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Radical cystectomy under continuous antiplatelet therapy with acetylsalicylic acid

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ABSTRACT

Introduction: Aim of this study was to analyse the perioperative outcome of patients undergoing radical cystectomy under continuous antiplatelet therapy with acetylsalicylic acid.

Materials and methods: Using prospectively maintained databases of two departments of urology, we identified 461 consecutive patients who underwent radical cystectomy for bladder cancer (2011–2017). Patients were divided into three groups: 1) on-going antiplatelet therapy with acetylsalicylic acid (n = 50), 2) discontinuing antiplatelet therapy (n = 65) and 3) no antiplatelet therapy (n = 346). Perioperative outcome was compared between the three groups using ANOVA, likelihood ratio or Kruskal Wallis test with post-hoc testing. Uni- and multivariate analyses were performed to identify predictor for perioperative complications and transfusion.

Results: Group 1 showed an average estimated blood loss of 732 ± 424, group 2 752 ± 488 and group 3 810 ± 544 ml (p = 0.51). There was no significant difference in transfusion rate (44% in group 1, 45% and 39% in groups 2 and 3, p = 0.63). Severe complications occurred in 26%, 15% and 15% in groups 1–3 (p = 0.19). Ischemic complications were more often observed in group 1 (n = 4, 8%) and 2 (n = 5, 8%) than group 3 (n = 7, 2%), p = 0.02. 90-day readmission (n = 99, 22%) and mortality rate (n = 10, 2.2%) were low and did not show any significant differences between the groups. In uni- and multivariate analysis ongoing therapy with acetylsalicylic acid was no independent risk factor for transfusion or severe complications.

Conclusion: Perioperative continuation of therapy with acetylsalicylic acid in radical cystectomy is safe with no difference in intraoperative blood loss, transfusion rate, complications or mortality.

Introduction

Radical cystectomy (RC) with pelvic lymphadenectomy and urinary diversion is standard therapy for patients with non-metastatic muscle invasive bladder cancer (MIBC). Despite high standardization it remains a procedure with considerable morbidity and transfusion rate [1]. With the aging populations, patients admitted for surgery more frequently suffer from cardiovascular co-morbidities such as coronary heart disease (CHD) [2]. In respective patients, antiplatelet therapy with low dose acetylsalicylic acid (ASAC) is recommended as a lifelong secondary prophylaxis to reduce risk of cardiac events [3]. Major non-cardiac surgery such as RC can cause severe cardiac complications such as myocardial infarction in more than 5% [4,5]. Patients who have a history of cardiac illness are at an even higher risk for perioperative cardiac events. To reduce risk of perioperative cardiac complications, multiple studies have suggested to continue antiplatelet therapy perioperatively [6]. However, this may significantly increase the risk for haemorrhagic complications. The European guideline for cardiovascular assessment for non-cardiac surgery gives a recommendation that antiplatelet therapy with low dose ASAC should be continued perioperatively, if there is a higher risk for thromboembolic complications and if bleeding risk is not considered to be very high or if bleeding can cause a severe complication, e.g. in spinal surgery [7]. For urological operations with a high bleeding risk such as partial nephrectomy or radical prostatectomy, studies have shown that it is safe to continue

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Abbreviations

ASAC	acetylicsalicylic acid
ASAPS	American society of Anaesthesiologists physical status classification system
CHD	coronary heart disease
EGD	esophagogastroduodenoscopy
IMC	intermediate care unit
MIBC	muscle invasive bladder cancer
NOAC	new oral anticoagulants
RC	radical cystectomy
UD	urinary diversion

antiplatelet therapy [8–10]. Among urological surgeries, RC with pelvic lymphadenectomy decidedly harbours a significant risk of blood loss and bleeding complications. Current studies found a transfusion rate of up to 60% after RC [11,12]. Currently there is no study, which has investigated the effects of perioperatively continued antiplatelet therapy in patients undergoing radical cystectomy.

