

Original article

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Analysis of Trends in the Performance of Urinary Diversions After Total Cystectomy: 15-Year Experience

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Abstract

The aim of our study was to analyze trends in urinary diversion (UD) in patients who underwent radical cystectomy (RC) from 2008 to 2023, with special reference to the period of the COVID-19 pandemic. A total 283 study patients (pts) (243 men and 40 women, mean age 65,07±7,73 years) were divided by the type of UD into the following groups: Mainz pouch 2 (MP2) – 85 pts, Ileal conduit (IC) – 89 pts, Ureterocutaneostomy (UCS) – 105 pts, Percutaneous nephrostomy (PCN) – 4 pts. The relative share of incontinent and continent UD was 70% and 30%, respectively. MP2 was the most represented UD from 2008 to 2013, IC from 2014 to 2019, and UCS from 2019 to 2023. The most common UD was UCS (37.1%), followed by IC (31.4%), MP 2 (30.0%) and PCN (1.4%). Temporal UD trends were variable, with relatively stable annual share of MP2 and IC and the lowest annual share of UCS until the period of the COVID-19 pandemic, when it had significantly increased, with a peak in 2022. Trend analysis shows significant increase of UCSs in the period 2008-2023 ($p < 0.001$), without significant change of trends in the other groups ($p > 0.05$). The trends of continent and incontinent UD after RC shown in our study are consistent with the data reported in the current literature.

Key words: urinary diversions, trends, Mainz-pouch 2, ileal conduit, ureterocutaneostom

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Analiza trendova u izvođenju urinarnih derivacija nakon totalne cistektomije: petnaestogodišnje iskustvo

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Apstrakt

Cilj našeg istraživanja bio je da analiziramo trendove urinarnih derivacija (UD) kod pacijenata koji su podvrgnuti radikalnoj cistektomiji (RC) od 2008. do 2023. godine, sa posebnim osvrtom na period pandemije COVID-19. Ukupno 283 pacijenta (243 muškarca i 40 žena, prosečne starosti 65,07±7,73 godine) podeljeno je prema tipu UD u sledeće grupe: Mainz pouch 2 (MP2) – 85 pacijenata, Ileumski konduit (IC) – 89 pacijenata, Ureterokotaneostomija (UCS) – 105 pacijenata, Perkutana nefrostomija (PCN) – 4 pacijenta. Relativni udeo inkontinentnih i kontinentnih UD iznosio je 70% i 30%, ponaosob. MP2 bila najzastupljenija UD od 2008. do 2013, IC od 2014. do 2019, i UCS od 2019. do 2023. Godine. Najzastupljenija UD bila je UCS (37,1%), zatim IC (31,4%), MP2 (30,0%) i PCN (1,4%). Vremenski trendovi UD bili su promenljivi, sa relativno stabilnim godišnjim udelom MP2 i IC i najnižim udelom UCS do perioda pandemije COVID-19, kada je značajno povećan, sa vrhuncem u 2022. Analiza trenda pokazuje značajno povećanje UCS u periodu 2008-2023 ($p < 0,001$), bez značajnije promene trendova u ostalim grupama ($p > 0,05$). Trendovi kontinentnih i inkontinentnih UD nakon RC prikazani u našoj studiji, u skladu su sa podacima prikazanim u aktuelnoj literaturi.

Ključne reči: urinarne derivacije, trendovi, Mainz pouch 2, ileumski konduit, ureterokotaneostomija

Introduction

Recent epidemiological data show that bladder cancer (BC) is the 2th most common genitourinary malignancy and 10th among all cancers in the general population, with the incidence rates 9,5 in men and 2,4 in women (per 100 000), mortality rates 3,3 in men and 0,9 in women, and a total of 573 278 new cases in 2020 worldwide. Overall incidence rates range from 3.1 in low/medium human development index (HDI) countries to 11.7 per 100 000 in high/very high HDI countries (1). Reported age-standardized incidence rates are 20 and 4.6 for male and female population in Europe (2). About 70-75% of BCs are detected at \leq T1 stages, as non-muscle-invasive bladder cancer (NMIBC), which are amenable to treatment and associated with longer survival, while the remaining 25-30% are detected at later, \geq T2 stages, as muscle-invasive bladder cancer (MIBC) (2,3). Among all histopathological types of BC, the largest share belongs to urothelial carcinoma (UC) (>90%), while the total share of other types, including squamous cell carcinoma, adenocarcinoma and neuroendocrine carcinoma of the urinary bladder, is less than 10% (4,5). The primary treatment of choice for MIBC includes radical cystectomy (RC) with pelvic lymphadenectomy and urinary diversion (UD) (6,7). So far, numerous of UD techniques have been described, from simple ureterocutaneostomy (UCS) to orthotopic neobladder (ONB). There is still debate as to which UD is best in terms of feasibility, long-term outcomes, and patient quality of life. However, the more complex operative technique for creating UD, the higher criteria for patient selection.

