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Original Scientific Paper

PREDICTORS OF INTRAOPERATIVE HYPERTENSION IN NECK SURGERY: A SINGLE CENTER RETROSPECTIVE STUDY

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SUMMARY – Intraoperative hypertension (IOHTA) during neck surgery is undesirable because this type of surgery has a propensity to bleed profoundly even in normotensive anesthesia. The purpose of our study was to detect predictors of IOHTA in patients undergoing neck surgery. This single center retrospective study included 880 adult patients who underwent neck surgery under general anesthesia. The impact of gender, age, comorbidity, difficult tracheal intubation, anesthesia duration, and induced hypotension on IOHTA was studied. IOHTA was present in 57 (6.7%) patients. The highest incidence of IOHTA was recorded in patients with ASA 4 status and those with Cormack-Lehane grade 4,: (22.2% and 21.4%, respectively). Significantly more patients with hypertension, hyperlipoproteinemia and ventricular extrasystoles had IOHTA compared with patients without these comorbidities. Statistically significant predictors of IOHTA were age (OR 1.438; 95% CI 1.144-1.808; p=0.002), cardiac arrhythmia (OR 1.702; 95% CI 1.129-2.566; p=0.011), Cormack-Lehane grade (OR 1.407; 95% CI 1.054-1.878; p=0.020), and duration of anesthesia (OR 1.005; 95% CI 1.001-1.008; p=0.005). The risk of IOHTA occurrence was lower in patients with induced hypotension (OR 0.024; 95% CI 0.003-0.185; p=0.000). During neck surgery, special attention is needed in patients of older age, those with cardiac arrhythmia, difficult intubation, and longer anesthesia duration because they are at risk of IOHTA.

Key words: *Hypertension; Intraoperative period*

Introduction

The key factor of patient care for anesthetists is the perioperative blood pressure management[1]. A usual approach to intraoperative blood pressure management is to keep the intraoperative pressures in the range of ±20% of the baseline blood pressure[2] because prolonged changes of more than 20 mm Hg or 20% in relation to preoperative levels were significantly related to complications[3].

Intraoperative hypertension (IOHTA) is common and has many causes. In usually normotensive patients, the main cause of IOHTA is heightened sympathetic response, which is often triggered by perioperative stress factors such as fear, pain, laryngoscopy and tracheal intubation, inadequate anesthesia, hypercapnia and hypoxia. Blood pressures of patients with previous hypertension are similarly affected by the perioperative stressors[1,4,5].

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In the literature, there are many studies which showed that in case of severe IOHTA, or IOHTA of unknown cause, or if it fails to respond to routine measures, it could cause morbidity and mortality in some patients[6-9]. The prospective cohort observational study by Wiorek and Krzych found that increased postoperative 30-day mortality after non-cardiac surgery was associated with high systolic blood pressure (OR 4.55; 95% CI 1.48-13.93; p=0.008) and high diastolic blood pressure (OR 9.73; 95% CI 3.26-29.99; p<0.001)[10].

The head and neck have rich blood supply and surgical procedures in these regions have a propensity to bleed profoundly, particularly if blood pressure is high[11]. Maintaining normal blood pressure or even hypotension during neck surgery is very important for the following reasons: it reduces blood loss, ensures that the surgeon has a clear operative field, minimizes tissue swelling and bruising, and significantly decreases the incidence of hematoma postoperatively[12]. Because of all these reasons, IOHTA during neck surgery is undesirable.

The goal of our study was to investigate the predictors of IOHTA in patients during neck surgery.

Patients and Methods

This single center retrospective study included 880 patients who underwent neck surgery at the Hospital for Otorhinolaringology and Maxillofacial Surgery, University Clinical Center of Serbia. The Ethics Committee of the Medical Faculty, University of Belgrade, approved this study.

Inclusion criteria

The study included patients over the age of 18 who had neck surgery in the conditions of general anesthesia, American Association of Anesthesiologists (ASA) score 1-4. In case of emergency (partial airway obstruction caused by neck hematoma or laryngeal tumor) or urgency (phlegmon of the neck), patients with ASA score 4 underwent surgery in general anesthesia. Systolic blood pressure (SBP) elevated by ≥20% over the baseline value for at least 10 minutes or more was defined as IOHTA. The baseline blood pressure value was defined as the first blood pressure obtained in the operating theater before drug administration.

Perioperative management

Up to the day of surgery, patients took their antihypertensive drugs. If a β-adrenoceptor antagonist was part of chronic therapy, this drug was taken by the patients on the day of surgery.

