

VRAAG 3: KARAKTERISTIEKEN BEELDVORMING INCIDENTALOMA

Diagnostische studies

Study ID	Method	Patient characteristics	Intervention(s)	Results primary outcome	Critical appraisal of study quality
Kang HW 2004	<ul style="list-style-type: none"> Diagnostic study, retrospective Funding/Col: not reported Setting: single university centre, Korea Sample size: N=198 Duration: inclusion 1/1999-12/2000 	<ul style="list-style-type: none"> Eligibility criteria: patients referred for evaluation of palpable thyroid nodules < 1.5 cm, incidentally detected by routine US check-up of the thyroid gland, carotid artery, or other regions of the neck, and via other diagnostic modalities such as CT or PET scan Patient characteristics: <ul style="list-style-type: none"> Mean age: benign 49y vs. malignant 46y Females: 66% vs. 84% Prevalence of disease: 28.8% 	<p><u>Index test:</u> US (only performed on 184 cases, and reported for 179 cases)</p> <p><u>Reference standard:</u> (1) FNAB (2) Follow-up thyroid US: benign if no change in size after 2 consecutive exams</p>	<ul style="list-style-type: none"> Individual US criteria: <ul style="list-style-type: none"> Ill-defined margin: Se 30%, Sp 96%, PPV 68%, NPV 81% Irregular shape: Se 0%, Sp 100%, NPV 76% Solid echostructure: Se 98%, Sp 27%, PPV 30%, NPV 97% Hypo(iso)echoic : Se 98%, Sp 18%, PPV 27%, NPV 96% Calcification : Se 53%, Sp 92%, PPV 68%, NPV 86% US index points based on these 5 criteria: >3 for malignancy <ul style="list-style-type: none"> Se: 74% Sp: 89% PPV: 92% NPV: 90% 	<p>Level of evidence: B</p> <ul style="list-style-type: none"> Differential verification Blinding not reported Incorporation bias: US used as reference standard in some patients
Kim BH 2010	<ul style="list-style-type: none"> Diagnostic study, retrospective Funding/Col: not reported Setting: single university centre, Korea Sample size: N=159 Duration: inclusion 3/2005-12/2009 	<ul style="list-style-type: none"> Eligibility criteria: patients with focal thyroid incidentaloma on PET/CT for staging of cancer, treatment response evaluation, detection of recurrent and metastatic disease or evaluation for cancer of unknown primary origin Patient characteristics: <ul style="list-style-type: none"> Mean age: malignant 55.0y vs. benign 54.3y Females: 95% vs. 84% Prevalence of disease: 23.2% 	<p><u>Index test:</u> FDG-PET/CT</p> <p><u>Reference standard:</u> (1) FNAB (140/159) (2) High resolution thyroid US (19/159)</p>	<ul style="list-style-type: none"> Visual grade 3: <ul style="list-style-type: none"> Se: 70% Sp: 80% PPV: 52% NPV: 90% AUC: 0.782 SUVmax cut-off = 4.46: <ul style="list-style-type: none"> Se: 51% Sp: 80% PPV: 43% NPV: 84% AUC: 0.641 SUVmean cut-off = 2.03: <ul style="list-style-type: none"> Se: 84% Sp: 48% PPV: 33% NPV: 91% AUC: 0.605 CT attenuation ≤ 3: <ul style="list-style-type: none"> Se: 84% Sp: 36% PPV: 28% (wrongly reported in article) NPV: 88% (wrongly reported in article) AUC: 0.531 	<p>Level of evidence: B</p> <ul style="list-style-type: none"> Differential verification Blinding not reported High resolution US not established reference standard Optimal cut-offs determined with ROC analyses
Kim SJ 2011	<ul style="list-style-type: none"> Diagnostic study, retrospective Funding/Col: not reported 	<ul style="list-style-type: none"> Eligibility criteria: patients with incidentally detected thyroid nodule during cancer evaluation with PET/CT 	<p><u>Index test:</u> FDG-PET/CT</p> <p><u>Reference standard:</u></p>	<ul style="list-style-type: none"> Visual early > 3: <ul style="list-style-type: none"> Se: 33% Sp: 83% PPV: 30% 	<p>Level of evidence: B</p> <ul style="list-style-type: none"> Differential verification Blinded image evaluation, blinded

