


**Original Article**

# Increase of Neutrophil-Lymphocyte Ratio (NLR) during Urologic Laparoscopic Surgery with Intraoperative Complications in Dr. Sardjito Hospital

 Hidayu Permata Hardi<sup>\*</sup>, Ahmad Zulfan Hendri, Sakti R. Brodjonegoro

Division of Urology, Department of Surgery, Faculty of Medicine, Public Health and Nursing, Universitas Gadjah Mada/Dr. Sardjito Hospital, Yogyakarta, Indonesia

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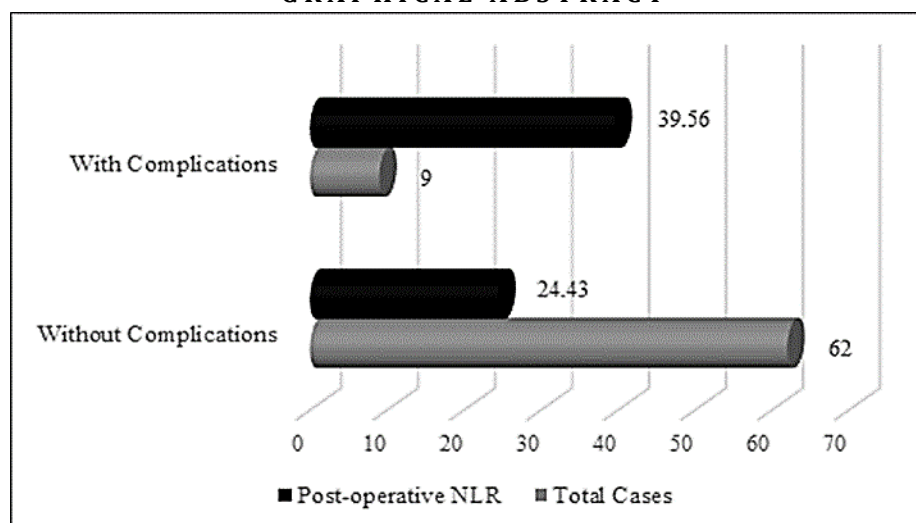
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**ABSTRACT**

Laparoscopy is a minimally invasive surgery using advanced technology, so the resulting surgical wound is smaller than conventional surgery. Laparoscopy, especially in the field of urology, is known to cause complications in patients. Intraoperative complications will cause physiological stress that causes an inflammatory response in the body. Neutrophils are one of the most important cells in producing the inflammatory response in the acute phase. Meanwhile, lymphocytes are the main cellular components of the immune system that are mediated by T cells and humoral cells. This study was conducted retrospectively and reviewed the patient's medical record data from intraoperative to outpatient admission. The sample included 71 patients who underwent laparoscopic urology in 2017-2019. There was a difference in NLR values between pre surgery and post-surgery ( $p < 0.05$ ). It is known that the postoperative NLR value is higher than preoperative. In addition, it was known that there were differences in postoperative NLR values between patients who did not experience complications and those who had complications ( $p < 0.05$ ). Where there is an increase in the postoperative NLR value in patients with complications, intraoperative complications lead to increased NLR. The greater the physiological stress experienced, the higher the NLR value. Increased NLR reflects poor output.

**GRAPHICAL ABSTRACT**

<sup>\*</sup> Corresponding author: Hidayu Permata Hardi

 ✉ E-mail: [hidayu.p.h@mail.ugm.ac.id](mailto:hidayu.p.h@mail.ugm.ac.id)

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## Introduction

Laparoscopy is a diagnostic and therapeutic surgical tool used to view intra-abdominal organs. Surgery using laparoscopy does have its advantages, but it should be noted that just like any other surgical intervention, laparoscopy also carries a risk of complications [1-3]. Significant complications from laparoscopy are mainly vascular, visceral, intestinal, and urological injuries. Therefore, careful identification and prompt management of complications is very important since the delay can cause morbidity and mortality in patients [4-6].

