ORIGINAL PAPER

THE IMPACT OF HYPOALBUMINEMIA ON PATIENTS WITH COMPLICATED COLON CANCERS, OPERATED IN EMERGENCY

Raul Mihailov[1,2], Georgiana Bianca Constantin[3], Cristina Șerban[2,3], Dorel Firescu[2,3], Dragoș Voicu[3], Laura Rebegea[2,3], Oana Mihailov[3], Corina Pălivan Manole[2,3], Adrian Beznea[2,3], Constantin Truș[2,3], Rodica Bîrlă[1], Traian Pătrașcu[1]

[1]"Carol Davila" University of Medicine and Pharmacy, Bucharest, Romania
[2]"Sf. Ap. Andrei" Clinical Emergency County Hospital, Galati, Romania
[3]"Dunarea de Jos" University, Faculty of Medicine and Pharmacy, Galati, Romania

Corresponding author: Rodica Bîrlă
Email: birlarodica@yahoo.com

ABSTRACT

The serum albumin was used as a parameter to assess the nutritional status of a patient, due to its free availability and low cost. We studied the clinical indications and the involvement of the serum albumin levels in the prognosis of patients operated in emergency for complicated colon cancers in a retrospective study including 451 patients, diagnosed and operated for complicated colon cancer in the Surgical Clinics I and II of the Clinical Emergency County Hospital "Sf. Ap. Andrei" from Galati, between 2008 and 2017. We found a major serum hypoalbuminemia in 5.10% cases, a minor hypoalbuminemia in 12.64% cases and the existing values correlated well with both the postoperative complications and the deaths resulting from the study. Although the albumin remains a weak marker of nutrition assessment, it offers a clear prognosis value in predicting the patient outcomes after colorectal surgery, but which would continue to benefit from further studies.

KEYWORDS: *hypoalbuminemia, colon cancer, deaths, complications*

INTRODUCTION

The albumin is a unique polypeptide, responsible for five main functions: [1] maintaining the colloid osmotic pressure; [2] linking and transporting solutions; [3] purification of free radicals; [4] inhibition of platelet function and antithrombotic effect and [5] beneficial effects on vascular permeability in the installation of shock and sepsis [1]. The albumin is a major source of sulfhydryl group, which sequesters both leukotoxin and nitric oxide, limiting permeability and vascular dilation. The serum albumin was used as an assessment of the nutritional status of a patient, due to its free availability and low cost. The reliability of this assessment is controversial, however, because hypoalbuminemia is an acute phase reactant and it is influenced by the systemic inflammation [6]. The increased need for specific amino acids for the synthesis of acute phase proteins degrades the available body protein, including the albumin [7] – [9].

The aim of this study is to analyze the clinical indications and the involvement of the serum albumin levels in the prognosis of patients operated in emergency for complicated colic neoplasms.

MATERIALS AND METHOD

This retrospective study involved 451 patients, diagnosed and operated for complicated colon cancer in the Clinics I and II of the Clinical Emergency County Hospital "Sf. Ap. Andrei" Galati, between 2008 and 2017. The serum albuminemia values were analyzed, as well as the correlations between these values, the postoperative complications and the deaths.

The database stores information as nominal or scalar variables. The relationships between the variables were established by calculating the values of the correlation coefficients at nominal level C and V, as well as the probabilities associated with them. If the associated probability has the value $p < \alpha = 0.05$, we can say that the variables are correlated. Another method for determining the degree of association between two categorical variables is the Pearson Chi-square test. For numerical variables we calculated the correlation coefficient r, Pearson's and the probability associated with it. If $p < \alpha = 0.05$, we admit that the two variables are correlated, the r value indicates the correlation level.

Davies, Charlson and Charlson scores adjusted for age were calculated on the studied group.

Davies score was applied for each patient and was obtained by cumulating the score of the following pathologies: Presence of neoplasia (1 point), Ischemic heart disease (1 point), Peripheral vascular disease (1 point), Left ventricular dysfunction (1 point), Presence diabetes mellitus (1 point), systemic vascular collagenosis (1 point), other significant pathology (1 point).

Depending on the value of the Davis score, the patients were categorized as follows: grade 0 (low risk) with score 0; grade 1 (medium risk) with a score of 1-2; grade 2 (high risk) with a cumulative score of at least 3.

