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## CARCINOMA OF THE PROSTATE

A STUDY OF THE PERCENTAGE OF CASES SUITABLE  
FOR THE RADICAL OPERATION

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In an editorial<sup>1</sup> published in *THE JOURNAL* in July 1942 I was quoted—and quoted correctly—as stating that of all cases diagnosed as carcinoma of the prostate in the Brady Urological Institute the radical operation was carried out in approximately 5 per cent. This question was raised in a discussion at a meeting of the New England branch of the American Urological Association, and without any available figures, in a desire to be conservative, I gave my impression that about 5 per cent of all cases of carcinoma of the prostate seen in any clinic would be found suitable for the radical operation.<sup>2</sup>

The publication of the aforementioned editorial, and particularly my statement, which was given purely as an impression and without the background of any statistical data, led me to make a study with as thorough a follow-up as possible to determine the end results of all cases in which the radical operation for carcinoma of the prostate was done in the Brady Urological Institute between Sept. 1, 1937 and Sept. 1, 1942. In this five year period a diagnosis of carcinoma of the prostate was made in 358 cases, of which 318 were admitted to the hospital. During this period 73 radical operations were performed by members of the visiting and house staffs. Thus the radical operation was carried out in 20.2 per cent of all cases seen and in 22.7 per cent of all hospital admissions with a diagnosis of carcinoma of the prostate (table 1).

These figures were so significant that it was deemed advisable to present them to the medical profession. I realize that this percentage of cases suitable for the radical operation is probably higher than would be seen in other clinics, but it can be explained by the fact that many patients are referred to this clinic with a diagnosis of early carcinoma for the express purpose of undergoing the radical operation.

In a similar series studied over a period of two years at the University of Virginia Hospital, Vest and Prince<sup>3</sup> made a diagnosis of carcinoma of the prostate in 77 cases. Of these, 7 cases, or 9 per cent, were

considered suitable for the radical operation with a good prognosis for complete cure.

The criteria for cases suitable for the radical operation have been previously stated and depend largely on careful rectal examination.<sup>4</sup> The malignant growth should not extend beyond the capsule of the gland, into the membranous urethra or beyond the base of the seminal vesicles, and, of course, metastases must not be demonstrable either on physical or on roentgenologic examination. In addition, the serum acid and basic phosphatase must be within normal limits, since the important researches of Huggins and his collaborators<sup>5</sup> and the Gutmans<sup>6</sup> have shown that an elevated acid phosphatase level in the blood serum should be interpreted as indicative of metastases from prostatic carcinoma unless some other definite cause for this elevation can be proved. Furthermore, no patient should be subjected to the radical operation unless the general physical condition is satisfactory, and the patient should have a fair span of life expectancy. Generally speaking, carcinoma of the prostate, especially in older persons, is a slowly progressive disease, and in every case in which the criteria for operability are satisfactory the question of life expectancy of the particular person must be carefully considered before operation is advised.

These criteria are not absolute, and in some cases radical operation has been carried out on persons in whom it seemed doubtful from the observations on rectal examination that a complete cure might be expected. George Gilbert Smith<sup>7</sup> some years ago advocated the radical operation in cases in which it was obvious that the whole malignant growth could not be removed, but he felt that even though some of the neoplasm might remain, usually in the region of the tips of the seminal vesicles, the patient's subsequent course was much more satisfactory than with any other method of treatment. The removal of the main mass of malignant disease around the neck of the bladder gave permanent relief of obstructive symptoms and effects, and in many cases the portion of the tumor which could not be removed, lying as it did well above the neck of the bladder, between it and the rectal wall,

4. Young, H. H.: The Radical Cure of Cancer of the Prostate. *Surg., Gynec. & Obst.* **64**: 472-482 (Feb. 15) 1937; *Surgery in Cancer of the Prostate*, *J. A. M. A.* **119**: 669 (June 20) 1942.

5. Huggins, Charles; Stevens, R. E., and Hodges, C. V.: Studies on Prostatic Cancer: II. The Effects of Castration on Advanced Carcinoma of the Prostate Gland, *Arch. Surg.* **43**: 209-223 (Aug.) 1941. Huggins, Charles; Scott, W. W., and Hodges, C. V.: Studies on Prostatic Cancer: III. The Effects of Fever, of Desoxycorticosterone and of Estrogen on Clinical Patients with Metastatic Carcinoma of Prostate, *J. Urol.* **46**: 997-1006 (Nov.) 1941.

