



## Effects of Total Intravenous Anesthesia vs. Balanced Inhalation Anesthesia on Hemodynamics and Recovery in Orthognathic Surgery

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### Abstract

**Purpose:** The main objective of the present study was to evaluate haemodynamics and recovery parameters in relation to two anesthetic techniques; remifentanyl-propofol based Total Intravenous Anesthesia (TIVA), vs. Fentanyl-sevoflurane based balanced inhalation anesthesia (BA) in orthognathic surgery. The second objective was to evaluate long duration local anesthesia administered after surgery on recovery parameters.

**Subjects and Methods:** Medical records were retrospectively reviewed from 269 patients who had undergone orthognathic surgery between 2003 and 2013. Ninety-four patients were audited due to strict inclusion criteria in order to compare the two anesthetic techniques. Haemodynamics were evaluated with parameters such as blood loss, Mean Arterial Pressure (MAP), values of systole and diastole, and heart rate. Recovery was investigated with parameters such as Postoperative Nausea and Vomiting (PONV), recovery time at the Postanesthesia Unit (PACU), pain and hospitalization. Furthermore, we analyzed possible influences of age, gender, Body Mass Index (BMI) and operating time.

**Results:** No significant differences regarding blood loss, operating time, recovery time, PONV and hospitalization were found between the two anesthetic techniques. There was a significant continuously improvement regarding reduced blood loss, operating time and (hospitalization) during the 10-year follow-up in all patients. TIVA facilitated hemodynamic stability through superior pain/stress control during surgery. The addition of long duration anesthesia (ropivacaine 7.5 mg/ml) given at the end of surgery significantly reduced hospitalization ( $p=0.0028$ ) when analyzed separately.

**Conclusions:** No significant differences between the two anesthetic techniques regarding blood loss, operating time, recovery time, PONV and hospitalization were found. TIVA facilitated hemodynamic stability. Long duration local anesthetics given at the end of surgery appears to improve mobilization of the patient and reduce hospitalization.

**Keywords:** Orthognathic surgery; Anesthesia; Hemodynamic; Remifentanyl; Propofol; Fentanyl; Ropivacaine

### Introduction

Improvements of the anesthetic technique are desirable to balance hemodynamics and to facilitate recovery parameters. Advancement and development in surgical technique, short acting reliable anesthetic drugs, pre- and postoperative care together coordinate the outcome and progress. Various anesthetic methods are used to secure hemodynamic and respiratory stability during the surgical procedure [1]. Current state of the art is to achieve anesthesia with at least a two-drug procedure, consisting of a sedative and an opioid. Two separate drugs are easier to regulate and therefore minimize side effects such as hemodynamic depression, prolonged waking time and the risk for overdoses. A volatile agent or intravenous propofol provides the sedative and hypnotic

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component. The opioid of choice provides analgesia. Remifentanyl is an ultra-short-acting opioid that can be rapidly titrated for various levels of surgical stimuli during surgery. Relatively large doses can be administered assuring intra-operative deep analgesia and stable hemodynamics while permitting rapid awakening and extubation at the end of the procedure. Additionally, higher doses of remifentanyl can be administered without residual opioid effects due to the faster elimination characteristics. Patients receiving remifentanyl might though experience postoperative pain after awakening if not compensated with appropriate analgesics.

Conversely, comparisons of remifentanyl with conventional opioids, such as fentanyl, have shown inconsistent results with respect to various outcomes such as hypotension, hypertension, more frequent postoperative analgesic requirements, and PONV [2,3].

Optimal dynamic pain relief and treatment of PONV is prerequisite for optimizing postoperative recovery and reducing morbidity and convalescence [4,5]. In this context, postoperative analgesia by the use of long duration local anesthetics in relation to early mobilization and recovery is not previously scientifically evaluated in the field of orthognathic surgery, although several studies are found in the field of surgery and orthopedics [6,7].

The orofacial region is highly vascularized, and bleeding can therefore reduce visibility and considerably impair surgical conditions [8]. A combination of methods such as head up tilt and local anesthesia with vasoconstrictor and modern anesthetic techniques can reduce blood loss to the extent that blood transfusion is uncommon [2]. Controlled hypotensive anesthesia may reduce intraoperative bleeding, although with conflicting results in the literature, and still with the main risk factor hypoperfusion of vital organs [9,10]. Several studies point out the role of total intravenous anesthesia with remifentanyl as superior in balancing hemodynamics with reduced blood pressure and intraoperative blood loss [11,12]. Modern anesthetic total intravenous techniques with remifentanyl can hopefully serve as a safe, more predictable and stable alternative regarding hemodynamics, and in minimizing blood loss, and promoting recovery in comparison with deliberate controlled volatile hypertensive techniques and longer acting opioids.

The present retrospective study was audited in order to evaluate the anesthetic techniques at our institutions with focus on hemodynamics and recovery parameters. Additionally, we wanted to evaluate possible effects of long duration anesthesia administered (ropivacaine 7.5 mg/ml) given immediately the end of the surgery with regard to recovery parameters.

