Cost-Effectiveness Analysis of Somatostatin Receptor Scintigraphy

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We analyzed the results of conventional imaging and somatostatin receptor scintigraphy in 150 patients with neuroendocrine tumors. **Methods:** The outcomes of combinations of imaging modalities were compared in terms of tumor localization, effect on patient management and financial cost. **Results:** In patients with carcinoids, a combination of somatostatin receptor scintigraphy, chest radiograph and ultrasound of the upper abdomen had a high sensitivity for tumor localization, and detected lesions in patients in whom no tumor was found with conventional imaging, justifying the greater cost. In patients with medullary thyroid carcinoma, somatostatin receptor scintigraphy adds little to the information obtained with conventional imaging and therefore should not be used as a screening method. In patients with paraganglioma, CT scanning of the region where a paraganglioma is suspected, followed by somatostatin receptor scintigraphy to detect multicentricity has the best cost-effectiveness ratio. In patients with gastrinomas, the combination of somatostatin receptor scintigraphy and CT scanning of the upper abdomen had the highest sensitivity. The relatively high cost of this process is outweighed by its demonstrating a resectable tumor. In patients with insulinomas, the highest yield against the lowest cost is obtained if somatostatin receptor scintigraphy is only performed if CT scanning fails to demonstrate the tumor. **Conclusion:** Somatostatin receptor scintigraphy should be performed in patients with small-cell lung carcinoma because it can lead to a change of stage and may demonstrate otherwise undetected brain metastases. The cost increase is outweighed by the omission of unnecessary treatment for some of the patients and by the possibility of irradiating brain metastases at an early stage, which may lead to a better quality of life.

Key Words: somatostatin receptor imaging; indium-111-octreotide; neuroendocrine tumors

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Since the introduction of somatostatin receptor imaging in 1989 (*1*), many reports on the usefulness and limitations of this technique have been published. Most of these concern the application of [^{111}In-DTPA-D-Phe^1]-octreotide in patients with neuroendocrine tumors. As with all new techniques, the enthusiasm about this new method to demonstrate tumor sites may interfere with a rational choice to only use it with patients for whom additional and essential information is expected to be obtained.

Optimal information on the localization of tumor sites may be important in several instances: (a) when localizing a solitary resectable tumor, (b) in staging a tumor when the choice of treatment depends on the stage and (c) in recording the extent of the disease to anticipate, and, when possible, prevent, future complications. For somatostatin receptor imaging, a fourth point of interest in its application may be that demonstrating the presence or absence of somatostatin receptors may in some tumors predict the usefulness of medical treatment, especially with somatostatin analogs.

In published reports on somatostatin receptor imaging in patients with neuroendocrine tumors, comparisons have been made with the outcomes of conventional imaging techniques and conclusions about its usefulness have been drawn based on the additional information it provided. However, studies that structurally analyze the benefits and the cost of somatostatin receptor imaging are lacking. Since dwindling budgets force the physician and hospital staff to evaluate diagnostic procedures, such an analysis seems both useful and necessary.

In this study, we analyzed the results of various conventional imaging techniques and somatostatin receptor scintigraphy in five groups of patients with neuroendocrine tumors, and compared the outcomes of several combinations of imaging modalities in terms of tumor localization, impact on patient management and financial cost.

METHODS

Patients

One hundred and fifty patients were included in the study. The results of somatostatin receptor scintigraphy and conventional imaging in the five groups of patients that were studied have been published previously (*2–6*). These were: 33 patients who either had histologically proven carcinoid tumors (n = 20) or were at risk of having a carcinoid tumor (n = 13) (*2*); 21 patients with histologically proven medullary thyroid carcinoma (MTC) (*3*); 34 patients who had known paragangliomas (n = 25) or had either undergone surgery or were clinically suspected to have a paraganglioma (n = 9) (*4*); 36 patients with endocrine pancreatic tumors (12 gastrinomas and 24 insulinomas) (*5*); and 26 patients with small-cell lung carcinoma (SCLC) (*6*).

Somatostatin Receptor Scintigraphy

Scintigrams were obtained either 4 and 24 hr or 24 and 48 hr after the injection of [^{111}In-DTPA-D-Phe^1]-octreotide (179-400 MBq). In patients with lung cancer, images were made only after 24 hr. SPECT images were analyzed in patients having paragangliomas and endocrine pancreatic tumors (*4,5*). The acquisition protocols have been described in the reports on which this study is based (*2–6*) and have been discussed extensively elsewhere (*7*).

