OBJECTIVE  
To better understand why children born with cloacal anomalies are at a high risk of renal insufficiency, this study aims to determine baseline renal volume in children with cloacal anomalies compared to controls. We hypothesized children with cloacal anomalies would be born with less renal volume.

METHODS  
An IRB approved database of children with cloacal anomalies was reviewed. Controls were female patients with 2-vessel umbilical cord or preauricular tags who underwent screening renal ultrasound. Children were included if they had a renal ultrasound in the first 3 months of life. Cloacal exstrophy, horseshoe kidney and cross-fused ectopic kidneys were excluded. Total and individual kidney volumes were compared between the 2 groups.

RESULTS  
The study cohort consisted of 109 patients, 46 (42.2%) cloaca patients and 63 (57.8%) controls. In unadjusted analyses, average total renal volume for cloaca and control patients was 22.4 cm³ vs 25.5 cm³ respectively (P = .1006), and there was no significant difference when adjusting for age (P = .3915). The estimated difference in renal unit volume between cloaca patients without solitary kidneys and controls was −1.6 cm³ (95%CI: −3.6, 0.4; P = .1201), and there was no significant difference when adjusting for age (P = .4725). The age-adjusted difference in renal unit volume between cloaca patients with solitary kidney and controls was 1.8 cm³ (95%CI: −1.1, 4.8; P = .2148).

CONCLUSIONS  
Children with cloacal anomalies have similar baseline renal volumes as children without cloacal anomalies. Therefore, the increased risk of renal insufficiency in this patient population appears to be due to renal injury postnatally.  

P  
Persistence of the cloaca during development results in the rectum, vagina and urinary tract joining into a single common channel opening at the perineum. This complex female anomaly is the most severe form of anorectal malformation, with an estimated incidence of 1 in 50,000 births worldwide. Patients with cloacal anomalies commonly have urinary tract anomalies, such as vesicoureteral reflux, ectopic ureter and renal structural abnormalities. The most common renal structural abnormalities are solitary kidney, renal dysplasia and hydronephrosis, but other anomalies include pelvic kidney, cross fused ectopic kidney, horseshoe kidney, duplex kidney, and ureteropelvic junction obstruction.

In addition to urinary tract anomalies, patients with cloacal anomalies are at a high risk of renal insufficiency. Studies have shown that 44%-75% of patients with cloacal anomalies develop renal dysfunction. However, it is not known if the cause of renal dysfunction is iatrogenic, or if patients are born with less renal volume compared to patients without cloacal anomalies. Renal volume has been described as a surrogate for nephron mass in neonates, therefore the goal of this study was to measure baseline renal volumes in patients with cloacal anomalies and compare them to controls. We hypothesized that patients with cloacal anomalies would have lower baseline renal volumes.

MATERIAL AND METHODS  
Patients  
An IRB approved prospectively maintained database of children with cloacal anomalies treated at our institution was reviewed. Patients were included if they had a renal ultrasound within the first 3 months of life. Patients with cloacal exstrophy were excluded as were patients with horseshoe or cross-fused ectopic kidney due to the complexity of volume measurement. Control patients were females diagnosed with 2 vessel umbilical cord or preauricular tags, who had a screening renal ultrasound within the first 3 months of life. For all patients, the earliest renal ultrasound was reviewed, and renal volume was calculated using the formula for volume of an ellipsoid (length x width x AP...
Renal structural abnormalities were recorded including: solitary kidney, multicystic dysplastic kidney (MCDK), hydrenephrosis or hydroureteronephrosis, duplication, ectopic location, or renal dysplasia. Patients with a MCDK were considered to have a solitary kidney. For cloaca patients, the presence of hydrocolpos and hydrometrocolpos on ultrasound was recorded. Voiding cystourethrograms were reviewed to determine the presence of vesicoureteral reflux in cloaca patients.

Statistical Analysis
Continuous data were reported as medians and interquartile ranges, while categorical data were reported as frequencies and proportions. Fisher’s exact test and Wilcoxon Mann Whitney test were used to determine differences between patients with cloaca and control patients. Demographic information such as race, ethnicity, and insurance was missing for many of the patients and thus was not included in the final analyses. Differences in total renal volume between cloaca and control patients were first estimated among patients with 2 kidneys. In order to rule out the effects of compensatory hypertrophy in cases of a solitary kidney, differences in renal volume between cloaca and control patients were also estimated for average individual kidney volume. Boxplots were used to compare renal volume between cloaca and control patients while trying to minimize confounding by age. Cloaca patients with solitary or MCDK were excluded from the analyses of total renal volume, but included in the analysis of individual kidney volume. Generalized linear model was used to assess the relationship between the total renal volume of cloaca and control patients. Mixed linear models were used for all assessments involving individual renal volumes. Age was the covariate in all generalized and mixed linear models. Findings were determined to be statistically significant at \( P < 0.05 \). All statistical tests were conducted on SAS Enterprise version 8.1.

