Section: General Surgery

Original Research Article

EVALUATION OF A SCORING SYSTEM FOR PREDICTING THE RISK OF MALIGNANCY IN THYROID NODULES USING CLINICAL, LABORATORY AND SONOLOGICAL DATA

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Abstract

Background: Many patients present to the surgical department with a thyroid nodule. However, not all require surgery; only 5-6% of these are malignant. The present study aimed to evaluate a scoring system using clinical, laboratory and sonological data for predicting the risk of malignancy in patients with thyroid nodules. **Material & Methods:** This prospective observational study involved 50 patients admitted to MMC, Chennai, with thyroid nodules. An analysis of a scoring system combined clinical findings, radiological features and laboratory findings such as TSH level and FNAC report. The final scores were compared with the post-operative histopathology of the patient, and the risk of malignancy was predicted. **Results:** The scoring system had a maximum score of 26. The observed score ranged from 3 to 19, with a mean score of 11. All the malignant cases were observed with scores greater than 11. The incidence of thyroid carcinoma for scores 1 to 11 was 0%, 12 to 13 was 20%, 14 to 18 was 75%, and ≥19 was 100%. The average risk of malignancy for a score ≤11 was 0%, and for a score >11 was 54.166%. The sensitivity and specificity were 70.2% and 100%, respectively. The positive and negative predictive value for the scoring system was 100% and 43.83%, respectively. A greater risk of malignancy was reported, with patients scoring higher than 11. The risk of malignancy increased with increasing scores and was found to be 100% for a score ≥16. **Conclusion:** This scoring system has proved to be accurate in predicting the risk of malignancy in patients with thyroid nodules.

INTRODUCTION

Thyroid nodules are extremely common (20 % to 76 %) in the general population, whose frequency has increased due to the widespread use of imaging, which leads to incidental detection of thyroid nodules.[1,2] There are several methods for the diagnosis of thyroid nodules. Palpation, the least sensitive method, can detect about 2 -6 % of nodules, while 19 -35% of thyroid nodules are detectable via ultrasonography (USG).[3] Despite the high prevalence of thyroid nodules, only 1.6% to 12% are malignant.[4]

A definitive diagnosis of thyroid cancer is made by fine needle aspiration (FNA) thyroid nodule biopsy. The biopsy results are reported in a standardised classification known as Bethesda.[5] Six diagnostic categories are used in Bethesda classification ranging from not diagnostic, unsatisfactory and benign to suspicious for malignancy and malignant.[6] Due to the high sensitivity of the Bethesda system, it is an effective classification that guides clinicians with a clear cytology report.[7] Although FNA is the most accurate method for diagnosing cancers, selecting those nodules that need FNA biopsy is challenging for endocrinologists. US is an accessible, noninvasive method that can detect patients with thyroid nodules and assist specialists in differentiating between benign and malignant tumours using specific US parameters.[8] Malignancy is more suspected in nodules with sonographic characteristics including hypoechogenicity, increased intranodular vascularity, irregular margins, microcalcifications, absent halo and a taller-than-wide shape measured in transverse dimensions.[9]

Clinical characteristics, laboratory investigations and imaging modalities have been associated with the risk of malignancy in thyroid nodules. These data have

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been integrated into various scoring systems. An ideal scoring system would reduce the need for costly imaging and unwanted exposure and, at the same time, increase the precision of decision-making.[10]

In our study, we have put together a scoring system using clinical, laboratory and radiological data for evaluating the risk of malignancy in thyroid nodules. These risk factors have been analyzed in various other studies and found to have specific predictive value for malignancy. Our study aims to evaluate this scoring system for predicting the risk of malignancy.

MATERIALS AND METHODS

The prospective and observational study was conducted on 50 Patients with clinically palpable thyroid nodules at an initial presentation at Rajiv Gandhi Government General Hospital, Chennai, from 01 August 2015 to 31 July 2016. The prior written consent and ethical committee approval were taken before the start of the study.

