Assessment of the Cost of Fine-Needle Aspiration Cytology as a Diagnostic Tool in Patients With Thyroid Nodules

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Key Words: Fine-needle aspiration cytology; Cost; Thyroid nodules; Diagnosis

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Abstract

Fine-needle aspiration cytology (FNAC) is the reference diagnostic tool in patients with thyroid nodules. Because the true diagnosis is based on histopathologic findings, the final diagnosis of nodules not operated on is postponed, impacting the cost. We aimed to determine the cost of FNAC by taking account of diagnostic mistakes, failures, and follow-up of patients who did not have surgery.

A Markov model described the management of patients according to initial cytopathologic results. Estimates for accuracy values and follow-up were derived from a retrospective study of 624 patients. Costs were computed from the hospital perspective. Sensitivity analyses were performed.

Of the lesions, 381 were cytopathologically classified as benign, 15 as malignant, 57 as “suspicious,” and 171 as unsatisfactory. The cost of diagnosis was 1,145 euros (€). Cost was significantly affected by the unsatisfactory specimen percentage (27.4%), without which the cost would be reduced by 35.5%, to €738.

Cost depends on cytopathologist performance and the unsatisfactory rate. In the future, routine ultrasound guidance and on-site assessment of cytopathologic adequacy would help reduce costs.

The prevalence of thyroid nodules is estimated at 4% to 7% in the general population.1 Because they are asymptomatic, most nodules are found incidentally. Only 5% are malignant,1,2 and the challenge for physicians is to identify the few malignant nodules among a large number of benign nodules. Fine-needle aspiration cytology (FNAC) is widely recommended for diagnosis of thyroid nodules2-4 because it is simple and safe. Cytopathologic results may be classified into 4 categories: benign, malignant, “suspicious,” and unsatisfactory. Surgery is performed when FNAC proves the lesion to be malignant or suspicious or when the nodule is large or causes compression symptoms.

Histopathologic results permit estimation of the diagnostic accuracy of the method. In a review of 18,183 FNAC cases from 7 large series,5 the mean sensitivity and specificity of the procedure were 83% and 92%, respectively, with low false-positive (mean, 3%) and false-negative (mean, 5%) results. The diagnostic accuracy of the method6-8 may be improved by ultrasound guidance (US-FNAC). Moreover, FNAC is a cost-effective diagnostic method9-14 compared with scintigraphy and biopsy, and this was studied in patients who underwent operation.5 FNAC generated a lower unit cost, significantly reduced medical costs by avoiding surgery in 25% of patients with benign thyroid disease (true-negative results), increased the percentage of malignant lesions found at surgery (from 14% to 39%), and shortened the postponement of treatment for thyroid cancer.

An extensive body of literature exists on the diagnostic accuracy and the cost of FNAC in patients who undergo operation,5,15-17 but the management of patients who do not has rarely been taken into account. Patients who do not undergo operation are usually followed up with a clinical
examination, ultrasound examination of the neck, or repeated FNAC, until the final diagnosis. Unsatisfactory specimens represent 10% to 30% of the prepared smears and lead to repeated FNAC procedures and delayed diagnoses. These additional procedures influence the cost, and no study has yet evaluated the cost of follow-up of patients who do not undergo operation.

The present study was, therefore, conducted to assess the cost of FNAC as a diagnostic tool for patients with thyroid nodules. We developed a Markov model that takes into account the accuracy of the procedure and unsatisfactory specimens and the follow-up of patients who do not undergo surgery.

Materials and Methods

Decision Model Structure and Assumptions

Determining the cost of a true (final) diagnosis was accomplished by using a decision-analytic model. We developed a Markov model, ie, a multistate transient model in which patients make transitions among various collectively exhaustive and mutually exclusive health states at different rates for extended periods (cycle). The aim of the model is to describe the management and the care process of patients with thyroid nodules according to initial cytopathologic results. Each clinically important event for the diagnosis, such as a repeated FNAC, thyroid surgery, or a clinical examination, is modeled as a transition from one state to another. Each Markov cycle corresponds to a follow-up visit.

