

How Dry is Dry? A Review of Definitions of Continence in the Contemporary Exstrophy/Epispadias Literature

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Abbreviation and Acronym

ICCS = International Children's Continence Society

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Purpose: Definitions of continence following surgery in children with exstrophy-epispadias complex vary widely. We assessed the most common definitions of continence and evaluated the clinical significance of usage patterns for those definitions.

Materials and Methods: We searched MEDLINE and EMBASE (2000 to 2011) for English language reports describing postoperative continence outcomes in children with exstrophy-epispadias complex. Articles were evaluated and data were abstracted by 2 reviewers. We assessed patient level factors such as age, preoperative diagnoses and use of additional therapies, as well as study level factors such as continence definition(s), country of origin and method of data collection.

Results: We identified 884 articles, of which 87 met inclusion criteria. In total these studies included continence outcomes data on 2,681 patients (57% male). Only 59 studies (68%) clearly defined the term "continence." The most common definition of continence was dry with voiding/catheterization every 3 hours (used in 23 studies, or 39%, defining continence). There was no association between publication date ($p = 0.17$), study location ($p = 0.47$) or study size ($p = 0.81$) and continence definition. There was a trend toward improved reporting of methods for continence ascertainment in more recent years ($p = 0.02$). Of the 2,681 children included 1,372 (51%) were dry by the definition used in their study.

Conclusions: The most frequent definition of continence was "dryness with voiding or catheterization at 3-hour intervals." However, definitions were highly variable and many authors did not define continence at all. To better define outcomes, we recommend that a standardized definition of continence be established and used in future reports.

Key Words: bladder exstrophy, epispadias, pediatrics, urinary incontinence, urology

THE exstrophy-epispadias complex represents a constellation of congenital anomalies of the lower abdominal wall, bladder, bony pelvis and external genitalia occurring when the abdominal wall fails to close appropriately during fetal development. Surgical treatment of exstrophy-epispadias has evolved continuously during the last 50 years.¹

However, despite advances in treatment, children affected by this condition often require multiple surgical interventions to optimize their quality of life.² In particular, children with exstrophy-epispadias are at significant risk for urinary incontinence, even following surgery to achieve continence.³ Continence outcomes are frequently

discussed in the exstrophy-epispadias literature, given that better urinary control has been correlated with improved social function in childhood and later in life.⁴ However, definitions of urinary continence following surgery among children with exstrophy-epispadias complex vary widely across studies.

A standardized definition of dryness is needed to better assess outcomes.⁵ The ICCS has offered definitions of urinary incontinence in an effort to standardize the terminology used to describe lower urinary tract function in children, with the express goal of generating a single nomenclature for research purposes.⁶ According to ICCS guidelines, incontinence is defined as “uncontrollable leakage of urine.” However, the guidelines do not define continence or dryness, and specifically the means by which continence is achieved. If a child can only be kept dry by frequent catheterization, medication use or urinary diversion, is that child truly continent? In addition, there is no general consensus on what methods researchers should use to assess continence. Should the patients or caregivers be asked directly instead of using surgeon reporting? Should a voiding diary be used?

Given the lack of consensus regarding definitions, it would seem that investigation into the standardization of continence definitions would be worthwhile. We reviewed definitions of urinary continence reported in the contemporary exstrophy-epispadias complex literature in an effort to assess the most common definitions used to describe continence and the most common methods by which authors determine continence rates.

PATIENTS AND METHODS

We searched the MEDLINE and EMBASE electronic databases for English language studies published between January 2000 and July 2011 based on Assessment of Multiple Systematic Reviews⁷ and Preferred Reporting Items for Systematic Reviews and Meta-Analyses⁸ guidelines. This date range was chosen to provide a contemporary selection of studies. We used the MeSH search terms “urinary incontinence” or “urinary” AND “incontinence.” The results were then restricted to articles retrieved under a second search for the MeSH terms “bladder exstrophy,” “exstrophy” or “epispadias.”

Selection Criteria

We reviewed all retrieved articles that assessed continence status in children 18 years or younger with bladder exstrophy, epispadias or cloacal exstrophy. No article was excluded based on study design, method of analysis, definition of success or perceived quality. We required that the number of patients treated and the fraction in whom the treatment was successful be reported and that all subjects in the study cohort meet our age requirements. For studies describing fecal and urinary continence rates we required that urinary continence be clearly delineated

separately from fecal continence. Reviews and meta-analyses that did not include a unique study population and instead aggregated data from other studies were excluded. In lieu of a formal ethics committee the principles of the Helsinki Declaration were followed.