6. Gutman, A. B.: Serum "Acid" Phosphatase in Patients with Carcinoma of the Prostate Gland: Present Status, *J. A. M. A.* **120**: 1112-1116 (Dec. 5) 1942.

7. Smith, G. G.: Total Perineal Prostatectomy for Carcinoma, *J. Urol.* **35**: 610-617 (June) 1936; *Total Perineal Prostatectomy*, Pennsylvania M. J. **44**: 1391-1401 (Aug.) 1941; *Surgery for Cancer of the Prostate*, *J. A. M. A.* **118**: 1514 (April 25) 1942.

From the Brady Urological Institute of the Johns Hopkins Hospital.

1. Carcinoma of the Prostate, editorial, *J. A. M. A.* **119**: 950-951 (July 18) 1942.

2. Colston, J. A. C.: The Surgical Treatment of Carcinoma of the Prostate, *New England J. Med.* **223**: 205-212 (Aug. 8) 1940.

3. Vest, S. A., and Prince, C. L.: Personal communication to the author.

might grow very slowly and not cause symptoms from its encroachment on either the bladder or the rectum. The following case illustrates this point very graphically:

## REPORT OF CASE

D. D. McM., aged 51, seen in June 1924, complained of burning on urination, frequency and blood in the urine. The general physical examination was essentially normal, except for mild

TABLE 1.—Percentage of Cases Suitable for Radical Operation Among All Cases Diagnosed as Carcinoma of the Prostate from Sept. 1, 1937 Through Aug. 31, 1942

	Number of Patients	Number of Radical Operations	Per Cent
Diagnosis: carcinoma of prostate.....	358	73	20.2
Admissions to hospital.....	318	73	22.7

hypertension. On rectal examination the prostate was slightly broader and undoubtedly firmer than normal, and in the right lobe there was an elevated, stony hard, fixed nodule and the induration extended up toward the base on the right side but apparently not into the seminal vesicle. X-ray examinations of the lumbar vertebrae, sacrum and bones of the pelvis were negative for metastases. Since the growth seemed to be entirely within the capsule of the prostate and had not extended into the membranous urethra or into the seminal vesicles, the case was considered suitable for radical operation. This procedure was carried out on July 2. The postoperative course was uneventful, except for a transient epididymitis. The patient was discharged on August 5, the perineal wound well healed, voiding freely without obstruction, with perfect control, able to retain urine throughout the night without arising and voiding every three hours during the day. He was seen at intervals following the operation and remained in excellent general condition with a perfect functional result. In June 1927, three years after the operation, an indurated area was noted high up between the rectum and the posterior wall of the bladder. In subsequent check-up examinations it was observed that this area grew very slowly and that the induration became gradually more pronounced. At the last examination, carried out in 1931, it was my impression that a definite recurrence was present. At no time had there been any urinary obstruction or other symptoms, and the functional result remained perfect. X-ray examinations showed no evidence of metastases. His general health had been good except for an attack of acute cholecystitis, for which a cholecystectomy was done in January 1928. He died on March 25, 1939 with a clinical diagnosis of coronary thrombosis. A complete autopsy was carried out by Dr. Nathan B. Friedman, then of the University of Chicago, who sent the indurated retrovesical mass to me for examination. Autopsy showed no evidence of metastases. The prostate was absent. Under the bladder the extremities of the vesicles were fused together in a firm mass 5 by 3 cm., most of which was on the right. On section this mass showed a group of thick walled tubules embedded in scar tissue. One region showed dilated cystic spaces up to 1 cm., each with reddish and yellow contents. Microscopic examination revealed the right seminal vesicle thickened and fibrotic with hyaline and mucoid interstitial changes and vascular sclerosis. The epithelium of the vesicle was relatively normal, although atrophic and desquamated in areas. Throughout the stroma and invading the nerves at the edges were numerous well differentiated adenocarcinomatous glandular structures.

It is obvious that the upper portion of the right seminal vesicle was not removed at the time of operation. It was probably invaded by the malignant process at the time of operation, but the neoplasm progressed so slowly that it never caused any functional disability by pressure on contiguous structures, located as it was

between the posterior vesical wall and the rectum, well above the neck of the bladder. This patient lived fifteen years completely free from urinary symptoms and with a perfect functional result, even though viable malignant cells were present behind the bladder wall during all this time.

