Feature Illustration: Vascularity

13

William D. Middleton

13.1 Nodular Lesions

There are certain situations where color Doppler clearly assists in the evaluation of thyroid nodules. The use of color Doppler may aid in distinguishing a predominantly cystic nodule from a vascular structure within or adjacent to the thyroid gland. In the setting of an isoechoic, solid nodule, the detection of peripheral vascularity can be helpful in confirming that a nodule is really present (Fig. 13.1). It can also help in defining the extent of the nodule and thus in accurately measuring the nodule. Color Doppler can also be useful in the assessment of complex cystic nodules that have internal regions of increased echogenicity. It is useful both for diagnosis and for targeting a biopsy to determine if the echogenic portion of a mixed cystic and solid nodule merely represents internal debris or hemorrhage or represents a true solid component. If the solid-appearing component has no detectable blood flow, it is often clotted blood, which can usually be confirmed by noting mobility while scanning the patient in an upright or decubitus position (Figs. 13.2 and 13.3). To improve the diagnostic yield, FNA of avascular components should be avoided in lieu of solid components with detectable vascularity.

The value of color Doppler in distinguishing benign and malignant nodules is much less certain. Many investigators have analyzed the degree and pattern of vascularity in thyroid nodules. Most have shown that intranodular vascularity is statistically more likely to be detected in malignant nodules (Fig. 13.4) than in benign nodules (Fig. 13.5). Unfortunately, they have also shown that malignant nodules have a range of vascular patterns as well as a range of degrees of vascularity (Fig. 13.6). In addition, benign nodules have been shown to have a broad range of vascular patterns and degrees, including hypervascular internal flow (Fig. 13.7). The amount of overlap in the vascularity of benign and malignant nodules substantially limits the value of vascularity in the differentiation of these nodules.

Table 13.1 summarizes the results of a number of studies that had histologic proof and specifically determined the statistics of nodule vascularity independent of gray-scale findings [1–12]. Most have divided flow patterns into peripheral and intranodular. The definition of flow that increases the risk of malignancy varies but included (1) any detectable peripheral or intranodular flow, (2) any detectable intranodular flow, (3) isolated or predominant intranodular flow, and (4) marked intranodular flow. Using these different criteria, the sensitivity, specificity, positive

W.D. Middleton, M.D. (✉)
Mallinckrodt Institute of Radiology, Washington University School of Medicine,
510 South Kingshighway Blvd., Saint Louis, MO 63110, USA
e-mail: middletonb@wustl.edu

M. Milas et al. (eds.), *Advanced Thyroid and Parathyroid Ultrasound*,
DOI 10.1007/978-3-319-44100-9_13

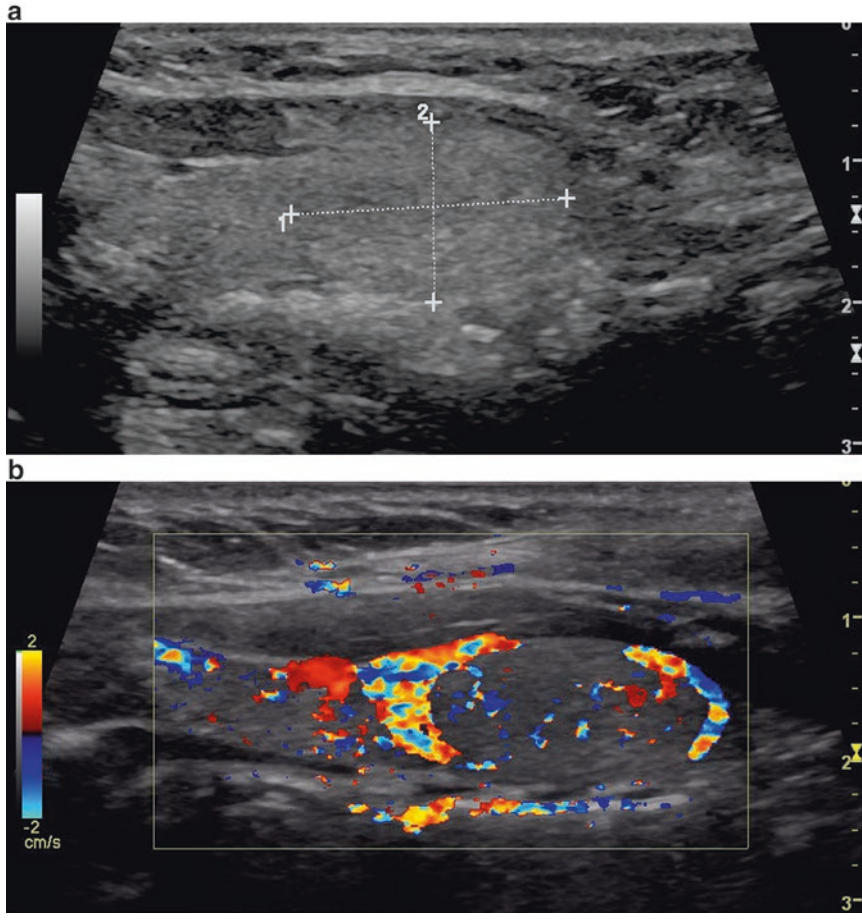

Fig. 13.1 Value of color Doppler with isoechoic nodules. (**a**) Longitudinal gray-scale view shows a solid isoechoic nodule that is very difficult to visualize and measure. (**b**) Longitudinal color Doppler view shows perinodular blood flow that defines the margin of the nodule

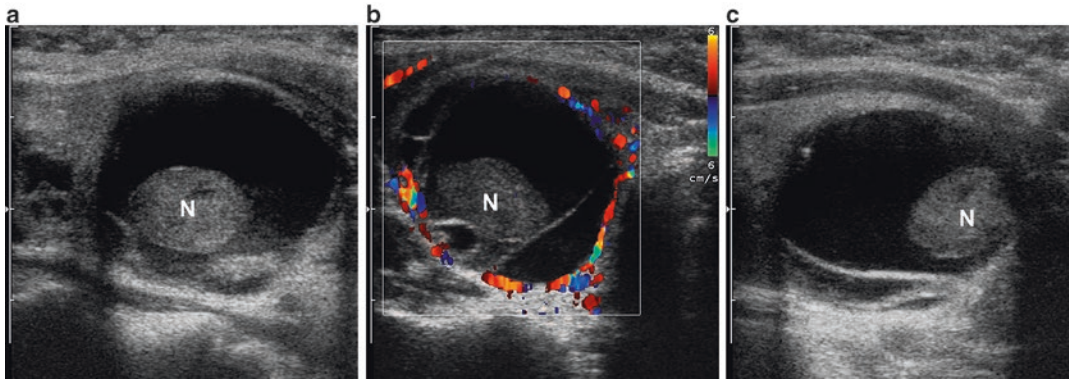

Fig. 13.2 Value of color Doppler with cystic nodules containing eccentric solid components. (**a**) Longitudinal gray-scale view shows a predominantly cystic nodule that has what appears to be a solid mural nodule (N). Because of this solid component, this patient had been scheduled for FNA. (**b**) Transverse color Doppler view shows lack of blood flow in the apparent solid mural nodule. This suggests the solid lesion may be a luminal blood clot and not a mural nodule. (**c**) Longitudinal view with the patient in the upright position shows that the avascular solid component has moved to the inferior portion of the cyst, confirming that it is mobile and not a mural nodule. In this case, FNA was canceled