Aim

The aim of the present study was to analyze trends in UD over a period of 15 years, in patients who underwent RC and UD in our clinic, with special reference to the period of the COVID-19 pandemic.

Material and methods

For the purposes of our retrospective study, we identified a total of 283 consecutive patients (243 men and 40 women, mean age $65,07 \pm 7,73$ years) who underwent RC and UD during a 15-year period, from 2008 to 2023. Based on the patients' medical records, the following data were analyzed: patient demographics, indication for RC, the date of the operation, type of UD and histopathological report of the RC specimen (type of the cancer, pathological grade and stage). In order to analyze temporal variations in UD trends, patients were examined both in relation to the type of UD and the time period, with special reference to the period of the COVID-19 pandemic. This study was conducted according to the Declaration of Helsinki ethical principles, with guaranteed discretion of personal data, and had been approved by the Ethics Committee of the University Clinical Center Nis, protocol number 28305.

According to the type of the UD, patients were divided into the following groups:

1. Group MP2 – 85 patients with sigma-rectum pouch (Mainz pouch 2) UD;
2. Group IC – 89 patients with Ileal conduit UD;
3. Group UCS – 105 patients with ureterocutaneostomy UD;
4. Group PCN – 4 patients with percutaneous nephrostomy UD;

Statistical data are presented in the form of arithmetic mean, standard deviation, minimum and maximum values. Comparison of categorical features was performed using the Chi-square test. For the trend analysis of the number of UD in the monitoring period, joinpoint regression analysis was used. The analysis was done in the program package Joinpoint regression analysis Joinpoint Regression Program, Version 4.8.0.1. April, 2020; Statistical Research and Applications Branch, National Cancer Institute). Other statistical analyzes were performed in the OpenEPI Info software package.

Results

Over the study period, a total of 283 patients underwent RC with UD. Of these, incontinent diversion (ID) was performed in 198 patients (70%), and continent diversion (CD) in 85 patients (30%). The annual number of cystectomies in the study period shows significant variations, ranging from 4 to 46 per year, without the existence of a linear trend of increase or decrease (Table 1). The lowest annual number of operations was performed in 2017 (n=4) and the highest in 2022 (n=46). Figure 1 shows the time trends and relative share of CD and ID after cystectomy.

