Retrospective Analysis of the Effects of Neutrophil / Lymphocyte Ratio on Intraoperative Acidosis Development and Hospitalization Time in Patients Underwent Radical Robotic Prostatectomy

Radikal Robotik Prostatektomi Uygulanan Hastalarda Nötrofil / Lenfosit Oranının İntraoperatif Asidoz Gelişimi ve Hastanede Yatış Süresine Etkisinin Retrospektif İncelenmesi

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ABSTRACT

Objective: This study aimed the predictive value of the neutrophil to lymphocyte ratio (NLR) for intraoperative acidosis and postoperative lenght of hospital stay in patients undergoing robotic assisted radical prostatectomy procedure.

Material and Methods: Patients with locally advanced prostate cancer undergoing elective robotic assisted radical prostatectomy procedure were included in the study. Inclusion criteria was being ASA I-II, and receiving sugammadex for recovery of neuromuscular block. Complete blood counts and blood-gas analyses were performed perioperatively. The neutrophil to lymphocyte ratio was calculated by dividing neutrophil counts to lymphocyte counts. Acidosis was defines as pH levels below 7.35.

Results: A total of forty-six patients (mean age 64.06±6.4 years) were included. Blood gas changes were detected in twenty three patients. Eighteen patients in the study population had combined acidosis. Twelve patients had acidosis according to pH levels, seven patients had $PaCO_2 \geq 45$ mmHg, and seven patients had Lactate ≥ 1.6 mmol/L. Median hospital stay was five days (0-10 days). NLR levels were not found to be significantly different between the groups, and were not correlated with patient age (p=0.907) or duration of hospital stay (p=0.654).

Conclusion: NLR was not found to be a marker for acidosis or predictive of prolonged hospital stay in patients undergoing the RARP procedure.

Key Words: Neutrophil lymphocyte ratio, Robotic assisted radical prostatectomy, Acidosis

ÖZ

Amaç: Bu çalışmada, robotik yardımlı radikal prostatektomi prosedürü uygulanan hastalarda, nötrofilin lenfosit oranının (NLR) intraoperatif asidoz ve postoperatif hastanede kalış süresi için öngörü değeri araştırıldı.

Gereç ve Yöntemler: Lokal ileri prostat kanseri olan ve elektif robotik destekli radikal prostatektomi prosedürü uygulanan hastalar çalışmaya dahil edildi. Hastalar ASA I-II sınıfında ve nöromusküler bloğu revers etmek için sugammadeks kullanıldı. Perioperatif tam kan sayımı ve kan gazı analizi yapıldı. Nötrofil lenfosit oranı, nötrofil sayılarının lenfosit sayılarına bölünmesiyle hesaplandı. Asidoz, 7.35'in altında pH seviyesi olarak tanımlandı.

Bulgular: Toplam kırk altı hasta (ortalama yaş 64,06 ± 6,4 yıl) dahil edildi. Yirmi üç hastada kan gazı değişikliği tespit edildi. Çalışma grubunda on sekiz hastada kombine asidoz saptandı. On iki hastada pH seviyesine göre asidoz, yedi hastada $PaCO_2 \geq 45$ mmHg, yedi hastada Laktat $\geq 1,6$ mmol/L saptandı. Ortalama hastanede kalış süresi beş gündü (0-10 gün). NLR düzeyleri asidoz grupları arasında anlamlı düzeyde farklı bulunmadı ve hasta yaşı (p = 0,907) ve hastanede yatış süresi ile ilişkili değildi (p = 0,654).

Sonuç: NLR, RARP prosedürü uygulanan hastalarda asidoz veya uzun süreli hastanede kalış tahmininde belirteç değildir.

Anahtar Sözcükler: Nötrofil Lenfosit oranı, Robotik yardımlı asiste radikal prostatektomi, Asidoz

INTRODUCTION

Prostate cancer is still one of the most frequent causes of cancer deaths among males in the world (1). The technological advances in the previous decade have shifted the practice pattern of radical prostatectomies from the retropubic approach to robotic-assisted radical prostatectomies (RARP). Currently, RARP's are the predominant and most widely used surgical procedure for prostate cancer surgeries. This approach has significant benefits including perioperative outcomes such as decreased blood loss and need for transfusions, decreased length of hospital stays, and increased quality of life (2). Nevertheless, there are also some drawbacks like longer operation times, deep Trendelenburg position, and high intraabdominal pressure (3). Moreover, increased intraabdominal pressure due to CO_2 decreases the lung volumes, and results in hypercarbia and decreased blood pH levels (4). Some studies suggested that decreased intraabdominal pressures during laparoscopic RARP surgeries are possible when deep neuromuscular block (NMB) is used for the anesthesia during the surgical procedure. The utilization of Sugammadex makes safe application of deep NMB possible, which improves the surgical working conditions during laparoscopic surgeries (5-7).

