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RESEARCH

NON-TRADITIONAL MORTALITY PREDICTORS FOR GERIATRIC INTENSIVE CARE UNIT PATIENTS

Abstract

Introduction: There is an increased number of elderly patients in intensive care units. Decreased physiological reserve and frailty makes them more vulnerable to illnesses.

Materials and Method: Geriatric intensive care unit patients (n=1093), who had no history of malignancy and chemotherapy with hospitalised more than 3 days were examined retrospectively. Clinical and laboratory values on admission and at the final, discharge or dead, were recorded. Non traditional mortality predictors neutrophil,to,lymphocyte count (NLR) and mean platelet volume (MPV), and timely changes of these parameters were examined.

Results: Readily measurable and effective markers foreseeing outcome are vital importance. In this retrospective cohort, we showed that neutrophil-to-lymphocyte count (NLR) and mean platelet volume (MPV) are independent mortality predictors in geriatric patients. In addition timely changed NLR and MPV were also independent mortality predictors [0.41 (95% CI 0.30-0.55) p<0.001 and 0.43 (95% CI 0.31-0.59) p<0.001, respectively].

Conclusions: These easily measurable and cheap parameters can be good patient follow-up parameters in geriatrics patients who have increased mortality due to cardiovascular and sepsis related diseases.

Keywords: Geriatrics, Cardiovascular disease, Inflammation, Mortality

ARAŞTIRMA

GERİATRİK YOĞUN BAKIM HASTALARINDA MORTALİTE ÖNGÖRÜCÜLERİ

Öz

Giriş: Yoğun bakımlarda izlenen geriatrik hasta sayısı giderek artmaktadır. Fizyolojik rezervlerin azalması ve kırılganlık, bu hastaları, daha savunmasız hale getirmektedir. Prognozu öngörmede, kolay ölçülebilen ve etkili göstergeler hayati önem taşımaktadır.

Gereç ve Yöntem: Bu çalışmada, yoğun bakım ünitesinde 3 günden fazla yatarak izlenen, herhangi bir malignite ve kemoterapi öyküsü olmayan geriatrik hastaların (n=1093) verileri retrospektif olarak incelenmiştir. Hastaların laboratuvar ve klinik verileri, kliniğe giriş ve sonlanım olmak üzere kaydedildi. Geleneksel olmayan mortalite öngörücüleri; nötrofil-lenfosit oranı (NLO) ve ortalama trombosit hacmi (MPV) ve bu parametrelerin zamansal değişimi incelenmiştir. Retrospektif kohort çalışmamızda, geriatrik hastalarda nötrofil-lenfosit oranı (NLO) ve ortalama trombosit hacminin (MPV) bağımsız mortalite prediktörleri olduğunu saptadık. Aynı zamanda, NLO ve MPV'nin zamanla değişiminin de mortalite göstergesi olduğunu saptadık [sırasıyla 0.41 (% 95CI 0.30-0.55) p<0.001 ve 0.43 (% 95CI 0.31-0.59) p<0.001].

Sonuç: Bu kolay ölçülebilen ve ucuz elde edilebilen göstergeler, kardiyovasküler ve sepsisle ilişkili hastalıklara bağlı mortalite oranı artmış geriatri hastalarında, iyi birer hasta başı takip parametresi olabilirler.

Anahtar sözcükler: Geriatri, Kardiyovasküler hastalık, İnflamasyon, Mortalite

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INTRODUCTION

There is an increased number of critically ill geriatric patients in hospitals who require intensive care unit (ICU) services. During ageing, diseases that involve multiple organ-systems and anatomical and physiological deteriorations occur in combination. Decrease in physiological reserve renders geriatric patients more vulnerable to illnesses and adverse events. In this population, preventive measures can be life-saving (1,2). The ratio of neutrophil-to-lymphocyte counts (NLR) and mean platelet volume (MPV) are easily measurable and novel inflammatory markers that can be used as indicators of systemic inflammation (3-5). In this retrospective study, we sought to investigate non-traditional mortality predictors for geriatric patients with generalised inflammation and cardiovascular complications.

