

# MIB- 1 DNA

· · · · ·  
\* · \* · \* · \*

=Abstract=

## Study for MIB- 1 Immunostaining and DNA Ploidy in Endometrial Carcinoma

K.T. Lim. M.D., T.J. Kim. M.D., H.W. Chung. M.D., G.H. Lee. M.D.,  
J.T. Park. M.D., I.S. Park. M.D., J.U. Shim. M.D., H.S. Kim. M.D.\*,  
Y.J. Kim. M.D.\*, Y.K. Chun. M.D.\*, S.R. Hong. M.D.\*, H.S. Kim. M.D.\*

*Department of Obstetrics and Gynecology, Department of pathology, College of Medicine,  
Sungkyunkwan university, Samsung Cheil women's hospital, Seoul, Korea*

**Objective:** The monoclonal antibody MIB-1 reacts with the same antigen as Ki67 antigen giving an estimate of growth fraction. The authors investigated whether MIB-1 staining, using semiquantitative analysis and DNA ploidy study, could be a prognostic indicator of recurrence in endometrial carcinoma.

**Methods:** The tumors from 45 consecutive patients receiving primary surgical therapy for endometrial carcinoma were evaluated with MIB-1 monoclonal antibody and DNA ploidy status. Growth fraction was quantified by counting stained nucleus in HPF. DNA ploidy study was evaluated by flow cytometry. The patients were followed for 5 years and their charts were reviewed to determine recurrence, stage, and grade.

**Results:** MIB-1 staining was significantly elevated in histologic high grade (grade 3 and 4) as opposed to low grade (grade 1 and 2) carcinoma ( $P = 0.038$ ). Aneuploidy was significantly increased incidence in advanced stage (stage 3 and 4) as opposed to early stage (stage 1 and 2) ( $P = 0.017$ ). MIB-1 staining and aneuploidy were associated with increased incidence of recurrence within 5 years of diagnosis, but not statistically significant.

**Conclusion:** In this series of 45 patients with endometrial carcinoma. MIB-1 monoclonal antibody staining and aneuploidy to be a prognostic indicators of recurrence.

가  
가 가  
가

- MIB- 1 DNA -  
 가 , 1988 가 .  
 FIGO  
 , 2.  
 1)  
 .1) 3 4 mm  
 Silane 12  
 xylen  
 10mm citrate Buffer가  
 800W 15 가 .  
 20 monoclonal  
 MIB-1 antibody(Immunotech.S.A.) 1: 50 60 ,  
 Biotinylated linked antibody 20 Ste-  
 ptoavidin 20 . MIB-1  
 가 , MIB-1  
 Semi-  
 .3) .4) .5) quantitative scoring . 400  
 6) , 5  
 (flow cytometry) 가 10 (Low) 10 20  
 DNA (moderate), 20 (High)  
 ,7-10)  
 .11-19) 5  
 가  
 ( MIB-1 ,  
 DNA  
 , 가  
 .  
 1. SAS Program .  
 1988 1 94 4  
 129 5  
 가 ,  
 DNA 가 가 가  
 가 45  
 1.  
 가 35 73  
 53 ,  
 (Endometrioid adenocarcinoma)

37 , (Adenosquamous carcinoma) 3 ,  
 (Mucinous adenocarcinoma) 2 ,  
 (Papillary serous adenocarcinoma) 2 ,  
 (Clear cell carcinoma) 1 .  
 32 , 1 , 11 ,  
 1 ,  
 grade 23 , grade 9 , grade 13 .  
 12 6  
 (Table 1).

Table 1. Clinicopathologic characteristics of the patients

Stage	Histologic Type				Total
	Endome*	Adesqu	UPSC	Others	
	28	1	0	3	32
	1	0	0	0	1
	7	2	2	0	11
	1	0	0	0	1
Total	37	3	2	3	45

\* Endome: Endometrioid Carcinoma

2. MIB-1 ,  
 1)  
 MIB-1 ,  
 33 11 , 33%  
 , 12 7 ,  
 58% .

.(Table 2)

Table 2. Relationship between MIB-1 staining and stage

Stage	MIB-1			Total
	mid	mod	sev	
	22	3	8	33
	5	2	5	12

Mantel-Haenszel chi-square  
 Probability 0.162

2)  
 Grade I 23  
 6 , 26% Grade  
 13 9 , 69%  
 . 가 MIB-1  
 ,  
 p-value 0.038 가 (Table  
 3).

Table 3. Relationship between MIB-1 staining and grade.

Grade	MIB-1			Total
	mild	mod	sev	
	17	1	5	23
	6	0	3	9
	4	3	6	13

Mantel-Haenszel chi-square  
 Probability 0.038

3. DNA ,  
 1)  
 DNA  
 33 5 , 15%가  
 , 12 6 , 50%  
 .  
 p-value 0.017 가 . (Table 4)

Table 4. Relationship between DNA ploidy and stage

Stage	DNA ploidy		Total
	Dipl	Aneu	
	28	5	33
	6	6	12

Mantel-Haenszel chi-square  
 Probability 0.017

2)  
 grade I 23 5 22%

가 , Grade 22 6  
, 27%가 가  
p-value 0.657  
(Table 5).

Table 5. Relationship between DNA ploidy and grade

Grade	DNA ploidy		Total
	Dipl	Aneu	
	18	5	23
	7	2	9
	9	4	13

Mantel-Haenszel chi-square  
Probability 0.657

#### 4. MIB-1 DNA

MIB-1  
27 2  
(7.4%) ,  
18 4 (22%) , MIB-1  
, (Table 6).

