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ORIGINAL ARTICLE

Differential Findings of Tc-99m Sestamibi Dual-Phase Parathyroid Scintigraphy Between Benign and Malignant Parathyroid Lesions in Patients with Primary Hyperparathyroidism

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Abstract
Purpose This study aimed to investigate the differential findings in clinical and biochemical features, and Tc-99m sestamibi (MIBI) dual-phase parathyroid scintigraphy for malignant and benign parathyroid lesions in patients with primary hyperparathyroidism.
Methods Subjects were 102 parathyroid lesions from 91 patients with primary hyperparathyroidism. Scintigraphic findings included radioactivity grade, uptake pattern, uptake contour, lesion size on early and delayed images, and degree of washout. Clinical and biochemical features were also evaluated. Histopathology confirmed the final diagnosis for all the patients.
Results Final diagnoses were 94 benign parathyroid lesions and 8 parathyroid carcinomas. The patients with parathyroid carcinoma were significantly older ($p=0.002$) and had significantly higher serum parathyroid hormone concentrations than those with benign parathyroid lesions ($p<0.001$). All malignant parathyroid lesions showed intense radioactivity similar to or greater than the submandibular gland activity on delayed images ($p=0.007$), and little radioactivity difference between early and delayed images ($p=0.012$). The cancer incidence for parathyroid lesions with both intense radioactivity and no washout was 17.0% (8/47). When parathyroid lesions with all of the abovementioned findings were regarded as malignant, the cancer incidence significantly increased from 17.0% to 33.3% (8/24, $p<0.001$).
Conclusion For Tc-99m MIBI dual-phase parathyroid scintigraphy, uptake grade on delayed images and washout were significantly useful diagnostic criteria for differentiating benign from malignant parathyroid lesions, along with age and parathyroid hormone serum concentration.

Keywords Primary hyperparathyroidism · Parathyroid carcinoma · Parathyroid adenoma · Parathyroid hyperplasia · Tc-99m Sestamibi · Parathyroid scintigraphy

Introduction

Parathyroid carcinoma is an uncommon malignancy that is the cause of primary hyperparathyroidism in less than 1% of cases [1–3]. A definitive treatment for parathyroid carcinoma is surgery only. En bloc resection of the tumor, including ipsilateral thyroid lobectomy, isthmectomy, tracheal skeletonization, and excision of any adherent muscle, is the initial therapy of choice [4, 5]. Open biopsy (including fine-needle aspiration cytology) in a suspected case of parathyroid carcinoma is not recommended because of the significant risk of capsule rupture with subsequent tumor spillage [6, 7].

Establishing a diagnosis of parathyroid carcinoma pre- or intraoperatively is difficult because of the lack of

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definitive diagnostic markers and overlap in clinical features with benign parathyroid disease. This results in frequent incomplete excision and a very high rate of recurrence. Therefore, the distinction between parathyroid carcinoma and benign parathyroid disease is important in patient management. A proper recognition of carcinoma at the time of initial treatment is the key to performing an adequate surgical procedure for a favorable outcome.

Generally accepted preoperative imaging modalities to localize parathyroid lesions include ultrasound, computed tomography (CT), magnetic resonance imaging (MRI) and Tc-99m sestamibi (MIBI) parathyroid scintigraphy. Tc-99m MIBI parathyroid scintigraphy is a useful and non-invasive method for localizing parathyroid tumors [8, 9]. The mean sensitivity of preoperative Tc-99m MIBI for the detection of solitary adenoma is 88.9% (87.4% to 89.4%). The mean sensitivity is 44.7% (41.1% to 47.8%) for detecting multiple gland disease and 30% (2.2% to 62.1%) for double adenomas [10]. However, diagnostic values for using this imaging modality to differentiate between parathyroid carcinoma and benign parathyroid disease have not been reported. Also, whether parathyroid scintigraphy can differentiate benign from malignant parathyroid lesions in patients with primary hyperparathyroidism is unknown.

The aim of this retrospective study was to investigate differential findings in clinical and biochemical features, and Tc-99m MIBI dual-phase parathyroid scintigraphy between malignant and benign parathyroid lesions in patients with primary hyperparathyroidism.

Materials and Methods

Subjects

We retrospectively analyzed the medical records of 100 consecutive patients with clinically and biochemically diagnosed primary hyperparathyroidism who underwent preoperative Tc-99m MIBI dual-phase parathyroid scintigraphy and subsequent operation at our institution from November 1998 to November 2008. Of 100 cases, Tc-99m MIBI scintigraphy could not be reviewed in 7 because of data error. These were removed from further data analysis. Pathological diagnoses for two patients confirmed normal parathyroid tissue. Therefore, 91 patients (63 women, 29 men; mean age±SD, 53.0± 14.0 years; age range, 14.0–88.0 years) with a total of 102 lesions were enrolled in this study. The average time interval between Tc-99m MIBI scintigraphy and surgery was 2.0±3.0 months. In all patients, a final diagnosis was confirmed by histopathology via surgical excision. Our institutional review board approved the protocol of this retrospective study.

