RESEARCH ARTICLE / *Araştırma Makalesi*

Regional Anesthesia vs General Anesthesia In Patients with Covid-19: The Effect on Critical Care Admission, Mortality Rates and Pulmonary Complications

COVID-19 Hastalarında Rejyonal Anestezi ve Genel Anestezinin Yoğun Bakım Başvurusu, Mortalite Oranları ve Pulmoner Komplikasyonlar Üzerine Etkisi

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Abstract

Introduction	The appropriate anesthesia method in patients requiring surgical treatment with confirmed or suspected new coronavirus disease (COVID-19) is unclear. This study aimed to compare regional anesthesia (RA) with general anesthesia (GA) in patients with COVID-19 infection in terms of admission to intensive care unit (ICU), rate of pulmonary complications and mortality.
Materials and Methods	Reviewed medical records between March 2020 and December 2021 added patients with COVID-19 that operated under RA or GA in the study. Patient data were obtained from the patient database program of our hospital. The patients were assigned into two groups: 1. patients operated under RA and 2. patients operated under GA. Demographic data, surgery types, anesthesia types, intensive care unit (ICU) admission rates, pulmonary, renal and hepatic labratory data, perioperative mortality rates, hemogram values were recorded. Primary outcomes were admission rates to the ICU, acute pulmonary, renal and hepatic complications and perioperative mortality rates.
Results	Included 123 patients in the study. While 97 (78.9 %) patients under RA and 26 (21.1 %) patients under GA were operated, the number of patients who underwent RA was statistically significantly higher (p<0.001). Although pulmonary complications were observed in 6 (6.2 %) patients in the RA group and in 2 (7.7 %) patients in the GA group no statistically significant difference was found (p=0.535). While the rate of admission to the ICU was 8.2 % in the RA group and 11.5 % in the GA group, no statistically significant difference was observed (p=0.422). Although perioperative mortality rates were lower in the RA group, no statistically significant difference was found (p=0.535).
Conclusion	Pulmonary complications, ICU admission, and perioperative mortality rates were lower in COVID-19 patients operated under RA however the differences were not statistically significant.
Keywords	Regional anesthesia, General anesthesia, COVID-19, ICU admission, Pulmonary complications

Öz

Amaç	*Yeni tip koronavirüs hastalığı (COVID-19) olan ve cerrahi tedavi gerektiren hastalarda hangi anestezi yönteminin uygulanacağı belirsizliğini korumaktadır. Bu çalışmada COVID-19 enfeksiyonu olan hastalarda rejyonal anestezi (RA) ve genel anestezi (GA)'nın pulmoner komplikasyon oranı, yoğun bakım ünitesine (YBÜ) kabul oranı ve mortalite açısından karşılaştırması amaçlandı.*
Yöntem ve Gereçler	*Çalışmaya Mart 2020 ile Aralık 2021 arasında RA ve GA altında ameliyat edilen COVID-19 hastaları dahil edildi. Veriler hastane bilgi sisteminden elde edilmiştir. Hastalar iki gruba ayrıldı: 1. Grup RA ile ameliyat edilen hastalar ve 2. grup GA ile ameliyat edilen hastalar. Demografik veriler, cerrahi tipleri, anestezi tipi, yoğun bakım ünitesine (YBÜ) kabul oranları, pulmoner, renal ve hepatik labratuar verileri, perioperatif mortalite oranları, hemogram değerleri kaydedildi. Birincil sonuçlarımız YBÜ kabul oranları, akut pulmoner, renal ve hepatik komplikasyonlar ve perioperatif mortalite oranlarıydı.*
Bulgular	*Çalışmaya 123 hasta dahil edildi. RA altında 97 (% 78.9) hasta, GA altında ise 26 (% 21.1) hasta opere edilirken RA uygulanan hasta sayısı istatistiksel olarak anlamlı derecede yüksekti (p<0.001). RA grubunda 6 (%6.2) hastada ve GA grubunda 2 (% 7.7) hastada pulmoner komplikasyonlar görülmesine rağmen istatistiksel anlamlı bir fark bulunamadı (p=0.535). YBÜ'ye kabul oranı RA grubunda % 8.2, GA grubunda % 11,5 iken istatiksel olarak anlamlı fark görülmedi (p=0.422). Perioperatif mortalite oranları RA grubunda daha düşük olmasına rağmen istatistiksel anlamlı fark bulunamadı (p=0.535).*
Sonuç	*Rejyonel anestezi ile ameliyat edilen COVID-19 hastalarında pulmoner komplikasyonlar, yoğun bakım yatışı ve perioperatif mortalite oranları daha düşük olmasına rağmen istatistiksel olarak anlamlı bir fark tespit edilememiştir.*