Midazolam (0.07 mg/kg) intramuscularly was used for premedication. All patients were induced in general anesthesia with fentanyl 3 μg/kg and propofol 2 mg/kg. In order to facilitate intubation, rocuronium 0.6 mg/kg was used. When difficult airway was predicted, succinylcholine 1.5 mg/kg was used. Further relaxation was maintained with rocuronium 0.3 mg/kg. A mixture of gases, i.e., air (1 L/min) and oxygen (1 L/min) and sevoflurane at appropriate concentration were used for maintenance of anesthesia. In order to achieve and maintain SBP below 100 mm Hg (in case of hypotensive anesthesia) or to maintain intraoperative SBP in the range of ±20% of the baseline blood pressure (in case of normotensive anesthesia), we titrated the dosage of remifentanil. Hypotensive anesthesia induced by remifentanil was practiced, except for the cases in which hypotension was contraindicated. Patients who had coronary artery disease, stenosis of carotid arteries, previous cerebrovascular insult and hypertension were contraindicated for induced hypotension. Intraoperatively, blood pressure values were recorded every 5 minutes using noninvasive methods and written in the anesthetic chart. If the recorded IOHTA persisted for 10 minutes or more, antihypertensive therapy was applied.

The impact of gender, age, ASA status, comorbidity (cardiovascular, non-cardiovascular and associated cardiovascular and non-cardiovascular comorbidity), difficult tracheal intubation (Cormack-Lehane grade 3 or Cormack-Lehane grade 4), anesthesia duration (minutes), and induced hypotension on the occurrence of IOHTA was studied. We observed the following comorbidities: hypertension, ischemic heart disease, cardiomyopathy, cardiac rhythm disorders (atrial fibrillation, supraventricular extrasystoles, ventricular extrasystoles and tachycardia), diabetes mellitus, hyperlipoproteinemia, and kidney disease (chronic and end-stage renal failure).

Statistics

Patient age and anesthesia duration as numerical variables were expressed as mean ± standard deviation (SD), and categorical variables were expressed as absolute numbers and percentages. Our patients were recognized as a group of patients with IOHTA and a group without IOHTA. Kolmogorov-Smirnov test was used to check for the normality of data distribution. In order to compare differences between the patients with and without IOHTA, Mann-Whitney U test was used. We used Pearson's χ^2-test to compare

differences in the frequency of categorical features. Logistic regression analysis determined predictors of IOHTA occurrence. The level of statistical significance was set at $p<0.05$.

Results

Most of the patients were male (70.1%) and older than 50 years (64.9%). The majority of patients were without any comorbidity (44.8%). The mean anesthesia duration was 91.94±64.04 minutes. Of the 880 patients, IOHTA was recorded in 57 (6.7%) and induced hypotension was achieved in 24.8% of our patients.

Comparative characteristics of patients with and without IOHTA are shown in Table 1. There was no significant gender difference. IOHTA was more frequently recorded in patients older than 50 years than in those aged ≤50 years. IOHTA was most common in patients with ASA 4 status and those with Cormack-Lehane grade 4 (22.2% and 21.4%, respectively). We recorded IOHTA significantly more often in patients without induced hypotension than in patients with induced hypotension (8.8% *vs*. 0.5%, p=0.000). The mean duration of anesthesia was longer in patients with IOHTA (p=0.003). Regarding comorbidity, IOHTA was most frequent in patients with associated cardiovascular and non-cardiovascular comorbidity (12%). Patients with a history of hypertension had IOHTA significantly more often (9.0% *vs*. 5.4%;

Table 1. Characteristics of patients with and without intraoperative hypertension

Variable	Patients with IOHTA	Patients without IOHTA	p value
	n=59 (6.7%)	n=821 (93.3%)	
Gender			0.852
Male; n (%)	42 (6.8)	575 (93.2)	
Female, n (%)	17 (6.5)	246 (93.5)	
Age (yrs)			0.010
18-50	7(2.3)	303 (97.7)	
>50	52 (9.1)	518 (90.9)	
ASA classification			0.012
ASA I	19 (4.8)	375 (95.2)	
ASA II	20 (6.3)	296 (93.7)	
ASA III	18 (11.2)	143 (88.8)	
ASA IV	2 (22.2)	7 (77.8)	
Cormack-Lehane			0.024
1 or 2	52 (6.2)	790 (93.8)	
3	4 (16.7)	20 (83.3)	
4	3 (21.4)	11 (78.6)	
Induced hypotension			0.000
Yes	1 (0.5)	217 (99.5)	
No	58 (8.8)	64 (91.2)	
Intraoperative transfusion			0.886
Yes	1 (7.7)	12 (92.3)	
No	58 (6.8)	809 (93.3)	
Anesthesia duration (min)			0.003
(χ±SD)	111±78.11	93±57.93	