MATERIALS AND METHOD

This retrospective report focussed on ICU patients treated between January 2010 and January 2017. We excluded patients younger than 65 years old and those older than 65 years old who had histories of malignancy, chemotherapy or death during the first 3 days of hospitalisation. We examined patients' laboratory and medical histories, including observational records, demographic characteristics and medications through Patient Database System.

Data of interest included demographics, such as age and sex. In addition, we examined patients' reasons for admission and comorbid clinical illnesses as specified in their medical histories. We recorded non-traditional inflammation markers, MPV, NLR and routine biochemical blood analyses with complete blood count (CBC). Records at baseline (baseline) and at discharge (final) were included in the statistical analyses. Changes in NLR and MPV during the hospital stay were summarised as ΔNLR, final NLR-baseline NLR, ΔMPV and final MPV-baseline MPV.

Posterior-anterior chest radiographs were obtained to regularly measure the cardiothoracic ratio (CTR) especially in hypertensive subjects, patients with histories of congestive heart failure (CHF) and those suffering from hypervolemic states. Analysis was done by the same operation team with the same computer software to ensure measurement accuracy. The CTR was calculated by dividing the maximal horizontal width of the heart by the horizontal diameter of inner borders of the rib cage (6).

Between two groups, alive and deceased patients, numerical variables are compared by Two-Independent Samples Student-t test. Categorical variables are compared by Pearson Chi-Square test. To determine the mortality predictors, univariate logistic regression and multiple logistic regression, by Forward stepwise likelihood ratio method, analysis were performed. Overall significance level is % 5. IBM SPSS ver 23.0 (SPSS Inc., Chicago, IL, USA.) is used for analyses.

RESULTS

We initially identified 3883 ICU patients. After application of exclusion criteria, 1093 geriatric patients were included in the final analyses. The mean age of the 1093 patients was 77.2±7.1 with a mean hospital stay of 7.7±6.0 days. Within our cohort, 40.5% were diabetic, 50.7% were female, 32.3% had congestive heart failure (CHF) and 72.9% had histories of cardiovascular disease (CVD). During the ICU stay, 24% died (n=262) due to various reasons including sepsis-related complications (n=132), cardiovascular complications (n=103), respiratory failure (n=2) and gastrointestinal bleeding (n=2).

The univariate analysis of clinical and laboratory characteristics of the study patients, whose alive or dead, are shown in Table 1a and 1b. Mortality predictors of study population in univariate and multivariate logistic regression analysis are shown in table 3a. When we compared living and deceased subjects, age and gender did not reach a level of statistical significance. However, hemodialysis dependence was significant mortality

predictor (1.64, 95% CI 1.23–2.19 p<0.001) in whole population. CTR also did not reached statistical significance (1.01, 95% CI 0.979–1.024, p=0.907) in whole population. However, N-terminal pro-B-type natriuretic peptide (NTproBNP) emerged as mortality predictor (1.002, 95% CI 1.001–1.004, p=0.006). Patients' NLR and MPV changes, while in the ICU, are represented in Figure 1.

We also performed univariate analysis in a subgroup (>80 years old) of study population (Table 2a and 2b). Mortality predictors that emerged from this analysis are represented in Table 3b. This subgroup included 372 patients, with a mean age of 85.2±3.4 and a mean hospital stay duration of 8.0±7.2 days. During the hospital stay, 26.3% of these patients died (n=98) from various reasons including sepsis-related complications (n=26), cardiovascular complications (n=64), and respiratory failure (n=8). Subgroup NLR and MPV changes, while in the ICU, are shown in Figure 2.

Table 1a. Univariate analysis of mortality predictors of ≥65 years old (Independent Samples t-Test).

