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# **PhD THESIS**

## **MULTIMODAL HYPNOSIS MONITORING IN SURGICAL PATIENTS UNDER GENERAL ANESTHESIA**

### **A B S T R A C T**

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## ABSTRACT

Developments in surgical techniques, diagnostic methods and the increasing surgical needs of the general population have led to the development of new substances and new techniques for the provision of general anesthesia. In order to increase the accessibility of specialized care to the general population, the rapid adaptation of multiparametric monitoring techniques in general anesthesia has been necessary to reduce waiting times, perioperative side effects and to improve patient safety.

The state of consciousness is defined by a series of variables that are experienced and felt, such as perceptions, sensations, emotions and memory/recall. This is the main reason why quantitative analysis of these states is impossible. One of the first theories emerged in 1949, when Hebb suggested that the physical translation of mental representations is due to neuro-cellular assembly, i.e. neuronal interconnection. Based on this first theory, after numerous studies, the N-methyl-D-aspartate (NMDA) synapses were discovered, with an agglomerated presence in the cortex. The various interactions, ionic exchanges, nitric oxide production and electrical stimulation generated by the opening and closing of ion channels produce the formation of inter-neuronal connections, hence complex neuronal activity. Loss of consciousness can have different causes, such as anesthesia, brain injury or sleep. In the case of anesthesia, the responses of the central nervous system are not totally suppressed; moreover, this state is reversible, which is the prerogative of modern medicine that has made it possible to develop surgery and invasive therapeutic and diagnostic interventions.

Electroencephalography (EEG) is the summation and recording of postsynaptic potentials in the pyramidal cells of the cerebral cortex. EEG is typically categorized according to frequency. It can be recorded on the scalp and forehead using surface electrodes and reflects the metabolic activity of the brain. The metabolic activity of brain cells requires energy. Problems or changes in energy production (increased demand or reduced supply) by brain cells can profoundly affect EEG activity. Monitoring the level of consciousness during general anesthesia using electroencephalography has become routine practice in the operating theater. For the patient, as well as for the anesthesiologist, the main concern regarding general anesthesia is the lack of consciousness and the avoidance of waking up during surgery. EEG patterns are known to change with the depth of the patient's anesthesia, and the assessment of hypnosis requires measurements of central nervous system electrical activity. Anesthetics act on the brain; thus, this organ should be monitored in addition to spinal cord reflexes and signs of the cardiovascular system, such as blood pressure and heart rate. Monitors used for EEG-based depth of anesthesia use algorithms to continuously analyze EEG signals and translate any changes into simple numeric indices corresponding to the level of consciousness. Monitoring the level of consciousness is complex and, despite rapid developments in this field, the benefits of EEG-based anesthesia monitoring are still controversial. The problem is that our understanding of human consciousness is incomplete and we do not yet fully understand the effects of general anesthesia on the brain. The depth of anesthesia is neither stable nor constant; rather, it is a dynamic action that depends on the balance between the dose of anesthesia and the pain caused by the surgery. The use of EEG signals to monitor the depth of anesthesia should reduce the incidence of intraoperative consciousness, lead to a reduction in drug consumption, prevent anesthesia-related adverse events, and allow for faster recovery. Multimodal monitoring techniques in general anesthesia refer to the use of all parameters

that can characterize this process. Thus, we are talking about the monitoring of the degree of hypnosis, the nociception-antinociception balance and the autonomic system. Classically, the principles of monitoring general anesthesia include the assessment of vital functions such as heart rate, blood pressure, temperature and other subjective clinical signs. In this situation, there is a risk of underdosage or conversely overdosage of anesthetic drugs, leading to an excessive degree of hypnosis with serious impairment of the prognosis of patients. Clinical signs such as hypertension, tachycardia and lacrimation have been used for a long time to guide general anesthesia, but they have been shown to be subjective and cannot guide anesthesia according to the real needs of patients.

The **primary objectives** of this study are the impact of multimodal monitoring on hemodynamic stability in patients under general anesthesia. Multimodal monitoring was represented by the monitoring of autonomic parameters (heart rate, blood pressure, peripheral oxygen saturation - SpO<sub>2</sub>, temperature) and the monitoring of the degree of hypnosis (entropy - RE/SE, qNOX and qCON).

The **secondary objectives** consist of analyzing the impact of multimodal monitoring on post-anesthetic recovery time. The statistical differences between the two techniques for monitoring the degree of hypnosis were also analyzed.

Prospective, observational, randomized, single-center, observational study conducted from January 2019 to March 2021 in the Anesthesia and Intensive Care Unit, "Pius Brînzeu" County Emergency Hospital Timișoara, Romania. The study was approved by the Ethics Committee of the institution, and was conducted in accordance with international regulations on clinical trials.

## 1. GENERAL ASPECTS

During general anesthesia, maintaining adequate tissue perfusion is one of the most important segments in perioperative management. Hypotension occurs frequently, especially after induction or rather, between induction and the start of surgery. Reich et al, reported a decrease in MAP by more than 40% (MAP < 70 mmHg or MAP < 60 mmHg) in the first 10 minutes after induction (P < 0.001) [1]. Moreover, in this study (n = 2,406 patients), significant increases in postoperative stay (13.3%, P < 0.05) and postoperative mortality (8.6%, P < 0.02) were reported in patients who developed intraoperative hypotension. Another interesting phenomenon emphasized by this group of authors is that post-induction hypotension occurred most frequently in the 5-10 minute timeframe, compared with the 0-5 minute timeframe. A similar study by Hug et al. reports that more than 15% of patients experience a drop in the systolic blood pressure (SBP) below 90 mmHg after propofol induction within the first 10 minutes of administration [2]. Studies demonstrate that Sevoflurane induction maintains hemodynamic stability and reduces the risk of hypotension, in contrast to Propofol induction, but this technique is much more difficult for patients to tolerate. Thwaites et al., conducted a study on patient satisfaction according to the type of induction: Sevoflurane (inhaled, 8%) vs. Propofol (i.v.). Thus, more than 14% of the patients consider induction with Sevoflurane to be

unpleasant, compared to induction with Propofol (0%). Also, more than 24% of the patients would not choose induction with Sevoflurane a second time, compared to induction with Propofol [3].