## Material and Methods

### Subjects

Medical records of 269 patients, who had undergone orthognathic surgery between 2003 and 2013, were enrolled and retrospectively reviewed (Table 1). Ninety-four patients were audited due to strict exclusion criteria. Inclusion criteria were; American Society of Anesthesiologists (ASA) physical status I-II; Bilateral Sagittal Split Osteotomies (BSSO), Le Fort I osteotomies and bimaxillary osteotomies on patients at NU Hospital Group in Trollhättan, Sweden (Figure 1).

The main objective was to evaluate haemodynamics and recovery parameters in relation to two anesthetic techniques; remifentanyl-propofol based Total Intravenous Anesthesia (TIVA),

**Table 1:** Demographic details and characteristics of TIVA and BA associated with subjects.

	Intravenous anesthesia (TIVA) n=18	Balanced anesthesia (BA) n=76	Two-sided p-value
Date of surgery (calendar year)	2010 ± 2	2007 ± 2	<0.001
Age (years)	25.6 ± 13.0	22.6 ± 8.2	0.29
Gender (% female)	39%	63%	0.11
BMI *	24.7 ± 3.7	23.4 ± 3.4	0.16
ASA **	22% (II)	13% (II)	>0.30
Smoking	6%	17%	>0.30
Osteotomy			
Mandibular	44% (n=8)	49% (n=37)	>0.30
Maxillary	33% (n=6)	16% (n=12)	0.18
Bimaxillary	22% (n=4)	36% (n=27)	>0.30
Subjects			
Systole at baseline	94.7 ± 11.7	97.9 ± 11.3	>0.30
Diastole at baseline	43.1 ± 14.0	36.0 ± 7.0	0.012
Heart rate at baseline	69.4 ± 9.4	71.8 ± 16.5	>0.30
MAP at baseline	60.3 ± 11.8	56.6 ± 6.5	0.091

\* Body-Mass-Index (Kg m<sup>2</sup>)

\*\* American Index of Anesthesiologists

vs. fentanyl-sevoflurane based balanced inhalation anesthesia (BA) in orthognathic surgery. The second objective was to evaluate long duration local anesthesia (ropivacaine 7.5 mg/ml) administered at the end of surgery. Data was collected from medical records, anesthetic charts, drug charts and recovery observation charts. Preparation of the data was compiled with the proforma shown in the appendix. The Regional Ethical Review Board in Gothenburg approved this retrospective study (Dnr 391-14). All segmentations and genioplasty procedures were initially excluded. In order to utilize two comparable study groups regarding the anesthetic techniques we excluded several drugs such as β-adrenergic antagonists, intraoperative atropine/glycopyrrolate due to occasions of bradycardia and ephedrine/phenylephrine due to occasions of severe hypotension, that influence the intraoperative hemodynamic stress responses. Patients with Body Mass Index >35 were excluded due to the risk of unpredictable distribution patterns of administered anesthetic drugs. Patients <18 years were excluded. Furthermore, we excluded patients with missing anesthetic charts, other anesthetic techniques (n=2), and concomitant surgical procedures such as bone augmentation, tooth extraction and implant installations. A total of 175 patients were excluded. Ninety-four patients were included in the study and divided into the TIVA group (n=18) and BA group (n=76) (Figure 1).

### Preoperative

All patients were subjected to routine preoperative assessment by the anesthesiologist. Preoperative medications were prescribed in order to prevent PONV, pain and could vary during the study period depending on changes in standard protocols (Table 2). All patients fasted from midnight and received the prescribed medications one hour before induction.

### Intraoperative

General anesthesia was induced with remifentanyl-propofol or fentanyl-sevoflurane (Table 2). Prior to induction all patients received approximately 5 ml/kg IV fluid (e.g. Ringer's solution). TIVA patients received an anticholinergic premedication of Glycopyrrolate 3 µg/kg

