Diagn Interv Radiol 2019; 25:122–126

INTERVENTIONAL RADIOLOGY

ORIGINAL ARTICLE

US-guided core needle biopsy under assistance of hydrodissection to diagnose small lymph node metastases adjacent to cervical large vessels

Zhigang Cheng
Ping Liang

PURPOSE
We aimed to evaluate the safety and effectiveness of ultrasonography (US) guided core needle biopsy (CNB) with hydrodissection to diagnose small lymph node metastases adjacent to cervical large vessels.

METHODS
From January 2013 to October 2017, 31 patients with 31 cervical lymph node metastases adjacent to large vessels presented for US-guided CNB. The mean maximal diameter of lymph nodes was 0.93±0.16 cm (range, 0.6–1.2 cm). All patients underwent US-guided CNB with 18-gauge true-cut biopsy needle after hydrodissection with saline. The separation success rate (SSR) of the hydrodissection, technical success rate (TSR) of CNB, histopathologic success rate (HST), and complications were assessed.

RESULTS
The SSR of hydrodissection was 100% (31/31). After effective separation between the lymph node metastases and the adjacent large vessels with saline injection, the procedures of CNB were performed with a TSR of 100% (31/31). The HST of the lymph node metastases was 100% (31/31). Two patients complained of mild cervical swelling sensation during saline injection. No major complications such as injury of the large vessels or massive hemorrhage occurred.

CONCLUSION
Hydrodissection can facilitate safely and effectively US-guided CNB of subcentimeter cervical lymph nodes adjacent to large vessels, potentially impacting further therapeutic decisions.

Cervical lymph nodes are one of the common metastatic sites for malignant tumors of multiple organs (1). Lymph nodes require careful assessment in patients with malignant tumors as they would change tumor stage and therapeutic strategies (2). Modern medical images including ultrasonography (US) (3), computed tomography (CT) (4), magnetic resonance imaging (MRI) (5) and positron emission computed tomography (PET-CT) (6) play important roles in detecting cervical lymphadenopathy (7), especially for impalpable nodes due to small size or deep locations (4), which require pathologic diagnosis from surgical resection (4) or biopsy (8) specimen to determine malignancy, histologic differentiation, and clinical staging (9). Image-guided percutaneous biopsies including fine needle aspiration (FNA) and core needle biopsy (CNB) (8) are the most common methods to obtain tumor tissue and have minimized the application of surgical resection for tumor biopsy (10, 11). US-guided CNB has become the first-line method in diagnosing cervical lymphadenopathy (12, 13) with obvious advantage of fewer insertions to achieve adequate sample tissue for pathologic diagnosis.

US-guided percutaneous CNB procedure is performed by automatic biopsy gun, which usually has two fixed ejection distances of 2.2 cm and 1.5 cm, so this biopsy technique was deemed impossible to obtain tissue samples from small suspicious lymph node metastases with a maximal diameter of about 1 cm close to the cervical large vessels, because of the high risk of vessel injury. FNA is commonly applied in cytologic evaluation for the small lymph nodes (14), with limitations such as low negative predictive value (13) for lymphoma

From the Department of Interventional Ultrasound (P.L. ✉ *liangping301@126.com*), Chinese PLA General Hospital, Beijing, People's Republic of China.

Received 2 May 2018; revision requested 8 June 2018; last revision received 2 July 2018; accepted 19 July 2018.

DOI 10.5152/dir.2019.18166.

You may cite this article as: Cheng Z, Liang P. US-guided core needle biopsy under assistance of hydrodissection to diagnose small lymph node metastases adjacent to cervical large vessels. Diagn Interv Radiol 2019; 25:122–126.

and carcinoma due to insufficient specimen and no immunohistochemical evaluation of the tissue structure and cell morphology (15) to draw a correct pathologic diagnosis. Therefore, it is essential to explore a method to safely and effectively complete the CNB of small suspicious lymph node metastases adjacent to the cervical large vessels.

