

available at www.sciencedirect.com
journal homepage: www.europeanurology.com



European Association of Urology



Platinum Priority – Infections
Editorial on pp. x–y of this issue

Irrigation of Continent Catheterizable Ileal Pouches: Tap Water Can Replace Sterile Solutions Because It Is Safe, Easy, and Economical

Frédéric D. Birkhäuser, Pascal Zehnder, Beat Roth, Leander Schürch, Katharina Ochsner, Rita Willener, George N. Thalmann, Fiona C. Burkhard, Urs E. Studer*

Department of Urology, University of Bern, Switzerland

Article info

Article history:

Accepted January 3, 2011
Published online ahead of
print on January 12, 2011

Keywords:

Continent urinary reservoir
Urinary tract infection
Irrigation
Isotonic solution
Water

Abstract

Background: Continent catheterizable ileal pouches require regular irrigations to reduce the risk of bacteriuria and urinary tract infections (UTIs).

Objective: Our aim was to compare the UTI rate, patient friendliness, and costs of standard sterile irrigation versus irrigation with tap water.

Design, setting, and participants: Twenty-three patients participated in a prospective randomized two-arm crossover single-center trial. Aseptic intermittent self-catheterization (ISC) combined with sterile sodium chloride (NaCl) 0.9% irrigation was compared with clean ISC and irrigation with tap water (H₂O) during two study periods of 90 d each.

Intervention: Patients underwent daily pouch irrigations with NaCl 0.9% solution or tap water.

Measurements: Urine nitrite dipstick tests were evaluated daily; urine culture (UC) and patient friendliness were evaluated monthly. Costs were documented.

Results and limitations: A total of 3916 study days with nitrite testing and irrigation were analyzed, 1876 (48%) in the NaCl arm and 2040 (52%) in the H₂O arm. In the NaCl arm, 418 study days (22%) with nitrite-positive dipsticks were recorded, 219 d (11%) in the H₂O arm, significantly fewer ($p = 0.01$). Of the 149 UCs, 96 (64%) were positive, 48 in each arm, revealing a total of 16 different germs. All patients preferred the H₂O method. Monthly costs were up to 20 times lower in the H₂O arm.

Conclusions: Pouch irrigation with sterile NaCl 0.9% solution and tap water had comparable rates of positive UC. Irrigation with tap water significantly lowered the incidence of nitrite-positive study days and was substantially less costly and more patient friendly than NaCl irrigation. We therefore recommend the use of tap water (or bottled water) instead of sterile NaCl 0.9% solution for daily irrigation of continent catheterizable ileal pouches.

Trial registration: Australian New Zealand Clinical Trials Registry, ACTRN12610000618055, <http://www.ANZCTR.org.au/ACTRN12610000618055.aspx>.

© 2011 European Association of Urology. Published by Elsevier B.V. All rights reserved.

* Corresponding author. Department of Urology, University Hospital of Bern, Inselspital, 3010 Bern, Switzerland. Tel. +41 31 632 3641; Fax: +41 31 632 2180.

E-mail address: urs.studer@insel.ch (U.E. Studer).

1. Introduction

For patients requiring urinary diversion, a continent catheterizable urinary reservoir can allow near normal physical integrity and a good quality of life. The need for intermittent self-catheterization (ISC), however, leads to an increased risk of bacteriuria [1]. To reduce the risk of urinary tract infections (UTIs) and mucus plug formation, daily pouch irrigation is recommended to eliminate microbes and evacuate the intestinal mucus [2]. Several studies have shown that the presence of mucus correlates with bacteriuria in patients with bladder substitutes or ileal conduits [3,4]. Pouch irrigation with a sterile solution (eg, isotonic saline or Ringer lactate solution) is considered standard.

A potential advantage of irrigation with tap water is its hypo-osmolarity. Levina et al showed that the exposure of *Escherichia coli* to a hypo-osmolar medium results in loss of viability and lysis of the microbes [5]. If tap water would prove to be as efficient at pouch irrigation as sterile solutions, it would likely be more patient friendly and less costly than sterile solutions. The aim of this study was to test this hypothesis.

2. Materials and methods

A consecutive series of 23 patients (3 men, 20 women; median age: 61 yr; range: 29–71 yr) with a continent catheterizable ileal pouch and no known preexisting chronic infection was randomized in a prospective two-arm crossover study. Patients were enrolled in the study a median of 38 mo (range: 3–121 mo) after pouch construction (Table 1). All patients gave written informed consent.

