

## Original Article

## Sonographic Features of Thyroid Nodules with Non-diagnostic Pathological Result

## Patolojik Sonucu Non-diagnostik Olan Tiroid Nodüllerinin Sonografik Özellikleri

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## ABSTRACT

**Aim:** FNAB is the most commonly used method in the pathological diagnosis of thyroid nodules, and it is an easy-to-apply, high diagnostic efficiency and low cost application. Sometimes not enough cells can be obtained as a result of thyroid fine needle aspiration biopsy and it may be insufficient for pathological evaluation. In our study, the ultrasonographic appearance of thyroid nodules that were obtained “non-diagnostic/inadequate” material for pathological evaluation with fine needle aspiration biopsy was investigated.

**Materials and Methods:** 186 patients were included in this retrospective study. Fine needle aspiration biopsy were performed under ultrasound guidance, using a 22 G needle and freehand technique. Pathological evaluations were made in accordance with the Bethesda classification. TIRADS score, size, composition of nodules, internal structure, echogenicity, shape, margin, echogenic foci, rim were evaluated by ultrasonography.

**Results:** From 186 nodules, 70 were solid, while 2 of them were completely or almost completely cystic. While 17 nodules were anechoic, 55 were hypoechoic, 102 were isoechoic, 12 nodules were detected as hyperechoic. There were 174 well-circumscribed, 12 lobulated contoured nodules. 156 had no echogenic focus, 15 had macrocalcification and 12 had microcalcifications. The TI-RADS score of 166 nodules were 2-4, while 5 of 4 nodules, 6 of 12 nodules, and 7 of 4 nodules.

**Conclusion:** Ultrasonographic features of thyroid nodules with inadequate pathology results were evaluated. In our study, it has been shown that although inadequate material results in features such as cystic dominance or macrocalcification increase, there is a possibility in all types of nodules.

**Keywords:** Thyroid nodules, thyroid ultrasonography, thyroid biopsy, bethesda, thyroid

## ÖZET

**Giriş ve Amaç:** İnce iğne aspirasyon biyopsisi tiroid nodüllerinin patolojik tanısında en sık kullanılan yöntem olup, uygulaması kolay, tanısal etkinliği yüksek ve düşük maliyetli bir uygulamadır. Bazen tiroid ince iğne aspirasyon biyopsisi sonucunda yeterli hücre elde edilemeyebilir ve patolojik değerlendirme için yetersiz kalabilir. Çalışmamızda, ince iğne aspirasyon biyopsisi ile patolojik değerlendirme için “tanısal olmayan / yetersiz” materyal elde edilen tiroid nodüllerinin ultrasonografik görünümü araştırıldı.

**Gereç ve Yöntem:** Bu retrospektif çalışmaya 186 hasta dahil edildi. İnce iğne aspirasyon biyopsisi, 22 G iğne ve serbest el tekniği kullanılarak ultrason rehberliğinde yapıldı. Bethesda sınıflandırmasına göre patolojik değerlendirmeler yapıldı. TIRADS skoru, boyutu, nodüllerin bileşimi, iç yapı, ekojenite, şekil, sınır, ekojenik odaklar, kenar ultrasonografi ile değerlendirildi.

**Bulgular:** 186 nodülden 70'i solid, 2'si tamamen veya neredeyse tamamen kistikti. 17 nodül anekoik, 55 tanesi hipoeikoik, 102 tanesi izoeikoik, 12 nodül hiperekoik olarak tespit edildi. 174 iyi sınırlı, 12 lobüle konturlu nodül vardı. 156'sının ekojenik odağı yoktu, 15'inde makrokalsifikasyon ve 12'sinde mikrokalsifikasyon vardı. 166 nodülün TI-RADS skoru 2-4 iken, 4 nodülün 5, 12 nodülün 6 ve 4 nodülün 7 idi.

**Sonuç:** Bu çalışmada patoloji sonuçları yetersiz olan tiroid nodüllerinin ultrasonografik özellikleri değerlendirildi. Yetersiz materyal sonucu olan nodüllerde kistik baskınlık veya makrokalsifikasyon gibi özellikler daha sık görülmekle birlikte, her tür nodülde bu olasılığın olduğu gösterilmiştir.