Many other studies on multimodal monitoring of the surgical patient show an improvement in the anesthetic process (Table 1).

**Table 1. Impact of hypnosis monitoring on clinical prognosis**

Author	Monitoring parameter/technique	Type of general anesthesia	Comments	Ref
Choi et al.	State Entropy (SE)	78 children (3-12 years) sevofluran	↓ use of sevoflurane ↓ time for postoperative recovery	[33]
Wu et al.	State Entropy (SE)	64 patients sevofluran	↓ use of sevoflurane ↓ use of antihypertensive drugs ↑ hemodynamic stability	[34]
Vakkuri et al.	State Entropy (SE)	368 patients propofol-alfentanil-N O <sub>2</sub>	↓ propofol use ↓ postoperative recovery time	[35]
Talawar et al.	Entropy (SE/RE)	50 patients isofluran-N O <sub>2</sub>	↓ postoperative recovery time	[36]
Elgebaly et al.	Entropy (SE/RE)	propofol	↓ use of propofol ↑ hemodynamic stability	[37]
Hernandez-Gancedo et al.	Bispectral index (BIS)	302 patients propofol-alfentanil-N O <sub>2</sub>	↓ use of propofol ↓ postoperative recovery time	[38]
Liu et al.	Bispectral index (BIS)	1383 patients day anesthesia	↓ consumption of anesthetic substances ↓ incidence for postoperative side effects (vomiting, nausea) ↓ postoperative recovery time	[39]
Bhardwaj et al.	Bispectral index (BIS)	50 pediatric patients; propofol	no effects on anesthetic drug use were observed; no effects on postoperative recovery time were observed;	[40]
Aime et al.	Bispectral index (BIS) and Entropy (RE/SE)	115 patients; sevofluran;	BIS & Entropy: ↓ sevoflurane consumption;	[41]
Liao et al.	Bispectral index (BIS) and A-line auto-regressive index (AAI)	116 patients; sevofluran;	BIS & AAI: ↓ sevoflurane consumption; ↓ postoperative recovery time;	[42]
May et al.	Composite auditory evoked potential index (cAAI)	20 pediatric patients; TIVA propofol and remifentanil;	↓ use of propofol; ↑ hemodynamic stability	[43]
Lai et al.	Narcotrend	40 patients; propofol and fentanyl;	↓ use of propofol; ↓ recovery time; No effects on PONV were identified;	[44]
Rundshagen et al.	Narcotrend	48 patients; propofol and remifentanil	no effects have been identified after propofol/remifentanil consumption; no effects on postoperative recovery time were identified;	[45]

The concept of Entropy, derived from thermodynamics, is successfully used in current clinical practice and applied to the analysis of EEG signals. In terms of the analysis mechanism, the EEG signal is initially subjected to Fast Fourier analysis to identify the sinusoidal components. Following the identification of the spectrum, the Shannon function is applied to identify the specific values of each highlighted frequency. By summing these values, a numerical value called Spectral Entropy is obtained. The first algorithm used in

clinical practice was defined and applied in the M-Entropy S/5 modules (GE Healthcare, Helsinki, Finland) (Figure 10). EEG data are collected via an adhesive sensor composed of three electrodes located in the fronto-temporal region [57].

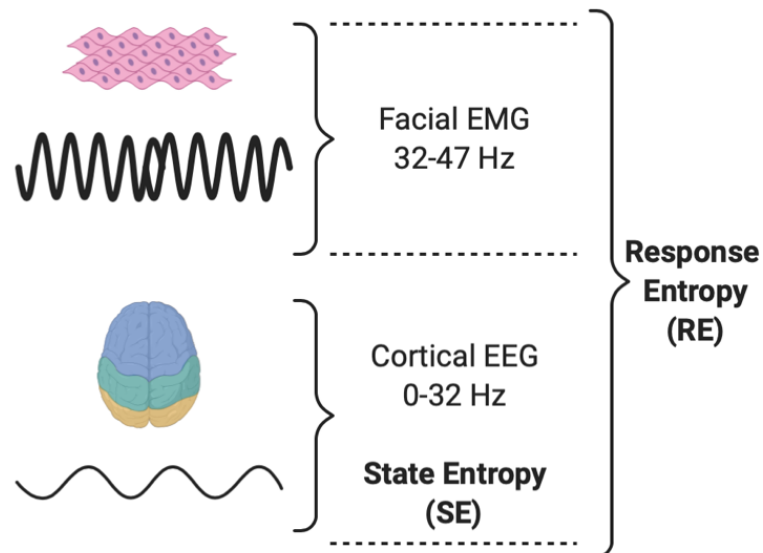


Figure 1. Graphical description of response entropy (RE)

The application of the concept in general anesthesia is based on the idea that when the brain is in the awake state, EEG signals are complex and highly irregular. When the patient falls asleep/is anesthetized, neuronal activity progressively decreases and EEG complexes become more regular. Applying this principle to Entropy, in patients under general anesthesia, a significant difference in the wave spectrum that is generated and in direct proportion to neuronal activity is observed. As the EEG signals are measured by electrodes placed frontally, an important percentage of the signals is represented by facial muscle activity and translated into electromyographic (EMG) signals. Thus, EEG signals are defined by frequencies up to 32 Hz, while EMG activity comprises signals higher than 32 Hz, and it is possible to discriminate between them. The M-Entropy mode (GE Healthcare, Helsinki, Finland), distinguishes the two frequencies and generates two parameters with important clinical applicability – “State Entropy – SE” and “Response Entropy – RE”. The SE (0.8 - 32 Hz) reflects the cortical status of the patients, respectively the RE (0.8-47 Hz) which includes both EEG and EMG activity. Values for SE range from 0 (EEG suppressed) to 91 (awake status) and RE is characterized by values ranging from 0-100. In usual clinical practice it is recommended to maintain RE/SE between 40-60 to obtain a degree of hypnosis adapted to the individual needs of the patients [57].

