

CA 125 가

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=Abstract=

The Clinical Significance of Increased Serum CA 125 in Asymptomatic Women

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Objectives: Our study was to determine the usefulness of CA 125 screening for asymptomatic female subjects. Though CA 125 has been used as a useful marker for the detection of ovarian cancer, its efficacy to detect early ovarian cancer in asymptomatic women has not been established.

Study Design: From April 1995 to December 1997, a total of 13,038 subjects who visited our Center for Health Promotion were screened. Serum CA 125 level was measured by a radioimmunoassay kit (Centocor, USA). In most cases transvaginal ultrasound was done at the same time. The specificity, sensitivity and positive predictive value were obtained on the basis of normal CA 125 range between 2.4 ~ 36.3 U/ml.

Result:

1) Two cases of ovarian cancer were detected out of 13,038 subjects screened. One ovarian cancer patient showed 1,625 U/ml of CA 125 level, on the other hand, the other level patient showed 27 U/ml.

2) Therefore, the sensitivity, specificity, and positive predictive value were 50%, 97.3%, and 0.3%, respectively. Since 346 cases out of 13,038 screened subjects showed false positive results on the basis of the upper limit of normal CA 125 level set at 36.3 U/ml, the false positivity was 2.6%.

3) The CA 125 levels in false positive cases ranged from 36.3 U/ml to 352.8 U/ml with the mean value of 66.19 ± 51.47 (S.D.).

4) The clinical features of the false positive cases included uterine myoma including adenomyosis (150), benign ovarian cyst (19), cervicitis (6), tuberculosis (3), pregnancy (2), and each one case of breast cancer, mammary cyst, endometritis, lung cancer, liver cirrhosis, pancreatic cancer, cervical cancer, renal cyst, uterine anomaly, and post TAH state. In the remainder of false positive 156 cases, no abnormal findings were observed. Among 258 patients who underwent combined tests of CA 125 and transvaginal ultrasound, the sensitivity of ovarian cancer was 100%.

5) The false positive rate was lower in the older age group (>50) than in the younger group (<50).

Conclusion: The prevalence of ovarian cancer in our study was 0.0153% (15.3 per 100,000 population) which is comparable to the rate of 15.8 per 100,000 population reported by the Korean Medical Insurance Corporation. Although the CA 125 test by itself shows a low positive predictive value, its clinical usefulness as a screening test can be enhanced dramatically by the combined use of transvaginal ultrasound examination, especially in postmenopausal women.

Keywords: CA-125, Ovarian, Cancer, Screen transvaginal sonogram

CA 125
Bast 3) CA 125 가 35 U/ml

5
1, 2 90 100% , 35 U/ml 65 U/ml
3, 4 20% .1) 가 가 13) CA 125
35 U/ml
가
가
가
14) CA
1981 Bast 2) CA 125 125 가 CA
35) CA
125
CA 125
6)
7)
1.
1995 4 1997 12
35) CA 125 가 CA CA 125 13,038
125
1985 Bast 39) CA 125가
12 80%
Zurawski 10) 18 kit(CA 125
50% CA 125가 30 U/ml RIA kit, CENTOCOR, USA) 2.4 36.3
40 1082 U/ml
CA 125 3
CA 125 가 2
20 CA 125 36.3 U/ml
Mann11) 1 23%가 347 74% 258
CA 125 Jacob Bast12) ACUSON 128 x
1 50% P4 EV-5, 5MHz
CA 125 3) CA 125 가 36.3 U/ml
가 , , ,

CA 125, 130,38 CA 125 12.87 U/ml (Table 1). CA 125가 36.3U/ml 347 65 U/ml 256 (73.8%) 95 U/ml 300 (86.3%) . 95 U/ml 47 1 1,615 U/ml 가 (Table 2).

CA 125 36.3 U/ml

CA 125 36.3

1994

20

Bayes

$$= \frac{x}{x + (1-x)} \times \frac{1}{1 + \frac{(1-x)}{x} \times \frac{1}{1-x}}$$

$$= \frac{x(1-x)}{x(1-x) + [(1-x) \times \frac{1}{1-x}]}$$

CA 125 가

SAS univariate, t-test

1. CA 125 13,038 CA 125 가 36.6 U/ml 12,691 36.3 U/ml 347 2.66% CA 125가 가 36.3 U/ml CA 125 11.3 U/ml 36.3 U/ml CA 125 70.7 U/ml

Table 2. Distribution of elevated Serum CA- 125 levels

CA-125(U/ml)	Numbers of 347 Subjects
< 65	256(73.8%)
< 95	300(86.5%)
> 96	47(13.5%)

2. CA 125 40 가 37.9%(4946), 50 가 29%(3777), 30 가 19.2%(2502), 60 가 10.8%(1410), 20 가 1.9% (248) 70 가 1.2%(155) 13,038 47.6 (Table 3). CA 125 가 가

가 (Table 4).

