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Risk factors for intraoperative hypotension during thyroid surgery

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G

ABCDEFG 1,2 Nevena Kalezic
CDEF 3 Marina Stojanovic
AB 3 Nebojsa Ladjevic
ABC 3 Dejan Markovic
ABC 1,2 Ivan Paunovic
ABC 3 Ivan Palibrk
CDE 3 Biljana Milicic
BCD 2 Vera Sabljak
BCD 2 Vesna Antonijevic
AFG 4 Branislava Ivanovic
AFG 5 Djordje Ugrinovic
ABCDEFG 1,2 Vladan Zivaljevic

1 Faculty of Medicine, University of Belgrade, Belgrade, Serbia
2 Centre for Endocrine Surgery, Clinical Centre of Serbia, Belgrade, Serbia
3 Centre for Anaesthesia, Clinical Centre of Serbia, Belgrade, Serbia
4 Clinic for Cardiology, Clinical Centre of Serbia, Belgrade, Serbia
5 Faculty of Medicine, University of Kragujevac, Kragujevac, Serbia

Corresponding Author: Nevena Kalezic, e-mail: casopis.anestezija@gmail.com
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Background: Hypotension is a common adverse effect of IV anaesthetics, especially during the induction of anaesthesia. The aim of our study was to determine the incidence and risk factors for intraoperative hypotension (IOH) in thyroid surgery, as well as to determine whether and to what extent IOH affects the occurrence of postoperative hypotension.

Material/Methods: The study included 1252 euthyroid patients, ASA 2 and ASA 3 status (American Society of Anesthesiologists physical status classification), who had thyroid surgery between 2007 and 2011. IOH was defined as a decrease in systolic blood pressure of >20% of baseline values. We studied the influence of demographic characteristics (sex, age, body mass index-BMI), comorbidity, type and duration of surgery, and anaesthesia on the occurrence of IOH. Univariate and multivariate logistic regression were used to determine predictors of occurrence of IOH.

Results: IOH was registered in 6.5% of patients. The most common operation was thyroidectomy. Patients with IOH were younger, had lower BMI, and significantly less often had hypertension as a coexisting disease. The multivariate regression model identified BMI and the absence of hypertension as a coexisting disease, and as independent predictors of occurrence of IOH. Significantly more patients with IOH had postoperative hypotension (9.9% *vs.* 2.4%, p=0.000).

Conclusions: IOH is common, even during operations of short duration and with minimal bleeding. It is necessary to pay special attention to these patients, given that many of these patients remained hypotensive during the postoperative period.

Key words: predictors • intraoperative • hypotension • thyroid gland • surgery

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2474 4 — 23

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Background

Maintaining hemodynamic stability is one of the main goals of anaesthesia. Intraoperative hypotension (IOH) is a common adverse effect of IV anaesthetics, but this effect is of short duration (usually 15 minutes or less), and is related to the period of induction of anaesthesia [1]. Operations of longer duration may be associated with significant fluid loss by perspiration, which may be followed by hypotension, even in the absence of significant intraoperative bleeding. If IOH lasts long enough, it may disturb organ perfusion and lead to irreversible ischemic damage. Previous studies have shown an association between IOH and perioperative myocardial infarction and stroke [2–4], as well as an influence on higher mortality in cardiac and non-cardiac surgery [5,6]. The influence of IOH has been confirmed in transplantation surgery. IOH is an independent predictor of kidney rejection [7], as well as the appearance of new onset atrial fibrillation (NOAF) after carotid endarterectomy [8].

However, there is little data about the impact of IOH on post-operative hypotension. Recently published results [4] indicate that precisely this post-operative hypotension could affect the occurrence of complications. Therefore, the primary objective of our study was to determine the incidence and risk factors for IOH in thyroid surgery patients with comorbidity. A secondary objective was to determine to what extent IOH affects the occurrence of postoperative hypotension.

Material and Methods

Study design

This prospective study was conducted between January 2007 and December 2011 at the Centre for Endocrine Surgery, University Clinical Centre of Serbia, Belgrade, where most patients with thyroid pathology in Serbia undergo surgery. The study was approved by the ethics committee of the Clinical Centre of Serbia; signed patient consent was waived because the treatment of patients did not differ from the usual; and no protected health information was collected.

