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Impact of Thyroid Incidentaloma on Liver Transplant: A Study of 1010 Recipients at a Single Center

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Background: Thyroid incidentalomas are typically nonpalpable thyroid nodules discovered during radiographic evaluation for a non-thyroid issue. Thyroid incidentalomas visualized by computed tomography (CT) and ^{18}F-flurodeoxyglucose (FDG) positron emission tomography (PET) before living donor liver transplantation (LDLT) are rare. The aim of the study was to analyze the clinical impact of thyroid incidentalomas discovered prior to transplantation.

Material/Methods: This retrospective study recruited 1010 patients undergoing LDLT between 2010 and 2019. CT was performed on each patient, whereas PET was performed on randomized patients (n=498).

Results: The prevalence and malignant risk of thyroid incidentaloma on CT was 2.3% (23/1010) and 13.0% (3/23), respectively. The prevalence of thyroid incidentaloma on PET was 3.0% (15/498). Approximately half of the FDG uptake on PET was diffuse uptake (n=7), whereas the other half was focal uptake (n=8). The malignant risk of PET incidentaloma with focal FDG uptake was 37.5% (3/8). Four asymptomatic thyroid cancers were identified incidentally. After total thyroidectomy followed by LDLT, these patients maintained cancer-free status.

Conclusions: Thyroid incidentalomas occurred at a rate of 2-3% in LDLT candidates. The malignant risk was 13.0% on CT incidentaloma, and 37.5% on PET incidentaloma with focal FDG uptake. Curative treatment of incidental thyroid cancer followed by LDLT without delay can achieve a favorable prognosis.

Keywords: **Incidental Findings • Liver Transplantation • Thyroid Diseases**

Abbreviations: **AJCC** – American Joint Committee on Cancer; **ATA** – American Thyroid Association; **CT** – computed tomography; **CNIs** – calcineurin inhibitors; **DM** – diabetes mellitus; **FDG** – flurodeoxyglucose; **FNA** – fine needle aspiration; **FT4** – free thyroxine; **HCC** – hepatocellular carcinoma; **HTN** – hypertension; **LDLT** – living donor liver transplantation; **LT** – liver transplant; **mTOR** – mammalian target of rapamycin; **PET** – positron emission tomography; **PTC** – papillary thyroid cancer; **SUV** – standard uptake values; **Tg Ab** – antithyroglobulin antibodies; **TPO Ab** – antithyroid peroxidase antibodies; **TSH** – thyroid-stimulating hormone; **US** – ultrasound

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Background

The prevalence of impalpable thyroid nodules in the general population may be up to 50% on autopsy, but most of these nodules are asymptomatic [1]. With advancement in imaging technologies and increased utility of imaging modalities, incidental thyroid nodules are being increasingly identified. Several studies have investigated the clinical impact of thyroid incidentalomas noted on computerized tomography (CT), magnetic resonance imaging, ultrasound (US), and 18F-flurodeoxyglucose (FDG) positron emission tomography (PET) in the general population for cancer screening or in patients with documented malignancy unrelated to the thyroid [2-4].

Liver cirrhosis is a leading cause of mortality and morbidity, with mortality rates rising globally between 1990 and 2017 [5]. Liver transplantation (LT) is the most effective surgical treatment for liver cirrhosis. However, several studies indicated that LT recipients had greater risks of de novo or recurrent cancers during follow-up [6-8]. The etiology may come from the immunosuppressive therapy, including attenuation of cytotoxic T-cell and natural killer cell function, as well as the disturbance of humoral interaction with macrophages [9,10]. Additionally, reports from animal studies demonstrated that calcineurin inhibitors (CNIs), one of the most common immunosuppressive drugs, have carcinogenic effect, which may be caused by activation of Ras pathway, induction of tumor growth, and disruption of angiogenesis and apoptosis [11-13]. Therefore, surveying of extrahepatic malignancy before LT and curative treatment of pre-existing malignancy is recommended, with sufficient time for observation of recurrence or metastasis [14].

