

# Stress hormone response to various anaesthetic techniques during thyreidectomy

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## Abstract

**Background.** Thyroidectomy is among the most frequently performed procedures in endocrine surgery. The hormonal response to surgery and anaesthesia depends in part on the anaesthetic techniques used; therefore, we measured serum concentrations of TSH,  $fT_4$ , and  $fT_3$  in patients scheduled for elective thyroidectomy under TIVA or VIMA.

**Methods.** Seventy-eight adult patients, of both sexes, with non-toxic or hyperthyroid nodular goitre, were divided into groups with regard to the goitre type and the technique of anaesthesia used during thyroid surgery. Serum concentrations of TSH,  $fT_4$ , and  $fT_3$ , were measured and the surgical stress was estimated using the E-PASS scale.

**Results.** In the groups examined, the mean serum concentrations of TSH remained unchanged during the period of observation. The initially high  $fT_4$  and  $fT_3$  concentrations gradually decreased, reaching their lowest level on the fourth day after surgery.

**Conclusion.** Both VIMA and TIVA can be regarded as safe techniques of anaesthesia for thyroidectomy.

**Key words:** hormones, thyroid; surgery, stress response; surgery, thyroid

Anaesthesiology Intensive Therapy 2012; 44: 4-7

Despite continuous advances in conservative treatment methods of goitre, its surgical removal remains one of the commonest endocrine surgical procedures. Strumectomy is associated with possible difficult intubation (particularly in cases of giant or retrosternal goitres and those markedly dislocating and distorting the trachea), cardiovascular disorders during thyroid manipulations, respiratory abnormalities after extubation, dyspepsia after surgery and serious postoperative complications (paresis of vocal cords, haemorrhage). The surgery is associated with a complex stress response characterized by changes in the neuroendocrine and immune system as well as metabolic disorders [1, 2, 3, 4, 5]. The stress response accompanying surgical interventions may significantly affect the production and release of thyroid hormones in the perioperative period [6, 7]. During strumectomy, increased release of thyroid hormones can result from the gland's pathology and the surgical technique used. The modulation and reduction of the effects of surgical stress response are extremely relevant as they improve the outcome, shorten the hospitalization and reduce the cost of treatment [8, 9].

The objective of the study was to compare the effects of various general anaesthesia methods, i.e. volatile induction and maintenance of anaesthesia (VIMA) with sevoflurane and total intravenous anaesthesia (TIVA) with propofol for strumectomy on the serum levels of thyroid-stimulating hormone (TSH), free fractions of triiodothyronine ( $fT_3$ ) and thyroxine ( $fT_4$ ). Moreover, the severity of surgical stress in the perioperative period was determined.

## METHODS

The study involved patients aged above 18 years of age, without cardiovascular or respiratory diseases, fulfilling the ASA I and II criteria. The patients with non-toxic or overactive nodular goitre, preoperatively euthyroid, scheduled for strumectomy, were divided into 4 groups according to the type of goitre and the method of anaesthesia: group I – with non-toxic goitre anaesthetised with VIMA, II – with overactive nodular goitre undergoing VIMA, III – with non-toxic goitre anaesthetised with TIVA and group IV – with overactive nodular goitre receiving TIVA. The control group (V) included patients

Patients	I	II	III	IV	V
Number	22	19	18	19	15
Gender					
women	16	18	15	18	11
men	6	1	3	1	4
Age (years)	44.5 ± 12.9	46.6 ± 9.4	52.0 ± 11.1	46.5 ± 14.3	45.8 ± 17.3
Body weight (kg)	69.5 ± 13.0	71.6 ± 14.4	74.4 ± 14.9	74.7 ± 12.9	67.1 ± 12.9
Time of anaesthesia (min)	111.4 ± 23.8	114.2 ± 20.6	101.9 ± 8.9	120.0 ± 6.2	105.0 ± 7.2
Time of surgery (min)	88.4 ± 22.0	90.5 ± 19.4	78.9 ± 19.6	93.9 ± 16.1	77.3 ± 16.9

Table 1. Characteristics of patients and time of surgery (number or mean ± SD)

scheduled for laparoscopic cholecystectomy anaesthetised using VIMA with sevoflurane.

Serum concentrations of TSH,  $sT_4$  and  $fT_3$  were determined at the following measurement points: 24 h before surgery (baseline values), immediately after strumectomy in the study group or after cholecystectomy in the control group, 1 h after the surgery completion, and on post-operative day 4.

To evaluate the safety of patients in the immediate perioperative periods, the severity of surgical stress was assessed using the estimation of physiologic ability and surgical stress (E-PASS) and its parts, i.e. the preoperative risk score (PRS) and surgical stress score (SSS).