Most of the complications of laparoscopy that arise are associated with the first entry of the trocar into the abdominal cavity. Laparoscopic control of the trocar as it penetrates any layer of the anterior abdominal wall is essential. Previous studies have suggested that initial trocar placement is the most dangerous aspect of using laparoscopy as a minimally invasive surgery. The consequences of errors during laparoscopic surgery are unpredictable and can vary from no side effects to fatal events. It is known that the laparoscopic surgical procedure also causes various complications to the patient. Complications that occur intraoperatively will have an impact on the physical condition after surgery [7-10].

When the body experiences high physiological stress due to these complications, an imbalance of the immune response forms between the pro-inflammatory and anti-inflammatory systems. Lymphocytes, macrophages, neutrophils, mast cells, and many other cells release cytokines that play an important role in pro-inflammatory and anti-inflammatory responses. Neutrophil Lymphocyte Ratio (NLR) is a simple parameter by assessing the neutrophil and lymphocyte ratio to determine the inflammatory condition in an individual. NLR is the result of divided, Relative Neutrophils (%) with Relative Lymphocytes (%). It is known that NLR reflects current physiological stress conditions. Interpretation of NLR is divided into 3 categories based on context, namely normal (NLR 1-3), mild stress (NLR 6-9), and severe stress (NLR > 9) [11-13].

## Material and methods

This study was conducted retrospectively and reviewed the patient's medical record data from intraoperative to outpatient admission. In this study, the results of the study were divided into 2 parts, namely primary results and secondary results. The primary outcome was the difference in postoperative NLR values in patients with intraoperative complications and without intraoperative complications. While the secondary results were gender, age, total length of stay after surgery, intraoperative bleeding, duration of surgery, and differences in preoperative and postoperative NLR values. Intraoperative complications are classified into 2 groups based on the Satava hierarchical system, namely error I where there are no dangerous consequences or errors that can be ignored and error II where errors must be immediately identified and corrected (serious complications).<sup>5</sup> The samples taken in this study were urology patients who were undergoing laparoscopic procedures at the Dr. Sardjito Hospital in the period January 2017 - December 2019. The sample inclusion criteria in this study were urology patients who underwent laparoscopy with pre-albumin, hemoglobin, electrolyte counts, and surgery within normal limits according to the reference value at Dr. Sardjito Hospital. Meanwhile, the exclusion criteria were patients who had previous surgery, patients with other comorbid diseases, and patients who did not undergo postoperative laboratory tests.

In this study, the analysis was carried out using statistical software SPSS ver. 22. To see whether there was a difference between the preoperative NLR and the postoperative NLR, the Wilcoxon test was computed and the hypothesis was accepted if the p value was < 0.05. Meanwhile, to determine whether there was a difference in the NLR value associated with intraoperative complications, the Mann Whitney test was calculated and the hypothesis was accepted if the p value was <0.05.

## Result and Dissection

In this study, it is known that the characteristics of the respondents are divided into gender, age,

length of stay after surgery, intraoperative bleeding, and duration of surgery, based on the gender of the respondents. Other characteristics

of the respondents were also considered, as shown in the following Table 1.

**Table 1:** Characteristics of the research sample

Average	Total Cases (71 cases)	Complicated Case (9 cases)
Gander		
• Man	39	3
• Woman	32	6
Age (year)	43	50
Postoperative length of stay (day)	7	16
Bleeding during surgery (ml)	676	2167
Duration of surgery (hour)	4	6

The general characteristics of patients from a total of 71 cases and 9 cases with complications are shown in Table 1. Various measures were taken to manage the complications that arose, so that there was no further morbidity and mortality. It should be noted that the incidence of complications in this study was about 11%. Gender in total cases was known to be higher in men than women, whereas in cases with complications the incidence of women was higher than that of men. On the other hand, the results of this study indicated that complications were evident in older patients. In terms of length of stay, in cases with complications, it took 2 times longer than the time required in total cases. In addition, the volume of bleeding during surgery

and the duration of surgery were markedly increased in patients with complications.

