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FACTORS IMPACTING MORTALITY IN TURKISH OCTOGENARIAN AND NONAGENARIAN PATIENTS WHO UNDERWENT COLORECTAL SURGERY

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ABSTRACT

Background & objective: Due to their physiological conditions, the postoperative mortality rates of elderly patients are higher compared to other age groups, albeit the postoperative care and intensive care conditions are better than in the past. In this retrospective study, it was aimed to present a model to predict mortality and factors affecting mortality in this patient group who underwent colorectal surgery. **Material & Methods:** The population of octogenarian and nonagenarian patients who were operated for colorectal surgery in our clinic between 2020 and 2021 were included in the study. Patients' age, gender, albumin, lymphocyte, monocytes, lymphocyte-monocyte ratio (LMR), prognostic nutritional index (PNI), delta neutrophil index (DNI), Charlson comorbidity index (CCI), length of hospital stay, modified systemic inflammatory score (mSIS)) values, operation type (emergency/ elective), operation classification (minor/ moderate/ major/ complex major), anesthesia type (general/ epidural), and contamination status (clean/ clean-contaminated/ contaminated/ dirty or infected) were obtained from the hospital system. **Results:** Case status, operation type, contamination status, DNI, duration of hospitalization, mSIS variables were statistically significant in univariate regression analyses. However, in multivariate regression analyses, DNI of ≥ 0.05 ($p< 0.015$; OR 3.984, 95%CI 1.302- 12.195) and contamination status ($p< 0.038$; OR 13,047, 95%Cl 1,150- 148,087) were found to be independent risk factors affecting postoperative mortality. **Conclusion:** In the geriatric patient population undergoing colorectal surgery, DNI and contamination of the surgical field are two important factors affecting mortality. We think that the mortality estimation model created for this patient population will also help physicians for the postoperative period of the patients.

Keywords: Colorectal Surgery, Mortality, Model, Nonagenarian, Octogenerian

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INTRODUCTION

Based on the data of the World Health Organization, the elderly population is increasing gradually. Correspondingly, the rate of emergency and elective abdominal surgery among octogenarian patients in the population, which currently accounts for nearly 60% of the general surgery workload, is increasing as well [1]. Dysfunction in organ systems is considered to begin at the age of 70, and comorbid conditions continue to increase dramatically after the age of 70 [2]. This brings comorbid conditions and the physiological age, at which activities of daily living take place, into the forefront rather than chronological age. The Charlson comorbidity index could also assist clinicians preoperatively for the octogenarian population through scoring many comorbid conditions [3]. The decrease in cardiac output with age, decrease in baroreceptor sensitivity, decrease in respiratory vital capacity by almost 50%,

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decrease in glomerular density, renal blood flow, and glomerular filtration rate, and high rates of protein-energy malnutrition lead to serious morbidity and mortality in every intervention performed in the octogenarian population [4-6]. Mortality was determined to be nearly 3 times higher in the elderly population operated for colorectal cancer and 4.6 times in those operated for trauma [7,8]. Due to such high mortality rates among the elderly population, in our study, we aimed to reveal the risk factors impacting mortality to predict the risk of mortality in elective colorectal surgery, to shorten the operation duration in emergency surgery, and to consider non-radical procedures, if possible, by evaluating the octogenarian and nonagenarian populations.

MATERIAL & METHODS

A total of 99 patients aged 80 years and older who underwent elective and emergency abdominal surgery for colorectal diseases in the general surgery clinic of our hospital between 2020 and 2021 were included in the study, which was designed retrospectively. In the study, in addition to demographic data such as age and sex, patients' albumin, lymphocyte, monocytes, lymphocyte-monocyte ratio (LMR), prognostic nutritional index (PNI), delta neutrophil index (DNI), the Charlson comorbidity index (CCI), duration of hospitalization, modified systemic inflammatory score (mSIS) values and operation type (emergency/ elective), anesthesia type (general/ epidural), operation classification (minor/ moderate/ major/ complex major) and contamination status (clean/ clean-contaminated/ contaminated/ dirty-infected) was evaluated as well. The operation grade was determined according to the criteria presented in **(Table I)** [9]. The patients were divided into two groups as clean-contaminated and contaminated-dirty based on their contamination status. DNI was computed via automatic cell analyzers operating with flow cytometry technique in blood. Cases with mortality within 30 days postoperatively were included in the study.