The Charlson score for comorbidity was calculated taking into account the following pathologies, each with its own score, as follows: Myocardial infarction (1 point), Congestive heart disease (1 point), Peripheral vascular disease (1 point), Cerebrovascular disease (1 point), Dementia (1 point), Chronic lung disease (1 point), Connective tissue disease (1 point), Ulcerative disease (1 point), Mild liver disease (1 point), Uncomplicated diabetes (1 point), Hemiplegia (2 points), Moderate or severe kidney disease (2 points), Diabetes with organ damage (2 points), Any tumor (2 points), Leukemia (2 points), Lymphoma (2 points), Moderate or severe liver disease (3 points), Solid tumor metastases (6 points), Acquired immune deficiency syndrome (6 points). As can be seen, the index includes 19 medical pathologies, marked from 1-6, so that the total score can range between 0 and 37.

The age-adjusted Charlson score was calculated by adding an extra point to each Charlson score for each decade of age.

Based on these scores, we evaluated the duration of hospitalization of patients, the type of surgery, the number and type of postoperative complications and the number of deaths.

The software package used for statistical analysis was IBM SPSS Statistics version 23.

RESULTS AND DISCUSSIONS

We found a major serum hypoalbuminemia in 5.10% cases and a minor hypoalbuminemia in 12.64% cases (Figure 1).

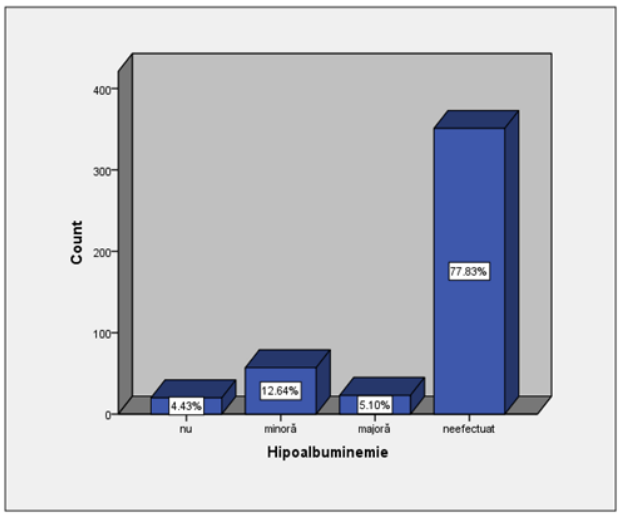

Table 1 – The distribution of cases according to the presence of hypoalbuminemia and its values

The correlation between the degrees of hypoalbuminemia and the post-operatory complications are written in Table 1.

The CHI^2 test shows that there is a link between hypoalbuminemia and post-operatory complications ($\chi^2 = 90.014$ and $p = 0.026 < \alpha = 0.05$) (Table 2).

Post-operatory complications	Hypoalbuminemia				Total
	Major	Minor	Not done	No	
Douglas abscess	0	0	1	0	1
Subphrenic abscess	0	0	1	0	1
peritoneal abscesses, colostomy necrosis, cardio-respiratory stop	0	0	1	0	1
Bronchopneumonia, acute respiratory insufficiency, cardio-respiratory stop	1	0	0	0	1
Clostridium difficile	0	0	3	0	3
Acute pulmonary edema, cardio-respiratory stop	0	0	1	0	1
Evisceration	0	0	1	0	1
Blocked evisceration	0	0	1	0	1
Anastomotic fistula	1	1	6	0	8
Anastomotic fistula, evisceration	0	2	0	0	2
Anastomotic fistula, wound hematoma	0	0	1	0	1
Anastomotic fistula, cardio-respiratory stop	0	0	2	0	2
Anastomotic fistula, pulmonary thromboembolism	0	0	1	0	1
Duodenal fistula	0	0	1	0	1
Enteral fistula	2	2	0	0	4
Pancreatic fistula	0	0	1	0	1
Heart failure, acute pulmonary edema	0	0	1	0	1
Acute renal insufficiency	0	0	1	0	1
Intestinal obstruction (adherencial syndrome)	2	3	2	0	7
Cardio-respiratory stop	3	4	15	0	22
Parietal suppuration	1	2	14	3	20
Total	**23**	**57**	**351**	**20**	**451**

Table 1 – The correlation between the hypoalbuminemia and the post-operatory complications

The values of the correlation coefficients at nominal level C and V as well as the probabilities associated with these values lead to the same conclusion ($p = 0.026 < \alpha = 0.05$, $C = 0.408$ and $V = 0.258$). The values of the coefficients show that this correlation existed but is weak.

We have also studied the correlation between the number of deaths and the hypoalbuminemia levels (Table 3).

