

Evaluation of Total Thyroidectomy with Prophylactic Central Neck Dissection as an Alternative to Total Thyroidectomy Alone in Clinically Node-Negative Papillary Thyroid Carcinoma

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Background: PTC is the most popular form of differentiated thyroid carcinoma. Total thyroidectomy is the preferred procedure for all PTC. In spite of CND is performed for clinically nodal-positive patients, it still controversial in cases with clinically negative nodes.

Aim of work: The purpose of this study is to compare the incidence of recurrence and complications of TT only with TT plus pCND in patients with clinically negative L.N and PTC.

Patients and methods: This retrospective study was conducted in the General Surgery Department at Ain Shams University Hospitals. The study involved 40 diagnosed cases of PTC with clinically node-negative disease, all of which were operated on between January 2021 and January 2023.

Results: The incidence of complications was similar in both groups. The rate of temporary recurrent laryngeal nerve injury was 5% in both groups. The rate of transient hypocalcemia was 5% in the TT only group and 10% in the TT with pCND group. Additionally, the rate of permanent hypocalcemia was 0% in the TT only group, while it was 5% in the TT with pCND group. pCND does not significantly reduce the local recurrence risk in cases of PTC.

Conclusion: Total thyroidectomy with pCND in clinically node-negative disease was not associated with increase in postoperative complications, in spite of having a longer operation time compared to total thyroidectomy without pCND. However, 40% of cases who performed total thyroidectomy with pCND were found to have lymph node metastasis.

Key words: pCND, total thyroidectomy, PTC, L.N metastasis.

Introduction

Papillary thyroid cancer is the most frequent form of differentiated thyroid carcinoma. In spite of its prognosis is relatively good with a 10-year cancer-specific survival over 90%, there is a high occurrence of locoregional recurrence.¹

Metastases in the L.N are frequent in PTC, in 20% to 50% of cases where there is no clinical evidence of central L.N involvement before surgery. These metastases typically occur in the central compartment of the neck (Level VI).²

L.N metastases are associated with a higher incidence of locoregional recurrence in patients with PTC. Numerous studies suggest that both the number of metastatic L.N in the central compartment and the lymph node ratio (LNR) serve as important prognostic factors for PTC. The primary goal of cancer treatment is the complete surgical resection of both the primary tumor and any clinically suspicious L.N metastases, as this is a critical factor that influences the outcomes in cases of differentiated thyroid carcinoma.³

Central compartment neck dissection (CCND) involves the surgical removal of all L.N from the sternal notch to the hyoid bone, located between each side of the carotid sheath (3). TT is considered the preferred procedure for all PTC cases. While CCND is typically performed on patients with clinically positive L.N, its necessity in patients with clinically negative nodes remains controversial.⁴

The pCND is defined as central-compartment L.N dissection in cases who show no evidence of L.N metastasis in the pre-operative radiological assessment or during the surgery. Many studies suggested that performing pCND along with TT is necessary in cases where there are no clinical signs of node involvement, in order to prevent locoregional recurrence, reduce the rate of post operative metastasis and assess the pathological indication for adjuvant radioactive iodine therapy.⁵

Some surgeons recommended routine CND to decrease postoperative thyroglobulin (Tg) levels, citing the high risk of positive L.N, the staging accuracy, better outcomes, reduce the rate of morbidity occurring with the initial operation and to prevent long-term secondary surgical dissection of central L.N.⁶

The 2015 American Thyroid Association (ATA) Guidelines recommended that pCND may be appropriate for cases with PTC who had advanced primary tumors (T3 or T4) and clinically negative central L.N.⁷

Others surgeons suggested that this procedure raise the risk of injury of the parathyroid glands and the recurrent laryngeal nerve with no proven advantages in the survival,⁸ and related to additional costs and longer stay in the hospital.⁹

Aim of work

The purpose of this study is to compare the incidence of recurrence and complications of total thyroidectomy only with total thyroidectomy plus

pCND in PTC patients with clinically negative L.N.

Patient and methods

This study was conducted in the Department of General Surgery at Ain Shams University Hospitals. Approval from the Ethical Committee was obtained. It is a retrospective study involving 40 patients diagnosed with PTC who had clinically negative L.N. These patients underwent surgery between January 2021 and January 2023, receiving either a TT alone or a TT with pCND. The patients were divided into two groups: Group 1 included 20 patients who underwent TT without pCND, while Group 2 consisted of 20 patients who underwent TT with pCND.