INTRODUCTION

Anesthesia management in patients requiring surgical treatment with confirmed or suspected new coronavirus disease (COVID-19) is challenging for all anesthetists. The safety of both patients and healthcare professionals should be considered a major issue when surgical procedures are performed for those patients. Patients undergoing surgery are a vulnerable group being at risk of exposure to the COVID-19 virus in the hospital. Besides, patients with confirmed or suspected COVID-19 disease may be particularly susceptible to pulmonary, renal and hepatic complications due to surgery, mechanical ventilation, and immunosuppressive responses.[1]

Elective surgery of patients with respiratory tract infections, including COVID-19 disease, should be postponed and rescheduled after the proper treatment of the infection.[2] During the SARS-CoV-2 pandemic, guidelines on surgery and anesthesia management have been published suggesting modalities of anesthesia management; however, these mainly consist of expert opinions.[3,4] In a single-center retrospective observational study, they reported that 49 patients with COVID-19 disease who underwent cesarean section (C/S) operation or orthopedic surgery under spinal anesthesia did not develop severe pneumonia and no mortality was reported.[5] A meta-analysis in 2020 investigated the factors affecting the death of operated patients with confirmed COVID-19 infection and reported that no death was seen in patients operated under regional anesthesia (RA).[6] However, the appropriate anesthesia method in patients requiring surgical treatment with confirmed or suspected COVID-19 is unclear, and data is needed from studies comparing RA with general anesthesia (GA).

Based on these studies, we hypothesized that the mortality rate, admission to intensive care unit (ICU), and pulmonary complications would be lower in patients operated under RA than patients operated under GA. The primary aim of this study was to assess RA and GA methods in surgically operated patients with COVID-19 infection in terms of pulmonary, renal and hepatic complications, admission to ICU, and mortality rates.

MATERIAL and METHODS

This study was planned as a retrospective comparative cohort study and was carried out in Sakarya Research and Training Hospital, Department of Anesthesiology and Reanimation. Study approval was obtained from Sakarya Universty Faculty of Medicine Local Ethics Committee (Approval number: 050.01.04.113329-67). Patient data were obtained from the patient database program of our hospital (Karmed, Kardelen Software).

We reviewed the records of the patients who operated under RA or GA between March 2020 and December 2021. Patients diagnosed with COVID-19 (confirmed by nasopharyngeal-oropharyngeal swab RT-PCR test) within seven days before the operation; were included in the study. Patients hospitalized in the intensive care unit in the preoperative period and patients who met the criteria for hospitalization in the intensive care unit were excluded from the study. The patients with respiratory, renal or hepatic symptoms before surgery were also excluded from the study.

The patients were assigned into two groups: patients operated under RA group and patients operated under GA group. The indications for surgery were classified as C/S operation, general surgery operations (colostomy, appendectomy, cholecystectomy) and other surgery operations (cardiovascular, urology, neurosurgery, orthopedics). The decision on the anesthesia method was based on the recommendations of the Regional Anesthesia and Pain Medicine (ASRA) and the European Society of Regional Anesthesia and Pain Therapy (ESRA) in patients with COVID-19.4 These recommendations are consistent with our institutional proposal of adopting RA as the primary anesthesia method in patients with COVID-19. In our clinic, spinal anesthesia in lower extremity surgeries and

(C/S), brachial plexus block in upper extremity surgeries are the anesthesia methods used routinely during the COVID-19 process.

