

Major Adverse Cardiac Events (MACE) do not occur more frequently in Patients Undergoing Cystectomy and Urinary Diversion with Perioperative Continuation of Blood Thinners

Christopher Soliman², Marc A. Furrer^{1,2}, Janine Abgottspon³, Markus Huber³, Dominique Engel³, Lukas M. Löffel³, Christian M. Beilstein³, Fiona C. Burkhard¹, Patrick Y. Wuethrich³

1. Department of Urology, Inselspital, Bern University Hospital, University of Bern, Bern, Switzerland

2. Department of Urology, The University of Melbourne, Royal Melbourne Hospital, Parkville, Victoria, Australia

3. Department of Anaesthesiology and Pain Medicine, Inselspital, Bern University Hospital, University of Bern, Bern, Switzerland

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OBJECTIVES

- Despite ongoing improvements in surgical technique and perioperative care, open radical cystectomy (ORC) with urinary diversion (UD) is still associated with **high early postoperative morbidity, substantial intraoperative blood loss and transfusion of packed red blood cells (PRBC) and/or fresh frozen plasma (FFP) in up to 60%**.
- The aim of this study is to assess if **uninterrupted blood thinners administration** affects rates of **major adverse cardiac events (MACE)**.

METHODS

- An **observational, single-centre cohort study** of a consecutive series of **1431 cystectomy patients**, between 2000 and 2020 was conducted.
- Open radical cystectomy was performed in patients with **uninterrupted low-dose aspirin (ASS), oral anticoagulants (OAC) with international normalized ratio (INR) goal of 2-2.5, or bridging with low weight molecular heparin (LWMH)**.
- We examined the occurrence of the **first major adverse cardiac events (MACE)**, a composite of cardiovascular death, myocardial infarction, coronary revascularization, stroke, heart failure and pulmonary embolism, within the context of a **time-to-event analysis (90 d)**.
- We used **propensity score matching analysis** to adjust for imbalances between groups with or without blood thinners.

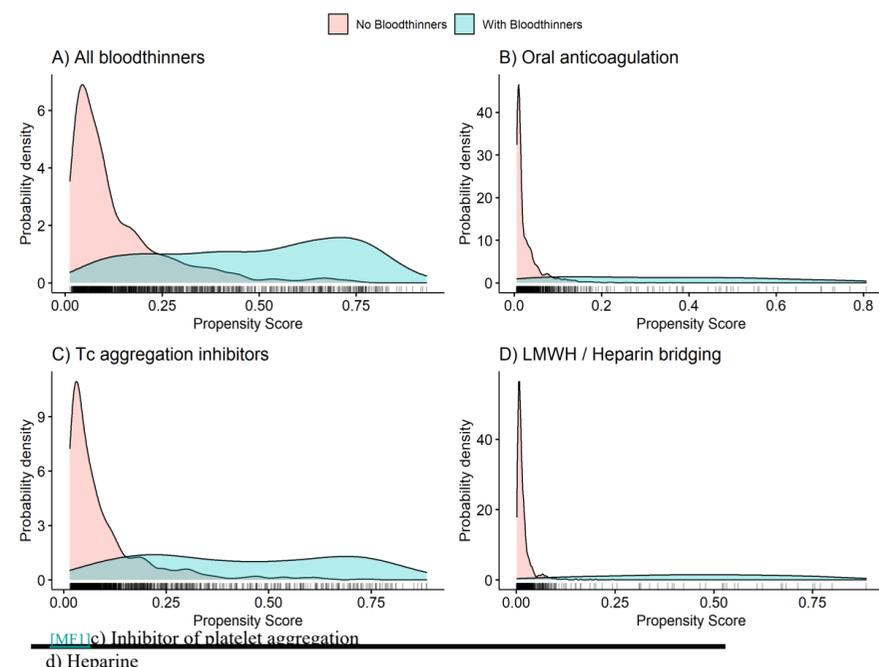
Patients' surgical and oncological characteristics (after PS matching)

