Prostate cancer diagnosis today

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Introduction

- Prostate cancer remains a major problem in the world and particularly in black people who have the highest incidence in the world. *(Ngugi/magoha)*
- Its incidence in the east African region has been rising
- The incidence rate for American black men is estimated to be ~55% that of American whites
- South Asian men living in England have a lower incidence than whites *(Metcalf et al)*

In East Africa in 1935 Vint reviewed 546 malignant male tumors and reported no prostatic carcinoma.

Davies reported the first three (2.1%) cases of prostate cancer in 143 cancers retrieved from 2162 male autopsies in Uganda.

Dodge in Uganda looked at prostate cancer in a 12 year period(period (1952-1963)

He reported histological diagnosis in 57 out of 97 patients.

In the other 40 patients diagnosis was based on radiological findings

Epidemiology

Epidemiology

Diagnosis of prostate cancer in the developed world has increased since the advent of the PSA.

In those countries It is diagnosed at an earlier age than before

Diagnosis

The first reported incidence of prostate cancer at 4.4/100000 was in 1966 in Uganda

Druly and Owuor reported that Ugandans had fewer latent prostate cancers than is reported in the WEST.

diagnosis

In 2000, Magoha showed that prostate cancer in Nairobi still presented late and that 25.42% of the patients had undifferentiated and poorly differentiated prostate cancer with Gleason scores of >7.

Twenty five per cent had moderately well differentiated tumors of Gleason score 6-7

diagnosis

In East Africa more men are being tested for prostate cancer with an increase in the number of patients diagnosed with prostate cancer.

introduction

- The diagnosis of prostate cancer continues to pose a challenge today as in the last millennium.
- Many patients diagnosed with early prostate cancer may not require treatment and others diagnosed with what appears to be early prostate cancer will still succumb to the disease despite all treatments available
- In east Africa the majority of the patients present late and the only treatment available is orchidectomy

Introduction

- The decision to biopsy the prostate has been traditionally been based on DRE and serum *t*psa.
- Other important factors include demographics and the presence of other risk factors.
- The DRE is subjective and has a marginal predictive value*(Shroder et al, Issa et al, Richie et al)*
- PSA has many flaws as it is prostate specific but not cancer specific

PSA

A human kallekrein secreted by prostate epithelialcells,

A normal component of the ejaculate.

These epithelial cells are also the progenitor cells of prostate adenocarcinoma

PSA

The adoption of PSA screening in the United States could not have been predicted from the initial reports.

A substantial overlap in values was found between patients with and without cancer

Initial recommendations for the upper limit of the normal range varied from 2.5 to 24 ng/mL

psa

- In the 1980s a cut-off level of 4.0 ng/mL was widely adopted arbitrarily
- virtually no patients with levels less than that underwent biopsy.
- For almost 2 decades prostate cancer was
- nerally thought to be almost nonexistent at PSA levels under 4.0 ng/mL.

PSA

Lack of specificity and of highly predictive methods for early detection and for differentiation of *indolent* from *aggressive* tumors results in poor prostate cancer survival

Contemporary use of PSA internationally

PSA testing for

- Men older of >50 years of age with life expectancy of >10 years have an annual PSA assessment. If PSA is elevated with no symptoms indicating higher risk for prostate cancer a DRE or *t*psa is performed at appropriate intervals
- If *tpsa* continues to rise or subsequent DRE results are suspect benign conditions are excluded using imaging, cystoscopy and measuring free psa/tpsa %.
- If these tests indicate sufficient risk for prostate cancer a biopsy is recommended.

PSA

Using *t*psa alone is risky as this can rise in many benign conditions including BPH and acute prostatitis.

A high BMI lowers the *tpsa* by dilutional effects

T psa is a poor indicator of the aggressiveness of the prostate cancer leading to over diagnosis and overtreatment for prostate cancer.

Lower urinary tract symptoms

- Older men with lower urinary tract symptoms need evaluation to eliminate the possibility of prostate cancer.
- Using the PSA for this purpose may be inadequate because of its limited sensitivity and specificity.
- The lack of specificity is due to temporal variation in psa levels that are not related to pathology*(Estherm et al)* and PSA being raised due to benign as well as malignant disease

LUTS

There is a weak association between LUTS and prostate cancer. *(Young et al)*

A recent case controlled study reported a strong association between LUTS and increased risk of clinically detected cancer *(Hamilton et al)2006*

Others have found no association but latest study from Cambridge *(Collin et al)* with 65,000men randomly selected who had psa and LUTS evaluation showed a strong correlation between PSA and LUTS

Gleason score

- It has been assumed that PSA level Gleason sum and clinical stage individually and independently predict outcome after radical treatments for CAP
- The study from Columbia shows that PSA and Gleason score used together give a better prediction than the sum total of individual predictions
- Thus PSA and Gleason scores are interrelated

Prediction of Gleason grade

Tumor grade is used as a surrogate for tumor aggressiveness and is important in selecting treatment

