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US Features of the Parathyroid Glands: An Intraoperative Surgical Specimen Study

부갑상선의 초음파 소견: 수술 중 수술 검체 연구

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Purpose This study aimed to evaluate the US features of the parathyroid glands (PTGs) using surgical specimens of normal PTGs obtained during thyroid surgery.

Materials and Methods This study included 34 normal PTGs from 17 consecutive patients who underwent thyroid surgery between December 2020 and March 2021. All normal PTGs were histologically confirmed by intraoperative frozen-section biopsy for autotransplantation. Surgically resected parathyroid specimens were scanned in sterile normal saline using high-resolution US prior to autotransplantation. The US features of echogenicity (hyperechogenicity or hypoechogenicity), echotexture (homogeneous or heterogeneous), size, and shape (ovoid or round) were retrospectively evaluated. The echogenicity of the three PTGs was compared with that of the thyroid parenchyma of the resected thyroid specimens in two patients.

Results All PTGs showed hyperechogenicity similar to that of gauze soaked in normal saline. Homogeneous hyperechogenicity was observed in 32/34 (94.1%) patients, and the echogenicity of the three PTGs was hyperechoic compared with that of the thyroid parenchyma. The long diameter of the PTGs ranged from 5.1 mm to 9.8 mm (mean, 7.1 mm) and the shape of the PTGs was ovoid in 33/34 (97.1%) patients.

Conclusion The echogenicity of normal PTG specimens was consistently hyperechoic, and the small ovoid homogeneously hyperechoic structure was a characteristic US feature of the PTGs.

Index terms Parathyroid Gland; Ultrasonography; Thyroid Gland; Thyroidectomy

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INTRODUCTION

Postsurgical hypocalcemia due to hypoparathyroidism is a common complication of thyroid surgery (1-3). Preoperative localization of normal parathyroid glands (PTGs) could be useful for surgical planning and preventing possible PTG injury during thyroid surgery. However, preoperative imaging-based localization of normal PTGs has not been established. US is an essential primary tool for the evaluation and localization of parathyroid lesions and is advantageous for localization of small normal PTGs because of its high resolution and feasible application. However, normal PTGs are rarely detected on US (4-7), and the US features of normal PTGs have not yet been established (6, 8, 9).

Some researchers have suggested that the echogenicity of normal PTGs was hypoechoic (10, 11) or isoechoic to hyperechoic (12-14) based on their experience. A recent study by Xia et al. (8) reported that 91.3% of PTGs identified by surgeons during thyroid surgery in 13 patients were hyperechoic compared to the neck muscle on intraoperative US. Cohen et al. (9) recently reported that normal PTGs confirmed by tissue washout parathyroid hormone or autofluorescence showed homogeneous hyperechogenicity in 6 patients. However, the detailed US features of normal PTGs identified by histopathological or biochemical methods remain to be elucidated, and there has been no study on the US findings of normal PTGs confirmed by histopathology.

Thus, we evaluated the US features of the PTGs using surgical specimens of normal PTGs confirmed by histopathology of frozen biopsy for autotransplantation during thyroid surgery.

MATERIALS AND METHODS

This retrospective study was approved by our Institutional Review Board with a waiver of the requirement for informed consent (IRB No. 2021-08-011).

STUDY POPULATION

Between December 2020 and March 2021, 19 consecutive patients with thyroid disease underwent thyroidectomy (total thyroidectomy, $n = 11$; hemithyroidectomy, $n = 6$) performed by a single experienced head and neck surgeon with 15 years of experience in high-volume thyroid surgeries in a tertiary hospital. Parathyroid autotransplantation of at least one PTG was routinely performed to prevent permanent hypoparathyroidism during thyroid surgery (15). An intraoperative frozen section of potential PTGs identified by surgeons was selectively used to confirm parathyroid tissue prior to autotransplantation. The inclusion criteria of this study were patients in whom autotransplantation of normal PTG was performed during thyroid surgery and transplanted PTGs were confirmed by frozen section biopsy. The exclusion criteria were patients in whom normal PTG was not identified by frozen section biopsy or patients with clinical history of parathyroid disease or parathyroid abnormality on preoperative laboratory data or US examination. One patient who underwent hemithyroidectomy was excluded from this study because the normal PTG was not identified by the frozen section biopsy, while another patient who had concurrent parathyroid adenoma and indeterminate thyroid nodule was excluded. Therefore, a total of 34 normal PTGs of 17 patients (15 female and 2 male; mean age, 54.8 years; age range 20–75 years) were included in this study. The preoperative serum calcium levels were within the normal range in all patients. All the normal PTG specimens were brownish-red in color at the time of US examination (Fig. 1), and none showed blue-black discoloration, which is a sign of severe vascular compromise (16). Patient demographics are summarized in Table 1.

