Preoperative impact of albumin to fibrinogen ratio (AFR) on oncological outcomes in patients with muscle invasive bladder cancer (MIBC) treated with radical cystectomy

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INTRODUCTION AND OBJECTIVES

Recent evidence has demonstrated that coagulation is associated with tumor progression in various cancers[1]. Fibrinogen, a plasma glycoprotein and an acute phase element that plays a key role in clot formation and wound healing and binds to platelets to support platelet aggregation, which is the final step in the coagulation cascade plays an important role in cancer: different studies have reported that high preoperative fibrinogen level is associated with tumor development and indicates poor prognosis in some malignancies[2]. Moreover, it is known that malnutrition is a predictor of progression in several types of cancer and albumin is a commonly used index in clinical practice to assess nutritional status[3].

The albumin to fibrinogen ratio (AFR) consists of serum albumin and plasma fibrinogen, indicating nutritional status and coagulation as well as the inflammatory condition of cancer patients. The aim of the study was to investigate the ability of the AFR to predict survival outcomes in patients affected by muscle invasive bladder cancer (MIBC) treated with radical cystectomy (RC).

MATERIALS AND METHODS

We retrospectively evaluated data from 122 patients who underwent RC for MIBC at our Institute with a minimum follow-up of 12 months. AFR score was calculated based on the serum albumin concentration and plasma fibrinogen. Patients were classified into two groups: those with low AFR and those with high AFR. Univariate and multivariate analysis were performed. Recurrence-free (RFS) and Overall Survival (OS) rates were calculated and compared between the two groups. To the best of our knowledge no study in literature have combined albumin with fibrinogen in patients with MIBC.

RESULTS

Cut-off value to discriminate between low and high AFR score was determined calculating the ROC curve: the area under the curve was 0.78 with an optimal cut-off of 9.53 points. 41(33.6%) patients had low AFR. Distribution of data in low and high AFR groups as mean age at surgery (72.3 ± 8.8 vs 71.1 ± 8.9, p=0.35), sex (male 23 vs 44 and female 18 vs 37, p=0.85), presence of high grade disease (39 vs 72, p=0.33) lymphovascular invasion (LVI) (16 vs 27, p=0.55), adjuvant chemotherapy (24 vs 58, p=0.16), mean BMI (25.2 ± 3.9 vs 26.4 ± 4.3, p=0.17) and urinary diversion were not statistically different between two groups. Pathological features as pT and pN stages were statistically different (0.01 and 0.03 respectively).

Table 1. Clinical and pathological features in low and high AFR groups

	total	low AFR	high AFR	p
n.patients	122	41	81	
Gender				1.00
male	67	23	44	
female	55	18	37	
Mean age at surgery (±SD)	71.6(±8.9)	72.3(±8.8)	71.1(±8.9)	0.35
Mean BMI (±SD)	26(±4.2)	25.2(±3.9)	26.4(±4.3)	0.17
Mean follow-up (±SD)	49.6(±38.3)	37.7(±34)	55.3(±39.2)	0.02
Charlson Comorbidity Index				0.82
0	23	9	14	
1	19	6	13	
≥2	80	26	54	
ASA score				0.02
≤2	75	19	56	
≥3	47	22	25	
pT stage				0.01
T2(a,b)	59	13	46	
T3(a,b)	42	16	26	
T4(a,b)	21	12	9	
pN stage				0.03
negative	96	27	69	
positive	26	14	12	
Grading				0.33
high	111	39	72	
low	11	2	9	
LVI				0.55
no	43	16	27	
yes	79	25	54	
Adjuvant CT				0.16
yes	82	24	58	
no	40	17	23	

OS and RFS rates were calculated with a mean follow-up greater in high AFR group (55.2 ± 39.2 vs 37.7 ±34, p=0.02). Results of the multivariate analysis, after adjustment for age, pT, pN, LVI, surgical margins (R) and ASA score, revealed that AFR was an independent predictor of RFS (HR 4.21, 2.25-7.88; p<0.001) and OS (HR 1.82, 1.01-3.32, p<0.001).