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	<ul style="list-style-type: none"> Setting: single university centre, Korea Sample size: N=50 Duration: not reported 	<ul style="list-style-type: none"> Patient characteristics: mean age 58y, females 80% Prevalence of disease: 18% 	(1) FNAB (2) Pathology	<ul style="list-style-type: none"> NPV: 85% AUC: 0.593 Visual delayed > 3: <ul style="list-style-type: none"> Se: 44% Sp: 73% PPV: 27% NPV: 86% AUC: 0.629 SUVmax cut-off = 2.9: <ul style="list-style-type: none"> Se: 56% Sp: 63% PPV: 25% NPV: 87% AUC: 0.604 SUVmax cut-off = 3.1: <ul style="list-style-type: none"> Se: 89% Sp: 44% PPV: 26% NPV: 95% AUC: 0.652 %ΔSUVmax ≤ 9.09: <ul style="list-style-type: none"> Se: 33% Sp: 88% PPV: 38% NPV: 86% AUC: 0.531 	pathology review not reported
Nam-Goong IS 2004	<ul style="list-style-type: none"> Diagnostic study, retrospective Funding/Col: not reported Setting: single university centre, Korea Sample size: N=267 with 317 nodules Duration: inclusion 1/2000-12/2001 	<ul style="list-style-type: none"> Eligibility criteria: patients who underwent US-guided FNA of impalpable thyroid nodules (detected by US) Patient characteristics: <ul style="list-style-type: none"> Mean age: 51y Females: 78% None of the patients had any radiation therapy to the head and neck area Mean size nodules: 0.9 cm (range 0.2-1.5 cm) Prevalence of disease: 16.4% (including inadequate samples) 	<u>Index test:</u> US <u>Reference standard:</u> Cytological findings on FNA	<ul style="list-style-type: none"> Individual US criteria: <ul style="list-style-type: none"> Ill-defined margin: Se 48%, Sp 73%, PPV 31%, NPV 84% Solid echostructure: Se 91%, Sp 33%, PPV 26%, NPV 93% Hypoechoic : Se 68%, Sp 53%, PPV 27%, NPV 87% Punctuate calcification : Se 36%, Sp 85%, PPV 39%, NPV 84% Combination of criteria <ul style="list-style-type: none"> Solid echostructure + hypoechoic: Se 64%, Sp 69%, PPV 35%, NPV 88% Solid echostructure + punctuate calcification: Se 36%, Sp 92%, PPV 53%, NPV 85% Hypoechoic + punctuate calcification: Se 20%, Sp 97%, PPV 60%, NPV 83% Solid echostructure + hypoechoic + punctuate calcification: Se 20%, Sp 98%, PPV 75%, NPV 83% 	Level of evidence: B <ul style="list-style-type: none"> Selection bias: only inclusion of patients that underwent FNA, possibly exclusion of some patients with simple cysts Blinding not reported Only per-lesion analysis available; 101 inadequate samples were excluded from analysis
Pagano L 2011	<ul style="list-style-type: none"> Diagnostic study, retrospective Funding/Col: supported by "Progetto Ricerca 	<ul style="list-style-type: none"> Eligibility criteria: patients with incidental thyroid PET/CT uptake in a study performed for the following: (i) metastasis 	<u>Index test:</u> FDG-PET/CT <u>Reference standard:</u>	<ul style="list-style-type: none"> SUVmax cut-off = 5.0: <ul style="list-style-type: none"> Se: 87% Sp: 65% PPV: 50% 	Level of evidence: B <ul style="list-style-type: none"> Potential selection bias: selection based on receiving of thyroid

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	<p>Sanitaria e Finalizzata" (protocol no. 2997 of 2008 to G.A.) from Regione Piemonte; no Col declared</p> <ul style="list-style-type: none"> • Setting: single university centre, Italy • Sample size: N=52 • Duration: 2005-2009 	<p>evaluation in the follow-up of patients with nonthyroid cancer; (ii) localization of a primitive cancer, in presence of metastases of unknown origin; (iii) localization of an infective or inflammatory process in patients with fever of unknown origin; thyroid function evaluation, US and US-FNAB, thyroid Tc99 scintigraphy when indicated, performed for the diagnostic work-up of the incidental thyroid uptake</p> <ul style="list-style-type: none"> • Patient characteristics: <ul style="list-style-type: none"> ○ Mean age: 64.1y ○ Females: 73% ○ Diffuse uptake: 31%; focal uptake: 69% • Prevalence of disease: 28.8% 	US-FNAB	<ul style="list-style-type: none"> ○ NPV: 92% • Focal uptake: <ul style="list-style-type: none"> ○ Se: 93% ○ Sp: 41% ○ PPV: 39% ○ NPV: 94% 	<p>function evaluation, US and US-FNAB</p> <ul style="list-style-type: none"> • From 191 cases with incidental thyroid uptake, 139 were excluded because they didn't satisfy all inclusion criteria • Blinding not reported
Bartolotta TV 2006	<ul style="list-style-type: none"> • Diagnostic study • Funding/Col: not reported • Setting: single university centre, Italy • Sample size: N=233 with 711 nodules • Duration: 1/2003-10/2003 	<ul style="list-style-type: none"> • Eligibility criteria: patients with incidentally detected thyroid nodules through Doppler US of the epiaortic trunks; no history, symptoms or signs of thyroid disease • Patient characteristics: <ul style="list-style-type: none"> ○ Mean age: 59.4y ○ Females: 61% • Prevalence of disease: 0% 	<p><u>Index test:</u> High-resolution US Real-time spatial compound sonography</p> <p><u>Reference standard:</u> (1) FNAC (2) Yearly follow-up with US</p>	<ul style="list-style-type: none"> • Hypoechoic: <ul style="list-style-type: none"> ○ Sp: 35% • Intranodular flow: <ul style="list-style-type: none"> ○ Sp: 76% 	<p>Level of evidence: B</p> <ul style="list-style-type: none"> • Differential verification • Incorporation bias: for patients without suspicious US criteria, US was used as reference standard • Blinded image review, unclear if pathology review was blinded • Only per-lesion analysis available

Abbreviations: AUC: area under the curve; Col: conflict of interest; CT: computed tomography; FDG: fluoro-deoxy glucose; FNAB: fine-needle aspiration biopsy; FNAC: fine-needle aspiration cytology; NPV: negative predictive value; PET: positron-emission tomography; PPV: positive predictive value; ROC: receiver operating curve; Se: sensitivity; Sp: specificity; SR: systematic review; TT: total thyroidectomy; US: ultrasonography.

References

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