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ORIGINAL PAPER

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# Diverse patterns of acid-base abnormalities associated with a modified sigmoid neobladder

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**Abstract** In this study, we analyzed the pattern of metabolic acidosis in patients following the construction of a sigmoid neobladder and then search for the risk factors which affecting this. In 23 men aged 43–73 years and nine women aged 49–74 years who underwent sigmoid neobladder surgery, we performed physical examinations and blood tests every 3 months for 13–75 months ($38.7 \pm 16.6$: mean ± SD). We monitored acid-base balance, serum electrolytes, creatinine, lipid and liver function in patients for up to 6 years postoperatively. Creatinine clearance over 24 h was determined preoperatively. According to pH and base excess measured during follow-up, patients were classified into three groups (normal, 17 patients; temporary acidosis, eight patients; persistent acidosis, seven patients). Patients with temporary acidosis could compensate spontaneously by 1 year without being given sodium bicarbonate; those with persistent acidosis could not compensate spontaneously and five of them required medication with sodium bicarbonate after 1 year. Serum creatinine in patients with persistent acidosis was consistently higher during follow-up than in the other two groups. Preoperative creatinine clearances in the normal, temporary, and persistent groups were $94.25 \pm 27.47$, $95.19 \pm 18.63$, and $69.18 \pm 16.18$ ml/min/1.73 $m^2$, respectively, being significantly lower in the persistent group ($P < 0.05$). In this group, patients with creatinine clearances less than 70 ml/min/1.73 $m^2$ could not compensate for metabolic acidosis. Normal and temporary groups showed different changes of serum chloride and bicarbonate during follow-up (respectively higher and lower) although the renal functions of the two groups were similar. Chloride and bicarbonate varied reciprocally with pH and base excess. Temporal hyperchloremic metabolic acidosis was observed until a year after surgery. In conclusion, temporary acidosis can be caused in some patients in spite of normal renal function, although it is difficult to predict it. In addition, careful follow-up is required, especially in patients with a creatinine clearance $< 70$ ml/min/1.73 $m^2$ who can encounter persistent acidosis.

**Keywords** Metabolic acidosis · Sigmoid neobladder · Renal function

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## Introduction

A variety of surgical procedures using an intestinal segment as a bladder substitute have been widely used. However, a potential risk exists of increased water loss [25] and metabolic acidosis [2, 16] because of mucosal shifts of water and solutes. Water movement follows the osmotic gradient and is dependent upon the tightness of the membrane. Compared with the ileum, the colon's tight junctions are fairly impermeable to water and are capable of maintaining significant osmotic differences between blood and lumen. With colon segments, there is less tendency to lose water. In contrast, patients with ileal segments often lose water. In addition, both segments secrete sodium and bicarbonate ions and reabsorb ammonia, ammonium, hydrogen ions and chloride ions when exposed to urine, causing metabolic acidosis. Metabolic acidosis reportedly develops in 86% of patients following rectosigmoid bladder construction [6], while it is rare or absent with a continent caecal reservoir [8], and the Hautmann [24], the Gilchrist [35], Kock [5, 17], Camey [21], Lebag [20], Mainz [37], and Koch [16] procedures. The likelihood of acidosis is dependent on the portion of intestine, type of urinary diversion, and length of the intestinal segment. The degree of acidosis is

considered to be related to the surface area of bowel exposed to the urine and the duration of exposure. Active and passive transport systems responsible for intestinal mucosal absorption and secretion appear to be similar in the ileum and colon [9, 39]. An animal study failed to demonstrate a metabolic advantage with intestinal reservoirs that incorporate ileum rather than colon or vice versa [26]. In patients with intestinal urinary tract substitutes, most authors consider impaired renal function to be a prerequisite for symptomatic metabolic acidosis [19], although Stamey demonstrated that acidosis may occur despite normal renal function [32]. The renal functional reserve is important in compensation for metabolic disorders; Kristjansson et al. [19] reported that a glomerular filtration rate of approximately 55 ml/min/1.73 $m^2$ was the minimum required to compensate for the ongoing endogenous acid load.

The aim of the present study was to elucidate how a modified sigmoid neobladder affected acid-base balance and to determine which patients compensate for acidosis during follow-up.

