RESEARCH ARTICLE

Editorial Process: Submission:01/05/2024 Acceptance:04/11/2024

Sparing Swallowing-Related Structures Reduces Post-Radiotherapy Dysphagia in Oropharyngeal Cancer

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Abstract

Objective: To identify swallowing-related structures (SRSs) predicting post-radiotherapy dysphagia in oropharyngeal carcinoma patients. **Material and methods:** Between September 2020 and October 2022, oropharyngeal cancer patients who had completed radiotherapy at least one year before without recurrence or residuals were selected. They underwent flexible endoscopic evaluation of swallowing (FEES) assessments and dysphagia grading. The mean radiation doses delivered to their SRSs were recalculated. The correlation between radiation doses to each SRS and FEES scores was analysed. **Results:** Twenty-nine participants, aged 51–73 years, were enrolled. Six patients had received two-dimensional radiotherapy, eight had undergone three-dimensional conformal radiotherapy, and fifteen had received intensity-modulated radiation therapy. Radiation doses to the inferior pharyngeal constrictor, cricopharyngeus and glottic larynx significantly predicted dysphagia for both semisolids ($p = 0.023$, 0.030 and 0.001) and liquid diets ($p = 0.021$, 0.013 and 0.002). The esophageal inlet significantly predicted swallowing outcomes for only the liquid diet ($p = 0.007$). **Conclusions:** This study supports that SRS-sparing during radiotherapy for oropharyngeal cancers improves swallowing outcomes.

Keywords: Dysphagia- Oropharyngeal cancer- Radiation doses- Radiation therapy- Swallowing-related structures

Asian Pac J Cancer Prev, **25 (4)**, 1451-1456

Introduction

Radiotherapy plays a crucial role in the treatment of cancer, particularly oropharyngeal cancer. Therapeutic radiation therapy utilises higher energy X-rays than diagnostic radiology. While high doses of radiation can eliminate cancer cells, they can also harm adjacent normal cells [1]. The acute effects of radiation therapy typically persist for approximately 8 to 12 weeks after treatment cessation. Additionally, there are long-term effects, such as soft tissue fibrosis and xerostomia. Tissue fibrosis affects the mobility of the tongue and pharyngeal muscles and the elevation of the larynx and hyoid [2]. Dysphagia, a significant complication of head and neck radiation therapy, becomes particularly pronounced when the radiation area encompasses a large portion of the neck. Consequently, dysphagia can profoundly impact patients' quality of life [3].

Advancements in computer technology have facilitated the transition from basic 2-dimensional radiotherapy (2DRT) to a more sophisticated approach known as 3-dimensional conformal radiotherapy (3DCRT). 3DCRT has been developed to limit the radiation dose to the planning target volume while minimising radiation spillage beyond the target area [4]. Intensity-modulated radiotherapy (IMRT) is a novel radiation treatment approach employing computer-controlled linear accelerators to deliver precise radiation doses to malignant tumours or specific areas within a tumour [5-7]. IMRT allows for the concentration of higher radiation doses on the intended target while minimising radiation exposure to surrounding normal structures.

The structures involved in swallowing (swallowing-related structures or SRSs) comprise the superior, middle and inferior posterior constrictor muscles; cricopharyngeus muscle; esophageal inlet; base of the tongue; supraglottis; and glottic larynx. These structures may be impacted during radiotherapy for oropharyngeal cancers. Therefore, an advanced radiation technique that reduces the radiation dose to the SRSs could help mitigate swallowing problems [1, 8, 9].

Flexible endoscopic evaluation of swallowing (FEES) is a standardized, precise and highly safe objective procedure for assessing swallowing parameters [10-12]. We hypothesized that different doses delivered to each SRS would provide different swallowing parameters and

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FEES scores. Thus, if some of SRSs are protected during radiotherapy, the patients' swallowing function would improve.

This cross-sectional study aimed to identify (1) SRSs that could serve as predictors for dysphagia and (2) the optimal radiation dose to deliver to each SRS to prevent post-therapeutic dysphagia.

Materials and Methods

This cross-sectional study was conducted on Thai patients treated for oropharyngeal cancer at the ear, nose, and throat oncology clinic of Siriraj Hospital, Bangkok, Thailand, between September 2020 and October 2022.