The neutrophil to lymphocyte ratio (NLR) is being used as a rapidly accessible, cheap, non-invasive and valuable marker for the assessment of systemic inflammation in general practice (8). The calculation of NLR from routine complete blood count is being used as a prognostic factor in many cancers (9). Prostate cancer is one of those cancers, but only with limited and mostly controversial data (10). However, there is no data regarding its role in RARP cases. Particularly when the increased risk of intraoperative metabolic changes during RARP are taken into consideration, predicting acidotic states using a reliable biomarker will provide both better intraoperative and postoperative management of the patients. This study aimed to evaluate the effects of NLR on intraoperative acidosis and postoperative hospital stay in RARP patients.

MATERIAL and METHOD

This retrospective study was conducted at the Department of Antalya Training and Research Hospital, between 2017-2018. The Local Ethics Committee of Antalya Training and Research Hospital approved the study (2018-128).

Data from a total of 46 patients were included in the study. The study population included 46 patients between 44 and 75 years of age, who had undergone an elective RARP operation, and received sugammadex for recovery of neuromuscular block after completion of the surgical procedure. Patients who were transferred to the intensive care unit postoperatively were excluded from the study.

Patients were graded as ASA I or II according to the American Society of Anesthesiologists criteria. The selected patients had no electrolyte impairment, no blood or plasma transfusions due to anemia during the operation, base is not open or there was no surplus.

After obtaining the anesthesia, monitoring was ensured with electrocardiogram, intra-arterial and central jugular catheter pressure reading, pulse oximetry, capnography, neuromuscular blockade, and urine output. In the induction of anesthesia, intravenous propofol (3 mg/kg), rocuronium (0.6 mg/kg), remifentanil (1µg/kg) were administered to the patients. For maintaining anesthesia, remifentanil (0.5 µg/kg/min) and 50% medical air and oxygen with desflurane 4-6 % v (≈ 1 MAC) as inhalation agent were used. Neutrophil/Lymphocyte (NLR) ratios in preoperative and postoperative hemogram values in the first 24 hours were compared.

Additionally, arterial blood PH values were evaluated during the operation for assessment of intraoperative acidosis.

The patients who developed respiratory or metabolic acidosis in the blood at the beginning of the operation and in the 2nd hour were included in the study. The pH levels below 7.35 were regarded as acidosis in the analyses.

Statistical Analysis

Descriptive analyses were presented with mean, standard deviation, median, minimum and maximum for numerical variables. Comparisons between 2 independent and dependent groups were done with Mann-Whitney U test and Wilcoxon Signed Rank test, respectively. The correlations between numerical variables were analyzed with Spearman's rho test. A p value lower than 0.05 was considered statistically significant. PASW 18.0 for Windows software was used for the analyses in this study.

RESULTS

A total of 46 patients with a mean age of 64.06±6.4 were included in the study. The mean duration of anesthesia was 197.2 min and the mean duration of surgery was 157.1 minutes. The liquid requirement of patients was met with isolyte-s input and the urine output was observed with a urethral catheter during the operation (Table I).

The mean NLR was 2.05±0.65 (range, 0.72 to 3.39) among the patients. The median hospital stay was 5 days (0-10 days). The pH levels ranged from 7.17 to 7.49, $PaCO_2$ levels ranged from 30.6 to 70.3 mmHg, and lactate levels ranged from 0.4 to 3.6 mmol/L. The biochemical analyses are summarized in Table II.

In 23 out of 46 patients, intraoperative acidosis was detected and 18 patients had combined acidosis. When the patients were grouped as those with and without acidosis according

to pH levels, 12 patients were found to have acidosis. $PaCO_2 \geq 45$ mmHg was present in 7 patients, and Lactate $\geq$ 1.6 mmol/L in 7 others. The comparison of NLR between groups is presented in Table III. Accordingly, NLR was not found to be significantly different between the groups.

The comparison analysis between NLR and the patient age (p=0.907) and duration of hospital stay (p=0.654) revealed that NLR was not correlated with any of these parameters (Table IV).