The CHI^2 test shows that there is a link between hypoalbuminemia and deaths ($\chi^2 = 42{,}936$ and $p < 0.001 < \alpha = 0.05$). The values of the correlation coefficients at the nominal level C and V as well as the probabilities associated with these values lead to the same conclusion ($p < 0.001 < \alpha = 0.05$, $C = 0.269$ and $V = 0.178$). The values of the coefficients show that this correlation is weak. We note that the death rate is 39.13% in those with major hypoalbuminemia, 17.54% in those with minor hypoalbuminemia, while the death rate in patients without hypoalbuminemia is 0%. Most of the deaths occurred after more than 96 hours post-operatory (Table 4).

	Value	df	Asymptotic Significance (2-sided)
Pearson Chi-Square	90.014a	66	.026
Likelihood Ratio	60.233	66	.677
N of Valid Cases	451		

Table 2 – Statistical analysis of the correlation hypoalbuminemia – post-operatory complication

Deaths	Hypoalbuminemia				
	Major	**Minor**	**Not Done**	**No**	**Total**
<24 hours post-operatory	2	1	3	0	6
>48 hours post-operatory	4	2	5	0	11
>72 hours post-operatory	1	1	2	0	4
>96 hours post-operatory	2	6	24	0	32
No	14	47	317	20	398
Total	**23**	**57**	**351**	**20**	**451**

Table 3 – The correlation between the deaths and the hypoalbuminemia

	Value	**df**	**Asymptotic Significance (2-sided)**
Pearson Chi-Square	42.936[a]	12	.000
Likelihood Ratio	26.629	12	.009
N of Valid Cases	451		

Table 4 – Statistical analysis between the values of hypoalbuminemia and the deaths in the study

In the early 1950s, there's been found that hypoalbuminemia has a negative influence on the postoperative development [10,11]. This finding was followed by Harvey's studies, which reported that low serum albumin level was the best indicator for concomitant sepsis [12]. A high incidence of malnutrition was first described in 1974 by Banh [13] and Butterworth [14]. Currently, the data available show that malnutrition has a prevalence of 30% to 50% in hospitalized patients and is one of the most important determinants in the prognosis of the patient, which affects the length of hospitalization, costs, morbidity and, finally, mortality [15], [16]. In particular, hypoalbuminemia is associated with poor tissue healing, decreased collagen synthesis and granuloma formation in surgical wounds, eventually delaying healing [17] – [21]. Usually, serum albumin levels have been used as a biochemical marker of preoperative nutritional status. It is regarded as an accurate indicator of preoperative prognosis in a variety of surgical procedures, including cardiac [22], trauma [23] and general surgery [10], [24] – [26], especially for digestive cancers [27] – [29].

The patients undergoing colorectal surgery are often undernourished due to advanced neoplasia or to inflammatory intestinal disease, leading to poor oral intake, blockages, intestinal fistulas, poor absorption capacity and high-volume loss of the gastrointestinal tract [30].

The hypoalbuminemia has also been associated with delayed recovery of postoperative intestinal function, further aggravating postoperative nutritional recovery [31]. The preoperatory albumin levels have been shown to be the best predictor of mortality after colorectal cancer surgery [16], [32].

Although the classic definition for hypoalbuminemia is the albumin value less than 3.0 g/dL, the definitions vary widely in different studies from <2.7 to <3.5 g/dL [16], [33], [34]. Using the American College of Surgeons National Quality Improvement Program (NSQIP) database to measure postoperative surgical outcomes, Moghadamyeghaneh et al [16] emphasized the effect of moderate hypoalbuminemia, defined by serum albumin levels between 3.0 and 3.4 g/dL. The mortality rate in patients with moderate hypoalbuminemia and without hypoalbuminemia was 6% and 1.7%, respectively, and the risk of morbidity was also higher [adjusted rate (AOR) = 1,876; 95% CI 1.51-2.05; P <0.01]. The highest rates of morbidity (60.4%) and mortality (26.2%) occurred at serum albumin levels below 2 g/dL. In addition, this study showed a linear correlation between the albumin level and the post-operatory mortality, which means that any decrease in serum albumin level from normal (> 4 g/dL) had serious consequences on colorectal resection results. The rate of increase in mortality and morbidity was estimated to be approximately 49% and 24% respectively for each 1 g / dL decrease in albumin level (P <0.05). Colon cancer patients had a higher rate of moderate hypoalbuminemia compared to patients with rectal cancer (AOR = 1.55; P <0.01).

None of the three scores correlated with the number of hospitalization days because the

probability associated with the Person test is greater than the significance threshold, $\alpha = 0.05$ ($p = 0.871$ for the Davies score, $p = 0.852$ for the Charlson score, and $p = 0.706$ for adjusted Charlson score).