Data Abstraction

Two reviewers (JCL, SMS) independently assessed study abstracts in parallel, with questions and disagreements resolved by consensus between the 2 reviewers. The full texts of articles appearing to meet selection criteria were reviewed and study data were abstracted. Abstracted data included country in which the study was performed, study period, study design, total number of patients, patient gender, patient age, underlying disorder, operations performed, duration of followup, definition of continence, method for determining continence, use of clean intermittent catheterization of the native urethra, use of anticholinergic medications or desmopressin analogues, and use of continent catheterizable channels. When authors did not provide sufficient information in their articles to complete our data set, we included the study but noted the missing data. In cases of ambiguity or where study reporting made evaluation difficult, we chose to err on the side of strictly interpreting the author intentions, rather than using inference that may have been mistaken. Our primary outcome of interest was the definition of continence used by various authors.

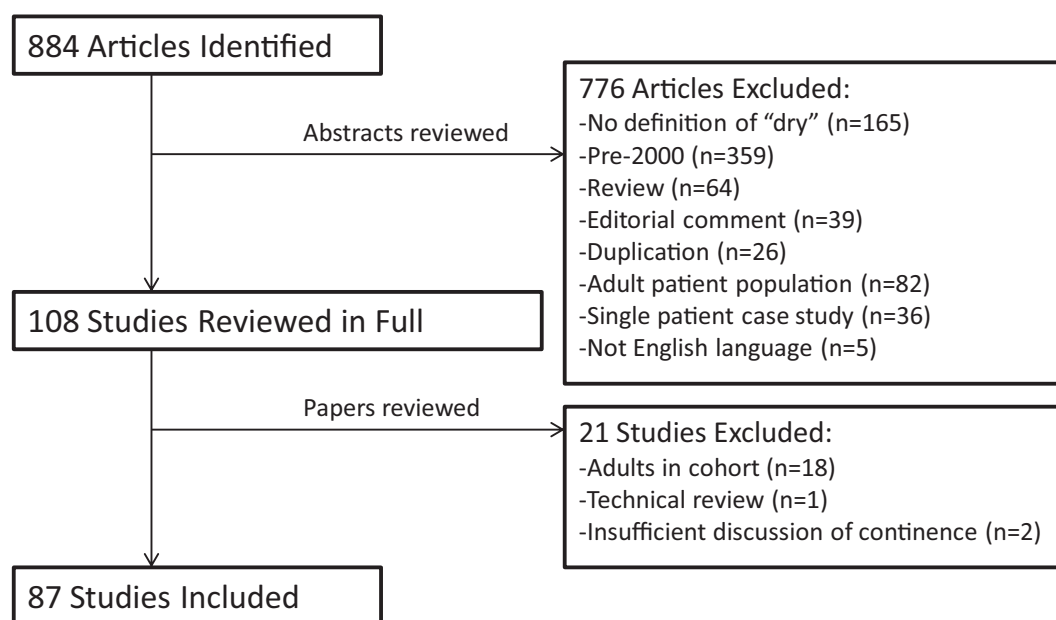
Statistical Analysis

We performed bivariate tests of association between predictor variables and study outcomes using the Fisher exact test, Mantel-Haenszel trend or Kruskal-Wallis test as appropriate based on data characteristics. Statistical analyses were performed using SAS®, version 9.2.

RESULTS

Our systematic review of the literature identified 884 abstracts. After our initial screening of abstracts and titles 108 studies were reviewed in full, and 87 studies met our inclusion criteria (see figure). In total, 23 countries were represented, with the United States (39%), United Kingdom (7%) and Egypt (7%) being the most frequent. Studies were almost universally case series (97%), with a small number of case-control studies (2%) and prospective cohort studies (1%). Mean \pm SD followup was 5.1 ± 3.4 years (median 4.2, range 0.7 to 18). Most studies were modest in size, with a mean \pm SD of 31 ± 25 patients (range 2 to 122) included. A total of 15 journals were represented, with the most frequent being *The Journal of Urology*® (51%). Of the 87 articles included 21 (24%) appeared to have crossover of patients with at least 1 other study.