Image 1,2. Overall Survival and Recurrence-free Survival rates

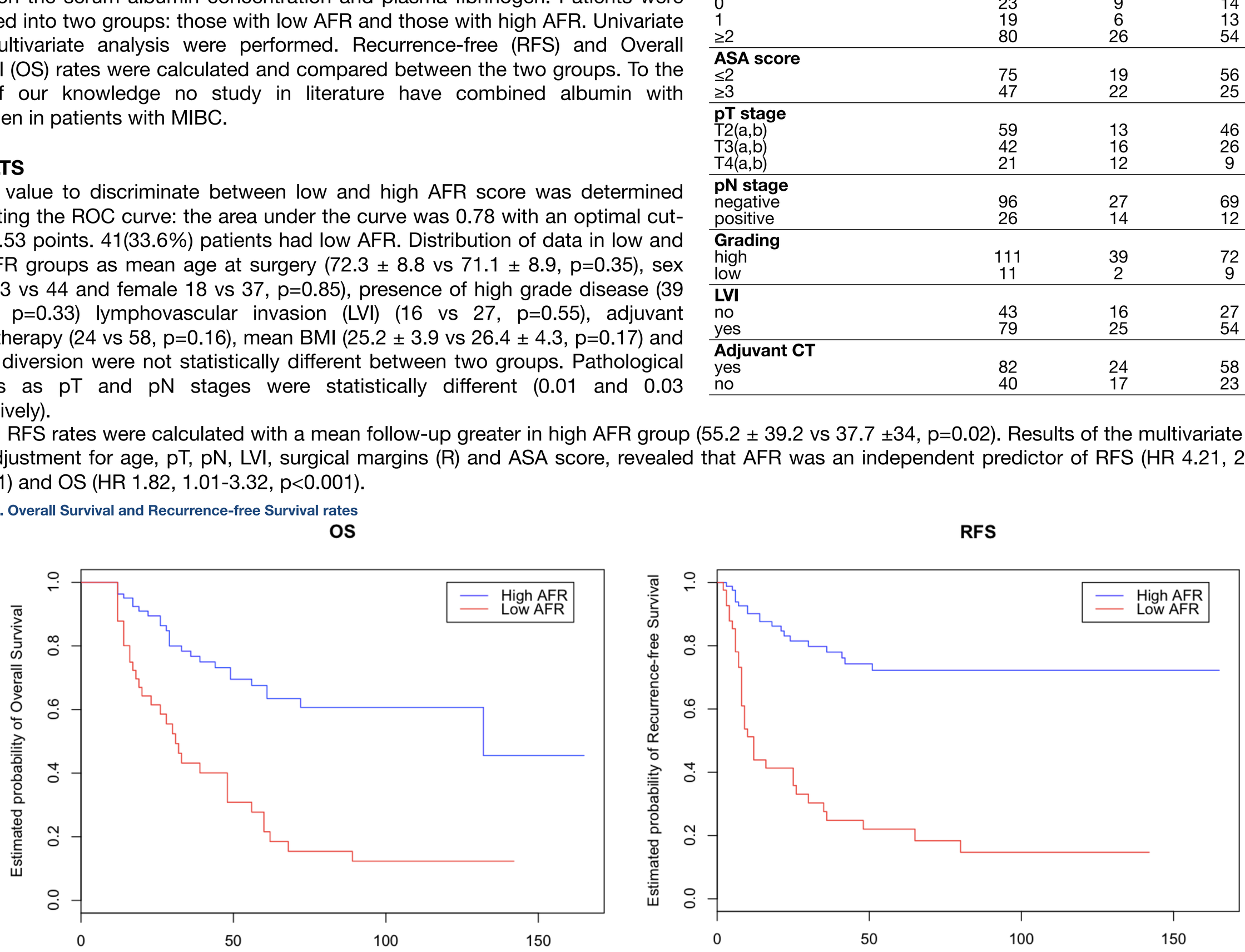

Image 2,3. Univariate and Multivariate analysis

Variable	RFS (95% IC)	p	OS (95% IC)	p
Age (as continuous)	1.86(1.01-3.40)	0.045	1.99(1.11-3.56)	0.02
pT≥3 (ref<3)	2.97(1.64-5,39)	0.0003	2.06(1.20-3.53)	0.008
pN positive (ref. negative)	3.92(2.23-6.97)	<0.0001	3.02(1.74-5.28)	0.0001
LVI positive (ref. negative)	2.71(1.55-4.72)	0.0004	2.27(1.31-3.96)	0.004
concomitant cis (ref. no)	1.13 (0.51-2.50)	0.77	1.37(0.64-2.90)	0.41
Surgical magrins (ref. negative)	2.88(1.01-8.28)	0.05	2.46(0.84-7.21)	0.09
Low AFR (ref. high)	4.21(2.25-7.88)	<0.0001	2.90(1.63-5.12)	0.0002
CCI≥2 (ref. <2)	0.86(049-1.51)	0.59	0.89(0,51-1,56)	0.69
ASA score≥3 (ref.<3)	1.85(1.01-3.39)	0.045	1.82(1.01-3.32)	0.48

Variable	RFS (95% IC)	p	OS (95% IC)	p
Age (as continuous)	1.67 (0.88-3.18)	0.11	1.60(0.85-3.01)	0.14
pT≥3 (ref<3)	1.56(0.76-3.19)	0.22	1,20(0.62-2.33)	0.58
pN positive (ref. negative)	1.52(0.60-3.83)	0.37	1.62(0.62-4.20)	0.32
LVI positive (ref. negative)	1.49(0.61-3.70)	0.38	1.33(0.52-3.37)	0.54
Surgical magrins (ref. negative)	2.88(1.01-8.28)	0.05	2.46(0.84-7.21)	0.09
Low AFR (ref. high)	4.21(2.25-7.88)	<0.0001	2.90(1.63-5.12)	0.0002
ASA score≥3 (ref.<3)	1.85(1.01-3.39)	0.045	1.82(1.01-3.32)	0.48

CONCLUSIONS

AFR is a potential prognostic predictor of both OS and RFS in patients with MIBC who underwent surgery. Further investigations should be necessary to confirm the good potential of this malnutrition-inflammation related tools.

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