## 2. MATERIALS AND METHOD

### 2.1. STUDY POPULATION

This is a prospective, observational, randomized, single-center, observational study conducted between January 2019 and March 2021 in the Anesthesia and Intensive Care Unit of the "Pius Brînzeu" County Emergency Hospital, Timisoara, Romania. The study was approved by the Ethics Committee of the institution and was conducted in accordance with international regulations on clinical trials. The study is part of the research platform of the Romanian Society of Anesthesia and Intensive Care ([www.srati.ro](http://www.srati.ro)).

To analyze the variables and the clinical impact, three research groups were set up as follows:

- Group 1 (control group). Patients in this group received standard monitoring according to existing international guidelines and recommendations. Thus, heart rate (HR), systolic (SBP) and diastolic blood pressure (DBP), peripheral blood oxygen saturation (SpO<sub>2</sub>), temperature (°C) and minimum alveolar concentration (MAC) were monitored in these patients.
- Group 2 (study group): Patients included in this group were monitored for the standard parameters found in the control group, plus the degree of hypnosis, using Entropy - *State Entropy (SE)* and *Response Entropy (RE)* (B650 Monitor, E-Entropy Module, GE Healthcare, Helsinki, Finland).
- Group 3 (study group): Patients included in this group were subject to the monitoring of the standard parameters listed above, plus monitoring of the degree of hypnosis using qNOX, qCON, qCON (2000 Monitor, Quantium Medical, Fresenius Kabi, Mataró, Spain).

The **criteria for the inclusion** of patients in the analysis were: above 18 years of age, both sexes, elective surgery with an estimated duration of more than 30 minutes, general inhalation anesthesia with sevoflurane.

The **criteria for exclusion** from the study were surgical emergencies, severe polytrauma and burns, pregnant women and general anesthesia combined with loco-regional anesthesia, intravenous general anesthesia with propofol, respectively. Patients were randomized into study groups using online allocation software ([www.randomization.com](http://www.randomization.com)). Figure 13 shows the study methodology structured according to the Consort protocol.



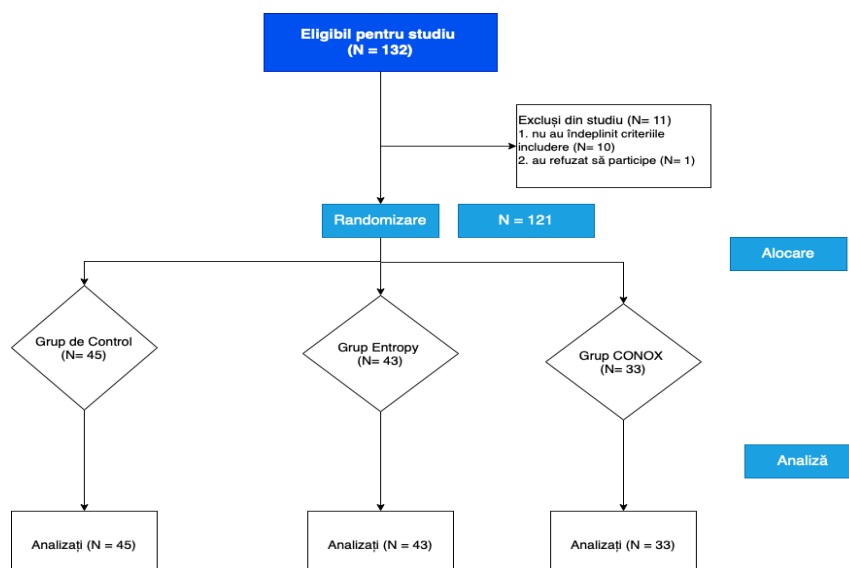


Figure 2. Study Flowchart

### 3. FINDINGS

#### 3.1. DEMOGRAPHIC AND CLINICAL DESCRIPTION OF ANALYZED GROUPS

In this study, 132 patients were enrolled according to the inclusion and exclusion criteria during the analyzed period. By applying the randomization process, 45 patients were assigned to Group 1, 43 patients were assigned to Group 2, 33 patients were assigned to Group 3 and 11 patients were left out as they did not meet the eligibility criteria. Descriptive statistical analysis of the groups revealed a homogeneous distribution of patients between the three study groups. Age was an important demographic parameter in the detailed analysis of the study groups.

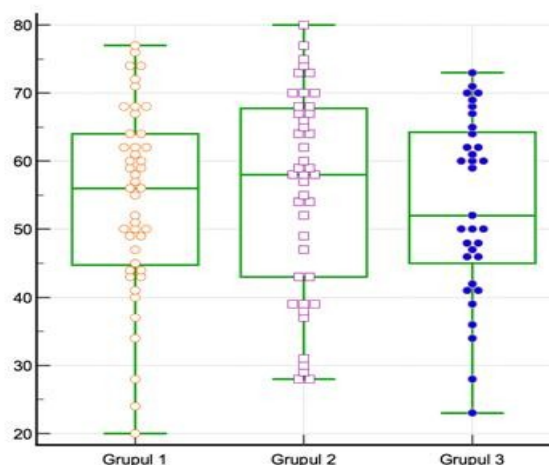
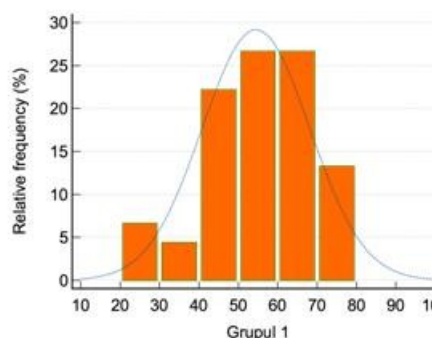


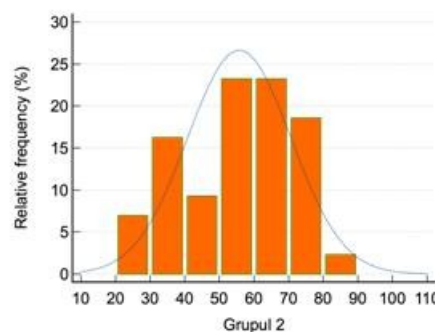
Figure 3. Age statistical distribution (Box-and-whisker, Plot all Data, expressed for mean and 95% CI of the mean)

Patients in the Control Group (Group 1) had a mean age of 54.467 (95% CI 50.356 - 58.578, median 56, standard deviation 13.6841), in Group 2 the mean age was 55.744 (95% CI 51.133 - 60.356, median 58, standard deviation 14.9843), and in Group 3 the mean age was 53.395 (95% CI 48.687 - 58.101, median 52, standard deviation 13.2758) (Figure 15).



