Is Ultrasound of the Prostate Indicated for Screening Purposes?

An Affirmative View

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The American Cancer Society predicts that in 1988 prostate cancer will be the second leading cause of death from cancer, claiming the lives of an estimated 29,000 men. Ninety-six thousand new cases of prostate cancer will be diagnosed each year thereafter.[1] Prostate cancer is commonly found in men over 50 years of age, a population in which autopsy studies have shown its prevalence to be as high as 30 percent.[2]

Currently, prostate cancer is diagnosed by digital rectal examination or from tissue removed at transurethral resection of the prostate. The majority of patients have advanced cancer when diagnosed, and chance for cure is small.[3]

Because current therapeutic methods of treatment for cancer confined within the prostate can provide long-term survival,[4] a screening procedure for early detection of prostate cancer may effect a decrease in the mortality rate. Contradiction between autopsy (30 percent) and clinical (3.7 percent) prevalence rates creates a dilemma in screening for prostate cancer.[5] The effectiveness of a screening test can be determined only when it can be learned which prostate cancers, diagnosed by screening, would actually become clinically evident in a man's lifetime. Indirect information may be obtained from autopsy and radical prostatectomy data to study this issue.

PREVALENCE OF PROSTATE CANCER

There appears to be good correlation between the volume of a tumor and its potential for malignant behavior. Small cancers tend to be well differentiated and have low malignancy potential. Large cancers display poor differentiation with tumor extension.

In an analysis of 100 prostate cancers obtained at autopsy, McNeal and colleagues[6] found that tumors 1.0 cm^3 in size exhibited invasive growth. The majority of tumors greater than 3 cm^3 showed local or distant spread. Tumors greater than 1.0 cm^3 made up 30 to 35 percent of the total (100) cancers.

With this correlation between tumor volume and malignancy potential, it is possible to define those cancers one would wish to diagnose. If a screening program limits diagnoses to those prostate cancers that are larger than 0.5 cm^3, 35 percent may be diagnosed.

Of the 436 prostates studied by McNeal et al, 100 cancers were found (prevalence = 23 percent); therefore, 8 percent (35 percent of 23 percent) of the cancers would have been greater than 0.5 cm^3 in size. This 8 percent prevalence is probably a maximum value, since it is derived from an autopsy series and not from a series of healthy, asymptomatic men.

Applying population and cancer statistics, Scardino[7] developed the following method to define screening prevalence:

1. If the autopsy prevalence for prostate cancer is 30 percent for men aged over 50 years, and there are 27,310,000 men older than 50 years in the United States, then there are 8,195,000 cancers in the men over 50 years of age in the United States (30 percent of 27,310,000).
2. If a man over 50 years of age has a risk of 0.35 percent for having prostate cancer diagnosed per year (96,000/27,310,000), and the average American man over 50 years of age is 64 years old and has a life expectancy of 15 years, then the risk for the average man aged over 50 years to develop prostate cancer in his lifetime is 5.3 percent (15 × 0.35).
3. Ideally, if all men aged over 50 years were screened, 5.3 percent would have prostate cancer diagnosed.

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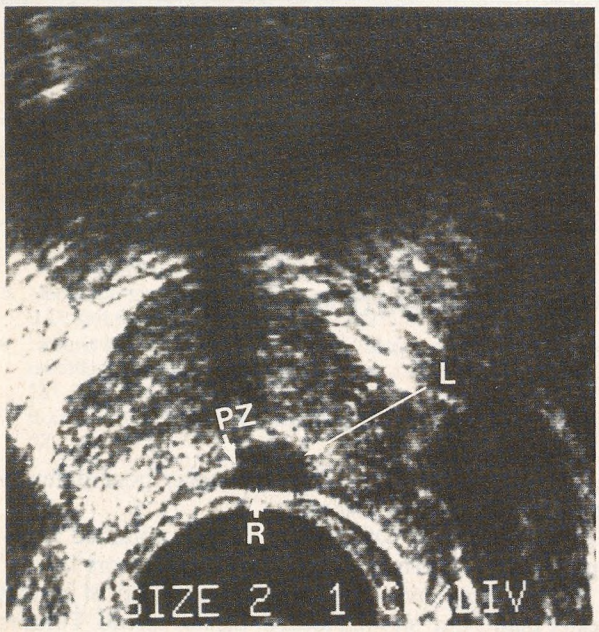