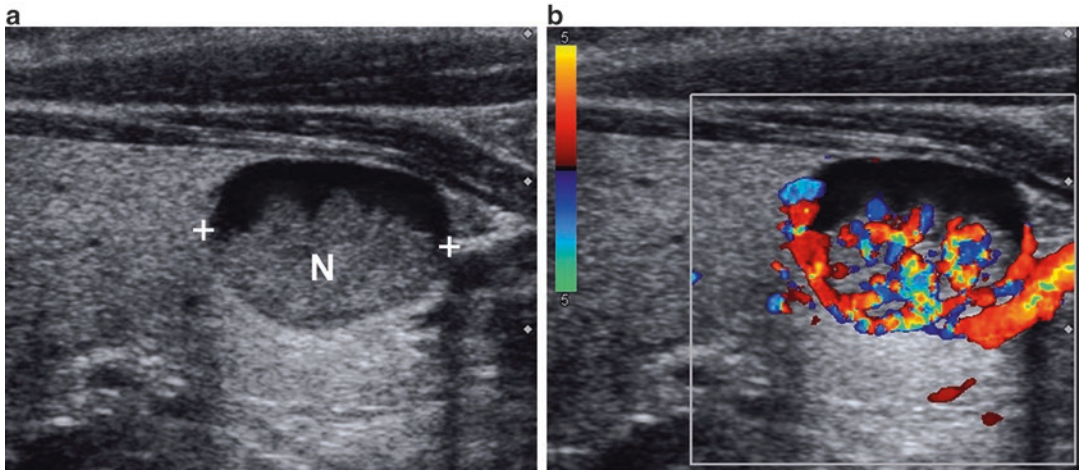

Fig. 13.3 Value of color Doppler with cystic nodules containing eccentric solid components. (**a**) Longitudinal gray-scale view shows a nodule (*cursors*) with a cystic component in the nondependent portion and a solid component (N) in the dependent portion. The differential diagnosis based on this image is a cyst with dependent debris or clot versus a cyst with a solid eccentric mural nodule. (**b**) Corresponding color Doppler view shows intense hypervascularity in the solid component, confirming it is a mural nodule. Cytology was interpreted as a follicular lesion of undetermined significance

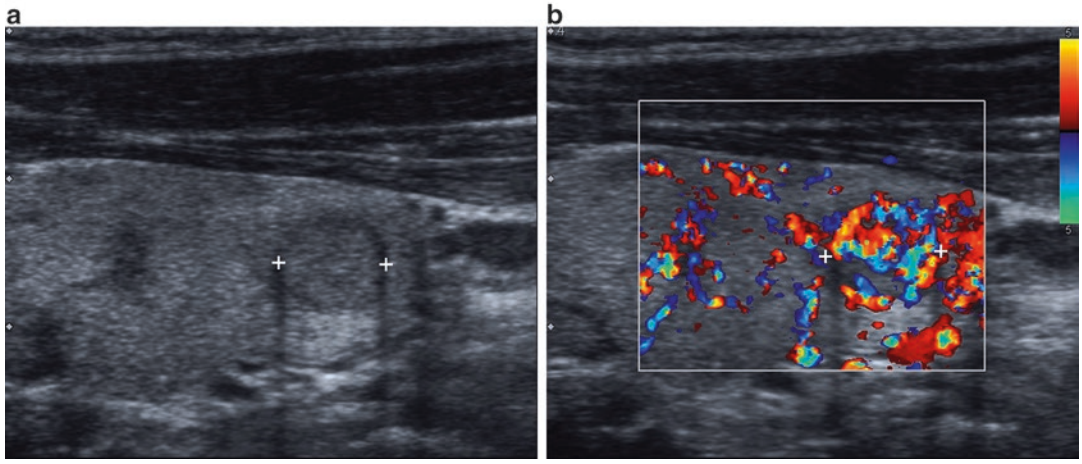

Fig. 13.4 Papillary thyroid cancer with hypervascular intranodular blood flow. (**a**) Longitudinal gray-scale view shows an intermediate suspicion, entirely solid, slightly hypoechoic smoothly marginated nodule (*cursors*) with refractive shadowing and no calcifications. (**b**) Corresponding color Doppler view shows marked intranodular blood flow

predictive value, and negative predictive values ranged from 15 to 75%, 34 to 96%, 6 to 61%, and 28 to 97%, respectively. In addition to the statistics mentioned above, one can use an odds ratio to compare the risk of malignancy of a positive result (for instance, intranodular flow) to the risk of malignancy of a negative result (for instance, no intranodular flow). A ratio of 5 would indicate that a nodule with intranodular flow was five times more likely to be malignant than a nodule without intranodular flow. As Table 13.1 shows, the odds ratios ranged from 0.2 to 9.4. In most cases the odds ratio was less than 2. In a study that included 31 malignant nodules, Papini

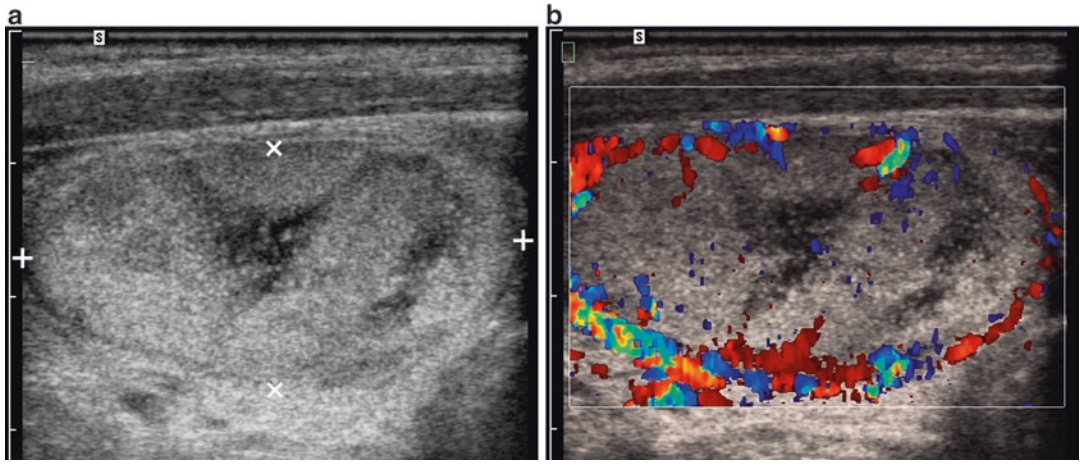

Fig. 13.5 Benign nodular hyperplasia with predominantly peripheral flow. (**a**) Longitudinal gray-scale view shows a low suspicion, almost entirely solid, isoechoic, smoothly marginated nodule (*cursors*) with no calcifications. (**b**) Corresponding color Doppler view shows abundant peripheral flow and almost no central flow

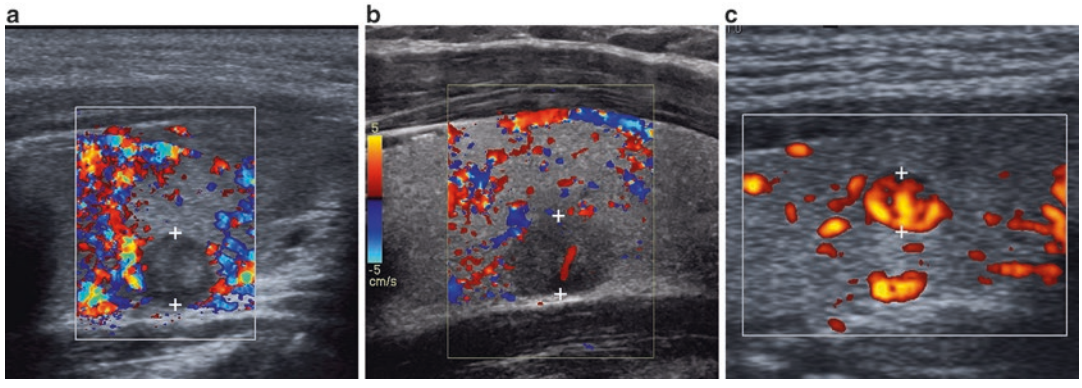

Fig. 13.6 Spectrum of vascularity in malignant thyroid nodules. (**a**) Papillary thyroid cancer (*cursors*) with no detectable blood flow. (**b**) Papillary thyroid cancer (*cursors*) with minimal internal blood flow. (**c**) Medullary thyroid cancer (*cursors*) with hypervascular internal blood flow