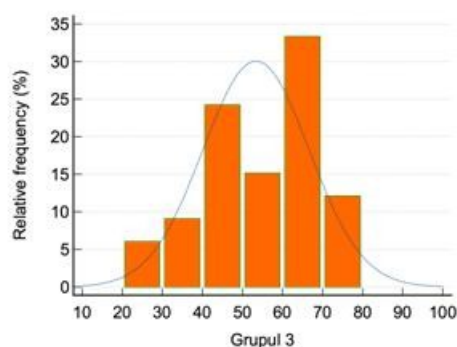
Variable	Grupul 1
Sample size	45
Lowest value	20.0000
Highest value	77.0000
Arithmetic mean	54.4667
Standard deviation	13.6841

Inte	Number of c
10 to	0
20 to	3
30 to	2
40 to	10
50 to	12
60 to	12
70 to	6
80 to	0
90 to	0



Variable	Grupul 2
Sample size	43
Lowest value	28.0000
Highest value	80.0000
Arithmetic mean	55.7442
Standard deviation	14.9843

Inter	Number of c
10 to	0
20 to	3
30 to	7
40 to	4
50 to	10
60 to	10
70 to	8
80 to	1
90 to	0
100 to	0



Variable	Group 3
Sample size	33
Lowest value	23.0000
Highest value	73.0000
Arithmetic mean	53.3939
Standard deviation	13.2758

Interval	Number of cases	%
10 to 20	0	0.00
20 to 30	2	6.06
30 to 40	3	9.09
40 to 50	8	24.24
50 to 60	5	15.15
60 to 70	11	33.33
70 to 80	4	12.12
80 to 90	0	0.00
90 to 100	0	0.00

**Figure 2. Age distribution in the study groups and descriptive statistical analysis**

Statistical analysis of the age of the patients included in the five study groups did not reveal statistically significant differences, as follows: Group 1 vs. Group 2 ( $p = 0.6466$ ), Group 1 vs. Group 3 ( $p = 0.9069$ ). Detailed statistical analysis is shown in Table 7.

**Table 2. Statistical analysis of age in the five study groups**

Statistical parameter	Group 1 vs Group 2	Group 1 vs Group 3
Mean difference	1.3954	-0.3636
Standard deviation of differences	19.8149	17.7302
Standard error of mean difference	3.0218	3.0863
95% CI of difference	-4.7027 to 7.4934	-6.6505 to 5.9233
Test statistic t	0.463	-0.119
Degrees of Freedom (DF)	42.00	32.00
Two-tailed probability	$P = 0.6466$	$P = 0.9069$

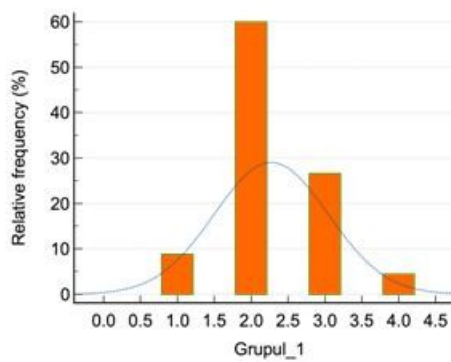
In terms of gender distribution, no statistically significant differences were found between the three groups. Table 8 summarizes the gender distribution in the three study groups.

**Table 3. Gender distribution of patients included in the three study groups**

Sex (M/F)	Control Group (Group 1)	Entropy Group (Group 2)	CONOX Group (Group 3)
F	21	21	15
M	22	22	18
N =	45	43	33

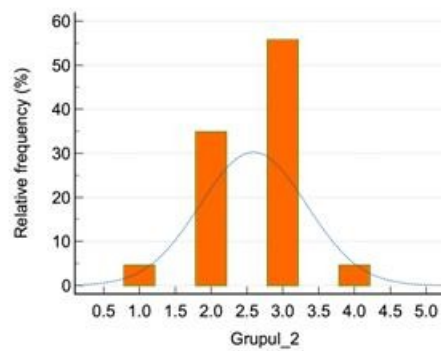
Another important feature in defining the study groups is the ASA score. In Group 1, the median for ASA score was 2 (min 2, max 3, 25% Percentile 2, 75% Percentile 3, range 3, coefficient of variation 30.33%, test for normal distribution, D'Agostino - Pearson test  $p = 0.2598$ ). The median ASA in Group 2 was 3 (min 1, max 4, 25% Percentile 2, 75% Percentile 3, range 2, coefficient of variation 25.33%, test for normal distribution, D'Agostino - Pearson test  $p = 0.4587$ ), respectively in Group 3, the median for ASA was 3 (min 1, max 3, 25% Percentile 2, 75% Percentile 3, range 2, coefficient of variation 29.43%, test for normal distribution, D'Agostino - Pearson test  $p = 0.1453$ ).

No statistically significant differences were found between the three groups (Figure 16).