Material and methods

Study design and data collection

After approval of the local ethical committee we identified patients admitted for RC from the prospective databases of two high-volume urological departments. Only patients with bladder cancer as indication for RC were included. Cases with missing clinical data were excluded. Overall, 461 consecutive patients were included (Mannheim, $n = 320$, 2011–2017 and Munich-Planegg, $n = 141$, 2013–2016). The procedure was performed by 7 different surgeons in Mannheim and 2 in Munich-Planegg. Data was analysed retrospectively, and patients were stratified into three groups: Surgery under continuous antiplatelet therapy with ASAC, group 1 ($n = 50$, Mannheim $n = 45$), RC with cessation of (group 2, $n = 65$, Mannheim $n = 39$) or without antiplatelet therapy (group 3, $n = 346$, Mannheim $n = 236$). Patients continuing ASAC in group 1 usually had a history of coronary stent implantation, history of stroke or (non-)cardiac bypass operation. In group 2 ASAC was paused for a median of 25 days. Postoperatively, ASAC was taken again after a median of 15 days. Other anticoagulants, such as NOAC and Cumarin derivatives, were taken in 29 cases. These were preoperatively paused accordingly to the professional information of the specific drug and postoperatively usually bridged with weight-adapted low weight molecular heparin.

Predefined pre-, intra- and postoperative parameters were obtained for each patient.

Surgical technique

Patients received oncological open RC with pelvic lymphadenectomy for bladder cancer. Pelvic lymphadenectomy included dissection of obturatoric fossa, external, internal and common iliac lymph nodes up to the aortic bifurcation with the genitofemoral nerve as lateral margin [13]. Surgery was performed under general anaesthesia. Postoperatively patients were monitored on an ICU or intensive care unit. Standardized perioperative prophylaxis for thrombosis at both institutions consisted of low molecular weight heparin s.c. once daily for 4 weeks postoperatively, first applied on the evening after surgery. Transfusion was given according to the current German Cross-Sectional Guidelines for Therapy with Blood Components and Plasma Derivatives [14]. Haemostatic agents were only used in selected cases. For urinary diversion ileum conduit, neobladder, pouch (usually ileocecal or ileal pouch) or in some cases ureterocutaneostomy was used. Intraoperatively inserted ureter catheters were regularly extracted on the 11th postoperative day, cystograms with extraction of the catheter were normally performed on the 14th (neobladder) or 21st (pouch) postoperative day.

Statistical analysis

For statistical analysis JMP® version 13.0.0 was used. For continuous variables mean, standard deviation und interquartile ranges were calculated. To compare statistical differences likelihood ratio was calculated for categorial variables, for statistical differences on continuous variables ANOVA or Kruskal-Wallis test was used with a two-sided 0.05 significance level. If significant differences were found, post-hoc testing was performed (Tukey test or Fishers exact test with Bonferroni correction). Finally, uni- and multivariate analysis were performed to identify predictor for surgical outcome, in particular for transfusion rate and severe complications.

Results

Patient characteristics

Detailed patient characteristics are shown in Table 1. The groups showed a significantly different ($p = 0.02$) Body Mass Index (BMI) with a significantly higher BMI in group 1 (28.5 ± 5.4) in comparison to group 3 (26.7 ± 4.3 kg/m^2). Also, group 1 showed a higher percentage of male patients than group 3 (94% in group 1, $n = 47$ vs. 76%, $n = 264$), $p < 0.01$. Regarding CHD, all groups were significantly different (group 1 66%, $n = 33$, group 2 34%, $n = 22$ and group 3 4%, $n = 15$), $p < 0.01$. Group 2 (23%, $n = 15$) had significantly fewer continent UDs than group 3 (48%, $n = 165$), $p < 0{,}01$.

Oncological outcome

Detailed oncological outcomes are stated in Table 1. There were no significant differences between the three groups. In group 1 46% ($n = 23$) had locally advanced MIBC (T3 or T4), 51% ($n = 31$) in group 2 and 52% ($n = 179$) in group 3 ($p = 0.66$). The rate of nodal positive lymph nodes was 17% ($n = 8$), 25% ($n = 15$) and 26% ($n = 87$), $p = 0.34$. A positive resection margin was seen in 8% ($n = 4$) in group 1, in 11% ($n = 7$) and also 11% ($n = 36$) in groups 2 and 3, $p = 0.83$.