During the ablation of cervical lesions, such as benign thyroid nodules (16, 17) and cervical recurrence of papillary thyroid cancer (18, 19), hydrodissection has been used to separate the target lesions and the adjacent structures, such as nerves, trachea and esophagus, to avoid or minimize damage to these structures and assist safe and effective ablation of target lesions. In this study, the safety and effectiveness of US-guided hydrodissection during CNB of lymph nodes adjacent to cervical large vessels were evaluated retrospectively.

Methods

Patients

From January 2013 to October 2017, clinical data from 31 patients (18 males and 13 females) with a mean age of 60.5±9.9 years (range, 38–75 years) were retrospectively evaluated (Table 1). All patients had histories of malignant tumors, pathologically proven by surgical section or biopsy; tumors were located in lung (n=13), breast (n=5), stomach (n=5), thyroid (n=3), esophagus (n=2), colon (n=2), and ovary (n=1), respectively. The total number of the target cervical lymph nodes was 31 (right, n=9; left, n=22) with the mean maximum diameter 0.91±0.15 cm (range, 0.6–1.2 cm).

Main points

- The procedure of hydrodissection with saline to separate target small lymph node metastases from adjacent cervical large vessels can be safely performed under US guidance with excellent (100%) separation success rate (SSR).
- US-guided core needle biopsy (CNB) under hydrodissection assistance can be used to obtain tissue samples from small lymph node metastases adjacent to cervical large vessels with excellent (100%) technical success rate.
- US-guided CNB under hydrodissection assistance is a safe method to obtain tissue samples from small lymph node metastases adjacent to cervical large vessels without major complications, such as injury to the vessel by cutting needle.

Pre-procedure evaluation

The selection criteria for the patients were as follows: 1) the target lymph nodes in the neck impalpable and detected by medical images including US or PET-CT at follow-up after surgery or during systematic chemotherapy or targeted agent treatment; 2) further clinical managements were required to determine the pathological diagnoses for the lymph nodes because their presentations were suspected metastases on images; 3) all the nodes were closely adjacent to cervical large vessels, such as internal jugular vein, common carotid artery and subclavian artery; 4) the lymph nodes could be detected on US imaging. The exclusion criteria were prothrombin time >25 s, prothrombin activity <40%, and platelet count $<50\times10^9$ cells.

Anticoagulation and antiplatelet agents were temporarily omitted 5–7 days prior to CNB and could be retaken one day after the procedure (20). Pre-procedure evaluation included: 1) skin intactness at puncture site; 2) no blood vessels across the needle approach on color Doppler flow imaging; 3) careful assessment of the target lymph node such as size, location, blood flow and adjacent structures; 4) the feasibility of hydrodissection with saline injection and percutaneous biopsy. All participants had given written informed consent and were enrolled in institutional protocols approved by our institutional review board.

Hydrodissection and CNB procedures

Hydrodissection and CNB procedures were performed under a color Doppler US device guidance (Mylab Twice, Esaote S.p.A.) with a 10-5 MHz linear-array transducer.

Separation success of hydrodissection was defined as sufficient separation area created by saline between the target lymph node and the adjacent vessel to reach the ejection distance of automatic biopsy gun without damage to the adjacent vessels. Separation success rate (SSR) was defined as the number of patients with separation success after saline injection accounted for the number of the total patients. Technical success of CNB was defined as presence of adequate amount of target lymph node tissue observed on gross examination after CNB. Technical success rate (TSR) was defi-

Table. Clinical features of the patients, tumors, and complications

Variables	Data
Analysis of patients	
No. of patients	31
Gender (male/female)	18/13
Age (years), mean±SD (range)	60.5±9.9 (38–75)
Analysis of cervical lymph node metastases	
No. of tumors	31
Diameter (cm), mean±SD (range)	0.91±0.15 (0.6–1.2)
Lung cancer, n (%)	13 (41.9)
Breast cancer, n (%)	5 (16.1)
Gastric cancer, n (%)	5 (16.1)
Thyroid cancer, n (%)	3 (9.7)
Esophageal cancer, n (%)	2 (6.5)
Colon cancer, n (%)	2 (6.5)
Ovarian cancer, n (%)	1 (3.2)
Analysis of complications, n (%)	
Major complications	0
Minor complications	2 (6.5)

