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〔原著〕

A STUDY ON THE CLINICAL SIGNIFICANCE OF A COMPUTER-AIDED MULTIVARIATE PATTERN ANALYSIS SYSTEM (CAMPAS) IN OVARIAN TUMORS

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SUMMARY

A computer-aided multivariate pattern analysis system (CAMPAS) based on 10 discriminant formulas with 8 tumor markers, ie, cancer antigen 125 (CA 125), immunosuppressive acidic protein (IAP), tissue polypeptide antigen (TPA), lactic dehydrogenase (LDH), C-reactive protein (CRP), carcinoembryonic antigen (CEA), amylase and alkaline phosphatase, was developed and practised retrospectively and prospectively as a pretherapeutic serological diagnostic means to distinguish epithelial ovarian carcinomas from benign ovarian tumors. The CAMPAS is chronologically classified to 3 types of CAMPAS I, II and III.

In ovarian tumors and uterine neoplasms as well, these 3 types of CAMPAS were compared with one another, CA 125 and a squamous cell carcinoma-associated antigen (SCC) with the reference to the sensitivity, specificity and accuracy. In ovarian tumors the accuracy reached 71.9 and 73.2 % in CAMPAS I and II & III respectively, while the rate of CA 125 stayed at 58.8 %.

The present study demonstrate the potential clinical significance of the CAMPAS as a newly designed combination assay of tumor markers for ovarian cancers, although the diagnostic system still carries some problems to be solved, ie, its insufficient accuracy, low cost-effectiveness and unsatisfied combination of markers.

Key words: Tumor marker, Combination assay, CAMPAS, CA 125, Ovarian cancer

I. Introduction

Measurement of tumor markers is widely used as a serodiagnostic method for preoperative diagnosis of ovarian tumors[1-5]. With the development of many tumor markers in recent years[6], a combination assay with several tumor markers has been devised besides the single use of individual markers and utilized so as to improve the quality of diagnosis for ovarian tumors. However, while sensitivity inevitably increases with the increase in the number of tumor markers in a simple combination assay,

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Table 1. Eight tumor markers applied in CAMPAS

Tumor markers	Assay method	Company or laboratry	Upper limits
CA 125	solid phase RIA*1	Centocor (Pennsylvania)	35U/ml
CEA	solid phase RIA	Dainabot (Tokyo)	2.5ng/ml
TPA	solid phase RIA	Daiichiradioisotope (Tokyo)	110U/L
IAP	Laser NM*2	Sankoujuniyaku (Tokyo)	500μg/ml
LDH	UV method*3	Wakoujunuyakukogyo (Tokyo)	200~360U/L/37°C
CRP	Laser NM	Hoechst Japan (Tokyo)	350ng/ml
Amylase	Enzyme method	Kantokagaku (Tokyo)	60~200IU/L/37°C
ALP	RNP substrate method*4	Wakoujunyakukogyo (Tokyo)	68~220IU/L/37°C

*1 RIA : radioimmunoassay
*2 Laser NM : laser nephrometry
*3 UV method : ultragioletabsorption method
*4 RNP substrate method : ribonucleoprotein substrate method

specificity drops on the contrary (in relation to trade off) raising the problem of lowering the diagnostic efficiency.

Thus, since 1987, we have been trying to develop a computer-aided multivariate pattern analysis system (CAMPAS)[7,8] with the focus on ovarian tumors using a discriminant analysis, which is one of multivariate analyses, to raise specificity while retaining sensitivity of a combination assay as much as possible. We applied this CAMPAS which was developed in collaboration with SRL (Tokyo, Japan) under the guidance of Prof. Y, Terashima. (Jikei University School of Medicine, Tokyo, Japan) in clinical cases to examine usefulness and limits of the method in the diagnosis of ovarian tumors.

II. Subjects and Method

A total of 267 cases consisting of 64 cases of benign ovarian tumors, 51 cases of uterine myoma, 45 cases of endometriosis, 44 cases of ovarian cancer, 25 cases of cervical carcinoma, which were examined and operated by laparotomy in our department from December, 1987, to September, 1991, were assigned as subjects; all the cases were confirmed histopathologically.