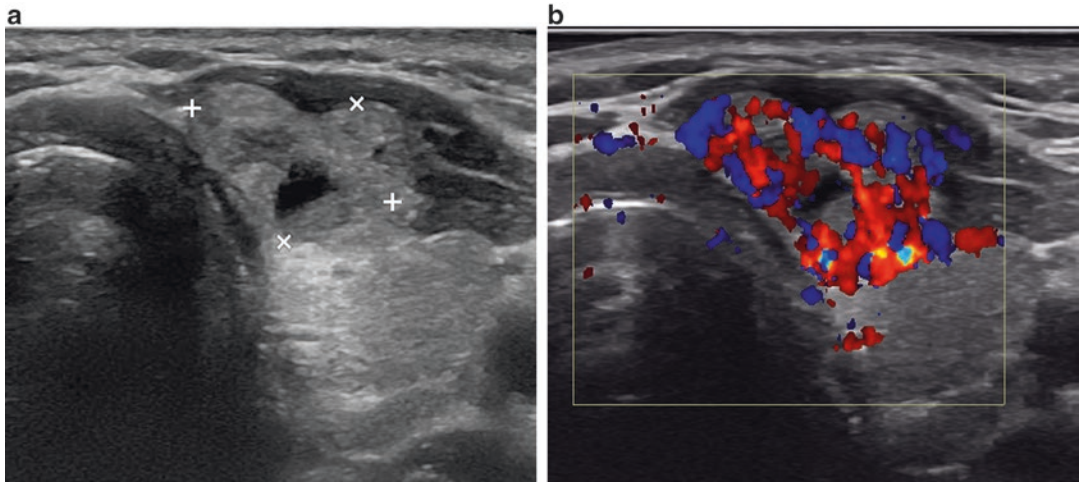

Fig. 13.7 Benign nodular hyperplasia with hypervascular internal blood flow. (**a**) Transverse gray-scale view shows an intermediate suspicion, lobulated, predominantly solid, slightly hypoechoic smoothly marginated nodule (*cursors*) with no calcifications. (**b**) Corresponding color Doppler view shows hypervascular internal blood flow

Table 13.1 Relationship to the pattern of nodular blood flow and risk of malignancy

Study	Criteria used	# of nodules	% malignancy	Sens (%)	Spec (%)	PPV (%)	NPV (%)	Odds ratio	Conclusion
Sharma 2011 [8]	Detectable flow anywhere	67	23 (16/67)	75	60.80	37.50	88.60	3.3	Not helpful
Rosario 2015 [12]	Intranodular flow	1502	10.6 (160/1502)	70	36	11.50	91.00	1.28	Not helpful
	Isolated or predominant intranodular flow	1502	10.6 (160/1502)	15	96	31.60	90.50	3.3	Not helpful
Cappelli 2006 [4]	Intranodular flow	6135	4.6 (284/6135)	62	50	5.60	96	1.4	? Not included in final recommendations
Popowicz 2009 [6]	Intranodular flow	316	8.5 (27/316)	51.90	56.70	8.90	92.70	1.2	Not helpful
Rago 1998 [1]	Marked intranodular flow	104	28.8 (30/104)	49	67	34	78	1.5	Not helpful
Brito 2014 [11]	Increased central flow	7578		48	53				Not helpful
Papini 2002 [2][a]	Intranodular flow	402	7.7 (31/402)	74 (23/31)	80.8 (300/371)	24.50	97.40	9.4	Helpful—included in recommendations
Frates 2003 [3]	Extensive intranodular flow	209	15.3 (32/209)	43.80	85.30	35.00	85.30	2.4	Limited usefulness
	Small to moderate or greater intranodular flow	209	15.3 (32/209)	62.50	57.10	20.80	79.50	1	Limited usefulness
Lyshchik 2007 [5]	Intranodular flow (all nodules)	86	53.5 (46/86)	65.20	52.50	61.20	56.80	1.4	Qualitative analysis of vascularity was not helpful
	Intranodular flow (nodules <2 cm)	43	67.4 (29/43)	65.50	85.70	90.50	54.50	2	Qualitative analysis of vascularity was not helpful
	Intranodular flow (nodules >2 cm)	43	39.5 (17/43)	64.70	34.60	49.30	60.00	1.23	Qualitative analysis of vascularity was not helpful
Lee 2011 [9]	Predominant intranodular	191	37.7 (72/191)	11.1	94.1	53.3	63.6	1.5	Not useful
Ozel 2012 [10]	Any intranodular	363	6.10 (22/363)	63.6	34	10.1	96.4	2.8	Useful
Moon 2010 [7]	Any flow	1083	24.8 (269/1083)	40.1	43	18.9	68.5	0.6	Negative correlation between vascularity and malignancy
	Intranodular flow	1083	24.8 (269/1083)	16.7	69.3	15.3	28.4	0.21	Negative correlation between vascularity and malignancy

Sens = sensitivity, Spec = specificity, PPV = positive predictive value, NPV = negative predictive value

[a]Nonpalpable nodules 8–15 mm

et al. had the highest odds ratio of 9.4 using any intranodular flow as the criterion [2]. In this study, intranodular flow had a 24.5 % risk of malignancy and no intranodular flow had a 2.6 % risk of malignancy.

In a recent study of 1342 benign and 160 malignant nodules (malignant rate of 10.6 %), suspicious flow was defined in two different ways [12]. Intranodular flow of any degree regardless of the presence or degree of peripheral flow had an odds ratio of 1.28 and a positive predictive value of 11.5 %. Intranodular flow without peripheral flow or exceeding peripheral flow had an odds ratio of 3.3 and a positive predictive value of 31.6 %. The authors concluded that Doppler evaluation of blood flow was not helpful.

In another large study of 5851 benign and 284 malignant nodules (malignant rate of 4.6 %), intranodular flow of any degree was considered suspicious for malignancy [4]. Using this criterion, the odds ratio was 1.4 and the positive predictive value was 5.6 %. Doppler findings were not included in the final recommendations of this study.

In a study of 814 benign and 269 malignant nodules (malignant rate of 24.8 %), suspicious flow was defined in two different ways [7]. In both cases there was actually a negative correlation with malignancy.

A meta-analysis of studies including 7578 nodules used increased intranodular flow as the criterion for malignancy and found a sensitivity of 48 % and a specificity of 53 % [11]. The authors did not conclude that analysis of vascularity was helpful.

