EVALUATION OF A DECISION-SUPPORT SYSTEM FOR PREOPERATIVE STAGING OF PROSTATE CANCER

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The usefulness and effectiveness of a decision-support system for preoperative staging of prostate cancers (PCES) were evaluated. The study population consisted of 43 consecutive patients with the preoperative diagnosis of prostate cancer who underwent surgical operation. Results obtained using the PCES were compared with staging by four urology attending physicians and five urology residents. The effect of PCES consultation on the physicians' staging of prostate cancer was also evaluated. To confirm the usefulness of the clinical findings of prostate-specific antigen, prostate-specific antigen density, prostate volume, and abnormal Gleason score in the PCES, their receiver operating characteristic (ROC) curves for diagnosis of advanced prostate cancer were plotted. The values of the areas under the curves were 0.772, 0.800, 0.531, and 0.752. The stage of prostate cancer was correctly determined by the PCES for 38 of the 43 patients, yielding 88.4% preoperative diagnostic accuracy. The PCES was significantly more accurate than two of the attending physicians and all residents. PCES consultation improved the residents' staging accuracy to approximately that of the attending physicians. The effect of PCES consultation on the residents' staging was significantly ($p < 0.001$) greater than the effect on the physicians' staging. The PCES may be useful in the preoperative staging of prostate cancers, especially during residency. The system's accuracy in determining the stage of advanced prostate cancer may make it possible to avoid unnecessary surgical operations. *Key words*: decision-support system; expert system; prostate cancer. **(Med Decis Making 1999;19:419–427)**

Accurate preoperative staging of prostate cancer is a difficult process. About a third of patients thought preoperatively to have organ-confined prostate cancer are found to have extraprostatic involvement at the time of operation.[1] Preoperative staging for prostate cancer is very important because the methods of management of localized and advanced prostate cancers differ. Surgical operation is usually the method of choice for localized prostate cancer. Radiotherapy and/or hormone therapy are usually the method of choice for advanced prostate cancer.[2]

A medical decision-support system is a computer-based consultation system using artificial intelligence technique to emulate the decision-making behavior of a human medical expert.[3] Decision-support system training has been reported to be useful in making management decisions for patients with prostate cancer.[4] Since 1991, we have developed an expert system to help residents diagnose renal masses more accurately preoperatively.[5] In 1993, we developed another decision-support system, the prostate cancer expert system (PCES), to preoperatively evaluate patients undergoing operation for prostate cancers.

The standard technique to detect the extent of prostate cancer is prostate-specific antigen (PSA) determination, followed by digital rectal examination (DRE), transrectal ultrasonography (TRUS) with biopsy, abdominal computed tomography (CT), and magnetic resonance imaging (MRI). For diagnosis of prostate cancer, serum PSA is one of the most important tumor markers. PSA elevations to values greater than 4 ng/mL may warrant prostatic biopsy. The higher the PSA concentration, the less likely a prostate cancer is to be localized.[6] However, the predictive value of PSA alone is too low to be clinically useful for individual patients. DRE provides clinical information about the size and location of prostate cancer. However, staging of prostate cancer by DRE alone is inaccurate and is dependent on the examiner's experience. TRUS has been used for many years to assess both the volume of cancer within the prostate and extracapsular extension. The sensitivity

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of TRUS in detecting extracapsular extension of prostate cancer has been reported to be 59–87%.[7] TRUS has also been reported to be a valuable method for the staging of prostate cancer.[8] However, even if TRUS could accurately assess tumor volume, its predictive value is too low for sole use in making treatment decisions.[9] We believe that combining PSA levels and the findings of DRE and TRUS can increase the accuracy of preoperative assessment of the extent of prostate cancer. By utilizing a Bayesian probabilistic inference engine and a frame-based knowledge base, the PCES provides physicians with a preoperative staging of prostate cancer when PSA, DRE, TRUS, and other clinical findings are given. The PCES was developed in an effort to improve the interpretation of preoperative staging techniques to discriminate between localized and advanced prostate cancers. In this study, we evaluated the usefulness and effectiveness of the PCES in the preoperative staging of localized and advanced prostate cancers and compared the accuracy of results obtained using the PCES with the accuracy of staging performed by four attending physicians in urology and five urology residents.