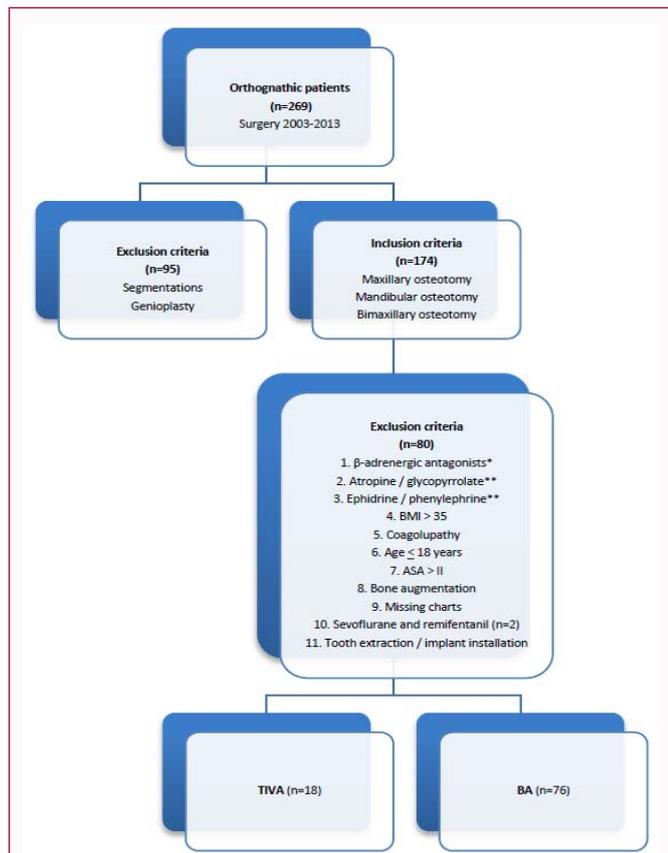


Figure 1: Selection of study population.

\* Medications excluded preoperatively (β-adrenergic antagonists)

\*\* Medications excluded intraoperatively hypotension (atropine/glycopyrrolate, ephedrine/phenylephrine) at occasion of bradycardia or severe hypotension

to 5 µg/kg as standard protocol. Antibiotics were given according to department routines; Penicillin G 3 g intravenously or clindamycin 600 mg in case of allergy, at induction and postoperatively during admittance. Betamethasone was administered with 16 mg in double jaw cases and 8 mg in single jaw surgery cases as standard protocol (Table 2). All bimaxillary procedures received tranexamic acid 1 g in order to minimize blood loss. Administration of clonidine 1.5 µg/kg, varied in the study population, due to the choice of the anesthesiologist in charge, in order to reduce intraoperative and postoperative stress response (Table 2). Additionally, all patients received infiltration with local anesthesia, lidocaine 2% epinephrine (1:200,000), before surgery in order to minimize hemodynamic stress response, consumption of anesthetic drugs, blood loss and to facilitate intraoperative surgical visualization. Single jaws received 7.2 ml and double jaws received 14.4 ml lidocaine 2% epinephrine (1:200.000) as standard protocol (Table 2).

For endotracheal intubation rocuronium bromid 0.5 mg/kg or atracurium 0.5 mg/kg was used.

Monitoring included Electrocardiography (EKG), Pulse-Oximetry (SpO<sub>2</sub>), capnography, end tidal gas analysis, body temperature, Bispectral Index (BIS) and neuromuscular transmission (TOF; Transmission with Four stimulus). Operating time was calculated from incision until the oral mucosal wound was closed. Anesthetic time was calculated from induction until awareness. Data regarding systole, diastole and heart rate were extracted from the

Table 2: Demographic details and characteristics of TIVA and BA associated with pre- and intraoperative variables.

	Intravenous anesthesia (TIVA) n=18	Balanced anesthesia (BA) n=76	Two-sided p-value
<b>Preoperative</b>			
Paracetamol	89%	99%	>0.30
Triazolam	6%	51%	<0.001
NSAID*	11%	29%	0.2
Morphine/oxycodone	78%	28%	<0.001
Meklozine	56%	20%	0.0081
<b>Intraoperative</b>			
Lidocaine 2% epinephrine	100%	100%	-
Betamethasone (g)	13.8 ± 5.4	13.6 ± 5.3	>0.30
Tranexamic acid	78%	66%	>0.30
Ondansetron/droperidol	67%	45% (n=75)	0.17
Clonidine	None: 56% (n=10) Preoperative: 44% (n=8) Intraoperative: 0	None: 92% (n=70) Preoperative: 5% (n=4) Intraoperative: 3% (n=2)	0.0014****
Rokuroniumbromid/atracurium	89%	99%	>0.30
Glycopyrrolate	100%	-	-
TIVA propofol	9.7 ± 4.2	0.00 ± 0.00	-
TIVA remifentanyl	0.2 ± 0.01 (n=17)	0.00 ± 0.00	-
Gas (MAC) (fentanyl)	0.00 ± 0.00	1.44 ± 0.19 (n=74)	-
Ketorolac, Parecoxib	44%	43%	>0.30
Ketobemidone/morphine	44%	43%	>0.30
MAP (mean)**	64.3 ± 6.9	57.6 ± 6.7	<0.001
MAP (max)	77.8 ± 11.5	72.9 ± 13.2	0.19
Systole (mean)	98.9 ± 8.8	98.6 ± 9.9	>0.30
Systole (max)	113.3 ± 11.1	117.9 ± 16.9	>0.30
Diastole (mean)	47.1 ± 7.4	37.2 ± 7.4	<0.001
Diastole (max)	63.6 ± 13.4	52.6 ± 15.8	0.015
Heart rate (mean)	69.0 ± 8.2	81.6 ± 12.7	<0.001
Heart rate (max)	76.7 ± 10.2	93.0 ± 15.1	<0.001
Operating time (minutes)	128.0 ± 51.0	151.2 ± 216.2 (n=75)	0.25
Anesthetic time (minutes)	193.2 ± 61.3	224.0 ± 84.7	0.18
Blood loss (ml)	176.4 ± 149.1	265.3 ± 216.2	0.12
Ropivacaine***	None: 4 (22%) Infiltration: 14(78%)	None: 67 (88%) Infiltration: 9(12%)	<0.001