**Anahtar Kelimeler:** Tiroid nodülleri, tiroid ultrasonografi, tiroid biyopsisi, bethesda, tiroid patolojisi, tanısal olmayan ince iğne aspirasyon biyopsisi

## Introduction

Thyroid nodules are common lesions, and increasing use of imaging methods, especially ultrasonography, are increasingly encountered. While superficial and large nodules can be detected by inspection and palpation at the time of diagnosis, the use of ultrasound is very valuable in small sized and deeply located nodules. In addition, it is very difficult to differentiate between malign and benign nodules detected by palpation, and the use of ultrasound reduces unnecessary attempts.

Biopsy has an important place in the management of detected thyroid nodules. Malign-benign distinction can be made with high success rates with ultrasound findings, but histopathological examination is required for a definitive diagnosis. The methods commonly used in histopathological evaluation are fine needle aspiration biopsy (FNAB) and thick needle biopsies(1, 2).

FNAB is the most commonly used method in the pathological diagnosis of thyroid nodules, and it is an easy-to-apply, high diagnostic efficiency and low cost application(1, 3). Complication rates are low and complications observed are often mild. If done with ultrasound, the success rate increases and the complication rates decrease(4). However, sometimes not enough cells can be obtained as a result of thyroid FNAB and it may be insufficient for pathological evaluation. In this case, methods such as biopsy repetitions, new biopsy in different techniques, follow-up or operation are followed, and the cost increases and patient satisfaction decreases in this process.

In our study, the ultrasonographic appearance of thyroid nodules that were obtained “non-diagnostic/inadequate” material for

pathological evaluation with FNAB was investigated.

## Materials and methods

### Study Design and Patients

Our study is a retrospective study and approved by our hospital's ethics committee. Informed consent is obtained after the biopsy purpose and procedure are discussed with the patient.

Out of 1162 patients aged 18 years and over who underwent thyroid biopsy in the Interventional Radiology Clinic of our hospital between January 2019 and July 2020, 216 patients whose thyroid biopsy results were “non-diagnostic/inadequate” were included in the study. 30 of these patients were excluded from the study due to the lack of ultrasound information included in our study in the ultrasound reports in the data system of our hospital. The remaining 186 patients were included in the study.

### Biopsy Procedure

Patients are referred to our clinic from internal medicine, endocrinology, otolaryngology and general surgery clinics for biopsy, and the nodules found in the patients are primarily evaluated by ultrasonography. If there is a single nodule in the patient's thyroid, biopsy is performed from this nodule, from the one with more suspicion of malignancy if there is more than one nodule, and from the largest one if the nodules have a similar malignancy risk. Malignancy risk of nodules is assessed by TIRADS scoring (5). Thyroid aspiration biopsies were performed by an interventional radiologist with 8 years (board certified, OFA) thyroid biopsy experience. All procedures were performed under ultrasound (Affiniti, Philips Healthcare, Bothell, Washington) 5-12 Mhz linear array



Figure 1. Sonographic evaluation at the beginning of the procedure

transducers with a sterile cover placed over its head. While the patient was lying in the supine position and the patient's neck was in the light extension position, the target lesion was detected and the area where the biopsy would be taken was cleaned with 10% povidone-iodine solution (Figure 1). Local anesthetic was not used before the procedure. Biopsy procedures, after the area where the needle will be inserted was sterilized, the transducer was placed on the lesion and possible vascular structures were evaluated with color Doppler mapping. It was stated to the patient that she/he should not swallow during the procedure. Biopsy was performed using a disposable 10 ml injector with 22 G needle and freehand technique with the needle in parallel or perpendicular position to the transducer. Aspiration was attempted from all parts of the nodule and the needle was imaged simultaneously with each movement of the needle (Figure 2).

