

**S1 Table.** Multivariate Cox regression analyses of risk factors for bladder recurrence in patients without previous history of bladder cancer and in patients with early T1-2 stage

Variable	No previous bladder cancer data set				Early stage (T1, T2) data set			
	Univariate		Multiple <sup>a)</sup>		Univariate		Multiple	
	HR (95% CI)	p-value	HR (95% CI)	p-value	HR (95% CI)	p-value	HR (95% CI)	p-value
<b>Bladder recurrence</b>								
Operation								
ONU	1 (Ref)		1 (Ref)		1 (Ref)		1 (Ref)	
LNU	0.816 (0.681-0.977)	0.027	0.782 (0.651-0.937)	0.008	0.858 (0.690-1.068)	0.170	0.871 (0.699-1.087)	0.222
Age (yr)	1.002 (0.994-1.011)	0.610	-	-	1.002 (0.992-1.013)	0.688	-	-
Sex								
Male	1 (Ref)		-	-	1 (Ref)		-	-
Female	0.842 (0.684-1.035)	0.103	-	-	0.845 (0.652-1.095)	0.203	-	-
BMI (kg/m <sup>2</sup> )	0.976 (0.950-1.002)	0.067	-	-	0.983 (0.952-1.016)	0.308	-	-
ASA score								
1	1 (Ref)		-	-	1 (Ref)		-	-
2	1.075 (0.876-1.319)	0.490	-	-	1.050 (0.815-1.353)	0.706	-	-
3	1.225 (0.831-1.805)	0.306	-	-	1.265 (0.775-2.064)	0.347	-	-
Unknown	0.862 (0.403-1.846)	0.703	-	-	0.790 (0.290-2.155)	0.645	-	-
Previous bladder cancer								
No	-	-	-	-	1 (Ref)		1 (Ref)	
Previous bladder tumor Hx.	-	-	-	-	1.831 (1.366-2.454)	< 0.001	1.701 (1.258-2.298)	< 0.001
Concomitant bladder tumor Hx.	-	-	-	-	2.083 (1.455-2.982)	< 0.001	2.172 (1.507-3.132)	< 0.001
Concomitant bladder cancer								
No	-	-	-	-	1 (Ref)		-	-
Yes	-	-	-	-	1.909 (1.339-2.723)	< 0.001	-	-
Tumor location								
Renal pelvis	1 (Ref)		-	-	1 (Ref)		1 (Ref)	
Ureter	0.946 (0.780-1.148)	0.576	-	-	1.028 (0.810-1.306)	0.820	0.941 (0.739-1.199)	0.624
Both renal pelvis and ureter	1.200 (0.929-1.550)	0.162	-	-	1.493 (1.109-2.010)	0.008	1.285 (0.947-1.744)	0.108
Tumor grade								
I	1 (Ref)		-	-	1 (Ref)		-	-
II	1.301 (0.724-2.339)	0.378	-	-	1.541 (0.679-3.497)	0.301	-	-