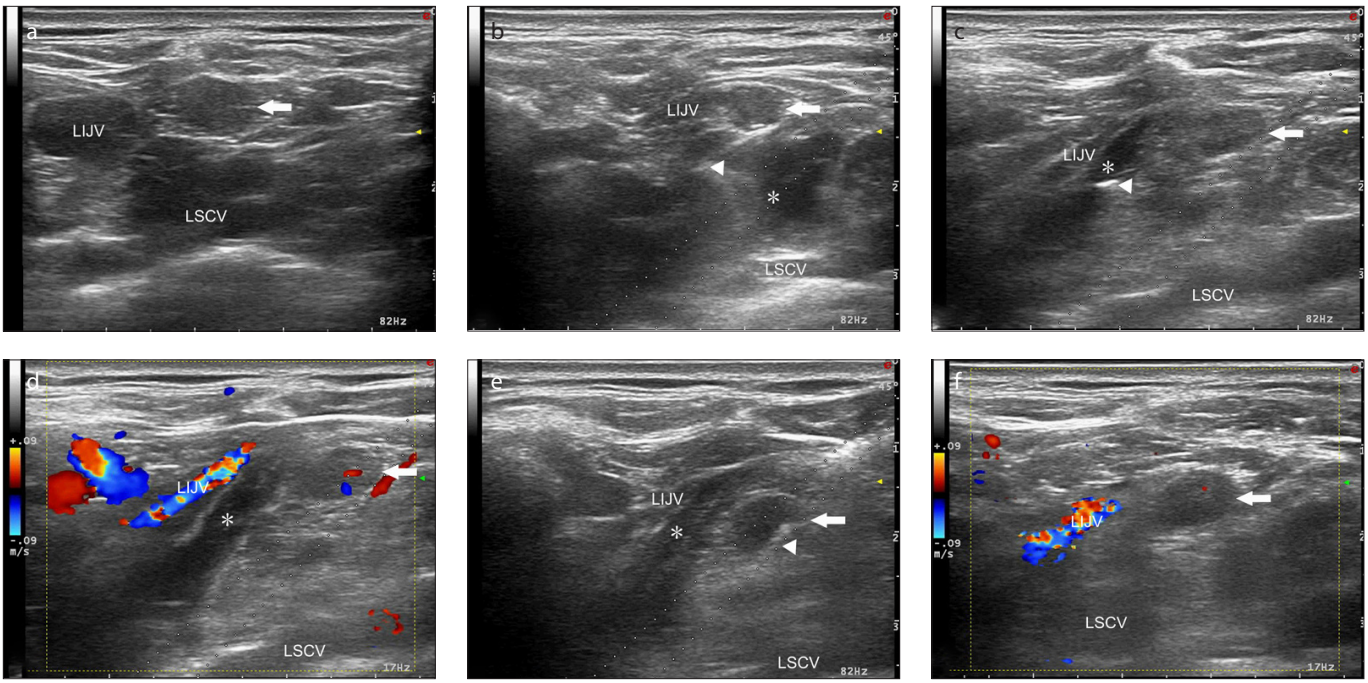

Figure 1. a–f. A 56-year-old man had surgical resection of lower esophageal squamous cell carcinoma 12 months before. Gray-scale US image **(a)** shows a nearly round lymph node in his right neck with maximal diameter of 0.9 cm *(arrow),* adjacent to left internal jugular vein (LIJV) and left subclavian vein (LSCV). Image **(b)** shows US-guided hydrodissection with a 21-gauge Chiba needle *(arrowhead)*, separating the node *(arrow)* and the adjacent LSCV. Image **(c)** shows US-guided hydrodissection with a 21-gauge Chiba needle *(arrowhead)* separating the node *(arrow)* and the adjacent LIJV. After hydrodissection **(d)**, the target lymph node *(arrow)* is successfully separated from the LIJV and LSCV. US-guided core needle biopsy (CNB) with an 18-gauge biopsy needle (**e,** *arrowhead)* is safely performed for the target lymph node *(arrow)*, and metastasis from esophageal squamous cell carcinoma is histopathologically proven. No injury of the large vessels or massive hemorrhage is present on US imaging **(f)** half an hour after CNB, and the injected saline has been absorbed. The *asterisk* indicates the injected saline.