In the decision-analysis model, the first decision node for a given patient is the first FNAC result: patients are then distributed into 4 transient states according to cytopathologic results, ie, malignant, benign, suspicious, and unsatisfactory. If a patient undergoes thyroid surgery, the histologic result provides the final diagnosis (benign or malignant) that is considered the “gold standard,” and the patient makes a transition into 1 of 4 absorbent states. These 4 absorbent states are defined, corresponding to the cytopathologic result, when the histopathologic diagnosis is known, ie, true-positive, true-negative, false-positive, and false-negative. When a second FNAC is performed in a patient who does not undergo surgery, the patient makes a transition into the state corresponding to the cytopathologic result of the second FNAC. The patient who has only a clinical examination remains in the same transient state. The simulation is then run for a hypothetical cohort of patients, up to 3 cycles. The diagnosis is defined as true (or final) when the status of the nodule can definitively be classified as benign or malignant by histologic examination for patients who undergo operation or when patients who do not undergo surgery remain in the same transient state during 3 cycles. At the end of these 3 cycles, the assumption is made that all patients remaining in the suspicious or unsatisfactory transient states will end up in an absorbent state following surgery.

Data

We derived estimates for diagnostic variables and accuracy values from a retrospective study reviewing all consecutive patients who underwent a first thyroid FNAC examination between January 2003 and December 2005 at the Institut Gustave Roussy (IGR), Villejuif, France. Data on patient characteristics (age, sex, nodule size, number and type of nodules) and surgical and follow-up procedures were extracted from the hospital computerized medical record. Data concerning FNAC examination (date, name of practitioner, under guidance or not) and cytopathologic (coded into 1 of the following 4 categories: malignant, benign, suspicious, and unsatisfactory) and histologic results were extracted from the database of the pathology department at IGR. Data on the follow-up of patients, repeated FNAC, and clinical examinations performed for patients who did not undergo surgery were also collected until June 30, 2006.

Cytopathology

According to Faquin, lesions derived from follicular cells may be classified as follows: (1) benign when aspirates are hypocellular to moderately cellular with moderate to abundant colloid and follicular cells have round nuclei of uniform size; (2) suspicious when aspirates suggest a follicular neoplasm, ie, hypercellular sample with scant colloid and a significant proportion of microfollicles, trabeculae, or crowded overlapping clusters of follicular cells (also includes lesions consisting of oncocytic [Hürthle cell] neoplasms); (3) malignant when cellular features of papillary, insular, undifferentiated, or medullary thyroid carcinoma are present; and (4) unsatisfactory for cytopathologic examination.

Costs

Costs were full costs estimated from the hospital perspective, which in France, corresponded to the payer’s perspective. A microcosting study was performed to determine the unit cost of FNAC examination at IGR. It included costs for all visits with a clinician and for performing the FNAC examination and processing and interpreting the sample. Resources included medical devices and supplies, personnel costs, and the depreciation cost of medical equipment, plus overhead costs. They were recorded at IGR via a prospective study of 167 consecutive thyroid FNAC examinations performed between January and October 2005. The time taken by each category of personnel (clinician, radiologist, technician, secretary, and cytopathologist) to perform the FNAC examination and process and interpret the sample was noted. The unit acquisition prices for consumables were based on 2005 rates.
expressed in euros ($\zeta$). Personnel costs were determined by using the average hourly wage of each professional category at IGR. The cost of a consultation was obtained by multiplying the mean duration of the consultation by the average hourly wage of a consultant at IGR.

The cost of the hospital stay for a thyroidectomy was extracted from the hospital cost accounting system. It included direct medical costs (medical supplies, laboratory tests, and radiology) and overhead costs and represents actual costs.

Because the study aimed at computing the cost of the diagnosis alone (rather than the cost of thyroid cancer treatment), we decided to use the following rules for attributing the cost of surgery. For patients who had malignant or suspicious cytologic findings and ultimately had a malignant tumor diagnosed by histologic examination (true-positive results), surgery was the treatment of choice of the carcinoma and its cost was, therefore, not considered a cost of the diagnosis. In patients with benign cytologic findings who had undergone surgery to relieve compression symptoms or for aesthetic reasons but not to confirm the cytopathologic diagnosis, the cost of surgery was not attributed to the failure of the FNAC procedure. For patients with an unsatisfactory FNAC specimen, the decision to treat the patient included the need to know the nature of the nodule (certainties of diagnosis) and the need for care (owing to a large nodule and/or compression symptoms). Because it is difficult to attribute the cost to one or another, in the basal model, the cost of surgery was applied to all patients with unsatisfactory cytologic results who had undergone surgery, whatever the final histopathologic result. Based on this critical assumption, a sensitivity analysis was performed. We considered that during the first 2 cycles of the model, surgery was performed for reasons unrelated to diagnosis (to relieve large nodules or for cosmetic reasons). Conversely, during the last (or third) cycle, FNAC failed to provide a diagnosis and the specimen was assessed to know the nature of the nodule (production of knowledge). Under this assumption, the cost of surgery was applied only for the last cycle.