DISCUSSION

In the current study, we have evaluated whether NLR can be utilized as a marker for intraoperative acidosis or postoperative hospital stay in patients who had undergone RARP surgery. According to our results, the NLR levels were not significantly different between patients with and without acidosis. This similarity has not changed based on the definition of acidosis or combined acidotic state, and likewise high levels of lactate and carbondioxyde. Moreover, NLR was not found to be significantly associated with the duration of hospital stay in the postoperative period.

Several changes in blood composition may be seen during these procedures. The current evidence in the literature suggests that systemic alterations in leukocytes, involving leukocytosis, neutrophilia and lymphopenia, can be observed in response to surgery (11). A previous study evaluating the effect of anesthetic techniques on the neutrophil to lymphocyte ratio after laparoscopy assisted vaginal hysterectomy revealed that significantly lower NLR can be observed 2 hours after surgery in patients that received propofol and remifentanil compared to the patients that received sevoflurane anesthesia (11). The mechanisms underlying these changes include hormonal changes, cytokine compositions, acute-phase reactants, inhibition of apoptosis of neutrophils, and apoptosis of lymphocytes (12). Neutrophils play a role in the inflammatory response by releasing lysosomal enzymes and free oxygen radicals when activated by chemotaxis, immunocomplexes or phagocytosis (13). These changes of immune mediators in surgical traumas are also associated with the anesthetic technique, and intravenous administration of anesthetics cause lower levels of these mediators than inhalation anesthesia (14).

Table I: Demographic and operational data.

Parameter	Mean value ± SD
Mean Age (years)	64.06 ± 6.4
Anesthesia Time (min)	197.2 ± 17.4
Operating Time (min)	157.1 ± 11.3
Isolyte-S input (ml)	1781.6 ± 132.8
Urine output (ml)	397.1 ± 47.6
Bleeding (ml)	238.2 ± 31.4

Table II: Biochemical variables of the patients.

	Mean ± SD	Median (min-max)
Hospital stay (days)	4.61±2.32	5 (0-10)
NLR	2.05±0.65	2.04 (0.72-3.39)
pH	7.35±0.07	7.34 (7.17-7.49)
$PaCO_2$	42.49±9.04	40.4 (30.6-70.3)
Lactate	1.46±0.72	1.3 (0.4-3.6)

Table IV: Relationship of NLR with age and hospital stay.

		NLR	
	N	rho	p
Age	23	-0.020	0.907
Duration of hospital stay	23	-0.068	0.654

* Spearman's rho.

Table III: NLR values in acidosis groups.

			Neutrophil/Lymphocyte		p*
		N	Mean ± SD	Median (min-max)	
Acidosis (Combined)	Present	18	1.98±0.61	2.05 (1.03-3.06)	0.280
	None	5	2.23±0.35	2.38 (1.74-2.6)	
Acidosis (pH <7.35)	Present	12	1.97±0.64	2.07 (1.03-3.06)	0.498
	None	11	2.11±0.49	2.1 (1.05-2.87)	
$PaCO_2 \geq 45$ mmHg	Present	7	1.91±0.71	1.96 (1.03-3.06)	0.548
	None	16	2.09±0.51	2.14 (1.05-2.87)	
Lactate $\geq$1.6 mmol/L	Present	7	1.9±0.61	2 (1.05-2.87)	0.403
	None	16	2.1±0.55	2.22 (1.03-3.06)	

* Mann Whitney U.

Despite the possible changes in blood composition during surgery, and increased risk of acidosis in RARP procedures, we did not observe a significant difference regarding NLR in our study population. This may be related with the timing of the biochemical analyses of complete blood counts to compute NLR, and arterial blood gas analyses during the surgery. NLR increases might not be observed in the early periods of surgery. This lag time between surgery and NLR changes are also consistent with the above mentioned underlying mechanisms of blood composition changes in response to surgery. Preoperative NLO may be a predictor factor for the amount of bleeding in prostatectomy operations and therefore in determining the duration of operation (15). Since we conducted biochemical analyses perioperatively in our study, the changes in NLR may not have occurred yet.

CONCLUSION

In this study, we evaluated the effects of NLR on different acidosis groups. The NLR value may indicate inflammation in surgery, but according to the results of this study, NLR was not found to be an important indicator of acidosis. It is also not predictive of prolonged hospital stay in patients that have undergone the RARP procedure. More research about its molecular and biochemical effects should be carried out.

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