Table 1 • Probabilistic Frame for Prostate Cancer with Lymph-node Involvement: Posterior Probability 0.769

	Status	Cost	True-positive Rate	False-positive Rate	Likelihood Ratio LR+	Likelihood Ratio LR−
Prostate-specific antigen (ng/mL)						
normal ≤ 4.0	45.0					
21–30		$30	0.42	—	4.66	0.09
31–40			0.58	—	19.30	0.03
41–50			0.70	—	25.40	0.02
>50			0.75	—	28.50	0.02
Transrectal ultrasonography shows						
hypoechoic lesions in both peripheral and transitional zones		$60	0.45	1.63	4.50	0.10
or						
tumors have an irregular outline and capsular distortion			0.52	1.87	5.20	0.10
or						
tumor involves seminal vesicles			0.80	4.75	16.00	0.05
Digital rectal examination shows						
a palpable mass, involves both lobes			0.48	1.67	3.69	0.13
or						
a palpable mass, involves seminal vesicles			0.70	2.93	5.83	0.12
or						
a palpable mass, outside capsule			0.60	2.25	6.00	0.10
Abdominal CT scan shows enlargement of pelvic lymph nodes		$300	0.90	8.50	6.00	0.15
Bone scan shows no bone metastasis		$300	0.85	2.33	1.70	0.50
Chest film (PA) shows no lung metastasis		$10	0.80	1.50	1.14	0.70
Gleason score		$20				
5–6			0.30	—	2.00	0.15
7–8			0.60	—	7.50	0.08
>8			0.82	—	8.00	0.01
Prostate-specific antigen density (normal < 0.15)						
0.15–0.30			0.30	—	1.00	0.30
0.31–0.44			0.40	—	1.02	0.39
>0.45			0.60	—	1.17	0.50

Table 2 • Prostate Cancer Expert System Categorization of Prostate-specific Antigen, Digital Rectal Examination, and Transrectal Ultrasonography Findings

	Prostate-specific Antigen	Digital Rectal Examination	Transrectal Ultrasonography
1	≤4	Nonpalpable	No hypoechoic lesion
2	5–10	Palpable, less than one lobe, surrounded by normal tissue	A small hypoechoic lesion (≤0.7 cm) in the peripheral zone
3	11–15	Palpable, less than one lobe	A larger hypoechoic lesion (>0.7 cm) in the peripheral zone
4	16–20	Palpable, one entire lobe	A hypoechoic lesion in the transitional zone with normal peripheral zone
5	21–30	Palpable, involves both lobes	Hypoechoic lesions in both peripheral and transitional zones
6	31–40	Palpable, outside capsule, not into seminal vesicles	Tumors have an irregular outline and capsular distortion
7	41–50	Palpable, involves seminal vesicles	Tumor involves seminal vesicles
8	>50		

Materials and Methods

The PCES for preoperative staging of prostate cancer was developed and run on an IBM-compatible personal computer. It was developed using the IL-IAD shell, which is a large expert system for differential diagnosis.[10] The PCES decision-support system contains 12 prostate cancer probabilistic frames. Table 1 shows the probabilistic frame for prostate cancer with lymph-node involvement. The probabilistic frame is designed by knowledge engineers using the true-positive rate and the false-positive rate to represent the relationships of abnormal findings to stages of prostate cancer. Much of the power of the PCES to mimic expert behavior is based upon the way these frames can interact with one another. These clinical findings are processed sequentially, using Bayes' theorem, which describes the relationship of a stage of prostate cancer to its manifestations, and provides a basis for explaining its conclusions.[11] Initially, 16 cases of prostate cancer (two cases in each stage) were used to train the model. Before beginning our study, the PCES was used in the diagnosis of prostate cancers for about six months and corrected as needed.

The clinical stages of prostate cancer are classified as A1, A2, B1, B2, C1, C2, D1, and D2. Stage A1 and A2 cancers occur in the transition zone of the prostate and are discovered incidentally during surgery for benign prostatic hyperplasia. Stage B1 and B2 cancers are confined to the prostate. Stage C1 and C2 cancers are those involving soft tissues outside the prostate. Stage D1 cancers involve pelvic lymph nodes. Stage D2 cancers involve distant organs. In our study, localized prostate cancer included stages A1, A2, B1, B2, C1, and C2, and advanced prostate cancer included stages D1 and D2. In the PCES, localized prostate cancer contains six probabilistic frames and advanced prostate cancer contains another six probabilistic frames.