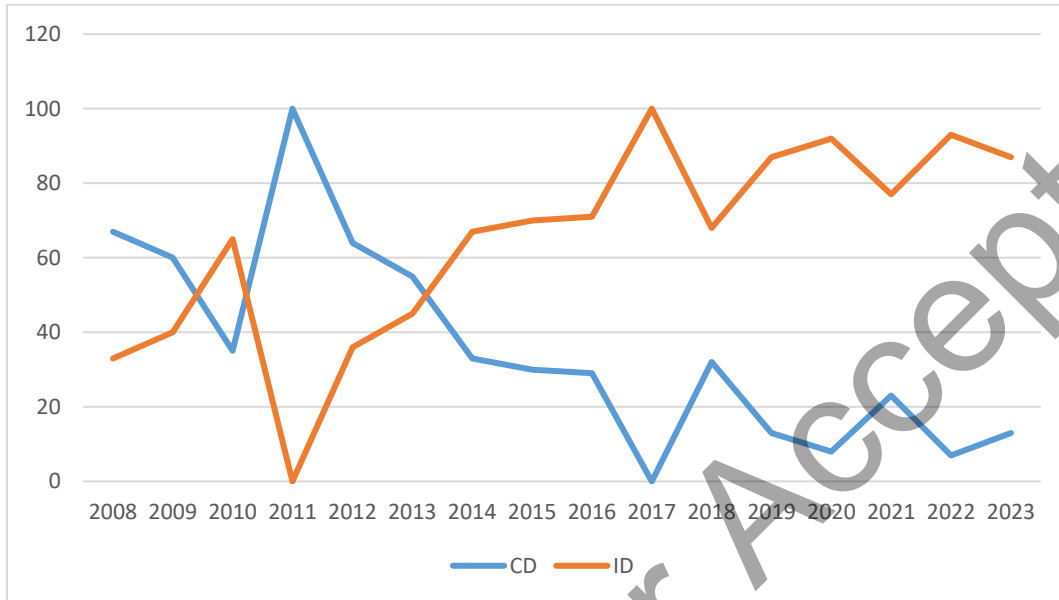


Figure 1. Time trends of CD and ID

In 2008, 2009, 2017 and 2023, the annual number of operations was low (<10 per year), while 2010, 2011, 2013, 2014 and 2015 had been characterized by a slightly higher number of operations (10-20 per year). During 2012 and 2018-2022, there were more than 20 operations per year, with largest annual number in 2022 (n=46). The annual number of operations is shown in Table 1.

Table 1. Number of cystectomies with UD by type

Year	Continent diversion (CD)		Incontinent diversion (ID)					CD + ID	
	MP2		IC	UCS	PCN	ID	TOTAL	TOTAL	
	No	%	No	No	No	No	%	No	%
2008	6	67	1	-	2	3	33	9	100
2009	3	60	1	-	1	2	40	5	100
2010	5	35	9	-	-	9	65	14	100
2011	11	100	-	-	-	.	-	11	100
2012	16	64	8	-	1	9	36	25	100
2013	6	55	5	-	-	5	45	11	100
2014	5	33	7	3	-	10	67	15	100
2015	3	30	5	2	-	7	70	10	100
2016	6	29	12	3	-	15	71	21	100
2017	-	0	3	1	-	4	100	4	100
2018	8	32	9	8	-	17	68	25	100
2019	3	13	10	10	-	20	87	23	100
2020	2	8	4	19	-	23	92	25	100
2021	7	23	9	15	-	24	77	31	100
2022	3	7	6	37	-	-	-	46	100
2023	1	13	-	7	-	-	-	8	100
TOTAL	85	100	89	105	4	198	100	283	100

Table 2 shows the demographic and clinical characteristics of the studied population. The average age of the entire examined population was $65,07 \pm 7,73$ years (37 years, 82 years). In relation to gender distribution, 83.5% of patients were male and 16.5% female. The most common UD was UCS (37.1%), followed by IC (31.5%), MP2 (30.0%) and PCN (1.4%). In terms of histological grade (HG), the most common was HG 3 (75,6%), followed by HG 2 (21,8%), HG 4 (1,8%) and HG 1 (0,8%) (Table 2). The highest relative share of pT4 stage was in the UCS group (35,2%), followed by MP2 group (10.6%), IC group (13.5%) and PCN group (25%). There is no statistically significant difference among the groups in terms of gender ($p=0.452$), age ($p=0.525$) and HG ($p=0.504$). In all groups, the most represented age category was 60-69 years (Table 2).

Table 2. Demographic and clinical characteristics of the studied population

Characteristic		MP2		IC		PCN		UCS		p
		No	%	No	%	No	%	No	%	
Gender	Male	73	85,9	73	82,0	3	75,0	94	89,5	0,452
	Female	12	14,1	16	18,0	1	25,0	11	10,5	
	Total	85	100	89	100	4	100	105	100	
Age	<50	3	3,5	2	2,2	1	25,0	5	4,8	0,525
	50-59	23	27,1	21	23,6	0	0,0	18	17,1	
	60-69	45	52,9	45	50,6	2	50,0	54	51,4	
	70-79	13	15,3	20	22,5	1	25,0	26	24,8	
	80+	1	1,2	1	1,1	0	0,0	2	1,9	
Histological grade (HG) *	I	1	1,2	1	1,2	0	0,0	0	0,0	0,504
	II	22	27,2	17	20,2	0	0,0	18	19,1	
	III	58	71,6	65	77,4	3	100,0	72	76,6	
	IV	0	0,0	1	1,2	0	0,0	4	4,3	
Pathological tumor stage (pT) **	NEM	0	0,0	1	1,1	0	0,0	0,0	0,0	
	pTa	5	5,9	3	3,4	0	0,0	6	5,7	
	pT1	6	7,41	8	9,0	0	0,0	4	3,8	
	pT2	25	29,4	24	27,0	1	25,0	20	19,0	
	pT3	37	43,5	41	46,1	2	50,0	34	32,4	
	pT4	9	10,6	12	13,5	1	25,0	37	35,2	

*Available for 275 patients; **available for 262 patients.