Inclusion criteria

Cases diagnosed with PTC with clinically negative L.N and belonging to either gender, aged between 18 and 60 years.

Exclusion criteria

Patients underwent prior surgery on the thyroid or parathyroid glands, Preoperative hypoparathyroidism, Preoperative hypocalcemia, clinically or radiologically positive cervical L.N (Lateral or central), Recurrent PTC, tumor with histological type other than PTC, Metastatic PTC, Pregnancy or lactation and patients who performed the surgery in less than 1 year.

Pre-operative assessment

The history and examination were conducted for such case, a diagnosis of PTC preoperative was confirmed through ultrasound (US)-guided fine-needle aspiration cytology. Before the operation, we conducted tests to measure free thyroid hormones (FT3 and FT4), the thyrotropin (TSH) level, and a high-resolution neck ultrasound. Clinically negative L.N were identified by the absence of suspicious nodes by ultrasound. Additionally, a pre-operative fibro-laryngoscopy was routinely carried out in all patients.

Operative details

All patients underwent TT using similar surgical techniques. The patient lying supine with hyperextended neck and the operative table tilted upward by 15 degrees. A horizontal incision was made 2 finger breadth above the sternal notch, the skin and platysma were incised and both the upper and lower flaps were raised. The deep fascia was then incised vertically in the middle, and the strap muscles were retracted aside. The pre-tracheal fascia was vertically incised exposing the thyroid gland. The middle thyroid vein was tied off, and the superior pedicle was dissected. The superior thyroid vein and artery were individually tied off and cut at the thyroid pole to prevent injury of the external laryngeal nerve. The dissection was carried out in a bloodless plane between the gland and the cricothyroid.

Both the upper and lower parathyroid glands were recognized and preserved. The recurrent laryngeal nerve was recognized and exposed through careful dissection along its entire path until inserted to the larynx. The inferior thyroid artery was ligated at the thyroid capsule level, and then the gland was resected.

In group (2), patients performed TT with pCND, which involved the area from the hyoid bone above to the brachiocephalic vein below, and included the carotid sheath on both sides. This procedure involved the removal of the pre-tracheal, pre-laryngeal, paratracheal, and tracheoesophageal LN.

Fig. 1 Total thyroidectomy with central neck dissection.

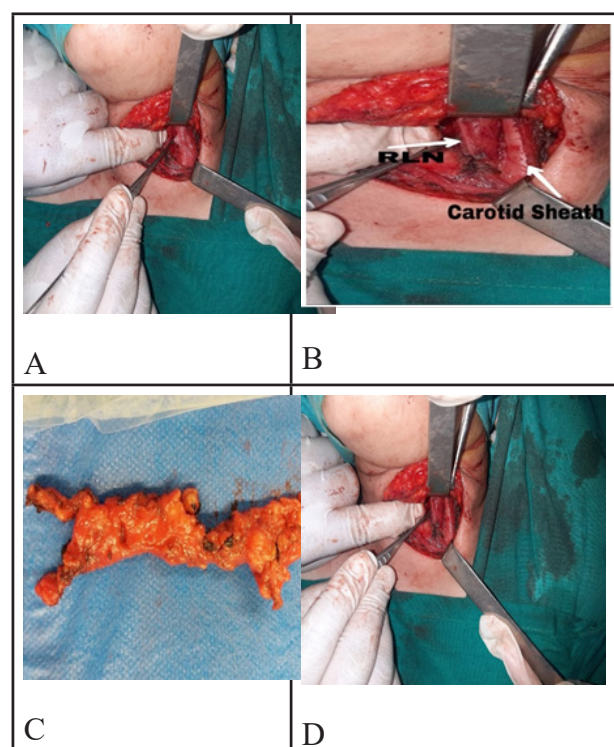


Fig 1: (A) Identification of the recurrent laryngeal nerve, (B) Identification of the carotid sheath, (C) Zooming on the identified recurrent laryngeal nerve and carotid sheath, (D) Central compartment neck dissection.

Data of the patients from their files and their surgical sheets were collected and assessed. Histopathological reports from two groups were reviewed, and operative data, including operation time and length of hospital stay, were recorded.