Eight tumor markers, carbohydrate antigen 125 (CA 125)[9,10], carcinoembryonic antigen (CEA)[11], tissue polypeptide antigen (TPA)[12], immunosuppressive acidic protein (IAP)[13], lactate dehydrogenase (LDH)[14], C-reactive protein (CRP), amylase[15] and alkaline phosphatase (ALP)[16] were used in the analysis and the method of measurement and upper limits in non-pathological women are shown in Table 1. Squamous cell carcinoma-associated antigen (SCC) was also measured with use of SCC RIA kit (Dainabot, Tokyo), and it's upper limit was set at 2.0 ng/ml. Serum specimens were obtained from the blood collected at the preoperative, untreated stage, separated immediately and kept frozen at −80 °C.

The discriminant is a linear equation obtained by putting a fixed weight onto the measurement values of various tumor markers with the purpose of raising objective of judgement and diagnostic accuracy by discriminating the comprehensive judgement either positively or negatively[7]. A CAMPAS is chronologically classified to 3 types of CAMPAS I, II and III.

CAMPAS I (Table 2) which was used from December, 1987, to March, 1988, can be considered as the original form and composed of 4 combinations and 7 equations. The method of judgement was such that the tumor was decided as the ovarian cancer when the values of both equations A and B except 3 A became above 0.

CAMPAS II (Table 3) was used from April, 1988, to January, 1989, and, with the modification of all the equations following the change of TPA kit, the number of discriminants became 10 in total consisting of 5 equations in both A and B. Similarly to CAMPAS I, judgement of ovarian cancer

Table 2. CAMPAS I Discriminants

[1-A]			
Z = −50.522			
+11.358	×	LOG	[CA125]
+0.0288	×		[IAP]
+14.787	×	SQR	[CEA]
+0.0144	×		[Alp]
[2-A]			
Z = 13.500			
+1.4670	×	SQR	[CA125]
+0.0229	×		[IAP]
−427.5	÷		[LDH]
−3.2640	×	LOG	[CRP]
+15.250	×	LOG	[CEA]
[3-A]			
Z = 291.85			
+58.862	×	LOG	[CA125]
+0.1602	×		[IAP]
+0.0400	×		[TPA]
+0.03556	×		[LDH]
+5.5445	×	LOG	[CRP]
−16.010	×	LOG	[CEA]
+0.0101	×		[Amy]
+0.0231	×		[Alp]
[4-A]			
Z = −17.061			
−5.4750	×	LOG	[CA125]
+0.0313	×		[IAP]
+0.1919	×		[TPA]
−0.0511	×		[LDH]
+9.7703	×	LOG	[CRP]
−6.0485	×	LOG	[CEA]
−0.0649	×		[Amy]
−0.0601	×		[Alp]

[1-B]			
Z = −27.718			
+0.0426	×		[CA125]
+0.0174	×		[IAP]
−0.5027	×	SQR	[TPA]
+0.0090	×		[LDH]
−0.0077	×		[CRP]
+5.4085	×		[CEA]
+0.0759	×		[Alp]
[2-B]			
Z = −2.2257			
+1.2097	×	SQR	[CA125]
−2830.1	÷		[AP]
−0.1943	×	SQR	[CRP]
+20.244	×	LOG	[CEA]
−0.0532	×		[Alp]
[4-B]			
Z = −15.996			
+0.2283	×	SQR	[CA125]
−0.0003	×		[IAP]
−0.0245	×		[TPA]
+532.97	÷		[LDH]
+0.4827	×	SQR	[CRP]
+1.1162	×	SQR	[CEA]

was given if the values of both equations A and B become above 0 even in one combination.

CAMPAS III (Table 4) has been used since February, 1989, up to now and the equations 4 A and 5 A in CAMPAS II were modified to reduce the rate of false positive. The method of judgement is the same as in the above.

The equations 1 A and 1 B were made with the intention for serous cystadenocarcinoma, 2 A and 2 B for mucinous cystadenocarcinoma, 3 A, and 3 B for endometrioid carcinoma, 4 A and 4 B for mesonephroma and early carcinoma, and 5 A and 5 B for advanced carcinoma.