Study patients

Eligible patients were those aged 18 years and older presenting for thyroid surgery at the University Clinical Centre of Serbia. From a total of 2293 patients, we excluded 758 patients with ASA 1 status (American Society of Anesthesiologists physical status classification, relating to the assessment of operational risk in relation to comorbidity) because these are patients without comorbidity. We also excluded 271 patients with hypo- and hyperthyroidism because of possible influence on hemodynamic instability during surgery. Twelve patients who had an average basal value of SBP less than 90 mmHg were excluded from the study. A total of 1252 euthyroid patients ASA 2 and ASA 3 were included. Our patients had the following admission diagnoses: 1) nodular goiter – 350 (28%); 2) multinodular goiter – 652 (52%); 3) thyroid gland cyst – 9 (0.7%); 4) recurrent goiter – 69 (5.5%); 5) papillary carcinoma – 78 (6.2%); 6) medullary carcinoma – 69 (5.5%); 7) Hürthle cell carcinoma – 8 (0.6%); 8) follicular carcinoma – 5 (0.4%); and 9) oxyphil lesion – 12 (0.9%).

Definition of intraoperative hypotension

Intraoperative hypotension (IOH) was defined as a decrease in systolic blood pressure (SBP) of ≥20% over the basal value, for 15 minutes. Baseline value of SBP was defined as the average value of SBP measured during the preoperative evaluation of patients in the operating room before induction of anaesthesia, thus the measurements required at least 1 blood pressure measurement before administration of drugs. We defined the time of induction as either the moment of administration of induction agents or 3 min before the first appearance of continuous expired carbon dioxide registration, whichever came first [9]. In the postoperative period, blood pressure values were also measured using a non-invasive method, every 15 min during the first hour, every 30 mins during the next 6 hours, and then every hour for 24 hours. If the registered intraoperative hypotension was maintained for more than 20 min, therapy was applied first using colloidal solution and then vasopressors, with the dose and duration decided by the treating anesthesiologist. Antihypertensive therapy in patients with diagnosed hypertension was applied on a daily basis including the day of surgery, except ACE-inhibitors, which were excluded for at least 24 hr before surgery because of their possible protracted hypotensive effect. The observed values of blood pressure were recorded at least every 5 min using non-invasive measurements and recorded in the list of anesthesia.

Variables studied

We investigated the influence of the following preoperative characteristics on the occurrence of IOH: age, sex, BMI (< or >25 kg/m^2), ASA score, admission diagnoses, and comorbidity. The following coexisting diseases were observed: hypertension, cardiomyopathy (CMP), angina pectoris (AP), cardiac rhythm disturbances (bradycardia, tachycardia, atrial fibrillation, ventricular and supraventricular extrasystoles VS/SVES), diabetes mellitus (DM) and DM course of treatment (insulin, oral therapy, diet), kidney disease (chronic and terminal renal failure), and anaemia (defined as hemoglobin (Hgb) value of less than 12 mg/dl).

We noted the influence of the following intraoperative characteristics: difficult intubation of trachea (defined as the inability

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to visualize the glottis during laryngoscopy, Cormack-Lehane grades 3 and 4), type of operation (total thyroidectomy *vs.* others), duration of surgery (min), and time under general anaesthesia (in minutes).

Type of anaesthesia

All surgery was performed during general anaesthesia. The patient's position on the operating table, adapted to the type of operation-thyroidectomy, involves the extension of the head and lifted shoulders, so that the head and thoracic part are raised to about 25° to the horizontal plane. This position was used in all patients. Patients were pre-medicated 20 min prior to surgery (Midazolam 0.1 mg/kg and Atropine 0.5 mg IM). During induction, all patients received Fentanyl 0.05–0.1 mg and Propofol in 1.5 mg/kg doses. To facilitate intubation, we used Succinylcholine 1.1 mg/kg, and maintained further relaxation with Rocuronium 0.5 mg/kg. Anaesthesia was maintained with Fentanyl (5 µg/kg) and a mixture of gases – air (2 L/min), oxygen (2 L/min), and Sevoflurane – at an appropriate concentration.