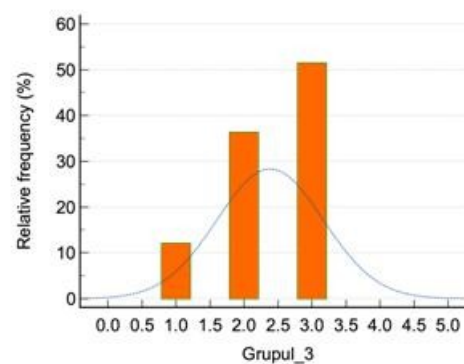
Variable	Grupul_1
Sample size	30
Lowest value	1.0
Highest value	4.0
Arithmetic mean	2.2
Standard deviation	0.6

Int	Number of
0.0	0
0.5	0
1.0	4
1.5	0
2.0	27
2.5	0
3.0	12
3.5	0
4.0	2



Variable	Grupul_2
Sample size	43
Lowest value	1.0
Highest value	4.0
Arithmetic mean	2.6
Standard deviation	0.6

Int	Number of
0.5	0
1.0	2
1.5	0
2.0	15
2.5	0
3.0	24
3.5	0
4.0	2
4.5	0

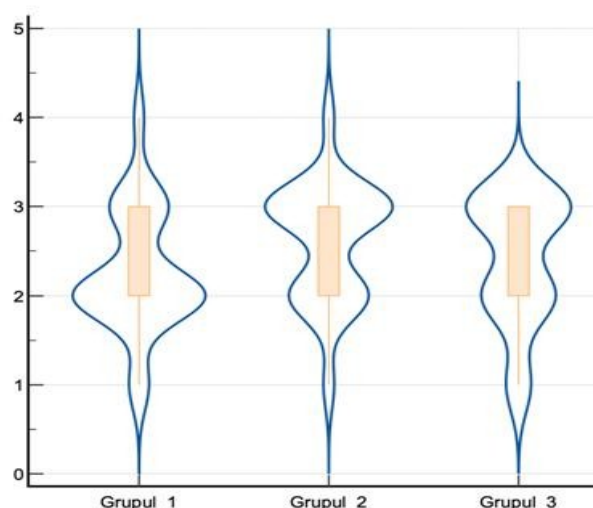


Variable	Grupul_3
Sample size	30
Lowest value	1.0
Highest value	3.0
Arithmetic mean	2.3
Standard deviation	0.7

Int	Number of
0.0	0
0.5	0
1.0	4
1.5	0
2.0	12
2.5	0
3.0	17
3.5	0
4.0	0
4.5	0

Figura 3. . ASA distribution in the study groups and descriptive statistical analysis

Figure 17 shows the distribution of the ASA score across the three study groups.



**Figure 6. Statistical distribution of the ASA score (Box-and-whisker, Violin Plot, Plot all Data, expressed for median and 95% CI of the median)**

In terms of type of surgery, in Group 1, 23 patients received laparoscopic cholecystectomy, 14 patients underwent surgery for umbilical hernia, and 8 patients underwent thyroidectomy. In Group 2, 19 patients underwent laparoscopic cholecystectomy, 20 patients umbilical hernia and 7 patients thyroidectomy. Laparoscopic cholecystectomy was applied to 9 patients in Group 3, 9 patients underwent umbilical hernia, and thyroidectomy was performed in 15 patients. (Table 9).

**Table 4. Distribution of patients in the three study groups by type of surgery**

Feature	Group 1	Group 2	Group 3
<b>Total no. of patients</b>	<b>45</b>	<b>43</b>	<b>33</b>
Laparoscopic cholecystectomy, N (%)	23 (51)	19 (35)	9 (30)
Umbilical hernia, N (%)	19 (29)	20 (40)	7 (24)
Thyroidectomy, N (%)	9 (20)	9 (26)	15 (45)

The heart rate on admission to the operating theater was  $74.82 \pm 13.20$  (lower 95% CI of mean 70.86, upper 95% CI of mean 78.79, coefficient of variation 17.65%) in Group 1,  $84.05 \pm 24.92$  (lower 95% CI of mean 76.38, upper 95% CI of mean 91.72, coefficient of variation 29.65%) in Group 2 and  $81.2 \pm 14.69$  (lower 95% CI of mean 76.00, upper 95% CI of mean 86.42, coefficient of variation 18.09%) in Group 3 (Figure 18).

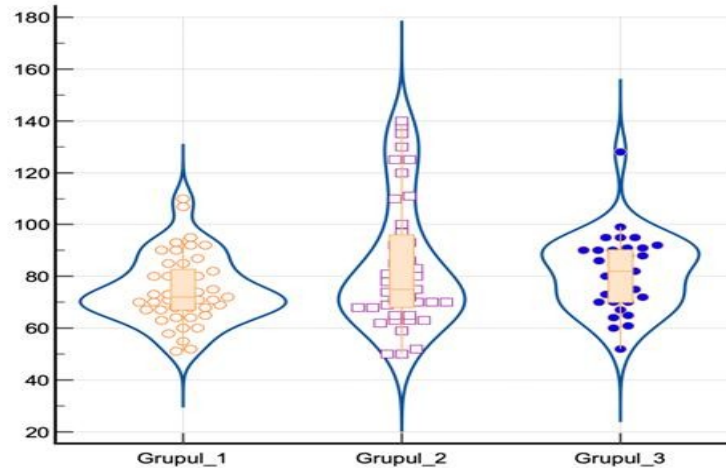


Figure 7. Statistical distribution of starting heart rate (on admission to the operating theater) (Box-and-whisker, Violin Plot, Plot all Data, expressed for the mean and 95% CI of the mean)

Statistical analysis for starting heart rate showed no statistical differences between groups as follows: Group 1 vs. Group 2 ( $P = 0.6558$ ), Group 1 vs. Group 3 ( $P = 0.0692$ ). Table 10 shows the statistical analysis in detail for heart rate within the five groups, the normal distribution and the corresponding histograms.