\* Non-Steroidal Anti-Inflammatory Drug

\*\* Mean Arterial Pressure

\*\*\* Local anesthetic infiltration given after surgery and before extubation

\*\*\*\* Nothing vs. something (preoperative of intraoperative)

anesthetic chart, from incision every 10<sup>th</sup> minute to the end of surgery. MAP values were calculated for all patients every 10<sup>th</sup> minute. Head up tilt was used as standard routine in cases of increased bleeding. Blood loss was measured through extracting the amount of saline used for rinsing/cooling from the total amount of fluids collected. Prophylaxis against PONV consisted of ondansetron or droperidol and was administered twenty minutes before extubation (Table 2). Ketorolac or parecoxib vs. ketobemidone or morphine was administered before extubation depending on the choice of the anesthesiologist. Infiltration with long duration local anesthesia (ropivacaine 7.5 mg/ml) at the end of surgery was introduced as standard protocol from

**Table 3:** Pre- and intra-operative variables related to blood loss, operating time, recovery time and hospitalization.

	Blood loss (ml)	Operating time (min)	Recovery time (min) PACU	Hospitalization (days)
<b>Preoperative</b>				
Date of surgery (calendar year)	0.0029-	0.0075-	0.025-	<0.001-
Gender	0.14	0.16	0.19	>0.30
Age	<0.001-	0.0081-	>0.30	>0.30
BMI *	0.26	0.21	>0.30	0.15
Smoking	>0.30	>0.30	>0.30	>0.30
ASA **	>0.30	0.069	>0.30	0.061
<b>Intraoperative</b>				
Operating time	<0.001+		0.0029+	<0.001+
Anesthetic time	<0.001+	<0.001+	0.0020+	<0.001+
MAP (mean) ***	>0.30	>0.30	>0.30	>0.30
MAP (max)	>0.30	0.14	0.087	0.043+
Systole (mean)	>0.30	>0.30	>0.30	>0.30
Systole (max)	0.28	>0.30	>0.30	>0.30
Diastole medel	0.11	0.27	>0.30	>0.30
Diastole (max)	>0.30	0.15	0.11	0.045+
Heart rate (mean)	0.0093+	0.032+	>0.30	0.23
Heart rate (max)	0.0036+	0.0085+	0.27	0.16
Ropivacaine ****	0.2	>0.30	0.3	0.0028-

\* Body-Mass-Index (Kg m<sup>2</sup>)

\*\* American Index of Anesthesiologists

\*\*\* Mean Arterial Pressure

\*\*\*\* Long duration local anesthetic infiltration administered after surgery and before extubating

August 2010. Single jaws received 5 ml and double jaws received 10 ml (ropivacaine 7.5 mg/ml) at the end of the surgery and before extubation (Table 2).

Surgery was performed with the same surgical standard protocol during the 10-year follow up despite that new team members were introduced in the surgical procedure from 2011.

Hence, differences in results due to variations in surgical technique were believed to be minimal in this single unit study.

### Postoperative

Recovery time was measured as the time for arrival to the PACU until departure. Parameters for nausea, vomiting and adverse effects were noted. Pain was measured with the Visual Analogue Scale (VAS) ranging from 0 to 10, with 0 indicating no pain and 10 indicating maximum pain. Rules for discharge was VAS<4, respiratory and hemodynamic stability, arrest of bleeding, minimal nausea, normal body temperature and acceptable bladder control. The length of hospitalization was specified as the number of nights spent at the ward from the operating day until discharge. Before discharge the patients had to be able to swallow fluids and medications, have normalized bladder control and be mobilized (Table 4).

### Statistics

Fisher's permutation, a non-parametric test, was used to compare

**Table 4:** Demographic details and characteristics of TIVA and BA associated with postoperative variables.

	Intravenous anesthesia (TIVA) n=18	Balanced anesthesia (BA) n=76	Two-sided p-value
<b>Postoperative (PACU) *</b>			
Recovery time (min)	207.5 ± 90.5	249.3 ± 226.7	>0.30
Pain (VAS) **	5.1 ± 2.5 (n=11)	4.9 ± 2.2 (n=41)	>0.30
Nausea	11%	32%	0.13
Vomiting (number of times)	0.0 ± 0.0	0.5 ± 1.6	0.28
Adverse effects	0%	1%	>0.30
Paracetamol (mg)	0.89 ± 0.32	0.97 ± 0.80	>0.30
Ketorolac (mg)	0.00 ± 0.00	0.39 ± 3.4	>0.30
Morphine (mg)	0.33 ± 1.41	0.04 ± 0.26	0.17
Ketobemidone (mg)	3.58 ± 4.46	4.73 ± 6.52	>0.30
Oxycodone (mg)	1.00 ± 2.59	0.39 ± 1.80	0.26
<b>Postoperative (ward)</b>			
Hospitalization (days) ***	1.5 ± 0.8	2.0 ± 1.0	0.068