		Mean	(±)sd	p
Age	A	77.03	7.00	0.281
	M	77.57	7.25	
CTR(%)	A	57.53	8.412	0.907
	M	57.64	10.21	
Urea (mg/dL)	A	121.99	80.35	**0.007**
	M	137.23	76.02	
Creatinine (mg/dL)	A	3.27	2.27	0.421
	M	3.41	2.21	
Albumin	A	3.36	0.66	**<0.001**
	M	2.91	0.63	
CRP (mg/dL)	A	9.85	9.53	**<0.001**
	M	14.55	10.69	
NTproBNP (x10^3 pg/mL)	A	14.20	17.06	**0.015**
	M	22.78	22.04	
PMNL (x10^3/μL)	A	10.28	7.15	**0.006**
	M	11.96	8.87	
L (x10^3/μL)	A	1.50	3.36	0.474
	M	1.31	4.16	
NLR	A	11.37	11.71	**<0.001**
	M	16.78	17.60	
MPV (fL)	A	10.60	1.36	**0.005**
	M	10.90	1.53	

A; Alive patients, M; Deceased patients, CRP; C-Reactive protein, PMNL; Polymorphous nucleated leucocytes, L; Lymphocyte, NLR; Neutrophil-to-lymphocyte count, MPV; Mean platelet volume.

Table 1b. Univariate analysis of mortality predictors of ≥65 years old (Chi-Square Tests).

			A	M	*p*
Gender	Male	Count	375	128	0.321
		% within mortality	45.1%	48.9%	
	Female	Count	456	134	
		% within mortality	54.9%	51.1%	
CHF	A	Count	572	164	0.095
		% within mortality	68.9%	63.3%	
	M	Count	258	95	
		% within mortality	31.1%	36.7%	
HD	A	Count	585	154	**0.001**
		% within mortality	70.5%	59.2%	
	M	Count	245	106	
		% within mortality	29.5%	40.8%	

A; Alive patients, M; Deceased patients, CHF; History of congestive heart failure, CTR; Cardiothoracic ratio, HD; Haemodialysis,

Table 2a. Univariate analysis of mortality predictors of >80 years old patients (Independent Samples t-Test).

		Mean	sd (±)	p
Age	A	85.12	3.47	0.633
	M	85.31	3.39	
Urea (mg/dL)	A	133.51	86.07	0.449
	M	140.62	76.83	
Creatinine (mg/dL)	A	3.26	2.75	0,999
	M	3.26	2.24	
Albumin	A	3.34	0.61	**<0.001**
	M	2.91	0.64	
CRP (mg/dL)	A	9.59	8.67	**<0.001**
	M	13.95	10.72	
NLR	A	12.39	12.58	**0.020**
	M	17.12	18.50	
MPV (fL)	A	10.52	1.45	**0.040**
	M	10.86	1.31	

A; Alive patients, M; Deceased patients, CRP; C-Reactive protein, NLR; Neutrophil-to-lymphocyte count, MPV; Mean platelet volume.

Table 2b. Univariate analysis of mortality predictors of >80 years old patients (Chi-Square Tests).

			A	M	p
Gender	Male	Count % within mortality	124 45.3%	46 46.9%	0.774
	Female	Count % within mortality	150 54.7%	52 53.1%	
CHF	A	Count % within mortality	184 67.2%	60 61.2%	0.289
	M	Count % within mortality	90 32.8%	38 38.8%	
HD	A	Count % within mortality	205 75.1%	65 66.3%	0.094
	M	Count % within mortality	68 24.9%	33 33.7%	

A; Alive patients, M; Deceased patients, CHF; History of congestive heart failure, CTR; Cardiothoracic ratio, HD; Haemodialysis,

Table 3a. Logistic regression analysis of the mortality predictors (≥65 years old).

	Univariate Logistic Regression			Multiple Logistic Regression		
	OR	95%CI	p	OR	95% CI	p
Age	1.01	0.99-1.03	0.283			
Gender (M)	1.16	0.88-1.54	0.283			
CHF	1.29	0.96-1.73	0.089			
CTR (%)	1.01	0.979-1.024	0.907			
HD	1.64	1.23-2.19	**<0.001**	2.17	1.39-3.39	**<0.001**
Urea mg/dL	1.002	1.001-1.004	**0.008**			
Creatinine mg/dL	1.31	0.09-1.12	0.876			
Albumin g/dL	0.34	0.27-0.44	**<0.001**	0.33	0.24-0.45	**<0.001**
CRP mg/dL	1.04	1.03-1.05	**<0.001**	1.02	1.00-1.04	**0.035**
NTproBNP pg/mL	1.002	1.001-1.004	**0.006**			
PMNL 10^3/μL	1.03	1.01-1.04	**0.003**	1.02	1.08-1.56	**0.034**
L 10^3/μL	0.78	0.64-0.93	0.491			
NLR	1.03	1.02-1.04	**<0.001**	1.02	1.01-1.03	**<0.001**
MPV fL	1.17	1.05-1.30	**0.005**			