Clinical and pathologic features as age, sex, size of the tumor, the resected LN number and TNM stage were recorded. Postoperative complications records were collected, such as neck hematomas that need re-operation, post-operative hemorrhage, permanent or transient vocal cord paralysis and permanent or temporary hypocalcemic symptoms and hypoparathyroidism.

Recurrent laryngeal nerve injury was identified as paralysis of the vocal cord and voice change which confirmed by laryngoscopic. Transient vocal cord paralysis was characterized by absent or reduced vocal fold movement which improved through six months postoperative. Permanent vocal cord paralysis was described as ongoing vocal fold dysfunction persisting longer than six months postoperative.

To assess hypoparathyroidism, serum calcium level was measured before the operation and daily postoperatively. Parathyroid hormone level was monitored daily with the normal range being 10–65 pg/mL. Hypoparathyroidism was identified as a parathyroid hormone level < 10 pg/mL. If the level of calcium was < 8.4 mg/dL and patients experienced symptoms such as circumoral numbness, tingling, carpopedal spasm, and tetany, they were diagnosed with symptomatic hypocalcemia.

Patients received 24-month follow-up after the operation to assess hypocalcemia and the possibility of recurrence.

Permanent hypoparathyroidism or hypocalcemia was determined by a continuous requirement for calcium or vitamin D supplementation lasting more than twelve months. Recurrence during the follow-up period was identified by the emergence of new suspicious lesion detected through physical examination, thyroid ultrasound, or CT and pathologically confirmed through FNAC.

Statistical analysis

The Statistical Package for Social Science [IBM SPSS] version 27 was used to gather, code, edit, and enter the data. When the quantitative data were parametric, they were displayed as mean, standard deviations, and ranges; when they were non-parametric, they were displayed as median and interquartile range [IQR]. Qualitative variables were also displayed as percentages and numbers. Numbers and percentages were used to display the qualitative data. p-values were regarded as significant. P>0.05 denoted non-significant (NS), P<0.05 denoted significant (S), and P<0.001 denoted highly significant (HS).

Results

Table 1: The distribution of the cases under study by age and sex

	No.= 40	All Cases
		No.= 40
Sex	Female	33 (82.5%)
	Male	7 (17.5%)
Age	Mean ± SD	41.88 ± 10.37
	Range	20 – 60

Table 1 Shows there were 33 female cases and 7 male cases, with ages ranging from 20 to 60 (Mean age: 41.88 years).

Table 2: Comparison of the studied groups' ages and sexes and Co morbidities

No. = 20		Group (1)	Group (2)	Test value	P-value	Sig.
		No. = 20				
Age	Mean ± SD	41.35 ± 9.35	42.40 ± 11.52	-0.317•	0.753	NS
	Range	25 – 55	20 – 61			
Sex	Female	17 (85.0%)	16 (80.0%)	0.173*	0.677	NS
	Male	3 (15.0%)	4 (20.0%)			
Co morbidities	No	14 (70.0%)	15 (75.0%)	0.125*	0.723	NS
	Yes	6 (30.0%)	5 (25.0%)			
	HTN	4 (80.0%)	2 (40.0%)			
	HCV	0 (0.0%)	1 (20.0%)			
	DM	2 (40.0%)	2 (40.0%)			

P-value<0.05 indicates significance (S); P-value<0.05 indicates non-significant (NS); and P-value <0.01 indicates highly significant (HS).

*: Chi-square test,•:Independent t-test.

Table 2 Shows that the number of males to females in group (1) was 3:17, while it was 4:16 in group

(2), and this was statistically insignificant.

Table 3: Comparison of pre-operative labs between the 2 groups:

Pre operative Labs		Group (1)	Group (2)
No. = 20		No. = 20	
Thyroid profile	Normal	20 (100.0%)	20 (100.0%)
Serum calcium preoperative	Normal	20 (100.0%)	20 (100.0%)

Table 3 the Thyroid profile and Serum calcium preoperative was normal in all cases in both operations.

Table 4 the Hospital stay in days ranged from 1 to 3 days in Group (1) with mean 1.20 ± 0.52 and 1 to 4 days with mean 1.40 ± 0.82 in Group (2), and this was statistically insignificant.

The Operative time in (mins) ranged from 80 to 130 in Group (1) with mean 107.00 ± 13.42 and 90 to 170 with mean 121.00 ± 20.49 in Group (2), and this was statistically significant.