The aspiration process has been carried out at least twice. Samples taken after the procedure were injected into a tube with formaldehyde



Figure 2. Ultrasound imaging during biopsy

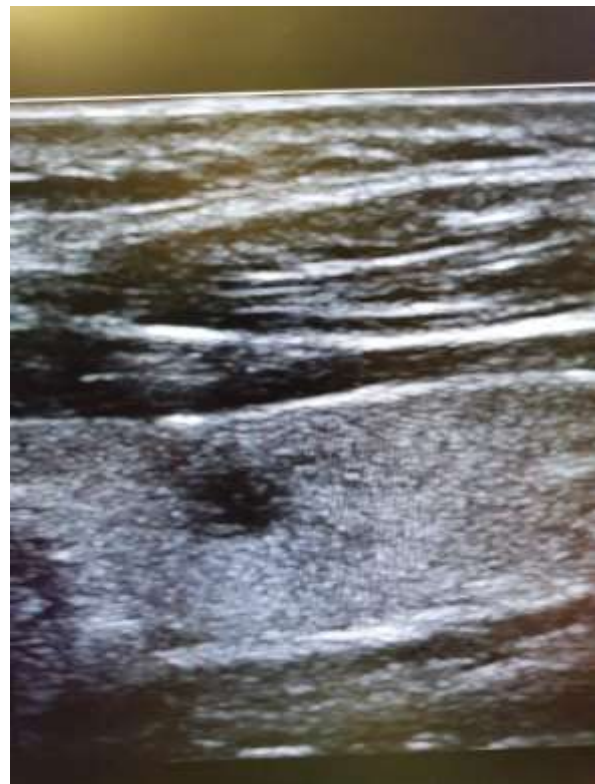


Figure 3. Pre-procedure sonographic evaluation. 8 mm hypoechoic nodule with microcalcification, no rim

Table 1. TI-RADS scores of nodules

TI-RADS Score	
2	66
3	52
4	48
5	4
6	12
7	4

and sent for pathological examination. Pathological evaluations were made in accordance with the Bethesda classification with appropriate fixation and staining methods. Aspirates without 6 follicle cell groups containing at least 10 cells were considered inadequate samples (Bethesda 1)(6).

#### Ultrasonographic Evaluation

Patients who undergo biopsy are evaluated by us before the procedure in our clinic, and we evaluate the presence of nodules, the character of the nodules, and which nodule or nodules to be biopsy in the presence of multiple nodules. Size, composition of nodules (cystic, mixed, solid), internal structure (heterogeneous, homogeneous), echogenicity (anechoic, hypoechoic, isoechoic, hyperechoic), shape (taller than wider, wider than taller), margin (well-circumscribed, lobule contoured, extrathyroidal extension), echogenic foci (absent, macrocalcification, peripheral calcification, microcalcification), rim (thin rim or no rim, thick rim) were evaluated by ultrasonography. TIRADS scoring was made according to these features (Figure 3).

#### Results

In our study, the average age of the patients was 52.5 +/- 13. The age distribution was between 18 and 76. 36 of our patients were men and 150 were women.

The average size of the nodules resulting from inadequate material was 24.5 mm, and the size range was 4-81 mm. 92 of the nodules were mixed, 70 were solid, while 2 of them were completely or almost completely cystic. While the internal structure of 104 nodules was heterogeneous, 82 of them were homogeneous. While 17 nodules were

anechoic, 55 were hypoechoic, 102 were isoechoic, 12 nodules were detected as hyperechoic. The anteroposterior length of all nodules included in our study was shorter than the transvers length.

In our study, there were 174 well-circumscribed, 12 lobulated contoured nodules. There is no nodule with extrathyroidal extension.

When nodules were evaluated in terms of echogenic focus, 156 had no echogenic focus, 15 had macrocalcification and 12 had microcalcifications. Peripheral calcification was detected in 3 nodules.

The rim was evaluated as thin or absent in 174 nodules, and thick rim was observed in 12 of them.

TI-RADS scores of the nodules are shown in table 1.

In our study, 29 of 49 patients whose results were inadequate material were found to be dominant in the cystic area. 19 were hypoechoic, 17 were isoechoic and 3 were hyperechoic. Three of the nodules with Bethesda 1 results were spongiform. While the internal structure of 22 nodules was homogeneous, 37 nodules were found to be heterogeneous.

#### Discussion

Thyroid FNABs performed under ultrasound guidance are among the most common procedures performed in interventional radiology clinics. It is important because of the high diagnosis rates, low complication rates and low cost (1). Those diagnosed as malignant as a result of FNAB are treated surgically, while those diagnosed with benign diagnosis can be followed up; It can be treated with radiofrequency or surgical methods (7, 8). Apart from these, inadequate material' found in different rates in the literature can come as a pathological result. With this result, patients are faced with repetitive biopsy procedures, naturally the cost increases. In addition, patient satisfaction rates are decreasing. In this patient group, we think that talking about the possible outcome of personal inadequacy according to the characteristics of the nodule will increase patient satisfaction

and strengthen the patient-physician relationship after ultrasonographic evaluation.