Postoperative patients experience high stress, so the higher the stress on the body, the higher the NLR. In this study, to determine the difference in preoperative and postoperative NLR values, the Wilcoxon test was used because the data were paired and not normally distributed. The Wilcoxon test results showed  $p < 0.05$ , so it can be concluded that there was a difference in the NLR value between pre operation and post operation. Postoperative NLR value was higher (13.61) than preoperative (4.54), as displayed in Table 2.

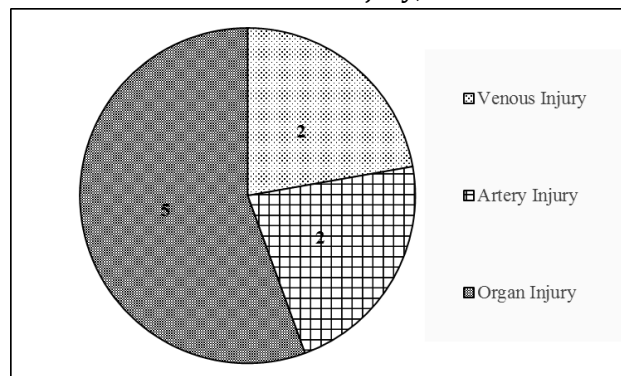
**Table 2:** The difference between preoperative and postoperative NLR

	NLR Pre-operative	NLR Post-operative
Maximum	25.78	69
Minimum	0.32	1.43
Average	4.54	13.61

Differences in NLR Associated with Intraoperative Complications

In this study, it was found that there were nine complications that occurred during the operation. The types of complications that occurred are shown in Figure 1, which consists of vascular injury and organ injury. The incidence of vascular

injury and organ injury is almost the same, namely in this study 4 vascular injuries were found including inferior vena cava injury (2 cases), iliac artery injury (1 case), and abdominal aortic injury (1 case), and organ injury (5 cases) included 1 case of pleural injury, 1 case of ileal injury, and 3 cases of rectal injury

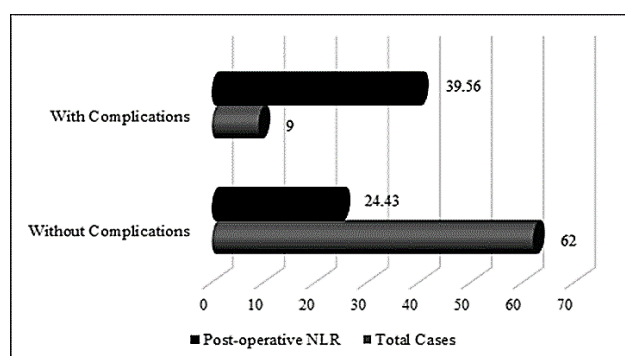


**Figure 1:** Type of complications in laparoscopic urology

**Table 3:** Complications due to various urological laparoscopic procedures

Laparoscopic Urology	Without Complications	With Complications
Unroofing kidney cyst	4	0
Cryptorchidismus (diagnostic)	3	0
Insertion of the catheter	3	0
Adrenalectomy	4	0
Ureterolithotomy	3	0
Nephroureterectomy	2	1
Pyeloplasty	2	0
Nephrectomy	10	1
Neoimplantation of the ureter	3	0
Retroperitoneal tumor	1	0
Nephrectomy Partial	3	0
Nephrectomy (living donor)	13	1
Cystectomy Partial	2	0
Cystectomy Radical	5	5
Nephrectomy Radical (>T1)	3	1
Prostatectomy Radical	1	0
Total	62	9 (14.1%)

Table 3 describes the various urological laparoscopic procedures that can cause complications. Of the 62 cases, in nine cases (13.41%) complications occurred.