IOHTA = intraoperative hypertension; n = number of patients; ASA = American Association of Anesthesiologists

Table 2. Coexisting diseases in patients with and without intraoperative hypertension

	IOHTA		
			p value
With		Without	
n=59 (6.7%)		n=821 (93.3%)	
Comorbidity			**0.009**
Without comorbidity	18 (4.6)	373 (95.4)	
Cardiovascular	10 (5.2)	181 (94.8)	
Non-cardiovascular	11 (8.3)	121 (91.7)	
Cardiovascular and non-cardiovascular	20 (12.0)	146 (88.0)	
Preoperative hypertension			**0.042**
Yes	28 (9.0)	282 (91.0)	
No	31 (5.4)	539 (94.6)	
Preoperative cardiomyopathy			**0.746**
Yes	2 (8.3)	22 (91.7)	
No	57 (6.7)	799 (93.3)	
Preoperative ischemic heart disease			**0.747**
Yes	2 (5.4)	35 (94.6)	
No	57 (6.8)	786 (93.2)	
Cardiac arrhythmias			**0.001**
No cardiac arrhythmias	51 (6.1)	785 (93.9)	
Atrial fibrillation	4 (17.4)	19 (82.6)	
SVES	1 (14.3)	6 (85.7)	
VES	3 (37.5)	5 (62.5)	
Tachycardia	0	6 (100)	
Preoperative diabetes mellitus			**0.715**
Yes	6 (7.7)	72 (92.3)	
No	53 (6.6)	749 (93.4)	
Hyperlipoproteinemia			**0.015**
Yes	6 (16.7)	30 (83.3)	
No	53 (6.3)	791 (93.7)	
Kidney disease			**0.328**
Yes	1 (16.7)	5 (83.3)	
No	58 (6.6)	816 (93.4)	

IOHTA = intraoperative hypertension; n = number of patients; SVES = supraventricular extrasystoles; VES = ventricular extrasystoles

p=0.042). Significantly more patients with hyperlipoproteinemia had IOHTA compared to patients without hyperlipoproteinemia (16.7% *vs*. 6.3%, p=0.015). IOHTA was more often recorded in patients with coexisting ventricular extrasystoles than in those without cardiac rhythm disturbances (37.5% *vs*. 6.1%, p=0.001). We did not record significant differences between the groups according to the incidence of preoperative comorbidities such as cardiomyopathy, ischemic heart disease, diabetes mellitus, and kidney dis-

Table 3. Predictors of intraoperative hypertension in neck surgery

Logistic regression analysis				
Univariate			Multivariate	
Variable	OR (95% CI)	p value	OR (95% CI)	p value
Age	1.422 (1.175-1.722)	0.000	1.438 (1.144-1.808)	0.002
ASA classification	1.726 (1.015-2.936)	0.044	0.788 (0.364-1.709)	0.547
Comorbidity	1.430 (1.149-1.780)	0.001	1.349 (0.834-2.183)	0.223
Preoperative HTA	1.621 (1.177-2.231)	0.003	1.001 (0.493-2.032)	0.997
Cardiac arrhythmias	1.521 (1.079-2.146)	0.017	1.702 (1.129-2.566)	0.011
Hyperlipoproteinemia	2.985 (1.190-7.487)	0.020	1.797 (0.632-5.110)	0.272
Cormack-Lehane	1.425 (1.107-1.835)	0.006	1.407 (1.054-1.878)	0.020
Anesthesia duration	1.004 (1.002-1.007)	0.003	1.005 (1.001-1.008)	0.005
Induced hypotension	0.048 (0.007-0.349)	0.003	0.024 (0.003-0.185)	0.000

OR = odds ratio; CI = confidence interval; ASA = American Association of Anesthesiologists; HTA = hypertension

ease (Table 2). The independent predictors of IOHTA, determined by multivariate logistic regression analysis, were age (OR 1.438, 95% CI 1.144-1.808, p=0.002), Cormack-Lehane grade (OR 1.407, 95% CI 1.054-1.878, p=0.020), history of cardiac arrhythmia (OR 1.702, 95% CI 1.129-2.566, p=0.011) and anesthesia duration (OR 1.005, 95% CI 1.001-1.008, p=0.005). The risk of IOHTA occurrence was lower in patients with induced hypotension (OR 0.024, 95% CI 0.003-0.185, p=0.000) (Table 3).

