical packages; and 4) procedures for importing data from external sources. The Vanderbilt Institute for Clinical and Translation Research provided support for REDCap and the Synthetic Derivative (1 UL1 RR024975 from NCRR/NIH) [8].

Statistical analysis was performed using Prism 5.0 (GraphPad Software, La Jolla, CA, USA) and SPSS 21 (IBM, New York, NY, USA). Descriptive statistics were generated using Fisher's exact test for categorical data and the Student's *t* test for continuous data. Odds ratios for potential risk factors for upper urinary tract stone development were evaluated in a univariate fashion using Fisher's exact test reporting *p* values and the 95% CI. Multivariable logistic regression was used to identify factors significantly associated with upper tract stone disease. Model variables were all dichotomous, including the dependent outcome variable. A p value <0.05 was determined significant for all tests.