The effects of 'Adequacy of Anesthesia' monitorization in general anesthesia on hemodynamics, recovery, and the cost of anesthetic drugs

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Original Article

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ABSTRACT

Objective: Adequacy of Anaesthesia provides information about electrical activity of the brain with entropy, and analgesic response of the body with surgical pleth index. In this study, we aimed to evaluate the effects of anesthetic management performed using adequacy of anaesthesia monitorization on intraoperative hemodynamics, postoperative recovery and the cost of anesthetic drugs.

Design: Prospective, randomized, a controlled study

Setting: Necmettin Erbakan University, Meram School of Medicine Department Of Anesthesiology and Reanimation, Konya, Turkey

Subject: A total of 120 patients scheduled for thyroidectomy operation under general anesthesia were included in the study.

Intervention: Patients divided into two equal groups as Group Adequacy of Anesthesia (Group AoA, n=60) and Group Control (Group C, n=60). For the induction, Group C was maintained with 1-2 mg/kg propofol and 1 µg/kg remifentanil injection, while based on the entropy and SPI values during the induction Group AoA was injected with propofol and remifentanil so as to provide state entropy and surgical pleth index values of 50 ± 10.

Main outcome measures: Hemodynamic data, times and recovery data were recorded and statistically analyzed.

Results: Extubation and recovery times were significantly shorter in Group AoA (p=0.29, p<0.01, p<<0.01; respectively). The cost of anesthesia calculated based on the amount of drugs used was significantly lower in group AoA (p<0.01).

Conclusion: In this study where we compared the use of adequacy of anesthesia with conventional anesthetic depth monitorization methods, we found that the use of adequacy of anesthesia provided positive contributions to the cost of anesthetic drugs, and post-anesthetic recovery.

KEY WORDS: adequacy of anesthesia, cost of anesthesia, depth of anesthesia, general anesthesia, recovery

INTRODUCTION

The term of anesthetic depth has largely changed with the advancement in technology, use of novel pharmacological agents, and modernization of anesthetic monitorizations[1].

General anesthesia has three components including hypnosis, analgesia, and immobility[2,3]. Today, among these three components of anesthesia, hypnosis is monitored with entropy, analgesia with surgical pleth index (SPI) and immobility with neuromuscular transition (NMT). AoA is an anesthetic monitorization software created by combining entropy and SPI.

Adequacy of anesthesia (AoA), a monitorization method used in general anesthesia practice is helpful in evaluation of the individual responses of patients in administration of intravenous hypnotics, opioids, and inhalationalanesthetics agents. AoA provides information about electrical activity of the brain with entropy, and analgesic response of the body with SPI. In addition, it shows muscle relaxation adequacy with NMT, providing monitorization of hypnosis, analgesia, and immobility that are the three components of general anesthesia. AoA is used in the evaluation of anesthetic depth, providing a combination of these non-invasive methods (Figure 1).

AoA aims to prevent both overuse of drugs by applying anesthesia deeper then needed, and wakefulness and awareness that occur due to superficial anesthesia applications during general anesthesia[4].

In this study, we aimed to evaluate the effects of anesthetic management performed on intraoperative hemodynamics, postoperative recovery and cost of anesthetic drugs using AoA monitorization.

SUBJECTS AND METHODS

This study was conducted after receiving the ethics committee approval (Ref. No:10643207-511.06-E.24117), in the operating room of our hospital between February 2018 and May 2018 in compliance with the Declaration of Helsinki. A total of 120 patients scheduled for thyroidectomy under general anesthesia with a physical status of ASA I-II according to the classification by the American Society of Anesthesiology (ASA), who were aged between 18 and 65 years, and gave informed consent were included in the study.

Patients with disrupted orientation and cooperation, severe psychiatric disorders, pregnant or breastfeeding women, emergency cases, patients with a history of cardiac dysrhythmia and heart failure, those with chronic smoking, alcohol or substance abuse, patients who needed intraoperative inotropic drugs, and those rejected to be volunteer were excluded from the study. Patients' demographic data were recorded. Patients were randomized with the sealed envelope method and divided into two equal groups as Adequacy of Anesthesia Group (Group AoA, n=60) and Control Group (Group C, n=60).

