

Prostate Cancer Site Analysis *by Timothy R. Coblentz, MD*



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Adenocarcinoma of the prostate is the most common cancer in men in the United States today, and is the second leading cause of cancer death in men. Approximately 1 in 6 US men will be diagnosed with prostate cancer, and approximately 1 in 36 will die from prostate cancer.¹ Approximately 200,000 new cases of prostate cancer are diagnosed annually, with most new cases occurring in men aged 50-80 years. African American men have an increased incidence of prostate cancer compared to white men, and the prostate cancer mortality rate in African American males is double that of contemporary white cohorts.¹ Socioeconomic position variations in prostate cancer diagnosis and death are also intriguing: men with higher levels of education are more likely to be diagnosed with prostate cancer, but men with lower levels of education are far more likely to die of prostate cancer or be diagnosed with distant disease. This phenomenon is thought to be the result of variations in screening.¹

Early prostate cancer is typically asymptomatic, while locally advanced cancers may cause hematuria, urinary tract obstruction, and pain. Distant metastases frequently involve bones of the axial skeleton and may cause pain and pathological fractures.

Due to the asymptomatic nature of prostate cancer in its earliest and most curable state, screening via the use of serum prostate specific antigen (PSA) and digital rectal examination (DRE) has been widespread in the United States since the early 1990s. Routine use of PSA

screening has come under recent scrutiny however, despite the observation that prostate cancer death rates declined 4.1% annually between 1994 and 2006.¹ The most provocative recent publication involved the Prostate, Lung, Colorectal, and Ovarian (PLCO) Cancer Screening Trial, which randomized 76,693 US men to annual prostate cancer screening with PSA versus “usual care” from 1993 through 2001. This trial, published in 2009, did not show a difference in prostate cancer deaths between the 2 groups at 7 to 10 years. The key weakness of this study is contamination of the control population. In fact, 52% of the “usual care” control subjects did get at least one PSA during the study.² The control population was therefore screened significantly, minimizing the differences between the two groups. The European Randomized Study of Screening for Prostate Cancer (ERSPC) was also published in 2009. 162,387 men were randomized to PSA screening or control and followed for a median of 9 years. Overall prostate cancer mortality decreased by 20% in the screened population.³ The American Urological Association (AUA) recommends that men over 40 years of age with a life expectancy of 10 years or more be offered prostate cancer screening, emphasizing informed consent.⁴ The American Cancer Society similarly recommends that asymptomatic men with 10 year life expectancy make an informed decision regarding prostate cancer screening after a discussion of risks and benefits.¹

The three most important prognostic factors for prostate cancer survival are TNM stage, Gleason score, and PSA level. T1 tumors are non-palpable by DRE, while T2 tumors are palpable. Stage T3 indicates extraprostatic

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extension including into the seminal vesicles. T4 tumors invade adjacent organs or the pelvic wall. The Gleason score is a tumor grading scale derived from pathologic review of prostate cancer tissue. The Gleason score ranges between 2 - 10, with higher scores indicating more aggressive disease. PSA levels are also used to assess risk of relapse, with higher pre-treatment PSAs being associated with worse long term prognosis.