cal success of CNB. Histopathologic success was defined as definite histopathologic diagnosis according to the tissue specimens after CNB. Histopathologic success rate (HST) was defined as the number of patients with histopathologic success divided the by the total number of patients.

Hydrodissection with saline injection was used to separate the target lymph nodes and the adjacent large vessels to avoid the injury of the large vessels. After the administration of local anesthesia (i.e., 1% lidocaine) at the puncture site, the sheath of a 21-gauge Chiba needle (Hakko Co. Ltd.) with 15 cm length was applied to perform the hydrodissection. The needle tip was advanced into the target lymph node and the proximal large vessel under US guidance, saline solution was rapidly injected so that a small local separation between the node and the vessel presented. The saline was continuously injected, while the needle tip was gradually advanced along the local liquid separation under US guidance until the separation between the node and the adjacent vessel was finally achieved on the US image. The sheath was kept for further saline injection when necessary. For the nodes close to two or more large vessels, additional hydrodissection procedure was performed at more than one site. After achievement of hydrodissection, CNB was performed with 18-gauge cutting biopsy needle ejected by an automatic ejection biopsy gun (Bard Biopsy Systems), and two to three biopsy samples were obtained from each target lymph node. Then, the sheath of Chiba needle was removed and 20 minutes of local compression was applied at the puncture site.

Patients were allowed to leave if no local bleeding or large vessel injury was observed 30 minutes after the procedure. Histopathologic success was evaluated according to the final pathologic diagnosis.

According to the Clavien-Dindo classification system for complications (21), the complications encountered in this study were defined as minor (Clavien–Dindo Classification Grade I and II) or major (Clavien–Dindo Classification Grade III, IV, and V), which were carefully recorded and timely managed.

Statistical analysis

Data analysis was performed with SPSS statistical software, version 22.0 (SPSS Inc.). Values for quantitative variables were expressed as mean ± standard deviation (range).

Results

All target lymph nodes were successfully separated from the adjacent cervical large vessels after hydrodissection with saline injection under US guidance. The SSR was 100% (31/31). An additional hydrodissection procedure was performed in two patients (6.5%) because of another large vessel close to the target lymph node. The remaining 29 patients (93.5%) achieved successful separation with a single hydrodissection procedure. The mean volume of injected saline was 23.9±7.0 mL (range, 10–40 mL).

After successful separation of the lymph nodes from the adjacent large vessels, CNBs were performed at ejection distances of 1.5 cm or 2.1 cm and TSR of 100% (31/31) was achieved. Sampling tissue length ranged from 0.5 to 1.2 mm. The pathologic diagnoses of the target lymph nodes were confirmed to be similar to the histopathologic types of the primary tumors, yielding HSR of 100% (31/31), including metastases from adenocarcinoma in 20 cases, squamous cell