In a slightly different analysis, Phuttharak compared the results of gray-scale findings alone versus the combination of gray-scale and Doppler findings [13]. Central hypervascularity that exceeded flow in the remainder of the nodule was considered suspicious for malignancy. The sensitivity, specificity, positive predictive value, and negative predictive value were 80 % (4/5), 84.6 % (22/26), 50 % (4/8), and 95.7 % (22/23), respectively, for gray-scale findings alone and 40 % (2/5), 96.2 % (25/26), 66.7 % (2/3), and 89.3 % (25/28) for combined gray-scale and Doppler findings. The authors concluded that Doppler findings were useful since they improved the specificity and the positive predictive values, albeit with a loss of sensitivity. A significant limitation of this study was the low number of nodules that were analyzed (only 31 total nodules and only five malignant nodules).

There is some data that suggests Doppler flow patterns may add clinically useful information for nodules that have been aspirated and have cytology indicative of follicular lesions of undetermined significance or atypia of undetermined significance [14–17]. Approximately 15–20 % of these indeterminate lesions ultimately are shown to be malignant. Currently there are no gray-scale sonographic features that assist in separating the benign and malignant nodules in this category. However, intranodular vascularity has been shown in several studies to be more closely associated with malignancy (Fig. 13.8). Sensitivity, specificity, positive predictive value, and negative predictive value range from 80 to 86 %, 39 to 90 %, 23 to 51 %, and 90 to 97 %, respectively. The odds ratio for a positive result ranges from 2.8 to 17.7. Table 13.2 shows the results of several studies that had histologic proof and specifically determined the statistics of nodule vascularity independent of gray-scale findings. DeNicola also evaluated measurement of RI values from the nodules and using a cutoff value of less than 0.75 as a sign of malignancy obtained a sensitivity of 40 %, specificity of 97 %, positive predictive value of 67 %, negative predictive value of 92 %, and an odds ratio for a positive result of 8.4 [15]. These results suggest a complimentary role for color Doppler in the management of follicular lesions. However, it is important to realize that in individual patients the presence of central flow (Fig. 13.9) does not ensure that a lesion is malignant and predominantly peripheral flow does not exclude a malignancy.

In summary, Doppler evaluation of nodule blood flow is much less helpful than gray-scale evaluation. While detection of intranodular vascularity may increase the risk of malignancy minimally, many benign nodules are hypervascular (Figs. 13.7 and 13.9), and the absence of

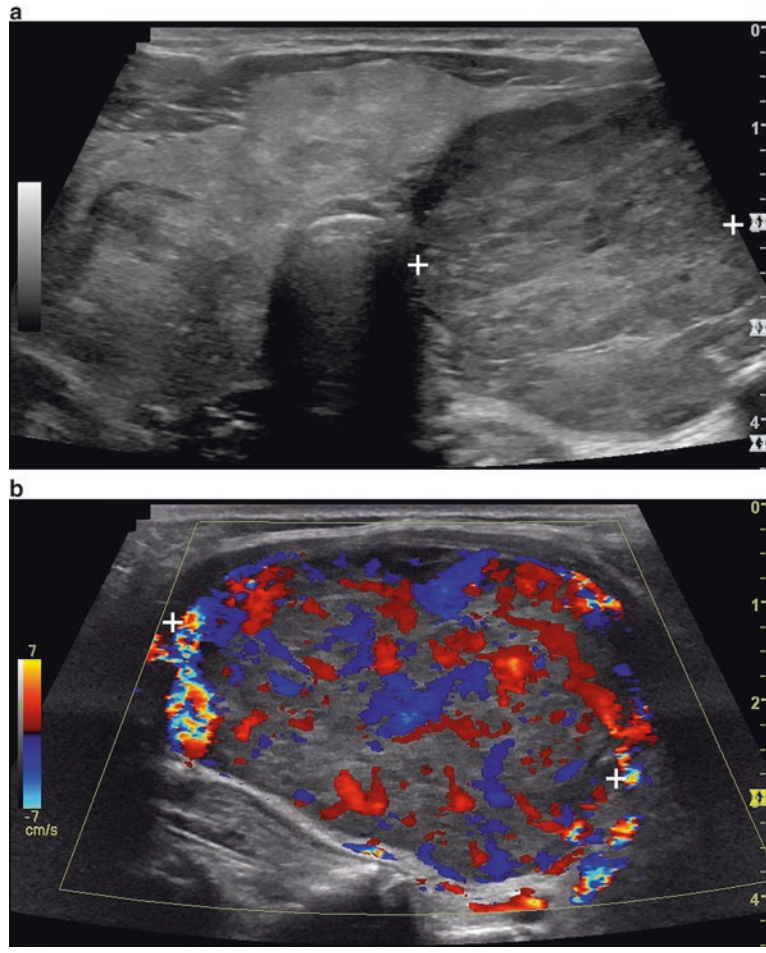

Fig. 13.8 Follicular cancer with predominant central internal blood flow. (**a**) Transverse gray-scale view shows a large, entirely solid, hypoechoic, intermediate suspicion nodule (*cursors*) with smooth margins and no calcifications. (**b**) Longitudinal color Doppler view shows readily detectable blood flow throughout the center of the nodule

Table 13.2 Relationship of the pattern of nodular blood flow and risk of malignancy for nodules with cytologic results of follicular neoplasm, follicular lesions of undetermined significance, or atypia of undetermined significance

Study	Criteria used	# of nodules	% malignancy	Sens (%)	Spec (%)	PPV (%)	NPV (%)	Odds ratio
Iared 2010 [17][a]	Predominant intranodular	457	14.7 (67/457)	85.1	86.2	51.4	97.1	17.7
Choi 2009 [16]	Intranodular flow	114	21.9 (25/114)	84	39	28	90	2.8
DeNicola 2005 [15]	Predominant intranodular	86	11.6 (10/86)	80	90	50	97	17.2
Fukanari 2004 [14]	Intranodular flow	310	14.2 (44/310)	86	52	23	96	5.4

Sens = sensitivity, Spec = specificity, PPV = positive predictive value, NPV = negative predictive value
[a]Meta-analysis

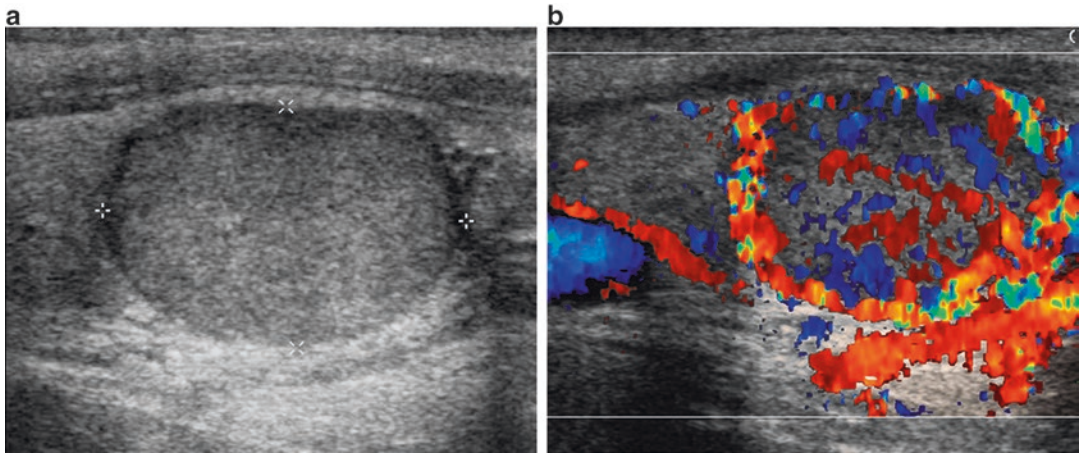

Fig. 13.9 Follicular adenoma with central and peripheral blood flow. (**a**) Longitudinal gray-scale view shows a large, entirely solid, hypoechoic, intermediate suspicion nodule (*cursors*) with smooth margins and no calcifications. (**b**) Longitudinal color Doppler view shows readily detectable blood flow throughout the center and periphery of the nodule

detectable internal flow in no way excludes malignancy (Fig. 13.6). In 2009 the American Thyroid Association guidelines for patients with thyroid nodules included increased intranodular flow as a malignant feature that warranted FNA at a smaller nodule size (along with several well-known gray-scale findings) [18]. The guidelines published in 2015 eliminated this Doppler finding in their recommendations for FNA of a thyroid [19].