Tc-99m MIBI Dual-Phase Parathyroid Scintigraphy

Tc-99m MIBI scintigraphy was performed using a dual-head gamma camera (Biad, Trionix Research Laboratory, Inc., Twinsburg, OH, for 75 patients and Infinia, GE Healthcare, Milwaukee, WI, for 16 patients). An anterior neck image using a pinhole collimator and anterior chest image using a parallel hole collimator were acquired 15 min and 3 h after the intravenous injection of 555 MBq Tc-99m MIBI.

Two nuclear medicine physicians retrospectively interpreted Tc-99m MIBI scans by consensus for intensity of radioactivity, uptake pattern, uptake contour, size of each lesion on early and delayed images, and degree of washout, as displayed on a workstation monitor with variable upper window threshold levels.

In most patients in our study, the submandibular gland showed higher radioactivity than the thyroid gland on both early and delayed images. Therefore, we evaluated the radioactive intensity of each lesion using a four-point visual grading system by adopting the submandibular gland and thyroid gland as reference organs on each early or delayed image, respectively (grade 0, similar to thyroid gland activity; grade 1, between the thyroid and submandibular gland; grade 2, similar to submandibular gland activity; grade 3, more than submandibular gland activity). For visual grading, various upper window levels were adopted using the activities of the thyroid gland, submandibular gland, and parathyroid lesion, if necessary (Fig. 1). Uptake pattern was classified into homogeneous or heterogeneous. Homogeneous uptake was defined as uniform uptake by the parathyroid tumor, and heterogeneous uptake was defined as spotted or mottled uptake in the parathyroid tumor. Uptake contour was classified into smooth or irregular margins (Fig. 2). Parathyroid lesion size was classified as smaller or larger than half of the corresponding thyroid lobe. For the evaluation of uptake pattern and contour, the activity of the submandibular gland was considered as an upper window level. The parathyroid lesions with grade 0 were determined to have heterogeneous uptake patterns and irregular margins. The degree of washout was defined by subtracting the radioactivity grade of a late image from the radioactivity grade of an early image (Fig. 3).

Statistical Analysis

The Mann-Whitney *U* test and Fisher's exact test were used to compare clinical, biochemical, and scintigraphic findings between benign and malignant parathyroid lesions. As biochemical markers, serum concentrations of total calcium, ionized calcium, and parathyroid hormone (PTH) were included. $P<0.05$ was considered statistically significant.

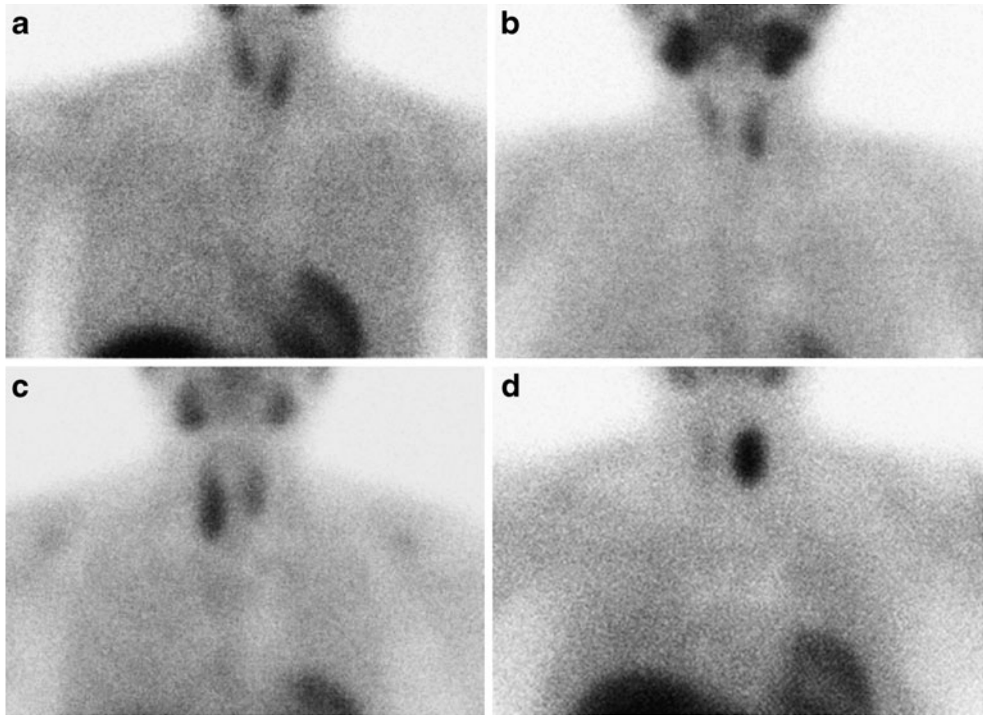

Fig. 1 Representative images of the 4-point visual grading system for parathyroid lesions (grade 0–3, **a**–**d**, respectively)