INTRAOPERATIVE US EXAMINATION

The US examinations of normal PTG specimens for autotransplantation was performed intraoperatively during thyroidectomy procedures. PTGs were routinely identified during surgery and preserved in situ if vascular pedicle was kept intact by the surgeon's judgement. Au-

Fig. 1. US features of normal parathyroid gland specimen in a 75-year-old female with multinodular goiter.
A. A photograph of the surgical parathyroid specimen shows an ovoid brownish red parathyroid gland.
B. US image of the same parathyroid specimen (long arrows) reveals that it has homogeneous hyperechogenicity similar to that of the adjacent gauze soaked in saline (short arrows). The long diameter was 7.2 mm and the shape of normal parathyroid gland was ovoid (long-to-short axis ratio: 2.9).

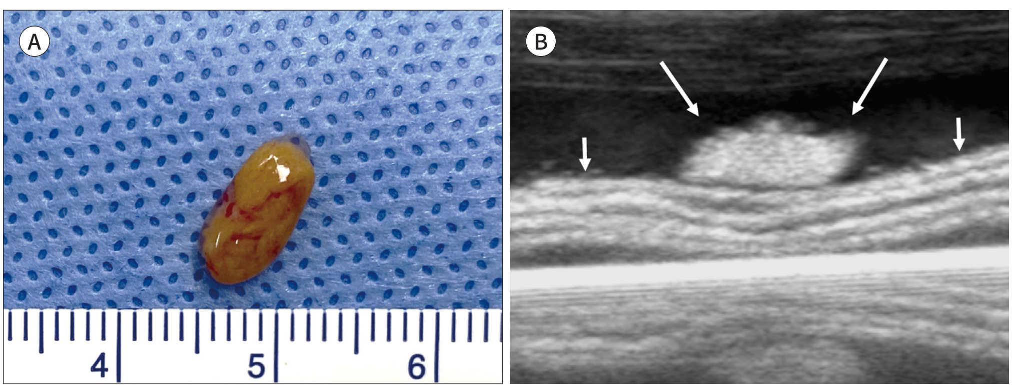

Table 1. Demographic Data of Patients

Parameter	Data
No. of patients	17
No. of female	15 (88.2)
Age (year), mean ± standard deviation	54.8 ± 15.1
No. of parathyroid glands	34
Thyroid surgery	
Total thyroidectomy	11 (64.7)
Hemithyroidectomy	6 (35.3)
Diagnosis of thyroid disease	
Papillary carcinoma	9 (52.9)
Follicular thyroid carcinoma	2 (11.8)
Graves' disease	2 (11.8)
Multinodular goiter	2 (11.8)
Nodular hyperplasia	1 (5.9)
Hurthle cell adenoma	1 (5.9)

Unless otherwise indicated, data are presented as numbers with percentages in parentheses for categorical variables.

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totransplantation was performed when devascularization or inadvertent parathyroidectomies occurred. Before autotransplantation, a small piece of the identified potential PTG (about 1–2 mm) was sent for frozen section, and the rest was placed in normal saline. The radiologist was ready to perform US in the operation room during surgery. After pathological confirmation, the parathyroid specimens were referred to the radiologist with 4 years' experience in thyroid US and US examinations were performed before autotransplantation during the surgery. The US examination of parathyroid specimens took 5–10 minutes in each patient, and there was no delay in surgery because of US examination.