The PCES stages prostate cancer by using the following information: 1) patient age; 2) PSA level; 3) prostate-specific antigen density (PSAD); 4) DRE findings; 5) TRUS findings; 6) Gleason score (from the prostate biopsy); 7) abdominal CT scan findings; 8) chest x-ray findings; 9) bone scan results; and 10) MRI findings. All of this information is important for staging the prostate cancer. However, surgical exploration is necessary to detect pelvic lymph-node involvement in patients with stage D1 prostate cancer. The output of the PCES is a list of probable diagnoses in descending order of their probability. The stage of prostate cancer was determined by the PCES if the diagnosis was listed as the most likely diagnosis and its calculated probability was greater than 50%. In this study, two diagnostic categories were considered: "localized" and "advanced" prostate cancers. Stage D2 cancers were easily diagnosed and were excluded from the study.

From January 1993 to November 1997, 674 consecutive patients at our hospital received the diagnosis of prostate cancer. Transrectal biopsies of the prostate histologically confirmed prostate cancer in all patients. Five hundred and twenty-six patients (78%) who had the diagnosis of stage D2 prostate cancer with positive findings in bone scanning were scheduled to receive radiotherapy and/or hormone therapy. One hundred and five patients who had the diagnosis of prostate cancer without metastasis refused surgical operation, and received radiotherapy and/or hormone therapy. The remaining 43 patients with the clinical diagnosis of prostate cancer were admitted to our hospital and underwent surgical operation. After patient admission to our department, a complete history was taken and a physical examination performed, followed by urinalysis and a plain film of the abdomen. All patients underwent the usual preoperative diagnostic evaluation for prostate cancer. The patients' ages ranged from 46

to 75 years, with an average age of 67 years. All patients had CT scan examinations, and ten patients had MRI examinations.

The findings of PSA, DRE, and TRUS utilized in the PCES are categorized in table 2. PSA, DRE, and TRUS are essential examinations for the diagnosis of prostate cancers. Prostate volume and PSAD are additional data that aid physicians in staging the cancers. Prostate volume is measured by TRUS and PSAD is the value of PSA divided by prostate volume. Most cases of advanced prostate cancer occur in patients who have higher serum concentrations of PSA and more abnormal Gleason scores in prostate biopsy.[12–14] To assess the accuracy of using the combination of PSA, PSAD, prostate volume, and Gleason score for the diagnosis of advanced prostate cancer, we used receiver operating characteristic (ROC) curves and calculated the areas under the curves (AUCs). ROC curves were produced by plotting the relationships of sensitivity and false positivity (1 − specificity) at various cutoff values.

Before surgical operation, four attending physicians in urology, a urology chief resident, two second-year urology residents, and two first-year urology residents were asked to categorize prostate cancers as being localized or advanced. The clinical findings of the patients were then input into the PCES by another physician. The final diagnoses of all cases were confirmed by pathologic examination after operation. The pathologic findings were used as the "gold standard" diagnoses.

The accuracy of preoperative staging of prostate cancers using the PCES was compared with the accuracies of the staging performed by the attending physicians and residents to test the validity of the PCES. Postoperatively, when the stage of the prostate cancer had been determined, the diagnosis made by the PCES was shown to all physicians (PCES consultation), and they were asked whether they would like to change their preoperative choices of staging for localized and advanced prostate cancers. The effects of PCES consultation on the physicians' staging of prostate cancer were evaluated.

McNemar's test was used to measure the significances of differences between PCES and physicians' stagings of localized and advanced prostate cancers. The paired t test was used to measure the significance of differences in staging by physicians before and after PCES consultation.

Results

In order to confirm the effectiveness of using the PSA, PSAD, prostate volume, and Gleason score to diagnose advanced prostate cancers, we subjected our results to ROC-curve analysis. Figures 1–4 depict the ROC curves and cutoff values for PSA, PSAD, prostate volume, and Gleason score; the values for the areas under the ROC curves were 0.772, 0.800, 0.531, and 0.752, respectively.

