Original Article

DOI: 10.7860/IJARS/2021/47306:2627

Radiology Section

Accuracy of Thyroid Imaging and Reporting Data Systems in Risk Stratification of Thyroid Nodules- A Retrospective Observational Study

ANTO J RICHIE[1], P MELLONIE[2]

ABSTRACT

Introduction: Thyroid cancer is the most common endocrine malignancy worldwide. Thyroid ultrasound reporting based on Thyroid Imaging and Reporting Data Systems (TIRADS) classification has enormously changed the clinical management of patients presenting with thyroid nodules.

Aim: To study the thyroid nodules using high-resolution ultrasound and to correlate the TIRADS and Bethesda system for thyroid cytopathology.

Methods and Materials: The present study was a retrospective observational study which was conducted in the Department of Radiology, Father Muller Medical College, Mangalore, Karnataka, India. Total 226 patients who came for thyroid ultrasound for evaluation of thyroid swelling were included. The thyroid nodules were evaluated based on features like shape, margin, echogenicity, internal composition, presence and type of calcification. Thyroid lesions were categorised using TIRADS classification. Diagnostic accuracy of TIRADS system was evaluated by comparing with the Fine Needle Aspiration Cytology (FNAC). Cytopathology report was considered to be the gold standard. The p-value and odds ratio were determined so that it was known how significantly the presence or absence of a specific ultrasound feature was seen associated with benign lesions and malignant lesions respectively in the study population. For each TIRADS category, the risk of malignancy was determined. Cervical lymph nodes were evaluated based on the size of lymph node, margin, necrosis, presence or absence of central echoegenic hilum and microcalcification. The percentage of cases that were accurately determined by TIRADS, (to avoid unnecessary FNAC) were determined. Data was statistically analysed using Statistical Package for the Social Sciences (SPSS Inc, Chicago, Illinois, USA), version 20.c2.

Results: The risk of malignancy in TIRADS categories 1 and 2 was found to be 0%, 0.5% in category 3, 3.85% in category 4A, 65.32% in category 4B, 84.22% in category 4C, and 100% in category 5. Out of the five sonological features assessed, shape (taller than wider) showed the highest Positive Predictive Value (PPV) (96.15%) for malignancy. Also, of the cervical lymph nodes studied, sonological features such as loss of central echogenic hilum, presence of an irregular margin, microcalcification and necrosis were found to have sensitivity of 100%, 67.15%, 43.56%, and 76.56%, respectively and specificity of 97.1%, 96.5%, 11.8%, and 35.3%, respectively to differentiate between benign and metastatic nodes. The estimated decrease in unnecessary FNACs was found to be 41.15%-84.30%.

Conclusion: The widespread use of imaging ultrasound techniques has generated an overwhelming increase in the recognition of thyroid nodules. This study will help to improve the ultrasound characterisation of thyroid nodules and establish risk groups to decide which patient should be evaluated for FNAC.

Keywords: Hypoechogenecity, Malignant nodule, Microcalcification, Thyroid cancer

INTRODUCTION

Thyroid nodule is a well demarcated area of altered echogenicity that is radiologically distinct from surrounding normal thyroid parenchyma [1]. The estimated prevalence of thyroid nodule worldwide ranges between 4-8% by palpation alone and the incidence increases to 20-48% with ultrasound examination [2]. In the last decade there has been an increase in the incidence of thyroid carcinoma due to improved ultrasound surveillance of thyroid nodules [3]. However, most of these thyroid nodules are benign, only 5-15% of thyroid nodules are malignant. Patients having high risk features such as radiation exposure and family history of thyroid cancer require thorough evaluation [4]. It is to be noted that thyroid nodules are more frequent in females as compared to males, however it is more aggressive and have higher risk of malignancy in males [5]. Hence detailed history, thorough clinical examination followed by ultrasound examination of thyroid is essential for evaluation of patients with thyroid nodule. TIRADS was first proposed by Horvath E et al., in 2009 and Kwal JY et al., recommended few modifications to it in 2011 [6,7]. The ultrasound features favouring a malignant nodule are irregular margins, solid nodules, hypoechoegenicity, microcalcification and shape taller than wider lesions. FNAC provides a rationale approach for management of patients with thyroid nodules. Bethesda system of reporting thyroid cytopathology will further risk stratify patients and help us to select patients for surgery [8,9]. Few studies have been done to risk stratify thyroid nodules by using TIRADS for thyroid ultrasound and Bethesda system for thyroid cytopathology based on Indian population. One such study done by Srinivas M et al., showed that the risk of malignancy for categories 3, 4A, 4B, 4C and 5 was 0.64, 4.76, 66.67, 83.33 and 100% respectively, also there is 0% risk of malignancy associated with category 1 and 2 [10]. Study done by Periakaruppan G et al., showed that the risk of malignancy for category 2,3,4 and 5 was 0%, 2.2%, 38.5%, and 77.8%, respectively [11]. Siddeshwar KP et al., in their study found that the risk of malignancy for category 2,3,4,5 was 0%,14.3%, 62.5% and 100%, respectively [12]. The aim of this study was to find the accuracy of TIRADS reporting in risk stratifying thyroid nodules by correlating with The Bethesda System of Reporting Thyroid Cytology (TBSRTC).

