MAGS Scoring: A Marker Of Tumor Angiogenesis And Prognostic Indicator In Carcinoma Breast

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Citation

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Abstract

Introduction: Angiogenesis is an important new prognostic indicator in breast cancer. Several works have been devoted to study the tumor angiogenesis asMicrovessel density, Doppler study, VEGF expression but all these techniques are expensive and require special laboratory to measure them. Microscopic Angiogenesis Grading System (MAGS) is an easy technique, can be carried out by any expert pathologist and does not require any extra preparation and needsonly H and E staining study which can be done in every biopsy specimen.
Material and Method: 30 cases of carcinoma breast and 10 cases of fibroadenoma underwent MAGS scoring by looking for Vasoproliferation (N), Endothelial Cell Hyperplasia (E) and Endothelial Cytology (X). and score was calculated as
MAGS SCORE = KnN + KeE + KxX
Results: Higher MAGS score was associated with advanced stage, higher grade and lymph node positive tumors($p<0.05$).
Conclusion: MAGS score is a good marker of tumor angiogenesis for prognostication in carcinoma breast and it is a marker of poor prognosis.

INTRODUCTION

Cancer is the most dramatic angiogenesis dependent disease . Progressive tumor growth and metastasis are angiogenesis dependent (Folkman J 1971). Without small blood vessels to supply the needed nutrients of the neoplastic cells, tumors cannot grow more than 2 to 3 mm^3 before diffusion alone is insufficient to meet basic metabolic requirements (Jones et al, 1998).There are many retrospective studies which show that angiogenesis is an important new prognostic indicator in breast cancers.

The vascular response to a neoplasm has been investigated by numerous workers who relied on such qualitative descriptions as “prominent small vessels”, “marked endothelial thickening” or such endothelial proliferation to analyze the histologic changes of angiogenesis. A more quantitative method of measuring the histologic extent of vascular proliferation was given by Brem S et al in 1972. They described a microscopic angiogenesis grading system (MAGS) which was based on 3 parameters; Vasoproliferation, Endothelial cell hyperplasia and Endothelial cytology. In our study, we have analysed the utility of MAGS scoring for the assessment of the biological behaviour of breast cancer.

This system provided a composite score ranging from 0 to 100, with biologically reasonable and quantitatively reproducible results. A formula was constructed to integrate the 3 components of endothelial cell regeneration.

MAGS = Kn N + KeE + KxX

(Vasoproliferation) (Endothelial cell hyperplasia) (Endothelial cytology)

MATERIAL AND METHODS

The study was conducted from March 2003 to March 2005 in University hospital, Varanasi, India. FNAC proven 30 patients of carcinoma breast and 10 patients of fibroadenoma were taken in study. All patients underwent detailed history and examination and investigations to look for metastasis.16 patients underwent modified radical mastectomy while 14 underwent Tru-cut needle biopsy followed by neoadjuvant chemotherapy (CAF). The tissue samples were collected in 10% formalin and were finally processed to paraffin wax. Detailed histology regarding type of tumor, grade, vascular invasion, lymph node status was performed. All the samples of carcinoma breast and fibroadenomas underwent MAGS scoring by looking for Vasoproliferation (N), Endothelial Cell Hyperplasia (E) and Endothelial Cytology (X) under

microscope on 4 m paraffin sections stained with Hematoxylin and Eosin under 500 times magnification and score was calculated as

MAGS SCORE = KnN + KeE + KxX

N represents the number of vessels per high power field. Kn is a constant used to correct for various fields of other microscopes so that they are equal to magnified area described. Ke is a constant with value of 3. E is the number of endothelial cell lining the cross section of capillary. Kx was a constant with value 6. X stood for histological appearance of an individual endothelial cell graded on the bases of regenerative appearance. X was given 0-5 points based on histological appearance of endothelial cells, normal endothelial cell was given 0 score, Plump clear nucleus,1 score, Plump clear nucleus with prominent nucleolus 2, Large hyperchromatic nucleus 3, Bizzare endothelial cell 4 and Mitotic figure 5 score. The MAGS score using the above mentioned formula ranges from 0 to 100.

STATISTICS

All the parameters were correlated with well known prognostic parameters of carcinoma breast as well as with themselves. Statistical analysis was done by SPSS version 10.0. Chi square test, paired T test, ANOVA test and Pearson Correlation were determined to assess the level of significance. P<0.05 were taken as significant.

RESULTS

Mean age of all the cancer patients was 43.1 ± 11.5 year (range 28-81 yrs). None of the patient were in stage I, 5 (16.7%)were in stage II, 21 (70%) in stage III and 4 (13.3%) in stage IV. All carcinoma breast tissues had MAGS score more than 20 but only one fibroadenoma tissue had MAGS score more than 20. 19 cancer patients (63.3%) had MAGS score more than 40 (Table 1). Highest MAGS score of carcinoma was 55 & of fibroadenoma was 22. Mean MAGS score in carcinoma breast was 41.9±8.23 and in fibroadenoma it was 18.9±1.96. This difference was statistically significant (p<0.001).