As the standard monitorization; electrocardiography (ECG), non-invasive blood pressure (NIBP), pulse oximetry (SpO_2), NMT, end-tidal carbon dioxide, and temperature were followed up. Patients in Group AoA were additionally monitored with entropy and SPI for AoA monitorization (Aisys CS^2 - GE Healthcare, CARESCAPE-B650-Finland). Recording times of the data are given in Table 1.

For the induction, Group C was injected with 1-2 mg/kg propofol (bolus) and 1 µg/kg remifentanil (infusion), Group AoA was injected with propofol and remifentanil so as to provide state entropy (SE) and SPI values of 50 ± 10. Rocuronium 0.6 mg/kg was administered for muscle relaxation, 2 mg/kg tramadol for postoperative analgesia, and 0.1 mg/kg ondansetron as antiemetic. Data of the 1st minute following anesthetic induction were recorded. All patients were intubated when the ratio of train-of-four (TOF) reached to zero, data were recorded post-intubation and after the patient was given the necessary position for thyroid surgery. Data were monitored during the surgical incision, and then with 10-minutes intervals.

For the maintenance of anesthesia, both groups were administered intravenous (iv) 0.25 µg/kg/min remifentanil infusion and 1 MAC sevoflurane as the inhalational agent. Whereas in Group C maintenance doses of sevoflurane and remifentanil were given based on clinical follow up, pulse, blood pressure, pupil reflex, and tear monitoring as in the conventional anesthetic applications; in Group AoA the anesthesia was maintained by providing optimum levels (SE: 50 ± 10, SPI: 50 ± 10) of Adequacy of Anesthesia chart values. During general anesthesia, if patient's heart rate drop down under 40/min, it was considered as bradycardic, and 0.5 mg atropine (iv) was applied to patients. If patient's systolic blood pressure (SBP) lower than 90 mmHg, it was considered as hypotensive, 10 mg ephedrine (iv) was applied to patients. When surgical skin suturing was completed, inhalational sevoflurane and remifentanil infusion were terminated. Fresh gas flow was raised to 10 L/min. Patients were awakened.

Anesthesia time was determined as the time from the initiation of induction to the extubation, and extubation time was defined as the time from termination of anesthesia maintenance to the extubation. The amount of anesthetic drugs, anesthesia time, and extubation time were recorded.

Heart rate, pulse oximetry, non-invasive arterial blood pressure, and fast-track recovery scores were monitored in patients taken to the postoperative recovery unit after wakening, and the patient with a fast-track score ≥ 12, providing none of the criteria were zero point, were referred to the ward (Table 2). The time between the extubation and referral to the ward was determined as the recovery time.

Statistical analysis

Data obtained were analyzed using SPSS v. 20 (Statistical Package for Social Sciences, Inc., Chicago, IL). The continuous variables are expressed as mean ± SD or number (%). The categorical variables are given as number and percentage. Normality of the data was tested using “Kolmogorov-Smirnov” test. Mann-Whitney U test was used in analysis of the continuous parameters (Age, weight, etc.). Chi-square test was used in the comparisons of paired groups and in the evaluation of the categorical variables. $p<0.05$ values were considered statistically significant.

RESULTS

This study was conducted with a total of 120 patients aged between 20 and 65 years, and no statistically significant difference was found between the groups in terms of the demographic data and ASA scores (p>0.05) (Table 3).

Whereas no statistically significant difference was found between the groups in terms of anesthesia times. Extubation and recovery times were significantly shorter in Group AoA (p<0.01) (Table 4).

Hemodynamic monitoring was performed based on heart rate, and SBP and diastolic blood pressures (DBP) were measured with a non-invasive method. There was no statistically significant difference between the groups in hemodynamic parameters (p>0.05) (Figure 2,3).

The cost of anesthesia calculated based on the total amount of anesthetic drugs used was significantly lower in Group AoA (p<0.01) (Tables 5, 6) (Figure 4).

No significant difference was found between the groups in neuromuscular block drugs. The mean entropy and SPI values observed in Group AoA are given in Figure 5.

DISCUSSION

In this study, in which the use of AoA was compared with conventional anesthetic depth monitorization methods, we found that the use of AoA provided positive contributions to the amount of drugs consumed, cost of drugs, and post-anesthetic recovery.