	Davies score	Charlson score	Adjusted Charlson score
Number of hospitalization days	-.008	.009	-.018
Pearson correlation	.871	.852	.706
N	451	451	451

Table 5 – Correlations between the number of hospitalization days and the scores (Davies, Charlson)

Deaths	N	Mean	Std. Deviation	Std. Error	95% Confidence Interval for Mean		Min.	Max.
					Lower bound	Upper bound		
Davies score								
No	398	1.74	.763	.038	1.66	1.81	1	4
<24 hours post-operatory	6	1.67	.516	.211	1.12	2.21	1	2
>48 hours post-operatory	11	2.64	.674	.203	2.18	3.09	1	3
>72 hours post-operatory	4	2.25	.500	.250	1.45	3.05	2	3
>96 hours post-operatory	32	2.09	.963	.170	1.75	2.44	1	4
Total	451	1.79	.788	.037	1.71	1.86	1	4
Charlson score								
No	398	4.00	2.626	.132	3.74	4.26	2	12
<24 hours post-operatory	6	3.00	.632	.258	2.34	3.66	2	4
>48 hours post-operatory	11	7.64	2.618	.789	5.88	9.40	4	11
>72 hours post-operatory	4	6.75	3.304	1.652	1.49	12.01	3	10
>96 hours post-operatory	32	5.25	2.747	.486	4.26	6.24	2	13
Total	451	4.19	2.704	.127	3.94	4.44	2	13
Adjusted Charlson score								
No	398	10.27	3.036	.152	9.97	10.57	5	19
<24 hours post-operatory	6	9.17	1.329	.543	7.77	10.56	7	10
>48 hours post-operatory	11	14.64	2.248	.678	13.13	16.15	12	18
>72 hours post-operatory	4	14.25	3.500	1.750	8.68	19.82	10	18
>96 hours post-operatory	32	12.44	2.839	.502	11.41	13.46	9	21
Total	451	10.55	3.128	.147	10.26	10.84	5	21

Table 6 – Correlation between the deaths and the Davies and Charlson scores

	Sum of Squares	df	Mean Square	F	Sig.
Davies score					
Between Groups	12.919	4	3.230	5.402	.000
Within Groups	266.647	446	.598		
Total	279.565	450			
Charlson score					
Between Groups	215.685	4	53.921	7.820	.000
Within Groups	3075.295	446	6.895		
Total	3290.980	450			
Adjusted Charlson score					
Between Groups	395.390	4	98.848	11.004	.000
Within Groups	4006.237	446	8.983		
Total	4401.627	450			

Table 7 – Analysis of variances for Table 6 (ANOVA)

The ANOVA table contains the test result:

- F = 5,402; p <0.001 <α = 0.05 for the Davies test;
- F = 7.820; p <0.001 <α = 0.05 for the Charlson test;
- F = 11.004; p <0.001 <α = 0.05 for the adjusted Charlson test;

According to these results, we obtain that there are significant differences in the averages of the three scores between the defined groups of deaths. Analyzing the descriptive table, we notice that the scores are lower if the deaths occurred faster.

Complications	N	Mean	Std. Deviation	Std. Error	95% Confidence Interval for Mean		Min.	Max.
					Lower Bound	Upper Bound		
Davies score								
No	354	1.74	.749	.040	1.66	1.82	1	4
Peritoneal abscesses	2	1.50	.707	.500	-4.85	7.85	1	2
Peritoneal abscesses, colostomy necrosis, cardiac complications	1	1.00	.	.	.	.	1	1
Clostridium difficile	3	1.00	.000	.000	1.00	1.00	1	1
Cardiac complications	22	2.05	.899	.192	1.65	2.44	1	4
Cardiac and pulmonary complications	18	2.44	.705	.166	2.09	2.79	1	3
Parietal complications	22	1.64	.790	.168	1.29	1.99	1	3
Fistulas	14	2.00	.961	.257	1.45	2.55	1	4
Fistulas, cardiac complications	2	1.50	.707	.500	-4.85	7.85	1	2
Fistulas, parietal complications	2	3.00	.000	.000	3.00	3.00	3	3
Fistulas, hematoma	1	2.00	.	.	.	.	2	2
Fistulas, pulmonary thromboembolism	1	4.00	.	.	.	.	4	4
Acute renal insufficiency	2	2.50	2.121	1.500	-16.56	21.56	1	4
Intestinal post-operatory obstruction	7	1.43	.535	.202	.93	1.92	1	2
Total	451	1.79	.788	.037	1.71	1.86	1	4