In this series, there were 43 consecutive patients with prostate cancers who underwent surgical operation. The PCES correctly identified the localized and advanced prostate cancers in 38 of the 43 cases, yielding an 88.4% overall preoperative staging accuracy, which compared with the four attending physicians' accuracies of 74.4%, 67.4%, 76.7%, and 83.7% (average 75.6%). The accuracies of the residents (chief resident, second-year residents 1 and 2, and

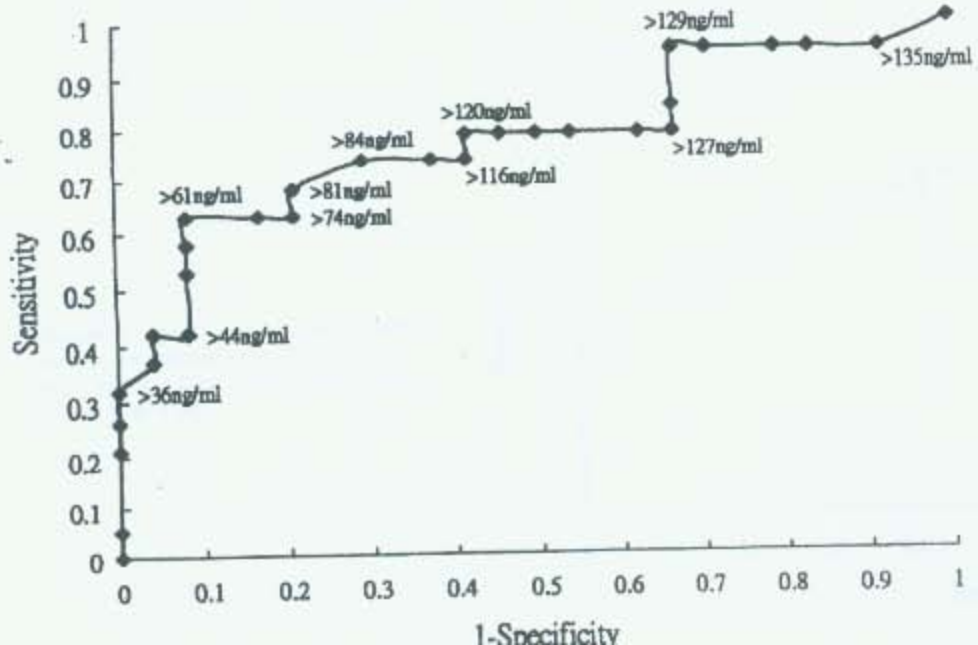

FIGURE 1. ROC curve and cutoff values for prostate-specific antigen (PSA). The area under the curve was 0.772.

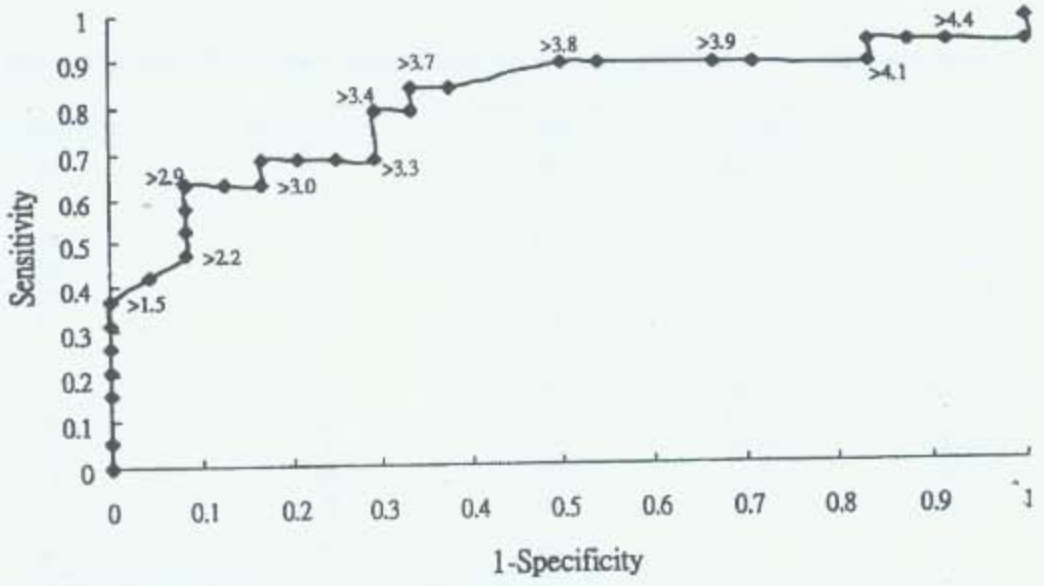

FIGURE 2. ROC curve and cutoff values for prostate-specific antigen density (PSAD). The area under the curve was 0.800.