\* Post-anesthetic care unit

\*\* Visual analogue scale

\*\*\* Duration of hospital stay

the two anesthetic techniques. Pitman test was used to test correlations between variables. Two-sided test was used and p<0.05 was regarded as statistically significant. To study the associations between year of operation and blood loss and operating time a spline regression model was fitted using knots at the 10<sup>th</sup>, 50<sup>th</sup> and 90<sup>th</sup> percentiles year of operation to, as recommended by Harrell FJ 2001 [13]. The splines were second-order functions between the breakpoints and linear functions at the tails resulting in a smooth curve. The effect of ropivacaine was separately evaluated with a univariate statistical model.

## Results

### Subjects

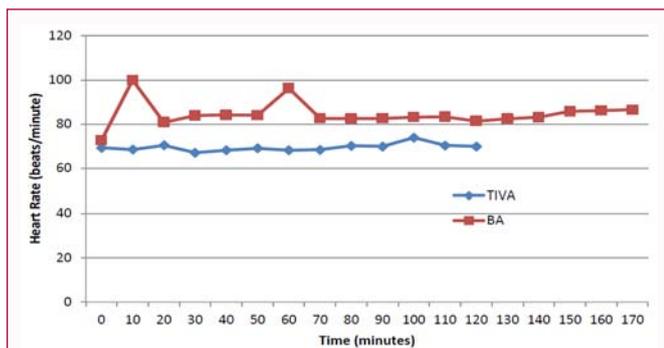
Ninety-four patients (55 females and 39 males) with the mean age of 23.2 years (range 18 to 62 years) underwent maxillary (n=18), mandibular (n=45) or bimaxillary surgery (n=31). There was a significant difference between the two anesthetic groups regarding date of surgery and diastole. We found lower diastolic values at baseline in the BA group. The TIVA group was followed from approximately 2010 ± 2 years. No significant preoperative differences were found between the two anesthetic techniques regarding age, gender, BMI, smoking, osteotomies, and systole at baseline, heart rate at baseline or MAP at baseline (Table 1).

### Preoperative

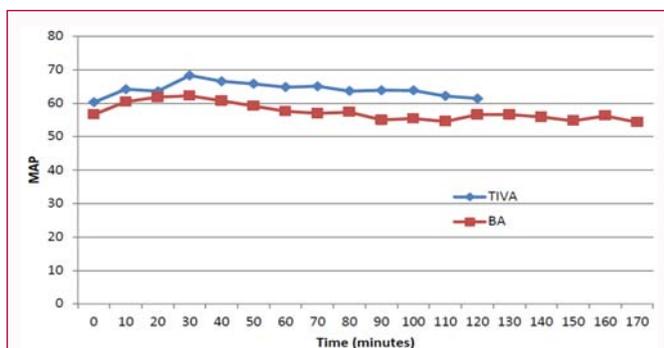
There was a significant difference between the two anesthetic groups regarding preoperative administration of triazolam, morphine/oxycodone and meclizine. No differences were found between the two anesthetic techniques regarding preoperative administration of paracetamol and Non-steroidal Anti-Inflammatory Drugs (NSAID) (Table 2).

### Intraoperative

Graphics showed that TIVA facilitated hemodynamic stability through superior pain control during the surgical procedure in comparison to the BA group (Figure 2). Furthermore, significant differences between TIVA and BA regarding hemodynamic



**Figure 2:** Heart rate measured every 10<sup>th</sup> minute during surgical procedures. Mean value of heart rate for TIVA (n=18) and BA (n=76).



**Figure 3:** Mean Arterial Pressure (MAP) measured every 10<sup>th</sup> minute during surgical procedures. Mean value for MAP and TIVA (n=18) and BA (n=76).

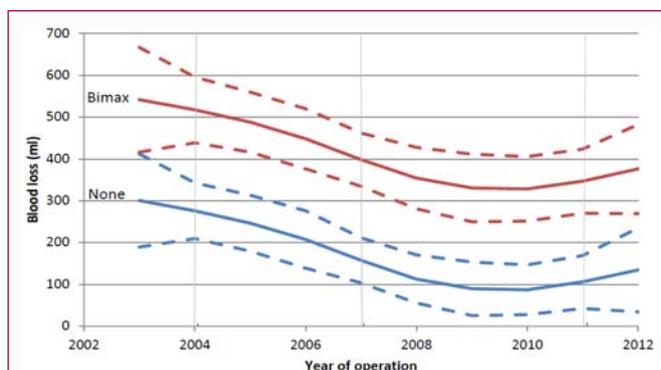
characteristics were found. MAP values (mean) and diastole (mean & max) were significantly higher in TIVA (Table 2, Figure 3). Heart rate values (mean & max) were significantly higher in BA (Table 2, Figure 2). The usage of clonidine was significantly different between the two anesthetic techniques.