Figure 1

Table 1: Distribution of MAGS score in Fibroadenoma and carcinoma breast patients

MAGS score	Carcinoma breast (n=30)		Fibroadenoma (n=10)	
	No.	%	No.	%
<20	0	0	9	90
20-40	11	36.7	1	10
>40	19	63.3	0	0

MAGS score was higher in larger and vascular invasion positive tumors but the differences were not statistically significant. MAGS score in lymph node metastasis positive patients was 46.05 ± 5.86 and those without lymph node metastasis was 33.6 ± 5.58, this difference was statistically significant (p<0.001). Highest mean MAGS score (50.5 ± 4.04) was associated with stage IV tumor then stage III i.e. 41.21 ± 7.81 and stage II 33.0 ± 7.07. And the difference between these scores were statistically significant (p<0.05). Grade was significantly related to MAGS score. With increasing grade, tumor showed higher MAGS score, and the differences of scores between different grades were statistically significant (p<0.001). Tumors with distant metastasis had significantly higher MAGS score than tumor without distant metastasis (p<0.05) (Table 2).

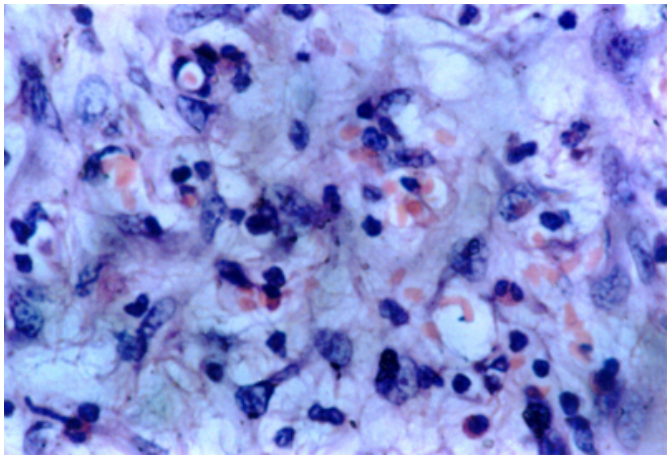
Figure 2

Table 2: Correlation of MAGS score with various parameters

Parameters	MAGS Score	p-value
Size of tumor		
2-5 cm (5)	38.4 ± 0.60	
> 5cm (25)	42.6 ± 7.96	NS
Lymph node metastasis		
Present (20)	46.05 ± 5.86	
Absent (10)	33.6 ± 5.58	<0.001
Metastasis		
Present (4)	50.5 ± 4.04	
Absent (26)	40± 57 ± 7.94	<0.05
Stage		
Stage II (5)	33.0 ± 7.07	
Stage III (21)	41.21 ± 7.81	
Stage IV (4)	50.5 ± 4.04	<0.05
Grade		
Grade I (5)	29.0 ± 2.73	
Grade II (7)	41.28 ±5.67	
Grade III (18)	45.72 ±6.16	<0.001
Vascular invasion		
Present (17)	42.94 ±7.96	
Absent (13)	40.53 ± 8.70	NS

Figure 3

Figure 1: Microphotograph of Invasive ductal carcinoma with high MAGS score (x 400)



DISCUSSION

Management of primary breast cancer involve the need for prognostication. The well known prognostic parameters are age, menstrual status, parity, stage, tumor size, histological type, grade, vascular invasion, lymph node status, ER/PR status. Several studies have indicated that tumor angiogenesis is also a prognostic indicator in carcinoma breast. Using immunohistochemical and biochemical methods, several studies have shown a worse prognosis for those patients with tumors with high angiogenic activity. Tumor angiogenesis can be studied by various parameters like estimation of expression of VEGF, MVD, Chalky counting, MAGS scoring, Color Doppler study.

MAGS scoring is a quantitative technique of measuring degree of angiogenesis in a tumor. This is based on three parameters, vasoproliferation, endothelial cell hyperplasia and endothelial cytology. It provides a composite score ranging from 0 to 100. This was first demonstrated by Steven Brem et al in year 1972 in a series of brain neoplasms, higher degrees of scores were consistently displayed by more malignant neoplasms. When MAGS was applied to a wide range of human neoplasms, different classes of tumors varied in their ability to elicit new endothelial growth although adenocarcinomas did not score as high as glioblastomas, these 2 classes of tumors were both categorized as “endothelial rich”. Based on the MAGS score attained by different tumors clinical course, virulence and prognosis of a malignant tumor can be assessed (Brem et al, 1972). MAGS may also be very helpful to evaluate the effectiveness of drug or antibodies against Tumor Angiogenesis Factor (TAF) which might diminish vascualrization (Salsberry et al, 1970) or inhibit angiogenesis.

In our study higher MAGS score was associated with malignancy as compared to fibroadenoma. Kumar M et al (2004) reported that higher MAGS score was associated with poorly differentiated prostatic carcinoma. In our study also higher MAGS score was associated with higher grade tumor and the difference between them was statistically significant. We also found positive significant correlation of VEGF with, lymph node status, distant metastasis and stage of tumor. Higher scores were found in tumors with lymph node metastasis / distant metastasis / advanced stage tumors.

CONCLUSION

Our study was designed to evaluate the prognostic importance of MAGS score in breast cancers. We compared all these parameters with tumor size, stage, histological grade, lymph node status, vascular invasion and metastasis. It was found that higher grade, and lymph node positive metastatic and advanced stage tumors had higher MAGS score. Therefore, our study suggests that MAGS score which can be done on H & E stained slides is a good and cheep alternative to study tumor angiogenesis for prognostication in carcinoma breast and it is a marker of poor prognosis.

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