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Risk Factors for New Onset Atrial Fibrillation during Thyroid Gland Surgery

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Highlights of the Study

- Incidence of new onset atrial fibrillation during thyroid surgery in euthyroid patients is similar to the incidence in other types of surgery.
- Previous heart rhythm disturbances are a strong predictor of new onset atrial fibrillation.
- Perioperative monitoring of these patients is required, especially if they have risk factors.

Keywords
Thyroid surgery · Atrial fibrillation · Risk factor · Anaesthesia

Abstract
Objective: Thyroid dysfunction is a common cause of atrial fibrillation (AF). Incidence of AF is high in patients with both expressed and subclinical hyperthyroidism. The aim of our study was to determine the incidence and predictors of new onset atrial fibrillation (NOAF) in euthyroid patients undergoing thyroid surgery. ***Subject and Methods:*** The study included 1,252 euthyroid patients with American Society of Anesthesiologists (ASA) physical status ASA 2 and ASA 3, who were 18 years and older and were in sinus rhythm. Patients without comorbidity and patients with persistent AF were excluded. We investigated the influence of the following preoperative characteristics on the occurrence of NOAF: age, sex, body mass index, ASA score, admission diagnoses, and comorbidity. We noted the influence of difficult intubation of trachea, type and duration of surgery, and time under general anaesthesia. Univariate and multivariate logistic regression were used to determine predictors of occurrence of NOAF. ***Results:*** NOAF was noted in 0.72% of patients. Patients with NOAF were older (63.11 vs. 56.81 years) than patients without NOAF, but this was not statistically significant. Significantly more patients from the NOAF group had preoperative heart rhythm disturbance and a history of angina pectoris, in contrast to patients without registered NOAF ($p = 0.001$; $p = 0.017$). Multivariate analysis showed that a history of heart rhythm disturbance was an independent predictor of NOAF. ***Conclusions:*** Incidence of NOAF during thyroid surgery is similar to the other type of surgery, if the values of thyroid hormones are normal.

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Introduction

Atrial fibrillation (AF) is one of the most common cardiac dysrhythmias that require treatment. The prevalence of this arrhythmia increases with age; AF occurs in 0.1% of people younger than 55 years and rises to 9% for people of 80 years of age and older [1]. It is associated with an increase in morbidity and prolonged length of hospital stay, as well as with a higher cost of treatment of these patients [2]. Complications, especially ischaemic stroke, transient ischaemic attack, and other thromboembolic complications, are more frequent in patients with AF, resulting in higher perioperative mortality [3, 4]. The absolute risk of ischaemic stroke or transient ischaemic attack at 5 years for patients with perioperative AF is significant compared with those with no AF and rises to 10.7% [3, 5]. Similarly, an increased risk of all-cause death has been reported for patients with AF compared with those with no AF [3, 4].

The incidence of AF is highest in cardiac surgery; it is higher in patients undergoing valve surgery (up to 52.7%) than in patients undergoing coronary artery bypass surgery (27%) [6, 7]. It is also one of the most frequent complications of thoracic surgery, with a reported incidence ranging between 12.3% and 38% [3, 8]. AF occurs relatively rarely in non-cardiothoracic surgery (0.37% occurrence in ophthalmic surgery, 3.1–14.1% in orthopaedic surgery, 6.4% in nervous system procedures, 69% in urogenital surgery, 14% in vascular surgery, and about 9–13% in large colorectal surgery) [3, 9–12].

The underlying causes of AF are incompletely defined. Some of described mechanisms include intraoperative phenomena, such as inflammation, sympathetic activation, and cardiac ischaemia that combine to trigger AF, often in the presence of pre-existing factors, making the atria vulnerable to AF induction and maintenance [13]. Also, electrophysiological disturbances, metabolic imbalances, hypoxia, hyper/hypoglycaemia, and hypervolemia during the operation can cause AF [12]. It is known that thyroid dysfunction is a common cause of AF. Previous studies have shown a significantly higher incidence of AF in patients with both expressed hyperthyroidism and subclinical hyperthyroidism [1, 12]. However, there are little data on the incidence of AF in euthyroid patients undergoing thyroid surgery. Therefore, the aim of our study was to determine the prevalence and predictors of new onset atrial fibrillation (NOAF) in these patients.