Table 4: Comparison of operative data between the 2 groups

Operative Data		Group (1)	Group (2)	Test value	P-value	Sig.
		No. = 20	No. = 20			
Hospital stay in days	Mean \pm SD	1.20 ± 0.52	1.40 ± 0.82	-0.919•	0.364	NS
	Range	1 – 3	1 – 4			
Operative time in (mins)	Mean \pm SD	107.00 ± 13.42	121.00 ± 20.49	-2.556•	0.015	S
	Range	80 – 130	90 – 170			

P-value<0.05 indicates significance(S); P-value<0.05 indicates non-significant (NS); and P-value<0.01 indicates highly significant (HS).
*: Chi-square test, •: Independent t-test.

Table 5: Comparison of Post Operative Complication between the 2 groups

Post Operative Complication	No.	Group (1)		Group (2)		Test value*	P-value	Sig.
		%	No.	%	No.			
Hoarseness of voice	None	19	95.0%	19	95.0%	0.000	1.000	NS
	Yes	1	5.0%	1	5.0%			
Transient recurrent laryngeal nerve injury	None	19	95.0%	19	95.0%	0.000	1.000	NS
	Yes	1	5.0%	1	5.0%			
Permanent recurrent laryngeal nerve injury	None	20	100.0%	20	100.0%	–	–	–
Symptoms of hypocalcemia (Circumoral numbness, carp pedal spasm)	None	19	95.0%	17	85.0%	1.111	0.292	NS
	Yes	1	5.0%	3	15.0%			
Transient hypocalcemia	None	19	95.0%	18	90.0%	0.360	0.548	NS
	Yes	1	5.0%	2	10.0%			
Permanent hypocalcemia	None	20	100.0%	19	95.0%	1.026	0.311	NS
	Yes	0	0.0%	1	5.0%			
Postoperative hemorrhage	None	19	95.0%	19	95.0%	0.000*	1.000	NS
	Yes	1	5.0%	1	5.0%			
Wound Hematoma	No	19	95.0%	19	95.0%	0.000*	1.000	NS
	Yes	1	5.0%	1	5.0%			
Wound infection	None	20	100.0%	20	100.0%	–	–	–

P-value<0.05 indicates significance(S);P-value<0.05 indicates non-significant(NS);and P-value <0.01 indicates highly significant(HS).*:- Chi-square test, •:Independent t-test.

Table 6: Comparison of the Pathology between the 2 groups

No. = 20		Group (1)		Group (2)		Test value	P-value	Sig.
		No. = 20						
Positive LNs in pathology	None	0 (0.0%)		12 (60.0%)		NA	NA	NA
	Yes	0 (0.0%)		8 (40.0%)				
No. of dissected LNs	Mean ± SD	–		6.90 ± 1.94		NA	NA	NA
	Range	–		4 – 10				
No, of positive LNs	0	–		12 (60.0%)		NA	NA	NA
	1	–		3 (15.0%)				
	2	–		3 (15.0%)				
	3	–		2 (10.0%)				
Multifocality	No	16 (80.0%)		15 (75.0%)		0.143*	0.705	NS
	Yes	4 (20.0%)		5 (25.0%)				
Tumor size in (mm)	Median (IQR)	10 (8 – 29)		10 (8 – 26)		0.510£	0.613	NS
	Range	4 – 37		6 – 39				
T stage	I	11 (55.0%)		12 (60.0%)		0.102*	0.749	NS
	II	9 (45.0%)		8 (40.0%)				
Staging	I	12 (60.0%)		10 (50.0%)		4.468*	0.107	NS
	II	8 (40.0%)		6 (30.0%)				
	III	0 (0.0%)		4 (20.0%)				

P-value<0.05 indicates significance(S); P-value<0.05 indicates non-significant (NS); P-value<0.01 indicates highly significant (HS). *:Chi-square test,•:Independent t-test,£: Mann-Whitney test.

Table 6, while The Tumor size in (mm) ranged from 4 to 37 in Group (1) with Median 10 mm and 7 to 39 with median 10 mm in Group (2).

Table 7: Comparison of the Recurrence between the 2 groups

Recurrence	Group (1)		Group (2)		Test value*	P-value	Sig.
	No.	%	No.	%			
No	19	95.0%	20	100.0%	1.026	0.311	NS
Yes	1	5.0%	0	0.0%			

P-value<0.05 indicates significance(S); P-value<0.05 indicates non-significant (NS); P-value<0.01. indicates highly significant (HS). *:Chi-square test,•:Independent t-test,£:Mann-Whitney test.