## Materials and methods

We studied 23 men aged 43–73 years ($62.4 \pm 8.7$, mean ± SD) and nine women aged 49–74 years ($59.3 \pm 9.3$) all of whom had undergone surgery for transitional cell carcinoma of the urinary bladder and were alive with no evidence of recurrence at the most recent follow-up at 13–75 months postoperatively ($38.7 \pm 16.6$ months).

The standard surgical procedure was a radical cystectomy with construction of a neobladder using 30–35 cm of sigmoid colon as previously described [19]. The patients were followed up at 1 and 3 months after discharge from the hospital, and then every 3 months up to 6 years. At each follow-up the clinical examination was routinely accompanied by blood tests to evaluate acid-base balance (pH, base excess and bicarbonate); creatinine (0.5–1.3 mg/dl, normal range); phosphate; sodium (Na); potassium (K), and chloride (Cl); total proteins and albumin; cholesterol and triglycerides; and glutamic oxaloacetic transaminase (GOT), gamma-glutamyl transpeptidase ($\gamma$-GTP), serum glutamic pyruvic transaminase (GPT), alkaline phosphatase (ALP), lactate dehydrogenase (LDH), and total bilirubin (Bil). Preoperatively, 24-h urine samples were analyzed for creatinine, and 24-h creatinine clearance was calculated. No patient had any illness, such as severe pulmonary derangement, that could cause acidosis. Patients were not treated with any medication that could lead to metabolic acidosis or influence intestinal absorption. Patients with excessive metabolic acidosis (base excess less than –5) were treated with sodium bicarbonate if compensation was not expected because of impaired renal function at 1 year postoperatively.

Differences between the groups of patients were assessed by a post-hoc test or analysis of variance (ANOVA). A value of $P < 0.05$ was considered to indicate statistical significance.

## Results

Patients were classified into three types according to the changing patterns of pH or base excess observed during follow-up (Fig. 1A, B). Both base excess and pH were always within normal limits during follow-up in 17 patients (53%) (normal type). In contrast, eight patients temporarily showed low pH and low base excess, which was maximal at 9 months after surgery (temporary acidosis). These patients could compensate for the acidosis spontaneously by 1 year, without receiving sodium bicarbonate. The remaining seven patients showed continuing low pH and base excess and could not spontaneously compensate for acidosis, requiring treatment with sodium bicarbonate after 1 year (persistent acidosis). Despite this medication, the acidosis was never completely corrected to normal. Serum creatinine in the persistent group was consistently higher during follow-up than in the other groups (Fig. 2). No difference was observed in serum creatinine between normal and temporary groups. The preoperative creatinine clearances in normal, temporary, and persistent groups were $94.25 \pm 27.47$, $95.19 \pm 18.63$, and $69.18 \pm 16.18$ ml/min/1.73 $m^2$, respectively (Fig. 3). Creatinine clearance in the first two groups was significantly higher than in the persistent group ($P < 0.05$). In the persistent group, patients with a creatinine clearance of less than 80 ml/min/1.73 $m^2$ could not compensate for metabolic acidosis.

Bicarbonate (Fig. 1C) and Cl concentrations (Fig. 11) in each group showed changes that were reciprocal to those of pH and base excess. Serum chloride and bicarbonate differed between normal and temporary groups, even though renal function was similar. In the temporary group, the bicarbonate concentration was maximally decreased at 9 months, and recovered to normal by 1 year after surgery. The chloride level increased up to 9 months and decreased after 12 months. Temporary hyperchloremic metabolic acidosis was observed in the temporary group until 1 year after surgery. In the normal group, concentrations of bicarbonate and chloride were usually normal throughout follow-up. In the persistent group, the bicarbonate concentration was consistently lower than normal, while chloride was high during follow-up. Thus, ongoing hyperchloremic metabolic acidosis was observed.

Sodium, potassium, total protein, albumin, cholesterol, triglyceride, and liver function markers (GOT, GPT, ALP, $\gamma$-GTP, and Bil) did not differ significantly among the three groups or change significantly during the follow-up period.

## Discussion

Most patients with urinary diversion via a segment of intestine are at risk for metabolic disturbances. Several factors appear to exert an important influence on the severity of the metabolic acidosis seen, including the type of urinary diversion and the portion of intestine used. The surface area of the intestinal segment used for reconstruction and exposure time of urine to intestinal mucosa are important, as is the underlying renal function, including the ability to concentrate the urine and excrete an acid load.