**RESULTS**
The study cohort consisted of 103 patients, 40 (38.8%) cloaca patients and 63 (61.2%) controls. On average, controls were older than cloaca patients (0.9 months [IQR: 0.2, 1.7] vs 0.0 months [IQR: 0.1, 1.4] respectively, \( P < 0.0001 \) (Table 1). In the cloaca group, 10 patients (25%) had solitary kidneys (5 had an MCDK). Renal structural abnormalities in the cloaca group are outlined in Table 1. Patients with cross fused ectopic kidneys \( (n = 4) \) and horseshoe kidneys \( (n = 2) \) were excluded prior to data analysis. Of those patients with hydrenephrosis \( (n = 21) \), 11 patients also had hydrourer. Of those cloaca patients with hydronephrosis \( (n = 12) \), 6 patients had hydrenephrosis and 6 had hydroureteronephrosis. Of those cloaca patients with hydrocolpos \( (n = 7) \), 2 patients had hydrenephrosis and 2 had hydroureteronephrosis. No patient in the control group had a solitary kidney or renal structural abnormality.

Since 25% of cloaca patients had a solitary kidney, individual renal volumes were compared among cloaca patients with a solitary kidney, cloaca patients with both kidneys and controls (Table 2). After adjusting for age, cloaca patients with solitary kidneys had significantly larger renal volume compared to controls \( (5.3 \text{ cm}^3, 95\% \text{CI: } -1.8 \text{ to } 8.7; P = .003) \), consistent with compensatory hypertrophy. Cloaca patients with 2 kidneys had similar renal volumes compared to controls \( (0.2 \text{ cm}^3, 95\% \text{CI } -1.7 \text{ to } 2.2; P = .8242) \). When patients were stratified by age, 

<table>
<thead>
<tr>
<th>Table 1. General characteristics</th>
<th>Overall Cohort ( (n =103) )</th>
<th>Cloaca ( (n =40) )</th>
<th>Controls ( (n =63) )</th>
</tr>
</thead>
<tbody>
<tr>
<td>*Age, months (median, IQR)</td>
<td>0.4 (0.0-1.4)</td>
<td>0.0 (0.0-0.3)</td>
<td>0.9 (0.2-1.7)</td>
</tr>
<tr>
<td>Female (%)</td>
<td>103 (100)</td>
<td>40 (100)</td>
<td>63 (100)</td>
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<tr>
<td>Diagnosis (%)</td>
<td></td>
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<tr>
<td>2 vessel cord</td>
<td>47 (45.6)</td>
<td>0 (0)</td>
<td>47 (74.6)</td>
</tr>
<tr>
<td>Cloaca</td>
<td>40 (38.9)</td>
<td>40 (100)</td>
<td>0 (0)</td>
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<tr>
<td>Ear tag</td>
<td>16 (15.5)</td>
<td>0 (0)</td>
<td>16 (25.4)</td>
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<tr>
<td>Solitary kidney</td>
<td>10 (9.7)</td>
<td>10 (25)</td>
<td>0 (0)</td>
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<tr>
<td>Renal Structural Abnormalities</td>
<td></td>
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<tr>
<td>Hydrenephrosis</td>
<td>21 (20.3)</td>
<td>21 (52.5)</td>
<td>0 (0)</td>
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<tr>
<td>Dysplastic</td>
<td>8 (7.8)</td>
<td>8 (20)</td>
<td>0 (0)</td>
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<tr>
<td>Duplicated</td>
<td>2 (1.9)</td>
<td>2 (5)</td>
<td>0 (0)</td>
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<tr>
<td>Ectopic</td>
<td>1 (1.3)</td>
<td>1 (2.5)</td>
<td>0 (0)</td>
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<tr>
<td>Vesicoureteral Reflux (%)</td>
<td>18 (17.5)</td>
<td>18 (45)</td>
<td>0 (0)</td>
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<tr>
<td>Hydrometrocolpos (%)</td>
<td>12 (11.7)</td>
<td>12 (30)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Hydrocolpos</td>
<td>7 (6.8)</td>
<td>7 (17.5)</td>
<td>0 (0)</td>
</tr>
</tbody>
</table>

* \( P < 0.0001 \)

| Table 2. Individual kidney volume \( (\text{cm}^3) \) for cloaca and control patients |
|-----------------------------------------------|-----------------------------------------------|-----------------------------------------------|
| Unadjusted                                    | Adjusted                                      |
| Cloaca                                        | Mean Volume \( (\text{cm}^3) \)                | Difference (95%CI)                             | \( P \) Value |
|                                              | Mean Volume \( (\text{cm}^3) \)                | Difference (95%CI)                             | \( P \) Value |
| Yes                                           |                                              |                                              |                |
| Solitary Kidney n (Kidney Units)              |                                              |                                              |                |
| Yes \( n = 10 \)                              | 16.1                                          | 3.3 (−0.4 to 7.0)                             | .0829          |
| No \( n = 60 \)                               | 12.0                                          | −0.8 (−2.9 to 1.3)                            | .4572          |
| Age (Months)                                  | Reference                                    |                                              |                |
| Yes \( n = 126 \)                             | 2.1 (1.7 to 2.6)                             | **<.0001**                                    |                |
| No Controls                                   | 12.4                                          | 2.3 (1.9-2.8)                                 | **<.0001**     |