Study subjects

The participants were at least 18 years old, had been diagnosed with oropharyngeal cancer, and had undergone definitive radiotherapy or chemoradiation at our tertiary care hospital. The radiation therapy techniques used were 2DRT, 3DCRT and IMRT. All patients had completed radiotherapy at least one year before their enrolment in the study, with none showing evidence of residuals or recurrence. Patients were excluded if they had cerebrovascular diseases, a history of head and neck surgery, a history of neuromuscular dysphagia, or if they were physically or mentally incapable of participating. The sample size calculation was based on a study by Ozkaya-Akagunduz et al. [12] The mean difference between the FEES scores for the SRS-sparing (3DCRT/IMRT) and non-SRS-sparing (2DRT) techniques was 0.9 (standard deviation = 0.5), the significance level (α) was 0.05, and the power was 90%. The sample size calculated using the nQuery Advisor program was 24 participants.

Interventions and study variables

The primary outcome variable of interest was the patients' swallowing function. All participants underwent FEES performed by our swallowing specialists. The procedure was conducted with the patient in an upright sitting position. A trans-nasal flexible endoscope was inserted and positioned at the level of the oropharynx, after which the patients were instructed to swallow liquid (nectar) and semisolid food (coconut cream). Participants were required to consume 30 ml of each type of food. The parameters for evaluating swallowing function were premature oropharyngeal spillage, laryngeal penetration, aspiration, and post-swallow residues. All findings were scored according to the criteria of Topaloglu et al. [13] (Table 1). FEES scores were categorised into three groups: severe dysphagia (scores 1 and 2), moderate dysphagia (score 3), and mild or no dysphagia (scores 4 and 5).

The primary predictor variable was the radiation dose delivered to the SRSs. A blinded radiation oncologist recontoured and recalculated the mean radiation dose (Gy – Gray) delivered to the SRSs in each patient who received 3DCRT and IMRT. Figure 1 demonstrates relevant computed tomographic slices illustrating the delineation of swallowing-related structures [14]. Radiation doses were estimated based on bony landmarks of the conventional radiation field related to the prescribed radiation doses for patients who received 2DRT. Subsequently, statistical analysis was performed to compare the radiation doses of the patients with higher FEES scores and of those with lower FEES scores. The radiation doses of each SRS were also compared in terms of higher and lower FEES scores and semisolid and liquid diets.

Statistical analysis

Baseline characteristics are presented as the mean ± standard deviation for continuous data and as numbers (percentages) for categorical data. T-tests were used to compare continuous data. Analyses were performed using IBM SPSS Statistics, version 26 (IBM Corp, Armonk, NY, USA). A p-value < 0.05 was considered statistically significant.

Results

Participant demographics

Twenty-nine participants were enrolled. All were male, with ages ranging from 51 to 76 years and a mean age of 60.2 ± 8.6 years. The most common primary site of the tumour was the palatine tonsil. The participants received different radiation techniques. The majority of the subjects (22/29) completed the radiation course within 1 to 5 years. Detailed characteristics, including staging and the type of radiotherapy received, are summarised in Table 2.

Comparison of swallowing outcomes of the non SRS-sparing group (2DRT) and the SRS-sparing group (3DCRT/IMRT)

Twenty-three patients underwent 3DCRT or IMRT, while 6 patients underwent 2DRT. None of the patients in our series had FEES scores below 3 for either the semisolid

Table 1. Endoscopic Findings for Evaluating Swallowing Function

FEES score	Swallowing parameters		
	Premature oropharyngeal spillage	Post-swallow residues	Laryngeal penetration/aspiration
1	Severe (> 75%)	Severe (> 75%)	Material entered trachea; cannot be discharged from airway
2	Significant (> 50%–75%)	Significant (> 50%–75%)	Material entered trachea; was discharged from airway
3	Moderate (> 25%–50%)	Moderate (> 25%–50%)	Material entered larynx; cannot be discharged from airway
4	Mild (< 25%)	Mild (< 25%)	Material entered larynx; was discharged from airway
5	None	None	Material did not enter the airway