Inclusion Study

Patients of either sex with clinically palpable thyroid nodules at initial presentation were included in the present study.

Exclusion Criteria

Patients have non-palpable thyroid nodules. Patients whose FNAC samples were unsatisfactory were excluded from the study.

Methodology

A detailed history was taken from the study group to establish the proper diagnosis per the proforma. A thorough physical examination was done in each case. FNAC, USG neck and Thyroid function test was done for all the patients. After proper evaluation and preparation, patients who required surgical management were taken up for surgery. Strict aseptic precautions were followed during the operation. Meticulous techniques were practised as far as possible. The operation procedure and related preoperative factors were immediately observed and recorded in the data collection sheet. The post-operative histopathological examination (HPE) report was collected. After completing the collection of data, it was compiled in a systematic way. The preoperative clinical, radiological and TSH levels were analysed, and a cancer risk score was assigned to each patient per the designed scoring system. This score was compared with the post-operative HPE report to predict the risk of malignancy. The observed results were subjected to statistical analysis. The following observations were made. The risk factors used in the scoring system were assigned scores based on the existing McGill Thyroid Nodule Scoring System. The parameters were assigned scores based on the previously demonstrated sensitivity and specificity of each parameter for carcinoma. A maximum cancer risk score of 26 is attainable with this scoring system.

Pre-tested structured questionnaires collected data. Data were collected from all the respondents by direct interview after getting informed written consent from them or their legal guardians.

Data Analysis

The data was gathered and entered into an Excel file. Frequencies mean percentages, standard deviations, chi-square coefficients of correlation, and p values were determined using the SPSS-16 software. The significance of a difference between two quantitative variables was calculated using the Chi-square test, and a p-value of less than 0.05 was considered significant.

RESULTS

This prospective study was done at the Institute of General Surgery at Madras Medical College, Chennai. The study period was from August 2015 to July 2016. The total number of cases was 50, of which the cases confirmed with malignancy was 13.

In the present study, female predominance (34) was reported, and 10 female patients reported malignancy, whereas only 3 male patients were found with malignancy. An equal number of patients reported more than 45 years of age and less than 45 years. Only one patient had a family history of thyroid malignancy, and none had a history of exposure to ionising radiation. A total of 13 patients on clinical had hard consistency of the thyroid gland. Among those diagnosed with malignancy, 12 had hard consistency of gland. Of all patients, 29 had serum TSH level >1.4mIU/L and 21 had TSH levels <1.4IU/L. Among those diagnosed to have malignancy, 12 had TSH levels>1.4IU/L [Table 1].

Thirty-nine patients had USG features taller than their thyroid's wider shapes. Among these patients, ten patients were diagnosed with malignancy postoperatively. Of 13 patients diagnosed with malignancy, three patients had a size of a gland between 2-2.9cm; four had a size between 3-3.9 cm, and 6 had a size ≥4 cm. A total of 26 patients had a solitary nodular goitre, and 24 patients had a multinodular goitre. The seven patients with malignancy had solitary nodules, and six had a multinodular goitre. A total of 39 patients showed the presence of hypoechogenicity nodules on USG. All the patients diagnosed with malignancy had hypoechogenicity nodules on USG. 13 patients had intra-glandular calcification determined by USG. Among these patients, ten were confirmed to have malignancy post-operatively. Of the 50 patients evaluated, 20 had cervical lymphadenopathy confirmed radiologically and 30 did not have lymphadenopathy. A total of 11 patients with proven malignancy had lymphadenopathy. The 33 patients showed vascularity of the gland on USG. All 13 patients with malignancy had increased vascularity [Table 1].