When chest CT or ^{18}F-FDG PET were arranged to survey malignancy [15,16], thyroid mass might be identified incidentally. Based on the current recommendations from American Thyroid Association (ATA), fine needle aspiration (FNA) was probably perceived to define the benign or malignant nature of the thyroid incidentaloma [17,18]. Once the patient was diagnosed of thyroid cancer, a decision had to be reached as to whether LT surgery should be delayed [14].

The aim of this study was to describe the prevalence and malignant risk of thyroid incidentaloma discovered on CT or ^{18}F-FDG PET in a large series of patients with liver cirrhosis or hepatocellular carcinoma (HCC) scheduled for upcoming LDLT. This study also aimed to evaluate the impact of untreated thyroid cancer discovered prior to LDLT on the clinical course and long-term outcome.

Material and Methods

Study Population and Design

The study sample comprised 1010 adults (all >20 years old) who underwent LDLT at Kaohsiung Chang Gung Memorial Hospital in Taiwan between January 2010 and December 2019. We maintained a longitudinal database of recipients and recorded all demographic, pre-operative, peri-operative, pathological, and follow-up information. All patients were followed up at our outpatient clinic every 3-6 months, with the observation period terminating in July 2021. The study was approved by the Institutional Review Board (IRB no. 202101208B0), and the need to obtain informed consent from patients was waived due to the study's retrospective design.

Patients were excluded if they had a previous thyroid disease or symptomatic thyroid mass. Two patients with underlying Graves' disease and 1 patient with benign nodular goiter post-lobectomy were excluded from the study.

The pre-operative assessment of LT candidates included screening for cardiovascular risk, psychological examination, and radiological assessment of the hepatic vasculo-biliary anatomy. The 64-raw multidetector chest CT (Aquilion 64; Toshiba Medical System; Japan) with both lung (window width 1500 H; window level -500 H) and soft tissue (window width 350 H, window level 50 H) settings was also performed routinely to survey lung lesions [15], and interpreted by the radiologists. FDG-PET scan (Discovery ST; GE Healthcare; USA), reviewed by the nuclear radiologists, was performed to exclude the possibility of distant HCC metastasis or extrahepatic malignancy [16], both of which are contraindication of LT [14]. Due to the prohibitively expensive cost of PET scan, it was performed on half of the sample participants in a randomized manner (n=498, 49%). For each patient with incidental thyroid mass on chest CT or PET scan, serum thyroid-stimulating hormone (TSH), thyroid hormone, and thyroid antibodies were measured, and thyroid US were performed.

Thyroid US (LOGIQ S8; GE Healthcare; USA) was performed by endocrinologists or general surgeons. FNA cytology with a 21-gauge needle was indicated when a definite solid nodule was noticed on US, and the specimen was examined by the same groups of cytologists. FNA was performed for every solid nodule without size limitation, but FNA was not performed for pure cystic lesions. If the cytology report indicated the presence of atypical cells, follicular neoplasm, and suspicious or confirmed malignancy, diagnostic thyroidectomy was recommended and performed prior to LT to confirm the diagnosis and cancer staging.

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Definitions

Excluding primary biliary cholangitis and primary sclerosis cholangitis, the diagnosis of autoimmune hepatitis was made based on the serological and/or histopathologic reports from the explants or on revised International Autoimmune Hepatitis Group scoring systems [19]. Diffuse uptake on PET scan was defined as FDG uptake over the entire thyroid gland, whereas focal uptake was defined as localized FDG uptake in the thyroid. Regions of interests were drawn for quantification FDG uptake on the visible lesions with increased tracer uptake, and maximum standard uptake values (SUVs) were calculated and recorded. Hypothyroidism was defined as a TSH level exceeding the reference range and a free thyroxine (FT4) level falling below the reference range, a documented history of hypothyroidism, or the use of thyroid hormone replacement therapy [20]. Autoimmune thyroiditis, also known as chronic lymphocytic or Hashimoto's thyroiditis, was defined by the presence of specific auto-antibodies in serum, including antithyroid peroxidase antibodies (TPO Ab) and antithyroglobulin antibodies (Tg Ab), and by varying degrees of thyroid dysfunction [21,22]. Papillary thyroid cancer (PTC) was staged according to the 8th edition American Joint Committee on Cancer (AJCC) TNM system.