Anesthetic depth is determined with the stress response and cognitive changes in a patient under neuromuscular block. According to the traditional practices, heart rate and blood pressure are guiding in evaluation of the stress response. Eyelash, cornea, and conjunctiva reflexes, and the reflexes such as pupillary diameter and light reaction as well as indirect monitorization are used for determination of cognitive changes. However, it has been concluded that these clinical findings show a poor correlation with anesthetic depth[5]. Today, many anesthetists adjust doses of pharmacological agents that they use, by measuring hemodynamic responses and minimal alveolar concentrations of inspired and expired inhaled anesthetic. Unnecessarily deep anesthesia may cause hypotension and late recovery, while insufficient anesthesia may lead to complications such as awareness[6]. Although monitorization of anesthetic depth has been shown to decrease the amount of anesthetic drugs used, effectively provide hemodynamic stabilization, and decrease times of wakening and extubation; the benefits that this method would provide in numerous issues including environmental pollution and costs are still underwork[7-9].

Methods based on electroencephalogram findings such as narcotrend, bispectral index (BIS) and entropy are used in the monitorization of anesthetic depth. AoA modul is a current system developed by combining entropy, and SPI which is used for the control of pain and stress response in general anesthesia, and it evaluates anesthetic depth and analgesia together. AoA is open to research in terms of the patient control under general anesthesia, post-anesthetic recovery, consumption and costs of anesthetic drugs.

When designing this study, we planned to apply AoA on thyroidectomy cases in order to prefer a surgery with sufficient time to also evaluate its effects on maintenance anesthesia period, and considering lower intraoperative external impacts. Adequacy of anesthesia charts were used for monitorization in Group AoA. Anesthetic target in this monitor was defined so as to provide entropy (40-60) values, providing surgical anesthetic depth, and SPI (50 ± 10) values enough to provide adequate analgesia[9,10]. End-tidal inhaler anesthetic concentration was used to adjust entropy values, while the doses of remifentanil infusion were adjusted to achieve SPI target.

Slavlov *et al*[11] examined mobility of patients, hemodynamics, and BIS values and observed increased blood pressure in mobilized patients, while they found no correlation between BIS and hemodynamic data. In a study with pediatric patients, effect of BIS monitorization alone on hemodynamics was not sufficient[12]. In another study in which BIS monitorization was used to monitor anesthetic depth for cranial surgery, monitorization of anesthetic depth had no contribution in the control of hemodynamics[13].

In the present study, we found that AoA monitorization showed similarity with the other monitorization methods, and obtained similar results in the hemodynamic evaluation with the conventional methods. However, systolic arterial pressure was under 90 mmHg in nine patients in Group C, while this finding was observed only in three patients in Group AoA. Significant difference between the groups in terms of the amount of drugs used, suggests that hemodynamics was also influenced. In our study, although hypotension was more common in Group C, the difference did not reach statistical significance, and we think that this result was due to the hypotension and bradycardia protocol used.

The relationship between monitorization of anesthetic depth and its effects on drug consumption is a commonly studied subject in anesthesia applications. Drug consumption values were similar in the anesthesia applications performed based on BIS and entropy[14]. In a study with patients who underwent laparoscopic sleeve gastrectomy surgery, the use of BIS was reported to decrease the consumption of desflurane[15]. In a study with elderly Asian population, the use of BIS was shown to provide a reduction in isoflurane consumption by 40%[16]. In a study by Banister *et al*, a deeper anesthesia was achieved in the control group which was given sevoflurane and N_2O, and the authors reported reductions by 25-40% in sevoflurane consumption in BIS group[17]. In a study examining effects of anesthesia application using SPI, it was reported that fentanyl consumption was decreased, while sevoflurane consumption was similar[18]. In our study, we used sevoflurane as the anesthetic agents for anesthesia maintenance, and provided analgesia with remifentanil infusion. Looking to the amount of drugs used during the maintenance per patient, the mean amount of remifentanil infusion was found as 1273.33 µg in Group C, and 932.66 µg in Group AoA. Whereas sevoflurane consumptions were found as 21.56 mL in Group C, and 16.18 mL in Group AoA. Therefore, the use of AoA decreased remifentanil consumption by mean 340.67 µg (26.75%) and sevoflurane consumption by mean 5.38 mL (24.95%). We concluded that the use of drugs for maintenance was significantly lower in Group AoA.