MATERIALS AND METHODS

This retrospective observational study was approved by our Institutional Scientific and Ethics Committee (protocol number: 220/20) and the study was conducted in the Department of Radiology, Father Muller Medical College, Mangalore, Karnataka, India. A total of 226 patients who underwent both ultrasound examination of thyroid in B-mode as well as FNAC of thyroid between August 2018 to August 2020 were included in the study.

Inclusion criteria: All patients who had thyroid nodule in B-mode ultrasound and also got thyroid FNAC done between August 2018 and August 2020 were included in the study.

Exclusion criteria: Normal thyroid scan (TIRADS 1) and confirmed case of thyroid malignancy (TIRADS 6) were excluded from the study.

Sample size calculator: Confidence level-95%, Confidence interval 5, population- 100 patients with thyroid nodules

Sample size needed = 80 patients.

Formula used - n = N /1+N*e2

The thyroid nodules were evaluated based on features like shape, margin, echogenicity, internal composition, presence and type of calcification. Thyroid lesions were categorised using TIRADS classification as follows: 1) normal thyroid gland; 2) benign lesions; 3) probably benign lesions; 4) suspicious lesions; 5) probably malignant lesions; and 6) biopsy-proven malignancy [13]. Diagnostic accuracy of TIRADS system was evaluated by comparing with the FNAC. Cytopathology report was considered to be the gold standard and it was done according to the TBSRTC as follows-

Category 1- non-diagnostic;

Category 2- benign lesion and non-diagnostic aspirates;

Category 3-Atypia of Undetermined Significance (AUS) or Follicular Lesion of Undetermined Significance (FLUS);

Category 4-follicular neoplasm or suspicious for a follicular neoplasm;

Category 5- suspicious for malignancy; and

Category 6-malignant [8].

Sensitivity, specificity, PPV, Negative Predictive Value (NPV), and accuracy were calculated for each TIRADS group. The p-value and odds ratio were determined so that we may know how significantly the presence or absence of a specific ultrasound feature was seen associated with benign lesions and malignant lesions respectively in the study population. For each TIRADS category the risk of malignancy was determined. Cervical lymph nodes were evaluated based on the size of lymph node, margin, necrosis, presence or absence of central echoegenic hilum and microcalcification. The percentage of cases that were precisely determined by TIRADS that could have avoided unnecessary FNAC was determined.

STATISTICAL ANALYSIS

Data was collected, tabulated, and statistically analysed using a personal computer with (SPSS Inc, Chicago, Illinois, USA), version 20.c2. The sensitivity, specificity and accuracy of TIRADS were calculated using appropriate statistical methods. Post-Hoc Tukey test was used to find the pair wise significance. Chi-square was used to find the significance of study parameters on categorical scale between two or more groups. The p-value of <0.05 was considered to be significant.

RESULTS

A total number of 226 patients were included in the study. There was a female preponderance noted as there were 187 female patients and only 39 male patients in the study population resulting in Male:Female ratio of 1:4.7. Also, the average age of the patients in present study was 32.5 (18-62 years) (Standard deviation=7.20) The average size of the thyroid nodules was 15.1mm (range of 3-42 mm) (Standard deviation=3.5). The size of malignant nodules ranged from 4-42 mm and the size of benign nodules varies from 3-37 mm.