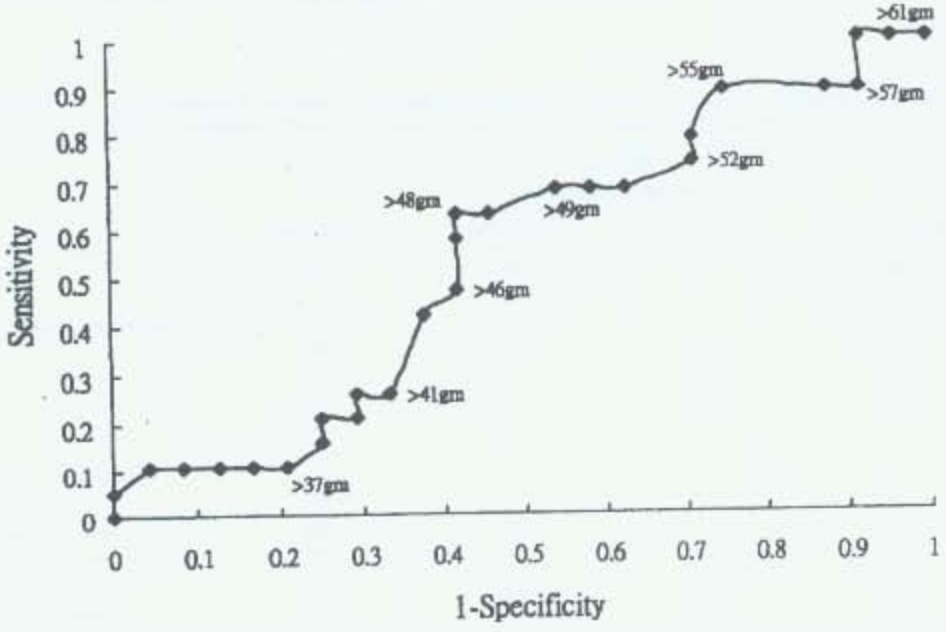

FIGURE 3. ROC curve and cutoff values for prostate volume. The area under the curve was 0.531.

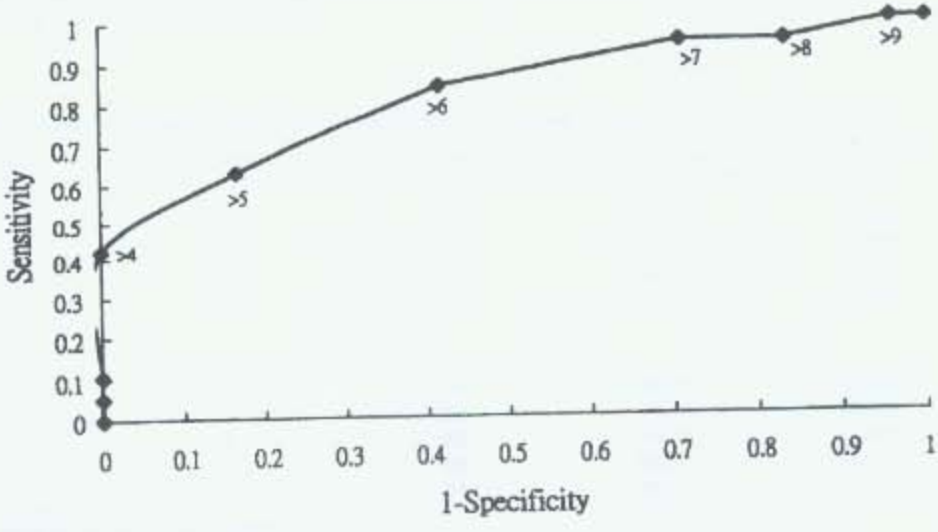

FIGURE 4. ROC curve and cutoff values for abnormality of the Gleason score. The area under the curve was 0.752.

Table 3 • Staging Accuracy for Prostate Cancers (PCs) of the Prostate Cancer Expert System (PCES) and of Physicians before PCES Consultation

	Localized PCs	Advanced PCs	Total	Accuracy	p†
PCES	22	16	38	88.4	
Attending physicians					
1	19	13	32	74.4*	0.042
2	19	10	29	67.4*	0.008
3	21	12	33	76.7	0.074
4	22	14	36	83.7	0.480
Urology residents					
Chief	16	9	25	58.1*	<0.001
Second year—1	15	12	27	62.8*	0.003
Second year—2	17	7	24	55.8*	<0.001
First year—1	9	13	22	51.2*	<0.001
First year—2	15	8	23	53.5*	<0.001
Pathologic stage	24	19	43		

*The PCES was significantly more accurate than attending physicians 1 and 2 and all urology residents.
†Compared with the accuracy of the PCES.