Methods

In this prospective observational study, we included patients who underwent thyroid surgery at the Centre for Endocrine Surgery, University Clinical Centre of Serbia, Belgrade, during January 2017–January 2021. As the treatment of patients did not differ from the usual treatments, the need for signed patient consent was waived and the study was institutionally approved.

All surgeries were performed during general anaesthesia. Intraoperatively, we noted the occurrence of NOAF, defined as the appearance of irregular atrial activity characterized by irregular RR intervals with a lack of p waves that lasted more than 30 s. Automatic arrhythmia detection and printed strip report were used. We confirmed the occurrence of AF by a complete 12 lead ECG (GE Medical Systems MAC 1200 version 5. 2) in all cases. During the postoperative period, patients were followed for the first 24 h continuously using bedside monitors and then once a day until hospital discharge.

We investigated the influence of the following preoperative characteristics on the occurrence of NOAF: age, sex, body mass index (< or >25 kg/m^2), ASA score, admission diagnoses, and comorbidity. The following coexisting diseases were observed: hypertension, cardiomyopathy, angina pectoris, cardiac rhythm disturbances (bradycardia, tachycardia, AF, ventricular and supraventricular extrasystoles [VES/SVES]), diabetes mellitus, kidney disease (chronic and terminal renal failure), anaemia (which we defined as a haemoglobin value of less than 12 mg/dL). We noted the influence of the following intraoperative characteristics: difficult intubation of trachea (defined as the inability 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 (min).

Statistical Analysis

SPSS software version 28 (SPSS Inc, Chicago, IL, USA) was used for statistical data processing. Numerical variables such as age, duration of surgery, and time under general anaesthesia are shown in the form of mean values ± standard deviation, while the other categorical variables are shown as absolute numbers and percentages. Patients were divided into two groups: with NOAF and without NOAF. The normality of data distribution was checked by the one sample Kolmogorov-Smirnov test. We used *t* test to compare the average values of the parametric features, while Pearson's χ^2 test was used to compare the differences in frequency of categorical features. Predictors of occurrence of NOAF were determined by logistic regression analysis. p values <0.05 were considered statistically significant.

Results

During the study period, 2,259 patients were treated at our centre. Among them, 192 patients with hypothyroidism, 183 patients with hyperthyroidism, and 362 patients with autoimmune thyroid disease were excluded. Also, patients without comorbidity (ASA 1 physical status) and patients with persistent AF were excluded. Finally, a total of 1,252 patients were analysed (Fig. 1).