Cost Analysis

The costs of various diagnostic procedures were calculated taking into account:

1. *Personnel Costs.* The wages for physicians, interns, radiologic and nuclear medicine workers and administrative personnel were divided by average working hours/year. The total number of working hours/year was calculated by subtracting weekend days, holidays and public holidays, educational furloughs and mean days of absenteeism, from a total

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TABLE 1
Cost of Various Imaging Techniques

Investigation	Duration (min)	Cost (DF1)			
		Personnel	Material	Equipment	Total
Head CT	20	83.40	29.60	67.20	180.20
Skullbase CT	60	154.80	37.90	201.50	394.20
Neck CT	30	98.10	53.30	100.80	252.20
Chest CT	40	112.80	69.90	134.30	317.00
Upper abdomen CT	25	90.70	25.50	84.00	200.20
Lower abdomen CT	25	90.70	25.50	84.00	200.20
Neck US	30	78.20	2.90	24.40	105.50
Upper abdomen US	30	78.20	2.90	24.40	105.50
Lower abdomen US	30	78.20	2.90	24.40	105.50
Chest radiography	10	31.90	6.00	11.10	49.00
Angiography	110	403.00	388.20	121.70	912.90
MRI	100	224.20	24.90	635.50	884.60
Bone scan	50	91.90	20.00	65.20	177.10
MIBG scan	125	150.20	865.50	162.90	1178.60
Octreotide scintigraphy	200	225.80	975.20	260.70	1461.70
SPECT with octreotide scintigraphy	60	64.80	5.70	241.70	312.20

Prices are in Dutch Florins (DF1), which equals approximately US $0.6. The difference in the cost of octreotide scintigraphy including SPECT (as compared to without SPECT) is largely due to the fact that SPECT investigations included the use of a three-head camera, which is more expensive than a single-head camera.

of 365 days, and multiplying the result with 8 hr/day, resulting in 1592 to 1688 working hr/yr. We included the cost of interns, because many of the investigations listed, and especially somatostatin receptor scintigraphy, are performed in university hospitals.

2. *Cost of Materials.* The cost of radiographs, injection systems, contrast liquid and kit material.
3. *Equipment Costs.* A yearly payment on an annuity basis at 8% and a term of 8 yr was used to calculate the cost of ultrasound equipment, scanners and gamma cameras. The prices of equipment are those of 1993. Maintenance cost was estimated at 8% of new value. Operating hr/yr were calculated by subtracting weekend days and public holidays and multiplying the result with 8 hr/day, resulting in 2128 hr/yr.
4. *Housing and Overhead Costs.* These were based on the number of square meters required to investigate a bedridden patient. They include the cost of furniture, cleaning, telephone and services of various overhead departments. Housing and overhead costs were based on 24 m^2 for all listed equipment at a price of DF1 681/m^2/yr. Hourly costs were computed as under item 3.

For each investigation, information on the cost of materials and the time needed in terms of equipment and personnel were provided by the departments of radiology and nuclear medicine. Costs are expressed in Dutch Florins (DF1), which approximately equals $0.6. The costs of the various imaging techniques are shown in Table 1.

Comparison of Somatostatin Receptor Scintigraphy and Conventional Imaging Techniques

To compute the sensitivities of the various imaging techniques in each of the five diagnostic groups of patients, the total number of lesions was assumed to be the total of lesions visualized by *any* technique. This assumption was based on several grounds:

1. It applies to any imaging technique that it can only demonstrate disease-related localizations within a certain probability. Histology, the ultimate proof, cannot always be obtained for every visualized lesion, especially if a tumor has metastasized.
2. Limitations in the capability to demonstrate tumors exist for all imaging techniques. In this respect, so-called "occult" tumors, like hormonally active tumors whose presence is certain on biochemical grounds, but cannot be visualized by any technique, are a good example.
3. In a number of patients in whom somatostatin receptor scintigraphy demonstrated otherwise unrecognized tumor localizations and in whom follow-up was available, histological proof was obtained afterwards (see Results).

In the five diagnostic groups that were investigated, the conventional imaging techniques applied in each patient were not identical. The sensitivities for each investigation were therefore calculated as a percentage of the lesions that were visualized in the group in which the imaging technique was applied, and thereafter this percentage was applied to the whole diagnostic group being investigated. Also, various combinations of imaging techniques applied partly to the same region of interest were analyzed for their combined sensitivity, and used in the same way as the sensitivities for the individual investigations.

RESULTS

Carcinoids

In 19 of 20 patients with histologically proven carcinoids, three of nine patients who were thought to be surgically cured of carcinoids, and four of four patients who were clinically suspected to have a carcinoid, accumulation of labeled octreotide at supposed tumor sites was found during somatostatin receptor scintigraphy (*2*). In 23 patients, accumulation of radioactivity at previously unsuspected localizations or sites not recognized with other imaging techniques was found. Histological or radiological evidence that these additional sites indeed represented tumor was obtained in eight patients for whom relevant follow-up was available.