According to the histopathological report of the RC specimen, the most common indication for RC was UC of the bladder, in 91.5%. Other indications were less prevalent, as follow: UC with squamous differentiation (3,6%), pure neuroendocrine carcinoma (1,1%), colonic adenocarcinoma (1,1%), undifferentiated UC (0,7%), urothelial adenocarcinoma (0,4%), UC of prostatic urethra (0,4%), prostate adenocarcinoma (0,4%), vesico-intestinal fistula (0,4%) and nonresectable inflammatory conditions of the bladder (0,4%).

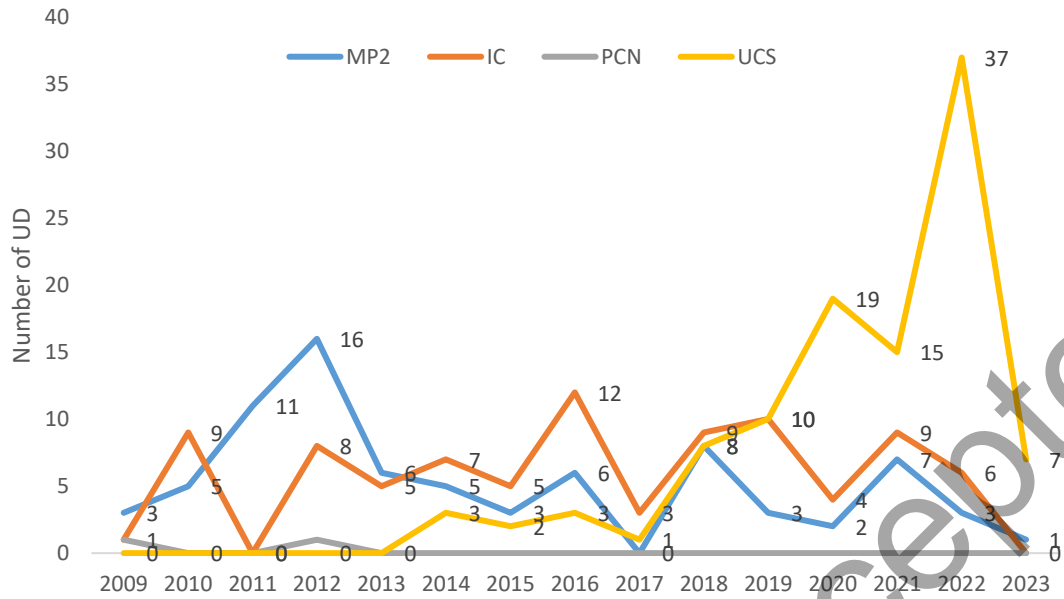
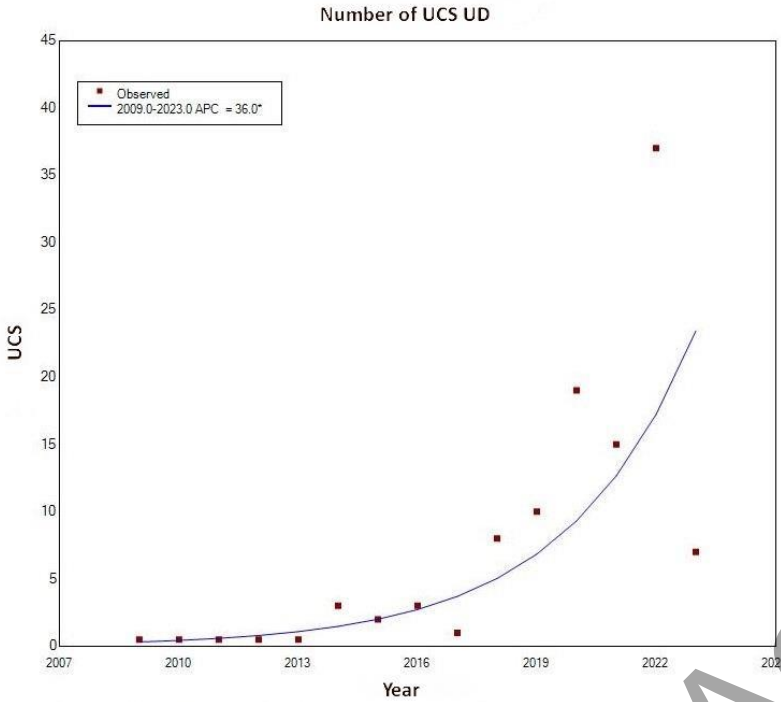


