

Chapter 8:

Urinary Diversions after Cystectomy: The Association of Clinical Factors, Complications and Functional Results of Four Different Diversions

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Abstract

Purpose: We present a single institute experience of the four most widely used diversions after cystectomy in 281 patients, and evaluated the association between clinical factors, complication rates, functional results and metabolic complications.

Materials and Methods: Between 1990 and 2005, 281 consecutive cystectomies were performed at our institute. Four different diversions were offered; an ileal conduit according to Bricker (IC; 118 patients), an Indiana pouch (IP; 51 patients), and orthotopic diversions after cystectomy/neobladder, (N; 62 patients) or Sexuality preserving Cystectomy and Neobladder (SPCN; 50 patients).

Results: 44% developed early complications; IC 48%, IP 43%, N 42%, and SPCN 38%. High ASA-score was the only variable significantly associated with early major complications (ASA 1 vs. 3: HR 0.32; 95%C.I. 0.14-0.72). Late complication rate was 51% with less complications in the IC-group; IC 39%, I 63%, N 59%, and SPCN 60% (HR 0.32; 95%C.I. 0.14-0.72), which was explained by less uncomplicated urinary tract infections (1/3 of all late complications) in the I.C. group. There were no differences in experienced late major complications. We found no significant association between tumour stage, ASA, age, pre-operative radiotherapy, gender and diversion related complication rates.

Complete day-night time continence was achieved in 96%-73% after IP, 90%-67% after Neobladder, and 96%-67% after SPCN. Metabolic changes were found in 24% of the patients; 21% after IC, 26% after IP, and 28% after orthotopic diversion (neobladder and SPCN combined). Low vitamin B12 was measured in 23%, 15% and 15% respectively.

Conclusions: Cystectomy with any subsequent diversion remains a procedure with considerable morbidity. High ASA-score was associated with more early complications. Orthotopic diversions provide good functional results, but at the cost of more late complications compared to ileal conduits. We found no evidence that age, ASA-score, positive lymph nodes, extravesical tumour growth, or previous radiotherapy are contraindications per se for any diversion.

Introduction

Radical cystectomy with a urinary diversion is still considered the gold standard for muscle invasive and refractory superficial bladder cancer. Different techniques and types of urinary diversions have been presented. The recent debate on cystectomy versus radiotherapy in the elderly underlines the controversies related to age and ASA-score in surgery, and controversies exist on whether any type of diversion can be used in any patient.^{1,2} Many considerations determine the final choice of urinary diversion in the individual patient; it should be oncologically safe, technically feasible and secure, provide good functional results, and comply with the patient's choice if possible. Some investigators advocate against the use of an orthotopic diversion after previous radiotherapy or in advanced stages of disease, while these factors are no exclusion criteria for others.^{3,4} A urinary diversion should allow sufficient urinary flow without compromising renal function, and in case of continent diversions provide good functional results. Increasingly emphasis is placed on decreased hospital stay for patients who undergo various surgical procedures, underlining the need for technically safe procedures reflected in low peri-operative and late complication rates.⁵ Continent urinary diversions may be of great psychological benefit to selected patients, but may be associated with different side effects. Hyperchloremic metabolic acidosis can occur because of re-absorption of ammoniumchloride and secretion of sodiumbicarbonate by ileal tissue of the neobladder.^{6,7} Resection of part of the ileum for urinary diversion may also lead to vitamin B12 or folic acid deficiencies.^{8,9}

Evaluating complications and functional results between different studies is hampered due to different definitions of complication rates, continence and voiding dysfunction, and the different surgical techniques used. In this study we assessed early and late complication rates, functional results, and metabolic changes in the four different urinary diversions that we have used between 1990 and 2005. We analyzed the association of tumour stage, ASA-score, age and previous received pelvic radiotherapy on these variables.

Patients and methods

Between 1990 and 2005, 281 consecutive patients underwent a cystectomy with subsequent urinary diversion at our institute. Median age was 63 years (range 32-85 years).