13.2 Hyperthyroidism

Distinction of Graves' disease, the most common cause of hyperthyroidism, and thyrotoxicosis caused by destructive thyroiditis (subacute thyroiditis, silent thyroiditis, pregnancy-related thyroiditis) is generally made based on a combination of clinical and laboratory findings. Radioactive iodine uptake and scanning have traditionally been used when imaging is necessary and are generally considered the gold standard. However, radioactive iodine is a relatively expensive and time-consuming examination that cannot be used in pregnancy or in breast-feeding women. Given its widespread availability, ultrasound and Doppler have now assumed an important complimentary role.

Ralls originally recognized the color Doppler hypervascularity of Graves' disease and coined the term "thyroid inferno" (Fig. 13.10) in 1988 [20]. Since then there have been a number of studies showing that there are statistically significant differences in the subjective categorization of Doppler vascularity between Graves' disease and destructive thyroiditis [21, 22] and from other forms of thyroid disease [23] and from euthyroid controls [23]. In a study of 65 patients, Kumar found mild to moderate patchy or diffuse increased flow in 32/34 patients with Graves' disease (sensitivity 94%) and only 1/31 patients with destructive thyroiditis (specificity 97%) [21]. Uchida et al. had much less encouraging results [22]. In a study of 215 patients, they found mild or marked increased flow in a patchy or diffuse distribution in 112/194 patients with Graves' disease (sensitivity 58%) and in 1/21 patients with painless thyroiditis (specificity 95%).

Given the inconsistent results with subjective analysis of parenchymal blood flow, some investigators have described quantitative techniques for measuring blood flow. These generally use

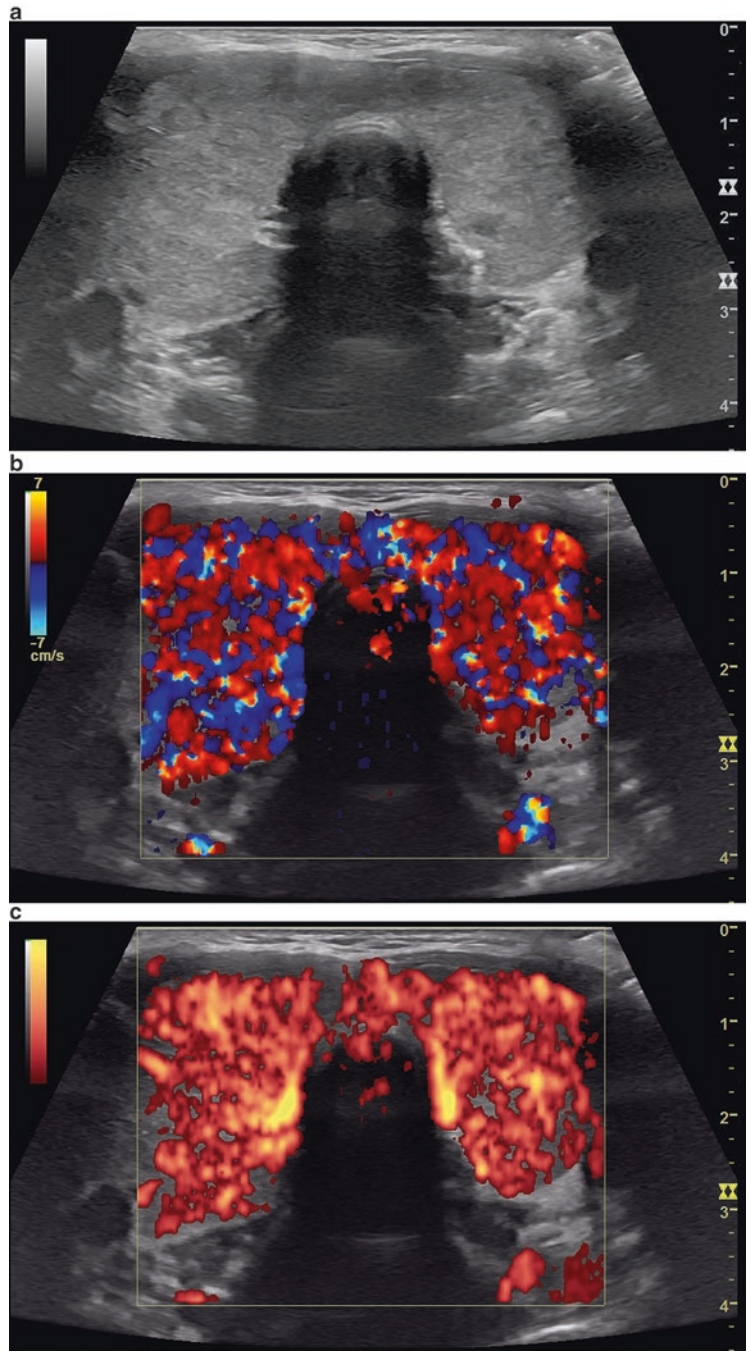

Fig. 13.10 Graves' disease with classic "thyroid inferno" hypervascularity. (**a**) Transverse gray-scale view shows an enlarged thyroid that is slightly hypoechoic and slightly heterogeneous. There are no nodules. (**b**) Corresponding color Doppler view shows intense, homogeneous, diffuse hypervascularity. (**c**) Corresponding power Doppler view shows findings similar to the color Doppler image

software that analyze color or power Doppler images of the thyroid and calculate a percentage of blood flow by comparing the number of pixels with color Doppler signals to the total number of pixels within a selected region of interest. In a study of 114 patients, Ota used proprietary software built in to their ultrasound unit and found mean thyroid total blood flow values of 14.9 % (±6.4 %), 0.8 % (±0.5 %), 0.9 % (±0.7), and 0.8 % (±0.5 %) for Graves' disease, painless thyroiditis,

subacute thyroiditis, and normal controls, respectively [24]. Using a cutoff of 4 % resulted in a sensitivity and specificity of 100 %. Using power Doppler and a different quantification method, Banaka also calculated the percent blood flow in the thyroid [25]. In the right lobe, they found values of 24.2 % (±16.3 %), 10.3 % (±7.1 %), 14.7 % (±13.8 %), and 3.7 % (±3.5 %), for Graves' disease, euthyroid Hashimoto's disease, hypothyroid Hashimoto's disease, and normal controls, respectively. Very similar values were obtained in the left thyroid lobe. Using a cutoff value of 7.4 % for the right lobe and 5.6 % for the left lobe, they obtained a sensitivity of 82–89 % and specificity of 85–88 % for distinguishing autoimmune disease (Graves' and Hashimoto's) from normal controls. Although these techniques can theoretically improve on subjective assessment of vascularity, they are cumbersome, very dependent on adjustment of technical parameters, and not uniformly available.