CHF; History of congestive heart failure, CTR; Cardiothoracic ratio, HD; Haemodialysis, CRP; C-Reactive protein, PMNL; Polymorphous nucleated leucocytes, L; Lymphocyte, NLR; Neutrophil-to-lymphocyte count, MPV; Mean platelet volume. Significant mortality predictors (p≤0.10) in univariate logistic regression were entered into multiple logistic regression analysis by forward stepwise likelihood ratio method.

Table 3b. Logistic regression analysis of the mortality predictors (>80 years old).

	Univariate Logistic Regression			Multiple Logistic Regression		
	OR	**95% CI**	**p**	**OR**	**95% CI**	**p**
Gender (M)	0.93	0.58-1.48	0.774			
CHF	1.29	0.83-2.08	0.290			
HD	1.53	0.92-2.52	0.09	2.07	1.15-3.72	**0.014**
Urea mg/dL	1.001	0.998-1.004	0.473			
Creatinine mg/dL	1.000	0.915-1.092	0.993			
Albumin g/dL	0.33	0.21-0.50	**<0.001**	0.34	0.20-0.56	**<0.001**
CRP mg/dL	1.048	1.02-1.07	**<0.001**			
NTproBNP pg/mL	1.000	1.000-1.000	0.080			
PMNL 10^3/µL	1.000	1.000-1.000	0.159			
NLR	1.02	1.00-1.03	**0.009**			
MPV fL	1.19	0.99-1.42	0.050			

CHF; History of congestive heart failure, CTR; Cardiothoracic ratio, HD; Haemodialysis, CRP; C-Reactive protein, PMNL; Polymorphous nucleated leucocytes, L; Lymphocyte, NLR; Neutrophil-to-lymphocyte count, MPV; Mean platelet volume. Significant mortality predictors (p≤0.10) in univariate logistic regression analysis were entered into multiple logistic regression analysis by forward stepwise likelihood ratio method.