Data Collection

Demographic and operative variables included age, sex, underlying etiology of liver disease, and presence of HCC. Preoperative and postoperative variables measured included body mass index (BMI) and the prevalence of hypertension (HTN) or diabetes mellitus (DM). Postoperative data included immunosuppressive therapy and outcome of thyroid cancer.

The primary outcome in this study was the incidence of thyroid incidentaloma on CT or PET in LT candidates. Secondary outcomes included the prevalence of subclinical thyroid cancer, the outcome of LT recipients with concurrent thyroid cancer, and the association with thyroiditis or hypothyroidism.

Immunosuppressive Therapy

All LDLT patients in the cohort received an initial standard immunosuppressive regimen comprising the CNI (tacrolimus) with mycophenolate mofetil. Target trough levels were 5-7 ng/mL for tacrolimus during the first year and 3-5 ng/mL after 1 year. Additionally, some patients were added on or converted to a mammalian target of rapamycin (mTOR) inhibitor for renal function preservation and anti-tumor effect.

Statistical Analysis

Data were collected and analyzed using SPSS Statistics v.20 software (IBM corporation, Armonk, NY). Qualitative variables were expressed as frequency of events and cumulative incidence (in percentage). Quantitative variables were expressed by their median with inter quartile range (IQR). Differences between groups were compared using the exact Fisher test for 2 qualitative variables and the nonparametric Mann-Whitney U test was calculated for differences in 2 groups for quantitative variables. The Wilcoxon signed-rank test was used to compare the repeated measurements on a single sample in a nonparametric group. A P value <0.05 was considered statistically significant.

Results

Thyroid Incidentaloma on CT

The cohort comprised 286 females and 724 males, with a mean age of 54.5±14.9 years. Chest CT identified 23 cases (2.3%, 23/1010) of thyroid incidentaloma in 1010 LT candidates without known thyroid disease (**Table 1**). The demographics of the 2 groups (CT thyroid incidentaloma and no CT thyroid incidentaloma) were comparable. Thyroid echo was performed exclusively in each CT-discovered thyroid incidentaloma case, followed by FNA to obtain the diagnosis. FNA was abandoned in 3 cases due to pure thyroid cysts. Among the 4 patients with FNA whose result were Bethesda category III, IV, and VI, diagnostic thyroidectomy was performed. One case was diagnosed with nodular goiter after right thyroidectomy, and another 3 cases were found to be papillary thyroid cancer (Patient No. 1, 3 and 4; **Table 2 and Figure 1**) after bilateral total thyroidectomy. Due to the well-differentiated thyroid cancer without LN or distant metastasis, the 3 thyroid cancer patients underwent LDLT surgery in 1 week after thyroidectomy.

In addition, the tumor sizes measured by CT and US differed significantly (median size: 1.5 cm vs 1.7 cm; P=0.003), indicating a size measurement discrepancy between CT and US, with the measured tumor size being larger on US than on CT.

Thyroid Incidentaloma in PET

The sample comprised 359 females and 139 males, with a mean age of 54.5±8.0 years. Among the 498 cases who underwent PET scan (**Tables 1, 2**), a total of 15 (3%, 15/498) thyroid incidentalomas were identified, including patterns of diffuse (n=7) and focal (n=8) uptakes. Although the demographics of both groups (PET thyroid incidentaloma and no PET thyroid incidentaloma) were similar, the prevalence rate of autoimmune hepatitis was higher in the group with PET thyroid incidentaloma than in the group without PET thyroid incidentaloma (6.7% vs 1.0%; P=0.049). Moreover, the pattern of diffuse FDG uptake (n=7, **Figure 2**) was suggestive of thyroiditis without definite mass on the CT scan and echo, and this pattern corresponded

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Table 1. Patient characteristics in liver cirrhotic patients waiting for liver transplantation.