Figure 2. Number of urinary diversion by type

The annual number of UD across all studied groups is shown in Figure 2. During the period 2008-2013, not a single UCS was performed. UCS has been implemented since 2014 (3 cases) and after that only a few cases were done per year, ending in 2017. From 2018, an increasing trend in the annual number of UCS was observed, peaking in 2022, with as many as 37 cases. There was no statistically significant trend of change in the number of cases in other studied groups ($p>0.05$).



* Indicates that the Annual Percent Change (APC) is significantly different from zero at the alpha = 0.05 level.
Final Selected Model: 0 Joinpoints.

Figure 3. Number of UCS UD in the study period

Figure 3 shows the annual number of UCS from 2008 to 2023. Trend analysis shows that there was a statistically significant trend of increasing the number of UCS in the period 2008-2023, with an annual percentage change (36.0, 95%CI 24.4-48.7, $p < 0.001$).

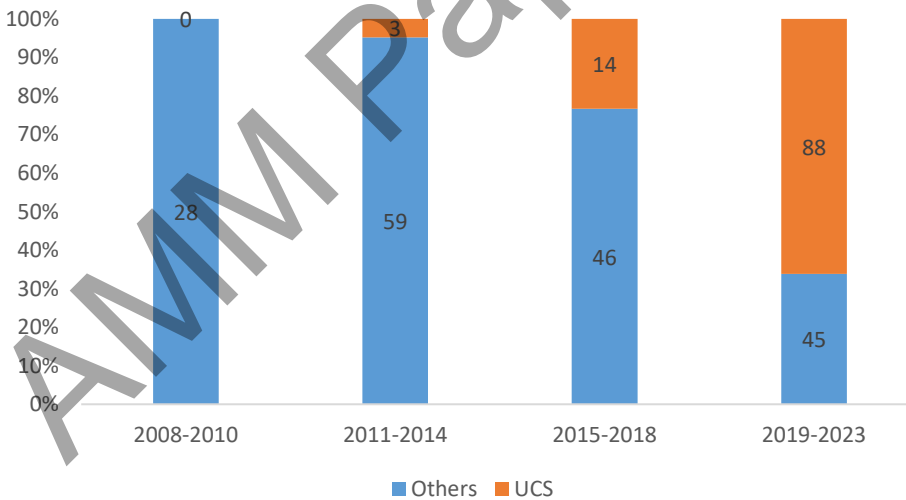


Figure 4. Proportion of UCS UD in the study period

Figure 4 shows the variability of the number of UCS UD performed over 4 time intervals during the entire period: 2008-2010, 2011-2014, 2015-2018, 2019-2023. The frequency of UCS changed statistically

significant during the study period ($p < 0.001$). In relation to the total number of UCS ($n = 105$), the relative share of the time interval 2019-2023 is 66.2%, while in other time intervals it is less: 23.3% for 2015-2018, 4.8% for 2011-2014, and 0% for 2008-2010.