Perioperative outcome

Detailed perioperative outcome results are stated in Table 2. Average duration of operation was not different between the groups ($p = 0.13$), 257 ± 79 min vs. 254 ± 80 (group 2) vs. 274 ± 87. Also, average blood loss was not significantly different (group 1 732 ± 424 ml vs. 752 ± 488 vs. 810 ± 544 in group 3; $p = 0.51$). In addition, there was a comparable transfusion rate (44%, $n = 22$ vs. 45%, $n = 29$ vs. 39%, $n = 136$; $p = 0.63$).

Severe complications occurred in 26% ($n = 13$) in group 1, in 15% ($n = 10$) and 15% ($n = 53$) in groups 2 and 3, showing no significant difference ($p = 0.19$). Ischemic complications occurred more often in group 1 ($n = 4$, 8%) and 2 ($n = 5$, 8%) than in group 3 ($n = 7$, 2%, $p = 0{,}02$).

Table 1
Patient characteristics and oncological outcome; *° or ^ showing significant difference between groups.

	All (n = 461)	G1 ASAC (n = 50)	G2 ASAC Stop (n = 65)	G3 No ASAC (n = 346)	p-value
Mean BMI (kg/m2)	26.9 ± 4.4	28.5 ± 5.4*	27,1 ± 3,7	26,7 ± 4,3*	0.02
Male, n (%)	362 (79)	47 (94)*	51 (78)	264 (76)*	<0.01
CHD, n (%)	70 (15)	33 (66)*^	22 (34)°^	15 (4)*°	<0.01
Coronary stent implantation, n (%)	56 (12)	32 (64)*^	16 (24)°^	8 (2)*°	<0.01
ASAPS 3 or 4, n (%)	149 (32)	33 (66)*	33 (50)°	83 (24)*°	<0.01
Median age, IQR (y)	70 (62–76)	72 (67–76)*	74 (70–81)°	69 (61–75)*°	<0.01
Continent UD, n (%)	198 (43)	18 (36)	15 (23)°	165 (48)°	<0.01
T0, T1 or Tis, n (%)	109 (24)	16 (32)	13 (20)	80 (23)	0.31
T2, n (%)	113 (25)	10 (20)	21 (32)	82 (24)	0.26
T3, T4, n (%)	233 (50)	23 (46)	31 (51)	179 (52)	0.66
Tx, n (%)	6 (1)	1 (2)	–	5 (1)	–
Nodal positive N+, n (%)	110 (24)	8 (17)	15 (25)	87 (26)	0.34
T4 or N+, n (%)	148 (32)	13 (26)	20 (31)	115 (33)	0.62
Positive margin, n (%)	47 (10)	4 (8)	7 (11)	36 (11)	0.83
Metastasis M1, n (%)	14 (3)	3 (6)	2 (4)	9 (3)	0.61

Table 2
Perioperative outcome; * or ° showing significant difference between groups; † = death following complication.