Thyroid nodules are common and mostly benign lesions. It is difficult to evaluate and manage only with clinical findings (9). Ultrasonography has an important place in the diagnosis as well as in the detection of the characteristics of the diagnosed nodule in the differentiation of malignant and benign (10). Ultrasound findings are valuable in the follow-up of the nodule and in making the biopsy decision. Different scoring systems have been developed in international platforms for the evaluation of nodules with ultrasonographic findings. American College of Radiology Thyroid Imaging Reporting & Data System (TI-RADS) and American Thyroid Association (ATA) scoring systems are the most commonly used scoring systems. These scoring systems are based on the ultrasound properties of the nodules. These features are taken into account by the composition, echogenicity, shape, borders and presence of echogenic foci of the nodule (11, 12).

In our study, ultrasonographic features of thyroid nodules with inadequate pathology results were evaluated. Different factors have been identified in the literature that affect biopsy results. These are cystic area dominance, macrocalcification, necrosis, and sclerosis (13-15). In addition, there are publications stating that the use of ultrasound, the experience of the specialist performing the biopsy, the number of insertions and the diameter of the needle used are related to the Bethesda 1 pathology result (16-18).

It was determined that 24 of 186 patients who had inadequate material were cystic, 92 were mixed and 70 were solid, in our study, Cystic areas were present in most of the nodules defined in a mixed structure. The ratio of almost complete cystic nodules to all biopsied nodules is low due to the low expectation of malignancy. On the other hand, the rate of nodules resulting from Bethesda 1 was found to be 12.9%. This rate is similar to the rates in the literature (15, 19). Two of the cystic nodules evaluated here have a pure cystic structure. In the study, it is possible that the

inadequate material increases with the increase in the number of pure cystic nodules. The number of examinable cells in the extracellular fluid content can be expected to be lower than in solid nodules.

When the nodules were evaluated in terms of TI-RADS scores, it was found that 166 were scored between 2-4. The score of 4 nodules was 5, 12 nodules was 6, while the TI-RADS score of only 4 nodules was 7. In the light of these data, it can be thought that nodules resulting from inadequate material have a low probability of malignancy. Management of patients with Bethesda 1 biopsy results has long been a difficult issue for physicians, and malignancy rates in nodules with inadequate results have been investigated (20). Malignancy rates in nodules resulting from inadequate material were found to be 2-7% in the literature. In the light of these rates, the result of Bethesda 1 should not be considered as benign.

While the boundaries of 12 of 186 nodules were irregular, 174 of them were reported as regular borders. Irregular border is a sonographic finding closely related to malignancy. Irregularly bordered nodules may be associated with cellular structures invading the surrounding tissues. In FNABs taken from these regions, dense cellular material is obtained and it is thought that the rate of inadequate material result decreases. There are not enough studies on Bethesda 1 pathology result in irregularly bordered nodules, and more studies are needed for a clear conclusion.

When nodules are examined in terms of echogenic focus, 156 of them have no echogenic focus, 15 of them have macrocalcification, 3 have peripheral calcification, and 12 have microcalcification. In the literature, non diagnostic cytology rates were found to be high in nodules containing macrocalcification (14). In nodules with macrocalcifications, the number of intact cells to be aspirated is relatively low. It can be difficult to apply the FNAB technique correctly in peripheral and internal dense calcified nodules. Calcified structures limit the needle movements and sometimes prevent

the needle tip from reaching the targeted areas. Increasing the number of macrocalcified nodules in biopsied nodules may increase the rate of inadequate results.

Halo sign-hypoechoic rim is a capsule-pseudocapsule structure consisting of imprinted thyroid tissue around the nodule. Inflammatory processes other than pressure cause this appearance. Thin and regular rim is frequently seen in benign nodules but is not specific enough in terms of benignity. Thin hypoechoic rim is frequently seen in follicular neoplasms. The absence of the halo sign has a low specificity of malignancy (21, 22). In our study, halo-peripheral hypoechoic rim properties of the nodules were evaluated. The result of 12 nodules with thick rim was Bethesda 1. Due to the low number of biopsied nodules with thick rim, the available data did not show a clear relationship between rim feature and inadequate material result. A study to be carried out with a higher number of nodules can provide more clear information on this issue, but the number of reports containing this information is low because rim features are an invaluable feature in the distinction between malignant and benign and have no place in scoring systems.