Table 6. Relationship between MIB-1 staining and recurrence

	Low	Mod-High	
No recurrence	25	14	39
Recurrence	2	4	6
	27	18	45

Table 8. Characteristics of survival patients in stage endometrial carcinoma

Case	Age	Type & Grade	Stage	Myometrial invasion Depth	MIB-1	Ploidy
1	53	ADENO	c	1/3	8	Diploidy
2	55	ADENO	c	1/2	5	Aneuploidy
3	73	ADENO	c	1/2	12	Aneuploidy
4	53	ADENO	a	1/2	6	Aneuploidy
5	54	UPSC	c	1/2	35	Diploidy
6	58	ADENO	a	1/3	15	Aneuploidy

DNA  
DNA  
(3/34) 8.8%  
, DNA  
(3/11) 27 %가 , DNA  
, (Table 7)

, 가  
1  
12 6  
6  
Table 8  
MIB-1 1

Table 7. Relationship between DNA ploidy and recurrence

	Diploidy	Aneuploidy	
No recurrence	31	8	39
Recurrence	3	3	6
	34	11	45

Table 9 . DNA  
6 4  
MIB-1  
, MIB-1

Table-9. Characteristics of recurrent patients in stage III-IV endometrial carcinoma.

Case	Age	Type & Grade	Stage	Myometrial invason	Depth	MIB-1	Ploidy
7	53	ADENO II	IIIc		Full	8	Aneuploidy
8	56	ADENO III	IIIc		1/2	4	Diploidy
9	51	ADENO III	IV		Full	40	Aneuploidy
10	55	ADENO II	IIIa		1/3	60	Diploidy
11	78	UPSC	IIIc		2/3	20	Diploidy
12	52	ADENO III	IIIc		2/3	80	Aneuploidy

[illegible]



15. van der Putten HW HM, Baak JPA et al: Prognostic value of quantitative pathologic features and DNA content in individual patients with stage I endometrial adenocarcinoma. *Cancer* 1989; 63: 1378.
16. Rosenberg P, Wingren S et al: Flow cytometric measurements of DNA index and S-phase and paraffin-embedded early stage endometrial cancer: An important prognostic indicator. *Gynecol Oncol* 1989; 35: 50.
17. Newbury R, Schurech C, Goodspeed N et al: DNA content as a prognostic factor in endometrial carcinoma. *Obstet Gynecol* 1990; 76: 251.
18. Symonds DA.: Prognostic value of pathologic features and DNA analysis in endometrial carcinoma. *Gynecol Oncol* 1990; 39: 272.
19. Hans HW et al: Prognostic value of quantitative pathologic features and DNA content in individual patients with stage I endometrial adenocarcinoma. *Cancer* 1989; 63: 1378.
20. Kerns BJ, M Jordan, Faerman et al: Determination of proliferation index with with in advanced ovarian cancer using quantitative image analysis. *Am J Pathol* 1994; 101: 12-17.
21. Hendricks, JB Wilkinson et al: Ki-67 expression in vulvar carcinoma *Gynecol Pathol* 1994; 13: 205-210.
22. Boon ME, Keinschmit-Guy et al: PAPNET for analysis of proliferating(MIB-1) cell populations in cervical smears *Eur J Morphol* 1994; 32: 78-85.
23. Cheung AN, Ngan H et al: Assesment of cell proliferation in hydatidiform mole using monoclonal antidody MIB-1 to Ki-67 antigen. *J Clin Morphol* 1994; 47: 601-604.
24. Garetti GG, Ciavattini et al: Ki-67 antigen immunostaining(MIB-1 monoclonal antibody) in serous ovarian tumors: Index of proloferation activity with prognostic significance. *Gynecol oncol* 1995; 56: 169-174.
25. Key G, Becker, Baron et al: New Ki-67 equivalent murine monoclonal antibodies generated against bacterally expressed parts of the Ki-67cDNA containing three 62 base pair repetitive elements encoding for the Ki-67 epitop. *Lab Invest* 1993; 68: 62-636.
26. John Geisler, Michael C Wiemann et al: Proliferation index determined by MIB-1 and recurrence in endometrial cancer. *Gyne oncol* 1996; 61: 373-377.
27. Geisinger KR, Homesley HD, Morgan. et el: Endometrial carcinoma: A multiparameter clinicopathologic analysis including the DNA profile and sex steroid status. *Cancer* 186; 58: 1518-1525.
28. Christopherson WM, Connelly et el: Carcinoma of the endometrium: An analysis of prgnostic factors in paitients with favorable subtypes and stage I disease. *Cancer* 1983; 51: 1705-1709.
29. Britton LC, Wilson, Gaffey et al: Flow ctometric DNA analysis of stage I endometrial carcinoma *Gynecol Oncol* 1989; 34: 317-322.
30. Iversen OE: Flow cytometric deoxyribonucleic acid index: A prognostic factor in endometrial carcinoma. *Am J Obstet Gynecol* 1986; 155: 770-776.
31. Newbury R, Schuerch, Goodspeed, et al: DNA content as a prognostic factor in endometrial carcinoma. *Obstst Gynecol* 1990; 76: 251-257.
32. Moberger B, Auer G, Forsslund G, et al: The prognostic significance of DNA measurements in endometrial carcinoma. *Cytomery* 1984; 5: 430-46.
33. Sorbe B, Risberg B, Thormthwaite J et al: Nuclear morphometry and DNA flow cytometry as prognostic methods for endomeria carcinoma. *Int J Gynecol Cancer* 1994; 4: 94-100.
34. Friberg LG, Noren H, Delle U et al: Prognostic value of DNA ploidy and S-phase fraction in endometrial cancer stage I and II. *Gynecol oncol* 1994; 53: 64-69.
35. . . . .  
41 DNA .  
1994; 37: 1423-1430.