With a combination of conventional imaging techniques and somatostatin receptor scintigraphy, 69 lesions were demon-

TABLE 2
Sensitivities of Applied Imaging Techniques for Carcinoids

Region	No. of lesions	Imaging technique CT (%)	Ultrasound (%)	Radiography (%)	Octreotide (%)
Head/Neck	2	100	—	—	100
Supraclavicular	2	—	—	—	100
Chest	15	67	—	20	100
Upper abdomen	17	46	20	—	100
Liver	12	86	82	—	58
Lower abdomen	21	20	—	—	100

Percentages reflect the number of patients studied.

strated in 33 patients. The lesions were divided into six regions easily recognized on octreotide scintigrams. The applied imaging techniques for each region and their sensitivities are listed in Table 2. Somatostatin receptor scintigraphy had the highest sensitivity in detecting extrahepatic sites, whereas CT or ultrasound were about equally effective in demonstrating liver metastases. Four combinations of imaging techniques were evaluated for their sensitivity and cost (Fig. 1). Because of the low numbers of patients with head and neck lesions in whom conventional imaging techniques were applied, this region was not taken into account. The most sensitive combination of conventional imaging (CT of the chest and abdomen) leads to the detection of only 49% of tumor localizations and fails to detect any localization in 15% of patients (Fig. 1). The combination of somatostatin receptor scintigraphy, chest radiograph and ultrasound of the upper abdomen leads to the detection of lesions in all patients in whom they can be demonstrated by any means, with a sensitivity of 100% in terms of the number of detected lesions (Fig. 1). The cost is DF1 162,000/100 patients versus DF1 72,000/100 patients for CT scanning of chest and abdomen (Fig. 1). The benefit is the detection of at least one lesion in 15% of patients in whom conventional imaging found no abnormalities. In terms of the number of lesions detected, the advantage is 51% of total.

We included radiography or CT scanning of the chest in the combinations of octreotide scintigraphy and conventional imaging that were investigated, although the combination of octreotide scintigraphy and ultrasound of the upper abdomen would suffice to reach equal results. The reason for this is that in our original study (*2*) thoracic lesions were not visualized in three patients who were injected with [^{123}I-Tyr^3]-octreotide.

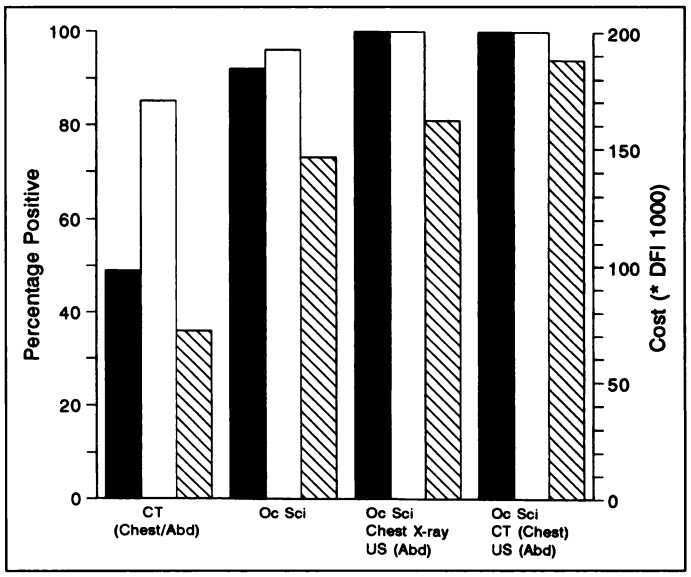

FIGURE 1. Sensitivity and cost of imaging combinations in patients with carcinoids. Our data were extrapolated to a group of 100 patients. Oc Sci = octreotide scintigraphy; US = ultrasound; black bars = percentage of localizations detected; white bars = percentage of patients in whom at least one lesion was detected; hatched bars = cost.

Also, in our experience, using [^{111}In-DTPA-D-Phe^1]-octreotide, bronchial carcinoids may not be visualized in a small percentage of patients.

Medullary Thyroid Carcinoma

[^{111}In-DTPA-D-Phe^1]-octreotide scintigraphy was performed in 21 patients with histologically proven MTC (*3*). In 14 patients (67%) accumulation of labeled octreotide at one or more tumor sites was found. With a combination of conventional imaging techniques and somatostatin receptor scintigraphy, 44 lesions were demonstrated in 21 patients.

The lesions that were found were divided into six anatomical regions that correspond to the metastatic pattern of MTC (Table 3), the seventh region representing upper abdominal pathology, found in two of our patients.

Because of their low sensitivity, chest radiographs and MIBG scanning were left out of our analysis.