The primary outcomes were acute pulmonary complications, admission rates to the ICU, and perioperative mortality. Secondary outcomes were perioperative hepatic and renal disorders. New onset of postoperative dyspnea, tachypnea, decrease in oxyhemoglobin saturation, need for additional oxygen supplementation and signs of pneumonia were considered pulmonary complications. Hepatic disorder was defined as an increase in liver enzymes. Renal disorder was defined as deterioration in renal laboratory parameters and the need for hemodialysis.

The criteria for admitting patients to the intensive care unit after surgery were as follows: Patients with respiratory distress (>30 breaths/min), oxygen saturation < 90 at rest under nasal oxygenation with 5–6 liters/min, arterial partial pressure of oxygen (PaO2) / fraction of inspired oxygen (FiO2) < 300 mmHg In addition to these, symptoms of shortness of breath, fever and/or cough, and significant comorbidities (chronic kidney disease, congestive heart failure, chronic obstructive pulmonary disease, and diabetes) which may significantly worsen with concomitant COVID-19 infection. Mechanical ventilation indications are the presence of hypercapnic acidosis and hypoxemia despite administration of high flow nasal oxygen.

Statistical analysis

Statistical analyzes were performed using the IBM SPSS Statistics 22 program. Categorical variables were expressed as numbers and percentages, while continuous variables were expressed as mean ± standard deviation or median (interquartile range). Chi-square and Fisher's exact tests were used for categorical variables. The distribution of numerical variables was evaluated by Kolmogorov Smirnov. Data of independent groups with normal distribution were compared with Student's t-test, and data without normal distribution were compared with the Mann-Whitney-U test. $p < 0.05$ was considered significant.

RESULTS

Included 128 patients in the study who were found eligible. Five patients were excluded from the study; three were indicated for intensive care hospitalization preoperatively; meanwhile, two patients were in ICU before the operation.

Data of 123 patients were analyzed. The mean age of the patients operated under RA (30.53 ± 10.60) was found statistical significantly lower than the patients operated under GA (44.72 ± 26.51) ($p<0.001$). Female patients number were statistical significantly high in the RA group ($p<0.001$). The demographic characteristic has been shown in Table 1.

Table 1. Demographic characteristics of patients. Data expressed as Mean ± Standard deviation, n (%), Median[IQR].

	Regional anesthesia (n=97)	**General anesthesia (n=26)**	**p**
Age, year	30.53 ± 10.60	44.72 ± 26.51	<0.001*
Gender, n (%)			
Male	9 (9,3)	9 (34,6)	<0.001*
Female	88 (90,7)	17 (65,4)	
Type of operation			
C/S	83 (91.2)	8(8.8)	<0.001*
General surgery	6 (6.2)	14 (53.8)	
Other a	8 (8.2)	4 (15.4)	
Urgent	46 (47.4)	15 (57.7)	0.352
Elective	51 (52.6)	11 (42.3)	
Operation time (min)	90 [80-105]	90 [90-120]	0.036*

a Other (cardiovascular, urology, neurosurgery, orthopedics), C/S: cesarean operation.
*statistically significant

We determined that 61 (49.6 %) of the 123 surgeries were emergency surgeries, and 62 (50.4 %) were elective surgeries. Ninety-seven patients were operated under RA (78.9 %); meanwhile, 26 patients (21.1 %) were operated under GA. In the RA group, infraclavicular block was applied to 2 (2.1 %) patients, while spinal anesthesia was adminis-

tered to 95 (97.9 %) patients. The rate of RA was statistically significant higher than GA rate (p=0.001) (Table 1). C/S operations (91.2 %) constituted the significance of patients who underwent RA (p<0.001). Twenty operations (16.3 %) were general surgery and 12 operations (9.8%) were other surgeries in the cohort. In the general surgeries, 6 (30 %) were operated RA and 14 (70 %) patients under GA. In the other surgeries, 8 (66.7 %) patients were operated under RA and 4 (33.3 %) patients under GA (Table 1). Mean operation time in the RA group was statistically significant shorter than GA group (p=0.036).