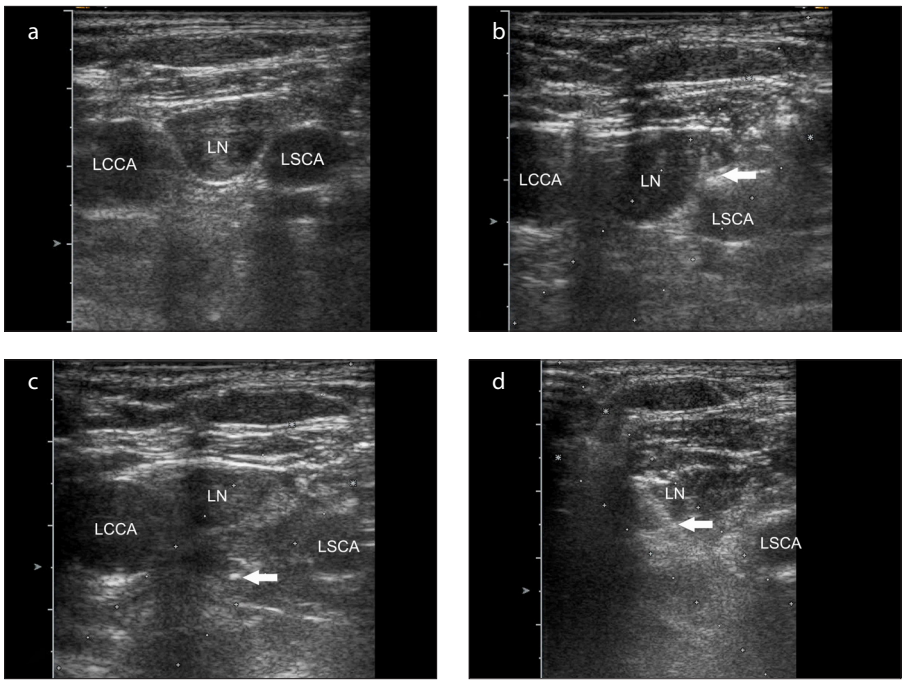

Figure 2. a–d. A 54-year-old woman had surgical resection of left lung adenocarcinoma 18 months before. Gray-scale US image **(a)** shows a nearly round lymph node (LN) in her left neck (maximal diameter 1.1 cm), adjacent to left common carotid artery (LCCA) and left subclavian artery (LSCA). Image **(b)** shows US-guided hydrodissection with a 21-gauge Chiba needle *(arrow)*, separating the lymph node and the adjacent LSCA. After hydrodissection **(c)**, the target lymph node is successfully separated from the LSCA (Chiba needle tip marked by *arrow)*. Image **(d)** shows successful US-guided CNB of the target lymph node using an 18-gauge biopsy needle *(arrow)*; metastasis from lung cancer was histopathologically proven from the biopsy sample. No injury to the large vessels occurred and there was no massive hemorrhage during follow-up.

carcinoma in 8 cases and papillary carcinoma in 3 cases (Table 1).

Minor complications occurred in two patients (6.5%), who complained of mild cervical swelling sensation, when 20 to 30 mL of saline was injected during the hydrodissection procedure. These two patients recovered a few minutes after the injection was ceased and the CNB procedures were successfully completed. No other minor complications occurred during the follow-up after the procedures. No major complications such as injury to a large vessel by cutting needle or massive hemorrhage at the puncture site were observed during or after the CNB procedures. Figs. 1 and 2 show the US presentations during hydrodissection procedures and CNB in two patients with cervical small lymph node metastases.

Discussion

Compared with FNA under US guidance, CNB showed a high diagnostic yield in cervical lymphadenopathy (12), but its clinical application was limited for the small lymph node metastases adjacent to the cervical large vessels because of the high probabilities of injury to the vessel wall leading to hematoma (13). Although ideally we strive to increase the diagnostic capability of imaging modalities to reduce the number of invasive procedures (22), it is still necessary to get pathologic results to guide further treatments in some cases. In our study, all lymph nodes were proximal to the cervical large vessels and had maximal diameter of 0.6 to 1.2 cm. Injury to the vessels might have occurred because the shortest ejection distance of the automatic biopsy gun was 1.5 cm, which was longer than the maximal diameters of the target nodes. To minimize the risks of CNB for the lymph node metastases close to the cervical large vessels, hydrodissection was employed to separate the target node and the proximal vessel during the CNB procedure. Our results showed that the procedures of hydrodissection during CNB were safely and effectively performed in all 31 patients and adequate specimens were obtained to draw pathologic diagnoses without injury to the large vessels or massive hemorrhage. Moreover, further therapeutic regimens were planned according to the pathologic diagnoses after CNB.