Table I: Classification criteria of operations.

Minor operations: Patients to whom resection could not be performed and underwent loop colostomy, diversion
Moderate operations: Patients who underwent minor concomitant intervention in addition to loop colostomy and diversion
Major operations: Hemicolectomy, Partial resections, Hartman procedure, Anterior resections, Miles operation
Complex major operations: Subtotal-total colectomies and surgeries with concomitant intervention in major surgeries

STATISTICAL ANALYSIS

All analyzes were conducted via the software of SPSS v23. Conformity of numerical data to normal distribution was checked by the Kolmogorov-Smirnov test. It was determined that none of the variables met the assumption of normal distribution. Continuous numerical variables were analyzed with the Mann-Whitney U test. The median, minimum, and maximum values of these variables were presented. Chi-square analysis was conducted for categorical variables. The frequency and percentage values of these variables were presented. Univariate regression analysis was conducted for each variable by taking the variables with significant p values in similar variables. Multivariate regression analysis with forward selection was conducted with the variables found to be significant. The Hosmer-Lemeshow test was used to analyze the goodness of fit. The results were considered significant at $p< 0.05$. To assess the success of the established logistic regression model, ROC curve analysis was conducted and performance measures were computed. In the definition of the predictive model, the area under the curve (AUC) values of > 0.8, 0.6-0.8, and < 0.6, were considered as excellent, good, and moderate, respectively. A p value of < 0.05 was considered significant.

RESULTS

The median age of 99 patients included in the study was 84(80-96). The population consists of 56(56.6%) male and 43(43.4%) female patients. The patients were operated mostly due to colorectal malignancy (57.6%), complications of diverticulum (16.2%), volvulus (15.1%), acute mesenteric ischemia (10.1%), and GI bleeding (1.0%). In addition, 58(58.6%) of the patients were operated emergency. There was mortality in 47(47.5%) of the cases, whereas there was no mortality in 52(52.5%) of the cases. The mean value of postoperative mortality time was 6.28 ± 1.28 days. The mortality was 13 times higher in patients who underwent emergency operation type compared to those who underwent elective surgery, and the difference between the two groups was significant ($p< 0.001$). Contaminated and Dirty-infected cases were 53(53.5%). Clean contaminated cases were 46(46.5%). Mortality rates were higher in contaminated and dirty cases. When the correlation between the contamination status of the cases and mortality was analyzed, it was determined that there was a significant difference. It was found that the mortality was 17.14 times higher in dirty-infected and contaminated cases compared to the clean-

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contaminated group (p< 0.001). Although there were 80(80.8%) major operations, there were 19(19.2%) complex major operations. Regarding the operation grade, it was observed that the mortality in major complex cases increased 2.93 times compared to complex cases, and this difference was significant (p= 0.042). A significant difference was determined between mSIS and mortality (p= 0.047). In the multinomial regression analysis performed afterward, no significant difference was determined between those who scored 2 and those who scored 0 (p= 0.175), whereas mortality was significantly increased 9.25 times in those who scored 1 compared to those who scored 0 (p=0.044). No significant difference was found between sex and type of anesthesia, which are other categorical data, and mortality (Tablo II-III).

Table II: Correlation between continuous numerical data and mortality

	Mortality	N	Median(min-max)	p
Age, years	Absent	52	84(80-90)	0.092
	Present	47	86(80-96)	
	Total	99	84(80-96)	
Albumin, g/dL	Absent	52	3.75(2.2-4.9)	0.451
	Present	47	3.5(1.9-4.3)	
	Total	99	3.7(1.9-4.9)	
Lymphocyte, 10^3/uL	Absent	52	1.15(0.34-3.03)	0.055
	Present	47	0.89(0.34-2.36)	
	Total	99	1.12(0.34-3.03)	
Monocyte, 10^3/uL	Absent	52	0.43(0.18-0.99)	0.774
	Present	47	0.45(0-1.52)	
	Total	99	0.43(0-1.52)	
LMR	Absent	52	2.67(0.65-8.19)	0.055
	Present	47	2.19(0.47-36)	
	Total	99	2.48(0.47-36)	
PNI	Absent	52	42.97(25.9-57.05)	0.055
	Present	47	39.65(24-54.8)	
	Total	99	41.8(24-57.05)	
DNI	Absent	52	0(0-36.4)	**<0.001**
	Present	47	2.3(0-67.5)	
	Total	99	0(0-67.5)	
CCI	Absent	52	5(4-7)	0.054
	Present	47	5(4-10)	
	Total	99	5(4-10)	
Hospitalization Duration, days	Absent	52	8(4-45)	**0.011**
	Present	47	5(0-61)	
	Total	99	7(0-61)	

[#] Mann-Whitney U test results were considered significant at p<0.05.