CA 125 가 100 U/ml 가 100 U/ml 가 (Table 5). 50 CA 125 가 100 U/ml 가 50 7976 CA 125 15.10 ± 16.31 , 50 5342 CA 125 9.67 ± 23.36 (Table 6).

3.

Table 1. Serum CA 125 Values of Subjects

	CA 125 < 36.3 U/ml	CA 125 ≥ 36.3 U/ml	Total
Numbers	12,691(97.34%)	347(2.66%)	13,038(100%)
Mean values	11.29 + 6.64 U/ml	70.66 + 97.75 U/ml	12.87 + 19.69 U/ml
Min`Max	0.1 36.3 U/ml	36.3 1615 U/ml	0.1 1615 U/ml

Mean values: mean + S.D.

Table 3. Age Distribution of Subjects

Age	Number(%)	CA 125 mean value (Min Max) U/ml
< 29	248(1.9%)	18.46 ± 27.46(1.5 381.7)
30 39	2502(19.19%)	15.38 ± 13.16(0.8 202.)
40 49	4946(37.94%)	14.79 ± 16.98(0.1 443.)
50 59	3777(28.97%)	9.94 ± 27.5(0.1 1615)
60 69	1410(10.81%)	8.85 ± 5.63(0.1 80.6)
> 70	155(1.19%)	10.47 ± 9.35(0.6 90.)
Total	13,038(100%)	12.87 ± 19.69(0.1 1615)

*Mean of Ages=47.63 ± 9.6(17 81) yrs old

Mean value=Mean ± S.D.

13,038 2
50 CA 125
1615 U/ml
5 cm 가
가

Table 6. Serum CA 125 values by age 50

Age	Number	Mean(U/ml)	S.D.
< 50	7696	15.1	16.32
> 50	5342	9.67	23.36
Total	13038	12.87	19.69

P value < 0.0001

Mean values=Mean ± S.D.

3
59 CA 125
가 27 U/ml 7
cm 가
1
4. CA- 125

Table 4 .Distribution of Serum CA- 125 Values according to ages of subjects

Age	< 29	30 39	40 49	50 59	60 69	> 70	Total
CA 125							
< 36.3 U/ml(%)	235(1.8)	2408(18.5)	4739(36.4)	3751(28.8)	1405(10.8)	153(1.2)	12691(97.3)
Column(%)	94.8	96.2	95.8	99.3	99.6	98.7	
> 36.3 U/ml(%)	13(0.1)	94(0.7)	207(1.6)	26(0.2)	5(0.04)	2(0.02)	347(2.7)
Column(%)	5.2	3.8	4.2	0.7	0.4	1.3	
Total(100%)	100	100	100	100	100	100	

Column(%): proportion of serum CA 125 values in same age group

Table 5. Specificity of different CA125 values according to age group

Age	CA 125 (U/ml)					Number
	< 20	< 35	< 65	< 100	< 200	
< 29	73.79	94.35	97.58	98.79	99.6	248
30 39	79.78	95.44	99.32	99.64	99.92	2502
40 49	82.55	95.27	98.81	99.43	99.88	4946
50 59	95.66	99.18	99.81	99.92	99.95	3777
60 69	96.67	99.43	99.93	100	100	1410
> 70	91.61	98.06	99.35	100	100	155
Total	87.28	96.9	99.3	100	99.92	13038
P value	0.001	0.001	0.001	0.001	0.351	

13,038
13,036 CA 125 가
12,691 CA 125 가
347 2
1 CA 125 가 1
CA 125 36.3 U/ml
CA 125 50%,
97.3% (Table 7). 1994
20
10 15.81 (Table 8).
15.31
Bayes
CA 125 0.3%,
99.9% .