The surgical technique employed to construct the ileal pouch is similar to that used for orthotopic bladder substitution except for the outlet nipple [6]. An ileal segment of 54 cm resected 25 cm proximal to the ileocecal valve was used. The ureterointestinal anastomoses were performed refluxive according to the Nesbit technique into a 15- to 18-cm-long afferent tubular ileal segment. The nipple preferably was

Table 1 – Patient characteristics

Patients with continent catheterizable ileal pouch included, n (%)	23 (100)
Median age, yr (range)	61 (29–71)
Sex	
- Male, n (%)	3 (13)
- Female, n (%)	20 (87)
Reason for continent catheterizable ileal pouch	
- Malignant tumor, n (%)	16 (70)
- Neurogenic bladder dysfunction/pelvic pain syndrome, n (%)	4 (17)
- Bladder exstrophy, n (%)	2 (9)
- Trauma, n (%)	1 (4)
Median time from construction of pouch to beginning of study, mo (range)	38 (3–121)

formed using the appendix vermiformis. If absent, the ileum was reconfigured according to the Yang-Monti technique [7] or the fallopian tube was used instead and fixed to the umbilicus.

The two standardized irrigation techniques studied were aseptic ISC combined with sterile sodium chloride (NaCl) 0.9% irrigation and clean ISC combined with tap water (H₂O) irrigation. In general, the concentration of calcium (Ca⁺⁺) and magnesium (Mg⁺⁺) ions varies from 120 to 420 ppm, nitrate concentration from 1 to 28 mg/l, and pH from 6.9 to 7.7 in Swiss tap water [8].

The crossover from one study arm to the other took place after 90 d. Because of the need for continuous daily pouch irrigations, there was no washout period between study arms. Twelve patients started with NaCl irrigation and 11 with H₂O (Fig. 1). Each patient was asked to keep a diary documenting the results of the nitrite test. Every patient received written step-by-step procedural descriptions.

In NaCl-arm patients, the umbilicus was cleaned with a solution containing octenidine dihydrochloride and phenoxyethanol (Octenisept; Ionto-Comed, Karlsruhe, Germany). Self-catheterization was done using a sterile ready-to-use disposable hydrophilic-coated catheter (12–14F; length: 20 cm; SpeediCath [Coloplast, Humlebaek, Denmark] Easy Cath [Rusch, Teleflex Medical Co, Kenosha, WI, USA]). The pouch was irrigated three times using a sterile 60-ml syringe with sterile NaCl 0.9% solution. In H₂O-arm patients, the umbilicus was cleaned with tap water. Catheters

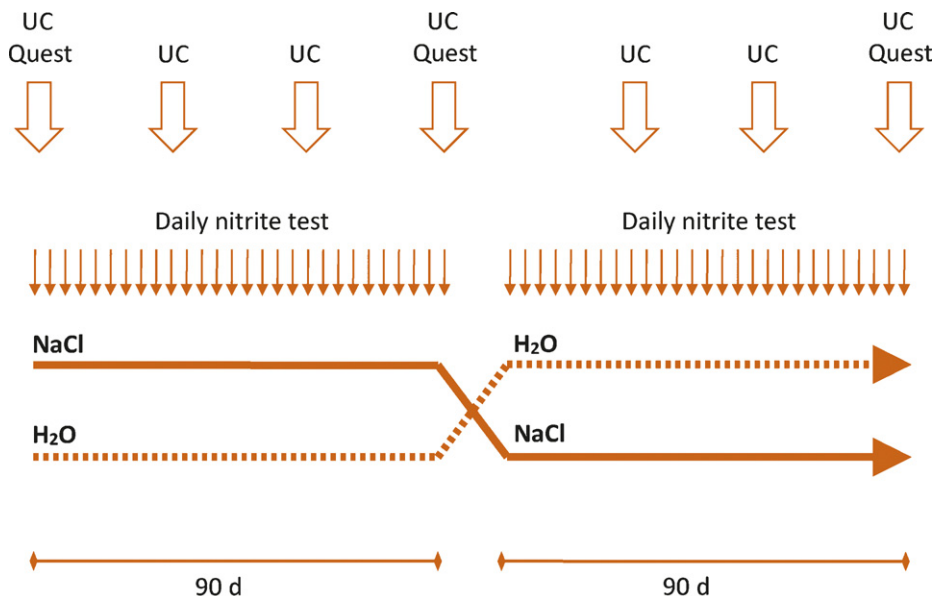


Fig. 1 – Study design of the two-arm crossover study. NaCl = sodium chloride 0.9% solution; H₂O = tap water; Quest = questionnaire; UC = urine culture.

and syringes were used up to five times after cleaning with tap water and drying at room temperature. The remainder of the procedure was the same as for the NaCl arm except tap water replaced the NaCl 0.9% solution.