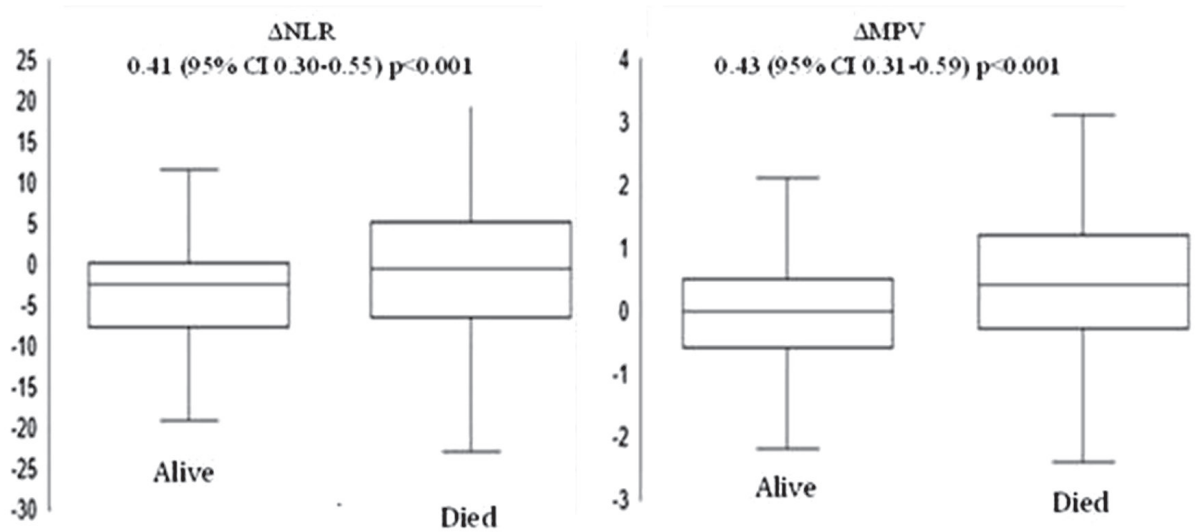

Figure 1. Odds ratios represent the effect of NLR and MPV change during the intersive care unit course in multiple logistic regression analysis. As compared to increments in ΔNLR and ΔMPV, same or decreased values are independent life saving parameters.

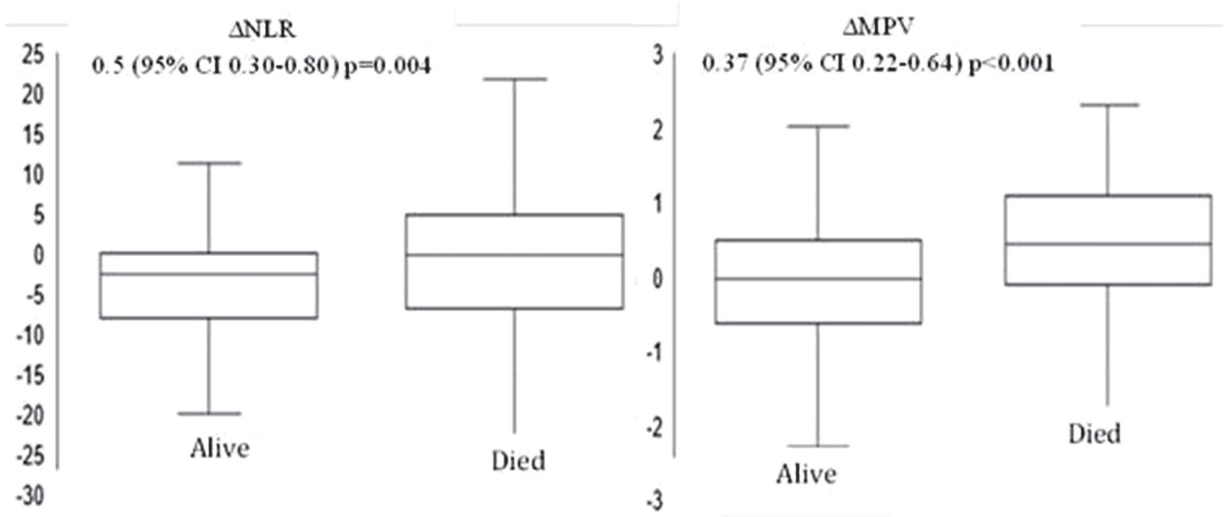

Figure 2. Odds ratios represent the effect of NLR and MPV change during the intersive care unit course in multiple logistic regression analysis in subgroup population (>80 years old). As compared to increments in ΔNLR and ΔMPV, same or decreased values are independent life saving parameters.

DISCUSSION

According to results of logistic regression, to need hemodialyis, serum urea, albumin, CRP, NTproBNP, NLR and MPV values with PMNL count were detected as mortality predictors in whole geriatric population. In the >80 years old population, to need hemodialysis, serum albumin, CRP and NLR values were independent mortality predictors in univariate logistic regression analysis. To avoid multicollinearity, we applied multiple logistic regression analysis by forward stepwise likelihood ratio method. In multiple logistic regression model, to need hemodialysis, serum albumin, CRP and NLR values with PMNL count were detected as independent mortality predictors in whole population while serum albumin level and to need hemodialysis were detected as independent mortality predictors in >80 years old population. In this retrospective study, we determined that change in NLR and MPV during the ICU stay are reliable predictors of mortality in geriatric patients.