Pulmonary disorders developed totally in 8 patients in the cohort. Of these, 6 (6.2 %) patients were in the RA group and two (7.7 %) were in the GA group. No statistically significant difference was found (p=0.535) (Table 2).

Eleven patients were admitted to the ICU (8.9 %). In the RA group, 8 patients (8.2 %) were admitted to intensive care and in the GA group, three patients (11.5 %) were admitted to the ICU (Table 2). Although there was a higher rate of intensive care hospitalization in the GA group, the difference was not statistically significant (p=0.422) (Table 2).

The perioperative mortality rate was 5.7 % (7 patients) in our cohort. The mortality rate was 5.2 % (5 patients) in the RA group and 7.7 % (2 patients) in the GA group. Despite the proportionally higher mortality rate in the GA group, no statistically significant difference was found (p=0.457). We have made a subgroup of C/S operations that consisted of most of the operations performed in patients with COVID-19. C/S was performed in 91 patients (74 % of the cohort). Of these patients, 83 patients received RA group and eight received GA group. The rate of pulmonary disorders, admission to ICU and perioperative mortality were similar in RA and GA groups in the obstetric population (Table 3).

During the postoperative follow-up period of the patients, we observed that three (3.1 %) patients needed renal replacement therapy in the RA group; meanwhile, one (3.8 %) patient required renal replacement therapy in the GA group. No statistically significant difference was found in the necessity of renal replacement therapy (p=0.618). An increase in liver function tests was observed in 9 patients (9.3 %) in the RA group and four in the GA group (15.4 %). The difference was not statistically significant (p=0.282). The rates of pneumonia, ICU admission rates and mortality rates were also stated in Figure 1.

Table 2. Outcome of pulmonary disorders, ICU Hospitalization, perioperative mortality, liver and renal disorders, and laboratory data. Data expressed as Mean ± Standard deviation, n (%), Median[IQR].

	Regional anesthesia (n=97)	General anesthesia (n=26)	p
Pulmonary disorder	6 (6.2%)	2 (7.7%)	0.535
ICU Hospitalization	8 (8.2%)	3 (11.5%)	0.422
Perioperative mortality	5 (5.2%)	2 (7.7%)	0.457
Increase in liver enzymes	9 (9.3%)	4 (15.4%)	0.282
Renal Replacement Therapy	3 (3.1%)	1 (3.8%)	0.618
Blood urea nitrogen	14 [11-22]	22 [14-31]	0.090
Creatinine	0.5 [0.4-0.7]	0.6 [0.5-1]	0.129
WBC	8.3 [6.6-11.3]	11 [7.8-15]	0.040*
PLT	210 [165-268]	259 [186-307]	0.266
HGB	11.2 [10-12]	11 [9.7-13.5]	0.226

*statistically significant ICU: Intensive Care Unit, WBC: white blood cell, PLT: Platelet count, HGB: Hemoglobin

Table 3. Outcome of C/S operations. Data expressed as Mean ± Standard deviation, n (%), Median[IQR].			
	Regional anesthesia (n=83)	General anesthesia (n=8)	p
Urgent	6 (6.2%)	2 (7.7%)	0.535
Elective	38 (45.8 %)	3 (11.5%)	0.422
45 (54.2 %)	6 (75 %)	2 (7.7%)	0.457
2 (25 %)	0.113	4 (15.4%)	0.282
Operation time (min)	90 [80-90]	85 [75-90]	0.196
Renal Replacement Therapy	1 (1.2 %)	0	0.912
Increase in liver enzymes	3 (3.6 %)	0	0.756
Blood urea nitrogen	13.9 [11.2-17.9]	15.8 [14-23]	0.261
Creatinin	0.5 [0.4-0.6]	0.5 [0.5-0.8]	0.202
WBC	8.4 [6.7-11.5]	9.5 [7.6-11.9]	0.771
PLT	204 [161-272]	270 [221-301]	0.387
HGB	10.8 [9.9-11.5]	11 [10.9-12.6]	0.073
Pulmonary disorder	1 (1.2 %)	0	0.912
ICU hospitalization	2(2.4 %)	0	0.831
Perioperative mortality	1 (1.2 %)	0	0.912
*statistically significant ICU: Intensive Care Unit, WBC: white blood cell, PLT: Platelet count, HGB: Hemoglobin			