Figure 1. Prostate cancer, axial scan shows a hypoechoic lesion (arrows) in the peripheral zone (PZ), R—rectum, L—left

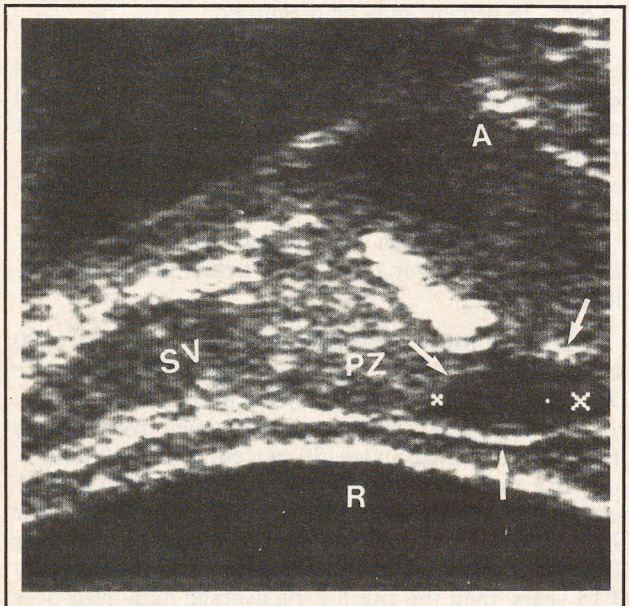

Figure 2. Prostate cancer, sagittal scan shows the hypoechoic lesion (arrows) in the peripheral zone (PZ), R—rectum, SV—seminal vesicle

Figure 3. Prostate cancer, axial histologic section shows solid tumor (arrows) in peripheral zone (PZ)

This scenario serves the purpose of supplying an approximate detection rate to be expected from a screening program. Sensitivity of a test for clinically important cancers (>0.5 cm^3) may then be derived accurately from a detection rate, if a screening program could indeed select out those 5.3 percent of men with prostate cancer. Only time can determine whether a screening test will identify the cancers that warrant diagnoses within this 5.3 percent.

Tumor volume is currently the best "gold" standard in diagnosing prostate cancer. A screening test diagnosing macroscopic cancer and not exceeding a 5.3 percent detection rate is probably not excessive in diagnosing cancer.

TRANSRECTAL ULTRASOUND

With transrectal ultrasound the normal internal anatomy of the prostate may now be demonstrated. Recent technological developments in ultrasound have allowed the differentiation between normal and abnormal anatomy. Currently, the majority of investigators using high-resolution equipment have accepted the criterion for prostate cancer to be a hypoechoic (dark) lesion (Figures 1 to 3). Using this criterion, various reported studies show yields of cancer from 21 to 41 percent within biopsy groups.[8,9]

The criterion for cancer being a hypoechoic lesion proves valuable nevertheless, since transrectal ultrasound is so easily combined with biopsy. Transrectal biopsy, taking multiple tissue cores from a site where cancer is suspected, provides the histological background of a lesion seen on ultrasound. The following questions are therefore important:

TABLE 1. AGE DISTRIBUTION AND INCIDENCE OF PROSTATE CANCER IN 784 MEN

Age (years)	Patients (No.)	Cancers No. (%)
60–64	431	6 (1.4)
65–69	223	9 (4.0)
70–74	90	6 (6.7)
>75	40	1 (2.5)

TABLE 2. STATISTICAL RESULTS (percent) OF A SCREENING STUDY (N = 784) FOR PROSTATE CANCER (prevalence = 2.8%) USING TRANSRECTAL ULTRASOUND AND DIGITAL RECTAL EXAMINATION

Statistical Tests	Transrectal Ultrasound	Digital Rectal Examination
Sensitivity	91	45
Specificity	94	97
Positive predictive value	31	34
Negative predictive value	100	98

1. Can transrectal ultrasound be used as a screening tool for prostate cancer?
2. Does transrectal ultrasound perform better than digital rectal examination?
3. If improved sensitivitiy is achieved using transrectal ultrasound, is it at the cost of diminished specificity?