US examinations of parathyroid specimens were performed in the operation room with a gentle and aseptic technique, following the steps described below. A surgical stainless-steel tray was filled with normal saline and a piece of flat gauze was placed at the bottom of the surgical tray. The parathyroid specimens were sunk in the tray with caution. All US examinations were performed by a radiologist with surgical aseptic technique using a real-time US system (IU22, IU22, Philips Medical Systems, Bothell, WA, USA) and a 5–12-MHz linear probe sheathed with a sterilized cover. The US probe was placed gently on the surface of the saline solution filled in the surgical tray and US images of specimens were obtained. In two patients who underwent hemithyroidectomy, the resected thyroid specimens were scanned in the same manner as parathyroid specimens to compare the echogenicity of PTG and thyroid parenchyma after thyroid surgery was completed. The obtained US images of specimens were transferred to the picture archiving and communication system workstation.

ANALYSIS OF US IMAGES

All US images of normal PTG specimens were retrospectively reviewed by two radiologists with 22 and 4 years of experience in performing thyroid US, respectively. The two reviewers assessed the echogenicity, echotexture, size, and shape (round, oval) of normal PTG specimens in a consensus. The echogenicity of PTGs was determined at the center of the parathyroid specimens as small fibrous or fatty tissues were attached around the parathyroid specimens and there were small tissue changes because of frozen section biopsy in the peripheral part of the PTGs. The echogenicity of normal parathyroid specimens was categorized as hyperechogenicity (similar echogenicity to the adjacent gauze soaked in normal saline) and hypoechogenicity (obviously hypoechoic relative to the adjacent gauze). The echotexture of PTGs was categorized as homogenous or heterogeneous. Homogeneous echotexture was defined as uniform echogenicity, while heterogeneous echotexture was defined as mixed echogenicity with more than one echogenicity category. If the lesion had a mixed pattern, the echogenicity of PTGs was determined by the predominant echogenicity. In two patients in whom US images of the resected thyroid specimens were obtained, the echogenicity of three parathyroid specimens were compared to the echogenicity of normal thyroid parenchyma in the resected thyroid specimens, and the echogenicity of thyroid parenchyma was compared between resected thyroid specimen and thyroid gland obtained from preoperative percutaneous US image. The size of normal PTGs was assessed by measurement of long and short diameters. The shape of normal PTGs was assessed using the long axis/short axis (L/S) ratio and was categorized as round (L/S ratio $\leq$ 1.5) or ovoid (L/S ratio > 1.5).

STATISTICAL ANALYSIS

Categorical variables are reported as frequencies and percentages for each category. Continuous variables are presented as the mean ± standard deviation or median (interquartile range), according to parametric or nonparametric distribution, respectively. Statistical analysis was performed using SPSS version 24.0 for Windows (IBM Corp., Armonk, NY, USA).

RESULTS

The US features of normal PTG specimens are summarized in Table 2. All PTGs showed hyperechogenicity similar to that of the adjacent gauze (Figs. 1, 2). Homogeneous echotexture was found in 32 (94.1%) of 34 PTGs, while heterogeneous echotexture was observed in two (5.9%) PTGs. The two PTGs showed focal ill-defined hypoechogenicity at the center of the PTG. The echogenicity of three PTGs was hyperechoic compared to that of the thyroid parenchyma and the echogenicity of thyroid parenchyma on preoperative US images was similar to the echogenicity of resected thyroid specimen in two patients in whom US images of resected thyroid specimens were obtained (Fig. 2). The parathyroid gland was hyperechoic than thyroid parenchyma in both surgical specimen and preoperative percutaneous US image in one patient (Fig. 2).

The long diameter of the PTGs ranged from 5.1 mm to 9.8 mm (mean, 7.1 mm), and the short diameter ranged from 2.1 mm to 4.3 mm (mean, 3.1 mm). The shape of the PTGs was ovoid (L/S ratio > 1.5) in 33 (97.1%) and round (L/S ratio ≤ 1.5) in 1 (2.9%).