The FNAC report of 30 patients under study was found to be benign, 13 patients had a lesion suspicious of malignancy, and seven patients had outright malignancy. Among the patients whose

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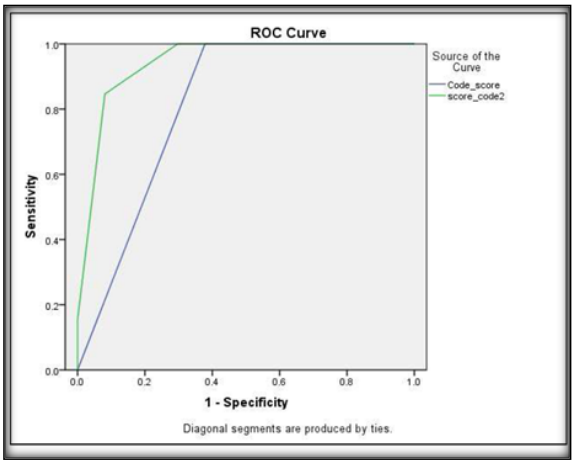
FNAC report was suspicious of malignancy, 6 out of 7 were malignant [Table 2].

The scores ranged between 3 and 19, with a mean score 11. The incidence of thyroid carcinoma for scores of 1 to 11 was 0% (0 out of 24 patients), 12 to 13 was 20% (2 out of 10 patients), 14 to 18 was 75% (9 out of 12 patients) and ≥19 was 100% (2 out of 2 patients). A score ≤11 correlated with a 0% risk of malignancy, whereas a score>11 implied a 54.166% risk of malignancy when correlated HPE report. This greater risk demonstrated for patients above a score of >11 is statistically significant ($p<0.0001$, $\chi 2 = 14.965$, df = 1) [Table 3].



Test Result Variable(s)	Area	Std. Error	Asymptotic Sig.	Asymptotic 95% Confidence Interval	
				Lower Bound	Upper Bound
Mean score	.811	.059	.001	.695	.926
MTNS score	.943	.031	.000	.881	1.000

Figure 1: ROC curve analysis

Table 1: Observation of demographic and other evaluation parameters of patients

Parameters (Score)	Frequency (n) (n=50)	
	Benign	Malignant
Age Group		
<45 (0)	18	7
<45 (1)	19	6
Gender		
Female (0)	34	10
Male (1)	3	3
Family history of malignancy		
Present (3)	0	1
Absent (0)	37	12
Exposure to ionising radiation		
Present (3)	0	0
Absent (0)	37	13
Hard consistency		
Present (2)	1	12
Absent (0)	36	1
TSH LEVEL		
> 1.4 mIU/L (1)	17	12
< 1.4 mIU/L (0)	20	1
Taller than wider shape		
Present (1)	29	10
Absent (0)	8	3
Size of the gland by USG		
2 – 2.9 CM (2)	8	3
3 – 3.9 CM (3)	15	4
≥ 4 CM (4)	14	6
Nodularity		
Solitary (2)	19	7
Multiple (1)	18	6
Hypoechogenicity by USG		
Present (1)	26	13
Absent (0)	11	0
Calcification		
Present (1)	3	10
Absent (0)	34	3
Cervical lymphadenopathy		
Present (2)	9	11
Absent (0)	28	2
Vascularity		
Increased (1)	20	13
Normal (0)	17	0

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FNAC report	Number of cases (n)
Benign (1)	30
Suspicious of Malignancy (2)	13
Malignant (3)	7

Table 2: Final pathology according to the scoring system

Score	Benign	Malignant	Percentage of Malignancy (%)
1	0	0	0
2	0	0	0
3	1	0	0
4	1	0	0
5	1	0	0
6	3	0	0
7	4	0	0
8	5	0	0
9	4	0	0
10	4	0	0
11	3	0	0
12	4	1	20
13	4	1	20
14	2	1	33.33
15	1	1	50
16	0	3	100
17	0	1	100
18	0	3	100
≥19	**0**	2	100

Table 3: Score versus HPE report

		Post-operative HPE		Total
		Benign	Malignant	
Score	≤11	26	0	26
	>11	11	13	24
Total		37	13	50

DISCUSSION

Increasing age is long recognised as a well-established threat for thyroid malignancy. Age >45 years is incorporated into the American Joint Committee on Cancer (AJCC) staging.[10] A study of the Surveillance, Epidemiology, and End Results (SEER database) found, among 9904 patients with papillary thyroid cancer (PTC), that age >45 years was significantly associated with bad outcomes on multivariate analysis.[11] Aged>45 years scored 1 in our study due to specificity limitations. 52% of malignant cases had age >45 years.