Many studies have considered metabolic disorders after urinary diversion. Reported frequencies of

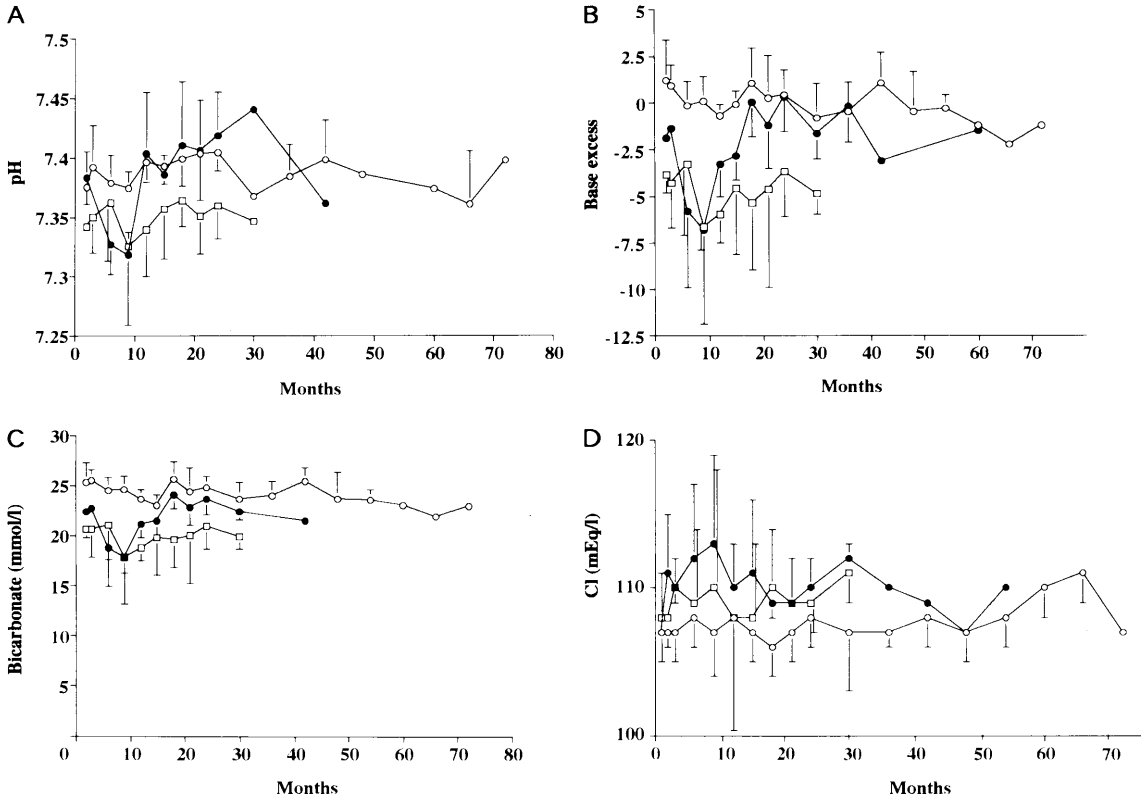


**Fig. 1A–D.** The postoperative metabolic changes. **A**, pH; **B**, base excess; **C**, bicarbonate; **D**, chloride. *Empty circle*, normal; *filled circle*, temporary; *empty square*, persistent. Normal; both pH and base excess were within the normal range during follow up. Temporary; both pH and base excess were temporarily lower than the normal range during follow up. Persistent; both pH and base excess were persistently lower than the normal range during follow up

metabolic acidosis in various studies are listed in Table 1. No acidosis were observed with Camey I type ileal enterocystoplasty [31], continent urinary colonic or ileocaeal reservoir [26, 30], continent Kock ileal reservoir [17], or continent colonic urinary diversion [16] including orthotopic bladder substitution [38] provided that the patients had well-preserved renal function. In addition, Koch [16] concluded that urinary diversion via a continent colonic reservoir imparts no significant metabolic acidosis over the short term to patients with normal renal and hepatic function. According to the frequency of acidosis in the patients (Table 1), there appeared to be no differences between colonic and ileal reservoirs. However, the absorption test for sodium and chloride in the intestinal reservoir revealed a decreased absorptive capacity of sodium and chloride through the mucosa with time [1], and that the absorption of $^{36}Cl$ was greater in the colonic reservoir than in the ileal one [7]. The ileal reservoir may be preferable because the low reabsoption of chloride is better, especially when the renal function is impaired and the intestinal reservoir is reconstructed.