Ten combinations of imaging techniques were evaluated for their cost and sensitivity (Fig. 2). Applying somatostatin receptor scintigraphy in patients with MTC, alone or in combination with other imaging techniques, does not lead to a higher sensitivity in terms of detected lesions or of the number of patients in whom at least one lesion is found. CT scanning of the neck, chest and upper abdomen, combined with bone

TABLE 3
Sensitivities of Applied Imaging Techniques for MTC Lesions in 21 Patients

Region	No. of lesions	Imaging technique CT (%)	Ultrasound (%)	Radiography (%)	Bone scan (%)	MIBG scan (%)	Octreotide scan (%)
Thyroid	5	100	100	—	—	0	60
Neck	11	100	100	—	—	0	82
Lung	4	50	—	50	—	0	75*
Mediastinum	9	100	—	20	—	0	78
Liver	7	100	100	—	—	33	0
Bone	6	—	—	—	100	100	50*
Other	2	100	0	—	—	100	50

*Detection of part of the lesions in one patient. Percentages pertain to the number of patients that were investigated.

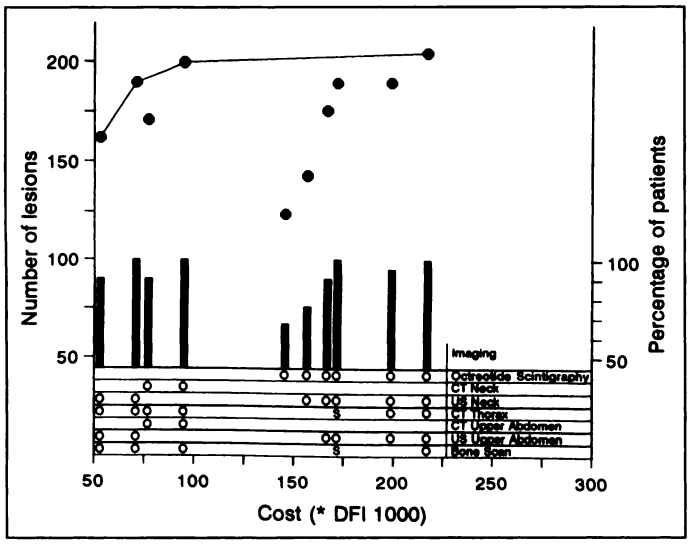

FIGURE 2. Sensitivity and cost of imaging combinations in patients with MTC. Right axis: percentage of patients with at least one lesion. Our data were extrapolated to a group of 100 patients. Closed circle = number of lesions; closed bar = percentage of patients; open circle = imaging techniques applied. Line between closed circles connects points with the most advantageous cost-effectiveness ratio. S = sequential investigations if all other listed imaging remained negative.

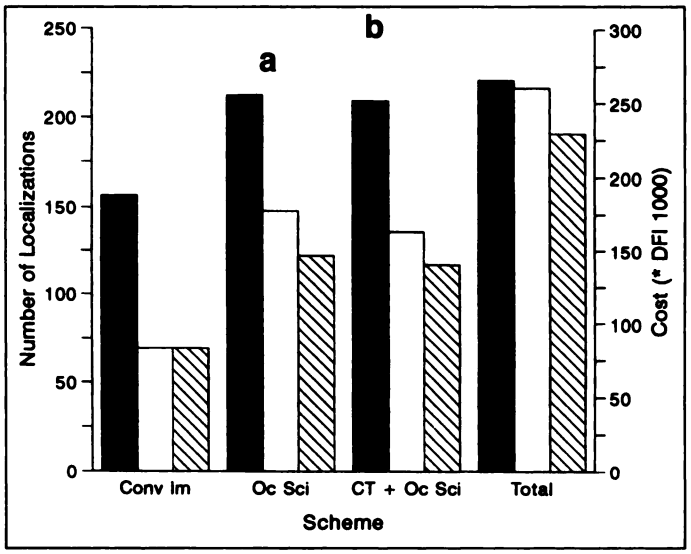

FIGURE 3. Sensitivity and cost of imaging combinations in patients with paragangliomas. Our data were extrapolated to a group of 100 patients. Conv Im = conventional imaging applied; Oc Sci = octreotide scintigraphy; CT + Oc Sci = CT of the region where tumor was suspected followed by octreotide scintigraphy; total = conventional imaging and octreotide scintigraphy combined; black bar = number of localizations; white/hatched bar = cost including octreotide scintigraphy with SPECT/without SPECT.

scintigraphy, leads to the detection of 95% of lesions in 100% of patients, at a cost of DF1 95,000/100 patients (Fig. 2). The most sensitive combination of somatostatin receptor scintigraphy, ultrasound of the neck and upper abdomen, CT scanning of the chest, and bone scintigraphy, will only lead to the detection of five extra lesions with a cost increase of DF1 122,000/100 patients (Fig. 2).