	Enhanced chest CT (n=1010)			^{18}F-FDG PET (n=498)		
	CT thyroid incidentaloma (n=23, 2.3%)	No CT thyroid incidentaloma (n=987)	*P* value	PET thyroid incidentaloma (n=15, 3.0%)	No PET thyroid incidentaloma (n=483)	*P* value
Recipient age (year)	58 (53-65)	55 (50-60)	0.061	55 (52-64)	55 (50-61)	0.233
Female sex, n (%)	10 (43.5%)	276 (28.0%)	0.103	10 (66.7%)	349 (72.3%)	0.635
BMI (kg/m^2)	26.6 (22-28)	24.9 (23-27)	0.405	23 (21-27)	25.2 (23-28)	0.149
MELD score	14 (9-20)	12 (8-17)	0.397	8 (7-14)	12 (9-16)	0.080
Child-Pugh score	9 (7-10)	8 (6-10)	0.114	7 (5-9)	8 (6-10)	0.066
Hypertension, n (%)	3 (13.6%)	143 (16.3%)	0.736	2 (13.3%)	86 (19.1%)	0.577
Diabetes mellitus, n (%)	8 (36.4%)	209 (23.8%)	0.172	2 (13.3%)	116 (25.6%)	0.281
HCC, n (%)	11 (47.8%)	472 (47.8%)	1.000	10 (66.7%)	253 (52.4%)	0.275
Primary liver disease*, n (%)						
HBV hepatitis	10 (43.5%)	453 (45.9%)	0.818	7 (46.7%)	212 (43.9%)	0.831
HCV hepatitis	6 (26.1%)	301 (30.5%)	0.649	4 (26.7%)	157 (32.5%)	0.634
Alcoholism	5 (21.7%)	202 (20.5%)	0.881	2 (13.3%)	111 (23.0%)	0.380
Autoimmune hepatitis	2 (8.7%)	37 (3.7%)	0.225	1 (6.7%)	5 (1.0%)	0.049
Others**	3 (13%)	68 (6.9%)	0.254	1 (6.7%)	32 (6.6%)	1.000
Postoperative outcome						
2-year patient survival rate	76%	91%	0.231	80%	87%	0.238

Data are shown as the median (interquartile range (IQR) 25-75) and number (%) * Some patients were diagnosed with combined viral hepatitis (ex: HBV+HCV) or viral hepatitis with alcoholism (HBV+alcoholism or HCV+alcoholism). ** Others include cryptogenic liver cirrhosis, Wilson's disease, polycystic liver kidney disease, Budd-Chiari syndrome...etc. BMI – body mass index, HCC – hepatocellular carcinoma, MELD – model for end-stage liver disease.

to autoimmune thyroiditis in 5 cases (71%, 5/7), according to serology test results. Four of 7 (57%) patients with diffuse FDG uptake in the thyroid had overt hypothyroidism without treatment (**Table 2**). For patients with focal FDG uptake in the thyroid (n=8), US and FNA were performed for each case. Three patients underwent total thyroidectomy because cytology results indicated Bethesda category ranging from 3-5, and they were postoperatively diagnosed with PTC (Patient No. 1, 2 and 4; **Table 3 and Figure 1**). Due to well-differentiated thyroid cancer without LN or distant metastasis, all patients underwent LDLT surgery in one week after thyroidectomy. For patients with PTC size >1 cm, radio-ablation therapy was scheduled according to ATA guidelines when the postoperative condition became stable [17], and these patients have maintained a thyroid cancer disease-free status to date. Moreover, in our analysis, the maximal value of SUV uptake was not associated with the occurrence of thyroid cancer (median SUV uptake of thyroid cancer vs benign nodule: 3.9 vs 3.7; *P*=0.840).

Discussion

Thyroid abnormality might be detected on the CT or PET imaging incidentally. In our cohort, thyroid incidentalomas occurred at a rate of 2-3% in LDLT candidates. The malignant risk was 13.0% for CT incidentaloma, and 37.5% for PET incidentaloma with focal FDG uptake. Additionally, diffuse FDG uptake on PET scan was an indicator of autoimmune thyroiditis with concurrent hypothyroidism. After curative resection of pre-LT discovered thyroid cancer, these recipients maintained a favorable outcome.