Statistical analysis

All data were presented and analyzed in SPSS database, version 12. Numerical variables such as age, duration of surgery and time under general anaesthesia are shown in the form of mean values ±SD (standard deviation), while the other categorical variables are shown as absolute numbers and percentages. Patients were divided into 2 groups; the group with IOH and the group without IOH. The normality of data distribution was checked by 1-sample Kolmogorov-Smirnov test. We used the t test to compare the average values of the parametric features, and Pearson's chi-square test was used to compare the differences in frequency of categorical features. Predictors of occurrence of IOH were determined by logistic regression analysis. P values <0.05 were considered statistically significant.

Results

The majority of our patients were women, ASA 2 status, with an average age of 56 years (Table 1). Most of them had a history of hypertension (66.5%), and the most common cardiac rhythm disturbances were atrial fibrillation (2.9%), tachycardia (1.9%) and extrasystoles (1.8%), while the rarest was bradycardia (0.2%). The most common admission diagnosis was benign goiter - 1080 (86.26%), whereas malignant tumours were rarely represented – 172 (13.74%).

Table 2 presents comparative characteristics of patients with and without IOH. IOH was registered in 81 (6.5%) patients. Patients with IOH were younger and had lower BMI. When we looked at age as a categorical variable, with 50 years as a cut-off value, more patients >50 years were registered in the group without IOH. Significantly more patients without IOH had a history of hypertension, as opposed to CMP and heart rhythm disturbances, which were more often registered in patients with IOH, but without statistical significance. Difficult intubation was also more often registered in patients with IOH compared to patients without IOH (14.8% *vs.* 12.1%), but without statistical significance. Significantly more patients who had IOH also had hypotension in the postoperative period (9.9% *vs.* 2.4%, p=0.000). We used the logistic regression model to determine the influence of each variable on the occurrence of IOH. Univariate analysis showed that younger age, lower BMI, and absence of hypertension as coexisting diseases influenced the occurrence of IOH (Table 3). Multivariate analysis showed that independent predictors for IOH were BMI <25 kg/m^2 and the absence of hypertension as a coexisting disease (Table 4).

Table 1. Patients characteristics.

Variable	n (%)
Age (Mean ± SD)	56.86±11.42
Sex (female)	1081 (86.3%)
(male)	171 (13.7%)
ASA	
ASA II	1004 (80.2%)
ASA III	248 (19.8%)
BMI >25 kg/m^2	823 (65.7%)
Hypertension	832 (66.5%)
CMP	98 (7.8%)
Cardiac rhythm disturbances	85 (6.8%)
Angina pectoris	62 (5.0%)
DM	149 (11.9%)
Insulin dependent	44 (3.5%)
Kidney disease	22 (1.8%)
Anaemia	43 (3.4%)
DI	153 (12.2%)
Type of surgery (total thyroidectomy)	959 (76.6%)
Duration of surgery (min) (Mean ±SD)	69.5±24.1
TUGA (min) (Mean ±SD)	79.43±24.67
Postoperative hypotension	36 (2.9%)

* SD – standard deviation; ASA – American Society of Anaesthesiologists; BMI – Body Mass Index; CMP – Cardiomyopathy; DM – Diabetes mellitus; DI – difficult intubation; TUGA – time under general anaesthesia.

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Table 2. Characteristics of the patients with and without IOH.

Variable	Patients with IOH* n=81 (6.5%)	Patients without IOH n=1171 (93.5%)	P value
Age (Mean ± SD)	54.4±1.8	57.03±11.4	**0.033
Sex (female) (male)	71 (87.7%) 10 (12.3%)	1010 (86.3%) 161 (17.7%)	0.722
ASA ASA II ASA III	 69 (85.2%) 12 (14.8%)	 935 (79.9%) 235 (20.1%)	 0.249
BMI >25 kg/m^2	38 (46.9%)	785 (67%)	**0.000
Hypertension	38 (46.9%)	794 (67.8%)	**0.000
CMP	8 (9.9%)	90 (7.7%)	0.478
Cardiac arrhythmias	9 (11.1%)	76 (6.5%)	0.110
Angina pectoris	4 (4.9%)	58 (5.0%)	0.995
DM	7 (8.6%)	142 (12.1%)	0.349
DM on insulin	2 (28.6%)	42 (29.6%)	0.983
Kidney disease	0 (0.0%)	22 (1.9%)	0.213
Anaemia	3 (3.7%)	40 (3.4%)	0.891
DI	12 (14.8%)	141 (12.1%)	0.561
Type of surgery#	58 (71.6%)	901 (76.9%)	0.362
Duration of surgery (min)	65.8±20.1	69.7±24.3	0.203
TUGA (min)	75.7±21.5	79.6±24.9	0.191
Postoperative hypotension	8 (9.9%)	28 (2.4%)	0.000