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Table III: Correlation between categorical variables and mortality

		Mortality			
		Absent N(%)	Present N(%)	Total N(%)	p
Gender	Male	33 (58.9%)	23 (41.1%)	56 (56.6%)	0.145
	Female	19 (44.2%)	24 (55.8%)	43 (43.4%)	
Operation Type	Emergency	17 (29.3%)	42 (70.7%)	59 (59.6%)	**<0.001**
	Elective	34 (85.0%)	6 (15.0%)	40 (40.4%)	
Anesthesia*	Epidural	1 (50.0%)	1 (50.0%)	2 (2.0%)	0.727*
	General	51 (52.6%)	46 (47.4%)	97 (98.0%)	
Operation Classification	Major	46 (57.5%)	34 (42.5%)	80 (80.8%)	**0.042**
	Complex Major	6 (31.6%)	13 (68.4%)	19 (19.2%)	
Contamination Status	Clean-contaminated	39 (84.8%)	7 (15.2%)	46 (46.5%)	**<0.001**
	Contaminated+ Dirty or Infected	13 (24.5%)	40 (75.5%)	53 (53.5%)	
mSIS	0	7 (87.5%)	1 (12.5%)	8 (8.1%)	**0.047**
	1	23 (57.5%)	17 (42.5%)	40 (40.4%)	
	2	22 (43.1%)	29 (56.9%)	51 (51.5%)	

Pearson chi-square test, *Fisher's exact test was considered significant at p<

When the statistical relationship between continuous numerical data and mortality was examined, a significant difference was found only between DNI, duration of hospitalization, and mortality (p< 0.001 and p= 0.011, respectively). For continuous numerical data with a significant difference, ROC analysis was performed and ideal cutoff points were determined individually. After the cut-off value was found to be 0.05 for DNI and 7.5 for the duration of hospitalization, logistic regression analysis was performed by converting the data into categorical data. The operation type, operation class, contamination status, having DNI of ≥ 0.05, hospitalization duration of ≥ 7.5 days, and mSIS, which were significant, were first subjected to univariate regression analysis. Then, independent risk factors were determined by applying multivariate regression analysis (Tablo IV). Having a DNI of ≥0.05 and contamination status were found to be two independent risk factors that increased mortality approximately 4-fold and 13-fold, respectively. The established mortality prediction model score was subjected to ROC analysis and the success of the test was revealed. The AUC value of the test to predict mortality was determined to be 0.876 (0.803- 0.948, 95% CI) (Fig. 1).

Table IV: Univariate and multivariate logistic regression analysis results

		Univariate Logistic Reg.			Multivariate Logistic Reg.		
		OR	95.0% CI	p	OR	95.0% CI	p
Operation Type	Emergency	1					
	Elective	12.987	4.608-35.714	**<0.001**			
Operation Classification	Major	1					
	Complex Major	2.931	1.011-8.495	**0.048**			
Contamination	Clean-Contaminated	1			1		
	Contaminated+ Dirty or Infected	17.143	6.186-47.503	**<0.001**	13.05	1.150-148.087	**0.038**
DNI	<0,05	1			1		
	≥0,05	9.708	3.875-24.390	**<0.001**	3.984	1.305-12.195	**0.015**
Duration of Hospitalization	<7,5	1					
	≥7,5	3.1	1.362-7.055	**0.007**			
mSIS	0	1		**0.078**			
	1	9.227	1.056-80.599	**0.044**			
	2	1.783	0.772-4.117	0.175			

OR: odds ratio CI: Confidence interval p<0.05 was considered statistically significant