Paragangliomas

In all 25 patients with known paragangliomas and one of nine patients referred because of symptoms consistent with paraganglioma or follow-up after surgical removal of a paraganglioma, supposed tumor sites were visualized with somatostatin receptor scintigraphy (*4*). Unexpected additional paraganglioma sites, not detected or not investigated with conventional imaging techniques, were found in nine of 25 patients (36%) with known paragangliomas, as well as in one of the nine remaining patients. In four patients in whom relevant imaging was subsequently performed, the additional sites were thereafter confirmed. With a combination of conventional imaging techniques and somatostatin receptor scintigraphy, 75 localizations were demonstrated in 26 patients.

The sensitivity of the combined conventional imaging techniques that were applied and somatostatin receptor scintigraphy were 53/75 lesions (71%) in 25/26 patients (96%), and 72/75 lesions (96%) in 26/26 patients (100%), respectively. The lesions were divided into four anatomically and surgically relevant categories and the sensitivities of the applied imaging techniques were calculated (Table 4). MRI was left out of the analysis because it did not have additional value over CT scanning in our patient group. Three schemes of imaging strategies were analyzed. Because of its high sensitivity, only somatostatin receptor scintigraphy was included as whole-body imaging technique (Fig. 3).

As is clear from Figure 3, the application of somatostatin receptor scintigraphy as a screening method (a), or used after the demonstration of a paraganglioma with CT scanning (b) leads to the detection of many more lesions than when only conventional imaging is applied. The increase in cost compared to conventional imaging is DF1 945/patient (a) and DF1 799/patient (b) if SPECT is included, and DF1 633/patient (a) and DF1 569/patient (b) without SPECT. In terms of the number of lesions detected, the cost of conventional imaging was DF1 532/lesion (53 lesions) versus DF1 690/lesion for somatostatin receptor scintigraphy if applied as a screening method (72 lesions) versus DF1 669/lesion if somatostatin receptor scintigraphy were applied only in patients in whom CT scanning demonstrated a paraganglioma in a clinically suspected region (71 lesions).

TABLE 4
Sensitivities of Applied Imaging Techniques for Paragangliomas

Localization	No. of lesions	Imaging technique				
		CT (%)	Ultrasound (%)	Octreotide scan (%)	Angiography (%)	MIBG scan (%)
Jugulotympanic	19	100	—	100	60	50
Vagal	10	88	—	100	100	0
Carotid body	23	67	90	96	60	0
Other	23	100	—	91	—	11

Percentages pertain to the number of patients that were investigated. Other localization refers to mostly thoracic and abdominal sites.

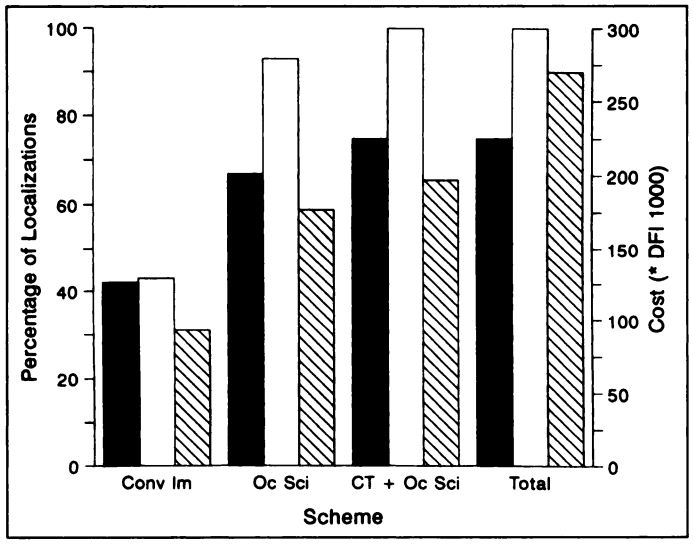

FIGURE 4. Sensitivity and cost of combinations of imaging techniques in patients with gastrinomas. Our data were extrapolated to a group of 100 patients. Abbreviations as in Figure 3. CT = CT of the upper abdomen; black bar = percentage of primary localizations; white bar = percentage of all localizations; hatched bar = cost.

Endocrine Pancreatic Tumors

Gastrinomas. Accumulation of labeled octreotide at supposed tumor localizations was found in 11/12 patients (92%) with gastrinomas (*5*). Conventional imaging, consisting of CT scanning of the upper abdomen (12 patients), ultrasound (seven patients), MRI (six patients) and angiography (three patients), failed to detect any lesion in six of 12 patients (50%) (*5*).