## OPERATIVE MORTALITY

During the period from Sept. 1, 1937 to Sept. 1, 1942 seventy-three radical operations were performed and there were four hospital deaths. An analysis of these fatalities shows that 3 patients were over 70, and in all of them evidences of varying degrees of arteriosclerotic cardiovascular disease were found. In 2 of them the cause of death was myocardial failure, and in the third a massive hemorrhage from unrecognized gastric ulcers was considered responsible for death, although here again myocardial disease was a contributing factor. The fourth death occurred from what must be considered a technical error in that, owing to a suspected occlusion of the ureter occurring at operation, it was thought necessary to insert a retained ureteral catheter, which was in all probability the source of a fatal staphylococcal bacteremia which developed.

It is an interesting commentary on the supposed danger of the radical operation that during the five year period fifteen such operations have been carried out by the various resident urologists of the Brady clinic without a death. This series, comprising as it does only a five year postoperative follow-up, is in no sense intended as a presentation of the percentage of cures following radical operation. It must be remembered that the study was undertaken primarily to determine the percentage of cases considered suitable for the radical operation from the total number of cases seen in the clinic over a five year period in which a diagnosis of carcinoma of the prostate was made. In this connection Lewis<sup>8</sup> made a study of the five year end results of the radical operation and found that approximately 50 per cent of the patients subjected to this procedure were alive and well without evidence of recurrence or metastasis more than five years after the operation.

In the present series of 69 patients who left the hospital after the operation, 10 have died from recurrence or metastasis, 11 are known to be alive with metastasis

TABLE 2.—Mortality and Immediate Results of Radical Operation for Carcinoma of Prostate (1937-1942)

Radical operation.....	73
Hospital deaths.....	4 (5.5%)
Died, recurrence or metastasis.....	10
Living, recurrence or metastasis.....	11
Living, no evidence of recurrence or metastasis.....	48

or recurrence or both, and 48 are living without evidence of recurrence or metastasis in periods ranging from six months to five years after the operation (table 2).

## RELATION OF GOOD PREOPERATIVE PROGNOSIS TO THE ULTIMATE RESULT

As has been previously stated, the preoperative prognosis, as far as the curability of the disease is concerned, is based entirely on careful rectal examination, provided,

8. Lewis, L. G.: Carcinoma of the Prostate: Young's Radical Perineal Prostatectomy, *J. Urol.* **47**: 302-305 (March) 1942.

of course, that no evidences of metastases are present, either clinically or roentgenologically. It has been the custom in the Brady Urological Institute for the examiner to state his impression, good or poor, from his observations on rectal examination. The sources of error lie in the extent of the disease, which may be impossible to recognize accurately on rectal palpation, and from the individual interpretation of the examiner. However, with these limitations in mind, from the preoperative examination in the 69 operative cases in which the clinical diagnosis was cancer the prognosis was classed good in 43 and poor in 26. Of the 43 patients with a good prognosis 41 are living and well without evidence of recurrence or metastasis, 1 has died from recurrence or metastasis and 1 has died from heart disease.

Of the 26 patients with cancer the extent of which caused the examiner to call the prognosis poor, 8 are living and well without evidence of recurrence or metastasis, 9 are living with evidence of either recurrence or metastasis, 8 have died from either recurrence or metastasis and 1 has died from other causes (table 3).

From a glance at these figures it is obvious that a good clinical preoperative prognosis is an important factor in the ultimate result; but it is equally evident

TABLE 3.—Cases Classified as Good or Poor Prognosis for Ultimate Cure: A Comparison of Results

Preoperative Prognosis	Number of Cases	Living and Well, No Evidence of Recurrence or Metastasis	Living and Well, with Evidence of Recurrence or Metastasis	Dead, Recurrence or Metastasis	Dead, Other Causes
Good	43	41	0	1	1
Poor	26	8	9	8	1

that patients classified under a fair or poor prognosis must not all be denied the opportunity for complete eradication of the disease which the radical operation affords, because 8 out of 26 patients with a poor prognosis are living and well without evidence of recurrence or metastasis. The excellent temporary results, often of surprisingly long duration, that may be obtained by eradication of the main mass of malignant disease in cases in which it is evident that complete removal of all the neoplasm is impossible have already been stressed.