Superficial veins, such as external jugular vein, can be easily compressed by US probe obscuring their presence on US imaging. In this condition, Chiba or biopsy needle puncture might pierce through the vein and cause unexpected damage. Careful evaluation by US imaging before operation, mild pressure of the probe on the skin and advancement under real-time US guidance played important roles in avoiding the unexpected damage to the superficial veins.

One of the essential points for a successful hydrodissection was tissue looseness in the neck, which enabled injected saline to create an ejection distance of 1.5 to 2.2 cm between the node and the close vessel and was helpful to complete the procedure of CNB. Additionally, although the hydrodissection has been shown to be a safe method to assist the CNB biopsy for small lymph node metastasis and only two patients suffered minor complications, it was necessary to monitor the Chiba needle tip by real-time US imaging and caution patients not to swallow during the hydrodissection procedure, to avoid piercing of the vessel wall or target lymph node by the sharp tip due to the neck movement.

Small cervical lymph nodes usually have tough capsules, which increase the difficulty of successful puncture. The biopsy needle with slanted tip was easy to slip off the target node. This difficulty was overcome by positioning the biopsy needle along the center of the target node and the slanted needle tip close and nearly vertical to the surface of the node. Also, the sampled tissue was carefully checked by an experienced operator on gross examination and extra biopsy was performed when necessary. In this study, the HSR was 100%, which was higher than the correct histopathologic diagnoses of 91.1% (73/79) after CNB for cervical lymphadenopathy published by Oh et al. (12). One reason for this could be that all the target lymph nodes in this study were already highly suspected to be metastases from primary malignancies according to the patients' history and clinical imaging presentations prior to CNB; biopsy was performed to determine the histopathologic diagnosis to decide on further therapeutic regimens.

This study has several limitations. This retrospective study only included a single participating center and had no comparative arm with the cytological results of FNA. Results of a prospectively comparative study between CNB and FNA would be more convincing. In addition, sample size

was small because only a minority of small lymph node biopsies need to be performed under the assistance of hydrodissection due to large vessel proximity, while the majority can be performed directly because of safe locations. Last but not the least, tumor seeding due to saline injection was cautiously considered. Reducing puncturing times and the volume of saline injection would be beneficial for minimizing the risk of tumor seeding.

In conclusion, hydrodissection can facilitate safely and effectively US-guided CNB of subcentimeter cervical lymph nodes adjacent to large vessels, potentially impacting further therapeutic decisions according to histopathologic and genetic results.

Financial disclosure

This work was supported by the National Key R&D Program of China (No. 2017YFC0112000) and the National Scientific Foundation Committee of China (Grants No. 81430039 & 81627803 & 81871374).

Conflict of interest disclosure

The authors declared no conflicts of interest.