DISCUSSION

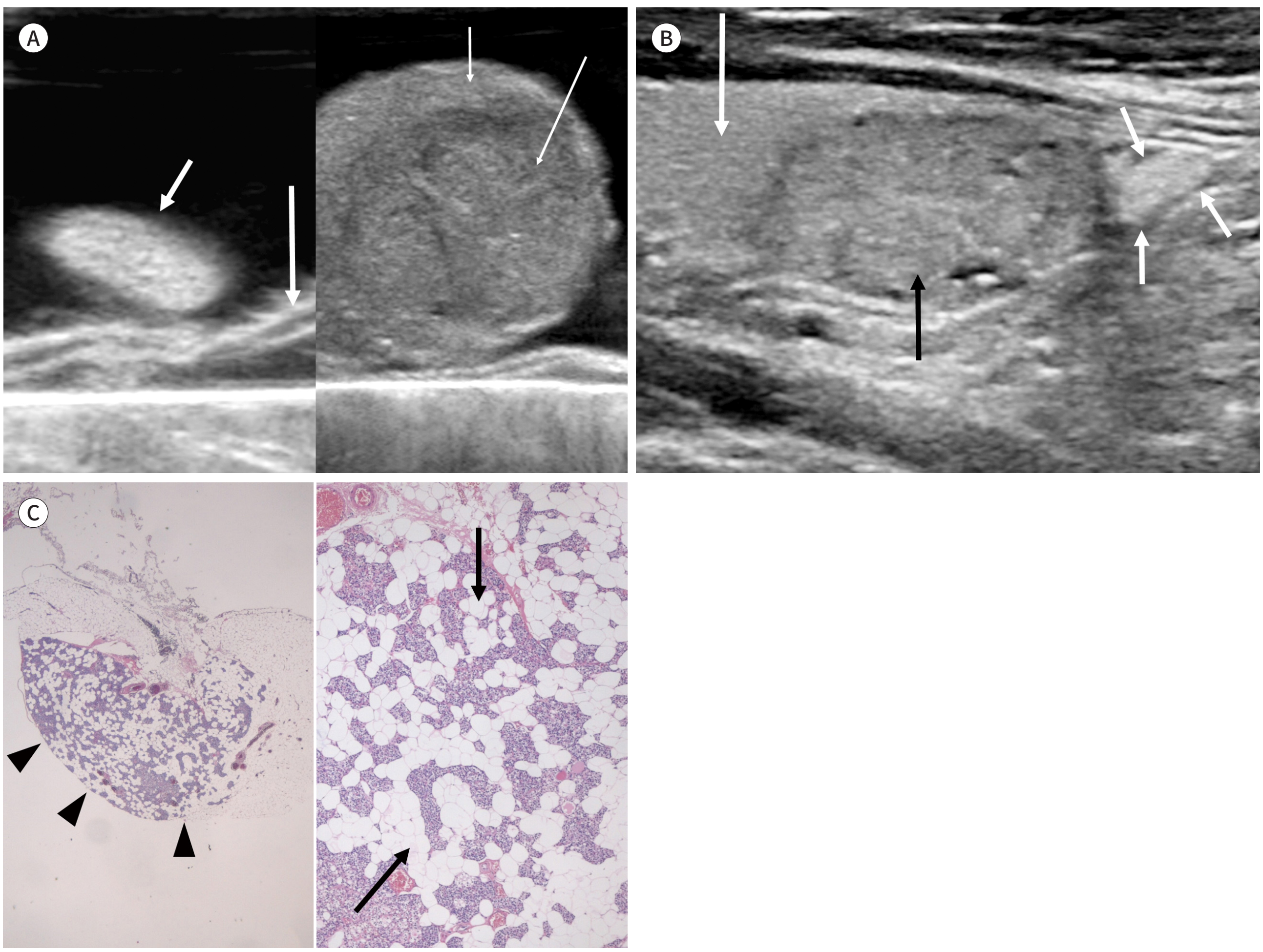
Our intraoperative surgical specimen study demonstrated that all normal PTG specimens

Table 2. US Features of Normal Parathyroid Glands

US Features	Data
Echogenicity	
Hyperechoic	34 (100.0)
Hypoechoic	0 (0)
Echotexture	
Homogeneous	32 (94.1)
Heterogeneous	2 (5.9)
Size (mm), mean ± standard deviation (range)	
Long diameter	7.1 ± 1.4 (5.1–9.8)
Short diameter	3.1 ± 0.7 (2.1–4.3)
Shape	
L/S ratio, median (IQR), range	2.3 (2.0–2.9), 1.5–5.1
Ovoid (L/S ratio > 1.5)	33 (97.1)
Round (L/S ratio ≤ 1.5)	1 (2.9)