III. Results

1. CAMPAS in ovarian cancer

1) Sensitivity of CAMPAS and CA 125 (Table 5)

Table 3. CAMPAS II Discriminants

〔1-A〕			〔1-B〕		
Z = −45.5789			Z = −78.8003		
+4.06562	LOG	〔CA125〕	+0.5986	SQR	〔CA125〕
+0.01008		〔IAP〕	+14.4713	LOG	〔IAP〕
+0.2200	SQR	〔TPA〕	+0.02890		〔TPA〕
+8.5010	LOG	〔LDH〕	+3.7284	LOG	〔LDH〕
+0.09111	SQR	〔CRP〕	−0.4112	SQR	〔CRP〕
+3.9269	SQR	〔CEA〕	+7.8678	SQR	〔CEA〕
+0.03180		〔Alp〕	+7.3218	LOG	〔Alp〕
〔2-A〕			〔2-B〕		
Z = −47.7854			Z = −22.3718		
+14.5174	LOG	〔CA125〕	+5.9354	LOG	〔CA125〕
+0.03505		〔IAP〕	+0.01974		〔IAP〕
+6.9591	LOG	〔TPA〕	+5,7644	LOG	〔TPA〕
−0.03425		〔LDH〕	−0.01491		〔LDH〕
+3.0137	LOG	〔CRP〕	+0.1248	SQR	〔CEA〕
+0.2463	SQR	〔CEA〕	−0.01353		〔Amy〕
			−0.02089		〔Alp〕
〔3-A〕			〔3-B〕		
Z = −41.6263			Z = −6.3132		
+12.9071	LOG	〔CA125〕	+0.8509	SQR	〔CA125〕
+3.5763	LOG	〔IAP〕	+6.9765	LOG	〔TPA〕
+12.9742	LOG	〔TPA〕	−10.3145	LOG	〔LDH〕
−11.2782	LOG	〔LDH〕	+10.0015	LOG	〔CEA〕
+3.5632	LOG	〔CRP〕	+0.03711		〔Amy〕
+7.9830	LOG	〔CEA〕	+3.5842	LOG	〔Alp〕
+4.0439	LOG	〔Alp〕			
〔4-A〕			〔4-B〕		
Z = −53.2054			Z = −49.5114		
−3.9754	LOG	〔CA125〕	+0.03214	LOG	〔CA125〕
+31.7452	LOG	〔IAP〕	+12.6774	LOG	〔IAP〕
+9.6533	LOG	〔TPA〕	+3.1219	LOG	〔TPA〕
−1.1597	SQR	〔LDH〕	+1.3499	LOG	〔LDH〕
−4.2949	LOG	〔CRP〕	−1.9853	LOG	〔CRP〕
+17.0429	SQR	〔CEA〕	+7.0022	LOG	〔CEA〕
+0.83067	SQR	〔Amy〕	+8.8044	LOG	〔Amy〕
−204.6840		〔Alp〕	−5.0444	LOG	〔Alp〕
〔5-A〕			〔5-B〕		
Z = −37.5139			Z = −521.472		
+0.022785		〔IAP〕	−36.950	LOG	〔CA125〕
−2.4285	SQR	〔TPA〕	+86.241	LOG	〔IAP〕
+16.0316	LOG	〔LDH〕	−105.612	LOG	〔TPA〕
+5.11458	LOG	〔CRP〕	+69.047	LOG	〔LDH〕
−42.9254	SQR	〔CEA〕	+8.0935	LOG	〔CRP〕
+10.3822	LOG	〔Amy〕	+142.065	LOG	〔Amy〕