Tumours were staged according to the UICC-classification rules of 2002. Pathological stage (pT) was assigned according to the highest stage after diagnostic TUR or cystectomy. In general patients with positive lymph nodes were treated with adjuvant or neoadjuvant chemotherapy according to trials open at the time of diagnosis. Four types of urinary diversions were used: an ileal conduit according to Bricker, a continent cutaneous diversion according to Indiana, an orthotopic neobladder after radical cystectomy (neobladder), and an orthotopic neobladder after a sexuality preserving procedure (SPCN).¹⁰

Selection of the type of diversion is essentially based on local tumour status, the capability of performing clean intermittent catheterisation (CIC), and renal

function: patients are primarily offered an orthotopic neobladder, with SPCN in highly selected patients (wish to preserve sexual function, no tumour in prostate and/or bladder neck). In patients with urethral tumours or cT4b tumours a heterotopic diversion was used. Additionally, an ileal conduit was advised to all patients with a compromised renal function or the incapability to perform CIC. The definite type of diversion was chosen after thorough consultation of the patient by the urologist and enterostomal-therapist accordingly.

Cystectomy included dissection of the lymph nodes as described earlier.¹⁰ An ileal conduit (Bricker) was constructed in a standard fashion, using the minimal amount of ileum. Indiana reservoirs were constructed according to the original description of Rowland.¹¹ Ureters were simply pulled through the reservoir wall and sutured to the colonic epithelium after placement of single-J stents. No attempt was made to construct an antireflux mechanism of the ureters. An orthotopic bladder substitute was constructed according to Studer.¹² The ureters were anastomosed with a spatulated elliptic end-to-side and side-to-end technique according to Nesbit (with single-J stents). From 1995 onwards, a Studer type bladder substitute was anastomosed to the rim of the prostate (or the urethra in females) with preservation of vasa deferentia, prostate and seminal vesicles in males (or all internal genitalia and anterior vaginal wall in females) in suitable patients.¹⁰

Postoperative routine comprised anticoagulants (heparin), early ambulation, serum electrolytes monitoring, and parenteral nutrition via central venous intravascular devices, since 2000 replaced by early enteral feeding via postpyloric tubes. Single-J stents and the suprapubic catheter were removed at the 10th day, preceded by a cystogram to exclude extravasation. All patients were intensely accompanied by an enterostomal-therapist for stoma care in case of incontinent diversions or voiding instructions in case of orthotopic diversions.

Patients were followed at 3-month intervals during the first year, semi-annually the next two years, and annually hereafter, or more frequent if indicated. Follow-up included physical examination, radiographic evaluation by pelvic-abdominal CT-scan, ultrasound and chest X-ray, cystoscopy in patients with an orthotopic diversion, and cytological examination of urine. During follow up blood gas pH, bicarbonate, and chloride were routinely obtained in the majority of patients, vitamin B12 and Folic acid at the discretion of the urologist. Hyperchloremic acidosis was diagnosed in patients with a chloride level above 105 mmol/l and a HCO₃⁻ value below 23 mmol/l at the same time. Hypochloremic acidosis was diagnosed in patients with a chloride level below 105 mmol/l and a HCO₃⁻ value below 23 mmol/l at the same time. To exclude metabolic acidosis in the early post-operative period these clinical laboratory values were excluded from analysis. Vitamin B12 injections were administered at vitamin B12 levels below 150 mmol/l. Over 90% of patients had one or more years of follow-up, 5 patients were lost to follow-up.

Morbidity was assessed with detailed hospital and outpatient clinical records. Early (postoperative) complications were defined as those occurring in-hospital or within 30 days after surgery in case of shorter stays. Thereafter, complications were classified as late. All events leading to a prolonged hospital stay or requiring medication or surgical intervention were scored as complication. Complications

were scored as minor (requiring no treatment or medication only) or major (requiring surgical intervention, prolonged hospitalisation and/or admission to an intensive care unit). The complications were stratified whether or not associated with the diversion used. Kidney function was assessed by serum creatinine, CT-scanning, ultrasound and/or intravenous pyelography. Lasix-renography was done in case of obstruction. If this confirmed functional outflow obstruction, patients were considered for treatment with percutaneous nephrostomy, double-J stenting, balloon dilatation or Acucise™ incision, open revision, or nephrectomy if renal function was below 10%.