A SCREENING STUDY

In an attempt to answer these questions, a screening and detection program was instituted at the Catherine McAuley Health Center comparing transrectal ultrasound with digital rectal examination.[10] A control group of patients was not included in this program; therefore, the issue of eventual patient survival may only be surmised.

Between 1985 and 1987, 784 men were examined. Ages ranged from 60 to 86 years with a median age of 65 years (Table 1). These men were healthy, predominantly white, and middle class, with 50 percent of them having had normal digital rectal examination results within one year before entering the study. All patients were studied in a blind fashion. Biopsy was performed when either transrectal ultrasound or digital rectal examination indicated an appropriate abnormality.

Seventy-seven men (9.8 percent) underwent biopsy. Eighty-three percent (64/77) of total biopsies resulted from transrectal ultrasound, and 38 percent (29/77) from digital rectal examination. The biopsy rate for transrectal ultrasound was slightly more than two times the rate of biopsy for digital rectal examination. Overall detection rate of transrectal ultrasound for cancer was two times greater than digital rectal examination (2.6 percent and 1.3 percent, respectively). Positive predictive values for transrectal ultrasound (31 percent) and digital rectal examination (34 percent) were nearly the same. In other words, for every three biopsies, a diagnosis of cancer was made.

TABLE 3. DETECTION RATES FOR PROSTATE CANCER BY TRANSRECTAL ULTRASOUND AND DIGITAL RECTAL EXAMINATION OF 784 PATIENTS

	Cancer No. (%)	Cancer and Displasia No. (%)
Overall	22 (2.8)	30 (3.8)
Transrectal ultrasound	20 (2.6)	28 (3.6)
Digital rectal examination	10 (1.3)	14 (1.8)

Sensitivity, specificity, and negative predictive values determined using the 2.8 percent detection rate from this study as probable clinical prevalence are displayed in Table 2. Sensitivity is a measure of the percentage of cancers that will be correctly diagnosed by a test. Sensitivity was two times greater for transrectal ultrasound than for digital rectal examination. The 2:1 advantage of transrectal ultrasound over digital rectal examination was thus reflected in a 2:1 detection rate of transrectal ultrasound for cancer (Table 3).

Autopsy and clinical pathological studies have shown that tumors 3.0 cc or smaller tend to be confined within the prostate gland.

Of the 22 patients who had cancer diagnosed, 17 had tumors of 1.5 cm or smaller. Eighty-two percent (14/17) of them had surgical staging lymphadenectomies, all of which were negative. Of those patients electing radical prostatectomies (n = 6), only one had a prostate showing complete capsular penetration. Though these numbers are small, if this trend is true, it may portend a decrease in the death rate from prostate cancer. Larger studies with similar results are needed to validate this trend, however.

Cost Effectiveness

The greater sensitivity of transrectal ultrasound and the equal positive predictive values of transrectal ultrasound and digital rectal examination are important in considering cost effectiveness of transrectal ultrasound. Intuitively, it is reasonable to assume digital rectal examination is most cost effective because implementation of digital rectal examination requires no capital investment.

Using currently accepted charges for digital rectal ex-

amination ($45), transrectal ultrasound ($150), biopsy ($100), and interpretation of pathologic findings ($100), total costs for the studies were considerably greater for transrectal ultrasound than for digital rectal examination. The costs per diagnosed cancer for transrectal ultrasound and digital rectal examination, however, were $6,520 and $4,108, respectively, a difference of 37 percent. This difference in cost may be further offset by comparing only those cancers with the most favorable prognosis (tumors $\leq$ 1.5 cm). Costs then become $7,671 for transrectal ultrasound and $5,869 for digital rectal examination, a difference of 23 percent.