Analysis of arterial waveforms has also received a great deal of attention. Measurement of velocity, flow volume, resistive index, and other parameters have been studied. Most studies have focused on the superior or inferior thyroidal artery. The results from several studies are summarized in Table 13.3 [21, 26–28]. The mean peak systolic velocity in either the ITA or STA ranged from 58 to 78 cm/s, 21 to 33 cm/s, and 17 to 33 cm/s, for Graves' disease, destructive thyroiditis, and euthyroid controls, respectively. Using cutoff values from 30 to 45 cm/s to distinguish Graves' disease from destructive thyroiditis, sensitivity has ranged from 76 to 95 %, and specificity has ranged from 81 to 100 % (Fig. 13.11).

Uchida et al. [22] compared PSV measurements to a subjective grading system of parenchymal blood flow in 194 patients with Graves' disease and 21 with painless thyroiditis. They found 27 patients with Graves' disease who had no parenchymal flow or flow seen as minimal color spots and 55 patients with patchy uneven distribution of flow. Seventy Graves' patients had a mild increased flow in a patchy distribution, and 42 had a marked increase in flow in a diffuse distribution. They concluded that subjective analysis of parenchymal flow was useful in making the diagnosis of Graves' disease when it was clearly increased, but that Graves' disease could not be excluded when parenchymal flow was decreased. Interestingly, in the group of Graves' patients with decreased parenchymal flow, measurement of STA-PSV remained higher than in the patients with painless thyroiditis (41 ± 32 cm/s vs. 27 ± 14 cm/s). Using a cutoff of 30 cm/s, they achieved a sensitivity of 74 % and a specificity of 77 %. A velocity cutoff of 45 cm/s produced a low sensitivity but a positive predictive value and specificity of 100 %.

Table 13.3 Comparison of peak systolic velocity in patients with Graves' disease and destructive thyroiditis

Article	#	Artery studied	Velocity mean			Cutoff	Statistics (%)
			Graves' disease	Destructive thyroiditis	Euthyroid controls		
Zuhur 2014 [27][a]	20	Mean ITA	59 ± 25 (13–146)	21 ± 5 (11–34)	17 ± 4 (7–29)	40 cm/s	Sens 76
							Spec 100
						30 cm/s	Sens 95
							Spec 95
Chen 2012 [28]	220	Mean STA	75 cm/s ± 2.8	33 cm/s ± 2.3	33 cm/s ± 3.5	45.25 cm/s	Sens 80.4
							Spec 81.4
Kumar 2009 [21]	65	Mean ITA	58 ± 13	22 ± 5		40 cm/s	Sens 94
							Spec 100
Uchida 2010 [26]	57	Mean STA	78 ± 36	28 ± 13	21 ± 8	45 cm/s	Sens 84
							Spec 92

ITA = inferior thyroidal, STA = superior thyroidal artery, Sens = sensitivity, Spec = specificity
[a]Pregnant patients with Graves' disease, destructive thyroiditis, and gestational thyrotoxicosis

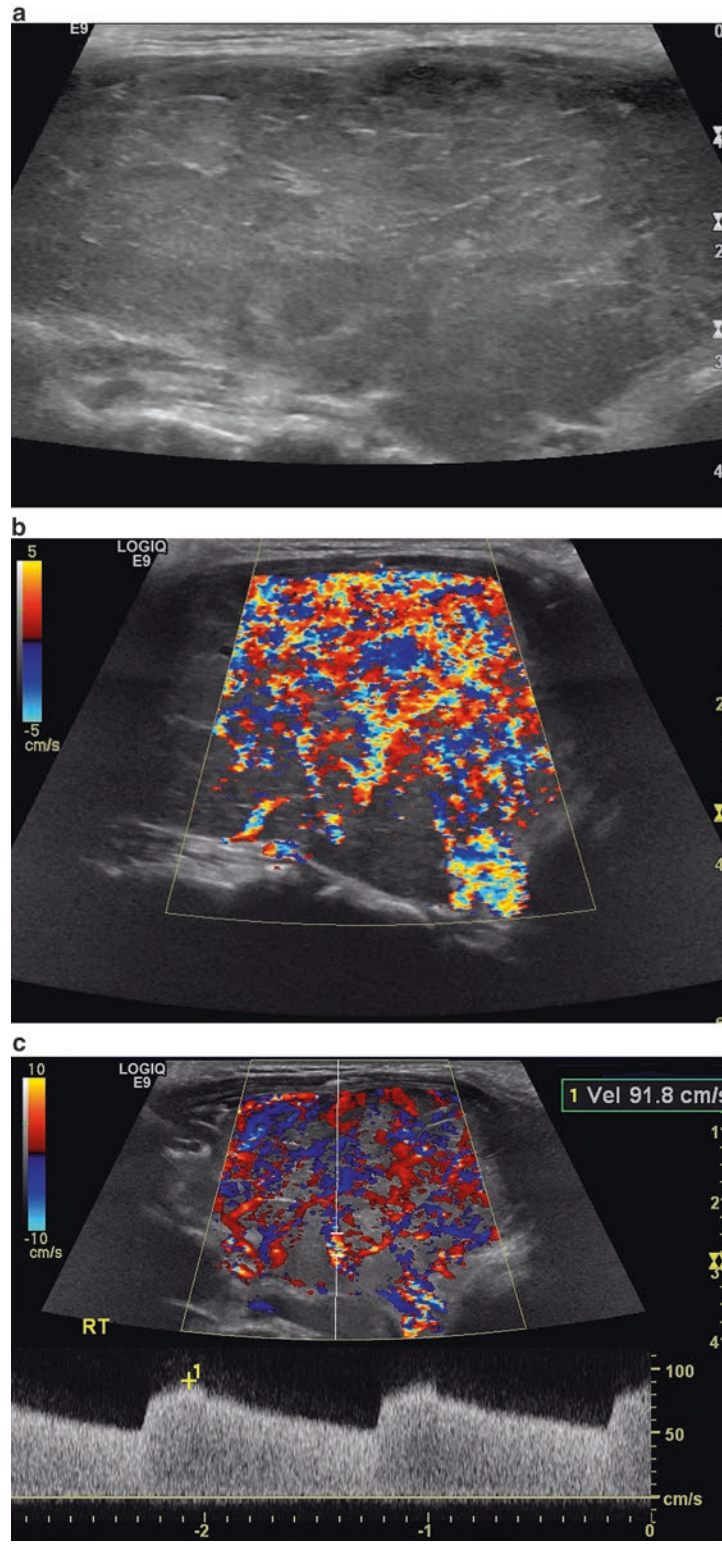

Fig. 13.11 Graves' disease with elevated inferior thyroidal artery peak systolic velocity. (**a**) Longitudinal gray-scale view shows an enlarged thyroid that is heterogeneous and hypoechoic. There are no nodules. (**b**) Corresponding color Doppler view shows intense, homogeneous, diffuse hypervascularity. (**c**) Pulsed Doppler waveform from the inferior thyroidal artery shows an elevated peak systolic velocity of 91.8 cm/s

Doppler analysis has also been shown to be helpful in distinguishing the two different types of amiodarone-induced thyrotoxicosis (AIT) [29, 30]. Type 1 AIT usually occurs in thyroid glands that have preexisting abnormalities such as diffuse or nodular goiters or Graves' disease prior to amiodarone therapy. It is usually treated with thionamides and potassium perchlorate therapy. These glands generally have an abnormal gray-scale appearance and increased parenchymal blood flow. Type 2 AIT is a destructive thyroiditis caused by cytotoxic effects of amiodarone on a normal gland. It is usually treated with glucocorticoids. These glands typically have a relatively normal gray-scale appearance and no vascularity [29]. Bogazzi subjectively graded parenchymal blood flow into four different patterns ranging from no flow or minimal color spots (grade 0) to markedly increased flow (grade 3). Pattern 0 was seen in all 16 untreated patients with type 2 AIT, all nine euthyroid patients on long-term amiodarone treatment, all nine patients with subacute thyroiditis, and all 26 normal controls. Of the 11 patients with type 1 AIT, seven had pattern 1, one had pattern 2, and three had pattern 3 [31]. In a follow-up study, Bogazzi et al. studied 55 patients with AIT. Of the 16 patients with type 1 disease, 13 had patchy parenchymal flow in an uneven distribution, two had mild hypervascularity in a patchy distribution, and one had marked hypervascularity in a diffuse homogeneous distribution. All 39 patients with type 2 disease had pattern 0 [32].