Table 4. CAMPAS Ⅲ Discriminants

〔1-A〕			〔1-B〕		
Z = −45.58			Z = −78.8		
+4.066	LOG	〔CA125〕	+0.5986	SQR	〔CA125〕
+0.01008		〔IAP〕	+14.47	LOG	〔IAP〕
+0.2200	SQR	〔TPA〕	+0.02890		〔TPA〕
+8.5010	LOG	〔LDH〕	+3.728	LOG	〔LDH〕
+0.09111	SQR	〔CRP〕	−0.4112	SQR	〔CRP〕
+3.9269	SQR	〔CEA〕	+7.868	SQR	〔CEA〕
+0.0318		〔Alp〕	+7.322	LOG	〔Alp〕
〔2-A〕			〔2-B〕		
Z = −47.79			Z = −22.3718		
+14.52	LOG	〔CA125〕	+5.935	LOG	〔CA125〕
+0.03505		〔IAP〕	+0.01974		〔IAP〕
+6.9591	LOG	〔TPA〕	+5.766	LOG	〔TPA〕
−0.03425		〔LDH〕	−0.01491		〔LDH〕
+3.0137	LOG	〔CRP〕	+0.1248	SQR	〔CEA〕
+0.2463	SQR	〔CEA〕	−0.01353		〔Amy〕
			−0.02089		〔Alp〕
〔3-A〕			〔3-B〕		
Z = −41.63			Z = −6.313		
+12.91	LOG	〔CA125〕	+0.8509	SQR	〔CA125〕
+3.576	LOG	〔IAP〕	+6.977	LOG	〔TPA〕
+12.97	LOG	〔TPA〕	−10.31	LOG	〔LDH〕
−11.28	LOG	〔LDH〕	+10.00	LOG	〔CEA〕
+3.563	LOG	〔CRP〕	+0.03711		〔Amy〕
+7.983	LOG	〔CEA〕	+3.584	LOG	〔Alp〕
+4.0439	LOG	〔Alp〕			
〔4-A〕			〔4-B〕		
Z = −55.155			Z = −49.511		
−8.658	In (In	〔CA125〕)	+0.03214	LOG	〔CA125〕
+38.325	In (In	〔AP〕)	+12.677	LOG	〔IAP〕
+12.610	In (In	〔TPA〕)	+3.1219	LOG	〔TPA〕
−6.428	In	〔LDH〕	+1.3499	LOG	〔LDH〕
−2.335	In (In	〔CRP〕)	−199853	LOG	〔CRP〕
−4.373%		〔CEA〕	+7.0022	LOG	〔CEA〕
			+8.8044	LOG	〔Amy〕
			−5.0444	LOG	〔Alp〕
〔5-A〕			〔5-B〕		
Z = −111.488			Z = −521.472		
+8.748	In (In	〔CA125〕)	−36.950	LOG	〔CA125〕
+70.424	In (In	〔IAP〕)	+86.241	LOG	〔IAP〕
+2.953	In	〔TPA〕	−105.612	LOG	〔TPA〕
−7.113	In	〔LDH〕	+69.047	LOG	〔LDH〕
−3.102	In (In	〔CEA〕+1)	+8.0435	LOG	〔CRP〕
			+142.065	LOG	〔Amy〕

Table 5. Sensitivity of CAMPAS and CA125 in ovarian cancer

n	CAMPAS I	CAMPAS II	CAMPAS III	CA 125
44	32 (72.7)*	29 (65.9)	28 (63.6)	25 (56.8)

*: No. positive (%)

Table 6. Sensitivity of CAMPAS and CA125 in ovarian cancer with regard to thelclinical staging

stage	n	CAMPAS I	CAMPAS II	CAMPAS III	CA 125
I a	12	4 (33.3)*	3 (25)	3 (25)	2 (16.7)
b	2	2 (100)	2 (100)	2 (100)	1 (50)
c	5	3 (60)	2 (40)	1 (20)	2 (40)
II a	1	1 (100)	0 (0)	0 (0)	1 (100)
b	4	2 (50)	2 (50)	2 (50)	1 (25)
c	4	4 (100)	4 (100)	4 (100)	4 (100)
III	10	10 (100)	10 (100)	10 (100)	8 (80)
IV	3	3 (100)	3 (100)	3 (100)	3 (100)
Metastatic carcinoma	3	3 (100)	3 (100)	3 (100)	3 (100)

*: No. positive (%)

Table 7. Sensitivty of CAMPASand CA125 in ovarian cancer with regard to histopatopathological cassification

	n	CAMPAS I	CAMPAS II	CAMPAS III	CA 125
Serous cystadenocarcinoma	15	10 (66.7)*	9 (60)	9 (60)	11 (73.3)
Mucinous cystadenocarcinoma	12	6 (50)	6 (50)	6 (50)	1 (8.3)
Endometrioid carcinoma	4	4 (100)	3 (75)	3 (75)	4 (100)
Mesonephroma	4	3 (75)	3 (75)	3 (75)	2 (50)
others	6	6 (100)	5 (88.3)	4 (66.7)	4 (66.7)
Metastatic carcinoma	3	3 (100)	3 (100)	3 (100)	3 (100)
Total	44	32 (72.7)	29 (65.9)	28 (63.6)	25 (56.8)