Results

Final histological results included 80 parathyroid adenomas (78.4%), 14 hyperplastic parathyroid glands (13.7%), and 8 parathyroid carcinomas (7.8%). Clinical, biochemical, and scintigraphic findings are compared between benign and malignant parathyroid lesions in Table 1. Histological confirmation was obtained via operation. Macroscopically, parathyroid carcinomas were not significantly larger than parathyroid adenomas or hyperplastic parathyroid glands (mean±SD, 1.9±0.8 cm for parathyroid carcinomas, 1.8±2.2 cm for parathyroid adenomas, 2.3±1.2 cm for hyperplastic parathyroid glands; $p=0.271$). Of the 91 patients, 6 (4 men, 2 women) had parathyroid carcinomas. All patients with parathyroid carcinoma were older than 40 years ($p=0.002$). Serum PTH concentrations for patients with parathyroid carcinomas were significantly higher than those with benign parathyroid lesions ($p<0.001$). However, no significant difference was observed in the serum concentrations of total calcium or ionized calcium in patients with parathyroid carcinomas or benign parathyroid lesions. All malignant parathyroid lesions showed intense radioactivity similar to or greater than submandibular gland activity on delayed images ($p=0.007$), and little difference in the radioactivity of early and delayed images ($p=0.012$) (Figs. 4 and 5). No significant differences were observed between benign parathyroid lesions and parathyroid carcinomas for the scintigraphic findings on size, grade of uptake, or uptake pattern and uptake contour on early or delayed images.

In this study, the cancer incidence for parathyroid lesions according to Tc-99m MIBI uptake was 7.8% (8/102) on a lesion-by-lesion basis or 6.6% (6/91) on a subject-by-subject basis. Significant differences were seen for age, Tc-

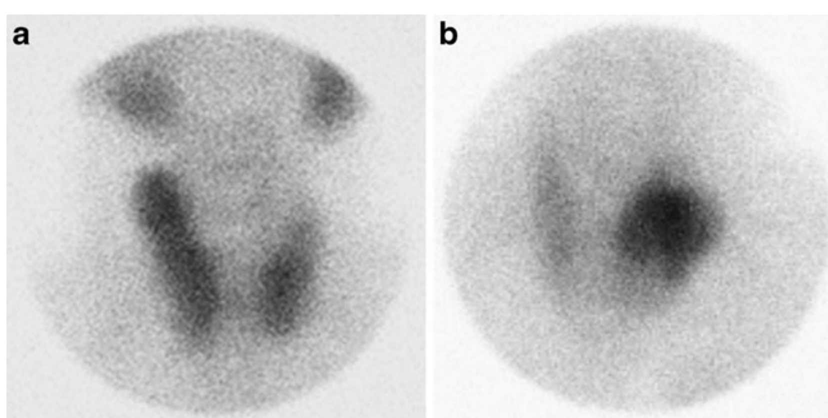

Fig. 2 Representative images showing the uptake pattern and contour of parathyroid lesions; homogeneous pattern and irregular contour (**a**), and heterogeneous pattern and smooth margin (**b**)

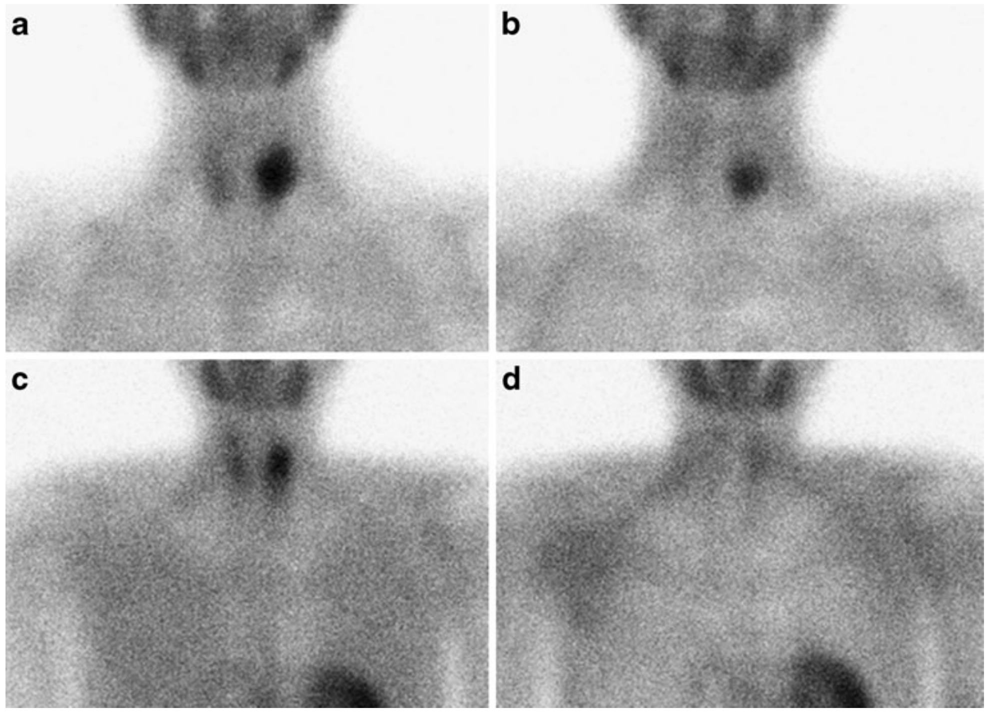

Fig. 3 Representative early and delayed images showing washout of parathyroid lesions; no washout (**a**, **b**) and positive washout (**c**, **d**)