It is well known that thyroid malignancies are more common in females than males. But male gender is a solid risk factor for carcinoma and hence was given a score of 1. In our study, 3 out of 13 patients diagnosed with malignancy were male (1:4.2), which is comparable to other studies.[12]

A family history of thyroid cancer, or in a first-degree relative, is also one of the few well-established risk considerations for carcinoma. Owing to the vast nature of support in the literature and the universally accepted nature of family history as a risk factor, it was also given 3 points within the scoring system.13 In our study, one patient had a history of thyroid malignancy in the mother, and this patient was also diagnosed with papillary cancer post-operatively.

The Canadian National Dose Registry reported elevated standardised incidence ratios (SIRs) for thyroid cancer for both male (SIR 1.35; 90% CI 0.97–1.75) and female (SIR 1.42; 95% CI 1.19–1.69) radiation workers.[14] As little doubt exists concerning this association, a history of significant previous radiation exposure was given a score of 3 in the McGill Thyroid Nodule Score (MTNS). None of the patients in our study had a history of exposure to ionising radiation.

Several authors have agreed that nodules felt to be ‘‘stone’’ or ‘‘bone’’ hard on palpation indicate a higher likelihood of carcinoma. Raber and colleagues demonstrated a predictive value of 57% and a relative risk of 2.6 for thyroid carcinoma in the presence of this feature (95% CI 1.2–5.6).15 Hence score of 2 was assigned. 12 out of 13 patients diagnosed with a malignancy in our study had hard consistency of gland on clinical examination.

Elevated serum TSH level, even within the higher end of the range, is associated with an augmented risk of malignancy. A well-designed study of over 800 patients conducted by Haymart et al. showed that the risk of carcinoma was significantly greater when TSH levels were between 1.40 and 4.99 mIU/L compared to lower levels (35% vs 25%, p = 0.002).16 Based on these findings, TSH serum levels >1.4 mIU/L were incorporated into the scoring system and given a risk score of 1. In our study, 12 out of 13 patients diagnosed with malignancy had a serum TSH level >1.4mIU/L which is comparable to the results of Haymart et al.[16]

When imaging a nodule in the transverse direction, a height greater than the width correlates with an increased likelihood of malignancy (specificity range of 60– 93%).[17] This represents aberrant, aggressive

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growth across the natural horizontal growth planes within the thyroid gland. It is also a reflection of tumour compressibility by an ultrasound probe. The sensitivity and specificity of this finding are variable. Thus a score of only one was assigned. However, in our study, 92.30% of patients with malignancy demonstrated this feature on ultrasound.

Nodule size has been consistently associated with a greater risk of malignancy. Tuttle and colleagues showed that nodules measured to be >4 cm to palpation had a 40% malignancy rate (vs 13% for smaller lesions).18 Raber and colleagues validated this correlation between size >4 cm and malignancy via sonography. In another study, 15 Nodules measuring 3 cm or more on a sonogram conferred a 55% risk (vs 23% in smaller nodules, p <0.0001). To account for these discrepancies in the literature, we proposed that nodules of 2 to 2.9 cm be scored 2, nodules of 3 to 3.9cm a score of 3, and nodules >4cm a score of 4 points. Our study also demonstrated a greater proportion of patients with malignancy (46%) with a size greater than 4 cm.