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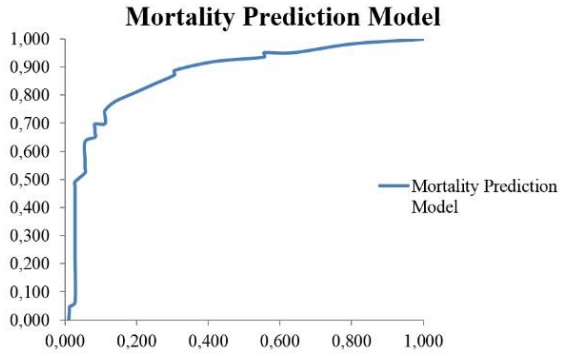

Figure 1. ROC analysis graph of the Mortality Prediction Model (x axis: Sensitivity y axis: 1- Specificitiy)

DISCUSSION

In our study, DNI, duration of hospitalization, operation type, operation grade, contamination status(surgical wound classification), and mSIS were found to be significant as a result of univariate analyzes, and from these variables, only the patient's contamination status, being contaminated,dirty-infected and having a DNI of ≥ 0.05 were shown as independent risk factors affecting mortality. In studies conducted in the octogenarian population, Green et al. [10] revealed the correlation between mortality and sepsis and accompanying malignancy, and Rubinfield et al. [11] demonstrated the correlation of ASA value and female gender with mortality while Hentati et al. [12] revealed the correlation between mortality and comorbid pulmonary disease, mesenteric vascular event, need for intensive care, and complications. Çalışmamızdaki sonuçlara göre DNI ≥0.05 ve contamine operasyonlarda preoperatif hasta seçiminde daha dikkatli olmamızı sağlamaktadır. Ayrıca hastalarımıza yoğun bakım kliniğinde organ yetmezlikleri açısından daha dikkatli olunmakta, geniş spekturumlu antibiotikler ivedilikle verilmektedir. Strikingly, no significant correlation was found between CCI and mortality in our study; however, many studies in the literature have revealed that CCI is an independent risk factor impacting mortality [3,13,14]. It is well-known that mortality and morbidity rates are remarkably higher in octogenarian and nonagenarian patients who underwent emergency surgery [15-17]. It has been shown to be an independent risk factor affecting mortality by Roque-Castellanove et al. [17]. In our study, although the fact that the type of operation was emergency was associated with mortality, this parameter could not be demonstrated as an independent risk factor. One of the most important reasons for this may be that the study was limited to patients who underwent colorectal surgery only.

DNI has been shown as a prognostic marker in many previous sepsis models [18-20]. Yet, studies on the usefulness of DNI in terms of predicting postoperative mortality are limited. In a recent study, it has been revealed that DNI is an independent predictive factor in predicting mortality in trauma patients who underwent emergency abdominal surgery [21]. In our study, it was revealed that a DNI of ≥ 0.05 is an independent risk factor that increases mortality 4 times in a significant way.

The significance of inflammatory markers regarding tumor metastasis and progression has long been emphasized [22]. The prognostic significance of albumin levels and LMR levels in colorectal cancers and clear cell type renal cell cancers have been proven [23,24]. Similarly, an increase in mSIS value has been shown to be associated with distant metastasis, local recurrence, peritoneal metastasis, and 5-year survival [25]. It was observed in our study that from the LMR, mSIS, albumin, and lymphocyte levels, which were used as inflammatory markers, only the increase in the mSIS value created a significant difference in mortality, particularly in the group with a score of 1 compared to the group with a score of 0.

STUDY LIMITATIONS

One of the biggest limitations of our study is its retrospective nature. In addition, the findings and our model need to be supported by validation studies in larger series. Octogenarian and nonagenerian patient populations can be homogenized, but they were not divided into groups due to the small number of nonagenarian patients in our study.

CONCLUSION

In the octogenarian and nonagenarian patient population, contamination of the surgical field and DNI in patients undergoing colorectal surgery is two important prognostic factors for mortality. It was demonstrated that the success of the model established in our study for predicting mortality in the elderly patient population was excellent[AUC= 0.876 (95% CI 0.803- 0.948)]. According to the results of our study, it enables us to be more careful while selecting preoperative patients in DNI ≥0.05 and contaminated operations. In addition, our patients are more careful in terms of organ failure in intensive care units, broad spectrum antibiotics are given urgently. We think that it can help clinicians to better serve the increasing geriatric populations by establishing consensus as a result of validation studies.

CONFLICT OF INTEREST: None

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