Indeed, a complementary analysis was performed to incorporate into the model the indirect costs related to day losses in active patients (ie, employed patients or those seeking employment), from the societal perspective. In France, loss of income is partially compensated by the National Sickness Fund, and the difference is the responsibility of the patient. Thus, by adding total hospital cost and sick leave costs, the total budgetary impact of the diagnosis was estimated. The estimation of the duration of sick leave was extracted from a study in process at our center, which involved the evaluation of the length and the cost of sick leave in patients with thyroid cancer treated by total thyroidectomy and radioiodine ablation. Data on sick leave duration was collected in active patients from the week before surgery to 3 months after radioiodine ablation. The value of 1 day of sick leave compensation was estimated at $\zeta27. Patients’ related costs represented uncompensated loss of income, and they were computed for active patients. In France, the daily amount can be calculated as the difference of the mean net income per day minus daily compensation received.

**Statistics and Sensitivity Analysis**

Cases that had been cytopathologically classified as malignant or suspicious and finally diagnosed as malignant at histologic analysis were considered true-positives. Cases with benign or unsatisfactory cytopathologic results and with a benign histologic confirmation or a benign clinical course were considered true-negatives. The false-positive category comprised cases with suspicious or malignant cytologic results and benign histologic findings, whereas false-negative diagnoses were cases with benign or unsatisfactory cytopathologic findings and malignant histologic findings.

We performed several 1-way sensitivity analyses for key model parameters, including the rate of initial unsatisfactory cytologic results, the rate of malignancy among suspicious cases, and the rates of false-negative and false-positive results.

To test the impact of a lower rate of unsatisfactory specimens on the cost of a true diagnosis, we assumed that the same proportion of patients would be distributed between the 3 other transient states (malignant, benign, and suspicious) as in our retrospective study. If $T_i_0$ was the initial rate of unsatisfactory results and $T_i_1$ a lower rate we wanted to test, then $T_i_1$ could be defined as $T_i_1 = T_i_0 \times k$, with $0 < k \leq 1$. The difference ($T_i_0 – T_i_1$) was distributed among the 3 other transient cytopathologic states. The corresponding new rate of malignant ($T_m_1$), benign ($T_b_1$), and suspicious ($T_s_1$) was calculated as follows:

$$T_m_1 = T_m_0 + [T_i_0 \times T_m_0 \times (1 – k)/(T_b_0 + T_m_0 + T_s_0)]$$

$$T_b_1 = T_b_0 + [T_i_0 \times T_b_0 \times (1 – k)/(T_b_0 + T_m_0 + T_s_0)]$$

$$T_s_1 = T_s_0 + [T_i_0 \times T_s_0 \times (1 – k)/(T_b_0 + T_m_0 + T_s_0)]$$

Retrospective and prospective data were collected on Epi Info software (version 3.3.2) (Centers for Disease Control and Prevention, Atlanta, GA). The model was developed using decision-analysis software from TreeAge Data 4.0 Software (TreeAge Software, Williamstown, MA).

**Results**

**Primary Data Sources and Identification of Baseline and Transition Probabilities**

Between January 2003 and December 2005, 624 patients with thyroid nodules underwent FNAC examination. The mean ± SD age of patients was 48.6 (± 14.8) years, and 508 (81.4%) were female. The mean ± SD diameter of the largest nodule was 26.8 (± 11.5) mm. Each FNAC sample was processed by 1 of 6 practitioners (4 endocrinologists and 2 surgeons), but
none was performed in the presence of a cytopathologist or in a
1-stop clinic. FNAC examination was initially performed under
ultrasound guidance in 186 patients (29.8%) with a smaller
nodule (22 vs 29 mm for classic FNAC).