99m MIBI uptake, and washout, and serum PTH level between benign and malignant parathyroid lesions. These were used as combined diagnostic criteria (Tables 1 and 2). Because it is clinically important to diagnose all malignant lesions without false negatives, we tried to find such diagnostic criteria. Defining high Tc-99m MIBI uptake on delayed images (grade 2, 3) as malignant gave a sensitivity of 100% (8/8), specificity of 58.5% (55/94), positive predictive value (PPV) of 12.7% (8/63), negative predictive value (NPV) of 100% (39/39), and accuracy of 46.1% (47/102) for using Tc-99m MIBI dual-phase parathyroid scintigraphy for diagnosing malignant parathyroid lesions. Defining no washout (uptake grade on early image minus uptake grade on late image=0) as malignant gave a sensitivity of 100% (8/8), specificity of 43.6% (41/94), PPV of 16.3% (8/49), NPV of 100% (53/53), and accuracy of 59.8% (61/102). Defining parathyroid lesions from subjects more than 40 years old as malignant gave a sensitivity of 100% (6/6), a specificity of 15.3% (13/85), a PPV of 7.7% (6/78), an NPV of 100% (13/13), and an accuracy of 20.9% (19/91). Defining high concentrations of serum PTH in 100 lesions (>154.1 pg/ml; the lowest value in malignant lesions) as malignant gave a sensitivity of 100% (8/8), a specificity of 47.8% (44/92), a PPV of 14.3% (8/56), an NPV of 100% (44/44), and an accuracy of 52.0% (52/100). When parathyroid lesions with both high delayed uptake and no washout were considered malignant, sensitivity, specificity, PPV, NPV, and accuracy were 100% (8/8), 58.5% (55/94), 17.0% (8/47), 100% (55/55), and 61.8% (63/102). When parathyroid lesions with all of the above criteria were considered malignant, sensitivity was 100% (8/8), specificity was 83.0% (78/94), PPV was 33.3% (8/24), NPV was 100% (78/78), and accuracy was 84.3% (86/102). This was a significant improvement in specificity, PPV, and accuracy over any single diagnostic criterion (Fig. 6). Using these combined criteria without false negatives significantly increased the cancer incidence from 7.8% (8/91) at baseline to 33.3% (8/24, $p<0.001$).

Table 1 Demographic features of the study patients

Characteristics	Adenoma/hyperplasia	Carcinoma	*P* value	Odds ratio (95% CI)
Sex				
Female	55	2	NS	3.667 (0.634–21.200)
Male	30	4		
Age at diagnosis (years)				
<40	13	0	0.002	NA
40–59	48	4		
>60	24	2		