Male	1 (Ref)		1 (Ref)		1 (Ref)		-	-
Female	1.255 (1.000-1.575)	0.050	1.054 (0.837-1.327)	0.655	1.453 (0.993-2.126)	0.055	-	-
BMI (kg/m <sup>2</sup> )	0.978 (0.947-1.009)	0.162	-	-	0.956 (0.907-1.009)	0.100	-	-
ASA score								
1	1 (Ref)		1 (Ref)		1 (Ref)		-	-
2	0.892 (0.704-1.131)	0.345	0.820 (0.638-1.054)	0.122	0.752 (0.505-1.12)	0.161	-	-
3	0.977 (0.610-1.565)	0.923	0.868 (0.528-1.427)	0.577	1.639 (0.853-3.151)	0.138	-	-
Unknown	2.270 (1.273-4.048)	0.006	1.721 (0.946-3.134)	0.076	2.066 (0.735-5.807)	0.169	-	-
Previous bladder cancer								
No	-	-	-	-	1 (Ref)		1 (Ref)	
Previous bladder tumor Hx.	-	-	-	-	1.811 (1.149-2.855)	0.011	1.417 (0.880-2.284)	0.152
Concomitant bladder tumor Hx.	-	-	-	-	0.712 (0.312-1.624)	0.419	0.607 (0.262-1.408)	0.245
Concomitant bladder cancer								
No	-	-	-	-	1 (Ref)		-	-
Yes	-	-	-	-	0.651 (0.287-1.479)	0.306	-	-
Tumor location								
Renal pelvis	1 (Ref)		1 (Ref)		1 (Ref)		1 (Ref)	
Ureter	1.275 (1.011-1.608)	0.040	1.186 (0.935-1.503)	0.160	2.171 (1.415-3.33)	< 0.001	1.845 (1.190-2.860)	0.006
Both renal pelvis and ureter	1.650 (1.235-2.205)	< 0.001	1.177 (0.867-1.597)	0.296	2.851 (1.725-4.71)	< 0.001	1.643 (0.953-2.835)	0.074
Tumor grade								
I	1 (Ref)		-	-	1 (Ref)		-	-
II	6.751 (0.938-48.604)	0.058	-	-	3.112 (0.429-22.561)	0.261	-	-
III	21.211 (2.966-151.692)	0.002	-	-	6.646 (0.916-48.243)	0.061	-	-
Missing/unknown	11.448 (1.602-81.829)	0.015	-	-	2.78 (0.384-20.139)	0.312	-	-
Tumor grade II								
Low grade	1 (Ref)		1 (Ref)		1 (Ref)		1 (Ref)	

High grade	4.731 (3.388-6.606)	< 0.001	1.884 (1.305-2.720)	< 0.001	2.785 (1.793-4.326)	< 0.001	1.978 (1.242-3.152)	0.004
Unknown	2.387 (1.007-5.653)	0.048	0.946 (0.356-2.510)	0.911	3.722 (1.294-10.705)	0.015	3.689 (1.228-11.086)	0.020
Pathological T category								
pTis/pTa	1 (Ref)		1 (Ref)		-	-	-	-
pT1	2.52 (1.218-5.212)	0.013	2.130 (1.024-4.428)	0.043	-	-	-	-
pT2	6.625 (3.285-13.362)	< 0.001	3.887 (1.884-8.019)	< 0.001	-	-	-	-
pT3	13.647 (7.007-26.577)	< 0.001	6.673 (3.297-13.505)	< 0.001	-	-	-	-
pT4	25.317 (11.275-56.843)	< 0.001	10.633 (4.529-24.962)	< 0.001	-	-	-	-
Unknown	86.112 (10.839-684.118)	< 0.001	49.605 (4.999-492.197)	< 0.001	-	-	-	-
Pathological N category								
pNx	1 (Ref)		1 (Ref)		1 (Ref)		1 (Ref)	
pN0	0.877 (0.693-1.109)	0.273	0.890 (0.695-1.139)	0.355	0.722 (0.496-1.05)	0.089	0.857 (0.581-1.263)	0.435
pN1	4.577 (3.435-6.099)	< 0.001	2.047 (1.493-2.807)	< 0.001	3.141 (1.621-6.089)	< 0.001	1.247 (0.599-2.594)	0.555
Concomitant LVI								
No	1 (Ref)		1 (Ref)		1 (Ref)		1 (Ref)	
Yes	3.248 (2.623-4.021)	< 0.001	1.588 (1.251-2.016)	< 0.001	1.768 (1.096-2.852)	0.019	1.365 (0.830-2.247)	0.220
Concomitant CIS								
No	1 (Ref)		1 (Ref)		1 (Ref)		1 (Ref)	
Yes	1.524 (1.143-2.033)	0.004	1.069 (0.795-1.437)	0.658	1.879 (1.233-2.862)	0.003	1.273 (0.819-1.980)	0.283
LN dissection								
Not performed	1 (Ref)		-	-	1 (Ref)		-	-
Performed	1.235 (1.002-1.521)	0.048	-	-	0.842 (0.592-1.198)	0.340	-	-
Adjuvant chemotherapy								
No	1 (Ref)		1 (Ref)		1 (Ref)		1 (Ref)	
Yes	3.229 (2.613-3.991)	< 0.001	1.185 (0.916-1.531)	0.196	6.223 (4.146-9.342)	< 0.001	4.716 (2.881-7.722)	< 0.001
<b>Overall survival</b>								
Operation								
ONU	1 (Ref)		1 (Ref)		1 (Ref)		1 (Ref)	