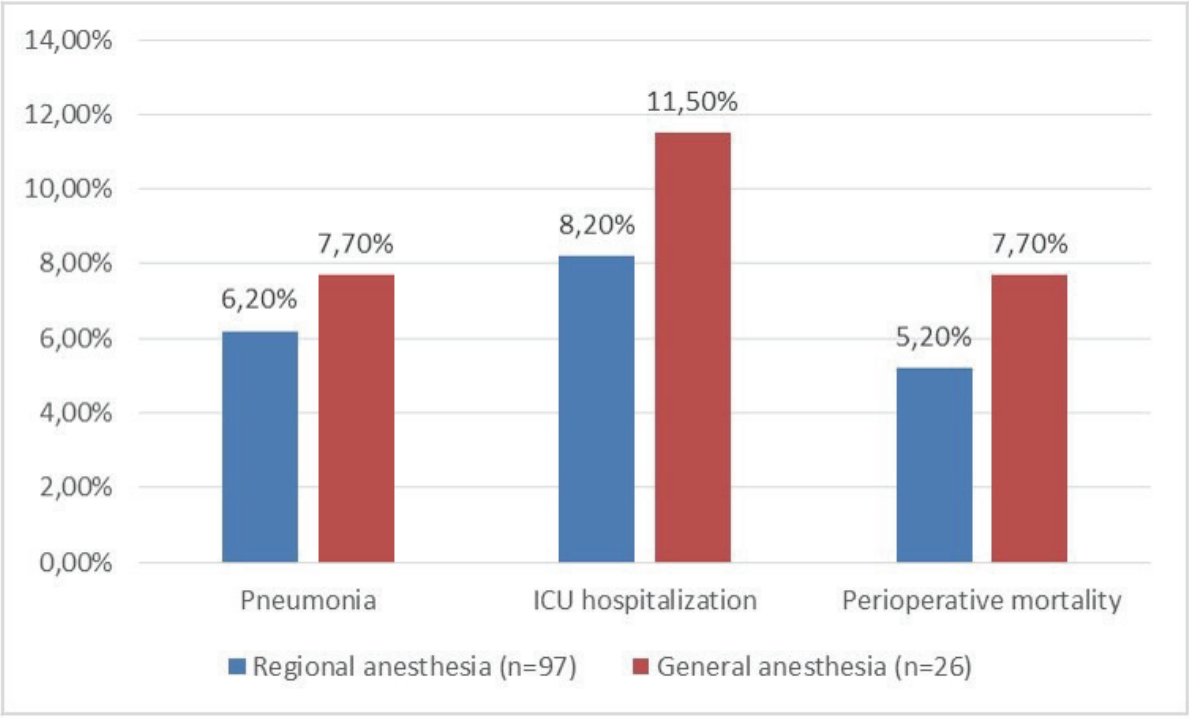

Figure 1. Data of pulmonary disorders, ICU Hospitalization, perioperative mortality, liver and renal disorders, and laboratory data. Data expressed as percentage.

DISCUSSION

The study results showed that acute pulmonary complications, admission to the ICU and perioperative mortality rates were similar when RA or GA was performed in patients with perioperative COVID-19 disease.