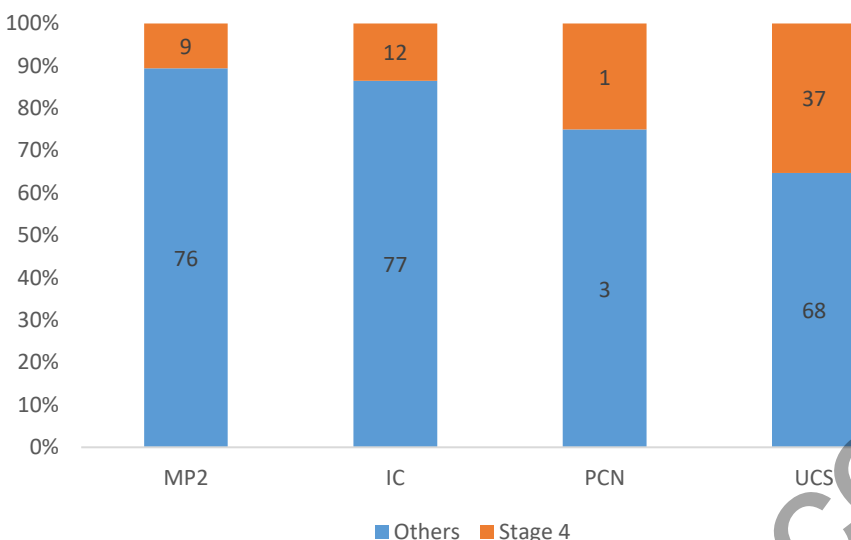


Figure 5. Proportion of T4 stage in the study period

There were a total of 59 patients (20.8%) with pT4 stage. The relative share of pT4 stage was the highest in the UCS group (35.2%) and this difference compared to the other groups is statistically significant (MP2-10.6%; IC-13.5%; PCN-25%) ($p < 0.001$) (Figure 5).

Discussion

A recent report by Farber et al. on the disparity in the use of CD after RC for BC, in a sample of 76,040 patients operated on in the United States of America (USA) from 2001 to 2012, showed IC and CD rates of 90.8% and 9.2%, respectively (8). The relative share of CDs had an increasing trend, with a peak in 2008 (almost 12%), with significant decreasing trend thereafter. A higher proportion of CDs was associated with urban areas, high-volume academic hospitals and patients from the western regions of the country. Similarly, the California group published an analysis of 10-year trends (2004-2013) in the USA on the use of ID and CD after RC in 27170 patients (6). It was shown that the relative share of ID and CD was 85.5% and 14.5%, respectively. However, the relative share of CD showed a statistically significant decrease, from 17.2% during the first three years to 12.1% during the last 3 years (6). Comparing early operative results of IC versus CD after RC for BC in the USA, Rezaee et al. reported that of 4755 RCs for BC in 2019 and 2020, 677 patients (14.2%) received CD (9).

In our series, the proportion of ID and CD was 70% and 30%, respectively. Temporal variations were most pronounced in 2011 (ID-0%; CD-100%) and 2017 (ID-100%; CD-0%), while in other periods the difference was more moderate. The increase in the share of ID compared to CD has been recorded since 2013/2014, with a relatively stable ratio until 2023 (Table 1, Figure 2). As in the presented series, the proportion of female patients in our series is significantly lower compared to men (6,8). When it comes to pathohistological indications for RC, UC was present in 91.5% of our patients. The relative share of other UC morphological subtypes and benign indications was 7.7% and 0.8%, respectively.

According to the 2022 WHO classification, as well as the data presented by Amin et al. and Comp erat et al, urothelial carcinoma is the most common morphological subtype of UC occurring in >90% of patients with MIBC, which is consistent with our results (4,5,10). Benign diseases as indications for cystectomy are very rare, including neurogenic bladder, post-irradiation conditions, interstitial cystitis and urinary incontinence (11-16).

Our results show evident temporal variability of UD during certain time periods in our series. Thus, MP2 was the most represented UD from 2008 to 2013, IC from 2014 to 2019, and UCS from 2019 to 2023.

Mainz pouch II is a modification of the ureterosigmoidostomy (USS) and was originally presented by Fisch in 1993 (17). It has fewer contraindications compared to ONB and is acceptable for a large number of candidates including those with advanced stages of BC. The operative technique is relatively simple compared to other CDs and has been promoted as their alternative, with low complication rates and good health related quality of life (HRQoL) (18-20). It has been successfully applied in our clinic since 1995, to overcome the drawbacks of UCS, USS and ONB, including insufficient support for the needs of stoma devices, postoperative care and nutrition, as well as the management of surgical and metabolic complications. Several series of our results have been published, confirming that the technique is associated with low complication rates and good HRQoL, with certain disadvantages such as malignant transformation of the ureterointestinal anastomosis and metabolic acidosis (18-21).