Discussion

A study conducted by Charlson *et al.* showed that prolonged intraoperative changes in blood pressure (more than 10 minutes) by more than 20 mm Hg or 20% in relation to preoperative levels were significantly related to complications[3]. According to Schechtman *et al.* , the criterion for IOHTA was a relative increase by >20% in the first SBP value measured prior to anesthesia induction[13]. In our previous studies (Kalezic *et al.* and Sabljak *et al.*), an increase in SBP by minimum 20% over the value before anesthesia induction, for 15 minutes, was a definition of IOHTA during thyroid and primary hyperparathyroidism surgery[14,15]. According to these studies, our criterion for IOHTA was an increase in SBP by 20% or more over the baseline value for at least 10 minutes.

We found that the incidence of IOHTA in our study population was 6.7%. In the study by Paix *et al.*, IOHTA was recorded in 1.75% of 4000 patients, but no data on the types of surgery were included in the study[16]. A publication analyzing blood pressure data from anesthesia information monitoring systems found hypertension in 20% of 16 913 anesthetic cases[17]. During thyroid surgery, 61.4% of patients had IOHTA[14], whereas in surgery for primary hyperparathyroidism the incidence of IOHTA was 56.9%[15]. Compared to the incidence of IOHTA in thyroid surgery and primary hyperparathyroidism surgery, our incidence of IOHTA was low, probably because we practiced induced hypotension, which was achieved in 24.85% of patients during neck surgery. Kearney *et al.* found that 26.4% of the global population were affected by hypertension[18]. In our study, 310 (35.2%) patients had hypertension as a coexisting disease. In

a huge study by Levin *et al*., which included 52 919 patients, 53% of them had hypertension as a comorbidity and 42% were treated by an antihypertensive medication[19]. In the study by Kalezic *et al*., previous hypertension was present in 66.5%[14]. The incidence of IOHTA in chronically hypertensive patients undergoing elective, noncardiac surgery appears to be less than 10%[20]. Consistent with the literature, our results showed that IOHTA was recorded in 9% of patients who had hypertension as a comorbidity, which was significantly more often compared to the incidence of IOHTA in patients who did not have hypertension in their history (5.4%, p=0.042).

We found no significant gender difference in the incidence of IOHTA. IOHTA was more often recorded in patients older than 50 years than in patients aged ≤50. This was also demonstrated in our previous studies[14,15]. In our research, older age was identified as an independent predictor of IOHTA. Franklin *et al*. performed an analysis of data from the Framingham Study population, which showed that there was a continuous rise in the pulse pressure through life in adults and that the rate increased in people older than 50 years[21]. Since elderly patients have more comorbidities than younger patients, this could explain why in our study, ASA 4 patients and patients with associated cardiovascular and non-cardiovascular comorbidities had the highest incidence of IOHTA.

Among patients with IOHTA, the most frequent cardiac rhythm disorders were ventricular extrasystoles. Haemars *et al*. in a controlled, preclinical relevant, novel closed-chest pig model showed that premature ventricular complexes were associated with the acute increase in blood pressure[22]. It is also well known that supraventricular and ventricular arrhythmias, particularly in a heart which is hypertrophic, are often aggravated and facilitated by the occurrence of myocardial ischemia, disturbances of electrolytes, a sympathovagal imbalance and transient blood pressure peaks which are quite common during anesthesia and surgery[23]. Because IOHTA is acute and usually a transient increase of blood pressure, this could be an explanation why ventricular extrasystoles were the most common cardiac rhythm disorder in patients with IOHTA and why cardiac arrhythmia was a predictor of IOHTA in our study.

In our study population, significantly more patients with hyperlipoproteinemia had IOHTA compared with patients without hyperlipoproteinemia. This result was not surprising because in a Korean multicenter cohort study of primary hypertension, out of 1318 patients with primary hypertension, 43.8% had hyperlipoproteinemia, which was the most common comorbidity[24].

Even in otherwise normotensive patients, IOHTA could be triggered by perioperative stress factors such as laryngoscopy and intubation, particularly in case of difficult intubation because these stressors can cause heightened sympathetic response[20]. In neck surgery, difficult tracheal intubation appears more often than in general population[25]. In our research, difficult intubation (Cormack-Lehane grade 3 and Cormack-Lehane grade 4) was recorded in 4.3% of cases. Bearing that in mind, it was not surprising that IOHTA was most common in patients with Cormack-Lehane grade 4, and that Cormack-Lehane grade was a significant predictor of IOHTA during neck surgery.