At first catheterization in the morning, patients in both arms were instructed to let the outflowing urine pass directly over a dipstick (Combur 4 Test N; Roche Diagnostics, Basel, Switzerland) to test for nitrite positivity. In case of nitrite negativity, ISC was repeated at 4-h intervals. In case of nitrite positivity, the nitrite test and irrigation were repeated at the next catheterization until nitrite testing became negative. A nitrite-positive study day was defined as a day with one or more nitrite-positive tests; a nitrite-negative study day was defined as a day with a negative nitrite test in the morning. Urine culture (UC) was defined as positive if any number of bacteria was detected (bacteriuria) and as negative when no bacterial growth was detected. A symptomatic UTI was defined as a nitrite-positive dipstick test and positive UC accompanied by symptoms such as fever or abdominal discomfort. In case of symptomatic UTI, antibiotic treatment was prescribed. UC were collected at enrolment and at monthly intervals. Nitrite test results, UC collections, and any antibiotic treatments were prospectively documented in the patient's diary.

At the beginning and after completion of each 90-d study arm, patient friendliness was assessed by a specific questionnaire with six questions. Due to lack of specificity, validated quality-of-life questionnaires could not be used. Monthly costs of the material used during each study period included expenses for catheters and syringes and, in the NaCl arm, Octenisept and NaCl 0.9% solution.

All statistical analyses were performed by the Institute of Mathematical Statistics and Actuarial Science of the University of Bern, Switzerland. The nonparametric approach was used for statistical analysis of the crossover design. Comparison of the nitrite test results for the two arms was done with the Mann-Whitney test (with exact *p* values) applying the nonparametric confidence interval of Hodges and Lehmann [9]. The paired data of the antibiotic analysis were calculated with the Wilcoxon sign-rank-test. The patient friendliness questionnaires were evaluated using the Mann-Whitney test (with exact *p* values). We assumed that no carryover effect occurred.

3. Results

All 23 patients completed both 90-d study periods except for 2 patients who refused the crossover to NaCl after the first study period with H₂O.

A total of 3916 (100%) study days were analyzed, 1876 d (48%) in the NaCl arm and 2040 d (52%) in the H₂O arm. There were 418 (22%) nitrite-positive days in the NaCl arm

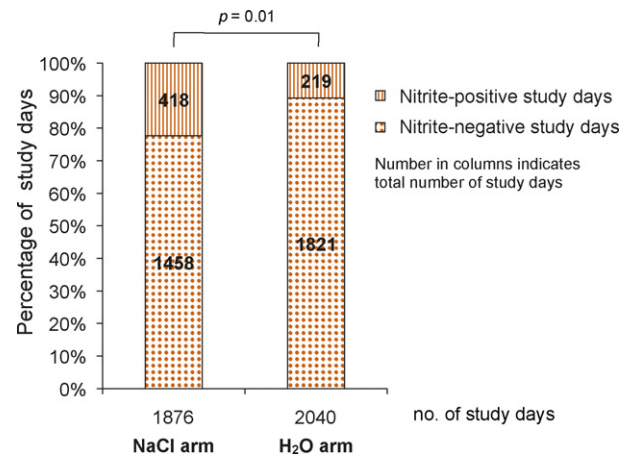


Fig. 2 – Percentage of nitrite-positive and nitrite-negative study days as determined by daily nitrite testing of urine.

and 219 (11%) in the H₂O arm, a significant difference (*p* = 0.01; 95% confidence interval, 0.03–0.26) (Fig. 2).

Of the 149 (100%) routinely collected UCs, 96 (64%) tested positive and 53 (36%) tested negative. Due to the different number of study days in the two arms, the ratio of positive UCs to the number of study days was 1 per 39 d in the NaCl arm and 1 per 43 d in the H₂O arm. There were also no statistically significant differences for positive UC at the level of both $\geq 10^4$ and $\geq 10^5$ colony forming units (CFU) per milliliter between the two arms (Table 2).