In the case of systolic blood pressure (mmHg) on admission to the operating theater, the mean value in Group 1 was  $143.8 \pm 25.02$  mmHg (lower 95% CI of mean 136.2, upper 95% CI of mean 151.3, coefficient of variation 17.41%), in Group 2 was  $138.3 \pm 34.79$  (lower 95% CI of mean 127.6, upper 95% CI of mean 149.0, coefficient of variation 25.15%), and in Group 3 the mean value was  $131.8 \pm 17.85$  (lower 95% CI of mean 125.5, upper 95% CI of mean 138.2, coefficient of variation 13.53%) (Figure 19).

Statistical analysis of the starting blood pressure (on admission to the operating theater) did not reveal statistically significant differences between the three groups analyzed, as follows: Group 1 vs. Group 2 ( $P = 0.4345$ ), Group 1 vs. Group 3 ( $P = 0.0500$ ). Table 11 summarizes the descriptive statistical analysis, normal distribution and histograms.

#### 3.3.2.4. Comparative statistical analysis of systolic blood pressure (Group 1 vs. Group 2; Group 1 vs. Group 3; Group 2 vs. Group 3)

For a statistically adequate assessment of the impact of multimodal monitoring on systolic blood pressure expression, it is important that the three study groups are statistically homogeneous. Specifically, it is important that systolic blood pressure values do not differ statistically significantly at the time of admission to the operating theater.

The statistical analysis of systolic blood pressure values (mmHg) at T0 identified no statistically significant differences between Group 1 and Group 2 ( $p = 0.3273$ , Fcrit 3.9518, F 0.9705, SS 909.1106) (Figure 55), respectively between Group 1 and Group 3 ( $p = 0.0778$ , Fcrit 3.9667, F 3.1952, SS 1434.3362) (Figure 56). Likewise, no statistically significant differences were found between the study groups in which multimodal monitoring of hypnosis was applied ( $p = 0.7328$ , Fcrit 3.9702, F 0.1173, SS 94.5074) (Figure 57).

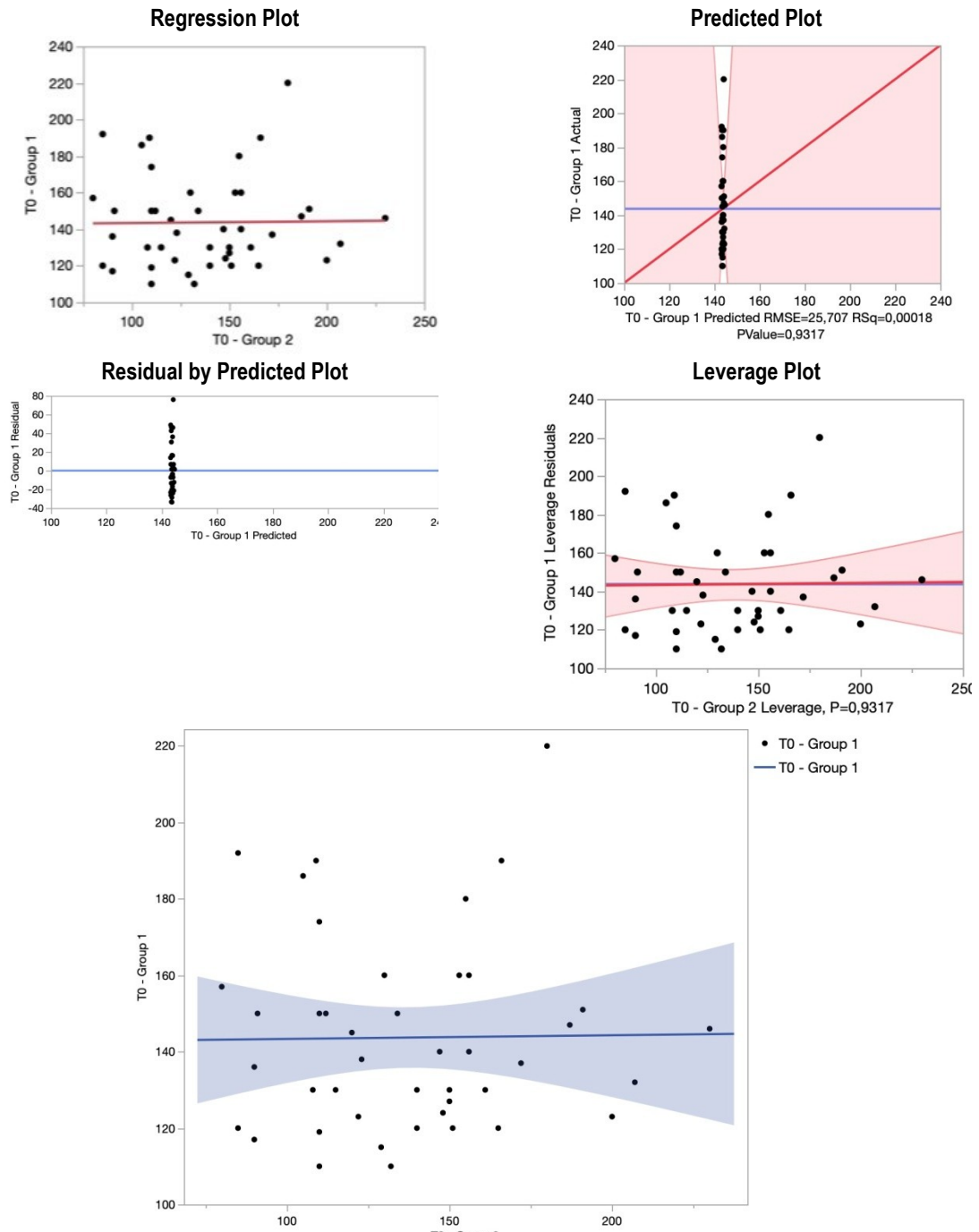


Figure 8. Descriptive statistical analysis of systolic blood pressure values (mmHg) on admission to the operating theater: Group 1 vs. Group 2