In our series of 1010 chest CT examinations among patients with liver cirrhosis and/or HCC, the prevalence of incidental thyroid lesions was found to be 2.3%, which is far lower than the 15-18% reported in other studies [2,23]. The discrepancy may arise from special populations studied; we focused on cirrhotic patients with viral or alcoholic hepatitis in majority, while other

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Table 2. Characteristics of the thyroid incidentalomas visualized on CT and PET.

	Thyroid incidentaloma detected by	
	Chest CT (n=23)	^{18}F-FDG PET (n=15)
PET uptake		
Diffuse, n (%)6		7 (46.7%)
Focal, n (%)		8 (53.3%)
SUV max		3.1 (2.4-6.0)
Tumor size measured by CT (cm)	1.5 (1.2-2.1)	–
Tumor size measured by echo (cm)	1.7 (1.4-2.9)	1.1 (1.8-3.1)
Hypothyroidism, n	0	4*
Pure thyroid cyst, n	3	0
Fine needle aspiration, n	20	8
Non-diagnostic, n	4	2
Benign, n	12	3
Atypia or follicular neoplasm, n	3	2
Suspicious or confirmed malignancy, n	1	1
Surgery		
Lobectomy, n	1**	0
Bilateral total thyroidectomy, n	3	3
Final pathology		
Nodular goiter, n	1	0
Papillary thyroid cancer, n (%)	3 (13.0%)	3 (37.5%)***

Data are shown as the median (interquartile range (IQR) 25-75) and number (%).* All patients had the diffuse FDG uptake of thyroid. ** Lobectomy was performed for the patient with nodular goiter. *** In the group of focal FDG uptake with definite thyroid nodule (n=8).

studies largely focused on general population. Furthermore, 13.0% (3/23) of the thyroid incidentalomas on CT were histologically proved to be malignant in our study. This incidence rate is comparable to that of a study by Yoon et al., who reported a 9.4% (15/160) prevalence rate of thyroid cancer in a cohort of 160 thyroid incidentalomas among 734 patients receiving CT scans [23]. Although the prevalence of CT thyroid incidentaloma was lower in LT candidates than in the general population, the risk of incidental thyroid cancer under CT was similar in both populations. Therefore, thyroid incidentaloma discovered on CT may alert clinicians to survey thyroid cancer more cautiously.

Several studies have demonstrated that both US and CT may overestimate the nodular size compared to pathologic examination [24,25]. Although lack of histology exam for each incidentaloma in our study, we noted a significant size discrepancy between the results of the CT and those of the US, with US measuring a bigger tumor size than CT. Our finding is in accordance with Tao's study, which showed a larger tumor size on US than on CT, probably explained by the apparent coalescence of thyroid nodules [24].

The prevalence of incidental thyroid FDG uptake was 3.0% (15/498) on FDG-PET scan, of which 1.4% (7/498) were diffuse and 1.6% (8/498) were focal types. Our findings were consistent to those of other studies that found prevalence rates ranging from 2.0% to 3.8%, with half being focal and half being diffuse lesions [26,27]. Notably, although the incidentally detected thyroid nodules on PET is fairly uncommon, the malignant risk of focal FDG uptake may up to 50% with dominant PTC on histological analysis [3,26,27]. In our study, cytological verification was only available in 6 of 8 focal thyroid FDG uptakes, and thyroidectomy were performed in 3 patients according to the Bethesda category of III or higher. Finally, these 3 patients (37.5%) were all diagnosed of PTC postoperatively. Moreover, our results also support the findings of several studies that the maximal SUV value was not useful in differentiating malignant from benign lesions [26,27]. Therefore, when PET revealed focal FDG uptake in the thyroid regardless of SUV value, thyroid echo and FNA for cytologic analysis was indicated [28].