Of the 2,681 patients included in this study 1,704 (64%) were diagnosed with classic bladder exstrophy, 242 (9%) with epispadias and 62 (2%) with cloacal exstrophy. An additional 241 patients (9%) were noted to have either bladder exstrophy or epispadias but the authors did not indicate the specific



Flow diagram of literature search and study review

pathology. Some studies included children with spina bifida, a history of pelvic trauma or other causes of bladder dysfunction, with these patients amounting to 16% of all subjects included. Of the subjects included 1,526 (69%) were male, although 9 studies did not differentiate patients by gender. Mean \pm SD age at enrollment was 5.8 ± 3.8 years (median 5.5, range 1 day to 14.5 years). Many children had undergone bladder and bladder neck procedures, including bladder augmentation (665, 25%), bladder neck reconstruction (1,360, 51%) and/or bladder neck closure (326, 12%), although, again, not all studies included these data.

Of the 87 articles included 10 (11%) described the use of medications to promote continence. In this subset of subjects 22% (62) required medications. At least 30 studies (34%) included patients with continent catheterizable stomas, whereas 48 authors (55%) did not include these patients. Nine studies (10%) did not provide this information. In those in which data were provided 544 children (20%) had stomas.

Of the 2,681 children included in the studies 1,372 (51%) were deemed continent by study authors. However, only 59 studies (68%) clearly defined what was considered to be continent. Definitions ranged from "always dry" (12 studies, 20%) to "dry with voiding/catheterization every 2 hours" (10, 17%), "dry with voiding/catheterization every 3 hours" (23, 39%), "dry with voiding/catheterization every 4 hours" (12, 20%), "use of security pads only" (1, 2%) and International Children's Continence Society definitions (1, 2%). The most commonly re-

ported definition of continence (23 studies, 39%) was "dry with voiding at 3-hour intervals" (table 1). Interestingly although all included studies referred to continence outcomes, 28 (32%) did not include a definition of continence. There was no association between publication date ($p = 0.17$), study location ($p = 0.47$) or study size ($p = 0.81$) and definition of continence.

The methods by which continence data were determined were less clear. Of the 87 studies reviewed 66 (76%) did not describe how continence status was ascertained (by patient report, parental report, voiding diary, etc). In studies that did characterize this aspect of data acquisition authors reported doing so by patient or family report (12 studies), survey (4), chart review (2), voiding diary (1) and pad weight (1). There was a trend toward improved reporting of methods for continence ascertainment in more recent years, with only 2 of 22 studies (9%) published between 2000 and 2002 describing the methodology,

Table 1. Reported definitions of continence

Definition	No. Studies (%)	% Studies Defining Continence
Always dry	12 (14)	20
Dry with voiding/catheterization every 2 hrs	10 (11)	19
Dry with voiding/catheterization every 3 hrs	23 (26)	39
Dry with voiding/catheterization every 4 hrs	12 (14)	20
Use of security pads only	1 (1)	2
Dry by ICCS definition	1 (1)	2
No definition given	28 (32)	Not applicable

Percentages may not equal 100 due to rounding.

compared to 10 of 23 (43%) published between 2009 and 2011 ($p = 0.02$ for trend, *table 2*).

DISCUSSION

The exstrophy-epispadias complex involves congenital urological anomalies that often require complicated reconstructive surgery and years of close urological followup. For urologists the primary goal in patients with exstrophy-epispadias complex is to achieve urinary continence. As such, continence outcomes are frequently discussed in the exstrophy-epispadias literature. However, definitions of continence across studies are highly variable. In our current analysis of 87 studies published since 2000 only 68% clearly defined the specific continence outcome used. The most common definition of continence was “dry with voiding/catheterization every 3 hours.” However, although all studies referenced continence outcomes, 32% of the included analyses did not define continence. This finding does not appear to be related to the study date, study location or study size. Overall, of the 2,681 children included in the studies 51% were dry by author definition.

Standardization of the definition of continence in the exstrophy-epispadias complex literature is essential. Only a uniform, standard definition will allow accurate comparisons between studies. Moreover, a single, widely accepted definition will increase the clinical usefulness and applicability of the exstrophy-epispadias literature, and allow researchers and clinicians to more readily apply these data to practice.