Generally, patients with a urinary diversion and normal renal and hepatic function appear to be able to

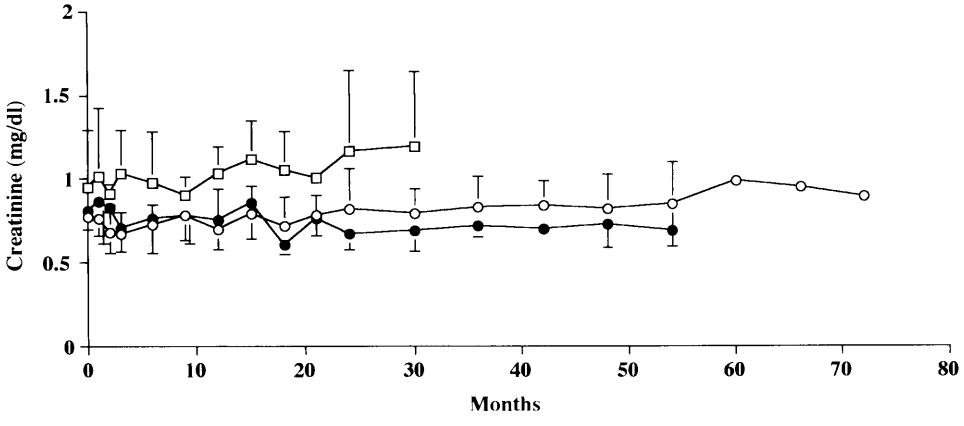


**Fig. 2.** The postoperative level of creatinine clearance. *Empty circle*, normal; *filled circle*, temporary; *empty square*, persistent. An *asterisk* indicates a significant difference ($P < 0.05$)

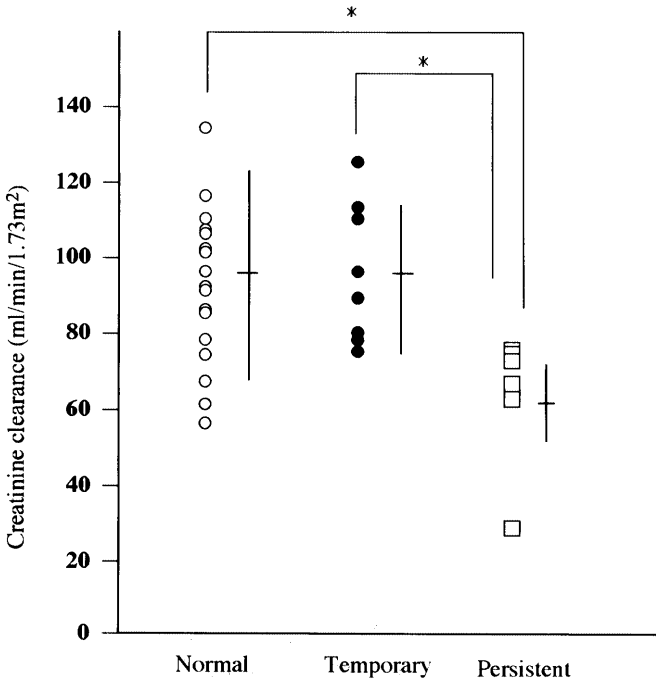


**Fig. 3.** The postoperative serum level of creatinine. *Empty circle* , normal; *filled circle*, temporary; *empty square*, persistent. Normal; both pH and base excess were within the normal range during follow up. Temporary; both pH and base excess were temporarily lower than the normal range during follow up. Persistent; both pH and base excess were persistently lower than the normal range during follow up. An *asterisk* indicates a significant difference ($P < 0.05$)

compensate for ongoing absorption of the acid by the neobladder. However, when patients with renal impairment undergo various modes of urinary intestinal reconstruction [40], the risk of metabolic acidosis is greater. Metabolic acidosis may persist over a long interval in less carefully selected patients with impaired renal function [34]. However, the degree of severity of renal impairment which is likely to affect the frequency of metabolic acidosis and preclude compensation for metabolic acidosis is unknown.