TIVA patients received clonidine 1.5 µg/kg preoperatively in 44% of the cases, in contrast to patients with BA who received 5% preoperatively and 3% intraoperatively (Table 2).

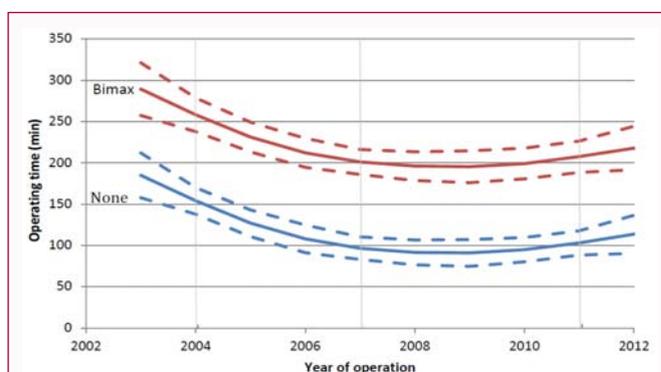
Nevertheless, the exclusion of clonidine from the two anesthetic techniques did not change the pattern regarding heart rate (Figure 2). Severe bradycardia, hypotension and/or awareness were not encountered in any cases.

Pre- and intraoperative variables were analyzed in relation to blood loss, operating time, recovery time at the PACU and length of hospitalization. Higher MAP (max) and diastole (max) values resulted in significantly prolonged hospitalization (Table 3). For every upturn in diastole with 16 mm Hg, hospitalization increased with 0.2 days (95% CI: 0.0, 0.3, SD 16) ( $p=0.0046$ ).

Prolonged operating time and increased blood loss may correlate with higher heart rates (mean & max) (Table 3). Longer operating time and anesthetic time resulted in more blood loss and increased hospitalization (Table 3). Higher age resulted in decreased blood loss and shorter operating time, which correlated with single jaw procedures (Table 3). There was a significant difference between the two anesthetic techniques regarding the use of (ropivacaine 7.5 mg/ml) (Table 2). Bimaxillary procedures increased hospitalization with 1.0 days (95% CI: 0.6, 1.3). No significant differences were found regarding blood loss and operating time between the two anesthetic techniques. A spline regression model reveals a trend towards



**Figure 4:** Blood loss associated with year of operation. The red and blue lines represent a spline regression model and the crosshatched lines visualize 95% confidence intervals. The vertical dashed lines represent the 10<sup>th</sup>, 50<sup>th</sup> and the 90<sup>th</sup> percentiles.



**Figure 5:** Operating time associated with year of operation. The red and blue lines represent a spline regression model and the crosshatched lines visualize 95% confidence intervals. The vertical dashed lines represent the 10<sup>th</sup>, 50<sup>th</sup> and the 90<sup>th</sup> percentiles. The betamethasone dose is adjusted, and set to mean value of 13.6 g.

continuously decreasing blood loss and reduced operating time during the study period regardless the anesthetic technique (Table 3, Figure 4, 5).

## Postoperative

Infiltration with long duration local anesthesia (ropivacaine 7.5 mg/ml) at the end of the surgery and before extubation reduced hospitalization significantly with 0.7 days (95% CI 1.1-0.2) ( $p=0.0028$ ). There was a weak trend towards prolonged hospitalization ( $p=0.068$ ) in the BA group with ( $2.0 \pm 1.0$ ) days, in comparison to the TIVA group with ( $1.5 \pm 0.8$ ) days. No significant differences were found between the two anesthetic techniques regarding PONV, pain, adverse effects, postoperative analgesics including opioids, recovery time at PACU and hospitalization.

## Discussion

The main objective with the present study was to evaluate hemodynamics and recovery parameters in relation to two different anesthetic techniques in orthognathic surgery. The second objective was to evaluate the effect of long duration local anesthesia given immediately after surgery on recovery parameters.

It was graphically exposed that the starting point of more painful surgical procedures were revealed in the BA group due to episodes of increased heart rates in contrast to the TIVA group. These findings were interpreted in favor for TIVA through facilitated hemodynamic