Baseline Data

The model and its initial transition probabilities are given
in Figure 1. The first node of the model for each patient cor-
responds to the results of the first FNAC, which were malign-
inant in 15 cases (2.4%), benign in 381 (61.1%), suspicious
in 57 (9.1%), and unsatisfactory in 171 (27.4%). These rates
represented the initial probabilities.

The 15 patients with a malignant FNAC result under-
went surgery, and all lesions were diagnosed as malign-
ant by histologic examination. Consequently, all of these
patients made a transition into the absorbent state called
true-positive in the model.

Of the 381 patients with a benign FNAC result, 93
(24.4%) underwent surgery because of compression symp-
toms or a recent increase in nodule size. At histologic exami-
nation, 87 specimens (94%) were benign (true-negative) and
6 (6%) were malignant (false-negative). Follow-up of the 288
patients who did not undergo surgery mainly involved clinical
examination (204 [70.8%]) or a repeated FNAC examination
(84 [29.2%]). The results of the second FNAC examina-
tion were as follows: malignant, 0 (0%); benign, 64 (76%),
suspicious, 6 (7%); and unsatisfactory specimen, 14 (17%).
Patients were then assumed to transit to the state correspond-
ing to the results of this second FNAC examination until a
new diagnostic event occurred.

The first FNAC result was suspicious in 57 patients who
underwent surgery (46 [81%]) or were followed up (11 [19%]).
Among the 46 patients who underwent surgery, 16 (35%) had
a malignant tumor diagnosed by histologic examination and,
thus, made a transition to the true-positive state, whereas the
other 30 (65%) patients with benign histologic findings made
a transition into the false-positive state. Follow-up of patients
who did not undergo surgery involved a clinical examination,
and these patients remained in the state called suspicious.

Of the 171 patients with initially unsatisfactory cyto-
pathologic specimens, 128 (74.9%) had a subsequent clinical
examination (47 [36.7%]) or another FNAC examination (81
[63.3%]) with the following results: benign, 48 (59%); suspi-
cious, 4 (5%); or unsatisfactory specimen, 29 (36%); none were
malignant. Patients were then assumed to transit to a state corre-
sponding to the results of this second FNAC examination. The
other 43 patients underwent surgery, and histologic examina-
tion showed a malignant tumor in 3 and a benign lesion in 40.

Valuation of Cost

Our prospective microcosting study included data for 167
patients. At a cost of a consultation (without FNAC) of
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tion showed a malignant tumor in 3 and a benign lesion in 40.
The cost (from $1,145 to $743) of the procedure would be obtained with an absence of unsatisfactory specimens. The sensitivity analysis, which consisted of applying the cost of surgery only during the last cycle for unsatisfactory cytopathologic results, showed the total cost of FNAC examination would be reduced to $516 per patient. This important reduction of the cost confirms that the cost of diagnosis is highly dependent on the rate of unsatisfactory specimens and on the clinician’s judgment of whether to perform surgery.

A sensitivity analysis involved the univariate variation of histology outcomes:

- **Malignant**
  - Histology +: 100%
  - Histology -: 0%
- **Benign**
  - Histology +: 6.6%
  - Histology -: 93.4%
- **Suspicious**
  - Histology +: 35%
  - Histology -: 65%
- **Unsatisfactory**
  - Histology +: 8.3%
  - Histology -: 91.7%

The model of the management of patients with thyroid nodules according to initial cytopathologic results is shown in Figure 1. FNAC, fine-needle aspiration cytology.
the rate of malignancy among patients whose lesions had first been classified as suspicious by cytopathologic examination and who subsequently underwent surgery. As shown in Figure 4, a 32.2% reduction (from $1,290 to $874) in the cost of the diagnosis could be obtained if the cytopathologist was always able to give an ascertained diagnosis. It is interesting that the cost was less impacted by the number of false-negative and false-positive results. For example, varying the rate of false-negative results observed in the literature (from 1.3% to 11.5%) would marginally increase the cost of diagnosis (from $1,108 to $1,179).

If all patients had a routine US-FNAC, the cost of diagnosis would only increase from $1,145 to $1,177. This small extra cost would easily be compensated by a slight reduction from 27.4% to 25.2% in the rate of unsatisfactory specimens with the use of US-FNAC (Figure 3). This could easily be achieved because the rate of unsatisfactory specimens in our series was 20% for patients who underwent US-FNAC.