Through further analysis it was determined that the costs for every cancer that would have become advanced if diagnosed without screening were $22,177 for transrectal ultrasound and $28,528 for digital rectal examination, a difference of 22 percent favoring transrectal ultrasound. Costs in a study such as this are related to changes in prevalence rates and changes in the stages of prostate cancer when diagnosed without screening.[11]

NATIONAL PROSTATE CANCER DETECTION PROJECT

In an attempt to achieve a universal standard of screening for prostate cancer with transrectal ultrasound, the Catherine McAuley Health Center, along with ten other institutions in North America, has formed the National Prostate Cancer Detection Project (NPCDP). With a follow-up period of five years, the NPCDP will screen nearly 5,000 men (aged 55 to 70 years) not at known risk for prostate cancer. This multidisciplinary group will utilize the same equipment and techniques. All patients will be screened with transrectal ultrasound, digital rectal examination, and serum prostate-specific antigen in a blinded fashion. There will be no control group of patients; however, an ethical and rational basis for comparison will be achieved through the criteria that all patients be self-referred and asymptomatic.

At present over 800 men have been successfully registered into the NPCDP. More ultrasound and digital rectal studies performed in multiple institutions, with long-term follow-up, will firmly address the important goal of early diagnosis of prostate cancer.

CONCLUSIONS

The following conclusions can be drawn from the Catherine McAuley Health Center screening study findings:

1. Transrectal ultrasound is twice as sensitive as digital rectal examination in the detection of prostate cancer.
2. The greater sensitivity of transrectal ultrasound is not due to an unreasonably high rate of biopsy, as reflected in the nearly equal positive predictive values of transrectal ultrasound and digital rectal examination.
3. The cancers diagnosed by transrectal ultrasound and undetected by digital rectal examination are of sizes typically considered to be potentially curable.
4. Specificities and negative predictive values for both transrectal ultrasound and digital rectal examination are high.

It is hoped that ultrasound will provide improved survival, with good quality of life, for men at increasing risk from prostate cancer in the aging national population. Based upon presently available evidence, a broader implementation and evaluation of transrectal ultrasound, a tool to be complemented by digital rectal examination, is advocated for the early detection of prostate cancer.

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An Opposing View

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In Seattle, a nightly advertisement during the 6 o'clock news carries ultrasound images of the prostate, presented by a physician who implies that the finger is outmoded, painful, and messy compared with rectal probe ultrasound; he advises all men over 40 years old to come to his office to have their prostates screened ultrasonically. Brochures come in the mail weekly containing advertisements for courses on ultrasonic examination of the prostate. Once a month an advertisement arrives from a manufacturer of ultrasonic equipment claiming some advantage over other devices built for this purpose. In the face of this deluge, it is difficult for the physician to resist the temptation to add the probe to his current equipment or to finance the purchase of an ultrasonic device capable of imaging the prostate.

What are the facts about the use of transrectal ultrasound in screening for prostate cancer? As documented in a recent issue of the *Journal of the American Medical Association*,[1,2] in the present state of the art, ultrasound is not recommended as a clinical device for screening the prostate for cancer. The educated index finger of the physician, albeit only 80 percent accurate, is still the "gold" standard for screening for cancer of the prostate.

To understand what may be misleading some sincere enthusiasts, it is necessary first to review the natual history of this disease. Then it is necessary to compare what is found by ultrasonic screening with the likelihood of arriving at the same or better diagnostic yields with other available modalities.

NATURAL HISTORY OF THE PROSTATE CANCER

Cancer of the prostate may be divided into two forms: (1) latent cancer of the prostate, which has no recognizable clinical manifestations, and (2) disease that is clinically manifest on the basis of symptoms, such as bone pain, on rectal examination or on skeletal x-ray films, radionucleide bone scanning, and so on. It is the latent form of the disease for which a new screening technique is desirable.

In a superb study, Breslow and colleagues[3] reviewed step-sectioned prostates from 1,327 consecutive autopies of men previously unsuspected of having prostate cancer. These autopsy specimens were collected in near equal numbers by pathologists from Hong Kong, Singapore, Israel, Sweden, Germany, Uganda, and Jamaica.