Charlson score								
No	354	3.97	2.605	.138	3.69	4.24	2	12
Peritoneal abscesses	2	6.50	6.364	4.500	-50.68	63.68	2	11
Peritoneal abscesses, colostomy necrosis, cardiac complications	1	8.00	.	.	.	.	8	8
Clostridium difficile	3	4.00	3.464	2.000	-4.61	12.61	2	8
Cardiac complications	22	4.95	2.627	.560	3.79	6.12	2	11
Cardiac and pulmonary complications	18	6.06	2.817	.664	4.65	7.46	2	10
Parietal complications	22	4.68	2.998	.639	3.35	6.01	2	11
Fistulas	14	4.21	2.293	.613	2.89	5.54	2	9
Fistulas, cardiac complications	2	3.50	.707	.500	-2.85	9.85	3	4
Fistulas, parietal complications	2	5.50	.707	.500	-.85	11.85	5	6
Fistulas, hematoma	1	10.00	.	.	.	.	10	10
Fistulas, pulmonary thromboembolism	1	13.00	.	.	.	.	13	13
Acute renal insufficiency	2	4.00	2.828	2.000	-21.41	29.41	2	6
Intestinal post-operatory obstruction	7	3.29	2.563	.969	.91	5.66	2	9
Total	451	4.19	2.704	.127	3.94	4.44	2	13
Adjusted Charlson score								
No	354	10.24	3.029	.161	9.92	10.55	5	19
Peritoneal abscesses	2	13.00	5.657	4.000	-37.82	63.82	9	17
Peritoneal abscesses, colostomy necrosis, cardiac complications	1	15.00	.	.	.	.	15	15
Clostridium difficile	3	10.67	3.786	2.186	1.26	20.07	8	15
Cardiac complications	22	11.91	2.741	.584	10.69	13.12	8	18
Cardiac and pulmonary complications	18	13.22	2.922	.689	11.77	14.68	7	18
Parietal complications	22	10.91	3.176	.677	9.50	12.32	5	18
Fistulas	14	10.71	2.673	.714	9.17	12.26	7	16
Fistulas, cardiac complications	2	11.00	.000	.000	11.00	11.00	11	11
Fistulas, parietal complications	2	12.50	.707	.500	6.15	18.85	12	13
Fistulas, hematoma	1	17.00	.	.	.	.	17	17
Fistulas, pulmonary thromboembolism	1	21.00	.	.	.	.	21	21
Acute renal insufficiency	2	11.50	2.121	1.500	-7.56	30.56	10	13
Intestinal post-operatory obstruction	7	9.00	3.512	1.327	5.75	12.25	6	16
Total	451	10.55	3.128	.147	10.26	10.84	5	21

Table 8 – Correlations between the post-operatory complications and the scores

	Sum of Squares	df	Mean Square	F	Sig.
Davies score					
Between Groups	23.771	13	1.829	3.124	.000
Within Groups	255.795	437	.585		
Total	279.565	450			
Charlson score					
Between Groups	245.429	13	18.879	2.709	.001
Within Groups	3045.551	437	6.969		
Total	3290.980	450			
Adjusted Charlson score					
Between Groups	416.288	13	32.022	3.511	.000
Within Groups	3985.339	437	9.120		
Total	4401.627	450			

Table 9 - Analysis of variances for Table 8 (ANOVA)

The results of the ANOVA test are as follows:

- F = 3,124; p <0.001 <α = 0.05 for the Davies test;
- F = 2,709; p = 0.001 <α = 0.05 for the Charlson test;
- F = 3,511; p <0.001 <α = 0.05 for the adjusted Charlson test;

According to these results, we obtain that there are significant differences in the means of the three scores between the groups defined by the postoperative complications.

The presence of comorbidities is a strong predictor of hospitalization and mortality. The Davies score is considered to be a good predictor for assessing morbidity and mortality in patients with associated comorbidities. In our study, the Davies Score was significantly associated with the age of the patients, as well as with postoperative deaths and complications.

CONCLUSION

Although the albumin remains a weak marker of nutrition assessment, it offers a clear prognostic value in predicting patient outcomes after colorectal surgery.

The hypoalbuminemia significantly influences the duration of hospitalization and the rate of complications, especially the post-operatory suppurations and the anastomotic fistulas. However, these studies are largely non-randomized small cohort retrospective studies or large-scale studies using national databases and this topic may benefit from further studies.

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