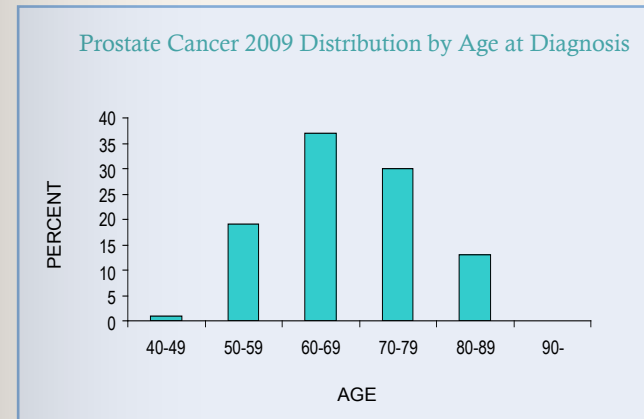
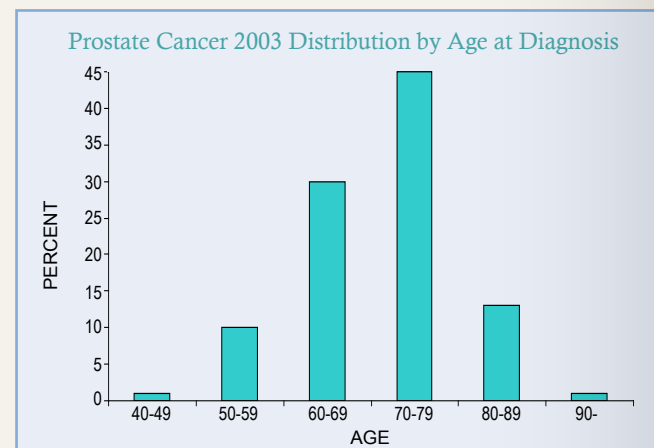
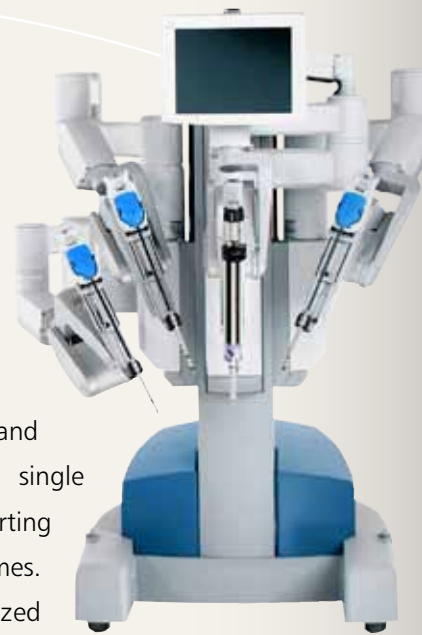
Based on the overall risk of recurrence, prostate cancer is usually stratified into 3 risk groups based on clinical stage, Gleason score, and PSA. The 2010 NCCN Clinical practice guidelines reaffirm this: Low risk patients (stage T1-T2a, Gleason <6, and PSA <10) are candidates for active surveillance, radical prostatectomy, external beam radiotherapy, or brachytherapy. Intermediate risk patients (stage T2b-T2c, Gleason 7, or PSA 10-20) are candidates for radical prostatectomy or external beam radiotherapy +/- short term androgen deprivation +/- additional brachytherapy. High risk patients (T3a, Gleason 8-10, or PSA >20) are frequently offered external beam radiotherapy with androgen deprivation, while select high risk patients undergo radical prostatectomy.⁵

The introduction of the da Vinci surgical robot (Intuitive Surgical, Sunnyvale, CA) has revolutionized the surgical treatment of prostate cancer since it received FDA approval for robot assisted laparoscopic radical prostatectomy (RARP) in 2001. RARP has been shown to have significantly less blood loss and shorter average hospital stay than open prostatectomy. Oncologic outcomes are similar to open prostatectomy. The improved visualization afforded by the 3-dimension high definition optics and precise motions of the unique wristed instrumentation afford

very precise dissection of the prostate. This precise dissection may lead to improvements in urinary continence and erectile function, with single surgeon series reporting excellent clinical outcomes. Large scale randomized data is lacking, allowing for some debate. Across the US, however, patients with prostate cancer are choosing RARP over open radical prostatectomy. Currently, more than three fourths of all radical prostatectomies performed in the US utilize the da Vinci robot. Aultman Hospital acquired a da Vinci Si surgical robot in 2010, and the first RARP at Aultman was performed July 1, 2010.