Table 4 • Confidence Intervals of the Sensitivities and Specificities of the Staging of Localized and Advanced Prostate Cancers by the Prostate Cancer Expert System (PCES) and by Physicians

		Sensitivity Confidence Intervals			Specificity Confidence Intervals	
	Sensitivity	Upper 95%	Lower 95%	Specificity	Upper 95%	Lower 95%
PCES	92	98	86	84	90	78
Attending physicians						
1	79*	85	73	68*	74	62
2	79*	85	73	53*	59	47
3	88	94	82	63*	69	57
4	92	98	86	74	80	68
Urology residents						
Chief	67*	73	61	47*	53	41
Second year—1	63*	69	57	63*	69	57
Second year—2	71*	77	65	37*	43	31
First year—1	38*	44	32	68*	74	62
First year—2	63*	69	57	42*	48	36

*The sensitivity of the PCES was significantly better than those of attending physicians 1 and 2 and all residents; the specificity of the PCES was significantly better than those of the attending physicians 1, 2, and 3 and all residents.

Table 5 • Physicians' Accuracies in Staging Prostate Cancers (PCs) after Prostate Cancer Expert System (PCES) Consultation

	Localized PCs	Advanced PCs	Total	Accuracy	p†
Attending physicians					
1	20	13	33	76.7	0.356
2	21	11	32	74.4	0.078
3	22	13	35	81.4	0.172
4	22	15	37	86.0	0.356
Urology residents					
Chief	20	11	31	72.1*	0.017
Second year—1	19	13	32	74.4*	0.008
Second year—2	22	10	32	74.4*	0.030
First year—1	17	13	30	69.8*	0.005
First year—2	20	11	31	72.1*	0.015

*PCES consultation significantly increased the staging accuracies of all residents.
†Compared with the accuracy before PCES consultation.

first-year residents 1 and 2) were 58.1%, 62.8%, 55.8%, 51.2% and 53.5% (average 56.3%). The PCES was significantly more accurate than two of the attending physicians and all of the residents (table 3).

Of the 43 patients undergoing surgical operation, 24 had localized prostate cancers and the remaining 19 had advanced prostate cancers. The PCES categorized the prostate cancers as localized or advanced in 38 of the 43 cases. Twenty-two of the 24 localized prostate cancers and 16 of the 19 advanced prostate cancers were correctly assigned, thereby producing three false-positive and two false-negative results. This yielded a sensitivity of 92% and a specificity of 84% for differential diagnosis of localized and advanced prostate cancers. The sensitivity of the PCES was significantly better than those of two attending physicians and all residents and the specificity of the PCES was significantly better than those of three attending physicians and all residents. Table 4 shows confidence intervals of the sensitivity and specificity of the staging of the localized and advanced prostate cancers by the PCES and the physicians.

The staging accuracies of the five residents were significantly different after PCES consultation. On average, the staging accuracy of the five residents increased from 56.3% before PCES consultation to 72.6% after PCES consultation, which was similar to the level of the attending physicians' accuracy. After PCES consultation, the four attending physicians changed their diagnoses, and increased their average staging accuracy from 75.6% to 79.6%. However, the change in the average staging accuracy of the attending physicians after PCES consultation was not significant. The numbers of correct choices of preoperative staging for localized and advanced prostate cancers made by the physicians after PCES consultation are shown in table 5. The effect of PCES consultation on the residents' staging for localized and advanced prostate cancers was significantly ($p < 0.001$) greater than the effect on the attending physicians' staging (fig. 5).

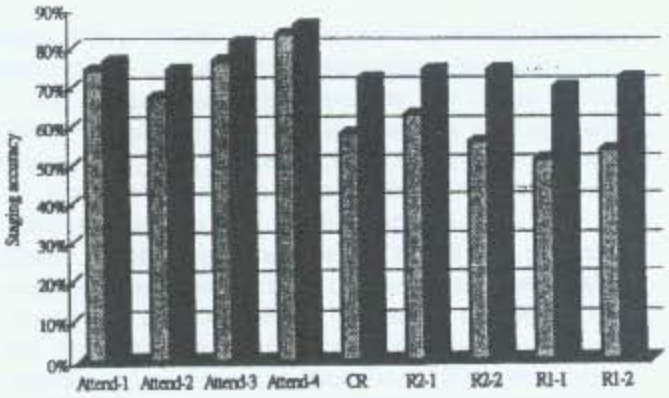

FIGURE 5. The increases of staging accuracy from before (light bars) to after (darker bars) prostate cancer expert system (PCES) consultation were significantly greater in urology residents than in attending physicians.