The distributions of measurements were not found to be normal, and therefore the data were compared using non-parametric tests. Medians and 25<sup>th</sup> and 74<sup>th</sup> percentile values with their ranges (minimum and maximum value) were presented. The differences in hormone levels were assessed using the Friedman ANOVA with post-hoc analysis for significant results. The inter-group differences were determined using the Kruskal-Wallis test. The dichotomous variables were evaluated using the  $\chi^2$  test. The differences were considered significant at  $p < 0.05$ .

## RESULTS

Ninety-three patients were encompassed in the study: group I – 22, II – 19, III – 18, IV – 19, and V (control) – 15. The characteristics of patients were presented in Table 1.

In all groups of patients, the mean serum concentrations of TSH did not change significantly throughout the observation period (Fig. 1), except for TSH levels 1 h after surgery, which was significantly lower in group II and IV compared to group I and III. The differences were found both in patients anaesthetised with inhalation method (by 55.8 %;  $p < 0.001$ ) and intravenous method (by 28.6 %;  $p < 0.05$ ).

The serum concentrations of  $fT_4$  in the individual groups gradually decreased at each successive measurement point, reaching the lowest values on day 4 after surgery (Fig. 2). Compared to baseline values, the biggest  $fT_4$  decrease was observed in group II and IV ( $p < 0.001$ ) and slightly smaller in group III ( $p < 0.05$ ). In group II and IV, irrespective of the anaesthesia method applied, a significant decrease in  $fT_4$  was found 1 h after surgery as compared to baseline

values. In group I, the serum  $fT_4$  level was significantly lower on postoperative day 4 in comparison with the value observed 1 h after the procedure.

Amongst the patients with overactive nodular goitre, higher concentrations of  $fT_4$  were found at all measurement points compared to patients with non-toxic goitre, yet the significant differences were only demonstrated in patients undergoing VIMA (group II) immediately after thyroidectomy. In the TIVA group (group IV), the  $fT_4$  concentration remained similar throughout the observation.

In all groups, the highest serum concentrations of  $fT_4$  were noted before surgery (Fig. 3). On postoperative day 4, the level of  $fT_3$  was markedly lower in all surgically treated patients. In the control group (V), however, the  $fT_3$  concentrations did not substantially change throughout the observation period.

Prior to surgery and immediately after thyroidectomy, the values of  $fT_3$  were found to be significantly higher in group II and IV compared to group V.

The inter-group differences in surgical stress severity in the perioperative period, including the evaluation according to PSS and SSS were not significant.

## DISCUSSION

The main goal of anaesthetic management is to provide patient safety in the perioperative period, which is achieved by relieving the pain and inhibiting the stress