In the 12 patients first performing pouch irrigation with NaCl, the incidence of positive UCs was 29 of 42 (69%) under NaCl irrigation and 23 of 31 (74%) under H₂O irrigation. In patients starting with H₂O irrigations, 23 of 38 positive UCs (61%) were noted under H₂O irrigations and 19 of 32 (59%) under NaCl. The differences were not significant.

In all positive UCs, 118 strains of bacteria were detected, 59 (50%) in each study arm. The two study arms had similar microbiologic spectra (Fig. 3). In UCs with ≤ 1000 CFU/ml, most germs were mixed gram-positive or mixed aerobic flora. Eleven symptomatic UTIs in the NaCl arm compared

Table 2 – Results of urine cultures, antibiotic treatments, and costs

	NaCl arm	H ₂ O arm	<i>p</i> value
Urine cultures total, <i>n</i> (%)	74 (100)	75 (100)	NS
- Positive urine cultures, any number of bacteria, <i>n</i> (%)	48 (65)	48 (64)	NS
- Positive urine cultures, $\geq 10\ 000$ CFU/ml, <i>n</i> (%)	33 (45)	33 (44)	NS
- Positive urine cultures, $\geq 100\ 000$ CFU/ml, <i>n</i> (%)	20 (27)	16 (21)	NS
Ratio of positive urine cultures to study days			
- Positive urine cultures, any number of bacteria, ratio	1:39	1:43	NS
- Positive urine cultures, $\geq 10\ 000$ CFU/ml, ratio	1:57	1:62	NS
- Positive urine cultures, $\geq 100\ 000$ CFU/ml, ratio	1:94	1:128	NS
Antibiotic treatment			
- Antibiotic treatments required, <i>n</i>	11	4	0.09
- Median duration of antibiotic treatment, d (range)	7 (5–14)	9 (6–11)	NS
Costs per month in CHF/EUR (not included: shipping, waste disposal)	940.00/700.00	50.00/37.00	

CHF = Swiss franc; EUR = euro; NaCl = sodium chloride 0.9% solution; H₂O = tap water; NS = not significant.