Somatostatin receptor scintigraphy combined with CT scanning of the upper abdomen is the most sensitive combination for the detection of gastrinomas, leading to the detection of primary sites in 75% (9/12) of patients, and of metastases in 100% (5/5). Compared to the conventional imaging applied in our group, it leads to a cost increase of DF1 1042/patient (Fig. 4).

Insulinomas. All 24 patients with insulinomas had a history of hypoglycemic attacks (*5*). Disproportionally elevated insulin/glucose ratios and severe hypoglycemia provoked by fasting, were present in all patients. Conventional imaging, consisting of CT scanning and ultrasound, combined with MRI in nine patients and angiography in 12, failed to localize the tumor

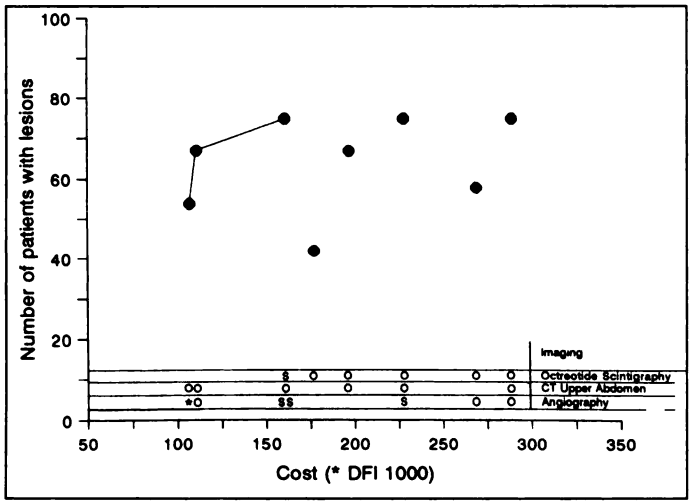

FIGURE 5. Sensitivity and cost of imaging combinations in patients with insulinoma. Our data were extrapolated to a group of 100 patients. Circles and lines as in Figure 2. S and SS = sequential investigation if other (S) or both other (SS) listed imaging techniques remained negative. *Investigation not applied in every patient.

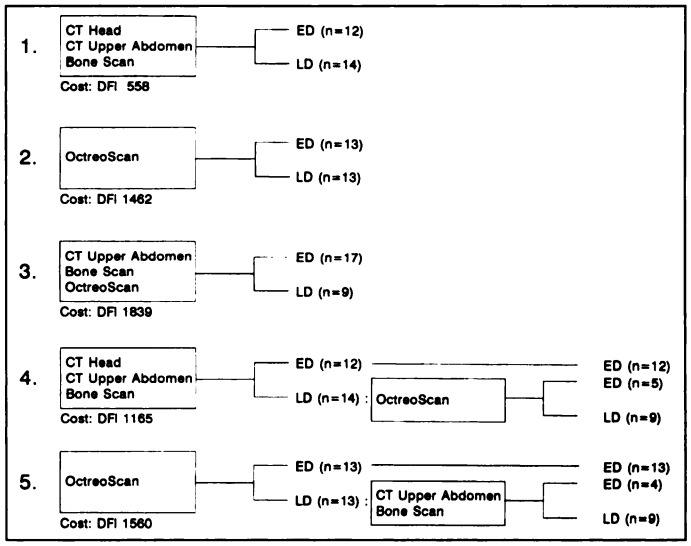

FIGURE 6. Staging and cost of five combinations of imaging techniques in patients with SCLC.

in 11 of 24 patients (46%). MRI and ultrasound of the upper abdomen had no additional value over CT scanning and were therefore omitted from the imaging strategies. It was found that a combination of conventional imaging and somatostatin receptor scintigraphy leads to the detection of more tumors than conventional imaging only (Fig. 5). The scheme in which somatostatin receptor scintigraphy is performed only when CT scanning shows no tumor, and angiography is performed only if CT scanning and somatostatin receptor scintigraphy remain negative, has a high rate of tumor detection and low cost (Fig. 5).

SCLC

The primary tumors, as well as 21 of 25 radiologically suspected sites of lymphatic spread and six of 20 often only radiologically confirmed sites of distant metastasis, were noticed during somatostatin receptor scintigraphy in 26 patients with SCLC (*6*). In 15 patients additional lesions were demonstrated. Of special interest are two groups of patients for whom the additional information provided by somatostatin receptor scintigraphy may have therapeutical consequences: those in whom unexpected cerebral metastases are found, and those for whom the additional information led to an upgrading [from Limited Disease (LD) to Extensive Disease (ED)].