*: No. positive (%)

For 44 cases of ovarian cancer, CAMPAS I judged 32 cases as cancer and its sentitivity was 72.7 % (32/44). Similarly, CAMPAS II judged 29 as such with the sensitivity of 65.9 % (29/44) and CAMPAS III judged 28 cases as cancer with sensitivity of 63.6 % (28/44). CA 125 which is the most widely used marker in the field of gynecology judged 25 cases as cancer and its sensitivity was 56.8 % (25/44).

2) Sensitivity of CAMPAS and CA 125 with regard to the clinical staging (Table 6)

CAMPAS I showed high sensitivity of 92 % and II and III of 88 % for the advanced carcinoma above the stage II. For the early carcinomas of the stage Ia, the sensitivity of CAMPAS I was 33.3 % (4/12) while that of II and III was 25 % (3/12); the sensitivity of CA 125 was 16.7 % (2/12).

3) Sensitivity of CAMPAS and CA 125 in relation to histopathological classifications (Table 7)

Sensitivity of CAMPAS I for serous cystadenocarcinoma was 66.7 % (10/15) while that of II and III was 60 % (9/15) and that of CA 125, 73.3 %

Table 8. Specificity of CAMPAS and CA125 in benign ovarian tumors

	n	CAMPAS I	CAMPAS II	CAMPAS III	CA 125
Serous cystadenoma	17	16 (94.1)	15 (88.2)	15 (88.2)	14 (82.4)
Mucinous cystadenoma	16	13 (81.3)	13 (81.3)	13 (81.3)	12 (75)
Dermoid cyst	29	25 (66.2)	27 (93.1)	27 (93.1)	18 (62.1)
Thecoma	2	2 (100)	1 (50)	1 (50)	1 (50)
Endometrial cyst	₮5	22 (48.0)	27 (60)	28 (62.2)	20 (44.4)
Total	109	78 (71.6)	83 (76.1)	84 (77.1)	65 (59.6)

*: No. negative (%)

Table 9. Accuracy of CAMPAS and CA 125 in ovarian tumors

	CAMPAS I	CAMPAS II	CAMPAS III	CA 125
Sensitivity	72.7*	65.9	63.6	56.8
Specificity	71.6	76.1	77.1	59.6
Accuracy	71.9	73.2	73.2	58.8

*: %

Table 10. Sensitivity of CAMPAS, CA125 and SCC in uterine carcinoma

	n	CAMPAS I	CAMPAS II	CAMPAS III	CA 125	SCC
Cervical carcinoma	25	7 (28)*	7 (28)	5 (20)	4 (16)	7(28)
Endometrial carcinoma	38	9 (23.7)	9 (23.7)	9 (23.7)	14 (36.8)	—

*: No. positive (%)

(11/15). For mucinous cystadenocarcinoma, CAMPAS I, II and III all showed sensitivity of 50 % (6/12) and CA 125, 8.3 % (1/12).

2. Specificity of CAMPAS in benign ovarian tumors (Table 8)

CAMPAS I judged 78 cases as benign out of 109 cases of benign ovarian tumors and its rate of specificity was 71.6 % (78/109). Similarly, CAMPAS II judged 83 cases and III 84 cases as benign and their specificity rates were 76.1 (63/109) and 77.1 % (64/109), respectively.

CA 125 judged 65 cases as benign and its specificity was 59.6 % (65/109).

3. Rate of diagnostic accuracy of CAMPAS in ovarian tumor (Table 9)

The rate of diagnostic accuracy of CAMPAS I in ovarian tumor was 71.9 % while that of II and III reached to 73.2 %.

The rate of diagnostic accuracy of CA 125 was 58.8 %.