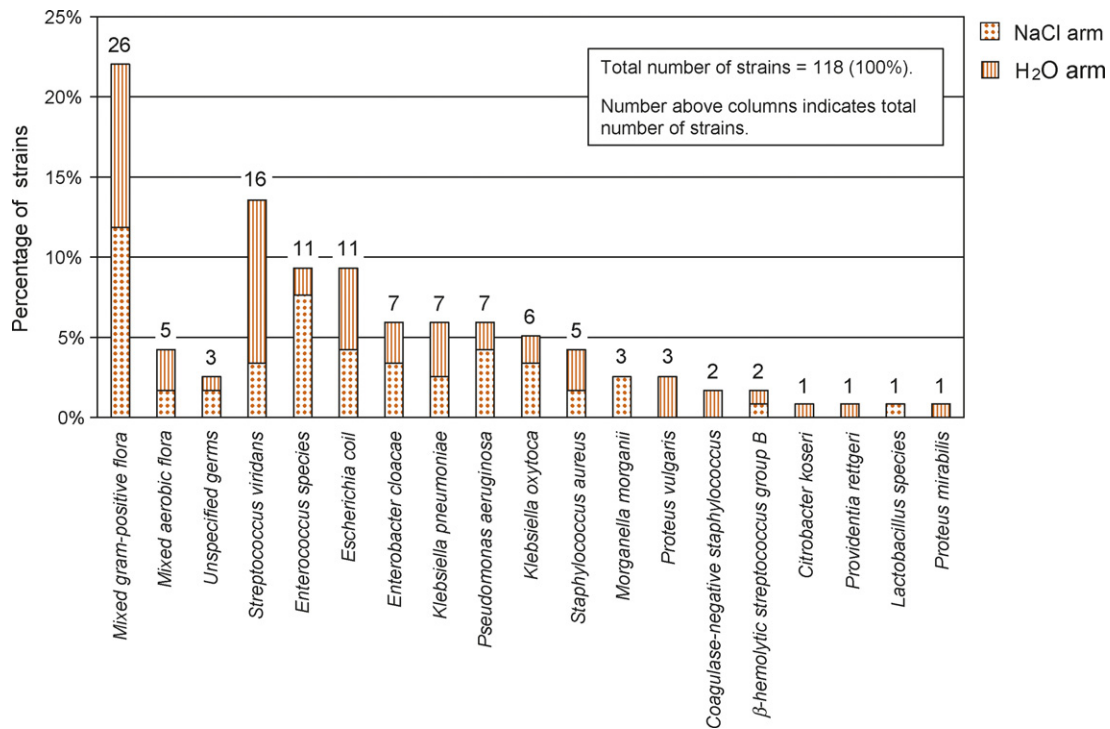


Fig. 3 – Microbiologic spectrum of the 96 positive urine cultures. More than one strain per urine culture is possible. NaCl = sodium chloride 0.9% solution; H₂O = tap water.

with four in the H₂O arm required antibiotic treatment ($p = 0.09$). The two arms had comparable durations of treatment (Table 2).

All patients preferred the H₂O method, adjudging the NaCl method to be significantly worse in terms of handling, time required, and impact on professional activity and daily life (Table 3).

With monthly minimal expenses of Swiss francs (CHF) 940.00 or euro (EUR) 700.00 (30 sterile syringes 60 ml [one per day], 180 sterile nonhydrophilic single-use catheters [six per day], NaCl 0.9% solution, aseptic solution), the costs for the NaCl arm were up to 20 times higher than for the H₂O arm with minimal monthly expenses of CHF 50.00/EUR 37.00 (2 syringes 60 ml, 10 nonhydrophilic single-use catheters, syringes, and catheters cleaned with tap water

and reused). In the NaCl arm, costs increased up to CHF 1360.00/EUR 1000.00 if commonly preferred disposable hydrophilic catheters were used.

4. Discussion

Patients with a continent urinary diversion are at high risk for UTI [1,10,11] and are therefore advised to irrigate their pouches regularly for their lifetime. They are usually instructed to irrigate the pouch with sterile NaCl 0.9% solution. This prospective study demonstrates that patients using sterile NaCl 0.9% solution had significantly more nitrite-positive study days (22%) than the same patients using tap water (11%). The ratio of positive UCs to number of study days did not differ significantly between the NaCl arm

Table 3 – Assessment of patient friendliness

Question	Answer options	NaCl Median (range)	H ₂ O Median (range)	p value
1. How was the handling of this method of reservoir irrigation?	1 ("very easy") to 10 ("very difficult")	4 (1–10)	1 (1–4)	<0.001
2. How much time did you need for catheterization and irrigation?	Minutes	12.5 (5–25)	10 (5–17.5)	<0.001
3. To which extent did this method affect your professional activity?	1 ("not at all") to 10 ("very much")	2 (1–10)	1 (1–8)	0.09
4. To which extent did this method have an impact on your daily life?	1 ("not at all") to 10 ("very much")	3.5 (1–9.5)	2 (1–5)	<0.001
5. How would you feel if you would have to catheterize and irrigate with this method until the end of your life?	1 ("excellent") to 10 ("miserable")	6 (1–10)	2 (1–8)	<0.001
6. Which method did you prefer? [question at the end of the study]	"NaCl" or "H ₂ O"	0	23	–

NaCl = sodium chloride 0.9% solution; H₂O = tap water.

(1 of 39) and the H₂O arm (1 of 43). Similarly, when only looking at UC with $\geq 10^4$ and $\geq 10^5$ CFU/ml, reflecting significant infections, the ratios were comparable in both arms and even showed a trend towards a lower incidence of positive UCs in the H₂O arm. In addition, a trend towards more antibiotic treatments ($p = 0.09$) for symptomatic UTI was noted in the NaCl arm ($n = 11$) versus the H₂O arm ($n = 4$).

Symptomatic UTI ($n = 15$) was much less common than asymptomatic bacteriuria ($n = 96$). The 64% incidence of asymptomatic bacteriuria found in our patients is at the upper end of what was reported in previous studies on continent urinary diversions (10–67%) [1,11–13]. The presence of mainly mixed gram-positive and aerobic flora, *Streptococcus viridans*, *Staphylococcus*, and UC with ≤ 1000 CFU/ml strongly suggests contamination of normal cutaneous flora [14].