With conventional imaging, cerebral metastases were detected in two patients. Somatostatin receptor scintigraphy suggested cerebral metastases in these two, and in another five patients as well. In these patients, CT scanning and/or bone scintigraphy showed no abnormalities. In four of them, cerebral metastases became manifest 5 and 8 mo later (*6*).

Five schemes of imaging were investigated. In those in which a combination of conventional imaging modalities and somatostatin receptor scintigraphy was evaluated, CT scanning of the head was omitted, because no known cerebral metastases were missed with somatostatin receptor scintigraphy. In the cost-effectiveness analyses, x-ray and CT scanning of the chest, bronchoscopy and biopsy of the tumor have not been taken into account, as these investigations are indispensable for the diagnosis. The results are presented in Figure 6.

Adding somatostatin receptor scintigraphy to the staging protocol in patients with SCLC will increase costs. By applying somatostatin receptor scintigraphy only in those patients who with a conventional work-up seem to have LD (Scheme 4, Fig. 6), the cost increase is lowest, (DF1 607/patient) if compared to conventional imaging only (Scheme 1, Fig. 6). The

benefit is an upgrading in five of 14 patients (36%) who seemed to have LD when screened with conventional imaging only.

Apart from an effect on grading, somatostatin receptor scintigraphy may be used for the early detection of brain metastases, as mentioned above. Applying Scheme 4 (Fig. 6) would leave brain metastases unnoticed in three patients with ED according to conventional imaging. If Scheme 3 or 5 were applied, brain metastases in these patients would be detected as well.

DISCUSSION

Carcinoids

With somatostatin receptor scintigraphy 92% of lesions in 96% of patients were demonstrated. Comparable percentages were found by other groups (*8,9*), who also report additional lesions in about a third of patients. It is important to determine whether a carcinoid has metastasized when the intended treatment is surgery. However, when the tumor has metastasized it may be important to assess the extent of tumor spread in order to evaluate medical treatment. We found that the combination of somatostatin receptor scintigraphy, chest radiograph and ultrasound of the upper abdomen leads to the detection of lesions in all patients in whom they can be demonstrated. The cost of the proposed imaging strategy is DF1 162,000/100 patients versus DF1 72,000/100 patients for the most sensitive combination of conventional imaging. The benefit is the detection of at least one lesion in 15% of patients in whom no abnormalities were found by conventional imaging alone. Another advantage is that twice as many lesions were detected. We think that the proposed imaging strategy justifies the greater cost compared to various combinations of conventional imaging techniques that may fail to detect some lesions.

Medullary Thyroid Carcinoma

With somatostatin receptor scintigraphy 26 of 44 lesions (59%) in 14 of 21 patients (67%) were found. We found that a combination of conventional imaging techniques led to a very high detection rate at reasonable cost. The addition of somatostatin receptor scintigraphy adds to the cost, but has a very low yield in localizations (2.5%) and does not lead to the detection of tumors in patients in whom otherwise no tumor would be demonstrated. Therefore, the use of somatostatin receptor scintigraphy as a screening method in patients with MTC should be discouraged. A different situation may be encountered in patients with minimal residual disease, in whom conventional imaging fails to demonstrate tumor. Dörr et al. (*10*) reported somatostatin receptor scintigraphy SPECT images to be concordant with the calcitonin gradient in selective venous sampling in five of seven patients with minimal residual disease. In these patients, therefore, somatostatin receptor scintigraphy might be of use.

Paragangliomas

High-resolution CT scanning in combination with MRI is an effective imaging regime for paragangliomas (*11,12*). However, this type of imaging is usually limited to the site where a paraganglioma is clinically suspected. In our series, CT scanning or MRI of the site where a paraganglioma was primarily expected was in most cases combined with ultrasound of the neck, to detect multicentricity. With somatostatin receptor scintigraphy, however, unexpected additional paraganglioma sites were found in 36% of patients with known paragangliomas.

In patients who are suspected of paraganglioma, the strategy with the best cost-effectiveness ratio is CT scanning of the region where a paraganglioma is suspected, followed by somatostatin receptor scintigraphy to detect multicentricity and metastases. This approach leads to a cost increase of DF1 799/patient, but is comparable to conventional imaging if the cost is expressed per lesion detected (DF1 532 versus DF1 669/lesion, respectively). The benefit in terms of patient management, i.e., surgery of additional lesions at an early stage, is obvious because small paragangliomas can usually be successfully resected, but surgical complications and mortality are high in larger tumors (*13*).