Effects of the monitorization of anesthetic depth on the cost of anesthesia remains controversial. In a review based on 22 studies controlling anesthetic depth with BIS, entropy, and narcotrend; although awareness issue was left disputable, monitorization of anesthetic depth has been reported to have drug cost reducing effects[19]. In a study investigating effectiveness of SPI on opioid consumption, it was underlined that combined use of SPI and entropy was effective in dose adjustment and decreased both the amount of opioids used, and hypnotic levels[4].

Similarly, in our study we found that reductions in the amount of sevoflurane and remifentanil used significantly decreased the costs. In the calculations of total drug cost; cost per patients was found as $8.75 in Group C, and $6.76 in Group AoA with a $1.99 (22.75%) contribution per patient.

In a study by Punjasawadwong *et al*[20], examining 36 studies, BIS monitorization was found to shorten length of stay in postoperative recovery unit by 6.75 minutes[21]. In addition, it was reported that BIS was not effective on time to discharge. Chhabra *et al*[21], reported that effects of the use of spectral entropy on weakening time has moderate reliable evidence, while Shephard *et al* reported shortened recovery time[19]. In a study examining 170 patients who underwent SPI guided day case anesthesia, remifentanil and propofol infusion doses were decreased and recovery times were shortened[4].

AoA which we found to have positive reflections on consumption and costs of drugs, also has effects facilitating post-anesthetic recovery. In the present study, no statistically significant difference was found between total anesthesia times. The mean recovery time was found as 6.58 minutes in Group AoA and 12.56 minutes in Group C, while the mean recovery time was found as 17.83 minutes in Group AoA and 32.33 minutes in Group C. Our results indicate that patients monitored with AoA experienced a more rapid recovery process.

CONCLUSION

This study has some limitations. We could not demonstrate effective results in hemodynamics with significant decrease in drug consumption, which we found. Also, at postoperative patient visit time, none of our patients presented similar information to intraoperative awareness, but we did not perform any test postoperatively.

Further controlled studies are needed to compare AoA and the other monitorization methods for anesthetic depth to evaluate hemodynamics, drug costs and recovery.

In conclusion, the use of AoA for the management of general anesthesia decreases the amount of drug, thus cost of anesthetic drugs, providing a more rapid recovery process in patients. We believe that development of targeted anesthetic management systems will provide a more controllable and more economical anesthetic management.

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Conflict of Interest: The authors declare that they have no conflict of interest.

Ethical approval: All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Authors contributions:

Design: A. TOPAL, Ş. TURK

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Article preparation: G. HACIBEYOGLU, A. TOPAL, R. YILMAZ

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Table 1: Recording times of data

Recording times	
T0	Basaline
T1	1 min after induction
T2	1 min after extubation
T3	Case position for surgery
T4	Surgery incision
T5	10. min after surgery incision
T6	20. min after surgery incision
T7	30. min after surgery incision
T8	40. min after surgery incision
T9	50. min after surgery incision
T10	End of surgery
T11	Termination of anesthesia
T12	Extubation

Table 2: Fast-Track Recovery point scoring table (MAP :mean arterial pressure)

Parameters	**Description of the patient**	**Score**
Level of consciousness	Score Awake and oriented	2
	Arousable with minimal stimulation	1
	Responsive only to tactile stimulation	0
Physical activity	Able to move all extremities on command	2
	Some weakness in movement of extremities	1
	Unable to voluntarily move extremities	0
Hemodynamic stability	Blood pressure ,15% of baseline MAP value	2
	Blood pressure 15%–30% of baseline MAP value	1
	Blood pressure .30% below baseline MAP value	0
Respiratory stability	Able to breathe deeply	2
	Tachypnea with good cough	1
	Dyspneic with weak cough	0
Oxygen saturation status	Maintains value .90% on room air	2
	Requires supplemental oxygen (nasal prongs)	1
	Saturation ,90% with supplemental oxygen	0
Postoperative pain assessment	None or mild discomfort	2
	Moderate to severe pain controlled with IV analgesics	1
	Persistent severe pain	0
Postoperative emetic symptoms	None or mild nausea with no active vomiting	2
	Transient vomiting or retching	1
	Persistent moderate to severe nausea and vomiting	0
Total score (max)		14

Table 3: Distribution of the demographics by groups

Demography	Group C (n=60)	Group AoA (n=60)	P Value
Age	46.20±11.55	44.48±11.42	0.47
Weight (kg)	77.18±14.50	76.63±11.31	0.73
ASA score (I/II)	43/17	47/13	0.26
Sex (M/F)	14/46	19/41	0.21

