

Utility of serum markers in the assessment of perioperative and postoperative morbidity and mortality after radical cystectomy for muscle invasive bladder cancer

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INTRODUCTION AND OBJECTIVES

Despite significant improvements in surgical techniques, radical cystectomy (RC) remains a highly morbid operation and greater than one-half of patients experience complications during their hospital stay and after discharge¹. The ability to predict complications and create prevention strategies is crucial in the surgical decision-making process and to optimise treatment outcomes. Methods of risk assessment include surrogates of comorbidity, such as the American Society of Anesthesiologists (ASA) Physical Status Classification and the Charlson Comorbidity Index (CCI) and it was reported previously that such tools possess a moderate capacity to predict post-RC outcomes, with a focus on mortality². Recently, there is growing interest in the association of preoperative inflammation and immuno-nutritional serum markers with postsurgical complications and survival outcomes. The aim of this study was to investigate and compare the ability of preoperative Controlling Nutritional Status (CONUT), Prognostic Nutritional Index (PNI), neutrophil to lymphocyte ratio (NLR), platlet to lymphocyte ratio (PLR), lymphocyte to monocyte ratio (LMR), systemic immune-inflammation index (SII), albumin, fibrinogen and PCR to predict perioperative and postoperative morbidity and mortality after RC.

MATERIALS AND METHODS

We retrospectively evaluated 164 patients who underwent open RC for muscle-invasive bladder cancer (MIBC) at our Institute between December 2004 and June 2018. We excluded those patients who received neoadjuvant therapy and those in whom postoperative complications were not recorded or

Table 1. Clinical and pathological features of population study

Ż		Total
Э	n. patients	164
t	Mean age at RC (±SD)	72.1±8.7
L 	Sex male (ref. female)	93(71)
ן	ASA score \geq 3 (ref. < 3)	74(90)
, ו פ	Charlson Comorbidity Index (CCI) 0 1 ≥ 2	31 25 108
I	pT stage ≥ 3 (ref. < 3)	97(67)
) t	pN stage ≥ 1 (ref. X or 0)	47(117)
	Grading high (ref. low)	152(12)
	LVI with (ref. without)	73(91)
	Adjuvant CT with (ref. without)	53(111)
r	Mean hospitalization time (±SD)	24.9±9.4
	Mean BMI (±SD)	25.7±4.4
) S	Surgical Margins (R) positive (ref. negative)	11(153)
)	Urinary diversion Ureterocutaneostomy Ileal conduit Orthotopic diversion	24 128 12



records were incomplete (table 1). Covariates were analyzed to determine associations with complication rates (according to the Clavien-Dindo system), mean hospitalization length, 30-days readmission rates and 90-days mortality. A multivariable binomial logistic regression determined associations with postsurgical outcomes taking into account age, sex, urinary diversion, pT stage and each serum marker, or American Society of Anesthesiologists (ASA) classification and Charlson Comorbity Index (CCI).

In all patients, blood samples were evaluated before surgery. CONUT score was calculated from the serum albumin concentration, total lymphocyte count, and total cholesterol concentratio, PNI was calculated based on the serum albumin concentration and total lymphocyte count, while NLR, PLR, LMR and SII were obtained with different combinations of peripheral neutrophil, lymphocyte ratio and platelet count.

Table 2,3. Mortality rates at 90-days, Readmission rates at 30-days

RESULTS

Cut-off values to discriminate threshold of CONUT score, PNI, NLR, PLR, LMR and SII were determined calculating the ROC curve and the maximum Youden index. We included 164 patients underwent RC for MIBC. The mean age at surgery was 72.1 years (range, 46-88) and the majority of urinary diversions were ileal conduit (78.1%). Overall, 44(26.8%) patients experienced a major complication (Clavien grade \geq 3) and there were 9(5.5%) deaths within 3 months of surgery. ASA, CONUT, NLR, PLR, SII and PCR showed statistically significant differences in distribution of complications (all p<0.05) (table 2,3). There were no differences in mean hospitalization length while CONUT, PNI, fibrinogen, PCR, SII and CCI were statistically associated with 30-days Fibrinogen was the only serum marker readmission. associated with 90-days mortality (p=0.01). Multivariable binomial logistic regression analysys confirmed the association of CONUT, SII, ASA, NLR, PCR and fibrinogen with surgical complications (all p < 0.05).

Mortality at 90 days				Readmission at 30 days				
	yes	no	р		yes	no	р	
total	9	155		total	46	118		
CONUT ow nigh	36	95 60	0.16	CONUT low high	18 28	80 38	0.002	
PNI ow nigh NLR ow nigh	3 6	65 90	0.87	PNI low high	26 20	42 76	0.02	
NĽR ow nigh	5 4	102 53	0.78	NLR ow high	26 20	81 37	0.2	
PĽR ow nigh	4 5	60 95	0.72	PLR low high	15 31	49 69	0.38	
LMR ow nigh	4 5	84 71	0.73	LMR low high	28 18	60 58	0.33	
Fibrinogen normal nigh	1 8	84 71	0.0015	Fibrinogen normal high	14 32	71 47	0.001	
PČR normal high	27	71 84	0.31	high PCR normal high	11 35	62 56	0.002	
Albumin normal low	63	120 35	0.74	Albumin normal low	31 15	95 23	0.11	
SII normal high	4 5	59 96	0.70	SII normal high	18 28	71 47	0.02	
AŠA score 1,2 3,4	3 6	87 68	0.32	ASA score 1,2 3,4	24 22	66 52	0.8	
CCI 0 1 ≥ 2	0 1 8	31 24 100	0.74	CCI 0 1 ≥ 2	11 8 27	20 17 81	0.001	