Discussion

The decision-making knowledge used in medical decision-support systems is often based on the experience and knowledge of medical experts in a specific field. The decision-making knowledge we used in the development of the PCES was based on the patient database of our hospital, the knowledge and experience of urologists in our hospital, and scientific clinical literature in the field of prostate cancer. The PCES was developed using the Bayesian theorem and thus cannot provide absolute and definitive stages of prostate cancer. It assigns a probability to each possible stage and, typically, bases its conclusion on the highest probability. When a parameter does not significantly discriminate between staging categories, the derived probabilities for that parameter will be approximately equal for all stages. Such a factor simply will have little mathematical consequence in the final calculations in the PCES. Bayesian theory has been used in many successful decision-support systems for years.[15–17]

The PCES uses clinical findings of previously evaluated patients to predict the diagnoses of new patients. These clinical findings were selected for their ability to discriminate between localized and advanced prostate cancers. The frequency with which each of these clinical findings was found in each diagnostic category made up a conditional probability that was incorporated into a Bayesian algorithm. The Bayesian algorithm then used the clinical experience embodied in the conditional probability to calculate the probability that the patient would fall into the group of localized or advanced prostate cancer. The major difficulty in creating the PCES system was the estimation of the false-positive rates of clinical findings in each stage. These rates greatly affected the staging accuracy of the PCES system. The false-positive rates for clinical findings were not easy for physicians to determine. The expert judgment of an experienced physician was always needed to get an appropriate false-positive rate.

The exact proportions of prostate cancers in the individual clinical stages at presentation vary. In 1990, the American College of Surgeons reported incidences of 27.0–29.3% for stage A prostate cancer, 26.0–37.7% for stage B, 12.5–13.0% for stage C, and 20.6–34.0% for stage D.[2] In our series, the incidence of stage D2 prostate cancer was higher. Aggressive and early diagnosis of prostate cancer is necessary. Therefore, we developed the PCES to aid urologists to make accurate diagnoses of prostate cancers.

ROC curves provide an index of accuracy by demonstrating the limits of a test's ability to discriminate between alternative states of disease over the complete spectrum of operating conditions. Each point on the ROC curve represents a sensitivity–specificity pair corresponding to a particular decision threshold. Qualitatively, the closer the curve is to the upper left corner, the higher the overall accuracy of the test.[18]

The measure most commonly used to quantify the diagnostic accuracy of a laboratory test is the area under the ROC curve. An AUC of 1.0 is characteristic of a perfect test, whereas below 0.5 indicates a test of no diagnostic value.[19] The AUCs for PSA, PSAD, prostate volume, and Gleason score all were greater than 0.5 in the diagnosis of advanced prostate cancer. This means that all these tests were useful for categorization of localized and advanced prostate cancers. For example, an AUC of 0.7 means that a randomly selected individual from the group of advanced prostate cancer has a laboratory test value larger than that for a randomly chosen individual from the group of localized prostate cancer 70% of the time.

In order to understand the usefulness of the PCES, we calculated the diagnostic accuracy of the PCES in this series and compared it with the diagnostic accuracies of four attending physicians and five urology residents (table 3). Significant differences between the accuracies of staging obtained by the PCES and the staging assigned by two of the attending physicians and all of the residents suggest that the inferencing algorithm and knowledge representation in the PCES may be useful in improving diagnostic accuracy in the staging of localized and advanced prostate cancers.

For preoperative staging of localized and advanced prostate cancer, the PCES had a sensitivity of 92% and a specificity of 84%. The sensitivity was significantly better than those of two of the attending physicians and all of the residents. The specificity was significantly better than those of three of the attending physicians and all of the residents (table 4). The high sensitivity and specificity of the PCES support its usefulness for the staging of prostate cancers. Since the PCES was intended not to replace urologists but rather to aid them, the system's diagnostic supportive value would have to be further investigated.

After PCES consultation, the physicians changed their preoperative staging of prostate cancers. The residents' staging accuracy significantly improved such that it was similar to that of the attending physicians. Although the increase in the attending physicians' diagnostic accuracy after PCES consultation was not significant, it did reflect some improvement (table 5). The increases in the residents' staging accuracy after PCES consultation were significantly greater than those of the attending physicians (fig. 5). This finding strongly supports the value of the PCES in training residents' and its role in diagnostic decision support. These urology residents changed their diagnoses because the PCES reminded them of clinical findings that need attention.