Table 4: Mean times calculated according to the groups

Times	Group C	Group AoA	P Value
Anesthesia time (min)	90.66±19.51	86.33±19.65	0.29
Extubation time(min)	12.56±2.84	6.58±2.14	<0.01
Recovery time(min)	32.33±8.10	17.83±7.38	<0.01

Table 5: Mean amounts of the drugs used for maintenance of anesthesia

Anesthetic Drugs	Group C (n=60)	Group AoA (n=60)	P Value
Remifentanil (µg)	1273.33±335.72	932.66±192.11	<0.01
Sevoflurane (ml)	21.56±5.49	16.18±3.80	<0.01
Propofol (mg)	142.83±29.9	129.50±22.43	<0.01

Table 6: Mean costs of the drugs used for maintenance of anesthesia

Anesthetic Drugs	Group C (n=60)	Group AoA (n=60)	P Value
Propofol ($)	0.52±0.11	0.47±0.08	0.04
Remifentanil ($)	1.54±0.41	1.13±0.23	<0.01
Sevoflurane ($)	5.66±1.44	4.25±1.00	0.01
Total ($)	8.75±1.77	6.76±1.17	<0.01

Fig. 1: Adequacy of Anesthesia chart images from the Aisys CS^2 – GE Healthcare, CARESCAPE-B650 monitor.