The functional results of continent diversions were evaluated with stringent norms on day- and night continence. Complete continence was defined as no involuntarily loss of urine and no pad use, satisfactory continence as incontinence requiring one pad or less per day/night, and poor continence as requiring multiple pads per day/night. Voiding function was evaluated by post-void residual measurements by ultrasound or clean intermittent catheterisation (CIC). Indications for regular CIC were symptomatic post-void residual urine of >150 cc or an α -symptomatic post-void residual of >250 cc.

Patients with a treatment related death or a survival of less than 30 days were excluded from the analysis of complication rates. Uni- and multivariate logistic regression analyses were performed to investigate the association between complication rate and organ confined disease, nodal status, age, type of diversion, previous radiotherapy, gender and ASA-score. Both the main and interaction effects were considered to include in the models. P-values lower than 0.05 were considered statistically significant. All analyses were performed in SAS 9.1.3.

Results

Patient characteristics

In total 212 male patients and 69 female patients underwent cystectomy. Of these patients 118 received an ileal conduit, 51 an Indiana pouch, 62 a neobladder, and 50 a SPCN. Patient characteristics according to type of diversion are summarized in table 1. Of all female patients 90% received a cutaneous diversion (ileal conduit and Indiana pouch combined), which was 50% in the male population. Patients with an orthotopic diversion (neobladder and SCPN combined) were younger than patients with a cutaneous diversion (mean 58.3 and 65.7 years respectively, t-test: $p < 0.001$), and had less often locally advanced disease (stage 3 + 4 in 34% and 53% respectively, $p = 0.02$) pre-operatively. Patients with an ileal conduit more often had a compromised renal function compared to the other patients (28% vs. 14%, $p = 0.003$).

Early complications

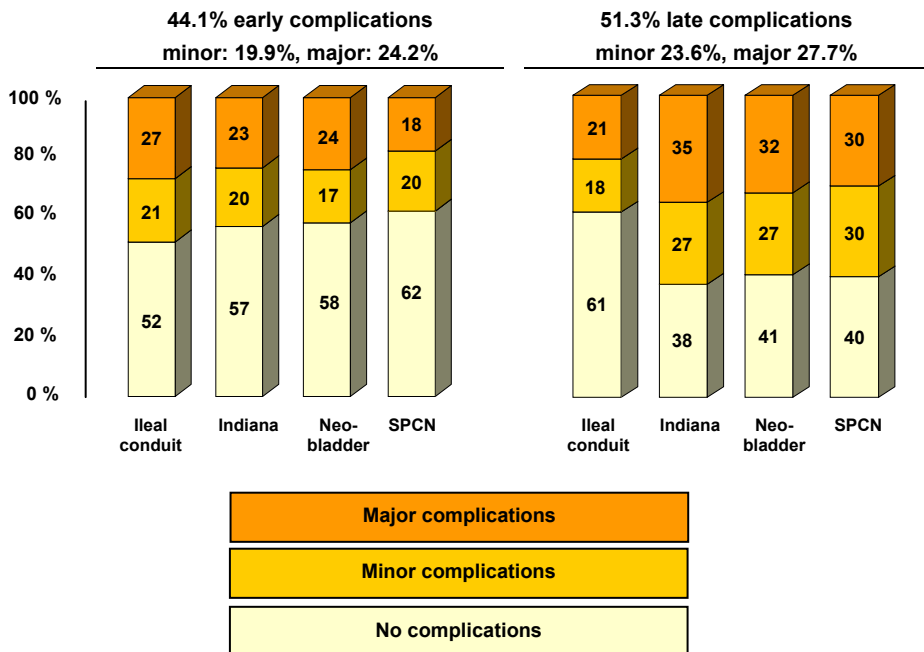
124 patients developed one or multiple complications within the first 30 days, leading to an early complication rate of 44%. There were no significant differences in early complication rates according to the different diversions used (figure 1). Early complications according to urinary diversion are summarized in table 2, eight patients (3%) died because of treatment.