Nitrite levels in the urine depend on the manner of its production and reduction. The human nitrate-nitrite-nitric oxide pathway is well known. Nitrate and nitrite are absorbed in the intestine and excreted by the kidneys [15]. In humans, nitrate-nitrite reduction requires the presence of bacteria because mammalian cells cannot effectively metabolize this anion [15,16]. False-negative urine nitrite tests despite the presence of bacteria may be caused by reduced nutritional uptake of nitrate or by infection with bacteria that do not reduce nitrate, such as *Staphylococcus* species, *Pseudomonas*, and some *Enterococci* [17]. In our study the significantly higher rate of positive nitrite tests in the NaCl arm cannot be attributed to differences in human factors because of the study's crossover design. It is probably due to a higher incidence of nitrate-reducing bacteria in the pouches irrigated with NaCl.

A possible explanation for the lower rates of nitrite-positive study days and of nitrite-reducing bacteria in the H₂O arm could be the hypo-osmolarity of tap water in contrast to the iso-osmolarity of the NaCl 0.9% solution. Microorganisms survive better in an iso-osmolar environment, whereas an osmotic shift toward a low (or high) osmolarity environment elicits dramatic changes in bacterial cell structure [18]. Tsapis and Kepes [19] described a leak of intracellular solutes (neutral and anionic sugars, endogenous nucleotides, and potassium) in *E. coli* when washed with hypo-osmolar solutions. The addition of various hypo-osmolar solutions caused transient damage to the cells via osmotic shock; however, no permanent damage was observed. Bacteria counts were unchanged when bacteria were diluted in distilled water and then inoculated onto a culture plate [19]. After an osmotic downshift, water uptake (phase 1) and release of intracellular solutes (phase 2) were complete within 1–2 min; the ensuing reaccumulation of solutes (phase 3) was complete within 10–20 min after the shift [18]. We speculate therefore that the daily, sometimes repeated irrigation with tap water may lead to a bacteriostatic state with impaired cell division and metabolism but not to bacteriolysis. This could explain the significantly lower rate of nitrite-positive study days in the H₂O arm but a similar rate of positive UCs with a comparable microbiologic spectrum

in both study arms when bacteria are brought back in a more friendly environment (UC medium). However, such speculation must be confirmed in further studies. Another possible reason for the similar rates of bacterial growth in the UCs of the NaCl and H₂O arms and a potential limitation of the study may be the practice of requiring patients to collect and ship urine samples themselves. Differences in urine collection technique and shipping times cannot be excluded.

From a practical point of view, patients described the irrigations with NaCl 0.9% solution as more complicated in handling ($p < 0.001$), more time consuming ($p < 0.001$), and having a bigger negative impact on their professional ($p = 0.09$) and daily lives ($p < 0.001$). The greater logistic effort of shipping, storing, and disposal of a large and heavy quantity of material was criticized as not being patient friendly. All patients preferred irrigations with tap water.

Regarding costs, irrigations with NaCl 0.9% solution (CHF 940.00/EUR 700.00 monthly costs) were far more expensive than irrigations with tap water (CHF 50.00/EUR 37.00 monthly costs). The determining cost factor for irrigating with NaCl 0.9% solution was the more frequent use of the expensive sterile ready-to-use disposable hydrophilic-coated catheters; the NaCl 0.9% solution itself and the aseptic cleaning solution and syringes were relatively cheap. In the H₂O arm the same catheter could be used repeatedly with cleaning. Even if in some countries tap water would have to be replaced by bottled drinking water, the costs would still be substantially lower than with aseptic irrigation with sterile NaCl 0.9% solution.

5. Conclusions

Using tap water for ileal pouch irrigation significantly reduced the incidence of nitrite-positive study days while not changing the positive UC rate compared with that of NaCl 0.9% irrigation with comparable microbiologic spectra. Similarly, a trend towards fewer antibiotic treatments for symptomatic UTI was observed in the H₂O arm versus the NaCl arm. All patients preferred the use of tap water as easier, more patient friendly, and considerably less expensive. We therefore recommend the use of tap water (or bottled water depending on the local circumstances) instead of NaCl 0.9% solution for the irrigation of continent catheterizable ileal pouches.

Author contributions: Urs E. Studer had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Study concept and design: Studer, Birkhäuser, Schürch, Burkhard, Willener, Ochsner, Zehnder, Thalmann.

Acquisition of data: Birkhäuser, Ochsner, Zehnder, Roth, Burkhard, Willener, Thalmann, Studer.