FUNCTIONAL RESULTS

There has, unfortunately, been an all too prevalent idea among both the general medical profession and some urologists who are not familiar with the operation that total incontinence of urine is an inevitable result of the radical operation. It might be argued that, even though this were so, if a complete cure of the malignant disease could be obtained a life of complete incontinence would be distinctly preferable to death from prostatic cancer, with its certain disability and suffering (table 4).

Incontinence of urine following the radical operation, in many instances at least, must be attributed to the sutures which anastomose the stump of the urethra to the neck of the bladder. The distal stump of the urethra contains the muscles of the external sphincter, and it is easy to understand that these structures may be constricted and their continuity severed by sutures tied directly through them. In 1940 Vest<sup>9</sup> described

9. Vest, S. A.: Radical Perineal Prostatectomy: Modification of Closure, Surg., Gynec. & Obst. 70: 935-937 (May) 1940.

his method of completing the anastomosis, which, briefly, depends on the principle of passing the anastomosing sutures out through the structures of the perineum and tying them there. By this method a snug approximation of the stump of the urethra to the neck of the bladder can be obtained, and no knots are tied directly over the muscles of the external sphincter, so that the suture

TABLE 4.—Urinary Control: Results on Leaving Hospital or at Last Report

Good control.....	50
Fair control.....	11
Poor control.....	8
Total number of cases.....	69

knot is cushioned by the soft tissues of the perineum. Since the introduction of this principle in the Brady clinic, the functional results have been appreciably improved (table 5).

The patients who survived operation and left the hospital have been classified with regard to urinary function as good, fair and poor. Under the first heading are classed those patients who are able to void freely without difficulty or obstruction or undue frequency and in whom urinary control has been retained to such a degree that no apparatus is necessary, either day or night. Under fair are classified those patients who have good control at night but when up and about dribble small amounts of urine at times, so that an apparatus is necessary at least part of the time. These patients are able to void freely without obstruction and the functional result is excellent except for the inability at times to control small amounts of urine. Under poor are classified those patients who have little or no control and require some form of apparatus both day and night. A good functional result can almost invariably be expected in the younger age group.

MISTAKES IN DIAGNOSIS

The operative specimen in 5 cases on microscopic examination failed to reveal evidences of malignant disease. In 3 of these cases fibrosclerotic areas which occurred in the posterior capsule were mistaken clini-

TABLE 5.—Urinary Control Since 1940, Since When the Modified Suture Technic Has Been Used in All Cases

Control good.....	30
Control fair.....	4
Control poor.....	3
Total number of cases.....	37

cally for malignant disease. All these patients had varying degrees of urinary obstruction and all recovered from the operation with a good functional result. In 1 case microscopic study showed that a large area of infarction had occurred in the prostate which clinically was considered to be carcinoma. In the fifth case microscopic sections of the operative specimen showed tuberculosis which had been mistaken clinically for malignant disease. This patient had symptoms of urinary obstruction, there were no other evidences of tuberculosis of the urinary tract and, following operation, healing was uneventful with an excellent functional result.

It should be an invariable rule that the clinical diagnosis should be confirmed at the operating table by a frozen section of the suspected area. This procedure is quite simple, and a satisfactory piece can be removed from any portion beneath the posterior capsule with the cautery knife without fear of disseminating malignant cells throughout the wound. The time required to prepare and study the section can be utilized in mobilizing the prostate and exposing it satisfactorily in preparation for the radical operation. If the section proves to be benign, the incision can be rapidly closed, and only a few days hospitalization is necessary, since, of course, the urinary tract is not opened.

The brilliant results which have been obtained by the endocrine control of carcinoma of the prostate, either by orchietomy,<sup>10</sup> introduced by Huggins, or by the administration of female sex hormone,<sup>11</sup> have raised the question in some minds whether the radical operation in early cases of this disease is ever justified.

The regression of bony and even pulmonary metastases<sup>12</sup> and the diminution in the size of the local growth, with relief of urinary symptoms even in extensive neoplastic disease are incontestable, and the results in the Brady Urological Institute in the treatment of these cases have fully confirmed the observations of Huggins. However, the ultimate fate of these patients, who may show a remarkable and prompt response to this method of treatment, is as yet unknown, since none of these cases have been followed over a sufficiently long period of time to make certain that the regression of the primary growth and metastases are permanent. Decided improvement persisting over varying periods of time up to a year may be followed by a gradual return of the symptoms and evidences of activity of the disease, which cannot be controlled by further treatment with the female sex hormone.