Since its introduction by Bricker in 1950, IC has become widely accepted due to the absence of metabolic complications and has since evolved into the gold standard for UD (22). Farber et al. reported that from 2001 to 2012 in the USA, IC was the UD of choice after RC in nearly 90% of cases (8). There are several reasons for this disparity in favor of IC, including the technical simplicity of the procedure, shorter operative time, better training of urologists for this type of procedure, fear of possible complications, the increasing use of robotic surgery and the poor financial benefit of CD (8,23). In a five-year series of the total number of cystectomies with UD from 2001 to 2005 in the USA, Gore et al. reported that out of 27,494 patients, 83.5% underwent IC and 16.5% underwent CD (24). Analyzing five-year trends in UDs at a high-volume tertiary urology clinic in the USA, Lowrance et al. stated that IC was the most frequent UD, with a relative participation of 63%, with an increasing time trend, while ONB was performed in 37% of cases. The authors also point out that there is a trend of IC, especially associated with female gender, advanced age, locally advanced disease and significant comorbidity factors (25). Furthermore, the recommendations of the American Urological Association (AUA) Guidelines include mandatory preoperative counseling with the patient regarding the choice of IC or CD as UD (26). In our series, IC was more prevalent compared to MP2 in the age group 70-79 years (15.3% vs. 22.5%), as well as in pT3/T4 stages (60% vs. 56%). A meta-analysis of 18 large studies on the overall HRQoL of patients after IC or CD did not find of significant differences (27).

The simple technique of UCS dates back to the 19th century, when Hayes Agnew from Philadelphia performed a ureterocutaneous stoma on the abdominal wall due to an injury to the ureter (2,20). In a recent systematic review comparing IC and UCS, Korkes et al. concluded that UCS is more feasible than IC, especially in elderly and fragile patients, not only because of the avoidance of bowel surgery, but also due to shorter operative time, perioperative care and hospitalization, as well as lower rates of bleeding, transfusion and complications (28). Deliveliotis et al. emphasize that UCS is particularly indicated in high-risk elderly patients, as well as in patients with a solitary kidney, with certain disadvantages including higher rates of ureterocutaneous stenosis and ascending UTIs, compared to techniques with ureteral diversion through intestinal cutaneostomy (29). The occurrence of stomal stenosis can be successfully prevented by postoperative ureteral double-J stenting, and Kozaciođlu reported positive experiences in this regard (30).

Comparing the complications of three UDs, including IC, UCS, and colon conduit (CC), a study by Picha et al. showed that major diversion-related complications were significantly more frequent in IC and CC and absent in UCS, while late reinterventions had occurred more frequently in IC (20%) compared to CC (5.8%) and UCS (2.4%), highlighting this as an important advantage of UCS, especially with regard to HRQoL (31). A recent meta-analysis by Nabil et al. on long-term outcomes between IC and UCS, including 10 studies with 3689 patients, showed advantages of UCS over IC in terms of length of stay, with similar results in terms of major complications, HRQoL and survival rates (32).

As already mentioned, there were 17 UCS from 2008 to 2018, and 88 from 2019 to 2023 in our series. A statistically significant increase in the number of UCS was observed throughout all analyzed time periods, with progressive peaks recorded during 2019, 2020 and 2022, making the relative share of UCS in this period as much as 66.2% of the total number of UCS in the entire series. In addition, the relative share of pT4 stage in the UCS group was 62.7% (37 out of 59 patients), significantly higher compared to the other groups. It is evident that the increase in the number of UCS coincides with the beginning of the COVID-19 pandemic and the corresponding restructuring of health capacities, in accordance with certain measures in the fight against the pandemic. These measures included a whole series of systemic solutions, related to patient admission protocols, repurposing of spatial capacities, redirection of human resources, preservation of equipment, prevention of iatrogenic infection, while giving certain priorities to elective oncological operations in circumstances of limited resources (33). In an attempt to precisely define the criteria for establishing priorities in the triage of uro-oncological elective operations, several clinical guidelines have been published containing the same provisions regarding urgent indications, including radical cystectomy for MIBC, radical or partial nephrectomy for renal cell carcinoma (RCC) in T3 tumors and nephroureterectomy for high-grade and/or clinical T1+ tumors (34,35).

Conclusion

in our study, a total of 283 RC with UD performed from 2008 to 2023 were analyzed. Of these, ID and CD were performed in 198 (70%) and 85 (30%) patients, respectively. The annual number of operations ranged from 4 to 46, depending on the number of patients. The most represented UD was UCS, followed by IC, MP2 and PCN. The highest relative share of pT4 stage was in the UCS group, followed by MP2 group, IC group and PCN group. The most common indication for cystectomy was urothelial carcinoma of the bladder. The annual share of MP2 and IC was relatively stable, with slight variations. The annual share of UCS shows lowest values until the period of the COVID-19 pandemic, when it increases significantly, with a peak in 2022. Due to its simplicity and feasibility, UCS has proven to be a suitable UD during the COVID-19 pandemic. The trends regarding ID and CD after RC shown in our study are consistent with the trends reported in the current literature.

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