FEES, flexible endoscopic evaluation of swallowing

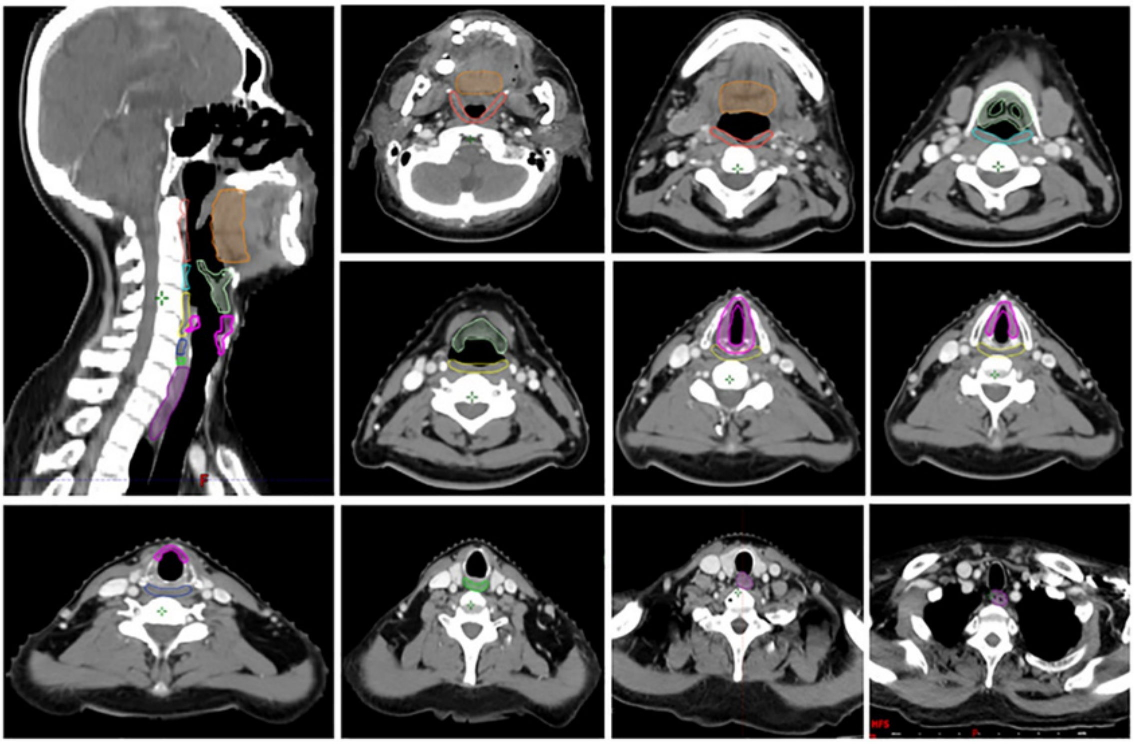

Figure 1. Relevant Computed Tomographic Slices Illustrating the Delineation of Swallowing-Related Structures. Shown in this Figure are the Superior Posterior Constrictor Muscle (PCM) (red), Middle PCM (light blue), inferior PCM (thyropharyngeal part) (yellow), cricopharyngeus (dark blue), esophageal inlet (lemon green), cervical esophagus (dark purple), base of tongue (orange), supraglottis (light green) and glottic larynx (magenta).

or the liquid diet. Pearson chi-squared analysis showed a significant difference in the FEES scores of the patients receiving 3DCRT/IMRT and those receiving 2DRT for both the semisolid and liquid diets. Table 3 demonstrates a significant difference between the FEES scores for the semisolid diet of these two patient groups. Patients undergoing 3DCRT/IMRT had better FEES scores than those receiving 2DRT ($p = 0.010$). This table also reveals that patients receiving any form of radiotherapy had good FEES scores for the liquid diet. However, a subgroup analysis of the mild dysphagia group (FEES score 4) and the no-dysphagia group (FEES score 5) showed that patients undergoing 3DCRT/IMRT had statistically better swallowing outcomes for the liquid diet than the 2DRT group ($p = 0.019$).

Correlation between radiation dose delivered to the SRSs and swallowing outcomes

Figure 2 illustrates comparison plots for radiation doses delivered to each SRS between subjects in the low FEES score group (score 3) and the high FEES score group (scores 4 and 5) for the semisolid diet examination.