	All (n = 461)	G1 ASAC (n = 50)	G2 ASAC Stop (n = 65)	G3 No ASAC (n = 346)	p-value
Mean duration of operation, SD (min)	269.2 ± 85.1	257.3 ± 79.3	253.8 ± 80.2	273.8 ± 86.5	0.13
Mean blood loss, SD (ml)	793.7 ± 525	732.9 ± 424.0	751.7 ± 488.4	810.2 ± 544.0	0.51
Resected lymph nodes, SD (n)	16.6 ± 9.1	15.4 ± 9.6	15.0 ± 8.9	17.1 ± 9.1	0.16
Mean loss of haemoglobin, SD (g/dl)	3.2 ± 1.6	2.7 ± 1.6	3.1 ± 1.8	3.2 ± 1.6	0.07
Transfusion rate, n (%)	187 (41)	22 (44)	29 (45)	136 (39)	0.63
Complications > II, n (%)	76 (17)	13 (26)	10 (15)	53 (15)	0.19
Abdominal wound dehiscence – fascial closure, n (%)	29 (6.3)	5 (10)	3 (4.6)	21 (6.0)	–
Urinoma, abscess or lymphocele - drain, n (%)	10 (2.2)	3 (6)	1 (1.5)	6 (1.7)	–
Myocardial infarction - coronary angiography ± stent, n (%)	7 (1.5)	1 (2.0)	3 (4.6)	3 (0.9)†	–
Perforation - Re-Laparotomy, n (%)	6 (1.3)	1 (2.0)†	1 (1.5)	4 (1.2)†	–
LAE or other severe thrombotic event - anticoagulation and monitoring on IMC, n (%)	5 (1.1)	1 (2.0)	0	4 (1.6)†	–
Ileus - Re-Laparotomy, n (%)	5 (1.1)	0	1 (1.5)†	4 (1.2)	–
Insufficient anastomosis - Re-Laparotomy, n (%)	3 (0.7)	1 (2.0)	0	2 (0.6)†	–
Haematoma/bleeding - Re-Laparotomy, n (%)	2 (0.4)	0	0	2 (0.6)	–
Dislocation of ureter stent - Re-Placement, n (%)	2 (0.4)	0	0	2 (0.6)	–
Sepsis - monitoring on IMC, n (%)	2 (0.4)	0	1 (1.5)	1 (0.3)	–
Ileus - monitoring on IMC, n (%)	2 (0.4)	0	0	2 (0.6)	–
Gastrointestinal bleeding – EGD	1 (0.2)	0	0	1 (0.3)	–
Cholecystitis - Re-Laparotomy, n (%)	1 (0.2)	1 (2.0)	0	0	–
Stenosis of anastomosis - Incision, n (%)	1 (0.2)	0	0	1 (0.3)	
Ischemic complications, n (%)	16 (3.5)	4 (8.0)*	5 (8.0)°	7 (2.0)*°	0.02
Thromboembolic complications, n (%)	11 (2.4)	2 (4.0)	1 (1.5)	8 (2.3)	0.70
Mean length of stay, SD (d)	18.0 ± 8.9	17.7 ± 8.6	18.0 ± 8.0	18.0 ± 9.2	0.98
30-day mortality rate, n (%)	6 (1.3)	1 (2.0)	1 (1.5)	4 (1.2)	0.88
90-day mortality rate, n (%)	10 (2.2)	1 (2.1)	1 (1.5)	8 (2.4)	0.91
30-day readmission rate, n (%)	58 (13)	9 (18)	7 (11)	42 (12)	0.48
90-day readmission rate, n (%)	99 (22)	12 (24)	16 (25)	71 (21)	0.70

30-day and 90-day Mortality rate was 1.3% (n = 6) and 2.2% (n = 10) respectively in our cohort with no significant difference between the groups (p = 0,88 and p = 0,91). 30-day and 90-day readmission rate was 13% (n = 58) and 22% (n = 99) respectively, also showing no significant, p = 0.07.

Uni- and multivariate analyses

Detailed results of uni- and multivariate analyses are stated in Table 3. Univariate and multivariate analyses identified BMI (multivariate OR = 2.43, p < 0.01) and male sex (OR = 2.44, p = 0,04) as independent predictors for severe complications. For transfusion, female gender (OR = 2.49, p < 0.01) and ASAPS>2 (OR = 1.57, p = 0.49) were identified as independent predictors in uni- and multivariate analysis. Continuation of ASAC therapy was not found to be a significant independent predictor for transfusion (OR = 1.12; p = 0.73) or severe complications (OR = 1.29; p = 0.51).

Subgroup analysis

Uni- and multivariate analyses were also performed as subgroup analysis for patients in group 1 and 2 only (see Appendix). Again, continuation of ASAC was not found to be an independent predictor for transfusion or severe complications.