These results indicate that the PCES can perform as well as human experts in the preoperative staging of localized and advanced prostate cancers. The PCES may provide sufficient information to help physicians to make early diagnoses of prostate cancers. Physicians' use of the PCES in combination with conventional staging methods may provide more accurate staging and thereby help in making treatment management decisions. The PCES may be especially important in preoperative consultation for urology residents. The accuracy of the PCES for determining the stage of advanced prostate cancer may make it possible to avoid unnecessary surgical operations by the use of this system to determine the tumor stages of advanced disease. This will also reduce unnecessary complications associated with surgical operation.

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References

1. Partin AW, Yoo J, Carter HB, et al. The use of prostate specific antigen, clinical stage and Gleason score to predict pathological stage in men with localized prostate cancer. J Urol. 1993;150:110–4.
2. Narayan P. Neoplasm of the prostate gland. In: Tanagho EA, McAninch JW (eds). Smith's General Urology. 14th ed. East Norwalk, CT: Appleton and Lange, 1995.
3. Shortliffe EH. Medical expert system—knowledge tools for physicians. West J Med. 1986;145:830–9.
4. Snow PB, Smith DS, Catalona WJ. Artificial neural networks in the diagnosis and prognosis of prostate cancer: a pilot study. J Urol. 1994;152:1923–6.
5. Chang PL, Li YC, Wu CJ, Huang MH, Haug PJ. Clinical evaluation of a renal mass diagnostic expert system. Comput Biol Med. 1994;24:315–22.
6. Hudson MA, Bahnson RR, Catalona WJ. Clinical use of prostate specific antigen in patients with prostate cancer. J Urol. 1989;142:1011–7.
7. Salo JA, Kivisaari L, Rannikko S, Lehtonen T. Computerized tomography and transrectal ultrasound in the assessment of local extension of prostate cancer before radical retropubic prostatectomy. J Urol. 1987;137:435–8.
8. Pontes JE, Eisenkraft S, Watanabe H, Ohe H, Saitoh M, Murphy GP. Preoperative evaluation of localized prostate carcinoma by transrectal ultrasonography. J Urol. 1985;134:289–91.
9. Gerber GS, Goldberg R, Chodak GW. Local staging of prostate cancer by tumor volume, prostate-specific antigen, and transrectal ultrasound. Urology. 1992;40:311–8.
10. Warner H, Haug P, Lincoln M, Warner H Jr, Sorenson D, Fan C. Iliad as an expert consultant to teach differential di-

agnosis. In: Proceedings of the 11th Symposium on Computer Applications in Medical Care. Washington, DC: IEEE Computer Society Press, 1987:371–6.
11. Edwards FH, Graeber GM. The theorem of Bayes as a clinical research tool. Surg Gynecol Obstet. 1987;165:127–9.
12. Kramer SA, Spahr J, Brendler CB, Glenn JF, Paulson DF. Experience with Gleason's histopathologic grading in prostate cancer. J Urol. 1980;124:223–5.
13. Danella JF, deKernion JB, Smith RB, Steckel J. The contemporary incidence of lymph node metastases in prostate cancer: implications for laparoscopic lymph node dissection. J Urol. 1993;149:1488–91.
14. Fournier GR Jr, Narayan P. Re-evaluation of the need for pelvic lymphadenectomy in low grade prostate cancer. Br J Urol. 1993;72:484–8.
15. Raeside DE. Bayesian statistics—a guided tour. Med Phys. 1976;3:1–11.
16. Chang PL, Li YC, Wu CJ, Huang MH. Using ILIAD system shell to create an expert system for differential diagnosis of renal masses. J Med Syst. 1993;17:289–97.
17. Chang PL, Li YC, Huang ST, Wang TM, Hsieh ML. Effects of a medical expert system on differential diagnosis of renal masses: a prospective study. Comput Med Imag Graph. 1996; 20:43–8.
18. Zweig MH, Campbell G. Receiver-operating characteristic plots: a fundamental evaluation tool in clinical medicine. Clin Chem. 1993;39:561–77.
19. Huguet J, Castineiras MJ, Fuentes-Arderiu X. Diagnostic accuracy evaluation using ROC curve analysis. Scand J Clin Lab Invest. 1993;53:693–9.