Although immunosuppression is essential after LT to prevent rejection, it also has several drawbacks, one of which is the

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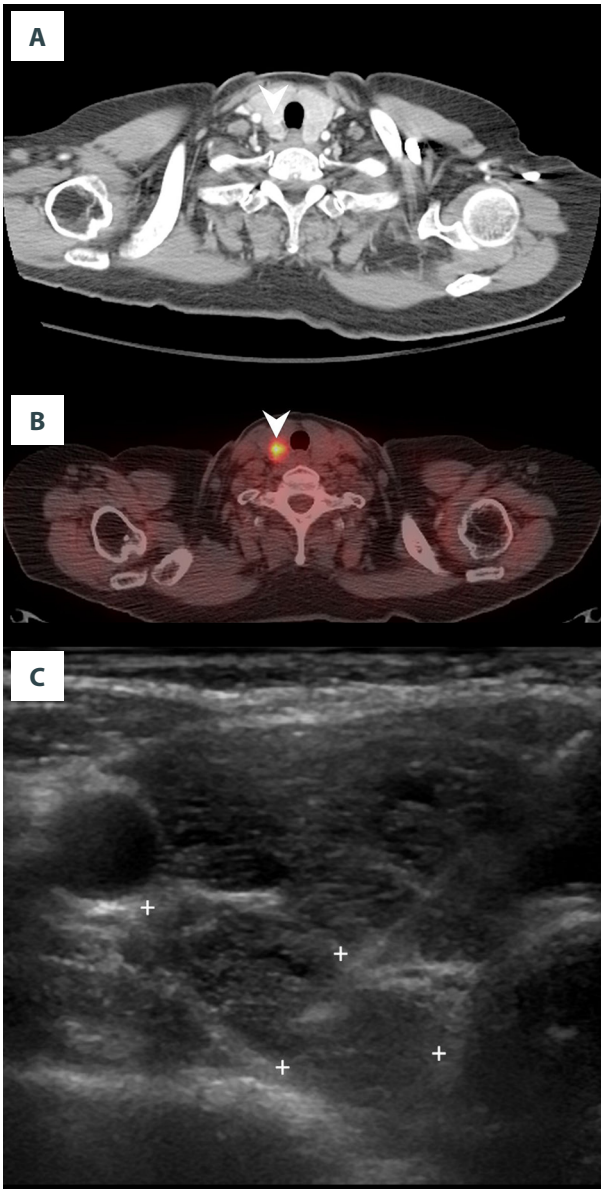

Figure 1. A 61-year-old woman (Patient No. 1) with hepatitis C-related liver cirrhosis and hepatocellular carcinoma was diagnosed with papillary carcinoma (stage I, pT1bN0M0) after total thyroidectomy. (**A**) Chest CT demonstrated a round isoechoic nodule with contrast-enhanced rim at right lower lobe; (**B**) ^{18}F-FDG PET/CT showed a hypermetabolic tumor with SUV_{max} up to 6.8 at right lobe; (**C**) Transverse view of thyroid echo revealed an ovoid isoechoic tumor at right lower thyroid, then fine needle aspiration disclosed atypical cells.