4. CAMPAS in uterine tumors

1) CAMPAS in uterine carcinoma (Table 10)

CAMPAS I and II judged 7 cases as malignant out of 25 cases of cervical carcinoma and the sensitivity was 28 % (7/25) while CAMPAS III gave the judgement of malignancy to 5 cases with the sensitivity of 20 % (5/25).

SCC, the tumor-related substance for uterine carcinoma, judged 7 cases as malignant the its sensitivity was 28 % (7/25).

All 3 CAMPAS formulae judged 5 out of 38 cases with endometrial carcinoma as malignant and the sensitivity was 23.7 % (9/38).

CA 125 judged 14 cases as malignant and its sensitivity was 36.8 % (14/38).

2) Specificity of CAMPAS in uterine myoma (Table 11)

CAMPAS I judged 45 cases out of 51 cases of uterine myoma as benign with 88.2 % of specificity (45/51) while CAMPAS II gave the judgement of

Table 11. Specificity of CAMPAS and CA 125 in uterine myoma

n	CAMPAS I	CAMPAS II	CAMPAS III	CA 125
51	45 (88.2)*	43 (84.3)	48 (94.1)	42 (82.4)

*: No. negative (%)

benign for 43 cases and CAMPAS III for 48 cases with 84. 3% (43/51) and 94.1% (48/51) respectively.

CA 125 judged 42 cases as benign and its specificity was 82.4% (42/51).

IV. Discussion

CA 125 has been used widely in diagnosis of ovarian cancer. It has many problems for clinical application because of low sensitivity in stage I of ovarian cancer and relative high false positive reaction in endometriosis although it gives the best results on diagnostic value such as sensitivity and specificity among the present tumor markers.

We tried all clinical inspection (13 markers such as CA 125, IAP, TPA, LDH, CEA, CRP, AMY, ALP, carbohydrate antigen 19-9 (CA 19-9), human chorionic gonadotropin (hCG) α-feto protein (AFP), ferritin and cancer antigen 15-3 (CA 15-3) that was considered as useful diagnosis for ovarian cancer at that time to improve these problems of CA 125 against patients with ovarian cancer and gynecological disease as control. Then we can improve an accuracy of diagnosis for ovarian cancer with clinical inspection by selecting useful marker for identification diagnosis for ovarian cancer by relative operating characteristic curve (R-O-C curve) analysis[17] and identification analysis, and judging cancer or not with identification function based on above inspection results. Fig. 1 shows the general idea of discriminant analysis. In cases of giving the judgement of being normal or not by 2 kinds of examinations, let us suppose that scatter diagram shown in Fig. 1 is given on the x_1-x_2 plane and the distribution patterns of the values in the normal and disease groups are already known. In this case, the discrimination efficiency is not high on either x_1 or x_2 alone due to the overlap of distribution of both groups. However, if a straight line, l, is drawn on the scatter diagram so as to

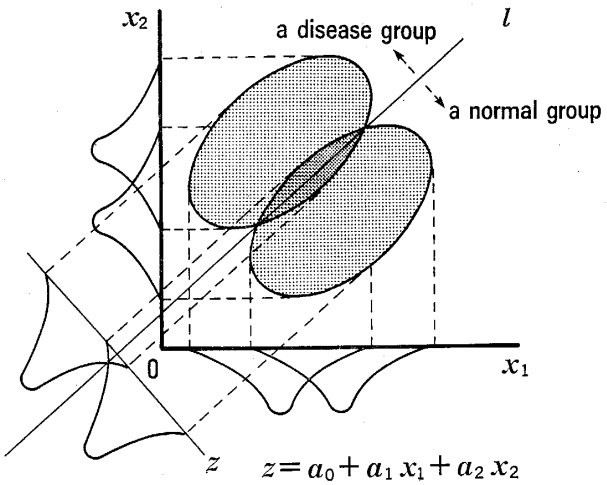

Fig. 1 A scatter diagram of the values of 2 kinds of examination (χ_1, χ_2) and the general idea of discriminant analysis

make the overlap to the minimum and take the z axis perpendicular to the line, high efficiency can be obtained by considering distributions of the two gropus on the z axis. The coordinates on the z axis are expressed in the linear combination of x_1 and x_2 as the z axis is a line on the x_1-x_2 plane. Thus, $z=a_0+a_1 x_1+a_2 x_2$ (*). By setting a_0 so as to make the point of intersection of the line, l, and the z axis as $z=0$, the individual concerned can be judged either normal or not by finding whether the value z obtained by substituting the values of the 2 examinations into (*) becomes positive or negative. The method is the same when the examination values more than 3 kinds.