* IOH – intraoperative hypotension; SD – standard deviation; ASA – American Society of Anaesthesiologists; BMI – Body Mass Index; CMP – Cardiomyopathy; DM – Diabetes mellitus; DI – difficult intubation; TUGA – time under general anaesthesia; # thyroidectomy; ** Statistically significant.

Discussion

Our results show that the incidence of IOH in thyroid surgery is 6.5%. BMI <25 kg/m^2 and hypertension (as a protective factor) were found to be independent predictors of occurrence of IOH.

Because of the very large number of different definitions mentioned in the literature, it is very difficult to determine the exact incidence of IOH. Bijker et al. found 140 different definitions of intraoperative hypotension in their meta-analysis, thus the incidence of intraoperative hypotension varied between 5% and 99% [9]. They also showed that the most commonly used definitions of IOH are SBP <80 mmHg or a decrease of more than 20% compared to baseline values. We decided to define IOH as decrease of SBP for more than 20% from baseline values, because we believe that this kind of a definition better reflects the hemodynamic instability. In our study, measurements were done using a non-invasive method. Wax et al. [10] showed that the values of BP measured by a non-invasive method were generally higher during periods of hypotension and lower during periods of hypertension, compared to values obtained by an invasive method.

Most studies have shown that age is an important risk factor for intraoperative complications [11–14]. However, in recent years greater attention is given to the so-called biological age compared to chronological age. In fact, it was shown that age alone does not affect the occurrence of complications if there are no comorbidities. Similar results were obtained in thyroid surgery. Passler et al showed that patients older than 75 years often exhibit intra- and postoperative complications, but age is not an independent predictor of their occurrence, in contrast to the ASA score [15]. Therefore, we decided to include only patients with comorbidity or ASA 2 and ASA 3 patients. In contrast to previous studies [11,12,14], in our study ASA score did not affect the occurrence of IOH. Probably because

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Table 3. Univariate logistic regression analysis.

Variable	OR (95%CI)		P Value
ASA	0.212	(0.878–1.647)	0.252
Age	1.019	(1.000–1.039)	**0.047
Sex	0.884	(0.446–1.749)	0.722
BMI	2.301	(1.463–3.620)	**0.000
Hypertension	0.383	(1.515–3.750)	**0.000
Cardiac arrhythmias	0.555	(0.267–1.153)	0.115
Angina pectoris	1.003	(0.355–2.863)	0.995
CMP	0.760	(0.355–1.626)	0.479
DM	1.459	(0.659–3.229)	0.352
Insulin dependent DM	1.018	(0.209–4.947)	0.983
Kidney disease	1.1E+0.8	(0.000–)	0.998
Type of surgery	1.080	(0.902–1.292)	0.404
Difficult intubation	0.851	(0.493–1.468)	0.562
Duration of surgery (min)	1.229	(0.918–1.645)	0.165
TUGA (min)	1.095	(0.834–1.439)	0.512

* OR-Odds Rations; CI – confidence interval; ASA – American Society of Anaesthesiologists; BMI – Body Mass Index; CMP – Cardiomyopathy; DM – Diabetes mellitus; TUGA – time under general anaesthesia; ** Considered statistically significant.

we included relatively younger patients with comorbidity, significantly more ASA 2 in relation to ASA 3 patients (1004 *vs.* 201), with hypertension as the most common comorbidity, which was well regulated.