Endocrine Pancreatic Tumors

Gastrinomas. Somatostatin receptor scintigraphy demonstrated lesions in 92% of our patients with gastrinomas. Previously unrecognized sites were found in five of 12 patients (42%). Scherübl et al. (*14*) reports positive scans in three of three patients, Zimmer et al. (*15*) in five of five patients and Joseph et al. (*16*) in ten of 11 patients. The last investigators also report additional findings in five of 11 patients. Recently, Reynolds et al. (*17*) from NIH, Bethesda reported positive scans in 72% of 57 gastrinoma patients and superior results of octreotide scintigraphy compared to CT, MRI and angiography. The sensitivity of CT scanning, MRI, ultrasound and angiography that we found (50% in terms of patients in whom any lesion was demonstrated) is comparable to data in other reports (*15,17,18*). Endoscopic ultrasound has been reported to have a detection rate of 83% for gastrinomas (*18*). In a prospective study by Zimmer et al. (*15*) this technique was compared with somatostatin receptor scintigraphy: endoscopic ultrasound was positive in four of five patients, somatostatin receptor scintigraphy in all patients. Limitations of endoscopic ultrasound are that only tumors in the duodenum and pancreas may be detected and the method requires skill and expertise.

With somatostatin receptor scintigraphy and CT scanning of the upper abdomen the detection rate of primary tumors in our group was 75%, and 100% of lesions demonstrated by any technique were found. Though causing a cost increase of DF1 1042 per patient compared to conventional imaging, it should be considered that the failure to demonstrate a gastrinoma that can be operated will lead in the worst case to repeated operations for gastric ulcers or even fatal complications, in the best case to prolonged medical therapy and frequent check-ups with repeated radiological investigations. Also of interest in this respect is a recent report by Lebtahi et al. (*19*) from Bichat Hospital, Paris: these investigators report that of 72 patients with metastatic carcinoid or islet cell tumors who according to conventional imaging were candidates for liver surgery, the results of somatostatin receptor imaging resulted in canceling planned partial hepatectomies or liver transplantations in 19 patients (26%).

Insulinomas. Somatostatin receptor scintigraphy demonstrated tumor localizations in ten of 24 (42%) of our patients. The failure to localize insulinomas in a substantial number of patients has also been reported by others (*8,14–16,20*), and may be due to the absence of somatostatin receptors or the presence of a somatostatin receptor that does not bind octreotide (*21*). From the cost-effectiveness analysis, we conclude that the highest yield in tumor detection against the lowest cost is obtained if CT scanning is applied first in all patients. Because nearly all insulinomas are solitary tumors, there is no need to combine this investigation with whole-body techniques if a tumor is demonstrated. If CT scanning shows no tumor, somatostatin receptor scintigraphy should be performed, followed by angiography if the latter investigation also fails in localizing the tumor.

SCLC

With somatostatin receptor scintigraphy, the primary tumors were demonstrated in all our (untreated) patients with SCLC, but only part of the metastases. Additional information, within some of the patients a potential impact on staging and treatment, was found in more than half of the patients. Leihta et al. (*22*), using [^{123}I-Tyr^3]-somatostatin receptor scintigraphy in treated patients, and O'Byrne et al. (*23*), using [^{111}In-DTPA-D-Phe^1]-octreotide scintigraphy in untreated patients, also report the visualization of 84% and 100% of primary tumors, respectively, and part of the known metastases. Both report the unexpected finding of brain metastases. Recently, Kirsch et al. (*24*) reported the absence of any additional information with somatostatin receptor scintigraphy, but their scanning protocol, using a whole-body scanning technique with a scan speed of 3 cm/min at 24 hr, may not be adequate. Also, separate lateral spot images of the head are important to detect brain metastases in SCLC. Therefore their conclusion, that somatostatin receptor scintigraphy does not have an impact on patient management, seems off-hand.

Inclusion of somatostatin receptor scintigraphy in the staging protocol of patients with SCLC led to an upgrading in 5 of 14 patients (36%) with LD. At lowest cost this could be achieved by only scanning those patients who with the conventional work-up seem to have LD. The cost increase (as compared to a conventional work-up only (DF1 607/patient)) must be weighed against unnecessary treatment in 36% of patients with LD (i.e., local chest radiotherapy if a complete remission is achieved). Applying somatostatin receptor scintigraphy only in patients with LD would leave brain metastases unnoticed in three patients in our group. In staging SCLC, CT scanning of the head has been abandoned in many centers because of its low sensitivity in detecting brain metastases. Irradiation of the brain is therefore postponed until neurological symptoms herald their presence. From a radiotherapeutical point of view, it would be preferable to irradiate brain metastases when they are small. Applying somatostatin receptor scintigraphy in the work-up of every patient with SCLC demonstrated otherwise undetected brain metastases in 19% of patients in our series. The cost increase compared to the conventional work-up is justified by the therapeutical consequences: irradiation of the brain at an early stage which may lead to a postponement of neurological symptoms and a better quality of life.

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