Aultman site analysis

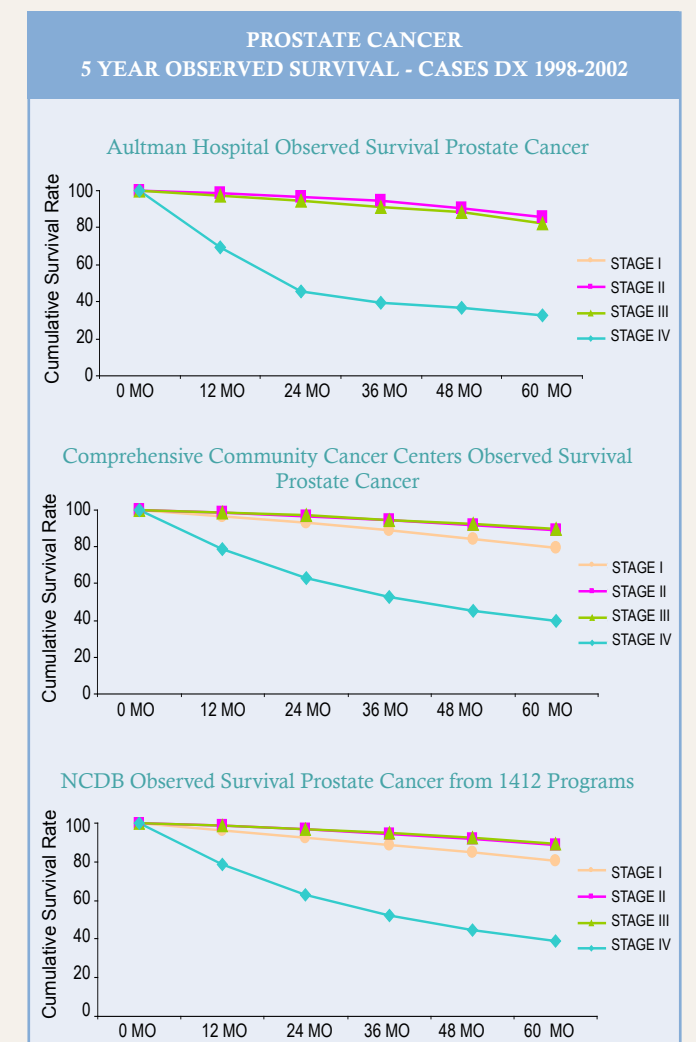
Analysis of age at diagnosis shows that men at Aultman were diagnosed with prostate cancer at younger ages in 2009 compared to 2003. Prostate cancer diagnoses declined markedly in patients over age 70 while there were modest increases in men under 70.



This may reflect a response to recent concerns in the urologic literature as well as the lay press regarding the possible overtreatment of prostate cancer in the elderly. This emphasis has received extensive national press coverage in the past two years.

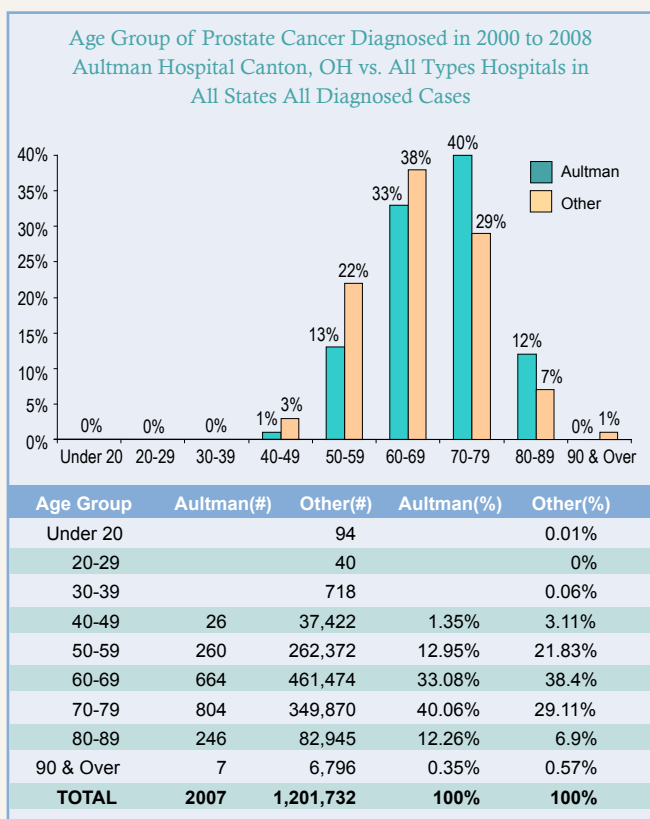
The most commonly treated prostate cancer is stage II, which includes most clinically organ-confined prostate cancers detected by screening. 5 year overall survival for stage II patients diagnosed at Aultman Hospital 1998-2002 was 85.5% compared to 88.9% for the American College of Surgeons Commission on Cancer's National Cancer Database (NCDB). Similarly, 82.3% of stage III patients diagnosed at Aultman survived 5 years compared to 89.6% for the NCDB. Among patients with metastatic disease at presentation (stage IV), overall 5 year survival at Aultman was 32.7% compared to 39.3% for the NCDB. While these numbers may suggest a slightly lower overall rate of survival for Aultman patients when compared to the NCDB, it bears repeating that patients during this time period were diagnosed at a significantly older average age, which likely skewed overall survival rates. While the stage of diagnosis is very similar at Aultman when compared

