

Inter Observer Agreement on Klintrup Makinen Scoring System in Breast Carcinoma

Klintrup
Makinen Scoring
System in Breast
Carcinoma

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ABSTRACT

Objective: To find out the reliability of Klintrup Makinen Scoring System (KMSS) by assessment of inter observer agreement among pathologists.

Study Design: Experimental study

Place and Duration of Study: This study was conducted at the Institute of Pathology and Diagnostic Medicine (IPDM), Khyber Medical University (KMU). Duration: July 2022 to January 2023.

Materials and Methods: 100 slides were made from 50 specimens of breast cancer. These slides were scored for Klintrup Makinen score by five pathologists. Inter observer agreement between these five pathologists was find out using kappa statistics.

Results: The mean kappa value for the pathologists was 0.61 which was in considerable range. There was considerable inter observer agreement between the pathologists for KM scoring showing the reproducibility of this scoring system.

Conclusion: In conclusion, the KMSS scoring system can be used in clinical practice for detection of breast cancer prognosis.

Key Words: Breast Cancer; Tumor; Pathology; Histological Grade

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INTRODUCTION

Among women, most common malignant neoplasm is breast cancer. One in every eight women is suffering with this disease. About 2.3 million women are diagnosed with the disease of breast cancer world wide and the disease is the chief cause of mortality among the females.¹

Knowledge of disease development and progression is necessary for improvement in breast cancer survival. There are numerous prognostic factors for disease detection. Lymph node metastasis is a strong predicting factor. Estrogen receptor alpha is also a good prognostic factor and is important for endocrine treatment. Other prognostic factors are progesterone receptor, Ki 67 protein estimation for proliferation rate detection, HER 2 receptor and histological grade of the breast cancer.^{2,3}

Prognosis can be determined through assessment of inflammatory reaction in the peritumoral area and optimal therapy can be determined regarding this.⁴ t the tumor, invasive border, inflammatory cells including neutrophils, lymphocytes, monocytes, macrophages and plasma cells can be assessed through KMSS. There is better five years survival rate in high grade inflammation and low grade inflammation is associated with poor prognosis.⁵

In many studies, work has been done on KM score assessment and on its prognostic value. KM score can be assessed through automated method and this can provide support to the pathologists clinically.⁵⁻⁷

Less work has been done on observer agreement for KM scoring system.^{4,5,8,9} The aim of the study is to find out the interobserver agreement among the pathologists for KM scoring so that reliability and reproducibility of this system can be assessed.

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MATERIALS AND METHODS

Samples were collected from HMC (Hayatabad Medical Complex) and KTH (Khyber Teaching Hospital). In the research, 50 patients of invasive breast cancer were included. From breast cancer patients, duly signed informed consent was taken. Before taking consent, aims and objectives of the research were explained to them. From each specimen of breast cancer, 2 blocks and 2 slides were made. So, 100 slides were obtained from 50 specimens of invasive breast cancer.

Slide Preparation: For making the slides, Specimen was fixed in 10% formalin for 24 hours so that its architecture may be preserved. Serial sectioning of the breast specimen was done 1 cm apart. Rectangular area of the tumor with normal parenchyma was cut and taken in the cassette. Processing of the tissue was done in the automated machine. Embedded tissue was placed in metallic mould and fresh molten wax was poured into it. Then it could settle and solidify.

In tissue cutting, first trimming was done at 30 microns, on microtome. Fine cutting was done at 5 microns. Water bath was preheated up to 60 degrees. Tissue was placed in the water bath and then lifted with help of plain glass slide.

For staining of slides, sections were fixed on glass slide in xylene. Then they were transferred to absolute alcohol for 3 minutes, rectified spirit (80% alcohol) for 3 minutes and methylated spirit for 2 minutes. Slides were washed in running water for one minute. They were put in hematoxylin for 3 to 5 minutes, washed in running water for 30 seconds, washed increased dye in 1% acid alcohol for 15 seconds, again washed in running water for 30 seconds. Then 2-3 dips in ammonia water were given. After washing with running water, counterstained with Eosin. Then mounted the slide with DPX oil and cover it with cover slip.