NS not significant, *NA* not applicable

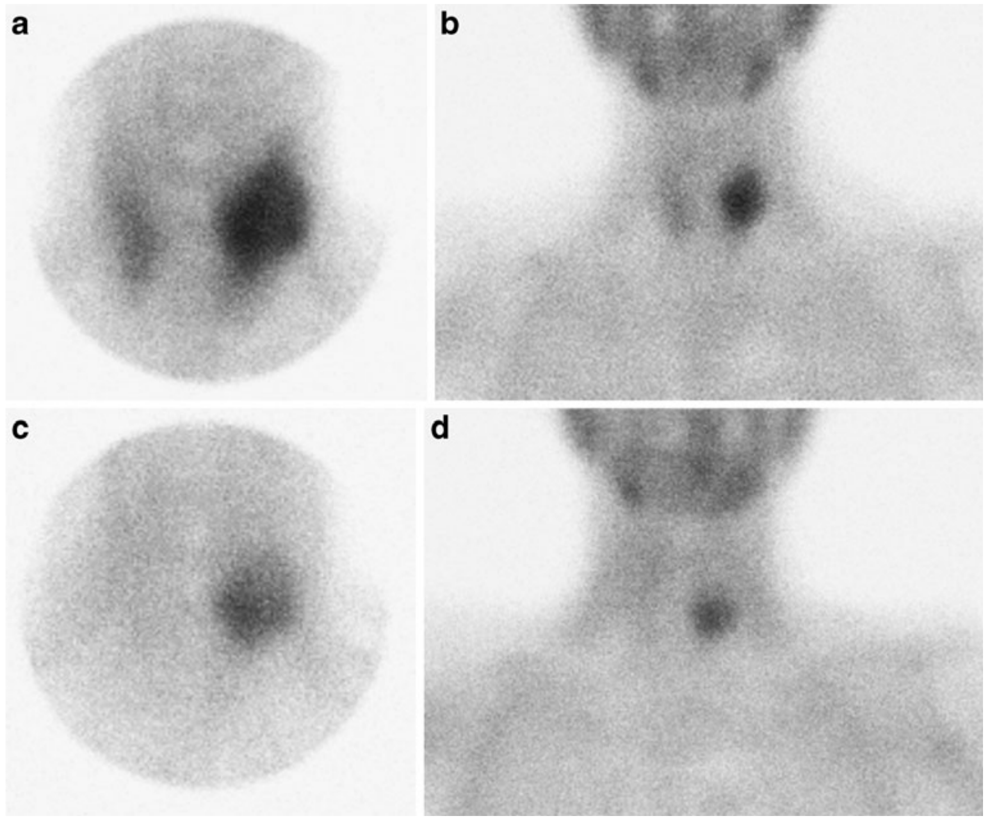

Fig. 4 Early (**a**, **b**) and delayed (**c**, **d**) images of neck and thorax Tc-99m MIBI parathyroid scan in a patient with parathyroid carcinoma. The images show a persistent intense tracer focus with nodular shape in the left thyroid bed

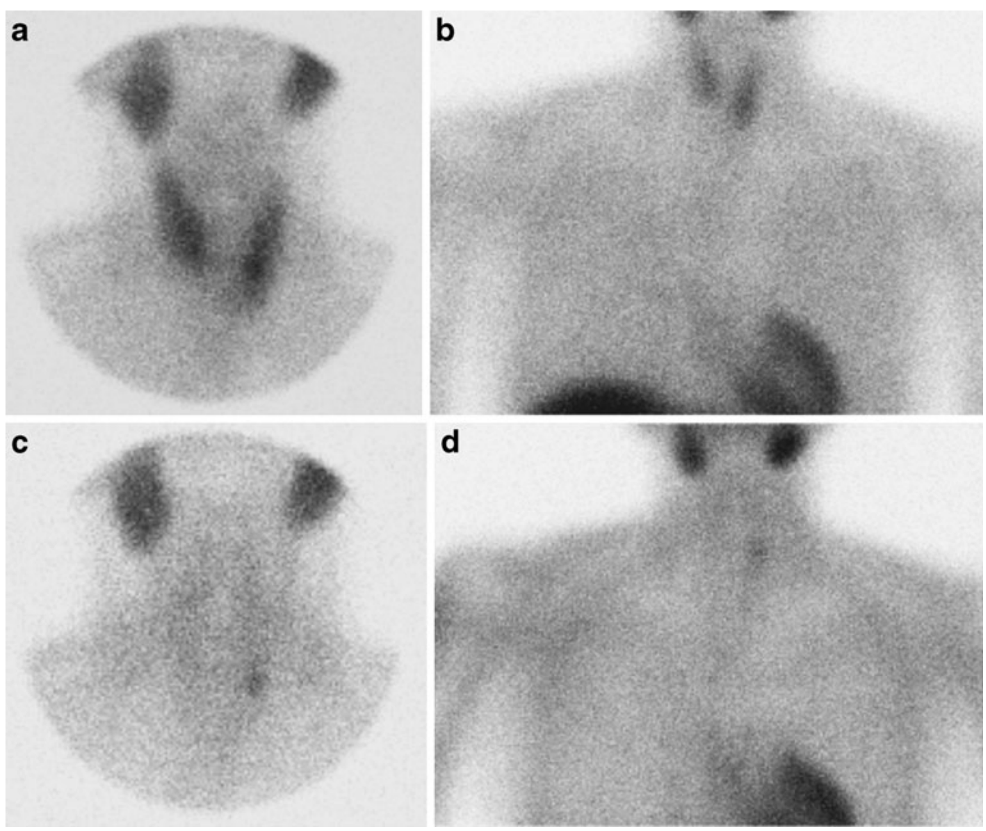

Fig. 5 Early (**a**, **b**) and delayed (**c**, **d**) images of neck and thorax images show a mild radio uptake in the left thyroid bed in a patient with parathyroid adenoma. The delayed images of neck and thorax show a faint tracer focus in the left thyroid bed

Table 2 Biochemical and scintigraphic findings between benign and malignant parathyroid lesions