As a result of that study, the authors defined two different types of latent prostate cancer. The first type, small latent cancer of the prostate, a lesion occupying less than two octiles of the prostate, was found at a constant rate of 12 percent in all age groups over 45 years. The mortality of this group with small latent cancer equaled the general age-related mortality for men in the region reporting. The second type, which they called larger latent cancer, occupied more than three octiles of the prostate. The mortality for this larger latent type of prostate cancer paralled the age-related mortality from cancer of the prostate in the region or country from which the individuals came. They concluded that small latent cancer of the prostate was clinically unimportant, but that larger latent cancer was clinically significant.

By compiling data from separate studies by Correa et al,[4] Heaney et al,[5] and Cantrell et al,[6] for a total of 207 cases of unsuspected cancer of the prostate discovered on tissue recovered during enucleation of the prostate followed for one to ten years, Catalona and Kelly[7] obtained similar findings (Tables 1 and 2). As is evident from these tables, progression of small latent disease occurred in only 5 percent of the patients in whom it was discovered at enucleation of the prostate, and there was only one death that was due to cancer of the prostate in 130 patients with small latent cancer. In contrast, in the 77 patients with the larger latent cancer discovered at enucleation of the prostate, over one third progressed and nearly one fifth died from cancer of the prostate.

It is reasonable to surmise from these figures that the course of latent cancer of the prostate discovered as a result of enucleation of the prostate can be divided into

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TABLE 1. PROGRESSION OF AND MORTALITY FROM SMALL LATENT CANCER FOUND AT ENUCLEATION OF THE PROSTATE

Number of Patients	Progression of Cancer No. (%)	Deaths No. (%)	Followed (years)
130	7 (5)	1 (1)	1–10

From Catalona and Kelly[7]

TABLE 2. PROGRESSION OF AND MORTALITY FROM LARGER LATENT CANCER FOUND AT ENUCLEATION OF THE PROSTATE

Number of Patients	Progression No. (%)	Mortality No. (%)	Followed (years)
77	29 (35)	14 (18)	1–10

From Catalona and Kelly[7]

the same two groups found in the autopsy study of Breslow et al, with similar conclusions, ie, small latent cancer of the prostate is clinically unimportant, but larger latent cancer of the prostate is clinically significant. It would indeed be useful to find some way of screening for larger latent cancer of the prostate.

TRANSRECTAL ULTRASOUND AS A SCREENING METHOD

How does transrectal ultrasound measure up as a screening method for detecting latent cancer of the prostate? There are only a few prospective studies that address this question. The answer in all of them is that transrectal ultrasound of the prostate lacks the sensitivity and specificity to do the job.[1,2] Ragde,[8] one of the most enthusiastic proponents of the use of transrectal ultrasound in detection of prostate cancer, recently presented a series of 1,051 men who visited his office in response to advertisements; his yield of positive biopsies obtained by ultrasonic guidance and rectal examination combined was 50, or 4.76 percent. It would be instructive to calculate what his yield of positive needle biopsies might have been had he directed a needle, without ultrasonic guidance, into portions of the prostate known from the Breslow et al study to be the most likely portions of the prostate to contain larger latent cancer.

Information of the location within the prostate of latent tumor from the study by Breslow et al is as follows:

1. Thirty percent of men over the age of 60 years have cancer of the prostate.
2. Fifty percent of these cancers will be larger latent lesions.
3. Sixty percent of all lesions will be in the outer rim of the prostate.
4. Sixty percent are in that transverse prostate segment located 5 to 15 mm from the apex of the prostate.

Multiplying the percentages from the four statements above produces a 5.4 percent probability of retrieving prostate cancer by needle biopsy of tissue in the area of the prostate determined by autopsy studies most likely to contain cancer (assuming here that the incidence of cancer of the prostate in the United States is the same as that found for the combined regions of the Breslow et al study).