Microscopy and Scoring: Microscopy and scoring were done in the Histopathology lab of IPDM, KMU.

100 slides, were scored by five pathologists, at 20X magnification, taken at point of maximum invasion for Klintrup Makinen score. Score 0 was given when there is no inflammation, score 1 was given for mild inflammation, score 2 for moderate inflammation and score 3 for severe inflammation.

In SPSS version 21, data was analysed. Cohen's kappa was used to find the interobserver agreement between the five pathologists. Per Landis and Koch's standards, kappa value less than 0 shows poor agreement. Kappa value of 0.21-0.40 shows fair agreement, kappa value of 0.41-0.60 shows moderate agreement, 0.61-0.80 shows considerable agreement and 0.81-1.00 shows nearly perfect agreement.

RESULTS

Total 100 slides, were scored by the five pathologists. The time taken by each pathologist, for KM scoring, was 5-8 minutes.

Symbols used for the pathologists were as follows,

A: Pathologist 1 B: Pathologist 2
C: Pathologist 3 D: Pathologist 4
E: Pathologist 5

The kappa score for the pathologists, in the pair wise fashion, was as follows:

AB: 0.60 AC: 0.61
AD: 0.67 AE: 0.73
BC: 0.56 BD: 0.51
BE: 0.78 CD: 0.52
CE: 0.57 DE: 0.55

The mean kappa score, for all these 10 pairwise kappa scores, was 0.61. Five pair wise kappa scores i.e., 0.56, 0.51, 0.52, 0.57 and 0.55 showed moderate level of agreement. The remaining five pairs i.e., 0.60, 0.61, 0.67, 0.73, and 0.78 showed substantial and considerable agreement.

The mean kappa value for the five observers, doing KM scoring, was 0.61 and range was 0.51-0.78.

Table No. 1: Shows Pairwise kappa score for Inter Observer agreement.

KM Score						
Observers						
Observers		A	B	C	D	E
	A		0.60	0.61	0.67	0.73
	B			0.56	0.51	0.78
	C				0.52	0.57
	D					0.55
	E					
Mean Kappa score: 0.61						

DISCUSSION

Interobserver agreement has been assessed in histopathological work like Gleason grading system in prostate biopsies, for IHC biomarkers in pancreatic ductal adenocarcinoma and also in radiologic interpretation. Two observers were involved in these studies.¹⁰⁻¹² Daniel et al worked on non-small cell subtypes of the lung cancer, in H & E and IHC specimens and found interobserver agreement between 3 pathologists.¹³ In the histopathological studies, mostly 2 to 3 observers are involved in the rating.^{12,14} The number of pathologists involved in our study was greater than the average number involved in most studies. This increases the reliability of Klintrup Makinen score interpretation.

From five pathologists, ten pairs were made to apply Cohen's kappa test. The mean kappa value for all the pairwise kappa score was 0.61. The value lies in the range of substantial agreement i.e. 0.61-0.80. This shows good agreement between the pathologists for KM scoring. Less work has been done on interobserver agreement related to KM scoring system. In a study, done by N. Kemi et al 2020, KM grading was done by two pathologists. The kappa value was 0.526 which showed moderate level of agreement that was comparable to our study.^{8,15}

CONCLUSION

There was considerable interobserver agreement between the pathologists for KM scoring showing the reproducibility of this scoring system and can be used clinically for detection of breast cancer prognosis.

Author's Contribution:

Concept & Design of Study: Amna Khalid
Drafting: Amna Khalid

Data Analysis: Amna Khalid
Revisiting Critically: Amna Khalid
Final Approval of version: Amna Khalid

Conflict of Interest: The study has no conflict of interest to declare by any author.

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