LNU	0.778 (0.621-0.975)	0.029	0.856 (0.678-1.081)	0.191	1.038 (0.723-1.491)	0.839	1.102 (0.758-1.603)	0.611
Age (yr)	1.042 (1.031-1.053)	< 0.001	1.043 (1.031-1.056)	< 0.001	1.059 (1.039-1.079)	< 0.001	1.066 (1.044-1.088)	< 0.001
Sex								
Male	1 (Ref)		-	-	1 (Ref)		-	-
Female	1.116 (0.884-1.410)	0.357	-	-	1.270 (0.859-1.877)	0.231	-	-
BMI (kg/m <sup>2</sup> )	0.968 (0.937-0.999)	0.043	0.976 (0.944-1.009)	0.150	0.963 (0.914-1.015)	0.158	-	-
ASA score								
1	1 (Ref)		1 (Ref)		1 (Ref)		1 (Ref)	
2	1.347 (1.036-1.752)	0.026	1.063 (0.808-1.398)	0.665	1.082 (0.708-1.652)	0.717	0.876 (0.565-1.359)	0.554
3	1.741 (1.126-2.692)	0.013	1.181 (0.746-1.870)	0.477	2.703 (1.446-5.053)	0.002	1.332 (0.677-2.622)	0.407
Unknown	4.514 (2.694-7.563)	< 0.001	2.940 (1.710-5.053)	< 0.001	3.476 (1.344-8.992)	0.010	3.028 (1.124-8.153)	0.028
Previous bladder cancer								
No	-	-	-	-	1 (Ref)		-	-
Previous bladder tumor Hx.	-	-	-	-	1.385 (0.839-2.288)	0.203	-	-
Concomitant bladder tumor Hx.	-	-	-	-	1.086 (0.567-2.080)	0.804	-	-
Concomitant bladder cancer								
No	-	-	-	-	1 (Ref)		-	-
Yes	-	-	-	-	1.043 (0.547-1.990)	0.898	-	-
Tumor location								
Renal pelvis	1 (Ref)		1 (Ref)		1 (Ref)		1 (Ref)	
Ureter	1.241 (0.984-1.566)	0.068	1.141 (0.900-1.446)	0.277	1.743 (1.162-2.612)	0.007	1.573 (1.042-2.374)	0.031
Both renal pelvis and ureter	1.633 (1.228-2.171)	< 0.001	1.220 (0.907-1.642)	0.189	2.206 (1.363-3.571)	0.001	1.533 (0.907-2.591)	0.110
Tumor grade								
I	1 (Ref)		-	-	1 (Ref)		-	-
II	2.146 (0.786-5.858)	0.136	-	-	1.265 (0.393-	0.694	-	-