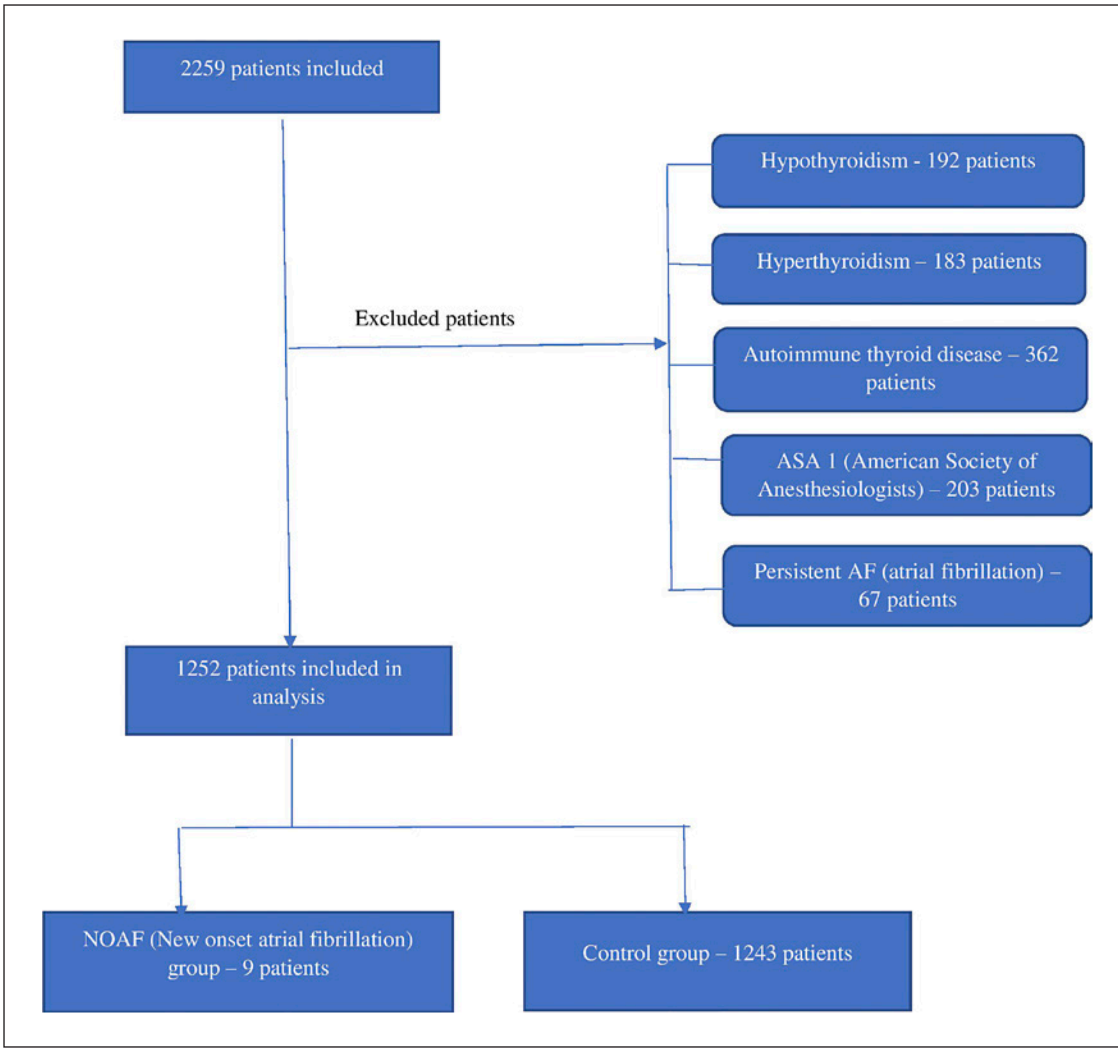

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Fig. 1. Flow chart of study population.

The descriptive statistics are shown in Table 1. The majority were women (86.3%) with ASA 2 status (80.2%). Eighty-five of our patients (6.8%) had preoperative heart rhythm disturbances, as follows: bradycardia 2 (2.4%), tachycardia 24 (28.2%), AF 36 (42.4%), VES/SVES 23 (27.1%). Our patients had the following admission diagnosis: nodular goitre – 350 (28%); multinodular goitre – 652 (52%); thyroid gland cyst – 9 (0.7%); recidivant goitre – 69 (5.5%); papillary carcinoma – 78 (6.2%); medullary carcinoma – 69 (5.5%); Hurthle cell carcinoma – 8 (0.6%); follicular carcinoma – 5 (0.4%); oxyphil lesion – 12 (0.9%). The most common type of surgery was total thyroidectomy (76.6%) while the other types of surgery (hemithyroidectomy, lobectomy, tumour reduction) were less common (23.4%).

Patients were divided into 2 groups: patients with NOAF registered during the intraoperative period and a control group – patients without NOAF (Table 2). Patients with NOAF were older (63.11 vs. 56.81), but this was not statistically significant ($p > 0.05$). More patients of ASA 3 status were in the group with NOAF compared to the group without NOAF (44.4 vs. 19.6%) but also without statistical significance. Bradycardia and tachycardia were registered only in patients without NOAF, while 2 patients had AF from the group of patients with NOAF and 34 from the group without NOAF (66.7 vs. 41.5%), while VES/SVES was present in 1 patient (33.3%) from the NOAF group and 22 patients (26.8%) from the group without NOAF. Significantly more patients from the NOAF group had a history of angina pectoris (33.3 vs. 6.8%, $p = 0.017$). There was no differ-