It is almost always easy to differentiate Graves' disease from Hashimoto's thyroiditis based on clinical and laboratory analysis. But patients may have ultrasound scans performed prior to the diagnosis. Since there is overlap in the gray-scale and color Doppler appearance of these conditions, Doppler waveform analysis has been used to help make the distinction.

Table 13.4 Peak systolic velocity measurements (mean and standard deviation) from the inferior thyroidal artery of the right and left lobes in patients with Graves' disease, Hashimoto's thyroiditis, and normal controls [25]

Condition	Right lobe (cm/s)	Left lobe (cm/s)
Euthyroid Hashimoto's thyroiditis	40 (±15)	43 (±14)
Hypothyroid Hashimoto's thyroiditis	52 (±36)	45 (±22)
Graves' disease	83 (±43)	88 (±46)
Normal controls	19 (±9)	20 (±9)

Erdogan et al. measured peak systolic velocity in perithyroidal arteries (not otherwise specified) and found statistically significant differences between Graves' disease (mean velocity in 29 patients = 48 cm/s ± 12) and Hashimoto's thyroiditis (mean velocity in 24 patients = 22 cm/s ± 8) [23]. Banaka et al. measured the peak systolic velocity in the inferior thyroid artery in patients with Graves' disease ($n = 29$), hypothyroid Hashimoto's thyroiditis ($n = 54$), euthyroid Hashimoto's thyroiditis ($n = 70$), and normal controls ($n = 48$) [25]. The mean velocities are shown in Table 13.4. There were significant differences between Hashimoto's thyroiditis and Graves' disease and between the entire group of patients and the normal controls. Using a cutoff value of 61 cm/s to distinguish Hashimoto's thyroiditis from Graves' disease, the sensitivity was 83 % and the specificity was 87 %. They found that peak systolic velocities were superior to quantitative measurement of vascularity index and superior to subjective analysis of parenchymal echogenicity (Fig. 13.12). Resistive indices were also calculated on the Doppler waveforms but were not useful.

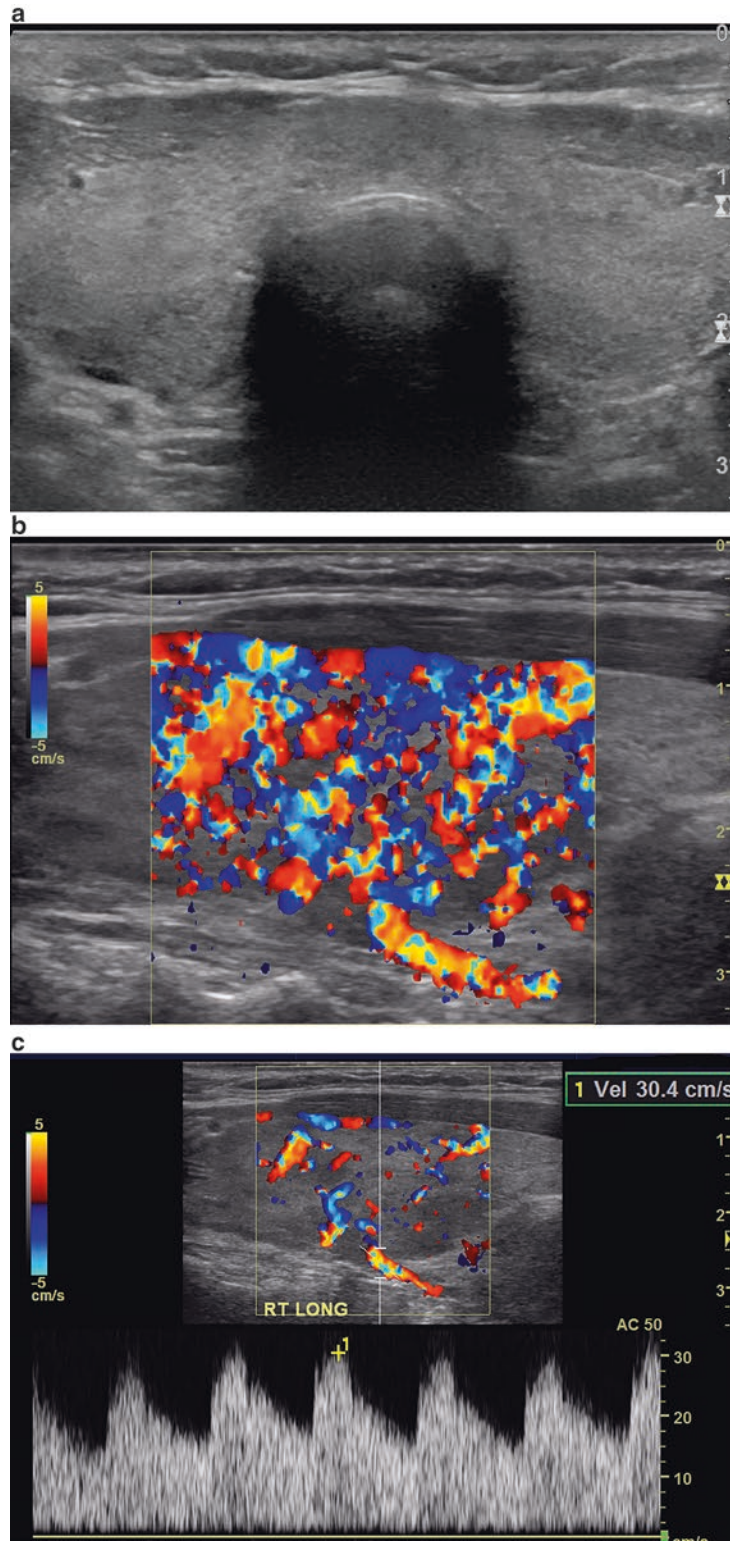

Fig. 13.12 Hashimoto's thyroiditis. (**a**) Transverse gray-scale view shows an enlarged thyroid that is slightly hypoechoic and slightly heterogeneous. There are no nodules. The gray-scale features are consistent with either Hashimoto's thyroiditis or Graves' disease. (**b**) Longitudinal color Doppler view shows intense, homogeneous, diffuse hypervascularity. The color Doppler features are consistent with either Hashimoto's thyroiditis or Graves' disease. (**c**) Pulsed Doppler waveform from the inferior thyroidal artery shows a peak systolic velocity of 30.4 cm/s. This is higher than normal but less than expected for Graves' disease. In this case the arterial velocity suggests Hashimoto's thyroiditis rather than Graves' disease