When the nodules in our study were examined in terms of size, it was found that the largest 81 mm, the smallest 4 mm, and the average 24.5 mm. It was considered depending on the necrosis areas observed in almost all of these nodules. Aspiration should not be made from necrotic tissues seen as cystic structures, and areas with solid appearance should be targeted whenever possible. Although it depends on the experience of the specialist performing the biopsy, it is not possible to understand exactly where the nodule has living tissue sonographically. In addition, in large nodules, the ideal number of needle passes of 3-5 times specified in the Bethesda Conference is insufficient and the number of needle entries may increase. In this case, the possibility of mixing blood and necrotic tissues increases. However, the size of the nodule alone was not sufficient and meaningful to evaluate the possibility of inadequate material result before biopsy.

The Bethesda System for Reporting Thyroid Cytopathology (TBSRTC) is the reporting system that sets the basic standards in the pathological evaluation of thyroid FNABs. Every material sent to pathology for examination by the clinician is first evaluated in terms of competence. In order for the examined sample to be evaluated as sufficient, there must be 6 follicular cell groups with at least 10 cells each. Although samples with abundant colloid material do not have enough cells to meet the criteria, it is recommended to report as benign, while samples containing pure cyst content and macrophages are recommended to be reported as non-diagnostic-inadequate. In cystic lesions with no suspicion of malignancy sonographically, it was recommended that the result of insufficient material be evaluated as benign by the clinician (6).

The technical competence of the specialist performing the biopsy, the experience of the pathologist who examined the material and sample used, and the experience of the pathologist in this field, play a role in the insufficient thyroid FNAB results. Apart from these, the characteristics of the biopsy nodule are important. Large areas of necrosis can be found in thyroid nodules. Finding an examinable cell block in aspiration biopsies made from these parts can be difficult for the pathologist. In addition, a small number of cell blocks in the fluid content aspirated from pure cystic nodules is expected. In the literature, the rate of insufficient results of FNABs taken from nodules containing macrocalcifications has been found to be high. In our study, the results are similar to the literature.

Our study has some important limitations. The study was conducted as a single center and retrospective. The biopsies included in the study were evaluated by different pathologists, and these pathologists may have experience differences. Relatively few patients were included in the study and only one type of syringe and needle tip was used. Apart from this, a comparison was not made on the number of needle passes recommended in the Bethesda Conference for 3-5 times, and

it was performed as a standard practice in all biopsies except for very large nodules.

## CONCLUSION

The pathological result of Bethesda 1 in thyroid biopsies is an issue that should be reduced as much as possible. In our study, it has been shown that although inadequate material results in features such as cystic dominance or macrocalcification increase,

there is a possibility in all types of nodules. Especially in biopsies taken from cystic dominant nodules, it may be beneficial to talk with the patient about the possible result beforehand. Even if the biopsy is taken by the most experienced hands, with the ideal technique and conditions, inadequate material results may be encountered. This information should be shared with the patient during the pre-procedure information.