High ASA-score was the only factor significantly associated with early major complications in both univariate (ASA 1 vs. 3: HR 0.32; 95%C.I. 0.14-0.72) and multivariate analyses (HR 0.36; 95%C.I. 0.14-0.91). None of the other variables were associated with early major or minor complications. There were no significant differences between the median length of hospital stay between the different diversion used; 17 days (range 6-53) following ileal conduit, 17 (range 9-42) following Indiana, 15 days (range 8-44) following neobladder, and 16 days (range 11-52) following SPCN.

Late complications:

Late complications occurred in 139 patients (51%), of whom 75 (28%) suffered from major complications (figure 1). Patients with an ileal diversion have lower risk of developing late complications (major and minor combined) compared to patients with a neobladder (univariate analyses: HR 0.32; 95%C.I. 0.14-0.72, multivariate analyses: HR 0.36; 95%C.I. 0.14-0.91).

Figure 1: Complication rates (number of patients with complication(s)) according to diversion.



There was no difference in major complications (HR 0.81; 95%C.I. 0.28-1.14). The most common complication was urinary tract infection treated with antibiotics and/or irrigation of the reservoir only (table 3). Positive lymph nodes was the only factor significantly associated with late complications in univariate analyses (HR 1.67; 95%C.I. 1.00-2.77), but not in multivariate analyses (HR 1.71; 95%C.I. 0.94-3.10). None of the other factors were associated with late major or minor complications.

Table 1: Patient characteristics according to type of diversion

	Ileal conduit		Indiana		Neobladder		SPCN		Total	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Gender										
Male	88	(75)	19	(37)	59	(95)	46	(92)	212	
Female	30	(25)	32	(63)	3	(5)	4	(8)	69	
Clinical tumor category										
No tumor (T0)	2	(2)	2	(4)	1	(2)	2	(4)	7	
Organ confined (≤ T2)	39	(33)	25	(49)	37	(59)	38	(76)	139	
Non organ confined (≥ T3)	77	(65)	24	(47)	24	(39)	10	(20)	135	
Nodal status										
Negative	70	(59)	38	(75)	47	(76)	35	(70)	190	
Positive	48	(41)	13	(25)	15	(24)	15	(30)	91	
Age in years										
Median [range]	70	[46-85]	61	[35-72]	62	[32-73]	55	[35-77]		
Previous radiotherapy										
Yes	35	(30)	15	(29)	5	(8)	7	(14)	62	
No	83	(70)	36	(71)	57	(92)	43	(86)	219	
ASA-score										
ASA 1 / 2	67	(57)	37	(73)	49	(79)	43	(86)	196	
ASA 3, >	25	(21)	2	(4)	4	(7)	0		31	
Unknown	26	(22)	12	(23)	9	(15)	7	(14)	54	
Total	118		51		62		50		281	

Table 2: Early complications according to diversion. In some patients multiple complications occurred

Complication	Total		Ileal conduit		Indiana		Neo bladder		SPCN	
	N	(%)	N	(%)	n	(%)	n	(%)	n	(%)
RELATED TO DIVERSION										
<i>Minor</i>										
Wound infection	23	(8.2)	14	(11.9)	4	(7.8)	1	(1.6)	4	(8.0)
Prolonged ileus	8	(2.8)	4	(3.4)	1	(2.0)	2	(3.2)	1	(2.0)
Urinary tract infection	36	(12.8)	14	(11.9)	7	(13.7)	9	(14.5)	6	(12.0)
Stoma necrosis	2	(0.7)	-		1	(2.0)	1	(1.6)	-	
<i>Major</i>										
Necrosis of diversion	2	(0.7)	1	(0.8)	-		1	(1.6)	-	
Rectal injury	2	(0.7)	2	(1.7)	-		-		-	
Fascial dehiscence	14	(5.0)	6	(5.1)	1	(2.0)	5	(8.1)	2	(4.0)
Ureteroileal leakage	3	(1.1)	1	(0.8)	-		-		2	(4.0)
Intestinal suture leakage	2	(0.7)	1	(0.8)	-		-		1	(2.0)
Pelvic/abdominal abscess	3	(1.1)	2	(1.7)	-		-		1	(2.0)
Bleeding	4	(1.4)	3	(2.5)	-		-		1	(2.0)
Death	8	(2.8)	3	(2.5)	3	(5.9)	2	(3.2)	-	
Fistula	1	(0.4)	-		-		1	(1.6)	-	
Sepsis	27	(9.6)	13	(11.0)	6	(11.8)	5	(8.1)	3	(6.0)
NOT RELATED TO DIVERSION										
<i>Minor</i>										
Pneumonia	22	(7.8)	13	(11.0)	4	(7.8)	3	(4.8)	2	(4.0)
Deep venous thrombosis	4	(1.4)	-		-		2	(3.2)	2	(4.0)
Sacral pressure ulcer	1	(0.4)	1	(0.8)	-		-		-	
Delirium tremens	2	(0.7)	2	(1.6)	-		-		-	
<i>Major</i>										
Pulmonary embolus	7	(2.5)	3	(2.5)	2	(4.0)	2	(3.2)	-	
Myocardial infarction	6	(2.1)	3	(2.5)	1	(2.0)	2	(3.2)	-	
Respiratory failure	3	(1.1)	2	(1.7)	-		-		1	(4.0)
PEG-leakage	1	(0.4)	-		-		-		1	(2.0)