References

1. Zhuang SM, Wu XF, Li JJ, Zhang GH. Management of lymph node metastases from an unknown primary site to the head and neck (Review). Mol Clin Oncol 2014; 2:917–922. [CrossRef]
2. Müller von der Grün J, Tahtali A, Ghanaati S, Rödel C, Balermpas P. Diagnostic and treatment modalities for patients with cervical lymph node metastases of unknown primary site - current status and challenges. Radiat Oncol 2017; 12:82. [CrossRef]
3. Chammas MC, Macedo TA, Lo VW, Gomes AC, Juliano A, Cerri GG. Predicting malignant neck lymphadenopathy using color duplex sonography based on multivariate analysis. J Clin Ultrasound 2016; 44:587–594. [CrossRef]
4. Shetty D, Jayade BV, Joshi SK, Gopalkrishnan K. Accuracy of palpation, ultrasonography, and computed tomography in the evaluation of metastatic cervical lymph nodes in head and neck cancer. Indian J Dent 2015; 6:121–124. [CrossRef]
5. Wu LM, Xu JR, Hua J, Gu HY, Zhu J, Hu J. Value of diffusion-weighted MR imaging performed with quantitative apparent diffusion coefficient values for cervical lymphadenopathy. J Magn Reson Imaging 2013; 38:663–670. [CrossRef]
6. Payabvash S, Meric K, Cayci Z. Differentiation of benign from malignant cervical lymph nodes in patients with head and neck cancer using PET/CT imaging. Clin Imaging 2016; 40:101–105. [CrossRef]
7. Forghani R, Yu E, Levental M, Som PM, Curtin HD. Imaging evaluation of lymphadenopathy and patterns of lymph node spread in head and neck cancer. Expert Rev Anticancer Ther 2015; 15:207–224. [CrossRef]
8. VanderLaan PA. Fine-needle aspiration and core needle biopsy: An update on 2 common minimally invasive tissue sampling modalities. Cancer 2016; 124:862–870.
9. de Bazelaire C, Coffin A, Cohen S, Scemama A, de Kerviler E. Biopsies in oncology. Diagn Interv Imaging 2014; 95:647–657. [CrossRef]
10. Ha EJ, Baek JH, Lee JH, et al. Core needle biopsy could reduce diagnostic surgery in patients with anaplastic thyroid cancer or thyroid lymphoma. Eur Radiol 2016; 26:1031–1036. [CrossRef]
11. Kaur I, Handa U, Kundu R, Garg SK, Mohan H. Role of fine-needle aspiration cytology and core needle biopsy in diagnosing musculoskeletal neoplasms. J Cytol 2016; 33:7–12. [CrossRef]
12. Oh KH, Woo JS, Cho JG, Baek SK, Jung KY, Kwon SY. Efficacy of ultrasound-guided core needle gun biopsy in diagnosing cervical lymphadenopathy. Eur Ann Otorhinolaryngol Head Neck Dis 2016; 133:401–404. [CrossRef]
13. Ryu YJ, Cha W, Jeong WJ, Choi SI, Ahn SH. Diagnostic role of core needle biopsy in cervical lymphadenopathy. Head Neck 2015; 37:229–233. [CrossRef]
14. Pusztaszeri MP, Faquin WC. Cytologic evaluation of cervical lymph node metastases from cancers of unknown primary origin. Semin Diagn Pathol 2015; 32:32–41. [CrossRef]
15. Lee YN, Moon JH, Kim HK, et al. Core biopsy needle versus standard aspiration needle for endoscopic ultrasound-guided sampling of solid pancreatic masses: a randomized parallel-group study. Endoscopy 2014; 46:1056–1062. [CrossRef]
16. Cheng Z, Che Y, Yu S, et al. US-guided percutaneous radiofrequency versus microwave ablation for benign thyroid nodules: a prospective multicenter study. Sci Rep 2017; 7:9554. [CrossRef]
17. Mauri G, Cova L, Monaco CG, et al. Benign thyroid nodules treatment using percutaneous laser ablation (PLA) and radiofrequency ablation (RFA). Int J Hyperthermia 2016;15:1–5.
18. Lim HK, Baek JH, Lee JH, et al. Efficacy and safety of radiofrequency ablation for treating locoregional recurrence from papillary thyroid cancer. Eur Radiol 2015; 25:163–170. [CrossRef]
19. Mauri G, Cova L, Ierace T, et al. Treatment of metastatic lymph nodes in the neck from papillary thyroid carcinoma with percutaneous laser ablation. Cardiovasc Intervent Radiol 2016;39:1023–1030. [CrossRef]
20. Kwok A, Faigel DO. Management of anticoagulation before and after gastrointestinal endoscopy. Am J Gastroenterol 2009; 104:3085–3097. [CrossRef]
21. Dindo D, Demartines N, Clavien PA. Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. Ann Surg 2004; 240:205–213. [CrossRef]
22. Rizzo S, Radice D, Femia M, et al. Metastatic and non-metastatic lymph nodes: quantification and different distribution of iodine uptake assessed by dual-energy CT. Eur Radiol 2018; 28:760–769. [CrossRef]