Discussion

Smoking is one of the main risk factors for cancer, in particular bladder cancer, as well as for CHD. Hence, it does not come as a surprise that there is a significant number of patients who need a

Table 3
Univariate and multivariate analysis.

	Univariate analysis			Multivariate analysis		
	OR	95%CI	p	OR	95%CI	p
Complications > II						
Age (>65y vs. ≤ 65y)	1.46	0.85–2.52	0.170	1.74	0.93–3.25	0.081
Sex (male vs. female)	3.10	1.37–6.97	0.006*	2.44	1.06–5.63	0.037*
ASAPS (>2 vs ≤ 2)	1.56	0.94–2.59	0.086	1.26	0.70–2.25	0.437
BMI (>30 vs. ≤ 30)	1.65	1.57–4.48	0.001*	2.43	1.41–4.19	0.001*
Continuation of acetylsalicylic acid	1.94	0.97–3.85	0.058	1.29	0.61–2.72	0.511
Continent urinary diversion (yes vs. no)	1.32	0.81-2-16	0.270	1.69	0.95–3.01	0.073
Advanced cancer (T4 or N+ vs. <T4 and N0)	1.04	0.62–1.76	0.872	1.23	0.71–2.14	0.461
Institution (Mannheim vs. Munich)	1.51	0.86–2.68	0.155	1.65	0.89–3.06	0.112
Transfusion						
Age (>65y vs. ≤ 65y)	1.41	0.95–2.10	0.091	1.12	0.63–1.78	0.631
Sex (female vs. male)	2.42	1.54–3.81	<0.001*	2.49	1.54–4.03	<0.001*
ASAPS (>2 vs ≤ 2)	1.81	1.22–2.69	0.003*	1.57	1.00–2.45	0.049*
BMI (>30 vs. ≤ 30)	1.16	0.75–1.80	0.499	1.24	0.78–1.98	0.354
Continuation of acetylsalicylic acid	1.17	0.65–2.12	0.600	1.12	0.59–2.12	0.732
Continent urinary diversion (yes vs. no)	0.41	0.28–0.61	<0.001*	0.52	0.33–0.81	0.004*
Advanced cancer (T4 or N+ vs. <T4 and N0)	1.23	0.82–1.82	0.313	1.34	0.88–2.04	0.176
Institution (Mannheim vs. Munich)	1.15	0.76–1.72	0.511	0.93	0.59–1.45	0.755

urological operation while taking ASAC as secondary prophylaxis for cardiovascular events. Indeed, studies have shown that especially patients which had coronary stent implantation are very likely to undergo a non-cardiac operation within two years after stent implantation [15]. For endoscopic urological procedures there is a consensus that ASAC can be continued, but for operations with a higher risk of bleeding recommendations are not as strong [16].

In our series, we demonstrated that RC with pelvic lymphadenectomy can be safely performed under continuing therapy with ASAC. Our data underlines, that patients with continuation of ASAC have more comorbidities, are more often of male gender and show a higher BMI in comparison to patients interrupting ASAC or without ASAC therapy. Regarding surgical outcome of RC, we found no difference in blood loss, rate of transfusion and severe complications in patients with continuation of ASAC. Regarding complications, there was a trend towards more complications in the ASAC group, but multivariate analysis showed that this mainly contributed to the differences between group characteristics rather than to continuation of ASAC. In addition, operation time and postoperative length of stay seems to be similar. Mortality and readmission rate were also comparable in all groups.