Table 3: Late complications according to diversion. In some patients multiple complications occurred

Complication	Total		Ileal conduit		Indiana		Neo bladder		SPCN	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Minor										
Urinary tract infection	89	(32.8)	26	(22.8)	20	(41.7)	24	(40.7)	19	(38.0)
Herniation	14	(5.2)	7	(6.1)	2	(4.2)	2	(3.4)	3	(6.0)
Diarrhea	2	(0.7)	-	-	-	-	1	(1.7)	1	(2.0)
Broken JJ stent	1	(0.4)	-	-	-	-	-	-	1	(2.0)
Dehydration/metabolic disorders	5	(1.8)	-	-	-	-	2	(3.4)	3	(6.0)
Major										
Ureteroileal stricture	29	(10.7)	13	(11.4)	5	(10.4)	5	(8.5)	6	(12.0)
Urethral stricture	12	(4.4)	-	-	-	-	10	(16.9)	2	(4.0)
Fistula	10	(3.7)	3	(2.6)	4	(8.3)	1	(1.7)	2	(4.0)
Herniation	25	(8.5)	4	(3.5)	6	(12.5)	9	(15.3)	6	(12.0)
Stoma stenosis	9	(3.3)	3	(2.6)	6	(12.5)	-	-	-	-
Lymphocele	4	(1.5)	2	(1.8)	2	(4.2)	-	-	-	-
Ileus	7	(7.4)	2	(1.8)	1	(2.1)	3	(5.1)	1	(2.0)
Vaginal prolapse	2	(0.7)	1	(0.9)	1	(2.1)	-	-	-	-
Severe reflux	1	(0.4)	-	-	-	-	1	(1.7)	-	-
Sepsis	27	(9.6)	13	(11.0)	6	(11.8)	5	(8.1)	3	(6.0)

Functional results:

Stoma stenosis occurred in three patients (3%) following ileal diversion and six patients (13%) after Indiana pouch, requiring surgical revision. Figures of day/night time continence and CIC-rates are summarised in figure 2.

Metabolic complications:

Of 271 patients surviving more than 30 days serum samples for acidosis were obtained in 237 patients, for vitamin B12 in 141 patients, and for folic acid in 117 patients.

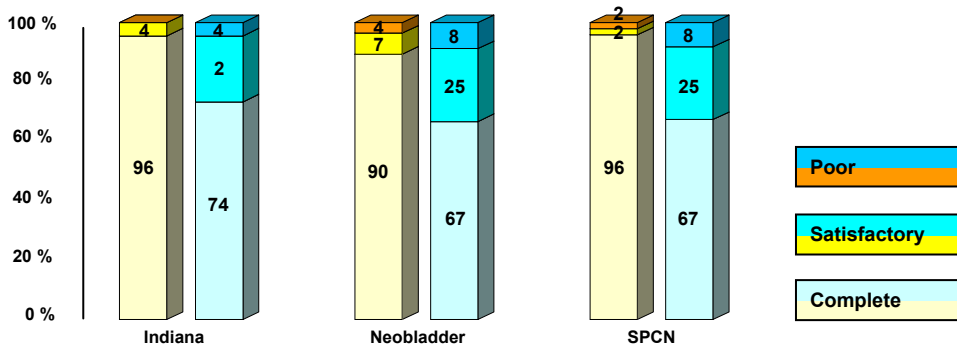
Hyperchloremic acidosis was found in 52 patients; with an incidence of 17% after ileal conduit, 24% after Indiana pouch, and 26% after orthotopic diversion (neobladder and SPCN combined)(table 4). 20 patients needed treatment with sodium bicarbonate and four patients were hospitalised because of acidosis and salt losing hypovolemia. All other patients experienced mild metabolic acidosis only, requiring no treatment.