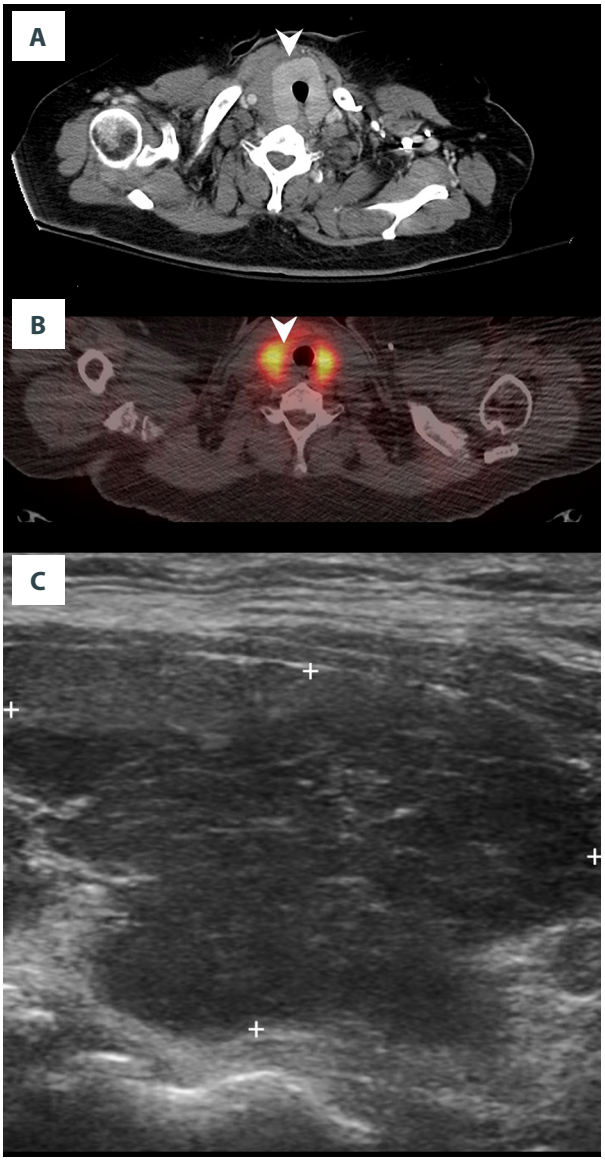

Figure 2. A 60-year-old woman with hepatitis C-related liver cirrhosis. (**A**) Chest CT showed an enlarged thyroid gland without mass; (**B**) ^{18}F-FDG PET/CT revealed diffuse uptake over bilateral thyroid with SUV_{max} up to 12.8; (**C**) Longitudinal view of thyroid echo disclosed hypoechoic parenchyma, compatible with thyroiditis change.

carcinogenic effect [6-8]. For LT candidates who have a history of extrahepatic malignancy, curative treatment and sufficient time for observation of recurrence or metastasis are recommended [14]. However, the behavior of malignancy varies substantially across cancers. Well-differentiated thyroid cancer was deemed less aggressive than other malignancies. Additionally, our PTC cases were classified as low risk for recurrence, according to the current risk stratification system from 2015 ATA guidelines [17]. Hence although thyroid cancer was newly diagnosed before LT, low risk malignancy and low possibility of recurrence or metastasis was anticipated [29]. In our series, 4 cases (0.4%) of PTC were identified incidentally among 1010 LT candidates (**Table 3**) and treated with total thyroidectomy immediately preceding LT and/or radio ablation therapy

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Table 3. Characteristics of LDLT patients diagnosed with incidental thyroid cancer.

Pt No.	Age (y)	Sex	Diagnosis	CT incidentaloma	PET incidentaloma	Cancer type	Cancer size	Treatment	8th AJC stage	Immunosuppression	Following time (m)	Outcome
1	61	F	HCV/HCC	+	+	PTC	1.3 cm	TTx+RAI	I (T1bN0M0)	Tacrolimus	64	No recurrence
2	51	F	HBV/HCC	–	+	PTC	0.7 cm	TTx	I (T1aN0M0)	Tacrolimus	57	No recurrence
3	67	F	HCV/HCC	+	–	PTC	0.1 cm*	TTx	I (T1aN0M0)	Sirolimus	43	No recurrence
4	55	M	HBV/HCC	+	+	PTC	2.8 cm	TTx+RAI	I (T2N0M0)	Tacrolimus+ sirolimus	24	No recurrence

* The 0.1 cm papillary microcarcinoma was discovered inside the 3.2-cm nodule goiter. AJCC – American join committee on cancer, PTC – papillary thyroid cancer, RAI – radioactive iodine, TTx – total thyroidectomy.

in 2 cases where the tumor size exceeded 1 cm after recovery from LT surgery. To date, the 4 PTC cases have maintained cancer-free status and normal liver function. Therefore, for patients with liver cirrhosis and HCC with suspected thyroid cancer discovered incidentally before LT, we preferred to first perform thyroidectomy to confirm the diagnosis and stratify the risk of recurrence. If classified as low-risk PTC, patients directly proceeded LT surgery and bypass the observation interval, followed by radio ablation if the tumor size surpasses 1 cm. The concern was raised about overtreatment of radical total thyroidectomy for papillary microcarcinoma or occult thyroid cancer, as thyroid cancer may present as subclinical malignancy with no or slow progress. However, due to the carcinogenic effect of immunosuppression, we believed curative surgical resection and/or radio ablation is adequate to minimize the risk of recurrent or metastatic thyroid cancer in these LT recipients. Finally, evidence from recent studies have demonstrated the risk of donor-transmitted cancer in transplanted recipients, with reported rate of 0.03% to 0.06% [30,31]. Although transmission is rare, the prognosis is poor, which it also highlights the importance of cancer surveillance in LT recipients.