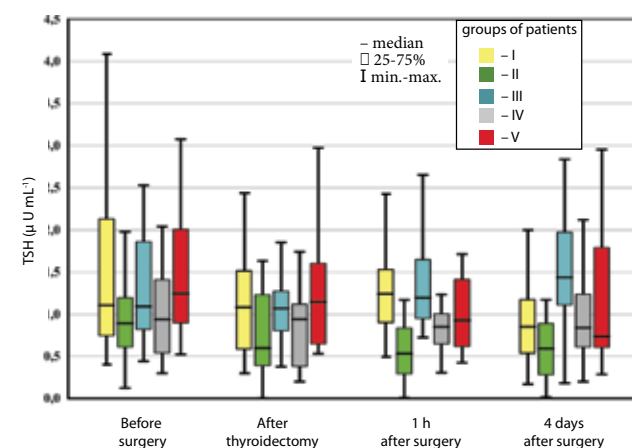


Fig. 1. Serum TSH concentrations at individual measurement points

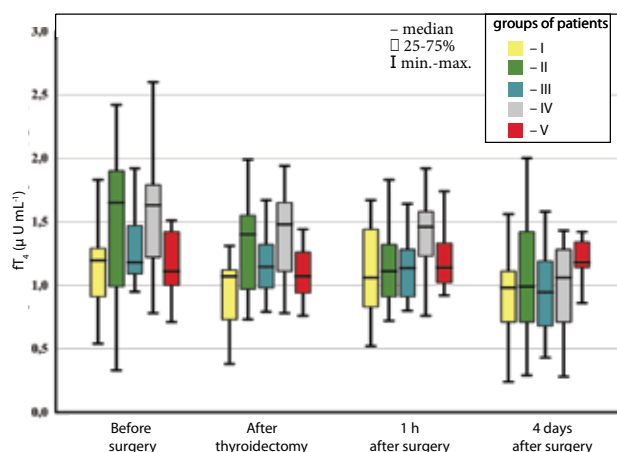


Fig. 2. Serum  $fT_4$  concentrations at individual measurement points

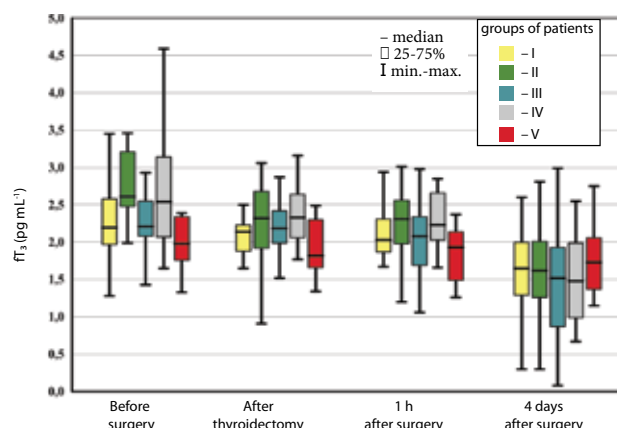


Fig. 3. Serum  $fT_3$  concentrations at individual measurement points

response resulting in for many intra- and post-operative complications [10]. The choice of an anaesthetic method and use of individual anaesthetics can markedly affect the production and release of thyroid hormones, the indicators of stress severity in the perioperative period.

According to the literature data, during abdominal surgeries the serum concentrations of  $fT_4$  and  $fT_3$  increase with the TSH levels unchanged [11, 12]. It is most likely that the increased unbound fraction of thyroid hormones is not caused by their higher total amounts but results from decreased concentrations of thyroxine-binding prealbumin (TBPA) and thyroxine redistribution between the extra- and intravascular spaces. Moreover, it has been demonstrated that serum concentrations of THS decrease during the first two postoperative hours and gradually return to baseline values; otherwise, the concentration of  $fT_3$  decreases markedly during the successive postoperative days [13].

Based on our findings, the concentrations of  $fT_4$  and  $fT_3$  gradually decreased with time both in VIMA and TIVA patients. Their lowest levels were observed on postoperative day 4. At each measurement point, the concentrations of  $fT_3$  and  $fT_4$ , however, were within the reference range. In contrast, in the control group, the levels of  $fT_3$  and  $fT_4$  in VIMA patients did not change throughout the study period. It is worth emphasizing that the changes in concentrations of free thyroid hormones depended on the type of surgery and not the method of anaesthesia used. Similar observations were reported by other authors [11]. Most likely, this is associated with the release of thyroid hormones from tissue reservoirs, mainly the liver, rather than the gland stimulation during surgery [12].

Furthermore, our results demonstrated that the serum THS concentration did not change substantially during the entire observation period in all groups of patients. This finding may evidence the inhibition of strong pain stimulation reaching the hypothalamus from

the operating site within the neck or peritoneum during inhalation anaesthesia with sevoflurane and intravenous anaesthesia with propofol. Similar results are found in the studies of comparable profiles [12]. According to some other reports, serum concentrations of  $fT_3$ ,  $rT_3$  and  $T_4$  are elevated during inhalation anaesthesia [7, 10].

Due to possible complications of surgical and anaesthetic treatment, the postoperative period is particularly hazardous [14, 15]. The studies in patients undergoing abdominal surgeries reveal that E-PASS enables to define the probability of complications, including deaths [16]. Low values of total PRS and SSS score correlate with low risks of postoperative complications and low mortality rates [17, 18]. The prognostic efficiency of E-PASS has been confirmed in patients undergoing thoracic, vascular and orthopaedic surgical procedures [18, 19, 20]. Our observations are similar; in all groups of patients, low E-PASS scores were associated with low risk of postoperative complications and good prognosis.

## CONCLUSIONS

1. The use of VIMA with sevoflurane and TIVA with propofol for thyroidectomy does not result in significant changes in serum concentrations of thyrotropin or free fractions of tyrosine and triiodothyronine, irrespective of the type of goitre, and enable the maintenance of euthyresis in the perioperative period.

2. VIMA and TIVA can be the alternative methods of anaesthesia in patients subjected to removal of various goitre types providing their safety in the immediate postoperative period.

## REFERENCES

1. Blackburn S: Surgical stress. *J Perinat Neonat Nurs* 2007; 21: 9-10.
2. Marana E, Scambia G, Colicci S, Maviglia R, Maussier ML, Marana R, Proietti R: Leptin and perioperative neuroendocrine stress response with two different anaesthetic techniques.