Discussion

FNAC examination has proved to be a simple, accurate, safe, and cost-effective method for the preoperative diagnosis of benign and malignant thyroid nodules. However, studies have considered the management, cost, and diagnostic accuracy values only for patients who undergo surgery. To our knowledge, this is the first study aimed at determining the cost of a true diagnosis of thyroid nodules using FNAC, by taking into account FNAC diagnostic mistakes and follow-up of patients who did not undergo surgery.

Our model shows that after 3 cycles, 9.4% of the hypothetical cohort would have had a final diagnosis of thyroid cancer. This rate is higher than that generally reported, which usually ranges from 3% to 5%. The difference may be

Table I
Unit Cost of FNAC and US-FNAC*

<table>
<thead>
<tr>
<th></th>
<th>FNAC</th>
<th>US-FNAC</th>
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<tr>
<td>Direct medical costs</td>
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<td>Personnel</td>
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<tr>
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<td>Radiologist</td>
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<tr>
<td>Laboratory technician</td>
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<td>Secretary</td>
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<tr>
<td>Total cost</td>
<td>107.7 ± 9.6</td>
<td>142.2 ± 21.8</td>
</tr>
</tbody>
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FNAC, fine-needle aspiration cytology; US, ultrasound guided.
* Data are given as cost or mean ± SD cost in euros.

Figure 2: Contribution of each cytopathologic result to the cost. FNAC, fine-needle aspiration cytology.

Figure 3: Sensitivity analysis showing the effect of the reduction in the unsatisfactory specimen rates on the cost of diagnosis in patients with thyroid nodules. US-FNAC, ultrasound-guided fine-needle aspiration cytology.

Figure 4: Sensitivity analysis showing the effect of an increased rate of malignancy on the cost of diagnosis in patients with thyroid nodules classified as “suspicious” by fine-needle aspiration cytology and who underwent surgery.
related to the effects of later detection of malignancy (follow-up) and diagnostic mistakes and also to the referral nature of IGR. False-negative results are a major pitfall in thyroid cancer diagnosis. In our model, the rate of false-negatives was estimated at 2.8%. This rate is not comparable to the 1.3% to 11.5% rate reported in studies that evaluated the diagnostic accuracy of FNAC examination, which reported incomplete results because they considered only surgically treated patients. In fact, our study takes into account follow-up data to estimate the rate of false-negative results and integrates the a posteriori detection of malignant nodules that were not detected at the first FNAC examination. Consequently, the false-negative percentage reported concerns the entire cohort of patients who underwent FNAC examination, including patients who did and did not undergo surgery. However, our results are consistent with the false-negative rates ranging from 0% to 2.3% reported in a few studies that investigated the long-term follow-up of patients with initially benign cytologic diagnoses. Finally, our false-negative rate may be underestimated given the potential development of a malignancy in a previously benign lesion, but this possibility seems rare, if it even occurs.

This low rate explains why false-negative results represented only 4.0% (46) of the cost of the diagnosis and that variation in the percentage did not significantly impact the cost. Moreover, the cost attributed to false-negative lesions is probably also underestimated because we failed to consider the economic consequences of a delayed diagnosis. Patients with false-negative results on FNAC examination and histopathologically proven thyroid carcinoma had a delay in surgical treatment for about 2 years, resulting in higher rates of vascular and capsular invasion and a 2-fold increased risk of persistent disease during follow-up, impacting the cost of the management of treatment and follow-up.

In our study, suspicious findings accounted for 9.2% of all specimens obtained by FNAC, of which 35% and 65%, respectively, proved to be malignant and benign by histologic examination (in the 81% of patients who underwent operation). From an economic perspective, specimens found to be suspicious by FNAC examination and benign by histologic examination were classified as false-positives because they corresponded to unnecessary surgeries for patients and avoidable expenses for the payer. False-positive results were found in 7.9% of patients. This rate is higher than the 0% to 7.7% rate previously reported among cases with malignant cytopathologic results and benign histologic findings. The sensitivity analysis showed that better diagnosis of malignant nodules in patients with suspicious results would decrease the cost from $1,140 to $868 per patient. In the future, the use of new techniques, such as immunocytochemical analysis with thyroid peroxidase or galectin 3 antibodies or gene expression studies should improve this rate, but these techniques are not yet recognized standards, nor are they widely available. False-positives amounted to $271, ie, 23.7% of the cost of diagnosis, and this cost is probably underestimated. The inclusion of indirect costs of sick leave increased costs up to $1,467.