The results of our research showed that on average, anesthesia in patients with IOHTA was notably longer compared to patients who did not have IOHTA (111±78.11 min *vs*. 93±57.93 min). The anesthesia duration was detected as an independent prediction factor of IOHTA. The research by Sabljak *et al*. identified the time under general anesthesia as a predictor of IOHTA in surgery for primary hypeparathyroidism[15]. With longer anesthesia duration, there is a higher possibility for the occurrence of various stimuli, which could be the cause of IOHTA, such as pain, inadequate depth of anesthesia, rapid intravascular volume shifts, excessive release of catecholamines, reduced baroreceptor sensitivity, peripheral vasoconstriction, renin-angiotensin activation, reperfusion injury, and altered cardiac reflexes[26].

In the literature, depending on definition, the incidence of intraoperative hypotension is 5% to 99%[27,28]. In our research, intraoperative hypotension was achieved in 24.8% of patients. Anesthetics, with their vasodilatory and negative inotropic properties, can prevent or treat intraoperative hypertension. This class of anesthetics includes opioids (in our research remifentanil), potent inhalation anesthesia, agents for induction of hypotension, and regional analgesia[29]. Our patients who were in normotensive anesthesia had IOHTA significantly more frequently than patients in hypotensive anesthesia. The reason for that could be the mechanism of remifentanil action, which was used as the main tool for hypotensive anesthesia. It is well known that remifentanil stimulates vagal nuclei

which cause bradycardia and consequent decrease of blood pressure. Furthermore, our results showed that remifentanil induced hypotension carried a lower risk of IOHTA than in the group of patients without induced hypotension (OR=0.024, 95% CI: 0.003-0.185, p=0.000). Bearing that in mind, induced hypotension should be considered even in surgeries which do not require hypotensive anesthesia, but future studies are warranted to investigate this assumption.

This study identified older age, longer anesthesia duration and previous cardiac arrhythmia as independent risk factors for IOHTA during neck surgery. Special attention is needed in patients with difficult intubation because they are also at risk of IOHTA occurrence.

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Sažetak

PREDIKTORI INTRAOPERACIJSKE HIPERTENZIJE U KIRURGIJI VRATA: RETROSPEKTIVNO ISTRAŽIVANJE U JEDNOM CENTRU

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Intraoperacijska hipertenzija (IOHTA) nije poželjna u kirurgiji vrata, jer kod ove vrste kirurgije postoji naročita sklonost ka krvarenju i u normotenzivnoj anesteziji. Cilj naše studije bio je utvrditi incidenciju i čimbenike rizika za pojavu IOHTA kod bolesnika podvrgnutih kirurgiji vrata. Ova retrospektivna studija je obuhvatila 880 odraslih bolesnika koji su u općoj anesteziji bili podvrgnuti kirurgiji vrata. Ispitivali smo utjecaj spola, dobi, supostojećih bolesti, otežane intubacije traheje, trajanja anestezije i inducirane hipotenzije na pojavu IOHTA. IOHTA je zabilježena kod 57 (6,7%) bolesnika. Bolesnici s ASA statusom 4 i oni s Cormack-Lehaneovim stupnjem 4 najčešće su imali IOHTA (22,2% odnosno 21,4%). Značajno više bolesnika s hipertenzijom, hiperlipoproteinemijom i ventrikulskim ekstrasistolama je imalo IOHTA u odnosu na bolesnike bez ovih subolesti. Značajni prediktori IOHTA bili su dob (OR 1,438; 95% CI 1,144-1,808; p=0,002), srčana aritmija (OR 1,702; 95% CI 1,129-2,566; p=0,011), Cormack-Lehaneov stupanj (OR 1,407; 95% CI 1,054-1,878; p=0,020), trajanje anestezije (OR 1,005; 95% CI 1,001-1,008; p=0,005). Rizik za pojavu IOHTA je bio manji u bolesnika s induciranom hipotenzijom (OR 0,024; 95% CI 0,003-0,185; p=0,000). Tijekom kirurgije vrata naročitu pozornost treba obratiti bolesnicima starije životne dobi, bolesnicima sa srčanom aritmijom, otežanom intubacijom i dužim trajanjem anestezije, jer su oni pod povećanim rizikom od razvoja IOHTA.

Ključne riječi: *Hipertenzija; Intraoperacijsko razdoblje*