Analysis and interpretation of data: Birkhäuser, Studer, Zehnder, Roth.

Drafting of the manuscript: Birkhäuser, Zehnder, Studer.

Critical revision of the manuscript for important intellectual content: Studer, Zehnder.

Statistical analysis: Hüsler (Institute of Mathematical Statistics and Actuarial Science of the University of Bern, Switzerland).

Obtaining funding: None.

Administrative, technical, or material support: Ochsner, Willener, Birkhäuser.

Supervision: Studer, Thalmann.

Other (specify): None.

Financial disclosures: I certify that all conflicts of interest, including specific financial interests and relationships and affiliations relevant to the subject matter or materials discussed in the manuscript (eg, employment/affiliation, grants or funding, consultancies, honoraria, stock ownership or options, expert testimony, royalties, or patents filed, received, or pending), are the following: None.

Funding/Support and role of the sponsor: None.

References

- [1] Wullt B, Holst E, Steven K, et al. Microbial flora in ileal and colonic neobladders. *Eur Urol* 2004;45:233–9.
- [2] Zehnder P, Dhar N, Thurairaja R, Ochsner K, Studer UE. Effect of urinary tract infection on reservoir function in patients with ileal bladder substitute. *J Urol* 2009;181:2545–9.
- [3] Reeves-Darby VG, Turner JA, Prasad R, et al. Effect of cloned *Salmonella typhimurium* enterotoxin on rabbit intestinal motility. *FEMS Microbiol Lett* 1995;134:239–44.
- [4] N'Dow J, Pearson J, Neal D. Mucus production after transposition of intestinal segments into the urinary tract. *World J Urol* 2004;22:178–85.
- [5] Levina N, Totemeyer S, Stokes NR, et al. Protection of *Escherichia coli* cells against extreme turgor by activation of MscS and MscL mechanosensitive channels: identification of genes required for MscS activity. *EMBO J* 1999;18:1730–7.
- [6] Studer UE, Ackermann D, Casanova GA, Zingg EJ. Three years' experience with an ileal low pressure bladder substitute. *Br J Urol* 1989;63:43–52.
- [7] Monti PR, Lara RC, Dutra MA, de Carvalho JR. New techniques for construction of efferent conduits based on the Mitrofanoff principle. *Urology* 1997;49:112–5.
- [8] Schweizerischer Verein des Gas- und Wasserfaches SVGW. Quality of potable water in Switzerland Web site. <http://www.wasserqualitaet.ch>.
- [9] Hodges JL, Lehmann EL. Estimates of location based on rank tests. *Ann Math Stat* 1963;34:598–611.
- [10] Falagas ME, Vergidis PI. Urinary tract infections in patients with urinary diversion. *Am J Kidney Dis* 2005;46:1030–7.
- [11] Studer UE, Burkhard FC, Schumacher M, et al. Twenty years experience with an ileal orthotopic low pressure bladder substitute—lessons to be learned. *J Urol* 2006;176:161–6.
- [12] Suriano F, Gallucci M, Flammia GP, et al. Bacteriuria in patients with an orthotopic ileal neobladder: urinary tract infection or asymptomatic bacteriuria? *BJU Int* 2008;101:1576–9.
- [13] Akerlund S, Campanello M, Kaijser B, Jonsson O. Bacteriuria in patients with a continent ileal reservoir for urinary diversion does not regularly require antibiotic treatment. *Br J Urol* 1994;74:177–81.
- [14] Mackowiak PA. The normal microbial flora. *N Engl J Med* 1982;307:83–93.
- [15] Lundberg JO, Weitzberg E, Gladwin MT. The nitrate-nitrite-nitric oxide pathway in physiology and therapeutics. *Nat Rev Drug Discov* 2008;7:156–67.
- [16] Stewart M. Urinary diversion and bowel cancer. *Ann R Coll Surg Engl* 1986;68:98–102.
- [17] Pollock HM. Laboratory techniques for detection of urinary tract infection and assessment of value. *Am J Med* 1983;75:79–84.
- [18] Wood JM. Osmosensing by bacteria: signals and membrane-based sensors. *Microbiol Mol Biol Rev* 1999;63:230–62.
- [19] Tsapis A, Kepes A. Transient breakdown of the permeability barrier of the membrane of *Escherichia coli* upon hypoosmotic shock. *Biochim Biophys Acta* 1977;469:1–12.