stability and with superior pain/stress control during surgery. These findings were confirmed by Nooh et al. [14] (Figure 2). Furthermore, significant differences between TIVA and BA regarding hemodynamics were exposed. These differences comprised of significantly higher MAP (mean) and diastolic values in TIVA compared to BA and significantly higher heart rate values in BA compared to TIVA. This resulted in a trend towards prolonged hospitalization ( $p=0.068$ ) in the BA group with ( $2.0 \pm 1.0$ ) days, in comparison to the TIVA group with ( $1.5 \pm 0.8$ ) days (Table 2, 4). It is hypothesized that higher cardiac output caused by increased heart rate is responsible for this result, which also is confirmed with the significantly increased blood loss in relation to higher heart rates (Table 3). Consequently, it was also shown that every upturn in diastole (max) with 16 mmHg significantly increased hospitalization with 0.2 days ( $p=0.0046$ ). Nevertheless, baseline values of diastole were significantly lower in the BA group and may influence these results ( $p=0.012$ ), which is due to variations in preoperative medication between the two study groups, where triazolam was significantly higher in the BA group, whereas morphine/oxycodone was significantly higher in the TIVA group (Table 1). Furthermore, the MAP (mean) values in TIVA were consistently higher during surgery in comparison with BA (Figure 3). These higher MAP (mean) values were non-significant in relation to blood loss and recovery parameters (Table 4). In accordance with our study Nooh et al. [14], showed higher heart rates in the fentanyl group during surgery in contrast to the remifentanyl group, although it should be emphasized that their prospective study design used propofol in both study groups. Conversely, the situation was contradictory regarding MAP (mean) values where Nooh et al. [14] exposed consistently lower MAP (mean) values in the remifentanyl group opposing the fentanyl group, whereas this present study showed consistently higher MAP (mean) values in the remifentanyl (TIVA) group in comparison to the BA group. These differences may partly be due to higher doses of remifentanyl ( $0.4 \mu\text{g}/\text{kg}/\text{min}$ ) in the study of Nooh et al. [14], resulting in a deeper anesthesia, in contrast to the present study with the dosage ( $0.2 \mu\text{g}/\text{kg}/\text{min}$ ) [14]. In order to further discuss the lower MAP values in the BA group, sevoflurane may have stronger vasodilational effect, in contrast to propofol, which may explain the lower MAP with mild hypotension in the BA group. Decreased MAP (mean) and heart rate could be explained by the stronger intraoperative analgesia causing increased vagal tone by the remifentanyl-induced autonomic nervous system effect [15]. The MAP (mean) values in BA were considered as mild controlled hypotension ( $\text{MAP } 57.6 \pm 6.7$ ) and equaled normotension for the TIVA group ( $64.3 \pm 6.9$ ) (Table 2).

The results of this study confirm previous evidence that indicate the superior effect of remifentanyl in preventing hemodynamic stress responses to noxious stimuli during surgery.

Notwithstanding, evaluations between TIVA vs. BA in orthognathic surgery are rare [2,14]. Lee et al. [16] evaluated TIVA and BA in thyroid surgery with a Quality of Recovery questionnaire (QoR-40), which significantly benefited TIVA regarding the quality of recovery [16]. Nooh et al. [14] showed in maxillary osteotomies that remifentanyl promotes hemodynamic stability, blunts the stress response to noxious stimuli and provides a better recovery profile [14]. Twersky et al. [17] confirmed improved hemodynamic control in respect to lower heart rate, earlier mobilization and discharge from hospital with the use of remifentanyl compared with fentanyl in elective surgery [17]. Komatsu et al. [3] evaluated ultra-short-acting remifentanyl with short-acting opioids (fentanyl, alfentanil

or sufentanil) in a meta-analysis study in elective surgeries, showing less response to noxious stimuli, deeper anesthesia and analgesia, faster recovery and conversely, no impact on PONV. In contrast to our present study more frequent episodes of bradycardia, more hypotension and more frequent postoperative analgesic requirements were demanded in the remifentanyl group [3]. Chegini et al. [2] reported significantly higher pain scores postoperatively, with non-significant trends towards shorter recovery times, while no differences were found in early postoperative opioid usage, hemodynamic parameters, or PONV in the remifentanyl group [2].

Interestingly, a recent study has pointed out that remifentanyl may reduce edema and ecchymosis of the upper and lower eyelids by reducing mean arterial pressure and amount of bleeding in rhinoplasty [12]. The literature shows that PONV has a high prevalence in patients undergoing orthognathic surgery [7]. We did not find any significant differences in respect of postoperative recovery variables such as pain, PONV, medication, time at PACU or hospitalization between the two anesthetic techniques in this present study.

Adverse results such as bradycardia and hypotension have been reported in several studies and may be addressed to high doses of drug infusion or bolus administration [14]. Wang et al. [18] reported noxious effects of remifentanyl in intraoperative analgesia and their study was terminated due to frequent incidences of bradycardia and asystolic episodes in the remifentanyl group. However, their patients were also taking  $\beta$ -adrenergic blocking medications preoperatively, resulting in slower a heart rate before induction [18]. Hall et al. [19] reported that severe episodes of hypotension could be repealed if remifentanyl was used with glycopyrrolate as pre-treatment. In contrast to Nooh et al. [14] and Hall et al. [19], this present study excluded intraoperative atropine and glycopyrrolate in occasions of bradycardia or severe hypotension at occasion, in order to utilize comparable groups [14,19]. Intraoperative administration of atropine and/or glycopyrrolate due to bradycardia and/or severe hypotension was administered at occasion. In this present study we excluded all patients who received these medications, intraoperatively, and nor did we encounter severe hypotension or bradycardia in the patients included. The hemodynamic stress response related to the maxillary osteotomy and down-fracture of the maxilla may release these occasions of severe bradycardia or hypotension. The frequent use of clonidine in the TIVA group, and young healthy adults (ASA I-II) in the study population, may minimize these occasions. Clonidine was used preoperatively only in the TIVA group (44%), in order to balance the vagal tone, and is an important drug in the balancing of hemodynamics.