Table 7. Sensitivity and Specificity of Serum CA 125

Ovarian Cancer	CA 125		Total
	< 36.3	36.3	
Negative	12690	346	13036
Positive	1	1	2
Total	12691	347	13038

Table 8. Prevalence of Ovarian Cancer Over the Age of 20 in Korea

ICD 183 (Ovarian Cancer)	Total No. of Cancer	Total No. of Admission	Prevalence
278	6042	1,758,832	0.0001581

5. CA 125가

13,038 CA
125 가 346 2.6%
45.1%(156),
43.3%(150), 1.7%
(6), 0.9%(3), 6%(2) 1
(Table 9). 1

CA 125 가 65.53 ± 9.34 U/ml .

Table 9. Clinical findings of false positive subjects

Diagnosis	Number	%	Mean (U/ml)
()	156	45.1	53.4
()	156	45.3	83.1
	19	5.5	46.9
	6	1.7	41.3
	3	0.8	89.6
	2	0.5	119.9
	1	0.4	37.2
	1	0.4	47.4
	1	0.4	53
	1	0.4	352.8
	1	0.4	62.7
	1	0.4	200.2
	1	0.4	41.3
	1	0.4	53.5
	1	0.4	126.5
	1	0.4	58.9
Total	346	100	66.19

1985 Bast 9) 가
1 CA 125 가
Zurawski 10)
CA 125
Einhorn 18) 5550
CA 125 30 U/ml
5550 175 (3.1%) 가
6
4 CA 125
가 3
35 U/ml 50
98.5% , 49
94.5% . Jacobs 19)
22,000 CA

125	0.2%	41	CA 125	CA 125	CA 125
CA 125	CA 125가 30 U/ml	11	7	CA 125	CA 125
CA 125	8	가		346 (2.6%)	
CA 125	CA 125	78.6%	35 U/ml	Zurawski8)	
13,038	347 (2.6%)	CA 125가 36.3 U/ml	Bast3)가	1.4%	3.9%
	1	가	13)	4.4%	
	2	가		43.3%	
가	CA 125				
가 1,615 U/ml	3	(c)	CA 125	66.19 ± 51.47(S.D.) U/ml	
, 27 U/ml	1	10	15.34	1994	20
	CA 125			20)	
2	10	15.81			
50%	CA 125	가	가	1000	3
100%	CA 125	가	가		
97.3%,	0.3%				
	CA				
125가			63		
가		CA 125	가		
			63		
Jacobs 19)	46	CA 125	가		
CA 125	73.02%		0.43 %		
1	78.6%	2	CA 125		
57.9%		가	가	1000	4
Helzlsouer20)					
20,305					가
CA 125					
3	57.1%	CA 125			
5	24%	CA 125		CA	
가	CA 125	125	가		
50%		CA 125	가		
CA 125		CA 125	50	50	
		CA 125	50	50	
CA 125가	347 (2.6%)	7,696	CA 125	15.10 ± 16.31 U/ml	
	Jacobs19)	16.3	2	95%	
0.2%	Einhorn18)	47.7 U/ml	50	5,342	9.67

± 23.36 U/ml
(P < 0.0001).
, 100 U/ml
가 (P < 0.001) 100 U/ml
가 .
50
47 U/ml
. CA
. CA 125
125 ,
가
.22) CA 125
.22)
CA 125
.2324)
CA 125
, , 가
, .
346 CA 125
190 156
, CA 125
156 CA 125
CA 125가 347
74% 258
CA 125가
3 CA 125
1
CA 125
2
50 가 41%
40 가 37.9%, 40 21.1%가
CA 125 가
가
CA 125
가
lkasian23) CA 125 가
90%
CA 125 가
Finkler25) CA 125

- References -

1. Berek JS, Fu YS, Hacker NF: CHAP.33. Ovarian cancer, in Berek JS, Adashi EY, Hillard PA(eds): Novak's Gynecology, Baltimore, USA. Williams & Wilkins. 12th ed 1996;PP1192.
2. Bast RCJ, Feeney M, Lazarus H, Nadler LM, Colvin RC, Knapp RC: Reactivity of a monoclonal antibody with human ovarian carcinoma. J Clin Invest 1981; 68:1331-7.
3. Bast RCJ, Klug TL, St. John E et al: A radioimmunoassay using a monoclonal antibody to monitor the course of epithelial ovarian cancer. N Engl J Med 1983;78:3199-203.
4. Schilthuis MS, Addlers JG, Bouma J et al: Serum CA 125 levels in epithelial ovarian cancer: Relation with findings at 2nd look operation and their role in the detection of tumor recurrence. Br J Obstet Gynecol 1987;94:202-7.
5. Canney PA, Moore M, wilkinson PM, James RD: Ovarian cancer antigen CA 125: A prospective clinical