Table 7 Shows there were no statistically significant difference between TT and PCND as regard

recurrence.

Discussion

The most common type of thyroid cancer is PTC, with incidence of 75% up to 85% of patients and occurring most commonly in women aged 20 to 55.¹⁰

40 cases were included in this study and divided into two groups: 20 patients in Group 1 had TT, and 20 patients in Group 2 had a TT combined with pCND.

In this study, the average patient's age was 41.88±10.37. In Kuo et al.¹¹ study on 1206 cases, 48.8±15.7 years was the mean age of PTC cases.

The PTC incidence was 82.5% in females and 17.5%

in males, which was the same results of Yildiz et al.¹² They documented in a retrospective study of 1885 cases that, 83% was the incidence of PTC in females and 17% in males.

The size of the tumor varied from (4-37mm) in Group (1) with a median of 10 mm, and from (6-39mm) with a median of 10 mm in Group (2). In Afif et al.,¹³ the tumor size in PTC cases was 22 mm.

In study Group (1), 20% of the cases had multifocal PTC, while in study Group (2), 25% of the cases had multifocal PTC. Multifocal PTC was present in 20% of the cases in Kiratli et al.¹⁴

In Group (1), 55.0% of cases were classified as T1 and 45.0% were T2, while in Group (2), 60.0% were T1 and 40.0% were T2.

Choi et al.¹⁵ discovered that 43.7% of PTC cases were in the T1 stage and 1.1% were in the T2 stage. Furthermore, Grogan et al.¹⁶ observed that, (26%) 71 patients had T1a tumors, (23%) 61 had T1b tumors, (19%) 5 had T2 tumors, (12%) 32 had T3 tumors, and (11%) 29 had T4 tumors.

In Group (2), 40% of cases exhibited node-positive disease by histopathology, and the average number of dissected central L.N in PTC patients was 6.90 ± 1.94 .

In a study by Robinson et al.¹⁷ 47.4% of cases had positive L.N. Onkendi et al.¹⁸ Reported that 40% of PTC cases were found to have node-positive. Additionally, Grogan et al.¹⁶ discovered that 42% of cases with PTC had node-positive. In the study by Matsuzo et al.,¹⁹ the average number of central L.N in PTC patient was 5.5 ± 1.7 , while Kutler et al.²⁰ Reported an average of 5.7 central LN.

In study group (1), the operation time varied from (80-130m), the mean time was (107.00 ± 13.42). Bakkar et al.²¹ reported an average operation time of 122 ± 10.31 minutes.

In study group (2), the operation time varied from 90-170 minutes, the mean time was (121.00 ± 20.49), while Lecerf et al.²² recorded that the average operation time was 180 ± 8.63 minutes.

The duration of hospital stays varied from 1 to 3 days, with mean (1.20 ± 0.52) in group (1). In the study by Kurukahvecioglu et al.,²³ the average length of hospitalization following TT was 2.90 ± 0.915 days.

In the study group (2), the hospital stays varied from 1 to 4 days with mean 1.40 ± 0.82 .

Kwak et al.,²⁴ reported that the mean hospital stays following TT and pCND was (4.98 ± 0.15 days).

In study group (1), only one patient developed voice hoarseness after surgery, while in group (2), only one patient also had voice hoarseness post-operative. Aluffi et al.²⁵ Reported that 6.5% of cases experienced hoarseness of voice post-operative.

In a study of 20 patients who underwent re-operation of the central L.N. dissection for recurrent or persistent PTC, Kim et al.²⁶, reported a 0% incidence of recurrent laryngeal nerve paralysis; other authors have also reported this finding.

In study group (1), just one case had temporarily postoperative hypocalcemia, and no cases had permanent hypocalcemia. In study group (2), two cases experienced temporary hypocalcemia postoperative, while only one patient experienced

permanent hypocalcemia.

In a series by Karamanakos et al.,²⁷ 6.3% of cases experienced hypocalcemia after their operation. Meanwhile, in a series documented by Seo et al.,²⁸ the incidence of hypocalcemia after operation was reported as 12.3%. In a study of 20 cases who performed re-operation of the central L.N dissection for recurrent or persistent PTC, Kim et al.²⁶ found that a 0.4% occurrence of permanent hypoparathyroidism following central L.N dissection. These findings had subsequently supported by other researchers.