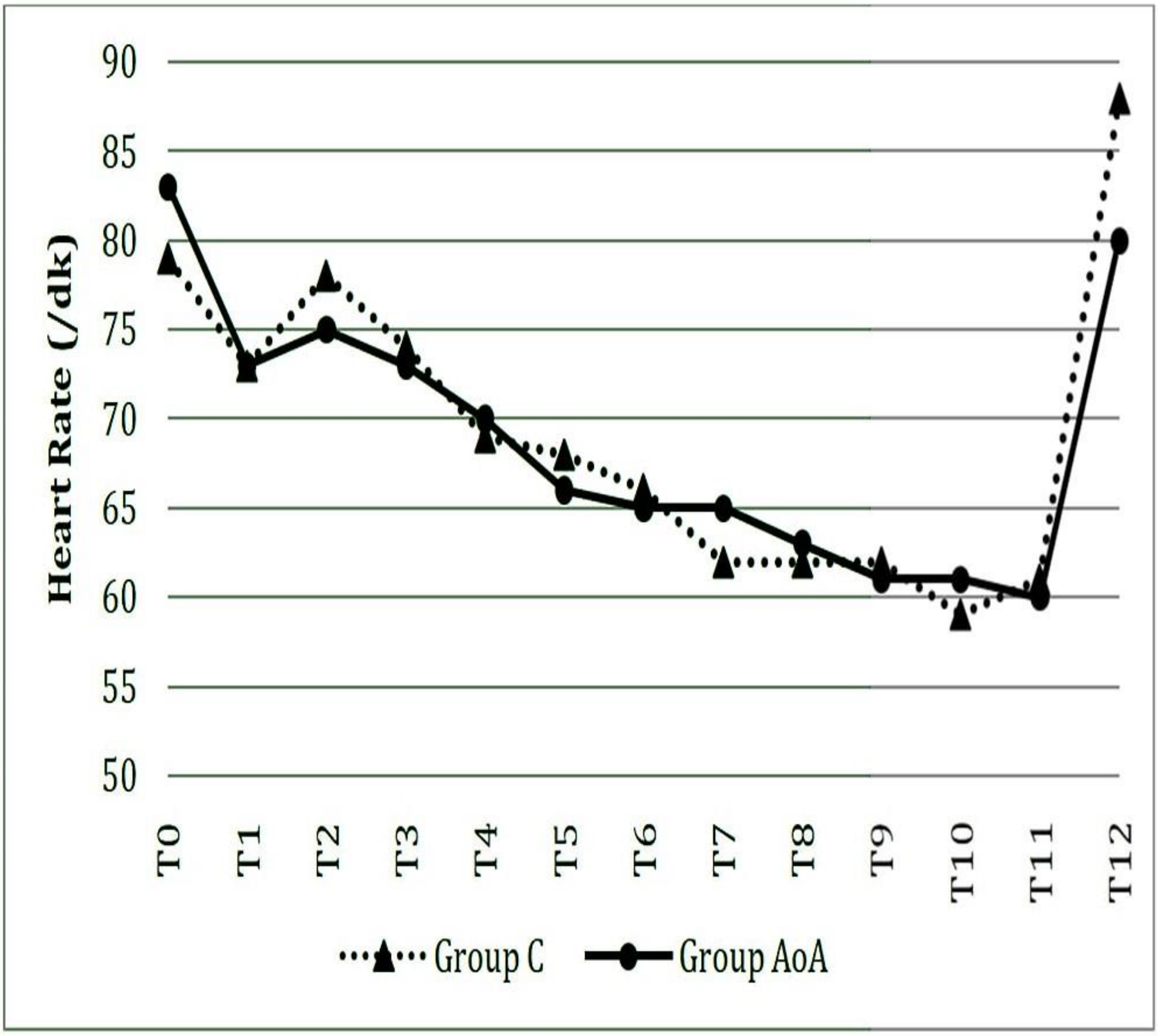

Fig. 2: Mean heart rate values of the groups

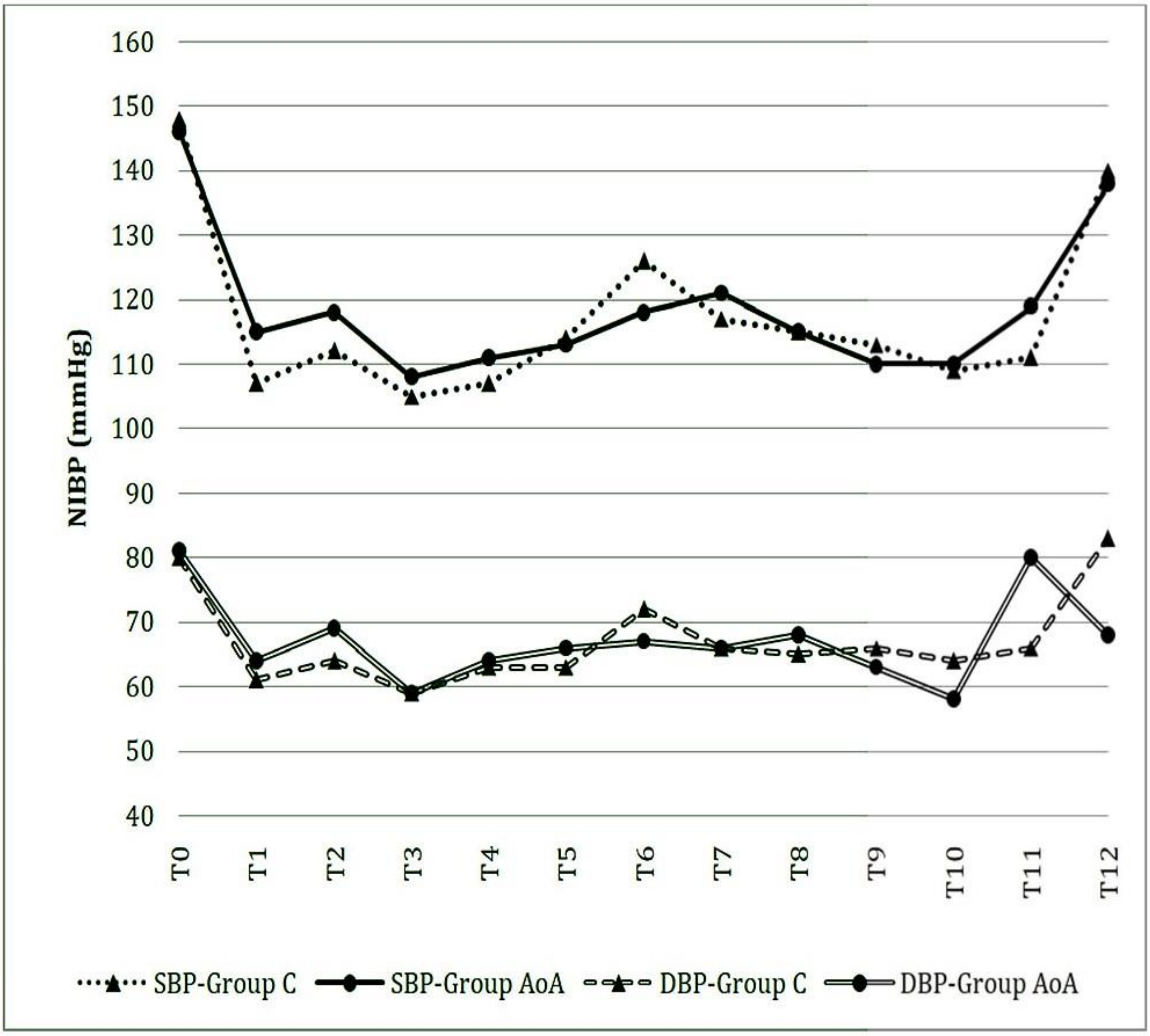