Diffuse FDG uptake on PET may be an indicator of thyroiditis. Yasuda et al [32] reported 36 cases (3.2%) of incidental diffuse thyroidal FDG uptake in 1102 healthy subjects, and only 1 patient (2.8%) was diagnosed with hypothyroidism. In our study, however, 7 cases (1.4%) of diffuse FDG uptake were found in 498 liver cirrhotic patients and 4 patients (57%) were also diagnosed with hypothyroidism. The discrepancy in prevalence rates may result from differences in the subjects studied; we focused on the cirrhotic patients rather than the general population. Five cases (71%) in our series tested positive for the presence of antithyroid antibodies, consistent with a diagnosis of autoimmune thyroiditis. Because LT is a complicated surgery, the clinical importance of hypothyroidism plays a crucial role during the postoperative recovery period [33]. Liver cirrhotic patients may appear chronically ill with poor daily functioning, which can be easily confused with symptoms of hypothyroidism. Therefore, early recognition of these weak LT candidates related to cirrhosis and hypothyroidism with thyroxine replacement therapy was important to prevent postoperative delirium, electrolyte imbalance, and prolonged hospital stay [20,33]. Furthermore, several studies had demonstrated that preoperative hypothyroidism is associated with worse outcome in LT recipients with HCC [20,34]. As symptoms and signs of hypothyroidism were not subjectively evident in every LT candidate, routine thyroid function examination before LT may be warranted.

A large retrospective study by Wong et al concluded that autoimmune hepatitis was strongly associated with concurrent extrahepatic autoimmunity (42%), and autoimmune thyroiditis was the most common presentation (18%) [35]. Our results from PET scan, however, found 1 (16.7%) case of autoimmune thyroiditis among 6 patients diagnosed with autoimmune hepatitis. Our findings are consistent with the previous report, and they also explain the higher prevalence of autoimmune hepatitis in patients with PET-discovered thyroid incidentaloma than in patients without thyroid incidentaloma (6.7% vs 1.0%; P=0.049), which was attributed to thyroiditis-related diffuse FDG uptake in the thyroid.

Study limitations

This study has several limitations. First, this retrospective study was conducted at a single medical center, and postoperative prognosis may vary among different hospitals by virtue of differences in management. Second, when the material obtained by FNA was insufficient, we did not repeat the procedure and the final diagnosis of one-fourth thyroid incidentaloma cases were inconclusive. Therefore, the real prevalence of malignancy in incidental FDG uptake thyroid nodules remained undetermined. Third, thyroid echo and thyroid function was not assessed in each patient, which may underestimate the true incidence of thyroid incidentaloma and thyroid dysfunction. Fourth, the observation duration for postoperative

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thyroid cancer was insufficient (median: 50 months; range: 24-64 months) to determine long-term prognosis. To overcome these limitations, larger prospective, randomized controlled trials are needed.

Conclusions

Incidental thyroid mass visualized on CT or ^{18}F-FDG PET in LT candidates was not uncommon, with a prevalence rate ranging from 2% to 3% in our study. Although diffuse FDG uptake on PET indicates benign thyroiditis, the cancer risk climbs up to 13.0% on CT and 37.5% on PET with focal FDG uptake. Due to low risk of thyroid cancer in the majority of our patients, total thyroidectomy followed by LT without delay can achieve tumor-free status with fair liver function.

Declaration of Figures' Authenticity

All figures submitted have been created by the authors, who confirm that the images are original with no duplication and have not been previously published in whole or in part.

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