In study group (1), only one patient experienced postoperative hemorrhage. Similarly, in study group (2) only one patient suffered from postoperative hemorrhage. Both patients required surgical intervention, and the bleeding vessels were ligated. Duclos et al.²⁹ reported that none of the patients who underwent TT experienced post-operative hemorrhage, while Efremidou et al.³⁰ Found that 0.2% of patients had post-operative hemorrhage.

Roh et al.³¹ examined the outcomes in a group of 155 PTC individuals, with 40 (or 25.8%) of them having TT with pCND even though they had cN0. They discovered that cases who had TT with pCND had higher overall morbidity in comparison to those who only had TT (50% vs. 12.3%; $p < 0.001$).

In study group (1), 5% of the cases developed recurrence after TT, whereas none of the patients in study group (2) experienced recurrence following TT with PCND. According to Roh et al.,³¹ the rate of locoregional recurrence after TT was 4.1%, while Zuniga and Sanabria.³² reported a local recurrence rate of 20.0% post TT with PCND.

Zetoune and colleagues³³ conducted a meta-analysis comparing 868 cases of PTC that underwent TT alone with 396 cases that had pCND. The results showed that pCND had no effect on the incidence of local recurrence.

Lang et al. ³⁴ recorded a meta-analysis comprising 14 series and demonstrated that individuals who had pCND and TT had a 35% lower risk of locoregional recurrence than those with TT only.

Zhao et al.³⁵ and Lang et al.³⁴ indicated that TT with pCND raised the incidence of postoperative transient hypoparathyroidism. Nevertheless, given the high incidence of recurrence (About 20% within 5–10 years) and the frequent development of irreversible hypoparathyroidism following re-operation (up to 27%), the incidence was considerably elevated compared to those following the initial surgery. As a result, pCND was advisable for individuals at the initial surgery.

Sanabria et al.³⁶ concluded that intrathyroidal

tumors without macroscopic ETE which categorized as low-risk PTC, did not necessitate Pcnd (TT only group recurrence rate versus TT with pCND:9/354 or 2.5% versus 11/409 or 2.7%; risk difference (RD),0;95%CI,-2% to 2%;p=0.98;NNT,500).

However, the rate of permanent hypoparathyroidism was higher in the TT + pCND group (RD,3%;95%CI, 0% to 6%; p=0.02; NNH=33.3).

Kim et al.²⁶ conducted a study on 11,569 cases diagnosed as PTC with negative LN. Out of 11,569 cases, 8,735 (75.5%) underwent pCND. The study showed that pCND did not significantly reduce the locoregional recurrence risk (P=0.392). Nevertheless, the pCND group showed greater incidence of complications postoperative, including transient vocal fold paralysis (P=0.001), transient hypoparathyroidism (P<0.001), and permanent hypoparathyroidism (p<0.001).

However, Zhao et al.³⁵ found in their meta-analysis that although transient recurrent laryngeal nerve injury and transient and permanent hypoparathyroidism were more common, performing pCND with TT significantly reduced the locoregional recurrence rate.

Conclusion

Total thyroidectomy with pCND in clinically node-negative patients was not associated with increase in postoperative complications, in spite of having a longer operation time compared to total thyroidectomy without pCND. However, 40% of cases who performed total thyroidectomy with pCND were found to have LN metastasis, the decision of whether to perform pCND or not is a complex and controversial that should be done case by case. Factors to be considered including the patient's age, tumor size, stage and overall health.

List of abbreviations

PTC: Papillary thyroid carcinoma.

LN: Lymph node.

TT: Total thyroidectomy.

PCND: Prophylactic central neck dissection.

FNAC: Fine-needle aspiration cytology.

Declarations

Ethics approval and consent to participate

Ethical approval was granted by the Ethics Committee at Ain Shams University Hospitals' Department of General Surgery.

Human ethics and consent to participate declaration: available.

Consent for publication

All patients provided signed written informed consent for publication.

Availability of data and materials

The datasets used and analyzed during this study are available from the corresponding author on reasonable request.

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Authors' contributions

YH drafted the manuscript. AS participated in the sequence alignment. DM participated in the design of the study and performed the statistical analysis and conceived the study. All authors read and approved the final manuscript.

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