Recent studies have shown that it is safe to continue ASAC therapy in terms of bleeding complications for radical prostatectomy [9] or partial nephrectomy [10]. Still, in terms of transfusion rate or complication rate, some of these series showed significant differences for patients taking ASAC which stands in contrast to our findings. Leyh-Bannurah et al. [9] published a series of 2061 patients undergoing open prostatectomy with 118 patients taking ASAC. They found a higher transfusion rate in these patients (12% vs. 8%, $p < 0.001$) whereas blood loss was not significant different after propensity score matching. In multivariate analysis continuing ASAC therapy was no independent factor for higher blood loss. They discussed more comorbidities, especially cardiac comorbidities, as a reason for higher rate of transfusion and recommended continuation of ASAC as complication rates did not show significant differences. These results are in accordance to our findings as their transfusion rate seems to be biased by the older and sicker population in the ASAC group. Packiam et al. [10] analysed a series of 214 patients undergoing partial nephrectomy with 49 patients taking ASAC perioperatively. They found a higher rate for 30-day complication with no statistical difference in transfusion and haemorrhagic complication rate although there was a statistically not significant trend towards more embolization in the ASAC group. The authors recommended continuation of ASAC but made a point for further studies with bigger sample sizes. Remarkably, in this study there was a higher rate of complications, which was not shown in our series. This could be explained by the fact that bleeding complications (e.g. haemorrhage, pseudoaneurysm, arteriovenous fistulas) are more dominant and potentially more severe in partial nephrectomy than in RC, where complications of urinary diversion are more dominant [17].

Ito et al. [8] published a series of 1097 patients with 67 patients continuing antiplatelet therapy while undergoing partial nephrectomy. They showed a higher rate of haemorrhagic complications (20.9% vs. 6.4%. $p < 0.0001$) with antiplatelet therapy as an independent risk factor ($OR = 2.2$). However, further analysis revealed that these complications mainly appeared in patients continuing clopidogrel with ASAC alone being no independent risk factor in multivariate analysis. The authors concluded that ASAC can be taken safely while clopidogrel should be paused. In our study clopidogrel was paused in all patients undergoing cystectomy. If patients are receiving clopidogrel after recent stent implantation, in our opinion, good collaboration with treating cardiologists is necessary to find an individual concept and time of operation for these patients.

In contrast to the above findings, a series on antiplatelet und anticoagulant therapy in partial nephrectomy by Pradere et al. [18] showed a higher rate of overall (39.2% vs. 17.4%) and haemorrhagic complications (32.7% vs. 9.6%). In subgroup analysis intake of ASAC was also associated with higher complications (45% vs 19%) and haemorrhagic complications (24% vs 13%). In multivariate analysis anticoagulation was the only independent factor for complications ($OR = 4.3$; $p = 0.03$) whereas taking ASAC showed a trend towards more complications although this was not statistically significant ($OR = 2.4$; $p = 0.15$). Because in their main analysis patients on anticoagulation or antiplatelet therapy were considered as one group, these patients were significantly older and had a higher ASAPS, the actual impact of ASAC in this study is, in our opinion, not completely certain.

Still, maybe the strongest argument, why ASAC should be continued, is the risk of major cardiac events if it is interrupted. Burger et al. [19] showed in their meta-analysis that a cessation of ASAC therapy (for secondary prevention) seems to be a risk factor for perioperative major cardiac events. Because of its impact, this study was considered in the ESC guidelines [7]. This was also supported by Shouten et al. [6], especially for early surgery after stent implantation. Therefore, recommendation for continuing ASAC therapy in RC is quite strong in our opinion.

Nevertheless, we did not find a different rate of ischemic complications in patients with cessation of ASAC in comparison to an ongoing ASAC therapy which could be explained by the fact that in our cohort many patients with cessation of ASAC were taking ASAC for primary but not secondary prevention. The higher rate of ischemic complications in both groups in comparison to the non-ASAC group can be explained by higher - especially cardiac – comorbidities and therefore increased risk for those complications.

Interestingly, Lyon et al. [20] just published a study to investigate a possible improved survival in patients which underwent radical cystectomy while taking ASAC permanently. They showed a significant better 5-year cancer-specific (68% vs. 60%; $p = 0.02$) and overall survival (59% vs. 52%; $p = 0.03$) for patients on ASAC. In multivariate analysis ASAC was independently associated with lower cancer-specific ($HR = 0.64$; $p = 0.01$) and overall mortality ($HR = 0.70$; $p = 0.02$). They also showed that there was no difference in bleeding complications and transfusion rate which is concordant to our findings. In contrast to our study, their patients continued ASAC for primary prophylaxis also, whereas in our study ASAC was only continued if it was taken for secondary prophylaxis (history of drug eluting stent implantation, bypass operation, myocardial infarction, strokes). Therefore, we recommend continuing perioperative intake of ASAC for these patients but cannot give this recommendation for ASAC use for primary prophylaxis, especially as other studies have shown higher haemorrhagic and general complications in non-cardiac surgery for patients taking ASAC for primary prophylaxis [21].