The risk of malignancy in TIRADS categories 1 and 2 was found to be 0%, 0.5% in category 3, 3.85% in category 4A, 65.32% in category 4B, 86.22% in category 4C, and 100% in category 5 [Table/Fig-1]. Out of the five sonological features assessed, irregular margins showed highest PPV (96.15%) for malignancy, followed by hypoechogenicity (93.44%) [Table/Fig-2].

Among the 226 cases of thyroid nodules studied, 61 cases had

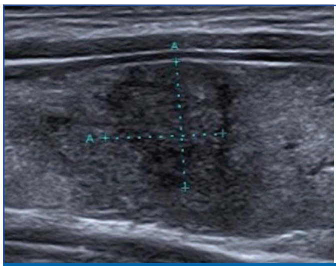
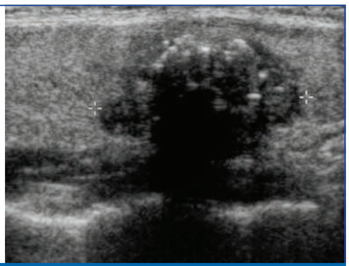
TIRADS category	Number of Malignant lesions	Number of Benign lesions	Total number of lesions	Risk of Malignancy %
1	0	0	0	0
2	0	102	102	0
3	1	94	95	0.5
4A	5	5	10	3.85
4B	2	2	4	65.32
4C	2	1	3	86.22
5	12	0	12	100

[Table/Fig-1]: Distribution of lesions according to TIRADS category with their risk of malignancy.

TIRADS features	Malignant lesion	Benign lesion	Total lesions	Odds ratio for malignant cytology	Odds ratio for benign cytology	Sensitivity in %	Specificity in %	PPV	NPV	p-value
Irregular margins										
Present	18	2	20	454.5	0.0022	81.81	99.01	96.15	98.05	<0.001
Absent	4	202	206							<0.001
Shape- Taller than wider										
Present	16	4	20	133.33	0.0075	72.72	98.03	80.67	97.08	<0.001
Absent	6	200	206							<0.001
Hypoechogenicity										
Present	15	1	16	435	0.0022	68.18	99.5	93.44	96.66	<0.001
Absent	7	203	210							<0.001
Microcalcification										
Present	13	5	18	57.4	0.0173	59.09	97.5	77.22	95.67	<0.001
Absent	9	199	208							<0.001
Solid composition										
Present	10	3	13	55.8	0.0179	45.45	98.5	76.92	64.36	<0.001
Absent	12	201	213							<0.001

[Table/Fig-2]: Sensitivity, specificity, PPV and NPV of sonological features of thyroid nodules.
Chi square test was used; The p-value of <0.05 was considered to be significant.

enlarged cervical lymph nodes also. Of these 11 were metastatic nodes and 50 were benign lymph nodes. Authors found that sonological features such as loss of central echogenic hilum, presence of an irregular margin [Table/Fig-3], microcalcification [Table/Fig-4] and necrosis have sensitivity of 100%, 67.15%, 43.56%, and 76.56% and specificity of 97.1%, 96.5%, 11.8%, and 35.3%, respectively for metastatic involvement [Table/Fig-5]. The estimated decrease in unnecessary FNACs was calculated and found to be 41.15%-84.30%.

[Table/Fig-3]: Hypoechoic thyroid nodule which is taller than wider with mildly irregular margins- suspicious for malignancy (TIRADS 4B category).
[Table/Fig-4]: Irregular hypoechoic lesion with multiple tiny microcalcifications in left lobe of thyroid- highly suggestive of malignancy (TIRADS 5 category). (Images from left to right)

Sonological Features of cervical lymphnodes	Sensitivity %	Specificity%	PPV	NPV	Diagnostic accuracy
Loss of central echogenic hilum	100	97.1	73.33	98.05	93.44
Presence of irregular margin	67.15	96.5	23.7	97.08	84.7
Microcalcification	43.56	11.8	45.6	96.66	49.8
Necrosis	76.56	35.3	36.8	95.67	32.6

[Table/Fig-5]: Sensitivity, specificity, PPV and NPV of sonological features of cervical lymph nodes.