The period of anaesthesia when hypotension is most frequent is the induction of anaesthesia, before surgical stimulation. Reich et al showed that severe hypotension after induction of anaesthesia is quite common, especially during the first 5–10 minutes after induction. They showed that 9% of patients experienced severe hypotension and that it was affected by age ≥50 years, hypotension before induction, the use of Propofol for induction of anaesthesia, ASA status (ASA III–V *vs.* ASA 1–2), and the increase of induction dose of Fentanyl. The mean dose of Propofol was 2.4 mg/kg/tt and it was shown that the IOH was significantly more frequent in patients who received higher doses, especially ASA III–V [14]. In contrast, we excluded patients with preoperative hypotension, while other patients received significantly lower doses of Propofol during induction (1.5 mg/kg). In patients with reduced coronary reserve, even the milder form of hypotension, which would be considered acceptable in a standard practice, can lead to significant myocardial ischemia. This is particularly true in ASA 3 and ASA 4 patients who received Propofol during induction of anaesthesia [16].

Table 4. Multivariate logistic regression analysis.

Variable	OR (95% CI)		P value
Age	1.005	(0.986–1.025)	0.589
BMI	2.016	(1.255–3.239)	**0.004
Hypertension	1.895	(1.152–3.118)	**0.012

* OR-Odds Rations; CI – confidence interval; BMI – Body Mass Index; ** Considered statistically significant.

Regarding antihypertensive therapy, there are differing opinions, especially when it comes to ACE inhibitors. Kheterpal et al. [17] showed that preoperative administration of ACE I in combination with diuretics led to significantly higher occurrence of IOH compared to patients who received only diuretics. Coriat and Colson came to similar conclusions in their research, pointing to a significantly higher incidence of IOH in patients treated with ACE inhibitors [18,19]. However, Reich [14] demonstrated that ACE inhibitors or other antihypertensive therapy did not affect occurrence of IOH. It was also shown that preoperative administration of furosemide, including on the day of surgery, does not affect the occurrence of IOH [20]. As recommended by cardiologists, we excluded ACE inhibitors 24 hr before surgery because of the possible influence on intra-and postoperative hypotension, while all other antihypertensive drugs were used regularly, including on the day of surgery. As in the previously mentioned studies, we found no association between antihypertensive therapy and IOH. Our results show that previous hypertension acted protectively on the occurrence of IOH, probably because they are relatively young patients (average age of our patients was 56 years).

We also showed that BMI was lower in patients with IOH, and duration of surgery does not affect the occurrence of IOH, in contrast to other studies [7,11,13]. Thyroid surgery is considered to be low or moderate risk surgery. These operations are of short duration and they do not entail great loss of blood or other complications, in contrast to major abdominal or cardiac surgery in which the operation can last several hours and may be accompanied by a significant loss of blood. These differences could be a possible explanation for our results.

Anaesthesia in thyroid surgery has a high incidence of difficult intubations (DI). We registered DI in 12.2% of patients, more frequently in patients with IOH (14.8% *vs.* 12.1%), but it was not singled out as a predictor of IOH. Our previous studies showed that the incidence of DI in thyroid surgery was 5.5%, but this study involved ASA 1 patients as well [21].

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Bijker et al. [22] showed no causal relation between IOH and 1-year mortality, and that lower blood pressures are tolerated for shorter durations, especially in elderly patients. In contrast to these studies, Monique et al showed that IOH is an independent predictor for 1-year mortality, and that every minute of anaesthesia with BP <80 mmHg increases the risk of mortality by 3.6% [23].

In his most recent study, Bijker et al. [4] showed that IOH (decrease in mean arterial BP for >30% compared to baseline values) influenced the occurrence of postoperative ischemic stroke, as well as the evolution of a postoperative stroke by compromising (collateral) blood flow to ischemic areas. The results of this study also indicate that each minute of hypotension increases the risk for stroke by 1.3%. They also pointed to the importance of postoperative hypotension, and doubted that IOH may affect postoperative hemodynamic instability, and that postoperative hypotension could also affect the occurrence of complications such as stroke. The results of our study confirm this assumption. Our results showed that there is a high statistical significance between intraoperative and postoperative hypotension. If the patient has IOH, there is a high probability that they will have postoperative hypotension.

Conclusions

Taking into account all the above, we conclude that IOH is a dynamic phenomenon that is affected by many factors. Our study found that lower BMI and the absence of hypertension as a coexisting disease was an independent risk factor for IOH. To prevent postoperative complications, it is important to determine risk factors for IOH in order to regulate it properly. It is necessary to pay special attention to these patients, both intraoperatively and postoperatively, to improve the final outcome.

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