Fig. 3: Mean systolic and diastolic blood pressure values of the groups

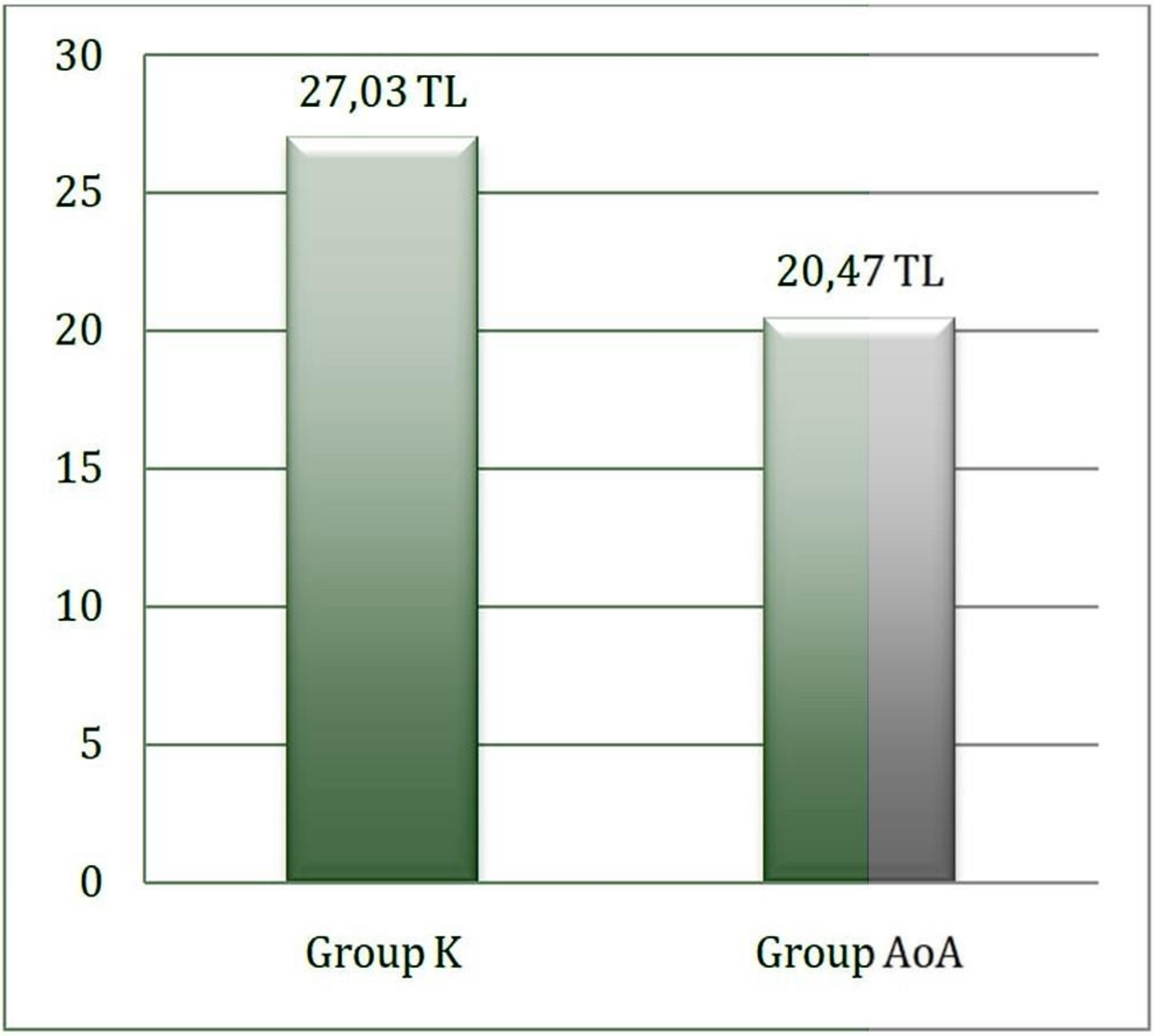

Fig. 4: Mean total cost of the