In other areas of medicine such variation has been noted to be problematic. There has been a strong trend toward standardized definitions, with a growing body of literature supporting the benefits of standardization.^{9–11} Additionally, numerous working groups have created reporting guidelines for the express purpose of making scientific literature more complete, clear and transparent.^{12–14} Because the population of children born with exstrophy-epispadias complex is quite small, being able to pool and

compare data across studies is particularly critical. Deficiencies in reporting, such as incomplete or selective reporting of outcomes, poor methodology descriptions or failure to clearly define outcomes (in this case continence), make this task even more challenging.¹⁵

Given that the ability to make informed clinical decisions depends in part on a high quality, knowledgeable comparison of research findings, standardization of reporting is vital and a standard for defining continence is long overdue. Based on our study, there are clear and significant discrepancies in the definition of continence among different researchers. Our results demonstrate that it is essential for all authors addressing continence outcomes in children with complex urological anomalies to clearly delineate their individual definition of continence. Indeed, given the pressure for timely, informed decisions in clinical practice and the explosion of information in the scientific literature, research results must be synthesized today more than ever. As such, standardization will continue to have an increasingly critical role in allowing accurate, meaningful comparisons of study results.¹³ Our analysis would seem to indicate an emerging trend in the definition of continence in the available exstrophy/epispadias literature, ie “dry with voiding/catheterization every 3 hours.” Therefore, we propose that this definition be used as the standard definition of continence in future studies. Alternatively a consensus definition should be developed by a multispecialty conference of pediatric urologists, patients and other stakeholders.

It is noteworthy that at least some of the children included in our analysis (22% of those in studies providing data) were taking medications to promote continence. Given the common use of prescription medications such as anticholinergics and desmopressin, we believe that our proposed definition of continence, “dry with voiding/catheterization every 3 hours,” should be used irrespective of medication use. Additionally 1 of the 89 studies we included measured pad weights, although the authors did not provide the numerical values of those pad weights.¹⁶ We are unaware of any preexisting pediatric guidelines for using pad weights to define continence in the exstrophy-epispadias population. As such, we hesitate to offer a strict pad weight benchmark.

Our review should be interpreted in light of its limitations. As with any systematic review, our analyses were limited by the data reported in the included studies. Published studies regarding continence outcomes in children with exstrophy/epispadias are predominantly case series, and their findings are rarely reported in a manner such that the data are readily amenable to comparison. Indeed, 32% of authors did not define continence at all, despite the fact that it was a measured study outcome.

Table 2. Studies describing method of continence ascertainment by year

	2000–2002	2003–2005	2006–2008	2009–2011	Totals
Not specified	22	16	13	13	64
Pt report	0	1	0	0	1
Pt or family report	0	0	6	6	12
Voiding diary	0	0	0	1	1
Pad wt	1	0	0	0	1
Survey	1	0	1	2	4
Chart review	0	0	1	1	2
Totals	24	17	21	23	85
Total providing specific ascertainment method	2	1	8	10	21

While some reviewers may have excluded these studies, we believe that drawing attention to this absence is meaningful to our work.

Of the 87 studies we evaluated 21 appeared to share a proportion of their subjects with at least 1 other study. Given the small number of patients with exstrophy-epispadias and the clinical need to follow them through time, it is not surprising that patients would be repeat sampled across studies at a given institution. In an analysis focusing on patient outcomes this practice would be quite worrisome, as outcomes at a given center could be overrepresented by patients who are serially sampled in repeat studies. However, our outcome was not a patient level factor, but rather the definitions authors used to define continence. Indeed, these definitions often did not agree across articles written by a single author at a single institution through time. Of the 7 distinct institutional series we identified only 2 used the same definition of continence in all of their studies. As such, we believe that the validity of our results did not suffer due to the inclusion of these studies.

We included some studies with subjects with exstrophy-epispadias complex as well as other urological conditions such as spina bifida, pelvic trauma and other causes of urinary incontinence. In total, 16% of the patients (432) included in our study suffered from these other conditions. Although these diagnoses were not our primary focus, the studies were included because excluding them would have essentially ignored the definitions of continence out-

comes in a large number of patients with exstrophy-epispadias in our cohort. Given the rarity of exstrophy-epispadias complex, we worried that valuable data would have been lost had we not included this minority of mixed population studies. In addition, our review attempts to capture data as presented to the reader by study authors. As such, if researchers find usefulness in grouping subjects with exstrophy-epispadias complex with other pediatric patients with voiding dysfunction, we believe we must work within the confines of the data we have been given.

Finally, we acknowledge that our decision to include only English language reports may have limited our search results. However, given the broad geographical representation of our included studies, it seems doubtful that excluding nonEnglish studies resulted in significant bias or that this decision meaningfully impacted our findings.

CONCLUSIONS

In the exstrophy-epispadias literature the most frequently used definition of urinary continence is “dryness with voiding or catheterization at 3-hour intervals.” However, reported definitions vary widely and nearly a third of authors fail to define continence. Given the importance of urinary continence to society in general, and to patients with congenital urological anomalies in particular, there is a clear need for increased standardization of definitions in the reporting of continence outcomes and continence ascertainment methods.

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