The kidneys are primarily responsible for maintaining a normal acid-base balance. Limited ability of the kidneys to excrete resorbed urinary solutes is considered the primary basis for metabolic derangement following urinary diversion [1, 11, 14, 27]. Kristjansson et al. [19] reported that patients with a glomerular filtration rate of at least 55 ml/min/1.73 $m^2$ have sufficient renal function to compensate for the chronic endogenous acid load resulting from urinary diversion, while those with a lower glomerular filtration rate develop metabolic acidosis. In our study, the creatinine clearance of patients without metabolic acidosis ($94.3 \pm 27.5$ ml/min/1.73 $m^2$) or patients able to compensate for temporary acidosis ($95.2 \pm 18.6$ ml/min/1.73 $m^2$) was higher than that of patients with persistent metabolic acidosis throughout follow-up ($69.2 \pm 16.2$ ml/min/1.73 $m^2$). In addition, our study showed that creatinine clearance in patients with persistent metabolic acidosis during follow-up was less than 70 ml/min/1.73 $m^2$. In spite of the treatment with

**Table 1.** Metabolic acidosis in patients with urinary diversion. N.D.: not described

| Author | No. of patients | Type of urinary diversion | Hyperchloremia only | Hyperchloremic acidosis | Reference no. |
|---|---|---|---|---|---|
| Djavan | 216 | ileal loop neobladder | N.D. | 42 | 10 |
| | 60 | ureterosigmoidostomy | N.D. | 41 | |
| Rogers | 20 | ileal neobladder | 4 (transient)<br>1 (persistent) | 1 (transient) | 29 |
| Tammela | 19 | neobladder (ascending colon) | 1 | 1 | 36 |
| Bejany | 25 | ileocolic neobladder | 2 | 0 | 4 |
| Stein | 4 | ileocolic (Mainz pouch I) | 0 | 2 | 33 |
| | 6 | colon conduit | 0 | 1 | |
| | 16 | rectal reservoir | 0 | 2 | |
| Weckermann | 15 | ileal neobladder | 1 | 4 | 41 |
| Davidsson | 10 | conduit (ileum or colon) | N.D. | 0 | 8 |
| | 8 | continent cecal reservoir | | 0 | |
| Studer | 100 | ileal neobladder (Studer) | no major change | depends on the length of ileum<br>30–38 cm: about 25%<br>40 cm: about 45%<br>45–60 cm: about 65% | 34 |
| Salomon | 17 | Carney-type I enterocystoplasty (35 cm ileum) | 1 | 0 | 31 |
| Jahnson | 51 | ileal conduit ureterostomy<br>Kock pouch<br>S-shaped bladder substitution | 17 | 2 | 15 |
| Lockhart | 17 | ascending colon (50–70 cm) | 12 | 0 | 22 |
| | 6 | ascending colon (30 cm) | 5 | 0 | |
| | 8 | stomach and ileum | 0 | 0 | |

sodium bicarbonate, the level of base excess did not recover to the normal level in any patients. Therefore, the patients with creatinine clearance $< 70$ ml/min/1.73 $m^2$ may not be suitable for the diversion using an intestinal segment.

However, the incidence of acidosis after urinary diversion may be influenced by factors apart from renal function. In our study, the normal and temporary groups showed similar preoperative renal function while only patients in the latter group showed temporary acidosis during the first postoperative year. The reason may involve individual differences in the absorption and excretion of electrolytes by the neobladder even though the portion of the intestine used to construct the neobladder was the same. Usually the bowel segment incorporated into the urinary tract secretes sodium and bicarbonate, while reabsorbing ammonia and hydrogen ions to maintain electrolytic neutrality [11, 23]. Chloride shift is considered a common phenomenon. In our study, the temporary group showed the increase of serum chloride and the decrease of bicarbonate in accord with a decrease of pH and base excess at 9 months after surgery. During this early period, kidneys with normal function could still not compensate for the effect of the abnormal transport of serum electrolytes. Therefore, individual differences in the transport of electrolytes through the interposed intestine are important determinants of the incidence of acidosis. Preoperative identification of patients inclined to develop temporary acidosis due to the high activity of the intestinal transport function after urinary diversion proved difficult. However, we demonstrated that acidosis with adequate renal function tends to improve within 1 year, possibly because of changes in the intestinal mucosa caused by exposure to urine eventually alter the transport activity of electrolytes in the neobladder. Metabolic acidosis reportedly decreases with time, in association with significant structural changes in the ileal mucosa such as atrophy of the intestinal villi, decrease of villi-to-crypt ratio and mucosal fibrosis after long-term exposure to urine. These are responsible for the time dependent decreased absorptive capacity of the intestinal mucosa [3, 18, 23, 28, 34]. Moreover, the absorption of chloride from an ileocecal reservoir (Mainz pouch I) is greatest during the first 6 months after surgery, and then declines markedly with time. A decreased absorption rate and consequent changes of acid-base profile in the blood were especially apparent in the first year after surgery [12], a pattern consistent with our finding in the temporary group. On the other hand, some patients with normal renal function did not improve metabolic acidosis. This may be because the absorptive capacity did not change despite progressive mucosal atrophy and morphological changes were minimal in the continent ileocolic urinary reservoirs after long-term exposure to urine [23].