Characteristics	After PS matching	
	With blood thinners	P
n	299	
Preoperative parameters		
Gender = Male (%)	230 (76.9)	0.259
Age	72.40 [66.40, 78.40]	0.861
Body mass index [kg/m ²]	26.80 [23.95, 30.05]	0.241
ASA (%)		0.025
ASA:2	49 (16.4)	
ASA:3	227 (75.9)	
ASA:4	23 (7.7)	
Charlson Comorbidity Index	6.00 [4.00, 7.00]	0.001
Nicotine (pack yrs)	20.00 [0.00, 45.50]	0.087
Hypertension = Yes (%)	227 (75.9)	0.306
Coronary heart disease = Yes (%)	176 (58.9)	0.004
Diabetes = Yes (%)	72 (24.1)	0.847
COPD = Yes (%)	69 (23.1)	0.488
BCG instillation preoperatively = Yes (%)	53 (17.7)	0.829
Intraoperative parameters		
Duration of operation (min)	368.00 [317.50, 419.00]	0.901
Administration of crystalloids (ml/kg/h)	3.92 [3.03, 5.42]	0.308
Administration of colloids (ml/kg/h)	0.00 [0.00, 0.00]	0.044
Administration of noradrenaline-(ug)	999.00 [420.50, 1561.50]	0.389
Laboratory values preoperatively		
Haemoglobin	125.00 [113.00, 139.50]	0.588
Hematocrit	0.37 [0.34, 0.41]	0.681
Thrombocytes	237.00 [197.00, 301.50]	0.223
Glomerular filtration rate (ml/min)	68.42 [49.99, 83.74]	0.611
Creatinine (umol/l)	92.00 [75.50, 116.50]	0.865

Histopathological parameters		
Histology n (%)		0.902
Urothelial cancer pure	223 (74.6)	
Urothelial cancer non-pure	34 (11.4)	
Other type of bladder cancer (e.g. adenocarcinoma, SCC)	9 (3.0)	
Other malignancies (e.g. prostate or cervical cancer)	2 (0.7)	
Benign conditions (e.g. shrunken bladder)	31 (10.4)	
Pathological TNM staging; n (%)		0.994
Tumor stage		
T:0-1	79 (26.4)	
T:2	72 (24.1)	
T:3	86 (28.8)	
T:4	31 (10.4)	
T: not applicable (benign condition)	31 (10.4)	
Nodal stage		
N:0	193 (64.5)	
N:1	61 (20.4)	
N:2	10 (3.3)	
N:3	4 (1.3)	
N: not applicable (benign condition)	31 (10.4)	
Tumour grade		
G:0 (no remaining tumor in specimen)	10 (3.3)	
G:1	3 (1.0)	
G:2	14 (4.7)	
G:3	241 (80.6)	
G: not applicable (benign condition)	31 (10.4)	
Vascular invasion		
V:0	199 (66.6)	
V:1	69 (23.1)	
V: not applicable (benign condition)	31 (10.4)	
Positive surgical margins		
R:0	253 (84.6)	
R:1	15 (5.0)	
R: not applicable (benign condition)	31 (10.4)	

RESULTS

Balance and overlap after IPTW matching



We identified **1457 consecutive ORC patients** who fulfilled the inclusion criteria. We excluded 26 patients (1.8%), 4 patients were on dual anti-aggregation therapy clopidogrel and ASS and 22 patients had missing data, resulting in 1431 patients included in the final analysis. **Median age was 69 years**. Overall, the **rate of 90 d postoperative MACE was similar between patients with vs. without blood thinners**. In the propensity-score matched analysis, the MACE rate was **8.7%** in the group with blood thinners compared to **9.1%** in those without blood thinners; **P=0.99**. After propensity-score matching, no statistically relevance has been detected between the treatment groups (log rank P=0.758).

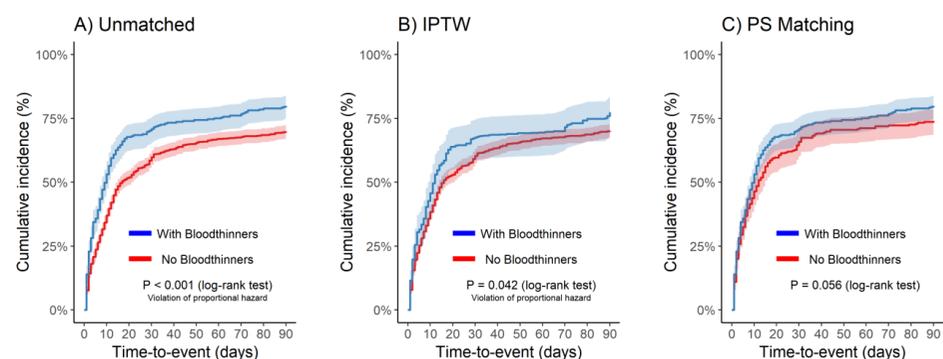


Figure 3: Cumulative incidences of postoperative complications (in %) occurring in the unmatched cohort, and after IPTW and PS matching.

A: Cumulative incidences among patients with blood thinners (red) and without (blue).

CONCLUSION

- Perioperative continuation of blood thinners during open radical cystectomy and urinary diversion **did not increase the occurrence of major adverse cardiac events (MACE) at 90 days postoperatively**.
- As a result, there is **no need for discontinuation** of chronic low dose aspirin, low molecular weighted heparin bridging or uninterrupted oral anticoagulant treatment aiming at an INR of 2-2.5.