Nevertheless, as mentioned before, the exclusion of clonidine from the two anesthetic techniques did not change the pattern regarding heart rate (Figure 2). The increase of anesthetic depth given by clonidine allows the reduction of propofol dosage to achieve a specific depth of anesthesia [20].

Adoption of anesthetic techniques used in orthopedic and neurosurgical operations has introduced deliberate hypotension in the maxillofacial field [21]. Maintenance of intraoperative controlled moderate hypotension reduces operating time, blood loss, provides a drier and clearer operative field and decreases occurrence of bradycardia [22,23]. On the other hand, Enlund et al. [10] present contradictory results regarding hypotension in orthognathic surgery. Neither the duration of surgery, nor the quality of the surgical field, was significantly influenced by hypotension [10].

Controlled moderate hypotensive anesthesia in order to reduce intraoperative blood loss remains controversial due to risks such as hypoperfusion of vital organs [9]. The definition of hypotension is a MAP 30% below a patient's usual MAP, with a minimum MAP of 50 mmHg in ASA Class I patients and a MAP not less than 80 mmHg in the elderly. This is suggested to be clinically acceptable [24].

The benefits of preoperative local anesthesia are showed in several studies. A mandibular block given preoperatively reduces intraoperative opioid consumption [25]. Inferior alveolar nerve block with ropivacaine before surgery increases patient comfort by decreasing PONV and postsurgical analgesia [26]. In this study preoperative local anesthesia (lidocaine 2% epinephrine 1:200.000) was administered by infiltration in the surgical field as standard procedure. The amount administered was equal in all patients in both TIVA and BA. The use of lidocaine 2% epinephrine was therefore not in conflict with the comparison of the two anesthetic groups.

Ropivacaine is a long-acting amide-type local anesthetic released for clinical use in 1996. In comparison with bupivacaine, ropivacaine is equally effective for subcutaneous infiltration, epidural and peripheral nerve block for surgery, obstetric procedures and postoperative analgesia. The pure (S-enantiomer) and its markedly lower lipid solubility have been suggested to significantly improve the safety profile of ropivacaine. This is confirmed in numerous studies showing that ropivacaine has less cardiovascular and CNS toxicity than racemic bupivacaine.

Ropivacaine also provides effective pain relieve after surgery, especially when given in conjunction with opioids or other adjuvants. Ropivacaine has a greater degree of separation between motor and sensory blockade relative to bupivacaine in the lower end of the dosage scale. In summary, ropivacaine has an efficacy similar to that of bupivacaine regarding postoperative pain relief, but causes less motor blockade and stronger vasoconstriction [27]. Patient satisfaction and analgesia were improved and the effect lasted for up to 48 h when ropivacaine was used opposed lidocaine in obstetric operations. A dosage with twenty milliliters lidocaine 10 mg/ml was compared with 20 ml (ropivacaine 7.5 mg/ml) [7]. These findings were confirmed by Peng et al. [28] who showed that ropivacaine provides effective anesthesia and superior postoperative analgesia compared to lidocaine when forearm intravenous regional anesthesia was used [28]. In BSSO surgery, mandibular nerve block with ropivacaine 0.5% decreased intraoperative bone bleeding during BSSO with a dry operation field, shortened mean time for osteotomy, reduced intraoperative opioid consumption and lowered pain scores in the recovery room [29-31]. As mentioned before, postoperative administration of ropivacaine reduced hospitalization in this present study. However, this retrospective study design was not able to show any reduction in postoperative opioid usage.

Infiltration with long duration local anesthesia (ropivacaine 7.5 mg/ml) at the end of surgery demonstrated a shortened hospitalization when analyzed separately (Table 3). To our knowledge this is the first study discussing the outcome of postoperative infiltration of the wound with long duration local anesthetics within the field oral and maxillofacial surgery.

The main shortcoming of this study was that data were collected retrospectively with limited possibility of controlling potential confounding factors and bias. Nevertheless, we believe that the use of intact standard protocols and application of strict exclusion

criteria have strengthened the study. On the other hand, this selection resulted in decimated study groups.

Given these limitations, results should be interpreted with caution. A larger study population with a randomized controlled prospective approach would be needed to address the objectives in this present study. This is though often difficult to achieve in limited surgical populations and smaller clinics.

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## Ethical Approval

This investigation was approved by: Regional Ethical Review Board in Gothenburg Dnr; 391-14.

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