Characteristics	Adenoma/hyperplasia	Carcinoma	*P* value	Odds ratio (95% CI)
Pathological size (cm)	1.9±1.1 (n=92)	1.9±0.8 (n=8)	NS	NA
Serum calcium (mg/dl)	10.9±1.0 (n=88)	11.2±1.7 (n=8)	NS	NA
Serum ionized calcium (mg/dl)	1.5±0.2 (n=75)	1.4±0.2 (n=8)	NS	NA
Serum parathyroid hormone (pg/ml)	284.2±412.8 (n=87)	1,187.0±746.4 (n=8)	<0.001	NA
Tc-99m MIBI scintigraphy				
Early image				
Radioactivity				
Grade 0	0	0	NS	NA
Grade 1	4	0		
Grade 2	60	3		
Grade 3	30	5		
Uptake pattern				
Homogeneous	89	7	NS	2.543 (0.260–24.879)
Heterogeneous	5	1		
Uptake contour				
Smooth	53	7	NS	5.415 (0.641–45.776)
Irregular	41	1		
Late image				
Radioactivity				
Grade 0	11	0	0.007	NA
Grade 1	28	0		
Grade 2	43	3		
Grade 3	12	5		
Uptake pattern				
Homogeneous	86	7	NS	1.536 (0.167–14.097)
Heterogeneous	8	1		
Uptake contour				
Smooth	71	7	NS	2.268 (0.265–19.417)
Irregular	23	1		
Grade of washout[a]				
≥1	53	0	0.012	1.195 (1.056–1.352)
0	41	8		
Size				
<1/2 of thyroid lobe	64	3	NS	3.556 (0.797–15.865)
≥1/2 of thyroid lobe	30	5		

NS not significant, *NA* not applicable

[a] Grade of washout was defined by subtracting the radioactivity grade on a late image from the radioactivity grade on an early image

Plus-minus values (±) are standard errors of the mean

Discussion

Although parathyroid carcinoma is a rare malignant neoplasm and an uncommon cause of hyperparathyroidism, differentiating malignant from benign parathyroid lesions is important because inadequate excision leads to very high recurrence rates [5]. Our results show that combined clinical and scintigraphic diagnostic criteria are helpful for screening potentially malignant parathyroid lesions while avoiding false negatives. The sensitivity and NPV of the combined criteria were 100% with a good accuracy of 84%, which may support a change in diagnostic and therapeutic decision making. For example, if the combined diagnostic criteria are negative for malignancy, we may avoid any unnecessary open biopsy and change the operative method from the conventional cancer surgery of an en bloc excision including the thyroid gland to the recent practice of minimally invasive parathyroidectomy with low morbidity and mortality.

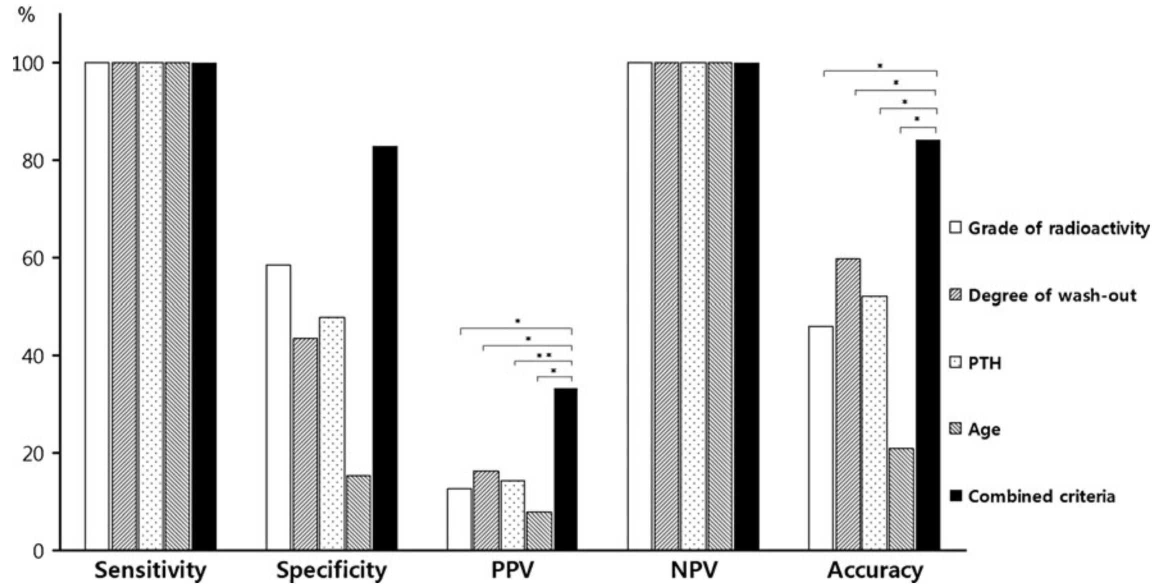

Fig. 6 Graph shows the comparisons of diagnostic efficacy between diagnostic criteria. Suggested combined criteria demonstrate the best PPV and accuracy for differentiating benign from malignant parathyroid lesions (*$p<0.001$; **$p<0.05$)

Before any surgical attempts, differentiating between malignant and benign parathyroid lesions is difficult because parathyroid carcinoma has no specific differentiating characteristics.

Only a few reports describe the detection of parathyroid carcinoma by Tc-99m MIBI parathyroid scintigraphy [11–16]. No reports include diagnostic values for this imaging modality for differentiating between parathyroid carcinoma and benign parathyroid disease. Our analysis found intense radioactivity similar to or greater than submandibular gland activity on delayed images, and little difference in the radioactivity of early and delayed images occurred more frequently in parathyroid carcinomas than in benign parathyroid lesions. Although parathyroid lesions with intense radioactivity on delayed images and no washout had a high likelihood of malignancy, not all that lesions with these characteristics were malignant. The PPV of scintigraphy was only 17.0% (8/47). Therefore, new combined criteria that include other clinical variables are necessary to improve the diagnostic value for differentiating between parathyroid carcinoma and benign parathyroid disease.