In conclusion, there are some patients who have temporary acidosis probably due to individual differences in the absorption of electrolytes in spite of their normal renal function. Therefore, careful follow-up including blood gas analysis should be performed for those patients as well as patients with low renal function (creatine clearance $< 70$ ml/min/1.73 $m^2$) who can develop persistent acidosis after urinary diversion. However, it is difficult from present study to predict temporary acidosis preoperatively.

## References


1. Akerlund S, Aronsson EF, Jonsson O, Kock NG (1991) Decreased absorption of $^{22}Na$ and $^{36}Cl$ in ileal reservoirs after exposure to urine. An experimental study in patients with continent ileal reservoirs for urinary or fecal diversion. Urol Res 19: 249
2. Akerlund S, Berglund B, Kock NG, Philipson BM (1989) Voiding pattern, urinary volume, composition and bacterial contamination in patients with urinary diversion via a continental ileal reservoir. Br J Urol 63: 619
3. Akerlund S, Nilsson LO (1986) Water and electrolyte absorption in ileal segments surgically transposed to the urinary bladder in the cat. Scand J Urol Nephrol 20: 63
4. Bejany DE, Politano VA (1993) Modified ileocolonic bladder: 5 years of experience. J Urol 149: 1441
5. Boyd SD, Schiff WM, Skinner DG, Lieskovsky G, Kanellos AW, Klimaszewski AD (1989) Prospective study of metabolic abnormalities in patient with continent Kock pouch urinary diversion. Urology 33: 85
6. Caprilli R, Frieri G, Latella G, Gallucci M, Bracci U (1986) Electrolyte and acid base imbalance in patients with rectosigmoid bladder. J Urol 135: 148
7. Davidson T, Akerlund S, Aronsson EF, Kock NG (1994) Absorption of sodium and chloride in continent reservoirs for urine: comparison of ileal and colonic reservoirs. J Urol 151: 335
8. Davidsson T, Lindergard B, Mansson W (1995) Long-term metabolic and nutritional effects of urinary diversion. Urology 46: 804
9. Davis GR, Morawski SG, Santa Ana CA, Fordtran JS (1983) Evaluation of chloride-bicarbonate exchange in the human colon in vivo. J Clin Invest 71: 201
10. Djavan B, Fakhari M, Roehrborn CG, Marberger M (1998) Metabolic consequences of urinary diversion with intestinal segments. Tech Urol 4: 177
11. El-Mekresh MM, Shebab El-Din AB, Fayed SM, Brevinge H, Kock NG, Gohneim MA (1991) Bladder substitutes controlled by the anal sphincter: a comparison of the different absorption potentials. J Urol 146: 970
12. Filipas D, Fisch M, Enein A, Fichtner J, Bockisch A, Hohenfellner R (1997) Chloride absorption in patients with a continent ileocaecal reservoir (Mainz pouch I). Br J Urol 79: 588
13. Fujisawa M, Gotoh A, Miyazaki S, Hara I, Okada H, Arakawa S, Kamidono S (2000) Sigmoid neobladder in women after radical cystectomy. J Urol 163: 1505
14. Hall MC, Koch MO, Halter SA, Dahlstedt SM (1993) Morphologic and functional alterations of intestinal segments following urinary diversion. J Urol 149: 664
15. Jahnson S, Pedersen J (1993) Cystectomy and urinary diversion during twenty years-complications and metabolic implications. Eur Urol 24: 343
16. Koch MO, McDougal WS, Reddy PK, Lange PH (1991) Metabolic alterations following continent urinary diversion through colonic segments. J Urol 145: 270
17. Kock NG, Nilson AE, Nilsson LO, Norlen LJ, Philipson BM (1982) Urinary diversion via a continent ileal reservoir: clinical results in 12 patients. J Urol 128: 469
18. Kollias G, Goulandris N, Kastriotis J, Paraschou E, Dimopoloulus C (1984) Absorbability of mucosa in total replacement of urinary bladder with jejunum. Urology 33: 51