Abnormal vitamin B12 values were measured in 24 out of 271 patients (8,8%) during follow-up. Low vitamin B12 was not associated with type of diversion (table 4). 16 patients with low vitamin B12 values were treated, 1 patient received treatment because of symptoms of low vitamin B12 while serum vitamin B12 was in the low range of normal values. The median time between cystectomy and abnormal vitamin B12 values was 41 months.

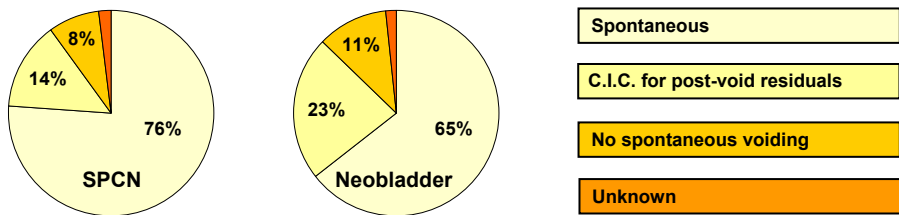
One patient (after ileal conduit) developed a low folic acid value together with a low vitamin B12, but was not treated.

Figure 2: Functional results according to diversion. Yellow bars represent continence rates at daytime, blue bars continence rates at night time. Complete continence: no involuntarily loss of urine and no pad use. Satisfactory continence: one pad per day/night. Poor continence: multiple pads per day/night. Pies represent voiding methods

Continence



Voiding methods



Discussion

Cystectomy with subsequent urinary diversion is still associated with considerable complications. Reported rates and types of complications vary widely, and many series report on one type of diversion, which makes them hard to compare. To evaluate complication rates and functional results of the four most commonly used diversions, we report on all consecutive diversions performed in our institute.

The early- (44%) and late complication rates (51%) at our institute are in the higher ranger of earlier reports rates, which vary widely between 16-61% (early) and 24-66% (late).^{4,5,9,13-21} Moreover the types of reported complications differ between reported series. Some series do not include urinary tract infections in the calculation of complication rates, which accounted for 1/4 of the early and 1/3 of the late complications in this series. Comparison of late complication rates between series is even more complex as these are highly dependent from duration of follow-up. Madersbacher illustrated that late complication rates might increase in time till over 90% after 15 years, and stated that the entire morbidity spectrum is only covered after one decade.¹⁷

Table 4: Metabolic complications according to diversion

Complication	Total		Ileal conduit		Indiana		Orthotopic	
	n	(%)	n	(%)	n	(%)	n	(%)
Hyperchl. acidosis								
No	185	(78.1)	77	(82.8)	32	(76.2)	76	(74.5)
Yes	52	(21.9)	16	(17.2)	10	(23.8)	26	(25.5)
<i>Measured</i>	<hr/> 237		<hr/> 93		<hr/> 42		<hr/> 102	
<i>Unknown</i>	34							
Hypochl. acidosis								
No	231	(97.5)	90	(96.8)	41	(97.6)	100	(98.0)
Yes	6	(2.5)	3	(3.2)	1	(2.4)	2	(2.0)
<i>Measured</i>	<hr/> 237		<hr/> 93		<hr/> 42		<hr/> 102	
<i>Unknown</i>	34							
Low vitamin B12								
No	117	(83.0)	31	(77.5)	22	(84.6)	64	(85.3)
Yes	24	(17.0)	9	(22.5)	4	(15.4)	11	(14.7)
<i>Measured</i>	<hr/> 141		<hr/> 40		<hr/> 26		<hr/> 75	
<i>Unknown</i>	130							
Low Folic acid								
No	116	(99.2)	29	(96.7)	23	(100)	64	(100)
Yes	1	(0.8)	1	(3.3)	0		0	
<i>Measured</i>	<hr/> 117		<hr/> 30		<hr/> 23		<hr/> 64	
<i>Unknown</i>	154							