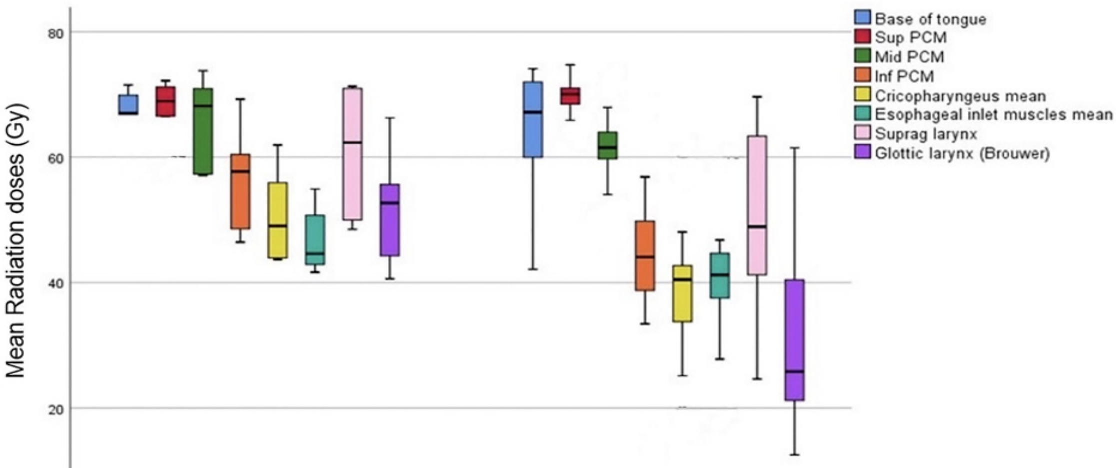

Figure 2. Plots Illustrating Radiation Dosage Delivered to each Swallowing-Related Structure between Groups for a Semisolid Diet

Table 2. Baseline Characteristics of Study Participants

Characteristics	Number (%)
Sex	
Male	29 (100%)
Female	0 (0%)
Primary site	
Tonsil	20 (69.0%)
Base of tongue	6 (20.7%)
Soft palate	3 (10.3%)
T stage	
T1	6 (20.7%)
T2	11 (38.0%)
T3	10 (34.4%)
T4	2 (6.9%)
N stage	
N0	7 (24.1%)
N1	6 (20.7%)
N2	12 (41.4%)
N3	4 (13.8%)
M stage	
M0	29 (100%)
M1	0 (0%)
Type of radiotherapy	
2DRT	6 (20.7%)
3DCRT	8 (27.6%)
IMRT	15 (51.7%)
Duration after finishing radiotherapy course	
1–5 years	22 (75.9%)
> 5 years	7 (24.1%)

2DRT, 2-dimensional radiotherapy; 3DCRT, 3-dimensional conformal radiotherapy; IMRT, intensity-modulated radiotherapy.

Table 3. Comparison of Scores for Flexible Endoscopic Evaluation of Swallowing between the 2DRT and 3DCRT/IMRT Groups

Type of diet	FEES scores	Type of radiotherapy		P-value
		2DRT n (%)	3DRT n (%)	
Semisolid	4, 5	1 (16.70%)	17 (73.90%)	0.01
	3	5 (83.30%)	6 (26.10%)	
liquid	5	1 (16.70%)	17 (73.90%)	0.019
	4	5 (83.30%)	6 (26.10%)	

2DRT, 2-dimensional radiotherapy; 3DCRT, 3-dimensional conformal radiotherapy; FEES, flexible endoscopic evaluation of swallowing

Table 4. Comparison of Mean Radiation Doses (Gy) Delivered to each SRS between Groups for a Semisolid Diet

	FEES scores for semisolid diet		
	3 (N = 17) Mean±SD	4, 5 (N = 6) Mean±SD	P-value
Base of tongue	66.50±5.07	64.82±8.98	0.671
Superior PCM	67.51±5.39	69.57±3.00	0.257
Middle PCM	65.89±7.07	60.63±7.28	0.14
Inferior PCM	56.68±8.31	42.41±13.21	0.023
Cricopharyngeus muscle	50.58±7.18	39.03±11.25	0.03
Oesophageal inlet	46.57±5.22	39.99±8.94	0.106
Supraglottis	60.89±10.39	50.97±12.83	0.104
Glottic larynx	52.02±9.03	30.03±13.51	0.001

FEES, flexible endoscopic evaluation of swallowing; PCM, posterior constrictor muscle

Table 4 illustrates the comparison of mean radiation doses (Gy) delivered to each SRS between the low-scoring group (score 3) and the high-scoring group (scores 4, 5) in the FEES for a semisolid diet. This table shows that among the SRSs, the inferior posterior constrictor muscle (PCM), cricopharyngeus muscle and glottic larynx were