The risk of malignancy in generalised swelling is about 3%, and in solitary thyroid nodules is about 15%. A study found malignancy in 10% of solitary nodule thyroid and 5% of multinodular goitre. In our study, 53.8% of patients with malignancy had a solitary nodule, and 46.2% demonstrated multinodular goitre.[18]

Hypoechogenicity, increased Doppler flow and calcifications are the most widely recognised characteristics that increase the index of suspicion for a malignant nodule. One study compounded the test characteristics for each feature of malignancy from seven additional studies and found hypoechogenicity to carry a 73% specificity, Doppler flows a 79% specificity, and calcifications a 91% specificity.[19] Because of high inter-observer variability and differing radiologic techniques, and because the various ultrasound findings are taken in constellation with one another, we assigned a score of 1 to each of these three features. In our study, 100 % of patients with malignancy demonstrated hypoechogenicity and increased vascularity of the gland, and 76.9% of patients with malignancy showed the presence of calcification within the gland.

Cervical lymphadenopathy is a common presentation in thyroid malignancy. The presence of cervical lymph nodes on ultrasound increased the predictive value of diagnosing thyroid cancer in suspicious nodules. Moon et al. demonstrated a 53–61% incidence of cervical lymphadenopathy in thyroid cancers.[20] In our study, cervical lymph node enlargement incidence among malignant patients was 76.92% and was assigned a score of 2.

Cytologic atypia on FNAC has been shown to represent a higher likelihood of malignancy on a relatively consistent basis. In a study by Raparia et al., FNAC predicted malignancy with a sensitivity of 86.8%, a specificity of 67.0%, a negative predictive value of 87.5% and a positive predictive value of 65.5%.[21] Our study categorised FNAC report as benign, suspicious of malignancy and malignant and assigned a score of 1, 2 and 3, respectively. In our study, 53.8 % of patients with malignancy correlated their FNAC and post-operative HPE finding. The remaining 46.2 % of patients had an FNAC report which was suspicious for malignancy, but their post-operative HPE was malignant.

The incidence of thyroid carcinoma for scores of 1 to 11 was 0% (0 out of 24 patients), 12 to 13 was 20% (2 out of 10 patients), 14 to 18 was 75% (9 out of 12 patients) and ≥19 was 100% (2 out of 2 patients). In our study, all the malignant cases had a score >11. 70.2% of benign cases had a score of ≤11, and 29.8% had a score of>11. The average risk of malignancy for patients with a score greater than the mean score of 11 was 54.166%. This greater risk demonstrated for patients above a score of 11 was also statistically significant ($p<0.0001$, $\chi 2 = 14.965$, $df = 1$). The area under the curve showed 81.1% sensitivity, similar to that of the MTNS scoring system.[10] The sensitivity and specificity for carcinoma are 70.27% and 100%, respectively. The positive and negative predictive values are 100% and 43.83%, respectively. In our study, a score ≥16 was associated with a 100% risk of malignancy.

In our study, 4 cases had pre-operative FNAC report as a benign lesion. But all four patients scored≥15 according to our scoring system, and their post-operative HPE was malignant. Thus the scoring system helps to minimise the false-negative rates of FNAC. It can make pre-operative decision-making much easier. Patients with a high score and thus a greater risk of malignancy can be carefully selected for surgery, and a more vigilant post–operative follow-up can be done.

Limitations of the study

The study was carried out over a limited period with a restricted number of patients, and there needed to be more financial and infrastructural support; it could not have been large enough to be of reasonable precision.

CONCLUSION

It can be concluded from the study's findings that this combined scoring system can serve as an accurate predictor for thyroid malignancy. It will help physicians better assess the risk that a thyroid nodule is malignant and formulate clinical decisions accordingly, in conjunction with a more informed patient. The scoring system brings high-risk patients to the forefront and is an extremely powerful and valuable resource for surgeons to aid in clinical decision-making.

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