On the basis of the above concept, we have developed and modified CAMPAS in order to offset the disadvantages of the combination assay of tumor markers used as the serodiagnosis the preoperative diagnosis for ovarian tumor and to improve objectivity of the diagnosis.

While the sensitivity of CAMPAS in ovarian cancer dropped accompanying the modification of the discriminant as the values 72.7% for the formula I, 65.9% for II and 77.1% for III, its specificity

rose from 71.5 % to 75.1 and 77.1 %, although the trade-off relationship could not be avoided even CAMPAS, the rate of diagnostic accuracy was improved from 71.9 % by the formula I to 73.2 % by II and III with the modification of the discriminant.

In the aspect of histopathology, sensitivity of CAMPAS I in serous systadenocarcinoma was 66.7 %, that of both II and III was 60 % while the sensitivity of CA 125 was higher as 73.3 %. For mucinous cystadenocarcinoma, on the other hand, the sensitivity of CA 125 was 8.3 %, which was much lower than that of all 3 CAMPAS formulae as 50 %. This shows the difficulty of giving accurate diagnosis for ovarian cancer with variegated histological forms by a single tumor marker.

Referring to the clinical stage of ovarian cancer, high sensitivities were shown in the cases above the stage IIa as 92 % by the formula I and 88 % by both II and III. For the cases of the stage I, the sensitivities of I, II and III became 47.4, 36.8 and 31.6 % and, limiting to the stage Ia, the values became markedly low as 33.3 % by CAMPAS I and 25 % by II and III though these were still higher than 16.7 % of CA 125.

As the method showed 20-28 % sensitivity in uterine malignancies, necessity of cytodiagnosis of uterine cervix and endometrium to exclude uterine malignancies examination was indicated.

From the above, the rate of diagnostic accuracy of CAMPAS for ovarian tumor reached 71.9 % by the formula I and 73.2 % by II and the method was considered useful as an auxiliary method for the diagnosis of ovarian cancers. However, when improvement of the rate of diagnostic accuracy for the early ovarian cancer and handiness including the cost were considered, necessity of modifying CAMPAS by the combination of fewer tumor markers which were highly sensitive to ovarian malignancies was pointed out.

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要　旨

既存の8種類の腫瘍マーカー cancer antigen (CA 125), immunosuppressive acidic protein (IAP), tissue polypeptide antigen (TPA), lactic dehydrogenase (LDH), C-reactive protein (CRP), carcinoembryonic antigen (CEA), amylase, allkaline phosphatase (ALP) を用いて多変量解析を行い，術前における卵巣腫瘍の質的診断（上皮性卵巣癌の鑑別診断）の向上を目的とした判別式 a computer-aided multivariate pattern analysis system (CAMPAS) を作成した。同判別式は主として特異度につき改良を重ね，年代順に CAMPAS I式，CAMPAS II式，及び CAMPAS III式とした。この CAMPAS を実施臨床に応用し，卵巣腫瘍診断における有用性を検討すると共に，子宮頸癌，子宮内膜癌等の他の子宮悪性腫瘍に対する陽性率を調べ，CAMPAS の上皮性卵巣癌に対する特異性の限界について検討した。

卵巣腫瘍に対する正診率は，CAMPAS I式は71.9 %，CAMPAS II式および CAMPAS III式は73.2%に達し卵巣腫瘍の診断に際し，有用な補助的診断法の一つと考えられた。一方，CAMPAS のタージェット外の婦人科悪性腫瘍である子宮頸癌，子宮内膜癌でもその陽性率は最高28%に達するため，CAMPAS 陽性の場合，これらの悪性腫瘍の可能性も考慮する必要性が示唆された。

また，卵巣悪性腫瘍における正診率もまだ不十分で，しかも，cost-effectiveness の面から腫瘍マーカーの選択を含めた CAMPAS の改良の必要性も示唆された。

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