to the national database, the historical propensity for diagnosis at older average ages is demonstrated when one compares age of diagnosis at Aultman versus the NCDB.



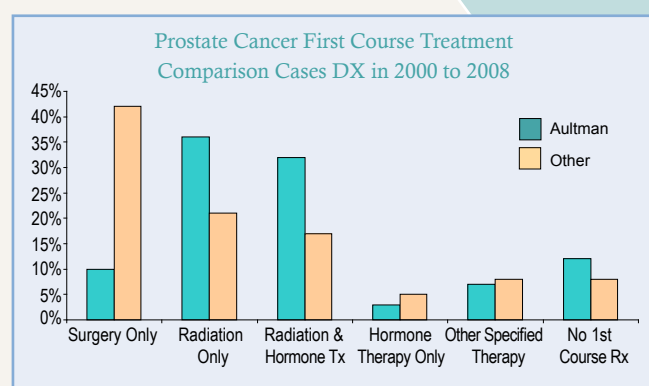
While there were too few cases of stage I patients at Aultman for significant observations, one may note that stage I patients in the Comprehensive Cancer Centers and NCDB databases exhibited lower overall survival than stage II or stage III patients. Stage I patients are typically low volume tumors diagnosed incidentally in men undergoing transurethral resection of the prostate

(cT1a) for bladder outlet obstruction. While these tumors frequently do not require active treatment, they also present in men at significantly older age ranges.



During 2000-2008 there was a strong predominance of radiotherapy as primary treatment for prostate cancer. 68% of patients at Aultman Hospital underwent radiotherapy with or without androgen deprivation, compared to 38% in the NCDB. Consequently, rates for radical prostatectomy were well below national data. Aultman Hospital has developed a very active interstitial prostate brachytherapy program, and the popularity of brachytherapy likely accounts for a significant portion of the radiotherapy. In addition, the rising popularity of robot assisted laparoscopic radical prostatectomy (RARP) in the latter half of the study

period also presented a unique challenge. Many of patients who were candidates for surgical therapy chose to go elsewhere for robot assisted surgery. Fortunately, this situation was ameliorated when Aultman Hospital installed a da Vinci robot in 2010.



Summary

Recent trends in prostate cancer at Aultman show increased focus on younger men with prostate cancer, who may benefit most from early diagnosis and treatment. Historical strength in radiotherapy-based treatment will be augmented by improvements in less invasive surgical techniques for localized prostate cancer.

References

1. American Cancer Society (2010) Cancer Facts and Figures 2010. www.cancer.org
2. Mortality Results from a Randomized Prostate-Cancer Screening Trial. NEJM 2009; 360:1310-1319.
3. Screening and Prostate-Cancer Mortality in a Randomized European Study. NEJM 2009; 360:1320-1328.
4. Early Detection of Prostate Cancer. AUA Policy Statement April 2009. www.auanet.org
5. NCCN Practice Guidelines in Oncology, version 2.2010. National Comprehensive Cancer Network, Inc. 5/27/2010.www.nccn.org