A joint statement by the American Society of Regional Anesthesia and Pain Medicine (ASRA) and European Society of Regional Anesthesia and Pain Therapy (ESRA) was reported in 2020 with recommendations on anesthesia methods in patients with COVID-19. These recommendations are usually consisted of expert opinions and do not include a previous comparative study. Avoiding GA was suggested, and RA was promoted whenever possible.[4] Neuraxial techniques are also recommended for surgical anesthesia and pain relief, especially in cesarean/section (C/S) operations.[7]

Many surgery clinics have postponed elective surgeries with the rapid spread of new coronavirus infection worldwide.[8] Although elective surgeries have been postponed, cancer surgeries, trauma surgeries, emergency operations, and especially obstetric surgery continued even in the presence of acute COVID-19. In our study, we observed that 74 % of our patient cohort consisted of C/S operations. Most of the C/S operations (91.2 %) were operated under RA. We also determined that 49.6 % of our cohort consisted of emergency operations. Since all elective surgeries have been stopped in our institution at that time period, this could be understandable. These results are consistent with the published literature. Nepogodiev et al. stated that 74.0% of the operated patients underwent an emergency operation. They also noted that 30-day mortality was 23.8% in operated patients with confirmed COVID-19. They could not find a statistically significant difference between GA and RA in mortality rates.[9] In the study of Chen et al., they implemented epidural anesthesia to 14 patients and GA to 3 patients in an obstetric cohort and reported no mortality.[10] In another study in which 28 patients were included spinal and local anesthesia was applied to 24 patients and GA was applied to four patients. All patients were operated under GA and transferred to intensive care and one death was reported postoperatively.[11] In our cohort, the mortality rate was 5.7 %, lower than the previous studies.

General anesthesia requiring airway intervention has a higher risk of perioperative pulmonary complications than regional anesthesia.[2] Postoperative pulmonary complications are the most common mid-term complications after surgery and significantly impact a patient's well-being and recovery.[12] The most important of these are pneumonia, atelectasis, acute respiratory distress and the need for mechanical ventilation.[13] A review also reported a lower incidence of postoperative pneumonia in patients undergoing neuraxial anesthesia than in patients undergoing GA.[14] Pulmonary dysfunctions resulting from subsequent restrictive lung injury have also been described in patients with severe COVID-19. Chen et al. reported that both RA and GA can be used safely in their study on COVID-19 positive pregnant patients.[10] In their study, Korkmaz et al. evaluated all patients with suspected COVID-19 who underwent surgery during the pandemic process and stated that mortality was associated with increasing age and GA application. At the same time, they reported that hospitalization in intensive care units, respiratory problems, acute renal failure and acute thrombotic events were the cause of death in patients.[15] In our study, pneumonia and respiratory distress were observed in 6 (6.2%) patients in the RA group and 2 (7.7%) patients in the GA group. At the same time In the RA group 8 patients (8.2%) were admitted to intensive care, and in the GA group three patients (11.5 %) were admitted to the ICU. Although pneumonia, respiratory complications and ICU admission rate were lower in the RA group compared to the GA group, this difference was not statistically significant. We guess that this is because the majority of our patient group consists of young and obstetric patients.

Liver enzymes in COVID-19 patients may be increased;

however, there is inconsistency about the effect of GA or RA on liver damage, even in patients with liver disease.[16] While an increase in liver enzymes occurred in 10.6 % of our patients, no statisticaly significant difference was found between the RA and GA groups.

One of the main concerns during the anesthesia management of patients with COVID-19 is the transmission of the infection to the healthcare staff via aerosol release, especially during GA.[17] This was not a subject of our study as there is no clear recommendation in the literature regarding the anesthesia method that should be used.

The study's main limitation seems to be the heterogeneous patient distribution due to the excess of C/S operations that consisted of the majority of our patients. We have analyzed the results of a subgroup consisting of C/S operations and found no statistically significant difference between RA and GA. The retrospective and observational characteristics of the study may also pose a limitation, and our findings need to be confirmed by prospective controlled studies.

In conclusion, pulmonary complications, ICU admission, and mortality rates were similar in patients operated under RA compared to GA. RA did not reduce the requirement of renal replacement therapy.

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