DISCUSSION

Horvath E et al., was the first to propose the TIRADS classification and suggested that mainly four features namely: irregular margins; multiple peripheral microcalcifications; hypoechogenicity; and hypervascularisation in combination were features of malignancy [6]. Present study results suggested that five independent sonological features namely irregular margins, microcalcifications, shape (taller than wide), marked hypoechogenicity, and solid composition, were associated with malignancy. Among these features, irregular margins was the most sensitive for malignancy followed by, hypoechogenicity, shape-taller than wider, microcalcification and solid component in that order. This finding was almost similar to the results derived by Kwak JY et al., in which irregular margins had the highest odds ratio for malignancy followed by taller than wide shape, marked hypoechogenicity, microcalcification, and solid composition of a thyroid nodule [7].

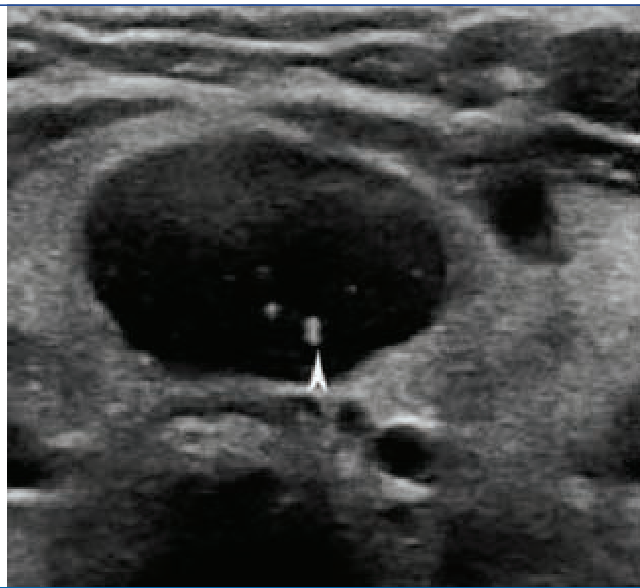
Fernandez Sanchez J in his study added an extra point to a TIRADS score when features of malignant cervical lymphadenopathy were found [14]. In the present study also, sonological assessment of cervical lymph nodes were included and it was found that sonological feature namely absence of fatty hilum showed 100% sensitivity and 97.1% specificity in classifying a node as metastatic. Kessler A et al., in their study showed that 70% of metastatic nodes, especially from papillary thyroid carcinoma had a cystic component. Thus, these metastatic nodes with cystic component had lower doppler indices compared to metastatic nodes without cystic component [15], which is in concordance with our study.

Many studies have stratified the risk of malignancy in each TIRADS category. It was observed that there were only minor differences in the values with the risk of malignancy steadily increasing from TIRADS 2 to TIRADS 5 category in all the studies summarised below [Table/Fig-6] [6,7,10,14,16].

In the present study, the sonological features which are highly sensitive and specific for benign lesion were evaluated. It was found that the three features namely hyperechogenicity or white knight appearance, completely cystic lesion [Table/Fig-7] and macrocalcification had 100% sensitivity for benignity. Similar findings were also seen in studies done by Bonavita JA et al., and Hoang JK et al., [17,18]. Popli MB et al., in their study observed similar results. All seven lesions which showed hyperechogenicity in their study were found to be benign on FNAC [19].

TIRADS category	Risk of Malignancy in percentage					
	Kwak JY et al., [7]	Moifo B et al., [16]	Fernandez Sanchez J [14]	Horvath E et al., [6]	Srinivas M et al., [10]	Current study
1	0	0	0	0	0	0
2	0	0	0	0	0	0
3	1.7	2.2	0	14.1	0.64	0.5
4A	3.3	5.9	9.5	45	4.76	3.85
4B	9.2	57.9	48	-	66.67	65.32
4C	44.4-72.4	-	85	-	83.33	86.22
5	87.5	100	100	89.6	100	100

[Table/Fig-6]: Comparison of risk of malignancy associated with each TIRADS category in various studies.



[Table/Fig-7]: Well-defined cystic nodule in right lobe of thyroid with echogenic colloid crystals within – colloid nodule (TIRADS 2 – Category).