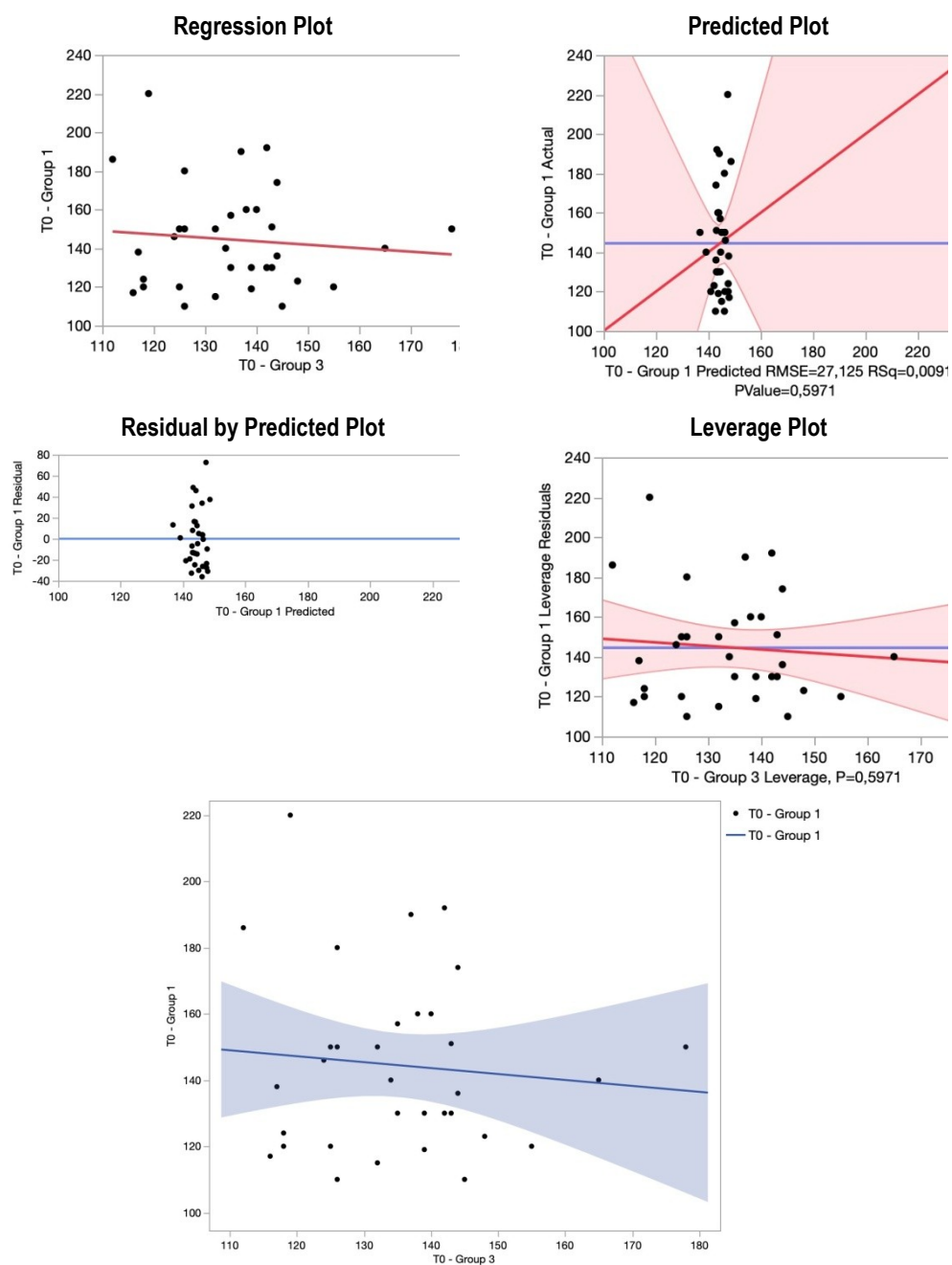
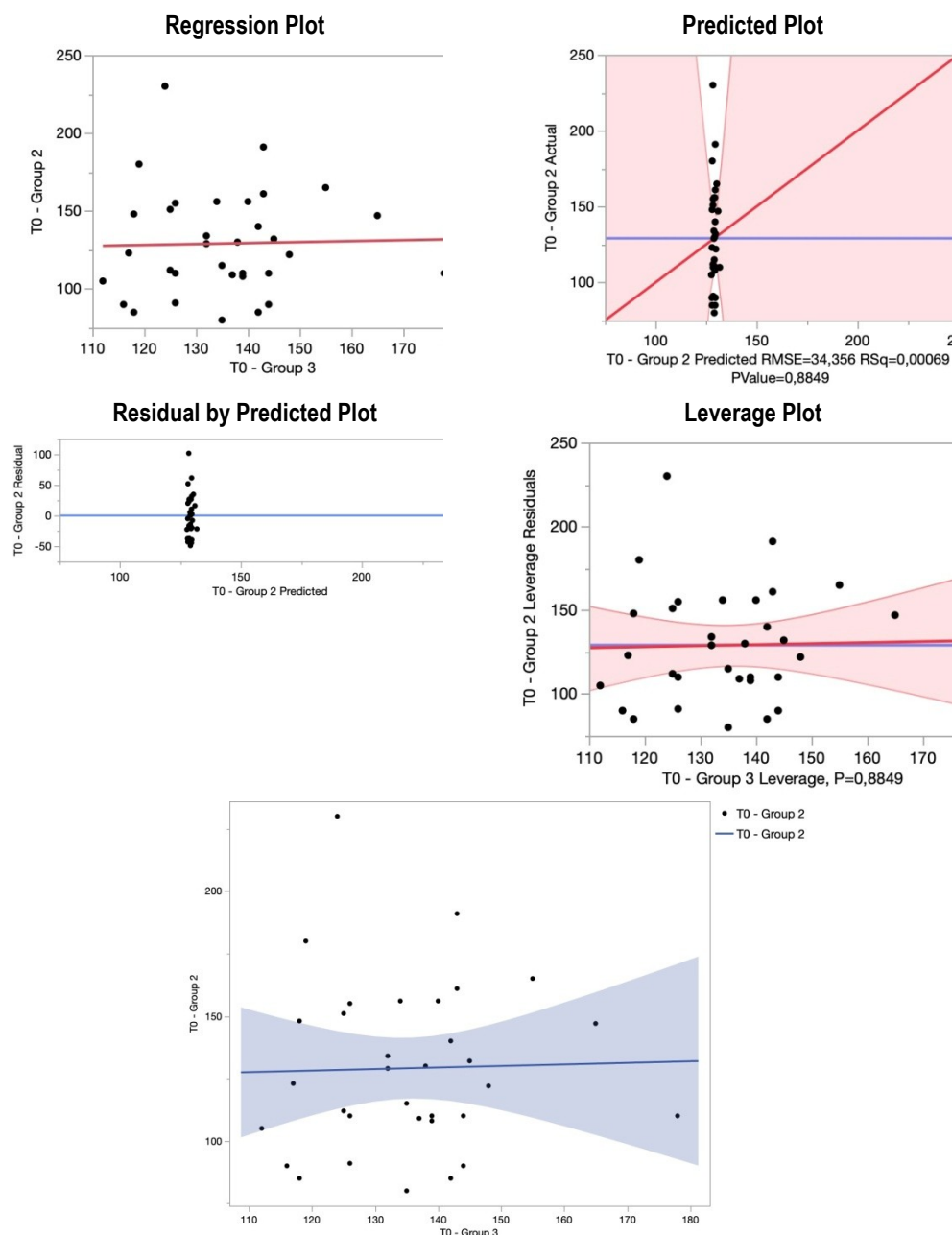