As shown in literature, low serum albumin levels, increased CRP, to need haemodialysis and increased serum Urea/Creatinine levels were also associated with higher mortality rates (7-11). Age was the leading cause of mortality in hospitalised patients, especially in ICUs. However, we did not observe a statistically significant correlation between age and mortality in our study. Besides increases in age-related mortality, the frailty frequently seen in geriatric patients, and its accompanying comorbidities, may play a larger role (12,13).

Our study patients demonstrated high rates of cardiovascular disease. CTR and NTpBNP were also examined. CTR is a cheap and readily obtainable parameter in patients suffering from cardiovascular complications. In addition, CTR is strongly associated with patient mortality (14,15). There is an increased data pertaining to NTpBNP levels and the relationship of these levels to cardiovascular and all-cause mortality in geriatric patients (16,17). In addition, generalised inflammation associated with various clinical conditions is strongly associated with higher NTpBNP levels. We did not confirm any relation like previously reported in literature between CTR values and mortality in our study. This

may have resulted from the small sample size of our cohort with posterior-anterior chest radiography reports. We found the NTpBNP level to be a significant mortality predictor in geriatric patients (1.002, 95%CI 1.001–1.004, p=0.006, n=222). Because of the small sample size we did not subject our findings to multiple logistic regression analysis. We believe that in a larger cohort, NTproBNP will emerge as a non-traditional mortality predictor in geriatric patients.

Acute kidney injury and dependence on haemodialysis are independent mortality predictors in ICU patients. In patients with acute kidney injury, especially those in ICUs, serum BUN levels and creatinine weakly correlate with the need for haemodialysis. In the geriatric population there is also an increased risk of sarcopenia associated with poor enteral feeding. This may mask elevated renal function tests. Generalised inflammation and cardiovascular insufficiency are the leading causes of acute kidney injury and the need for haemodialysis (18,19). In our study cohort, sepsis-related complications and cardiovascular complications are major causes of mortality. For that reason, the high mortality rates due to haemodialysis and acute kidney injury were no surprise. Haemodialysis was a significant independent predictor of mortality, both in univariate and multiple logistic regression analyses, whereas serum creatinine and BUN levels were not.

Unfortunately, there is little data concerning the most elderly patients who require ICU services. In our study due to the small number of patients ≥85 years old, we evaluated the mortality predictors in patients who were ≥80 years old instead. Low albumin levels, increased CRP and NLR values were independent mortality predictors. We also found that baseline NLR and MPV change during the ICU stay were independent mortality predictors among the most elderly patients. These were non-traditional risk factors for mortality in this population.

NLR and MPV are recognised non-traditional risk parameters for microvascular complications, generalised inflammation, and patient mortality and morbidity. There is a strong correlation between these non-traditional risk factors and patient mortality not only within the geriatric population but also in asymptomatic individuals (20–22). We found that baseline NLR and NLR changes during the hospital stay were independent mortality predictors in the population of geriatric ICU patients who have higher mortality rates due to sepsis, septic shock, and cardiovascular complications. NLR is a cheap and readily-available test for use in a high-risk population. MPV is another non-traditional risk factor for predicting mortality due to cardiovascular complications and generalised inflammation (23–25). Timely change in MPV may reflect mortality risk in geriatric patients. This was the first study to evaluate the relationship between MPV change and mortality in the most elderly patients.

There are some limitations to our study. First, it was performed in a retrospective fashion. Second, we did not complete comprehensive geriatric assessments on our patients during their hospital stays. Combining these non-traditional risk factors with comprehensive geriatric assessments in a prospectively-designed study will likely yield useful information. We also excluded patients who required ventilator support due to the small number of these patients, and their higher associated mortality rates. This may have affected the statistical results. However, our results contain a wide range of data to explain the complex pathophysiology of geriatric illnesses.

This pilot study sought to link demographic, clinical, and laboratory values with mortality outcomes in a cohort of elderly ICU patients. NLR and MPV have advantages for predicting the outcomes of geriatric patients in ICUs. Geriatric patients are more vulnerable to adverse events during hospital stays due to physiological changes inherent in this population. Early identification of critically ill geriatric patients will increase survival in this high-risk and frail population.

Conflict of interest

The authors declared no potential conflicts of interest with respect to the research and/or publication of this article.

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