- Acta Anaesthesiol Scand 2008; 52: 541-546.
3. *Hahnenkamp K, Herroeder S, Hollman MW*: Regional anaesthesia, local anaesthetics and surgical stress response. *Best Pract Res Clin Anaesthesiol* 2004; 18: 509-527.
  4. *Goździk W, Durek G, Maślanka P, Adamik B, Namięta K, Kubler A, Kustrzycki W*: Hormonalna odpowiedź na stres okołoperacyjny przy znieczuleniu całkowicie dożylnym z zastosowaniem ciągłego wlewu remifentanylu i propofolu TCI do zabiegów chirurgicznej rewaskularyzacji wieńcowej z zastosowaniem krążenia pozaustrojowego. *Anestezjol Intens Ter* 2003; 35: 157-164.
  5. *Pierro A*: Metabolism and nutritional support in the surgical neonate. *J Pediatr Surg* 2002; 37: 811-822.
  6. *Huiku M, Uutela K, Gils M, Korhonen I, Kymalainen M, Merilainen P, Paloheimo M, Rantanen M, Takala P, Viertio-Oja H, Yli-Hankala A*: Assessment of surgical stress during general anaesthesia. *Br J Anaesth* 2007; 98: 447-455.
  7. *Borner U, Klimek M, Schoengen H, Lynch J, Peschau C, Schicha H*: The influence of various anesthetics on the release and metabolism of thyroid hormones: results of two clinical studies. *Anesth Analg* 1995; 81: 612-618.
  8. *Marana E, Annetta MG, Meo F, Parpaglioni R, Galeone M, Maussier ML, R.Marana*: Sevoflurane improves the neuroendocrine stress response during laparoscopic pelvic surgery. *Can J Anaesth* 2003; 50: 348-354.
  9. *Nishiyama T, Yamashita K, Yokoyama T*: Stress hormone changes in general anesthesia of long duration: isoflurane-nitrous oxide versus sevoflurane-nitrous oxide anesthesia. *J Clin Anesth* 2005; 17: 586-591.
  10. *Miner JR*: The surgical stress response, preemptive analgesia, and procedural sedation in the emergency department. *Acad Emerg Med* 2008; 15: 955-958.
  11. *Chikenji T, Mizutani M, Kitsukawa Y*: Anaesthesia, not surgical stress, induces increases in serum concentrations of reverse triiodothyronine and thyroxine during surgery. *Exp Clin Endocrinol* 1990; 95: 217-223.
  12. *Bielski J, Szymańska-Kowalska M*: Wpływ anestezji z użyciem propofolu w operacjach tarczycy na stężenie hormonu tyreotropowego i hormonów tarczycowych. *Anestezjol Intens Ter* 1996; 28: 67-71.
  13. *Desborough JP*: The stress response to trauma and surgery. *Br J Anaesth* 2000; 85: 109-117.
  14. *Ghatge S, J.Lee, Smith I*: Sevoflurane: an ideal agent for adult day-case anesthesia? *Acta Anaesthesiol Scand* 2003; 47: 917-931.
  15. *Coloma M, Zhou T, White PF, Markowitz SD, Forestner JE*: Fast-tracking after outpatient laparoscopy: reasons for failure after propofol, sevoflurane, and desflurane anesthesia. *Anesth Analg* 2001; 93: 112-115.
  16. *Haga Y, Ikei S, Ogawa M*: Estimation of physiologic ability and surgical stress (E-PASS) as a new prediction scoring system for postoperative morbidity and mortality following elective gastrointestinal surgery. *Surg Today* 1999; 29: 219-225.
  17. *Haga Y, Wada Y, Takeuchi H, O.Kimura, Furuya T, Sameshima H, Ishikawa M*: Estimation of physiologic ability and stress (E-PASS) for surgical audit in elective digestive surgery. *Surgery* 2004; 135: 586-594.
  18. *Tang T, Walsh SR, Fanshawe TR, Gillard JH, Sadat U, Varty K, Gaunt ME, Boyle JR*: Estimation of physiologic ability and surgical stress (E-PASS) as a predictor of immediate outcome after elective abdominal aortic aneurysm surgery. *Am J Surg* 2007; 194: 176-182.
  19. *Yamashita S, Haga Y, Nemoto E, Nagai S, Ohta M*: E-PASS (the estimation of physiologic ability and surgical stress) scoring system helps the prediction of postoperative morbidity and mortality in thoracic surgery. *Eur Surg Res* 2004; 36: 249-255.
  20. *Hirose J, Mizuta H, Ide J, Nomura K*: Evaluation of estimation of physiologic ability and surgical stress (E-PASS) to predict the postoperative risk for hip fracture in elder patients. *Arch Orthop Trauma Surg* 2008; 128: 1447-1452.

received: 11.06.2011

accepted: 20.10.2011

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