III	4.418 (1.627-12.000)	0.004	-	-	4.072) 1.451 (0.436-4.823)	0.544	-	-
Missing/unknown	3.547 (1.315-9.571)	0.012	-	-	1.439 (0.451-4.599)	0.539	-	-
Tumor grade II								
Low grade	1 (Ref)		1 (Ref)		1 (Ref)		1 (Ref)	
High grade	3.072 (2.318-4.070)	< 0.001	1.635 (1.192-2.242)	0.002	1.785 (1.218-2.617)	0.003	1.357 (0.896-2.055)	0.150
Unknown	2.542 (1.299-4.977)	0.007	1.696 (0.805-3.571)	0.165	2.383 (0.931-6.099)	0.070	2.983 (1.104-8.061)	0.031
Pathological T category								
pTis/pTa	1 (Ref)		1 (Ref)		-	-	-	-
pT1	1.773 (1.050-2.996)	0.032	1.529 (0.900-2.597)	0.116	-	-	-	-
pT2	2.744 (1.618-4.655)	< 0.001	1.794 (1.034-3.112)	0.038	-	-	-	-
pT3	6.038 (3.775-9.658)	< 0.001	3.496 (2.089-5.850)	< 0.001	-	-	-	-
pT4	11.924 (6.189-22.972)	< 0.001	5.408 (2.679-10.918)	< 0.001	-	-	-	-
Unknown	25.844 (3.446-193.801)	0.002	13.385 (1.541-116.268)	0.019	-	-	-	-
Pathological N category								
pNx	1 (Ref)		1 (Ref)		1 (Ref)		1 (Ref)	
pN0	1.144 (0.912-1.434)	0.244	1.193 (0.939-1.514)	0.148	1.085 (0.763-1.544)	0.650	1.475 (1.013-2.148)	0.042
pN1	3.975 (2.906-5.438)	< 0.001	1.935 (1.370-2.732)	< 0.001	2.541 (1.162-5.554)	0.019	1.567 (0.654-3.756)	0.314
Concomitant LVI								
No	1 (Ref)		1 (Ref)		1 (Ref)		1 (Ref)	
Yes	2.946 (2.377-3.651)	< 0.001	1.591 (1.248-2.029)	< 0.001	1.845 (1.166-2.920)	0.009	1.745 (1.068-2.849)	0.026
Concomitant CIS								
No	1 (Ref)		1 (Ref)		1 (Ref)		1 (Ref)	
Yes	1.490 (1.110-2.002)	0.008	1.114 (0.823-1.508)	0.486	1.657 (1.070-2.565)	0.023	1.403 (0.889-2.213)	0.145
LN dissection								
Not performed	1 (Ref)		-	-	1 (Ref)		-	-
Performed	1.412 (1.145-1.742)	0.001	-	-	1.155 (0.820-1.627)	0.410	-	-

Adjuvant chemotherapy								
No	1 (Ref)		1 (Ref)		1 (Ref)		1 (Ref)	
Yes	2.370 (1.908-2.945)	< 0.001	1.070 (0.822-1.394)	0.616	3.201 (2.005-5.110)	< 0.001	2.486 (1.411-4.378)	0.002
<b>Cancer-specific survival</b>								
Operation								
ONU	1 (Ref)		1 (Ref)		1 (Ref)		1 (Ref)	
LNU	0.809 (0.626-1.045)	0.105	0.917 (0.703-1.196)	0.522	1.042 (0.66-1.645)	0.859	1.282 (0.804-2.045)	0.297
Age (yr)	1.028 (1.016-1.041)	< 0.001	1.031 (1.018-1.045)	< 0.001	1.039 (1.015-1.063)	0.001	1.045 (1.020-1.071)	< 0.001
Sex								
Male	1 (Ref)		-	-	1 (Ref)		-	-
Female	1.199 (0.918-1.565)	0.183	-	-	1.48 (0.911-2.405)	0.114	-	-
BMI (kg/m <sup>2</sup> )	0.987 (0.951-1.023)	0.470	-	-	0.988 (0.923-1.057)	0.716	-	-
ASA score								
1	1 (Ref)		1 (Ref)		1 (Ref)		-	-
2	1.173 (0.876-1.571)	0.283	0.993 (0.731-1.348)	0.963	0.737 (0.446-1.219)	0.234	-	-
3	1.254 (0.733-2.147)	0.409	0.993 (0.564-1.748)	0.981	1.71 (0.765-3.824)	0.191	-	-
Unknown	3.563 (1.918-6.618)	< 0.001	2.477 (1.301-4.717)	0.006	2.521 (0.757-8.399)	0.132	-	-
Previous bladder cancer								
No	-	-	-	-	1 (Ref)		1 (Ref)	
Previous bladder tumor Hx.	-	-	-	-	1.815 (1.013-3.253)	0.045	1.467 (0.788-2.732)	0.227
Concomitant bladder tumor Hx.	-	-	-	-	1.179 (0.509-2.732)	0.701	1.155 (0.491-2.719)	0.741
Concomitant bladder cancer								
No	-	-	-	-	1 (Ref)		-	-
Yes	-	-	-	-	1.078 (0.469-2.48)	0.859	-	-
Tumor location								
Renal pelvis	1 (Ref)		1 (Ref)		1 (Ref)		1 (Ref)	
Ureter	1.202 (0.916-1.578)	0.184	1.101 (0.834-1.454)	0.496	2.126 (1.231-3.671)	0.007	1.830 (1.049-3.193)	0.033
Both renal pelvis and	1.708 (1.232-2.367)	0.001	1.183 (0.841-1.666)	0.334	2.904 (1.55-5.441)	< 0.001	1.650 (0.825-	0.157