Table 1. Patients' characteristics

Variable	*n* (%)
Age (mean ± SD), years	56.86±11.42
Sex	
Female	1,081 (86.3)
Male	171 (13.7)
ASA	
ASA 2	1,004 (80.2)
ASA 3	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)
AP	62 (5)
DM	149 (11.9)
Insulin dependent	4 (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 (mean ± SD), min	69.5±24.1
TUGA (mean ± SD), min	79.43±24.67
Postoperative AF	22 (1.76)

SD, standard deviation; *n*, number of patients; ASA, American Society of Anesthesiologists; BMI, body mass index; CMP, cardiomyopathy; DM, diabetes mellitus; DI, difficult intubation; TUGA, time under general anaesthesia; AP, angina pectoris.

ence in the incidence of other comorbidities between the two groups. We also noted a higher incidence of complications during recovery from anaesthesia in patients with NOAF, in terms of prolonged awakening, and a higher incidence of postoperative nausea and vomiting in the same group. Significantly more patients with NOAF had AF in the postoperative period, compared to patients without NOAF (33.3 vs. 1.5%, $p = 0.000$).

We applied the logistic regression model to determine the influence of each variable on the occurrence of NOAF. Univariate analysis showed that history of earlier heart rhythm disturbances and angina pectoris influenced the occurrence of NOAF (Table 3). Multivariate analysis showed that a history of heart rhythm disturbances was an independent predictor of NOAF (Table 4).

Discussion

Our study results indicate that during the intraoperative period, the incidence of NOAF is 0.72%. History of heart rhythm disturbances, especially earlier absolute arrhythmia and extrasystoles, are independent predictors of occurrence of NOAF.

Thyroid dysfunction is an important risk factor for paroxysmal AF [14, 15]. The incidence of AF is significantly higher in patients with hyperthyroidism compared to euthyroid patients [15, 16]. The incidence of AF has been shown to be very high in patients with subclinical hyperthyroidism. In fact, subclinical thyroid dysfunction, which is biochemically characterized by an abnormal TSH value with normal values of thyroid hormones T3 and T4, is also very common, with a frequency of up to 12% which increases with age [17]. The results of two large prospective cohort studies [18, 19] and a cross-sectional study [14] indicate an association between subclinical hyperthyroidism and AF. Serum FT4 was demonstrated to be an independent predictor for AF, both in patients with proven thyroid dysfunction and in euthyroid patients [15]. It was also shown that the value of FT3 at admission is an independent predictor of AF [20]. Unlike the previously mentioned studies, we observed only euthyroid patients during the intraoperative and immediate postoperative period. Even though we included only patients with comorbidities (ASA 2 and ASA 3), we obtained a relatively low frequency of NOAF.

Thyroid hormones have many effects on cardiovascular function. Previous studies have shown that thyroid hormones can shorten the action potential in both atrial and ventricular myocytes, which could facilitate and promote the appearance of re-entry mechanism and the formation of atrial tachyarrhythmia. By acting on ion channels, thyroid hormones decreased the expression of L-type calcium channel mRNA and increased the expression of Kv 1.5 mRNA which leads to increased outward current and decreased inward current resulting in shorter action potential duration [21]. Thyroid hormones also increased spontaneous activity in pulmonary vein cardiomyocytes, increased the occurrence of delayed after-depolarizations in pulmonary vein beating and non-beating cardiomyocytes, and increased after-depolarizations in beating cardiomyocytes [22].

Although AF is a common cardiac complication of hyperthyroidism, it can also be the loading symptom of apathetic hyperthyroidism, especially in the elderly and can precipitate the onset of a thyroid storm [23]. On the other hand, surgery itself can be a trigger for a thyroid crisis, which is caused by the sudden release of excessive thyroid hormones into the circulation [24]. Senese et al. [25] examined the effect of thyroid surgery on the kinetics of thyroid hormones. They measured TSH, T3, T4, and thyroglobulin levels preoperatively, intraoperatively, and