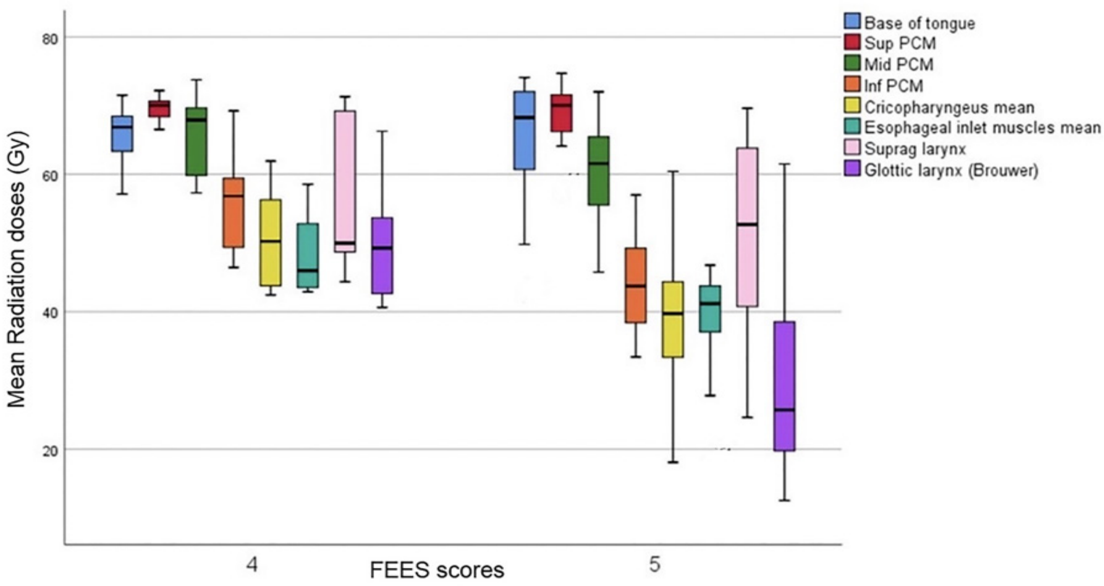

Figure 3. Plots Illustrating Radiation Dosage Delivered to each Swallowing-Related Structure between Groups for a Liquid Diet

Table 5. Comparison of Mean Radiation Doses (Gy) Delivered to each SRS between Groups for a Liquid Diet

	FEES scores for liquid diet		
	4 (N = 7) Mean±SD	5 (N = 16) Mean±SD	P-value
Base of tongue	65.60±5.20	65.11±9.20	0.898
Superior PCM	69.54±1.96	68.81±4.34	0.676
Middle PCM	65.43±6.36	60.50±7.57	0.145
Inferior PCM	55.72±7.98	41.94±13.50	0.021
Cricopharyngeus muscle	50.69±7.67	38.27±10.87	0.013
Oesophageal inlet	48.59±6.26	38.69±7.72	0.007
Supraglottis	57.35±11.94	51.90±13.19	0.36
Glottic larynx	49.82±9.13	29.61±14.10	0.002

FEES, flexible endoscopic evaluation of swallowing; PCM, posterior constrictor muscle

significantly associated with dysphagia according to FEES evaluation. Mean radiation doses to the inferior PCM, cricopharyngeus muscle, and glottic larynx were statistically lower in the high FEES score group than in the low FEES score group (p = 0.023, 0.030 and 0.001, respectively).

No patients had a FEES score of less than 4 for the liquid diet examination. Figure 3 displays comparison plots for radiation doses delivered to each SRS between the mild dysphagia group (FEES score 4) and the no-dysphagia group (FEES score 5) for the liquid diet examination. Table 5 illustrates the comparison of mean radiation doses (Gy) delivered to each SRS between the mild dysphagia group (score 4) and the no-dysphagia group (score 5) in the FEES for a liquid diet. This table shows that the inferior PCM, cricopharyngeus muscle, esophageal inlet and glottic larynx were significantly associated with dysphagia for the liquid diet according to FEES determination (p = 0.021, 0.013, 0.007 and 0.002 respectively).