Statistically significant \((P< 0.05)\).
**DISCUSSION**

Patients with cloacal anomalies are born with similar renal volumes as patients without cloacal anomalies. Renal volume has been described as a surrogate for nephron mass in neonates, therefore it can be deduced that cloaca patients are born with similar baseline renal function as controls. However on long term follow up of patients with normal nadir serum creatinine, 66% subsequently developed renal failure. The cause of renal insufficiency in patients with cloacal anomalies is most likely attributed to renal insult after birth. Retrospective reviews have demonstrated that independent predictors of chronic renal failure in cloaca patients include vesicoureteral reflux, renal dysplasia, new renal scarring and solitary kidney. A quarter of cloaca patients in our cohort had a solitary kidney and those with solitary kidney had larger renal volume compared to controls, consistent with compensatory hypertrophy.

| Table 3. Individual kidney volume (cm³) for hydrocolpos/hydrometrocolpos among cloaca patients |
|---------------------------------------------|---------------------------------|------------------------|------------------------|-----------------|-----------------|-----------------|-----------------|
| Hydrocolpos / hydrometrocolpos | Solitary Kidney | n (Kidney Units) | Mean Volume (cm³) | Difference (95%CI) | P Value | Mean Volume (cm³) | Difference (95%CI) | P Value |
| Yes | Yes | 3 | 13.3 | 0.5 (−8.0 to 9.1) | .8986 | 12.2 | 1.8 (−6.4 to 10.0) | .6555 |
| | No | 32 | 13.1 | 2.3 (−1.9 to 6.6) | .2721 | 13.2 | 2.8 (−1.2 to 6.8) | .1630 |
| No (No Hydrocolpos) | Yes | 7 | 18.1 | 7.4 (1.3 to 13.4) | .0192 | 18.7 | 8.3 (2.6-14.1) | .0063 |
| | No | 28 | 10.7 | Reference | – | 10.4 | Reference | – |
| Age (Months) | | | 1.7 (0.8 to 2.5) | .0544 | |
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Since cloaca patients with solitary kidney are more likely to experience chronic renal failure, this is likely due to a renal insult later in life and not because of renal maldevelopment in utero. Surprisingly, cloaca patients with hydrocolpos or hydrometrocolpos, had similar renal volumes compared to cloaca patients with 2 kidneys, indicating that in utero obstruction related to hydrocolpos or hydrometrocolpos may not negatively impact renal size. When looking at only hydronephrosis, those cloaca patients with hydronephrosis had larger renal volume compared to cloaca patients without hydronephrosis. The presence of hydronephrosis will result in larger renal volumes due to expansion of the renal unit and therefore this larger renal volume does not necessarily correlate to better function but what would be expected to see with this renal anomaly.

There are several limitations to this study. Renal ultrasounds were performed by more than 1 technician and there is the possibility that true kidney measurements are underestimated. However, all renal volumes were calculated by a single study member to ensure there was consistency in volume measurements. Imaging modalities such as nuclear renal scan or MRI may provide more accurate assessment of renal volume than ultrasound. However renal ultrasound is readily available, cost effective, and allows for the opportunity to compare to controls. Another limitation is that only renal size was measured and not renal function, but as mentioned earlier, renal size has previously been described as a surrogate for renal function. Ideally, functional MRI or nuclear scan would be used to measure renal function but these are more invasive tests and are not routinely available for controls. We did not assess follow up ultrasound images in cloaca patients or controls to see if sizes remained similar as patients grew older. Additionally, for this study, children with horseshoe or cross fused ectopic kidneys were excluded due to difficulty measuring renal volume on ultrasound, so there is the chance that this may not be an accurate assessment of renal volume for cloaca patients.

CONCLUSIONS

Children with cloacal anomalies have similar baseline renal volumes on ultrasound as children without cloacal anomalies. Although it is known that patients with cloacal anomalies are at higher risk for renal insufficiency, this is the first study to our knowledge that attempts to understand this further and demonstrates that since cloaca patients are born with similar renal volumes compared to controls, that the risk of renal insufficiency is due to a renal insult after birth. Future studies are needed to determine if early proactive management of the urinary tract can impact the long term renal outcomes for these patients.

SUPPLEMENTARY MATERIALS

Supplementary material associated with this article can be found in the online version at https://doi.org/10.1016/j.jurology.2020.08.010.

References