Ragde, with the aid of both digital rectal examination and transrectal ultrasonic guidance, obtained 4.76 percent positive biopsy results in asymptomatic men. As calculated, one might obtain a 5.4 percent positive response by blindly directing the needle to the area of prostate most likely to contain larger latent tumor. Since Ragde only recovered 4.76 percent combining digital rectal examination and ultrasonic guidance on a screening basis, it can be concluded that he would have done better without the ultrasound.

Lee, the leading radiological proponent of transrectal ultrasound as a screening method for the diagnosis of prostate cancer, has published a series of papers on the topic, the latest in Radiology in August this year.[9] The series is compiled of self-selected individuals who come to his facility to have a prostate ultrasound examination in response to advertisements in the media in the Ann Arbor area. In that August article, Lee and colleagues describe screening 784 men between June 1985 and April 1987 who ranged in age from 60 to 86 years with a median age of 65 years. Subjects were studied independently in a blind fashion. A digital rectal examination was done by the urologists in addition to transrectal ultrasound. Seventy-seven of the 784 patients had their prostates biopsied. Sixty-four biopsies were done on the basis of ultrasound findings, and 29 on the basis of findings on digital rectal palpation. Twenty-two of the 77 patients (2.8 percent) proved to have prostate cancer on biopsy. Ultrasound was positive in 20 cases, while ten cases were discovered by digital rectal examination. They conclude that ultrasound is twice as likely to pick up significant lesions as digital rectal examination. They do not emphasize the tabulated results that three fourths of the patients who were positive on ultrasound had negative findings on biopsy. Although they state that the incidence of carcinoma rises with age

in this series, in fact the incidence of 2.5 percent tabulated in their patients aged over 75 years is less than the 7.7 percent in the 70- to 74-year group and the 4.0 percent found in the group aged 65 to 69 years.

My argument is not with these inconsistencies but with the lack of true controls for the study. For a valid study, as indicated elsewhere in this article, Lee and colleagues should have biopsied an equal, age-matched group of individuals who were thought to be negative for carcinoma on both examinations. Chances are that if the biopsy needle were guided into the portion of the prostate most likely to harbor cancer, an equal or better yield of tissue positive for cancer would have been obtained. In other words, many of the cancer diagnoses obtained with the aid of ultrasound may have been the result of chance placement of the needle rather than the ultrasonic guidance of it. Chodak[2] has recently proposed a carefully controlled study to evaluate ultrasound in screening for prostate cancer. Such a study is needed, to answer the questions raised here and in *The Journal of the American Medical Association.*[1]

This raises the question of whether all men aged over 50 years should have a needle biopsy of the prostate to determine whether they harbor prostate cancer. Some answers to this question can be reached by looking at example cases first and then considering some prime targets for such intervention.

Case 1. An asymptomatic 85-year-old man comes into a physician's office because he has been watching the Phil Donahue show and learned from an expert on that program that all men aged over 50 years should have prostate examinations annually. On examination his prostate feels moderately enlarged but the consistency is benign. This man should not have a needle biopsy or ultrasound because his life expectancy of five years is the same life expectancy he could expect even if he were found to have far advanced prostate cancer.

Case 2. The wife of a 72-year-old man with advanced cardiac problems and severe obstructive pulmonary disease brings her husband in because since furosemide has been added to his diuretic regimen, he voids frequently from early morning to late afternoon. She fears he may be developing prostate cancer, based on what some friends tell her about that disease. His prostate feels lobularly irregular but not hard. In this case the man's symptoms are probably the result of his diuretic therapy, not his prostate. Furthermore, he is likely to die from his severe pulmonary and cardiac problems long before he would from any prostatic cancer. How is knowing he has asymptomatic prostate cancer, which will not be treated, going to help him? Why peform a needle biopsy of his prostate?

Individuals who have no symptoms referable to their prostates and have other systemic diseases that are life-threatening are not candidates for prostatic cancer detection. As a matter of fact, one can state that anyone aged over 75 years whose 20-year life expectancy is no more than 50 percent is not a candidate for radical surgical cure of his prostate cancer. If he has a surgically curable form of prostate cancer, his 50 percent life expectancy from the untreated cancer is 20 years, so there is no point in putting him through the surgery. There is no need to establish the diagnosis in such an asymptomatic individual because there is no evidence that early hormonal control therapy changes the life history of the disease. Hormonal control therapy is valuable palliation, but there is no need for palliation in an asymptomatic individual.