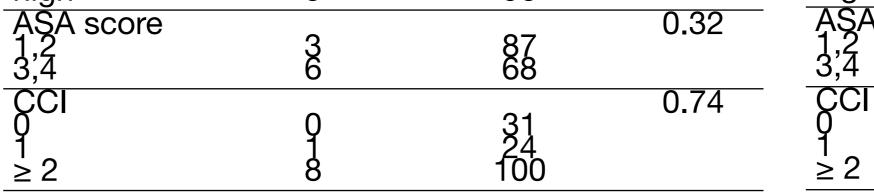


Table 4. Postoperative complications according to risk grouping

	C	omplicatior	•	to Clavien G	arade		
Percentage (No)							
Grouping	0	1	2	3	4	5	р
CCI 0 1 ≥ 2	19.3(6) 4(1) 7.4(8)	45.2(14) 40(10) 38.9(42)	22.6(7) 24(6) 24.1(26)	12.9(4) 32(8) 15.7(17)	0(0) 0(0) 8.3(9)	0(0) 0(0) 5.6(6)	0.09
ASA score < 3 ≥ 3	11.1(10) 6.8(5)	48.9(44) 29.7(22)	24.4(22) 23(17)	11.1(10) 25.7(19)	2.2(2) 9.6(7)	2.2(2) 5.4(4)	0.01
Albumine Iow normal	7.9(3) 9.5(12)	28.9(11) 43.7(55)	23.7(9) 23.8(30)	28.9(11) 14.3(18)	7.9(3) 4.8(6)	2.6(1) 4(5)	0.32
CONUT Iow high	12.2(12) 4.5(3)	40.8(40) 39.4(26)	28.6(28) 16.7(11)	11.2(11) 27.3(18)	5.1(5) 6.1(4)	2(2) 6.1(4)	0.03
PNI low high	7.4(5) 10.4(10)	35.3(24) 43.8(42)	22.1(15) 25(24)	26.5(18) 11.5(11)	7.4(5) 4.2(4)	1.5(1) 5.2(5)	0.13
NLR Iow high	11.2(12) 5.3(3)	40.2(43) 40.4(23)	28(30) 15.8(9)	11.2(12) 29.8(17)	5.6(6) 5.3(3)	3.7(4) 3.5(2)	0.049
PLR Iow high	9.4(6) 9(9)	32.8(21) 45(45)	34.4(22) 17(17)	10.9(7) 22(22)	6.3(4) 5(5)	6.3(4) 2(2)	0.048
LMR low high	6.8(6) 11.8(9)	44.3(39) 35.5(27)	17(15) 31.6(24)	22.7(20) 11.8(9)	6.8(6) 3.9(3)	2.3(2) 5.3(4)	0.08
SII Iow high	9(8) 9.3(7)	42.7(38) 37.3(28)	29.2(26) 17.3(13)	8.9(8) 28(21)	5.6(5) 5.3(4)	4.5(4) 2.7(2)	0.043
Fibrinogen	11 8(10)	11 7(38)	2/ 7(21)	15 3(13)	3 5(3)	0(0)	0.06

Table 5. Multivariable analysis adjusted for age, sex, pT and urinary diversion

variable	HR(95% IC)	p
SII	2.39(1.65 - 3.13)	0.02
CONUT	2.87(2.10 - 3.65)	0.008
PLR	1.29(0.52 – 2.06)	0.51
NLR	2.55(1.75 - 3.35)	0.022
LMR	1.63(0.87 – 2.39)	0.21
PCR	3.67(2.85 - 4.49)	0.002
Fibrinogen	2.27(1.52 - 3.01)	0.03
Albumine	2.05(0.96 - 2.84)	0.08
PNI	1.98(0.94 - 2.73)	0.073
ASA	3.80(3.02 - 4.59)	0.0008
CCI	1.59(0.77 - 2.37)	0.24

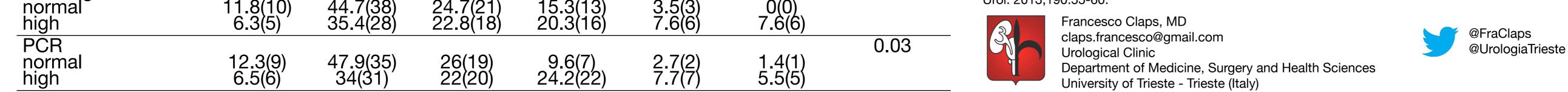
CONCLUSIONS

Preoperative inflammation and immuno-nutritional serum markers based on standard laboratory measurements may be simple and inexpensive potentially effective riskassessment tools to predict outcomes after RC. Further investigations should be necessary to confirm these results.

REFERENCES

1 - Shabsigh A, Korets R, Vora KC, et al. Defining early morbidity of radical cystectomy for patients with bladder cancer using a standardized reporting methodology. Eur Urol. 2009;55:164-174.

2 - Boorjian SA, Kim SP, Tollefson MK, et al. Comparative performance of comorbidity indices for estimating perioperative and 5-year all cause mortality following radical cystectomy for bladder cancer. J Urol. 2013;190:55-60.



Presented at the XXIX Congress of Italian Society of Uro-Oncology SIUrO, Bologna, Italy