Cystectomy appears to be safe in the elderly, but urologist should realize that the superiority of cystectomy above radiotherapy is still debated, especially in patients with high age and ASA-score.^{1,2} We found an (expected) association between early major complications and high ASA-score, but this was independent from the type of diversion that was used. Furthermore patients with an ileal conduit experienced less late complications. No specific complication was dominant in any type of diversion. Comparison however might still be hampered by inherent biases. Although the patient has great influence on the definite type of diversion, the clinician's preference and information remain an important determinant in choice, considering the differences in age and ASA between the patients opting for an ileal conduit and continent diversions. We found no significant association between tumour stage, ASA, age, pre-operative radiotherapy, gender and diversion related complication rates, but conclusions have to be interpreted with caution due to the methodological limitations inherent to retrospective studies. Additionally, the comparison of functional results of orthotopic and external diversions is highly debatable. The chance of involuntary urine loss however can be of significant importance for a patient in the decision of type of diversion. For this reason these figures are provided, but the reader has to be aware of the methodological restrictions when comparing these figures.

The high percentage (11%) of ureteroileal strictures is remarkable and deserves our attention. In 17 out of 23 patients an irreversible partial loss of renal function at the strictured site had occurred despite treatment. Reported rates vary between 0.6% and 9%.^{13,21,22} However, some report stricture-rates per renal unit, which would be 6% in these series. Madersbacher found deterioration in 2/3

of his patients after 5 years¹⁷, so our percentage might even increase over time. This and the irreversible partial or total loss of the ipsilateral kidney function, even after treatment, underline the importance of close monitoring of these patients.

The rates of satisfactory to complete continence of the SPCN are slightly better than those for neobladder. In the SPCN series mainly women experienced incontinence, while continence in males approached 100%. These rates are in accordance with other reports which vary between 88%-100%, although nightly incontinence was experienced frequently in the neobladder group.^{9,13,21,23,24} Many of these patients though experience periods of incontinence associated with UTI's, which decline after antibiotics.

Metabolic abnormalities can occur when intestine is incorporated in the urinary tract. Renal impairment, large bowel surface, and long contact are factors associated with the development and severity of the disorder. We found no difference in incidence of metabolic abnormalities according to the diversion used. Although 52 patients developed a hyperchloremic acidosis, only 20 needed treatment with bicarbonate and 4 were re-hospitalized. The risk of clinically important acidosis after urinary diversion therefore seems small but substantial and is in concordance with previous publications, although the incidence in the ileal conduit group is higher than described in the literature.^{9,17} Theoretically large resections of ileum lead to vitamin B12 malabsorption.⁶ As a consequence we expected more often deficiencies after continent diversions, but we found the opposite. However, serum samples were more often obtained as a routine procedure in the continent diversion groups, while patients with an ileal conduit are only tested when showing symptoms. Furthermore, insufficient intake instead of malabsorption might be another important cause for low serum samples.

Improved surgical techniques, such as laparoscopic cystectomy, and improvements in anaesthesia and peri-operative care may have resulted in reduced morbidity and shorter hospital stay.^{5,25} Nevertheless cystectomy remains associated with significant morbidity, but this seems not diversion related. In our opinion type of diversion should be selected according to local tumour stage, hand function and renal function, not by the presumed fear of complications.

Conclusions

Cystectomy with any subsequent diversion remains a procedure with considerable morbidity. High ASA score is associated with more early complications. Orthotopic diversions provide good functional results, but at the cost of more late complications compared with cutaneous diversions. Provided that patients' choice is based on thorough pre-operative consultation, we found no evidence that age, ASA-score, positive lymph nodes, extravesical tumour growth, or previous radiotherapy are contraindications per se for any diversion.

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