Among the SRSs, we analysed the radiation doses delivered to each structure to identify the optimal dose to reduce post-radiation dysphagia. Mean radiation doses less than 40 Gy delivered to the inferior PCM could reduce dysphagia with a sensitivity of 35.5% and specificity of 100%. For the cricopharyngeus muscle, mean radiation doses of less than 43 Gy could reduce dysphagia with a sensitivity of 76.5% and specificity of 100%. Regarding the glottic larynx, delivered mean radiation doses of less than 35 Gy could reduce dysphagia with a sensitivity of 64.7% and specificity of 100%.

Discussion

Radiotherapy plays a crucial role in treating oropharyngeal cancer. Advanced radiotherapy technology enables the precise delivery of high radiation doses to a target area while minimising the dose to surrounding normal structures, including the SRSs. The SRSs consist of the three PCMs, cricopharyngeus muscle, esophageal inlet, base of the tongue, supraglottis and glottic larynx. However, their proximity to the primary cancer area makes it challenging to spare the superior PCM, middle PCM, tongue base and supraglottic larynx during radiotherapy. This study aimed to identify which SRSs could serve as predictors for dysphagia following radiation therapy. We hypothesised that protecting the SRSs during radiotherapy would improve swallowing function. The study also set out to determine the optimal radiation dose for each SRS that would prevent post-therapeutic dysphagia in patients with oropharyngeal cancer.

The majority of participants in our study received 3DCRT or IMRT as a treatment for oropharyngeal cancer, while some received 2DRT. 3DCRT/IMRT resulted in significantly better swallowing outcomes, as determined by FEES scores, compared to 2DRT for both the semisolid diet (p = 0.010) and the liquid diet (p = 0.019). We performed FEES in all symptomatic and asymptomatic oropharyngeal cancer patients after they completed radiotherapy. FEES is an objective test widely used by otolaryngologists to directly assess the motor and sensory functions of swallowing. It is recognised globally and considered a reliable evaluation method for dysphagia problems [10]. In this study, participants generally obtained better FEES scores for the liquid diet than for the semisolid diet. This finding suggests that a liquid diet is easier and safer to swallow, with minimal retention in the oropharynx or hypopharynx [15].

In analysing the radiation dose, we observed differences in FEES scores based on the dose given to each SRS. The doses delivered to the inferior PCM, cricopharyngeus muscle and glottic larynx were significant predictors of dysphagia for the semisolid and liquid diets. In contrast, the esophageal inlet was a significant predictor only for the liquid diet. However, the base of the tongue, superior PCM, middle PCM and supraglottic larynx showed no significant mean differences in the radiation doses received between the higher and lower FEES score groups. Additionally, we identified that radiation dose thresholds of 40 Gy for the inferior PCM, 43 Gy for the cricopharyngeus muscle and 35 Gy for the glottic larynx could potentially reduce dysphagia problems.

In conclusion, the most significant structures which could be the dysphagia predictors in oropharyngeal carcinoma patients receiving radiotherapy were the inferior PCM, cricopharyngeus muscle, glottic larynx and esophageal inlet. Our data suggest that adjusting the radiation doses delivered to SRSs can reduce long-term side effects such as dysphagia after radiotherapy. Reducing the radiation dose delivered to these structures using an SRS-sparing technique (3DCRT or IMRT) can alleviate dysphagia problems and improve patients' quality of life.

Limitation

Limitation in this study was that we could not calculate radiation dose in the patients who had received 2DRT technique.

Author Contribution Statement

Chanin Wasuthalainun prepared the study conception and design. Phawin Keskool took the lead in writing manuscript in consultation with Janjira Petsuksiri. Sunun Ongard and Paiboon Sureepong took responsibility in data collection, research intervention and gathering knowledge information. All authors have accepted responsibility for the entire content of this manuscript and approved its submission.

Acknowledgements

We express our grateful appreciation to Miss Julaporn Pooliam and Assistant Professor Chulaluk Komoltri, our consulting statistician, as well as Miss Jeerapa Kerdnoppakhun and Miss Ngamrat Treerassapanich for their assistance with the manuscript preparation. We also extend our thanks to all the participants involved in this study.

Funding

This research project was supported by the Faculty of Medicine Siriraj Hospital, Mahidol University (grant number [IO] R016432011).

Ethics approval and consent to participate

The study was approved by Siriraj Institutional Review Board (approval number Si 767/2020). The research was conducted ethically, with all study procedures being performed in accordance with the requirements of the World Medical Association's Declaration of Helsinki. Written informed consent was obtained from each participant for study participation and data publication.

Competing interests

The authors declare that they have no competing interests.

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