Table 2. Characteristics of the patients with and without NOAF

Variable	Patients with NOAF *N* = 9 (0.72 %)	Patients without NOAF *N* = 1,243 (99.28 %)	*p* value
Age (mean ± SD), years	63.11±11.14	56.81±11.41	0.080
Sex			
Female	7 (77.8)	1,074 (86.4)	0.453
Male	2 (22.2)	169 (13.6)	
ASA			
ASA 2	5 (55.6)	998 (80.4)	0.064
ASA 3	4 (44.4)	243 (19.6)	
BMI (mean ± SD), kg/m^2	28.87±4.47	27.28±4.79	0.276
Hypertension	6 (66.7)	826 (66.5)	0.989
CMP	2 (22.2)	96 (7.7)	0.107
Cardiac arrhythmias	3 (33.3)	82 (6.6)	0.001*
AP	2 (22.2)	60 (4.8)	0.017*
DM	2 (22.2)	147 (11.8)	0.337
Kidney disease	0 (0)	22 (1.8)	0.687
Anaemia	1 (11.1)	42 (3.4)	0.205
DI	3 (33.3)	132 (10.6)	0.122
Type of surgery	7 (77.8)	952 (76.6)	0.758
Duration of surgery (mean ± SD), min	71.11±24.47	69.49±24.08	0.662
TUGA (mean ± SD), min	81.67±28.39	79.38±24.68	0.643
Complications during anaesthesia emergence	3 (33.3)	25 (2.0)	0.000*
Postoperative AF	3 (33.3)	19 (1.5)	0.000*
Postoperative nausea	3 (33.3)	139 (12.1)	0.053

Abbreviations as in Table 1. Values are *n* with percentages in parentheses unless indicated otherwise. * Statistically significant.

Table 3. Univariate logistic regression analysis

Variable	Odds ratio (95% CI)	*p* value
ASA	1.800 (0.932–3.476)	0.080
Age	1.056 (0.990–1.128)	0.100
Sex	0.551 (0.113–2.673)	0.459
BMI	1.060 (0.947–1.186)	0.312
Hypertension	1.010 (0.251–4.057)	0.989
Cardiac arrhythmias	7.079 (1.739–28.820)	0.006*
AP	5.633 (1.146–27.700)	0.033*
CMP	3.414 (0.699–16.660)	0.129
DM	2.130 (0.438–10.351)	0.348
Kidney disease	0.000 (0.000-)	0.998
Anaemia	3.574 (0.437–29.233)	0.235
Type of surgery	1.080 (0.902–1.292)	0.404
DI	2.328 (0.761–7.125)	0.139
Duration of surgery, min	1.003 (0.977–1.029)	0.840
TUGA, min	1.004 (0.979–1.029)	0.782
Complications during recovery from anaesthesia	24.360 (5.764–102.957)	0.000*
Postoperative AF	32.211 (7.495–138.434)	0.000*
Postoperative nausea	3.637 (0.899–14.706)	0.070

CI, confidence interval; BMI, body mass index; CMP, cardiomyopathy; DM, diabetes mellitus; DI, difficult intubation; TUGA, time under general anaesthesia; AP, angina pectoris. * Statistically significant.

Table 4. Multivariate logistic regression analysis

Variable	Odds ratio (95% CI)	*p* value
Cardiac rhythm disturbances	6.280 (1.512–26.088)	0.011*
AP	4.630 (0.911–23.537)	0.065

CI, confidence interval; AP, angina pectoris. * Statistically significant.

postoperatively and found that the manipulation of the thyroid gland during surgery causes significant changes in concentrations of hormones but without clinical effects, including thyrotoxicosis.

The risk for AF increases exponentially with age [2, 13]. It was shown that less than 5% of patients younger than 40 years, and more than one-third older than 70 years, have postoperative tachyarrhythmia. It was shown that with each decade of life, the risk for AF increases by 2.1 in men and 2.2 for women [26]. Amar et al. [27] found similar results in their study showing that the incidence of AF was significantly higher in patients older than 60 years and in those who had, preoperatively, a frequency greater than 74 (≥74 beats/min). The risk for AF was increased by 2.5 times between age groups (<60 years, 60–69 years, ≥70 years) and by 2.3 times, depending on whether the frequency was less or greater than 74/min. The combination of age >60 years and frequency >74 beats/min predicted the appearance of AF with a sensitivity of 73% and a specificity of 57%. Atrial changes caused by ageing, such as dilatation, muscle atrophy, decreased conductance, may explain this association. Unlike previous studies, age was not an independent predictor for NOAF in our study. Although patients with NOAF were older than patients without NOAF (63.11 vs. 56.81 years), this difference was not statistically significant. A possible explanation for this result lies in the fact that our patients were relatively young. The average age of our patients was 56 years.