References

1. Rago T, Vitti P, Chiovato L, De Liperi A, Miccoli P, et al. Role of conventional ultrasonography and color flow-Doppler sonography in predicting malignancy in 'cold' thyroid nodules. Eur J Endocrinol. 1998;138: 41–6.
2. Papini E, Guglielmi R, Bianchini A, Crescenzi A, et al. Risk of malignancy in nonpalpable thyroid nodules: predictive value of ultrasound and color-doppler features. J Clin Endocrinol Metab. 2002;87:1941–6.
3. Frates MC, Benson CB, Doubilet PM, Cibas ES, Marqusee E. Can color Doppler sonography aid in the prediction of malignancy of thyroid nodules. J Ultrasound Med. 2003;22:127–31.
4. Cappelli C, Castellano M, Pirola I, Gandossi E, et al. Thyroid nodule shape suggests malignancy. Eur J Endocrinol. 2006;155:27–31.
5. Lyshchik A, Moses R, Barnes SL, Higashi T, et al. Quantitative analysis of tumor vascularity in benign and malignant solid thyroid nodules. J Ultrasound Med. 2007;26:837–46.
6. Popowicz B, Klencki M, Lewinski A, Slowinska-Klencka D. The usefulness of sonographic features in selection of thyroid nodules for biopsy in relation to the nodule's size. Eur J Endocrinol. 2009;161: 103–11.
7. Moon HJ, Kwak JY, Kim MJ, Son EJ, Kim EK. Can vascularity at power Doppler us help predict thyroid malignancy. Radiology. 2010;255:260–9.
8. Sharma A, Gabriel H, Nemcek AA, Nayar R, Du H, Nikolaidis P. Subcentimeter thyroid nodules: utility of sonographic characterization and ultrasound-guided needle biopsy. AJR Am J Roentgenol. 2011;197: W1123–8.
9. Lee YH, Kim DW, In HS, Park JS, Kim SH, et al. Differentiating between benign and malignant solid thyroid nodules using an US classification system. Korean J Radiol. 2011;12:559–67.
10. Ozel A, Erturk SM, Ercan A, Yilmaz B, Basak T, et al. The diagnostic efficiency of ultrasound in characterization for thyroid nodules: how many criteria are required to predict malignancy? Med Ultrason. 2012;14:24–8.
11. Brito JP, Gionfriddo MR, Nofal AA, Boehmer KR, et al. The accuracy of thyroid nodule ultrasound to predict thyroid cancer: systematic review and meta-analysis. J Clin Endocrinol Metab. 2014;99:1253–63.
12. Rosario PW, da Silva AL, Borges MAR, Calsolari MR. Is Doppler ultrasound of additional value to gray-scale ultrasound in differentiating malignant and benign thyroid nodules. Arch Endocrinol Metab. 2015;59:79–83.
13. Phuttharak W, Somboonporn C, Hongdomnern G. Diagnostic performance of gray-scale versus combined gray-scale with colour Doppler ultrasonography in the diagnosis of malignancy in thyroid nodules. Asian Pac J Cancer Prev. 2009;10:759–64.
14. Fukanari N, Mitsuji Nagahama M, Sugino K, Mimura T, Ito K, Ito K. Clinical Evaluation of Color Doppler Imaging for the Differential Diagnosis of Thyroid Follicular Lesions. World J. Surg. 2004;28: 1261–1265.
15. De Nicola H, Szejnfeld J, Logullo AF, Wolosker AM, et al. Flow pattern and vascular resistive index as predictors of malignancy risk in thyroid follicular neoplasms. J Ultrasound Med. 2005;24:897–904.
16. Choi YJ, Yun JS, Kim DH. Clinical and ultrasound features of cytology diagnoses follicular neoplasm. Endocr J. 2009;56(3):383–9.
17. Iared W, Shigueoka DC, Cristofoli JC, Andriolo R, Atallah AN, et al. Use of color Doppler ultrasonography for the prediction of malignancy in follicular thyroid neoplasms. J Ultrasound Med. 2010;29:419–25.
18. Cooper DS, Doherty GM, Haugen BR, Kloos RT, Lee SL, Mandel SJ, Mazzaferri EL, McIver B, Pacini F, Schlumberger M, Sherman SI, Steward DL, Tuttle RM. Revised American Thyroid Association management guidelines for patients with thyroid nodules and differentiated thyroid cancer. American Thyroid Association (ATA) Guidelines Taskforce on Thyroid Nodules and Differentiated Thyroid Cancer. Thyroid. 2009;19(11):1167–214.
19. Haugen BR, Alexander EK, Bible KC, Doherty GM, Mandel SJ, 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.
20. Ralls PW, Mayekawa DS, Lee KP, Colletti PM, Radin DR, Boswell WD, Halls JM. Color-flow Doppler sonography in Graves disease: "thyroid inferno". Am J Roentgenol. 1988;150(4):781–4.
21. Kumar KVS, Pasupuleti V, Jayaraman M, Abhyuday V, Rayudu R, Modi KD. Role of thyroid Doppler in differential diagnosis of thyrotoxicosis. Endod Prac. 2009;15:6–9.
22. Uchida T, Shigihara N, Takeno K, Komiya K, et al. Characteristics of patients with graves disease and intrathyroid hypovascularity compared to painless thyroiditis. J Ultrasound Med. 2014;33:1791–6.
23. Erdogan MF, Anil C, Cesur M, Baskal N, Erdogan G. Color flow Doppler sonography for the etiologic diagnosis of hyperthyroidism. Thyroid. 2007;17: 223–8.
24. Ota H, Amino N, Morita S, Kobayashi K, Kubota S, Fukata S, Kamiyama N, Miyauchi A. Quantitative measurement of thyroid blood flow for differentiation of painless thyroiditis from Graves' disease. Clin Endocrinol (Oxf). 2007;67(1):41–5.
25. Banaka I, Thomas D, Kaltsas G. Value of the left inferior thyroid artery peak systolic velocity in diagnosing autoimmune thyroid disease. J Ultrasound Med. 2013;32:1969–78.
26. Uchida T, Takeno K, Goto M, Kanno R, et al. Superior thyroid artery mean peak systolic velocity for the

diagnosis of thyrotoxicosis in Japanese patients. Endocr J. 2010;57(5):439–43.
27. Zuhur SS, Ozel A, Kuzu I, Erol RS, Ozcan N, et al. The diagnostic utility of color Doppler ultrasonography, Tc-99m pertechnetate uptake, and TSH-receptor antibody for differential diagnosis of Graves' disease and silent thyroiditis: a comparative study. Endod Prac. 2014;20:310–9.
28. Chen L, Zhao X, Liu H, Wang Y, Li L, Lu B, Li Y, Hu R. Mean peak systolic velocity of the superior thyroid artery is correlated with radioactive iodine uptake in untreated thyrotoxicosis. J Int Med Res. 2012;40:640–7.
29. Alzahrani AS, Ceresini G, Aldasouqu SA. Role of ultrasonography in the differential diagnosis of thyrotoxicosis: a noninvasive, cost-effective, and widely available but underutilized diagnostic tool. Endod Prac. 2012;18:567–78.
30. Eaton SEM, Euinton HA, Newman CM, Weetman AP, Bennet WM. Clinical experience of amiodarone-induced thyrotoxicosis over a 3-year period: role of colour-flow Doppler sonography. Clin Endocrinol (Oxf). 2002;56:33–8.
31. Bogazzi F, Bartalena L, Brogioni S, Mazzeo S, et al. Color flow Doppler sonography rapidly differentiates type I and type II amiodarone-induced thyrotoxicosis. Thyroid. 1997;7:541–5.
32. Bogazzi F, Martino E, Dell'Unto E, Brogioni S, et al. Thyroid color flow Doppler sonography and radioiodine uptake in 55 consecutive patients with amiodarone-induced thyrotoxicosis. J Endocrinol Invest. 2003;26:635–40.