Our results show a higher frequency of parathyroid carcinoma in patients with primary hyperparathyroidism (7.8%) than the reported frequency of parathyroid carcinoma [2]. The high incidence may be due to the selective referral of patients with more serious conditions to our center. Parathyroid carcinoma usually presents most often in the 5th and 6th decades of life, approximately 10 years earlier than for patients with parathyroid adenomas, and has equal gender distribution [5, 17]. Our study found no parathyroid carcinomas in patients younger than 40 years, a factor that was included in the combined diagnostic criteria. However, we had a male-to-female ratio of 2:1 in our study, which may be because of the small number of patients.

PTH levels are frequently two to ten times the normal values in patients with parathyroid carcinoma, whereas PTH levels are commonly twice the normal value in patients with primary hyperparathyroidism [18–20]. In accordance with previous studies, we found that the serum PTH concentrations for patients with parathyroid carcinomas were significantly higher than for patients with benign parathyroid lesions. This was included in the combined criteria. The degree of hypercalcemia is often more pronounced in parathyroid carcinoma. Very high calcium levels, usually 3–4 mg/dl above the normal limit, are common. However, we found no significant difference in patients with parathyroid carcinomas or benign parathyroid lesions.

Our results suggest that the scintigraphic findings of grade of radioactivity on delayed images, degree of washout, patient age, and serum PTH concentration are diagnostically useful. Thus, the possibility of parathyroid carcinoma should be considered when a lesion has an intense radioactivity similar to or greater than the submandibular gland on delayed image, no washout between the radioactivity of an early and a delayed image, and a high PTH serum concentration in subjects older than 40 years. Using these combined diagnostic criteria gave no false-negative results for malignancy, and we obtained good diagnostic efficacy, including a high sensitivity with a 100% NPV, 83.0% specificity, and 84.3% accuracy.

Varying degrees of MIBI uptake in parathyroid carcinoma are reported [11–16]. Many previous studies suggest that Tc-99m MIBI uptake by parathyroid lesions is related to the volume or size of the lesion, serum calcium levels, oxyphil cell content, cellular mitochondria content, tumor blood flow or capillary permeability, expression of P-glycoprotein or multidrug resistance (MDR) related protein, or phosphorus level [21–23]. Although the Tc-99m MIBI uptake mechanism by tumor cells is not understood completely, hypothesized mechanisms involve mitochondria and a combination of blood flow and cell metabolic status [24]. No study has examined the uptake mechanism of Tc-99m MIBI in parathyroid carcinoma. Related studies suggest that intense uptake and delayed retention may be caused by high mitochondrial content, increased perfusion, or increased metabolic activity [25–27].

Our study is limited by the small number of patients with parathyroid carcinoma and retrospective design. Not all subjects who had primary hyperparathyroidism underwent Tc-99m MIBI scintigraphy. However, relatively speaking it was not small in number since parathyroid carcinoma is extremely rare. This is the first study on the diagnostic value of Tc-99m MIBI dual-phase parathyroid scintigraphy for differentiating benign from malignant parathyroid lesions. Further prospective studies in a larger number of patients to investigate the value of our suggested diagnostic criteria for parathyroid lesions are warranted.

In conclusion, the grades of Tc-99m MIBI uptake on delayed images and washout were significantly useful diagnostic criteria for using Tc-99m MIBI dual-phase parathyroid scintigraphy to differentiate benign from malignant parathyroid lesions. Additional useful criteria were age and serum PTH concentration. These combined criteria may be useful for screening parathyroid lesions with a high risk of malignancy. This may affect management and therapeutic planning for patients with primary hyperparathyroidism.

Conflict of interest statement All authors declare that they have no conflict of interest.