ureter							3.302)	
Tumor grade								
I	1 (Ref)		-	-	1 (Ref)		-	-
II	3.025 (0.740-12.374)	0.124	-	-	2.556 (0.35-18.692)	0.355	-	-
III	6.681 (1.644-27.155)	0.008	-	-	3.244 (0.434-24.243)	0.251	-	-
Missing/unknown	4.619 (1.141-18.703)	0.032	-	-	1.823 (0.247-13.437)	0.556	-	-
Tumor grade II								
Low grade	1 (Ref)		1 (Ref)		1 (Ref)		1 (Ref)	
High grade	4.775 (3.241-7.034)	< 0.001	1.966 (1.289-3.000)	0.002	3.314 (1.853-5.926)	< 0.001	2.317 (1.264-4.246)	0.007
Unknown	3.841 (1.682-8.772)	0.001	1.673 (0.655-4.273)	0.282	4.496 (1.29-15.663)	0.018	4.236 (1.163-15.435)	0.029
Pathological T category								
pTis/pTa	1 (Ref)		1 (Ref)		-	-	-	-
pT1	1.865 (0.838-4.152)	0.127	1.550 (0.692-3.472)	0.287	-	-	-	-
pT2	4.466 (2.071-9.630)	< 0.001	2.620 (1.184-5.795)	0.018	-	-	-	-
pT3	11.530 (5.675-23.425)	< 0.001	5.973 (2.811-12.695)	< 0.001	-	-	-	-
pT4	25.272 (10.803-59.120)	< 0.001	10.854 (4.407-26.732)	< 0.001	-	-	-	-
Unknown	53.101 (6.614-426.317)	< 0.001	22.269 (2.268-218.613)	< 0.001	-	-	-	-
Pathological N category								
pNx	1 (Ref)		1 (Ref)		1 (Ref)		-	-
pN0	0.918 (0.701-1.202)	0.535	0.939 (0.706-1.249)	0.666	0.754 (0.472-1.202)	0.235	-	-
pN1	4.200 (2.989-5.901)	< 0.001	1.781 (1.225-2.589)	0.003	2.423 (0.961-6.11)	0.061	-	-
Concomitant LVI								
No	1 (Ref)		1 (Ref)		1 (Ref)		1 (Ref)	
Yes	3.405 (2.664-4.352)	< 0.001	1.645 (1.249-2.165)	< 0.001	2.649 (1.566-4.483)	< 0.001	2.355 (1.363-4.069)	0.002
Concomitant CIS								
No	1 (Ref)		1 (Ref)		1 (Ref)		1 (Ref)	
Yes	1.650 (1.189-2.289)	0.003	1.185 (0.846-1.659)	0.324	2.164 (1.29-3.628)	0.003	1.455 (0.847-2.500)	0.174



LN dissection								
Not performed	1 (Ref)		-	-	1 (Ref)		-	-
Performed	1.243 (0.975-1.584)	0.079	-	-	0.839 (0.537-1.309)	0.439	-	-
Adjuvant chemotherapy								
No	1 (Ref)		1 (Ref)		1 (Ref)		1 (Ref)	
Yes	3.001 (2.347-3.837)	< 0.001	1.073 (0.802-1.435)	0.635	4.88 (2.882-8.264)	< 0.001	3.525 (1.928-6.445)	< 0.001

HR, hazard ratio; CI, confidence interval; ONU, open nephroureterectomy; LNU, laparoscopic nephroureterectomy; BMI, body mass index; ASA, American Society of Anesthesiologists; Hx, history; LVI, lymphovascular invasion; CIS, carcinoma in situ; LN, lymph node. <sup>a)</sup>Firth correction for hazard ratio and 95% profile likelihood confidence interval.