Figure 9. Descriptive statistical analysis of systolic blood pressure values (mmHg) on admission to the operating theater: Group 1 vs. Group 3





**Figure 10. Descriptive statistical analysis of systolic blood pressure values (mmHg) on admission to the operating theater: Group 2 vs. Group 3**

In Group 1 of the study (control group) a total of one episode of hypotension and 71 episodes of hypertension were recorded. Regarding the incidence of hemodynamic events associated with blood pressure, the analyzed data are presented in Table 32.

**Table 5. Incidence (%) of hemodynamic events associated with systolic blood pressure (mmHg) in Study Group 1**

	Group 1 (N = 45)						
	T15	T30	T60	T90	T120	Tfin	Total
No. of hypotension	0	0	0	0	0	1	1
No. of hypertension	14	18	19	12	6	2	71
% (incidence) hypo	0%	0%	0%	0%	0%	2%	2%
% (incidence) hyper	31%	40%	42%	27%	13%	4%	158%

Study Group 2 had a total of 5 hypotension and 46 hypertension events. The incidence analysis is shown in Table 33.

**Table 6. Incidence (%) of hemodynamic events associated with systolic blood pressure (mmHg) in Study Group 2**

	Group 2 (N = 43)						
	T15	T30	T60	T90	T120	Tfin	Total
No. of hypotension	1	0	1	0	2	1	5
No. of hypertension	14	10	6	7	7	2	46
% (incidence) hypo	2%	0%	2%	0%	5%	2%	12%
% (incidence) hyper	33%	23%	14%	16%	16%	5%	107%

Study Group 3 had 15 hemodynamic events of hypotension and 23 of hypertension, and the incidence analysis (%) is shown in Table 34.

**Table 7. Incidence (%) of hemodynamic events associated with systolic blood pressure (mmHg) in Study Group 2**

	Group 3 (N = 33)						
	T15	T30	T60	T90	T120	Tfin	Total
No. of hypotension	2	2	3	3	3	2	15
No. of hypertension	3	10	3	3	3	1	23
% (incidence) hypo	6%	6%	9%	9%	9%	6%	45%
% (incidence) hyper	9%	30%	9%	9%	9%	3%	70%

Statistical analysis of the total number of hemodynamic events between the three study groups did not reveal any statistical difference in hypotension between the control and entropy-monitored groups, but significant differences in favor of the CONOX-monitored group were found. Between groups, significant differences were found in the incidence of hypertension, with the control group being significantly higher than the groups in which either Entropy or CONOX was monitored. No significant differences were found between Groups 2 and 3 in the hemodynamic profile represented by the incidence of the number of episodes associated with systolic blood pressure (Table 41).

**Table 8. p-values - statistical analysis between groups**

	TOTAL % (incidence) hypo	TOTAL % (incidence) hyper
Group 1 vs. Group 2	P > 0.05	P < 0.05
Group 1 vs. Group 3	P < 0.05	p < 0.05
Group 2 vs. Group 3	p < 0.05	P > 0.05

## CONCLUSIONS AND OWN CONTRIBUTIONS

The present study highlighted the impact of multimodal monitoring in general anesthesia on both intraoperative status and postoperative recovery. A total of 121 patients were included in the analysis and randomized into three study groups. Thus, three study groups were set up, as follows: Group 1 - control group, where anesthesia was performed according to the conventional protocol, Group 2 - study group, where general anesthesia was titrated according to entropy parameters (RE and SE), and Group 3 - study group, where anesthetic management was performed using CONOX parameters (qNOX and qCON). Statistically, the groups were homogeneous, thus allowing statistical comparisons.

A positive impact of multimodal monitoring on hemodynamic stability was observed in the study groups, with a significant reduction in both heart rate and systolic blood pressure deviations from baseline. Interestingly, no major differences with statistical significance were found between the two methods used. In terms of post-anesthesia recovery, the use of modern techniques in monitoring the degree of hypnosis showed a significant impact, with reduced post-anesthesia awakening time and reduced incidence of post-anesthesia side effects (PONV). For these parameters, patients in group 2 reported a lower incidence of PONV than group 3, and a shorter awakening time. This emphasizes the characteristics of Entropy versus CONOX parameters, represented by the faster response of EEG and EMG stimuli, respectively the display of a higher accuracy response.

Another important aspect noted in the study is the statistically significantly lower fluid volume requirement in patients in whom general anesthesia was guided using the two monitoring methods. Also of note is that no statistically significant differences in fluid volume requirements were found between the two methods.