- assessment of its role as a tumor marker. *Br J Cancer* 1984;50:765.
6. Einhorn N: Ovarian cancer: Early diagnosis and screening. *Hematol Oncol Clin North Am* 1992;6:843-850.
 7. Bast RCJ, Boyer C, Olt G et al: Identification of markers for early detection of epithelial ovarian cancer, in Sharp F, Mason W, Leake R(eds): *Ovarian Cancer*, London, United Kingdom, Chapman & Hall 1989; PP265-75.
 8. Zurawski VRJ, Brodrick SF, Pickens P, Knapp RC, Bast RCJ: Serum Ca 125 levels in a group of unhospitalized women: Relevance of the early detection of ovarian cancer. *Obstet Gynecol* 1987;69:606.
 9. Bast RCJ, Siegal FP, Runowicz C et al: Elevation of serum CA 125 prior to diagnosis of an epithelial ovarian carcinoma. *Gynecol Oncol* 1985;22:115-20.
 10. Zurawski VRJ, Sjoval K, Schoenfeld DA et al: Prospective evaluation of serum CA 125 levels in a normal population, phase I: The specificities of single and serial determination in testing for ovarian cancer. *Gynecol Oncol* 1990;36:299-305.
 11. Mann W, Pastern B, Cohen H et al: Preoperative serum CA 125 levels inpatients with surgical stage I invasive ovarian adenocarcinoma. *J Natl Cancer Inst* 1988;80:208-9.
 12. Jacobs IJ, Bast RCJ: The CA 125 tumor associated antigen: A review of the literature. *Human Reprod* 1989;4:1-12.
 13. , , , , , .
CA 125
1992;35:1800-9.
 14.
1995.
 15. Zurawski VRJ, Orjaseter H, Andersen A, Jellum E: Elevated serum CA 125 levels prior to diagnosis of ovarian neoplasia: Relevance for early detection of ovarian cancer. *Int J Cancer* 1988;42:677-80.
 16. Jellum E, Andersen A, Lund-Larsen P, Theodorsen L, Orjasaeter H: Experiences of the Janus Serum Bank in Norway. *Environmental Health Perspectives* 1995;3:103
 - Suppl: 85-8.
 17. Jacobs IJ, Bridges J, Reynolds C: Multimodal approaches to screening for ovarian cancer. *Lancet* 1988; 2:268-71.
 18. Einhorn N, Sjoval K, Knapp RC, Hall P, Scully R, Bast RCJ: Prospective evaluation of serum CA 125 levels for early detection of ovarian cancer. *Obstet Gynecol* 1992;80:14-8.
 19. Jacobs I, Davies AP, Bridges J, Stabiel I, Fay T, Lower A: Prevalence screening for ovarian cancer in postmenopausal women by CA 125 measurement and ultrasonography. *Br Med J* 1993;306:1030-4.
 20. Helzlsouer K, Bush J, Reynolds C et al: Prospective study of serum CA 125 levels as markers of ovarian cancer. *JAMA* 1993;269:1123-6.
 21. 16
1995;16:62-492.
 22. Grover S, Quinn M, Weidman P: Factors influencing serum CA 125 levels in normal women. *Obstet Gynecol* 1992;79:511-4.
 23. Malkasian GDJ, Knapp RC, Lavin PT et al: Preoperative evaluation of serum CA 125 levels in premenopausal patients with pelvic masses: Discrimination of benign from malignant disease. *Am J Obstet Gynecol* 1988; 158:341-6.
 24. Vasilev SA, Schwartz JB, Campeau J, Morrow CP: Serum CA 125 levels in preoperative evaluation of pelvic mass. *Obstet Gynecol* 1988;71:751-6.
 25. Finkler NJ, Benacerraf B, Lavin PT, Wojciechowski C, Knapp RC: Comparison of serum CA 125. clinical impression and ultrasound in the preoperative evaluation of ovarian masses. *Obstet Gynecol* 1988;72:659-64.
 26. Jacobs IJ, Jeyerejah A, Davies AP, Woolas R, Skates S, Oram DH: High sensitivity of an annual multimodal screening strategy for ovarian cancer(Abstract). *Gynecol Oncol* 1996;60:102.
 27. Skates SJ, Xu FJ, Yu YH et al: Toward an optimal algorithm for ovarian cancer screening with longitudinal tumor markers. *Cancer* 1995;76(10 suppl):2004-10.