Chandramohan A et al., assessed the practical aspects and accuracy of TIRADS in daily clinical practice and observed that PPV for malignancy was 6.6%, 32%, 36%, 64%, 59%, and 91% for TIRADS 2, 3, 4A, 4B, 4C, and 5 categories, respectively [20]. Barbosa TLM et al., concluded that, TIRADS score can refine the malignancy risk assessment, suggesting a conservative approach for indeterminate Bethesda III thyroid nodules and surgical approach for Bethesda IV and V categories [21]. Chaigneau E et al., showed that TIRADS score 3, 4a, 4b and 5 had the malignancy risks as 20.5%, 29%, 63.4% and 100%, respectively [22]. Another study done by Vargas-Uricoechea H et al., showed that the high concordance between TIRADS and Bethesda system of cytology reporting was found among both, the low risk (TIRADS 2 and Bethesda II) and the high risk categories (TIRADS 4 and Bethesda IV) [23]. The results of Changneau E et al., and Vargas-Uricoechea H et al., are similar to the results of the present study. In present study, TIRADS category 2 and 3 had only 0% and a meagre 0.5% risk of malignancy, respectively. Hence, these lesions can be followed-up with ultrasound alone. FNAC can be avoided in these cases thus, reducing the number of unnecessary FNACs by around 41.15-84%.

Limitation(s)

However, the limitations of this study are the small sample size and histopathology correlation was not done. In future, studies may also include histopathological follow-up in cases undergoing surgery. Also, monitoring protocols can be designed for discordant cases.

CONCLUSION(S)

We conclude that TIRADS classification is a reliable imaging modality to differentiate benign lesions from the malignant lesions. Additionally, the presence of malignant cervical lymphadenopathy features will enhance the radiologist's confidence in classifying a lesion as malignant on TIRADS. In present study, all the nodules classified as category 2 turned out to be benign in FNAC. This will help us to avoid FNAC in TIRADS category 2 patients. This study will further improve the ultrasound characterisation of nodules and establish risk groups to decide which patient should be submitted to FNAC. Thus, TIRADS reporting will help to select patients for FNAC thereby minimising costs and maximising benefits.