References

1. Cohn K, Silverman M, Corrado J, Sedgewick C. Parathyroid carcinoma: the Lahey Clinic experience. Surg. 1985;98:1095–100.
2. Hakaim AG, Esselstyn Jr CB. Parathyroid carcinoma: 50-year experience at The Cleveland Clinic Foundation. Cleve Clin J Med. 1993;60:331–5.
3. Wang CA, Gaz RD. Natural history of parathyroid carcinoma. Diagnosis, treatment, and results. Am J Surg. 1985;149:522–7.
4. Holmes EC, Morton DL, Ketcham AS. Parathyroid carcinoma: a collective review. Ann Surg. 1969;169:631–40.
5. Koea JB, Shaw JH. Parathyroid cancer: biology and management. Surg Oncol. 1999;8:155–65.
6. Agarwal G, Dhingra S, Mishra SK, Krishnani N. Implantation of parathyroid carcinoma along fine needle aspiration track. Langenbecks Arch Surg. 2006;391:623–6.
7. Spinelli C, Bonadio AG, Berti P, Materazzi G, Miccoli P. Cutaneous spreading of parathyroid carcinoma after fine needle aspiration cytology. J Endocrinol Invest. 2000;23:255–7.
8. Shin JW, Ryu JS, Kim JS, Moon DH, Hong SM, Gong G, et al. Lesion localization in patients with hyperparathyroidism using double-phase Tc-99m MIBI parathyroid scintigraphy. Korean J Nucl Med. 1999;33:120–30.
9. Jeon TJ, Lee JD, Rhyu YH, Park JS, Jang HS. Comparison study of lesion localization in patients with primary and secondary hyperparathyroidism using double-phase Tc-99m sestamibi scintigraphy. Korean J Nucl Med. 1999;33:368–80.
10. Ruda JM, Hollenbeak CS, Stack Jr BC. A systematic review of the diagnosis and treatment of primary hyperparathyroidism from 1995 to 2003. Otolaryngol Head Neck Surg. 2005;132:359–72.
11. Lu G, Shih WJ, Xiu JY. Technetium-99 m MIBI uptake in recurrent parathyroid carcinoma and brown tumors. J Nucl Med. 1995;36:811–3.
12. Singhal T, Jacobs M, Mantil JC. Tc-99 m pertechnetate/sestamibi subtraction scan in a case of parathyroid carcinoma. Clin Nucl Med. 2008;33:196–7.
13. Clark P, Wooldridge T, Kleinpeter K, Perrier N, Lovato J, Morton K. Providing optimal preoperative localization for recurrent parathyroid carcinoma: a combined parathyroid scintigraphy and computed tomography approach. Clin Nucl Med. 2004;29:681–4.
14. Favia G, Lumachi F, Polistina F, D'Amico DF. Parathyroid carcinoma: sixteen new cases and suggestions for correct management. World J Surg. 1998;22:1225–30.
15. Kebebew E, Arici C, Duh QY, Clark OH. Localization and reoperation results for persistent and recurrent parathyroid carcinoma. Arch Surg. 2001;136:878–85.
16. Nakamura Y, Kataoka H, Sakoda T, Horie Y, Kitano H. Nonfunctional parathyroid carcinoma. Int J Clin Oncol. 2010;15:500–3.
17. Hundahl SA, Fleming ID, Fremgen AM, Menck HR. Two hundred eighty-six cases of parathyroid carcinoma treated in the US between 1985–1995: a National Cancer Data Base Report. The American College of Surgeons Commission on Cancer and the American Cancer Society. Cancer. 1999;86:538–44.
18. Cordeiro AC, Montenegro FL, Kulcsar MA, Dellanegra LA, Tavares MR, Michaluart Jr P, et al. Parathyroid carcinoma. Am J Surg. 1998;175:52–5.
19. Wynne AG, van Heerden J, Carney JA, Fitzpatrick LA. Parathyroid carcinoma: clinical and pathologic features in 43 patients. Med (Baltim). 1992;71:197–205.
20. Chen Q, Kaji H, Nomura R, Sowa H, Yamauchi M, Tsukamoto T, et al. Trial to predict malignancy of affected parathyroid glands in primary hyperparathyroidism. Endocr J. 2003;50:527–34.
21. Carpentier A, Jeannotte S, Verreault J, Lefebvre B, Bisson G, Mongeau CJ, et al. Preoperative localization of parathyroid lesions in hyperparathyroidism: relationship between technetium-99m-MIBI uptake and oxyphil cell content. J Nucl Med. 1998;39:1441–4.
22. Sun SS, Shiau YC, Lin CC, Kao A, Lee CC. Correlation between P-glycoprotein (P-gp) expression in parathyroid and Tc-99m MIBI parathyroid image findings. Nucl Med Biol. 2001;28:929–33.
23. Pons F, Torregrosa JV, Fuster D. Biological factors influencing parathyroid localization. Nucl Med Commun. 2003;24:121–4.

24. Arbab AS, Koizumi K, Toyama K, Araki T. Uptake of technetium-99m-tetrofosmin, technetium-99m-MIBI and thallium-201 in tumor cell lines. J Nucl Med. 1996;37:1551–6.
25. Hassan IM, Sahweil A, Constantinides C, Mahmoud A, Nair M, Oamr YT, et al. Uptake and kinetics of Tc-99m hexakis 2-methoxy isobutyl isonitrile in benign and malignant lesions in the lungs. Clin Nucl Med. 1989;14:333–40.
26. Petrovic NS, Grujicic D, Artiko VM, Sobic-Saranovic DP, Gajic MM, Jaksic E, et al. Investigation of blood perfusion and metabolic activity of brain tumours in adults by using 99m Tc-methoxyisobutylionitile. Nucl Med Commun. 2010;31:962–73.
27. Ak I, Gulbas Z, Altinel F, Vardareli E. Tc-99m MIBI uptake and its relation to the proliferative potential of brain tumors. Clin Nucl Med. 2003;28:29–33.