**Figure 2:** NLR values related to intraoperative complications

In Figure 2, to determine the difference in postoperative NLR values between patients who did not experience complications and those who experienced complications, the Mann Whitney test was used because the data were not paired and not normally distributed. The results of the Mann Whitney test showed  $p < 0.05$ , so it can be concluded that there was a difference in the NLR value between patients who did not experience complications (NLR = 24.43) and those who experienced complications (NLR = 39.56). Because there were significant differences, it can be seen that there is an effect of the incidence of intraoperative complications on increasing the postoperative NLR value.

This study showed that the postoperative NLR was higher than the preoperative NLR. This shows that surgery causes great physiological stress on the body. However, when there were intraoperative complications, it was known that the postoperative NLR of patients who had complications was higher than the postoperative NLR of patients who did not experience complications. NLR has been shown to be a simple and effective method for assessing systemic inflammation in individuals. Several studies<sup>6,7</sup> have been conducted to examine the relationship between NLR and outcomes, all of which found that increasing the NLR value resulted in poorer outcomes.

Neutrophils are one of the most important cells in producing the inflammatory response in the acute phase and the development of multiple organ dysfunction syndrome (MODS). Meanwhile, lymphocytes are the main cellular components of the T-cell-mediated and humoral immune system. In a state of injury and blood loss, the ability of T and B lymphocytes will be negatively affected. This cell-related abnormality in immunity was associated with decreased numbers of CD4 helper and natural killer (NK) T helper cells. A decrease in the total lymphocyte count after injury has been described as a potential contributor to severe sepsis and MODS. Patients who fail to normalize lymphopenia have increased mortality. Based on these results, in the inflammatory response secondary to trauma, the

number of neutrophils tends to increase and the number of lymphocytes tends to decrease. As a result, an increased NLR and this higher NLR could be associated with a worse outcome [14-17].

The inflammatory response associated with surgery can be considered surgical inflammation, which is an inflammatory process caused by surgery that consists of a series of phases. In response to injury, cells can develop defensive (inflammatory) mechanisms and progress to dangerous (necrotic) conditions. The occurrence of bleeding and the presence of intraoperative organ injury also causes an inflammatory reaction. As soon as blood vessel damage and bleeding occur, leukocytes begin to collect along the endothelium. HMGB1 secretion and cytokine production are initiated. Proinflammatory cytokines are produced after bleeding and high levels of IL-6 correlate with mortality in hemorrhagic shock [9-11, 17-20].

The local inflammatory response always occurs in association with tissue trauma. The injured cells will release HMGB1 thereby attracting neutrophils and macrophages to the injury site, increasing leakage of blood vessels, and reducing perfusion pressure in the microcirculation. Monocytes and endothelium in the area of injury release the most important proinflammatory cytokines being IL-1- $\beta$ , TNF- $\alpha$ , IL-6, IL-8 and IFN- $\gamma$ . TNF- and IL-1 are the first cytokines released following trauma. TNF- and IL-1 are both short-lived cytokines that have a similar impact on the immune system. TNF- and IL-1 have half-lives of 20 and 6 minutes, respectively. TNF- and IL-1 stimulate many important immune cells and can cause the release of proinflammatory cytokines like IL-6 and IL-8, as well as the anti-inflammatory cytokine IL-10. IL-1 can also cause a febrile response. Within one hour of trauma, IL-6 is detected in plasma. C-reactive protein (CRP) and procalcitonin are released by IL-6, which stimulates hepatic acute-phase protein synthesis. The amount of IL-6 secreted correlates with the severity of the trauma, the length of surgery, and the risk of postoperative complications [12-14, 21-26].

## Conclusion

Intraoperative complications are conditions that can increase physiological stress in the individual's body. Physiological stress is related to the NLR value; the higher the NLR value, the more severe the damage. An increase in the NLR value can occur due to changes, where the number of neutrophils increases, while the number of lymphocytes decreases. A worse output can be seen from a high NLR value.

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## Authors' contributions

All authors contributed toward data analysis, drafting and revising the paper and agreed to be responsible for all the aspects of this work.

## Conflict of Interest

We have no conflicts of interest to disclose.

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