REFERENCES

[1] Ferlay J, Soerjomataram I, Dikshit R, Eser S, Mathers C, Rebelo M, et al. Cancer incidence and mortality worldwide: Sources, methods and major patterns in GLOBOCAN 2012. Int J Cancer. 2015;136(5):359-86.
[2] Guth S, Theune U, Aberle J, Galach A, Bamberger CM. Very high prevalence of thyroid nodules detected by high frequency (13 MHz) ultrasound examination. Eur J Clin Invest. 2009;39:699-706.
[3] Hegedüs L. The thyroid nodule. N Engl J Med. 2004;351:1764-71.
[4] Gharib H, Papini E. Thyroid nodules: Clinical importance, assessment, and treatment. Endocrinol Metab Clin North Am. 2007;36:707-35.
[5] Rahbari R, Zhang L, Kebebew E. Thyroid cancer gender disparity. Future Oncol. 2010;6:1771-79.
[6] Horvath E, Majlis S, Rossi R, Franco C, Niedmann JP, Castro A, et al. An ultrasonogram reporting system for thyroid nodules stratifying cancer risk for clinical management. J Clin Endocrinol Metab. 2009;94:1748-51.
[7] Kwak JY, Han KH, Yoon JH, Moon HJ, Son EJ, Park SH, et al. Thyroid imaging reporting and data system for US features of nodules: A step in establishing better stratification of cancer risk. Radiology. 2011;260:892-99.
[8] Cibas E, Ali S. The 2017 Bethesda System for reporting thyroid cytopathology. Thyroid. 2017;27(11):1341-46.
[9] Cibas ES, Sanchez MA. The national cancer institute thyroid fine-needle aspiration state-of-the-science conference: Inspiration for a uniform terminology linked to management guidelines. Cancer Cytopathology. 2008;114(2):71-73.
[10] Srinivas M, Amogh V, Gautam M, Prathyusha I, Vikram N, Retnam M, et al. A prospective study to evaluate the reliability of thyroid imaging reporting and data system in differentiation between benign and malignant thyroid lesions. J Clin Imaging Sci. 2016;6:5.
[11] Periakaruppan G, Seshadri KG, Vignesh Krishna GM, Mandava R, Sai VPM, Rajendiran S. Correlation between ultrasound-based TIRADS and Bethesda System for reporting thyroid-cytopathology: 2-year experience at a tertiary care center in India. Indian J Endocrinol Metab. 2018;22(5):651-55.
[12] Siddheshwar KP, Agarwal BD, Mohapatra SSG, Sahu N, Dixit A, et al. Correlation between ultrasound-based ACR -TIRADS and Bethesda system for reporting thyroid-cytopathology: A prospective study at tertiary care center in eastern India. Paripex - Indian Journal of Research. 2020;9(3):ISSN No.2250-1991.
[13] Tessler F, Middleton W, Grant E, Hoang J, Berland L, Teefey S, et al. ACR Thyroid Imaging, Reporting and Data System (TI-RADS): White Paper of the ACR TI-RADS Committee. J Am Coll Radiol. 2017;14:(5);587-595.
[14] Fernandez Sanchez J. TI RADS classification of thyroid nodules based on a score modified according to ultrasound criteria for malignancy. Rev Argent Radiol. 2014;78:138-48.
[15] Kessler A, Rappaport Y, Blank A, Marmor S, Weiss J, Graif M. Cystic appearance of cervical lymph nodes is characteristic of metastatic papillary thyroid carcinoma. J Clin Ultrasound. 2003;31:21-25.
[16] Moifo B, Takoeta EO, Tambe J, Blanc F, Fotsin JG. Reliability of thyroid imaging reporting and data system (TIRADS) classification in differentiating benign from malignant thyroid nodules. Open J Radiol. 2013;3:103.
[17] Bonavita JA, Mayo J, Babb J, Bennett G, Oweity T, Macari M, et al. Pattern recognition of benign nodules at ultrasound of the thyroid: Which nodules can be left alone? AJR Am J Roentgenol. 2009;193:207-13.
[18] Hoang JK, Lee WK, Lee M, Johnson D, Farrell S. US features of thyroid malignancy: Pearls and pitfalls. Radiographics. 2007;27:847-60.
[19] Popli MB, Rastogi A, Bhalla P, Solanki Y. Utility of gray scale ultrasound to differentiate benign from malignant thyroid nodules. Indian J Radiol Imaging. 2012;22:63-68.
[20] Chandramohan A, Khurana A, Pushpa BT, Manipadam MT, Naik D, Thomas N, et al. Is TIRADS a practical and accurate system for use in daily clinical practice. The Indian Journal of Radiology and Imaging. 2016;26:145-52. doi:10.4103/0971-3026.178367.
[21] Barbosa TLM, Junior COM, Graf H, Cavalvanti T, Trippia MA, da Silveira Ugino RT, et al. ACR TI-RADS and ATA US scores are helpful for the management of thyroid nodules with indeterminate cytology. BMC Endocr Disord. 2019;19:112. https://doi.org/10.1186/s12902-019-0429-5
[22] Chaigneau E, Russ G, Royer B, Bigorgne C, Bienvenu-Perrard M, Rouxel A, et al. TIRADS score is of limited clinical value for risk stratification of indeterminate cytological results. Eur J Endocrinol. 2018;179(1):13-20.
[23] Vargas-Uricoechea H, Meza-Cabrera I, Herrera-Chaparro J. Concordance between the TIRADS ultrasound criteria and the BETHESDA cytology criteria on the nontoxic thyroid nodule. Thyroid Res. 2017;10:1.

PARTICULARS OF CONTRIBUTORS:
1. Associate Professor, Department of Radiology, Father Muller Medical College, Mangalore, Karnataka, India.
2. Assistant Professor, Department of Pathology, Father Muller Medical College, Mangalore, Karnataka, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Dr. P Mellonie,
1605, Tower A, Northern Sky City, Mangalore-575001, Karnataka, India.
E-mail: drmellonierichie@gmail.com

PLAGIARISM CHECKING METHODS: [Jain H et al.]
- Plagiarism X-checker: Oct 22, 2020
- Manual Googling: Dec 21, 2020
- iThenticate Software: Dec 23, 2020 (25%)

ETYMOLOGY: Author Origin

AUTHOR DECLARATION:
- Financial or Other Competing Interests: None
- Was Ethics Committee Approval obtained for this study? Yes
- Was informed consent obtained from the subjects involved in the study? No
- For any images presented appropriate consent has been obtained from the subjects. No

Date of Submission: **Oct 22, 2020**
Date of Peer Review: **Nov 05, 2020**
Date of Acceptance: **Dec 21, 2020**
Date of Publishing: **Jan 01, 2021**