Our study has several limitations. First, there is retrospective analysis of this data, which may cause several biases especially selection bias for holding ASAC depending on expected complicity of operation and surgeon preferences. Also, there were heterogenous indications for continuing therapy with ASAC. Sample size of patients taking ASAC was quite small, therefore this study might be underpowered regarding the chosen endpoints and larger studies are needed to confirm our results. There was a difference in percentage of continent urinary diversion and, although this was not significant, this may have made a difference. Naturally, patient groups characteristics and comorbidities were different especially in terms of cardiac comorbidities, sex and BMI although the ASAC group appears to be sicker and seems to be had rather more risk factors for cardiac events and need of transfusion.

Conclusion

To our knowledge, this is the first study investigating the impact of continuing antiplatelet therapy with ASAC during RC with pelvic lymphadenectomy on perioperative outcome. We could demonstrate that transfusion rate, intraoperative blood loss, perioperative complications, readmission and mortality rate are not significantly increased in patients, who continued ASAC intake perioperatively, despite a higher comorbidity rate. Further research with larger study populations is needed to confirm our findings.

Declaration of interest

None.

Administrative, technical, or material support

None.

Authors' contribution

Study concepts: F. Wessels, M.C. Kriegmair.
Study design: F. Wessels, M.C. Kriegmair.
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Appendix

Table A1
Uni- and multivariate analysis for patients taking or pausing ASAC only (group 1 and 2 only)

	Univariate analysis			Multivariate analysis		
	OR	**95%CI**	**p**	**OR**	**95%CI**	**p**
Complications > II						
Age (>65y vs. ≤ 65y)	1.97	0.53–7.29	0.309	2.75	0.59–12.78	0.197
Sex (male vs. female)	2.05	0.10–2.31	0.367	1.33	0.25–7.04	0.736
ASAPS (>2 vs ≤ 2)	1.20	0.47–3.04	0.706	1.12	0.40–3.16	0.823
BMI (>30 vs. ≤ 30)	2.17	0.83–5.73	0.116	1.89	0.69–5.17	0.217
Continuation of acetylsalicylic acid	1.93	0.78–4.87	0.162	1.87	0.69–5.44	0.251
Continent urinary diversion (yes vs. no)	1.43	0.54–3.78	0.472	1.62	0.51–5.15	0.417
Advanced cancer (T4 or N+ vs. <T4 and N0)	1.05	0.39–2.85	0.919	1.41	0.48–4.18	0.531
Institution (Mannheim vs. Munich)	1.05	0.37–2.98	0.916	0.81	0.25–2.62	0.724
Transfusion						
Age (>65y vs. ≤ 65y)	2.27	0.86–6.00	0.098	1.27	0.39–4.12	0.695
Sex (female vs. male)	1.99	0.70–5.65	0.199	1.44	0.45–4.61	0.542
ASAPS (>2 vs ≤ 2)	3.19	1.45–7.01	0.004*	2.20	0.92–5.22	0.075
BMI (>30 vs. ≤ 30)	1.96	0.84–4.55	0.117	2.39	0.92–6.21	0.073
Continuation of acetylsalicylic acid	0.98	0.46–2.05	0.948	1.10	0.45–2.72	0.831
Continent urinary diversion (yes vs. no)	0.18	0.07–0.49	<0.001*	0.22	0.07–0.70	0.010*
Advanced cancer (T4 or N+ vs. <T4 and N0)	0.99	0.44–2.21	0.974	1.06	0.42–2.66	0.908
Institution (Mannheim vs. Munich)	1.14	0.50–2.63	0.752	0.99	0.37–2.70	0.987

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