Randall<sup>13</sup> has recently reported 5 cases of extensive carcinoma of the prostate in which bilateral orchietomy was done seven, eight and nine years ago. Four of his patients died forty-three days, eight months, seventeen months and three and one-half years respectively after the operation. One is living six and one-half years after the operation, but x-ray examination shows massive metastases of the dorsolumbar spine, which have apparently been ameliorated by the use of diethylstilbestrol. Evidence has not been adduced to prove, therefore, that complete eradication of carcinoma of the prostate can be obtained by endocrine treatment, but the palliative results which are observed in approximately 80 per cent of the cases, even with extensive metastases, must be received without question. Some writers have contended that, on account of the early involvement of the perineural lymphatics,<sup>14</sup> carcinoma of the prostate can never be completely removed by surgical operation. Carcinoma in other locations

throughout the body also has a tendency to invade lymphatics, so that, if this contention was followed to a logical conclusion, an effort to remove a carcinoma anywhere in the body would not be justifiable.

It is the feeling, therefore, in the Brady Urological Institute that any patient with an early carcinoma of the prostate who fulfils the necessary criteria for the radical operation should have the benefit of this procedure. As far as our present knowledge goes, this operation in certain selected cases offers the only possibility for complete eradication of the disease.<sup>15</sup>

## COMMENT

A study of the radical operations for carcinoma of the prostate performed in the Brady Urological Institute by various operators during the five year period from Sept. 1, 1937 to Sept. 1, 1942 has been carried out. This study has been undertaken to determine the percentage of cases suitable for the radical operation out of the total number of cases seen in the clinic in which a diagnosis of carcinoma of the prostate was made. The study, of course, in no way attempts to evaluate the five year percentage of cures, but the subsequent course of the patients subjected to the radical operation has been followed as closely as possible, with special reference to recurrence and metastasis and to the functional result.

There were four hospital deaths in the series of seventy-three operations—a mortality of 5.5 per cent. These fatalities have been summarized and analyzed. The importance of a good preoperative prognosis for complete cure of the disease has been emphasized. Of 43 patients for whom the prognosis was good, 41 are living and well without evidence of recurrence or metastasis. Of 26 patients for whom the prognosis was poor, 8 are living and well at intervals varying from three months to five years.

Intensive follow-up of all patients with early cancer of the prostate subjected to Young's radical operation shows that more than 50 per cent are free from recurrence or metastasis from five to twenty-seven years after leaving the hospital. A study of the postoperative functional results has also been carried out on the 69 patients who comprise this series. In 49 the functional result was excellent, all patients having complete urinary control. The result was classified as fair in 11 cases in which there was occasional slight leakage during the day, and in 8 the result was evaluated as poor, as some form of apparatus was necessary during the day and in some instances during the night. It is important to complete the anastomosis between the neck of the bladder and the stump of the urethra by means of sutures introduced so that there will be no strangulation and subsequent necrosis and scarring of the muscles of the external sphincter. It is evident that sutures tied in such a way as to constrict the sphincter muscles must play a large part in the incidence of postoperative incontinence.

Frozen section biopsy, carried out with the patient prepared for the radical operation, is a simple means of avoiding mistakes in diagnosis.

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11. Herbst, W. P.: Biochemical Therapeutics in Carcinoma of the Prostate Gland: Preliminary Report, *J. A. M. A.* **120**: 1116-1120 (Dec. 5) 1942.

12. Alyea, E. P., and Henderson, A. F.: Carcinoma of the Prostate: Immediate Response to Bilateral Orchietomy; Clinical and X-Ray Evidence, *J. A. M. A.* **120**: 1099-1102 (Dec. 5) 1942.

13. Randall, Alexander: Eight Year Results of Castration for Cancer of the Prostate, *J. Urol.* **48**: 706-709 (Dec.) 1942.

14. Thompson, G. J.: Transurethral Resection of Malignant Lesions of the Prostate Gland, *J. A. M. A.* **120**: 1105-1109 (Dec. 5) 1942.

15. Hinman, Frank: Surgery in Cancer of the Prostate, *J. A. M. A.* **119**: 669 (June 20) 1942. Creevy, C. D.: The Diagnosis and Treatment of Early Carcinoma of the Prostate, *ibid.* **120**: 1102-1105 (Dec. 5) 1942.