19. Kristjansson A, Davidsson T, Masson W (1997) Metabolic alterations at different levels of renal function following continent urinary diversion through colonic segments. J Urol 157: 2099
20. Light JK, Engelmann UH (1986) Le bag: total replacement of the bladder using an ileocolonic pouch. J Urol 136: 27
21. Lilien OM, Camey M (1984) Twenty-five years experience with replacement of the human bladder. J Urol 132: 886
22. Lockhart JL, Davies R, Persky L Figueroa TE, Ramirez G (1994) Acid-base changes following urinary tract reconstruction for continent diversion and orthotopic bladder replacement. J Urol 152: 338
23. Mansson W, Willen R (1988) Mucosal morphology and histochemistry of the continent cecal reservoir for urine. J Urol 139: 1199
24. Matsui U, Toppoll B, Miller K, Hautmann RE (1993) Metabolic long-term follow-up of the ileal neobladder. Eur Urol 24: 197
25. Melchior H, Spher C, Knop-Wageman I, Persson MC, Juenemann KP (1988) The continent ileal bladder for urinary tract reconstruction after cystectomy. A survey of 44 patients. J Urol 139: 714
26. Mohler JL (1988) Metabolic acidosis after bladder replacement: comparison of severity and reversibility in ileal and colonic reservoirs. J Urol 139: 628
27. Nurse DE, Mundy AR (1989) Metabolic complications of cystoplasty. Br J Urol 63: 165
28. Philipson BM, Hockenstrom T, Akerlund S (1987) Biological consequences of exposing ileal mucosa to urine. World J Surg 11: 790
29. Rogers E, Scardino PT (1995) A simple ileal substitute bladder after radical cystectomy: experience with a modification of the Studer pouch. J Urol 153: 1432
30. Roth S, Semjonow A, Waldner M, Hertle L (1995) Risk of bowel dysfunction with diarrehea after continent urinary diversion with ileal and ileocecal segments. J Urol 154: 1696
31. Salomon L, Lugagne PM, Herve JM, Barre P, Lebret T, Botto H (1997) No evidence of metabolic disorders 10 to 22 years after Camey type I ileal enterocystoplasty. J Urol 157: 2104
32. Stamey TA (1956) The pathogenesis and implications of electrolyte imbalance in ureterosigmoidstomy. Surg Gynecol Obstet 103: 736
33. Stein R, Fisch M, Andreas J, Bockisch A, Hohenfellner R, Thuroff JW (1998) Whole-body potassium and bone mineral density up to 30 years after urinary diversion. Br J Urol 82: 798
34. Studer UE, Danuser H, Merz VW, Springer JP, Zingg EJ (1995) Experience in 100 patients with an ileal low pressure bladder substitute combined with an afferent tubular isoperistaltic segment. J Urol 154: 49
35. Sullivan H, Gilchrist RK, Merricks JW (1973) Ileocecal substitute bladder: long term follow-up. J Urol 109: 43
36. Tammela TL, Lindell OI, Vittanen JK, Hellstrom PA, Kontturi MJ, Lukkarinen OA (1991) Functional and urodynamic characteristics of bladder substitution with detubularised right colonic segment. Br J Urol 67: 298
37. Thuroff JW, Alken P, Reidmiller H, Engelmann U, Jacobi GH, Hohenfellner R (1986) The MAINZ pouch (mixed augmentation ileum and cecum) for bladder augmentation in continent diversion. J Urol 136: 17
38. Tschopp AB, Lippuner K, Jaeger P, Merz VW, Danuser H, Studer UE (1996) No evidence of osteopenia 5 to 8 years after ileal orthotopic bladder substitution. J Urol 155: 71
39. Turnberg LA, Bieberdorf FA, Morawski SG, Fordtran JS (1970) Inter-relationship of chloride, bicarbonate, sodium and hydrogen transport in the human ileum. J Clin Invest 49: 557
40. Wagstaff KE, Woodhouse CRJ, Rose GA, Duffy PG, Ransley PG (1991) Blood and urine analysis in patients with intestinal bladders. Br J Urol 68: 311
41. Weckermann D, Wawroschek F, Schipp J, Krawczak G, Harzmann R (1999) Metabolic changes and urodynamic findings after continent urinary diversion. Int Urol Nephrol 31: 665