Unless otherwise indicated, data are presented as numbers with percentages in parentheses for categorical variables and ranges in parentheses for continuous variables.
IQR = interquartile range, L/S = long axis/short axis

Fig. 2. US features of a normal parathyroid gland specimen in a 45-year-old male with Hurthle cell adenoma.
A. US image (left) shows the resected superior parathyroid specimen (short thick arrow), and reveals homogeneous hyperechogenicity similar to that of the adjacent gauze soaked in saline (long thick arrow). The long diameter was 6.6 mm and the shape of the normal parathyroid gland was ovoid (long-to-short axis ratio: 2.4). US image (right) shows the thyroid specimen that was resected using left hemithyroidectomy. The parathyroid gland (short thick arrow, left) is hyperechoic compared with the thyroid parenchyma (short thin arrow) around the tumor (long thin arrow).
B. Preoperative percutaneous US image of the left thyroid lobe reveals thyroid parenchyma (long white arrow), tumor (black arrow), and inferior normal parathyroid gland (short white arrows) located at the infrathyroid region adjacent to the left inferior thyroid pole. The parathyroid gland (short white arrows) has hyperechogenicity similar to that of the resected intraoperative parathyroid specimen (A, short thick arrow), and is hyperechoic compared with the thyroid parenchyma (long white arrow).
C. The image reveals the surgical pathology of the resected inferior parathyroid gland by the left central neck dissection (right, hematoxylin and eosin stain, × 40; left, hematoxylin and eosin stain, × 100). Histology of the surgical specimen of resected parathyroid gland demonstrates a typical ovoid shape (arrowheads) and abundant adipocytes (arrows) distributed within the parathyroid gland.



consistently showed hyperechogenicity, with most showing homogeneous echotexture. This study is the first to verify that the echogenicity of PTGs identified by histopathological method was hyperechoic using the surgical specimens. Our findings were consistent with the recent finding that the echogenicity of normal PTGs were homogeneously hyperechoic on preoperative percutaneous US (9).

The origin of hyperechogenicity of normal PTGs may be explained by abundant stromal fat content diffusely distributed in the PTG, accounting for 35%–50% of the glands (17-19). The heterogeneous glandular architecture composed of fat tissue and chief cells contain numerous interfaces, which may increase the echogenicity of normal parathyroid tissues. In parathyroid adenoma and hyperplasia, the stromal fat content is displaced because of the proliferation of chief cells (20-22), resulting in a homogenous architecture in the cellular proliferation area and hypoechogenicity on US in most adenomas or hyperplasias (22). In two cases (5.9%) of PTGs with focal intraglandular hypoechogenicity, the residual hyperechoic area consistently showed the same homogenous hyperechogenicity as the other PTGs. The histologic identity of intraglandular focal hypoechogenicity is uncertain; however, it might be an uncommon feature of normal PTG because Xia et al. (8) reported a similar finding; 3.8% of presumed PTGs uncommonly showed heterogeneous echotexture with focal hypoechogenicity inside the gland. The measured long diameter (5.1–9.8 mm) of PTGs was within the size range (2–12 mm) of normal PTGs reported by a previous cadaver study (23) and that (4–10 mm) reported by the percutaneous US study (8). Most PTGs in our study had an ovoid shape, which is consistent with the result of a previous study (8).

Our study suggests that a small (less than approximately 10 mm) ovoid homogeneously hyperechoic lesion is a characteristic US feature of normal PTG. This characteristic US feature of normal PTGs may provide useful information to preoperatively identify and localize normal PTGs in patients undergoing thyroid surgery. First, the hyperechoic US feature of a normal PTG clearly distinguishes it from perithyroidal normal or reactive lymph nodes, showing hypoechogenicity similar to neck muscles. However, normal PTGs should not be misdiagnosed as metastatic lymph nodes of thyroid cancer as these may show focal or diffuse hyperechogenicity of lymph nodes (24-26). Second, normal PTGs could be differentiated from perithyroidal fat tissue because perithyroidal fat usually shows ill-defined heterogeneous hyperechogenicity in contrast to the normal PTG with a circumscribed ovoid hyperechoic lesion. Further research is needed to determine the reliability and accuracy of advanced high-resolution US for the preoperative localization of normal PTGs in a large population of patients undergoing thyroid surgery.