Our sensitivity analyses showed that the cost may be significantly reduced, conditional to the performance of the cytopathologist and the rate of unsatisfactory specimens. Reduction of this rate from 27% to 0% would lead to a cost reduction of 35.1% (from $1,145 to $743 per patient). The results of the sensitivity analysis showed that the extra cost of routine US-FNAC would be offset if it permitted a relative reduction of the rate of unsatisfactory results of 2.2% or more (from 27.4% to 25.2%; Figure 3). The application of the Markov model to the subgroup of patients who had a US-FNAC as the first test showed a reduction of the cost (from $1,145 to $408 per patient). According to the literature, the routine use of US-FNAC allows a decrease in the rate of unsatisfactory specimens from 15% to 20% down to 5%. US-FNAC makes the diagnosis possible in 50% to 63% of initially unsatisfactory FNAC results. In addition, the on-site assessment of FNAC specimen adequacy increases the likelihood of accurate diagnosis because the risk of initial unsatisfactory cytologic specimens remains significant (5%-15%), and the rate of cancer in surgically resected nodules is higher in unsatisfactory than in benign FNAC results (7.1% and 2.1%, respectively). It was estimated that on-site evaluation allowed a benefit of $55 per case, based on a reduction of repeated FNAC owing to unsatisfactory specimens (1% vs 20%) and despite the additional cost of $177 per case for the immediate professional service.

The important distinguishing feature of the model is the consideration not only of the cost of FNAC examination but also the entire diagnosis process, combining specific characteristics of the test, relative skill of the cytopathologist, and the clinician’s judgment as to whether surgery should be performed. The model had 2 limitations. First, the model described joint production of diagnosis process and care, for which it is difficult to separate the costs. Two scenarios were calculated: if the cost of surgery was applied to all unsatisfactory results that resulted in surgery, the cost of diagnosis reached $1,145, whereas it reached only $516 when the cost was attributed only to a fraction of the lesions. Second, the contribution of the cost of surgery to the total cost of diagnosis is very important (Figure 2). The clinical judgment of whether to operate, which determined the surgery frequency by center, led to great variations in the diagnosis cost across institutions.

Data on the care process of patients and resources consumed were collected retrospectively from the computerized medical records of the hospital. Consequently, the perspective of the economic evaluation was restricted to the hospital per-
spective because of the absence of data on extrahospital costs. The hospital perspective was adopted because we wanted to inform clinicians and managers of the budgetary impact of the diagnosis of thyroid nodules. Certain costs, such as patient-related costs, loss of work income, litigation costs in case of diagnostic errors, and transport costs, were excluded from the basal analysis, leading to an underestimation of the cost of diagnosis. The hospital perspective can be considered a limit of the model: nations with different cost structures may prefer other perspectives. In the United States, a more appropriate perspective may be from the payer viewpoint because hospitals and services would generate more revenue based on unsatisfactory FNAC specimens because of repeated FNAC procedures. Nevertheless, a complementary analysis was completed by adding compensated and uncompensated sick leave costs. Data collection and the model were assessed at only 1 study site, so the generalization of our results remains questionable. However, the aim of this study was not to generalize the results from our particular center to practices throughout France, but to provide practitioners with a model allowing them to evaluate their own costs. More generally, our model can also be used by other centers to assess the performance and the cost of their own diagnostic process, from the initial FNAC examination to the final assessment of the patient’s status.

Conclusion

This study demonstrates that the cost of a given procedure for a true diagnosis exceeds its unit cost of production. The cost study of a diagnostic procedure should take into account its predictive value, ie, its errors and its failures (ie, unsatisfactory specimens). Thyroid FNAC failures generate a much higher cost than errors. Routine use of US-FNAC and on-site assessment of the adequacy of cytopathologic specimens should dramatically reduce the rate of failures and, thus, the cost of a true diagnosis.

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References