drugs used for anesthesia per one patient

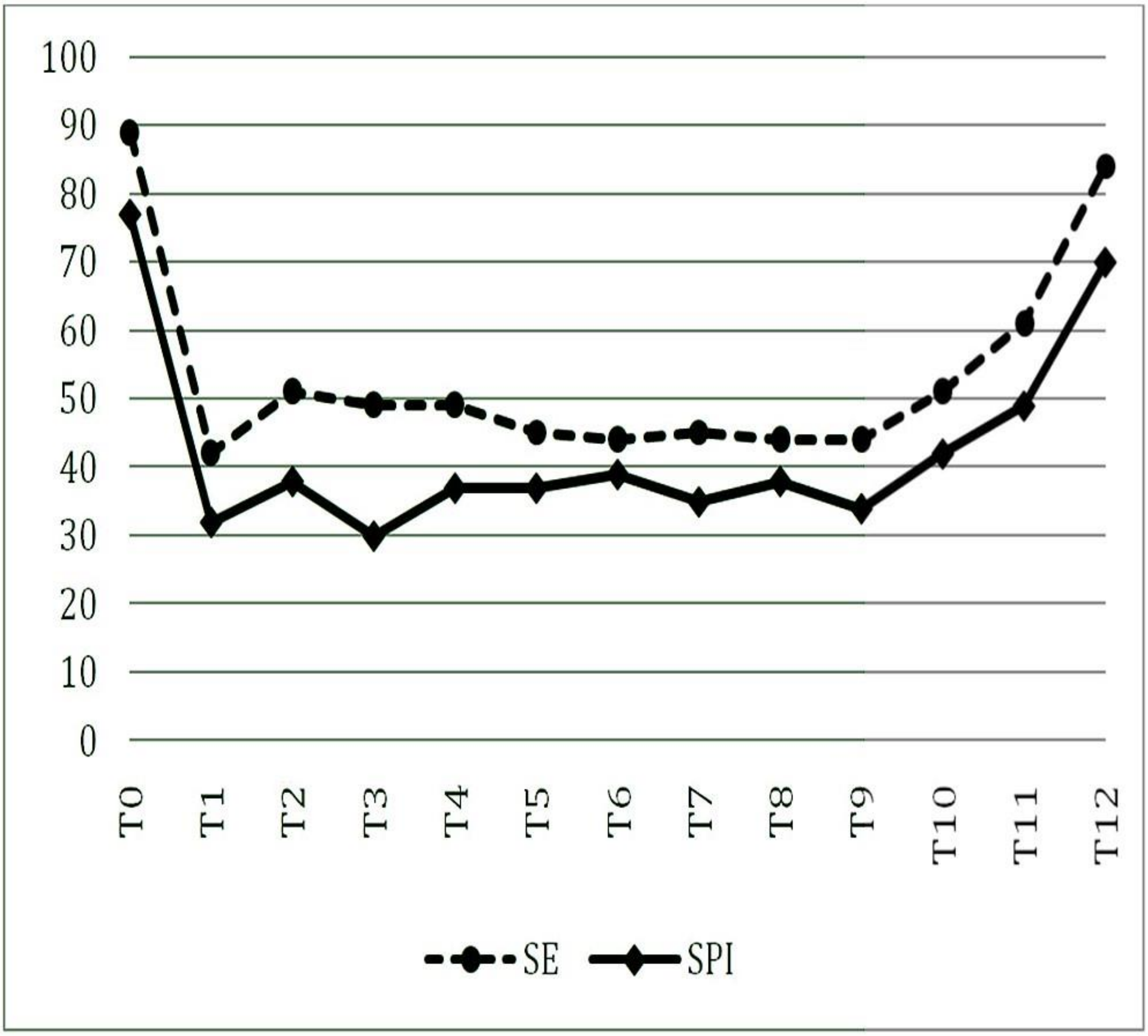

Fig. 5: Entropy and SPI values observed in Group AoA