This study has several limitations. First, we only evaluated the echogenicity of normal PTG using the resected surgical specimens. The surgical specimen of normal PTGs might show a difference in US echogenicity compared to the in vivo normal PTGs obtained by percutaneous US as resected PTGs may result in ischemic tissue change of the PTG. However, blue-black discolored PTGs associated with severe vascular compromise were not included in this study, and US examination of normal parathyroid specimens was performed shortly after surgical resection. The hyperechogenicity of normal parathyroid specimens found in our study was consistent with that of normal PTGs detected by percutaneous US in recent studies (8, 9). In one patient of our study, the echogenicity of PTG incidentally identified on preoperative percutaneous US image was similar to the echogenicity of the resected parathyroid specimen and the echogenicity of PTG was brighter than the thyroid parenchyma in both US image of surgical specimen and preoperative US image (Fig. 2). Second, we compared the echogenicity of normal PTGs with that of the thyroid parenchyma in only two patients because of difficulty in obtaining the appropriate US images in many cases with severe goiter and large thyroid nodules. Therefore, we could not verify if the echogenicity of normal PTG specimens was hyperechoic compared to the thyroid parenchyma in all patients. Third, we did not evaluate the US feature of parathyroid glands on preoperatively obtained US images and the reliability or accuracy of preoperative percutaneous US for the localization of normal PTGs in the patients because the US feature of normal PTGs was not well recognized during the study period.

In conclusion, the echogenicity of normal PTG specimens was consistently hyperechoic, and the small ovoid homogeneously hyperechoic structure was the characteristic US feature of normal PTGs. The knowledge and recognition of the characteristic US features of PTGs will help localize normal PTGs using preoperative US in patients undergoing thyroid surgery.

Author Contributions

Conceptualization, N.D.G.; data curation, P.W., L.J.C.; formal analysis, N.D.G., P.W.; investigation, all authors; methodology, N.D.G., P.W.; project administration, N.D.G.; resources, N.D.G.; supervision, N.D.G.; validation, N.D.G.; visualization, P.W., L.J.C.; writing—original draft, P.W.; and writing—review & editing, all authors.

Conflicts of Interest

The authors have no potential conflicts of interest to disclose.

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부갑상선의 초음파 소견: 수술 중 수술 검체 연구

백우열[1] · 이종철[2] · 노병주[3] · 나동규[4*]

목적 이 연구는 갑상선 수술 중 절제된 정상 부갑상선 검체를 이용하여 부갑상선의 초음파 소견을 알아보고자 한다.

대상과 방법 2020년 12월부터 2021년 3월까지 갑상선 수술을 시행한 17명 환자의 34개 부갑상선을 분석하였다. 모든 정상 부갑상선은 자가이식전 동결 절편을 통해 조직학적으로 진단되었고 부갑상선 검체를 무균 생리식염수에 넣은 상태에서 고해상 초음파 영상을 얻었다. 부갑상선 검체의 초음파 에코(고에코, 저에코), 에코결(균일, 불균일), 크기, 및 모양(난원, 원형)을 후향적으로 분석하였다. 두 명의 환자에서 얻은 3개의 부갑상선 에코를 절제된 갑상선 실질 에코와 비교하였다.

결과 모든 부갑상선은 생리식염수에 적신 거즈의 에코와 유사한 고에코를 나타냈다. 균일한 고에코는 32개(94.1%)의 부갑상선에서 관찰되었고 3개의 부갑상선은 갑상선 실질보다 높은 에코를 나타냈다. 부갑상선의 장경은 5.1–9.8 mm (평균 7.1 mm)였고, 모양은 33개(97.1%) 부갑상선에서 난원형을 보였다.

결론 부갑상선 검체의 에코는 모두 고에코를 나타냈고, 작은 크기의 균일한 고에코를 보이는 난원형 구조물은 부갑상선의 특징적 초음파 소견이었다.

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