## REFERENCES

1. Caruso D, Mazzaferri EL. Fine needle aspiration biopsy in the management of thyroid nodules. *The Endocrinologist*. 1991; 1(3):194-202.
2. Screatton NJ, Berman LH, Grant JW. US-guided core-needle biopsy of the thyroid gland. *Radiology*. 2003; 226(3):827-32.
3. Gharib H, Goellner JR. Fine-needle aspiration biopsy of the thyroid: an appraisal. *Annals of internal medicine*. 1993; 118(4):282-9.
4. Silverman JF, West RL, Larkin EW, et al. The role of fine-needle aspiration biopsy in the rapid diagnosis and management of thyroid neoplasm. *Cancer*. 1986; 57(6):1164-70.
5. Russ G, Bigorgne C, Royer B, Rouxel A, Bienvenu-Perrard M. The Thyroid Imaging Reporting and Data System (TIRADS) for ultrasound of the thyroid. *Journal de radiologie*. 2011; 92(7-8):701-13.
6. Cibas ES, Ali SZ. The 2017 Bethesda system for reporting thyroid cytopathology. *Thyroid*. 2017; 27(11):1341-6.
7. Chung SR, Suh CH, Baek JH, Park HS, Choi YJ, Lee JH. Safety of radiofrequency ablation of benign thyroid nodules and recurrent thyroid cancers: a systematic review and meta-analysis. *International journal of hyperthermia*. 2017; 33(8):920-30.
8. Kim Y-S, Rhim H, Tae K, Park DW, Kim ST. Radiofrequency ablation of benign cold thyroid nodules: initial clinical experience. *Thyroid*. 2006; 16(4):361-7.
9. Bruneton J-N, Balu-Maestro C, Marcy P-Y, Melia P, Mourou M-Y. Very high frequency (13 MHz) ultrasonographic examination of the normal neck: detection of normal lymph nodes and thyroid nodules. *Journal of Ultrasound in Medicine*. 1994; 13(2):87-90.
10. Kim SJ, Kim EK, Park CS, Chung WY, Oh KK, Yoo HS. Ultrasound-guided fine-needle aspiration biopsy in nonpalpable thyroid nodules: is it useful in infracentimetric nodules? *Yonsei medical journal*. 2003; 44(4):635-40.
11. Tessler FN, Middleton WD, Grant EG, et al. ACR thyroid imaging, reporting and data system (TI-RADS): white paper of the ACR TI-RADS committee. *Journal of the American college of radiology*. 2017; 14(5):587-95.
12. Haugen BR, Alexander EK, Bible KC, et al. 2015 American Thyroid Association management guidelines for adult patients with thyroid nodules and differentiated thyroid cancer: the American Thyroid Association guidelines task force on thyroid nodules and differentiated thyroid cancer. *Thyroid*. 2016; 26(1):1-133.
13. Bellantone R, Lombardi CP, Raffaelli M, et al. Management of cystic or predominantly cystic thyroid nodules: the role of ultrasound-guided fine-needle aspiration biopsy. *Thyroid*. 2004; 14(1):43-7.
14. Belfiore A, La Rosa GL. Fine-needle aspiration biopsy of the thyroid. *Endocrinology and Metabolism Clinics*. 2001; 30(2):361-400.
15. Choi SH, Han KH, Yoon JH, et al. Factors affecting inadequate sampling of ultrasound-guided fine-needle aspiration biopsy of thyroid nodules. *Clinical endocrinology*. 2011; 74(6):776-82.
16. Gursoy A, Ertugrul DT, Sahin M, Tutuncu NB, Demirer AN, Demirag NG. Needle-free delivery of lidocaine for reducing the pain associated with the fine-needle aspiration biopsy

of thyroid nodules: time-saving and efficacious procedure. *Thyroid*. 2007; 17(4):317-21.

17. Carpi A, Sagripanti A, Nicolini A, et al. Large needle aspiration biopsy for reducing the rate of inadequate cytology on fine needle aspiration specimens from palpable thyroid nodules. *Biomedicine & pharmacotherapy*. 1998; 52(7-8):303-7.

18. Ghofrani M, Beckman D, Rimm DL. The value of onsite adequacy assessment of thyroid fine-needle aspirations is a function of operator experience. *Cancer Cytopathology: Interdisciplinary International Journal of the American Cancer Society*. 2006; 108(2):110-3.

19. McHenry CR, Slusarczyk SJ, Khiyami A. Recommendations for management of cystic thyroid disease. *Surgery*. 1999; 126(6):1167-72.

20. Chow LS, Gharib H, Goellner JR, van Heerden JA. Nondiagnostic thyroid fine-needle aspiration cytology: management dilemmas. *Thyroid*. 2001; 11(12):1147-51.

21. Brito JP, Gionfriddo MR, Al Nofal A, et al. The accuracy of thyroid nodule ultrasound to predict thyroid cancer: systematic review and meta-analysis. *The Journal of Clinical Endocrinology & Metabolism*. 2014; 99(4):1253-63.

22. Remonti LR, Kramer CK, Leitao CB, Pinto LCF, Gross JL. Thyroid ultrasound features and risk of carcinoma: a systematic review and meta-analysis of observational studies. *Thyroid*. 2015; 25(5):538-50.

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