Most studies showed that, besides age, other important risk factors for AF are male sex, hypertension, diabetes, myocardial infarct, congestive heart failure, aortic atherosclerotic disease, chronic pulmonary disease, peripheral vascular disease, liver disease, and renal disease [2, 3, 12, 14]. It was shown that obesity affects the occurrence of AF indirectly through the increase in left ventricular mass. It is a novel risk factor for AF associated with a 50% increased incidence [28]. Genetic factors, specific clinical conditions (hypertension, diabetes, obstructive sleep apnoea, metabolic syndrome), coronary artery disease, ventricular adaptation, inflammation, oxidative stress, focal adiposity are involved in atrial remodelling, facilitating AF initiation and perpetuation in obese subjects. Wang et al. [28] showed that after adjustment for echocardiographic left atrial diameter in addition to clinical risk factors, body mass index was no longer associated with AF risk [29]. Our results also confirm that obesity is not a predictor for AF, in contrast to angina pectoris, which we have shown affects the frequency of occurrence of NOAF.

A study by Polanczyk et al. [2] on 4,181 patients younger than 50 years undergoing non-cardiac surgery (but including thoracic surgery) revealed the occurrence of supraventricular arrhythmias (which persisted or required treatment) in 2% intraoperatively and 6.1% postoperatively. The variables that were independently associated with the development of AF were earlier occurrence of AF, older age, left anterior hemiblock, and atrial beats on the preoperative ECG. This study [2], like ours, included a relatively young population, younger than 50 years. NOAF was registered in 2% of patients intraoperatively, in contrast to 0.72% in our study. However, even though this study by Polanczyk et al. [2] included only patients who underwent non-cardiac surgery, it also included patients who underwent thoracic surgery, unlike our study which involved only patients undergoing thyroid surgery. The appearance of AF significantly affects the further treatment of patients. Patients with NOAF have a higher mortality (23.4 vs. 4.3%), longer stay in the intensive care unit, and total hospital stay than patients without arrhythmias [3]. Goodman et al. [30] came to similar conclusions in their research showing that the APACHE 2 score was higher in the group with NOAF than in patients without arrhythmias, and the incidence of NOAF is very high in intensive care unit (in this study 9%) and is a marker of extremely high intrahospital and 1-year mortality.

A limitation of our study is the absence of a control group undergoing comparable non-thyroidal surgery. Patients without AF were control to patients with AF, while we compared the incidence of NOAF with other types of surgery where euthyroid patients were also included.

Conclusions

Incidence of AF in non-cardiothoracic surgery should not be ignored, despite lower incidence. When it comes to thyroid surgery, if the values of thyroid hormones are normal, the incidence of AF is similar to that in other types of low-risk surgery. It is known that manipulation of the thyroid gland during surgery leads to a significant change in the kinetics of thyroid hormone levels, but without significant clinical effects, especially when it comes to the incidence of NOAF. Considering higher morbidity and mortality of these patients, even when it comes to smaller operations and low-risk procedures, adequate preparation and perioperative monitoring of these patients are required, especially if they have risk factors.

Statement of Ethics

The study was institutionally approved. The requirement for signed patient consent was waived by the expert collegium of the Endocrine Surgery Clinic, University Clinical Centre of Serbia, as the treatment of patients did not differ from the usual (case number: 153-06-1422/2018-04).

Conflict of Interest Statement

The authors declare no conflicts of interest.

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None.

Author Contributions

Marina Stojanovic, Nevena Kalezic, and Vladan Zivaljevic designed the experiments and analysed the data. Biljana Milicic, Milana Zivkovic, Tjasa Ivosevic, and Mirko Lakicevic analysed the data and prepared the manuscript. All authors approved the final manuscript.

Data Availability Statement

The data that support the findings of this study are available on request from the corresponding author.

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