Case 3. A 62-year-old patient known and followed for years comes in, asymptomatic except for minor complaints, to have his annual checkup. He is examined, and during a rectal examination a firm nodule in the left lobe of his prostate is felt that was not there one year ago. What can be suggested for this individual? This person is one who is most likely to benefit from radical prostatectomy, if indeed his nodule proves to be a neoplasm. A plain x-ray examination of his pelvis should be done to rule out stones; prostatic acid phosphatase levels and prostate-specific antigens should be determined; and a needle biopsy of the prostate should be performed. There is no need for ultrasound; the lesion can be felt, and biopsy can be undertaken directly without the aid of ultrasound. If his biopsy result is positive, he should have some assessment of his lymph nodes (a computed tomographic scan or lymphangiogram) and a bone scan for metastases. If the bone scan is negative, and there are no abnormal nodes to justify a needle biopsy, he should have a formal node sampling, and if no cancer is found in the nodes, a radical prostatectomy.

The field can thus be narrowed to those under 75 years of age who may have latent cancer. Should all of these individuals have needle biopsy of the prostate? There are rare individuals aged over 70 but younger than 75 years who are physiologically in their 60s. Such individuals might be treated as if they were in their 60s, but the great majority of individuals aged over 70 years should be treated as though they were over 75 years as far as prostate cancer is concerned.

Should all men aged between 50 and 70 years have needle biopsy? One way to answer this question is to present the pros and cons and let the reader (and patient) choose:

Pro: Significant larger cancers will be discovered by needle biopsy in about 5 percent of men. Possibly 80 percent will be surgically or radiologically curable.

Con: Two thirds of the men aged over 60 years do not have cancer and will have their prostates biopsied unnecessarily. About 1 percent of those having needle biopsy of the prostate will develop complications such as infection or bleeding, necessitating treatment with antibiotics or by

evacuation of clots and fulguration of bleeders. Thirty percent of those treated surgically and 40 percent of those treated by radiation will become impotent. Up to 12 percent of those patients discovered to have prostate cancer may be treated unnecessarily because they will have a small, latent, clinically unimportant prostate cancer. Between 1 and 2 percent of those treated surgically will develop strictures or urinary incontinence. Between 1 and 2 percent of those treated by radiation will develop radiation colitis or cystitis, requiring long-term symptomatic treatment for this very unpleasant complication of treatment. Given present knowledge and technical developments, random screening by needle biopsy might cause as much or more harm to some as it does good for others.

CONCLUSIONS

Recent focus on the prostate problems of a very popular president, who has been very open with the public about his illnesses, combined with thorough discussion by such experts as Dr. Patrick Walsh on prime time television news programs, has resulted in a dramatic rise in the detection and surgical treatment of early cancer of the prostate. Some of this early discovery may also be indirectly related to publicity about ultrasonic examination of the prostate, which has led patients to consult physicians. The long-term value of ultrasound as a screening modality is at best unproven, however, and at this time is suspect as a commercial gimmick in some hands.

On the basis of the evidence from collected studies and calculations based on the natural history of the disease, transrectal ultrasound of the prostate is currently not a useful screening test for latent cancer of the prostate. One may justify its use on an investigational basis. Advertising its use on prime time television, playing on individuals' fears about cancer as a means of recruiting patients and fees, is to be condemned as professionally unethical and unacceptable by truth-in-advertising standards.

Any screening for latent prostate cancer in individuals aged over 75 years (with rare exceptions) is unwarranted because, given the natural history of this slowly progressive disease, they are far more likely to die of causes other than prostate cancer. A reliable, noninvasive screening modality for discovering larger latent cancer of the prostate in individuals aged 50 through 69 years is desirable but not yet available, certainly not, as of this writing, by means of transrectal ultrasound.

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