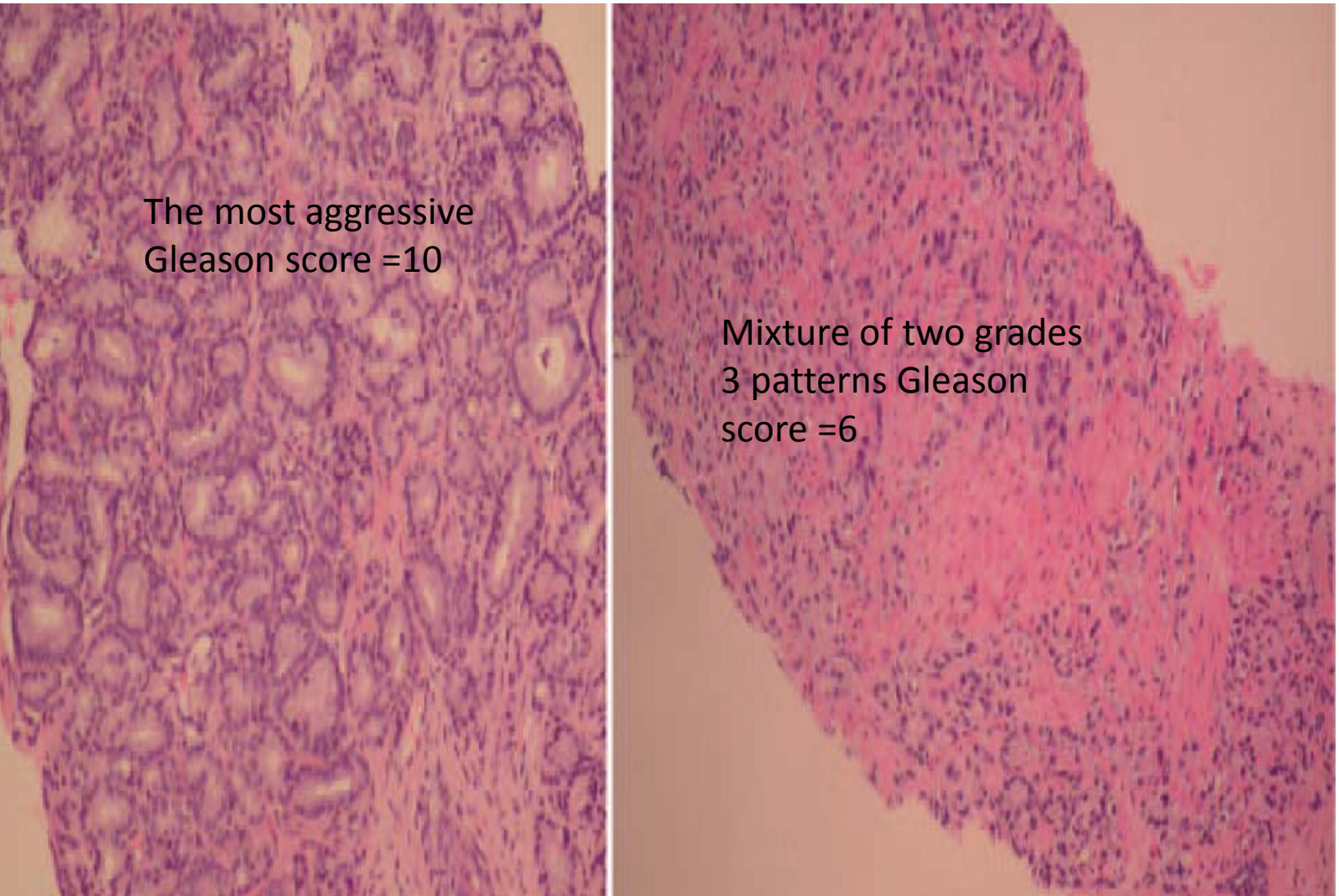
Gleason score correlates well with aggressiveness and prognosis and influences treatment of choice. *(master et al)*

Gleason score however depends on sampling and is subject to significant error

Gleason score

There is a correlation between biopsy Gleason score and RP Gleason score to those with Gleason **>7** than those **< 7**

Micrographs of thin slices of prostate cancer tissue.



biopsy

The posterior region of the prostate gland is where most cancers arise; biopsies are directed (somewhat randomly) to sample from that area

Number of biopsies

- The average number of biopsy cores taken varies by clinical practice.
- In initial screening studies, investigators obtained 4 biopsy cores
- In 1989, this increased to 6 cores
- more recently, numbers have ranged from 12 to 24 cores.

Number of biopsies

The prostate cancer detection has been enhanced by increasing the number of biopsies and reducing the PSA threshold for biopsy

Biopsy strategies are designed to detect the most clinically significant cancers while minimizing the detection of clinically insignificant lesions

Biopsies have increased from 6 through 12 to 36*(Rabets JC et al)*

Treatment outcomes the scandinavian study

RCT -radical prostatectomy (RP) vs watchful waiting - the Scandinavian Prostate Cancer Group Study group

Recently additional 3 years of follow-up data:

- differences in death from prostate cancer
- differences in death from any cause, distant metastases, and local progression

Treatment outcomes the scandinavian study

695 men from 14 centres from 1989 to 1999,

clinical stage T1 or T2 prostate cancer, a PSA level of <50 ng/mL and negative bone scans.

The patients were stratified according to:

tumour grade and randomization centre

randomly assigned to undergo either RP or watchful waiting.

Analysis was by intention to treat, with a 5% crossover in the RP group and a 10% crossover in the watchful-waiting group.

Treatment outcomes the scandinavian study

significant advantages in the RP group for:

death from prostate cancer *(30 vs 50 men, P = 0.01)*

deaths from any cause *(83 vs 106 men, P = 0.04)*.

no difference in the incidence of distant metastases in the two groups during the first 5 years

additional 3-year follow-up yielded an absolute risk reduction of 10% in favour of the RP group (*relative risk of 0.60*)

Treatment outcomes the scandinavian study

study was the first to show a clear advantage to RP over watchful waiting in a cohort of patients with clinically localized prostate cancer, either well or moderately differentiated.

mportant message from the study

- 5-year follow-up data in treatments for prostate cancer have limited value
- 8- or preferably 10-year data are necessary to discern important differences.
- The greater incidence of local progression and distant metastases in the watchful-waiting group would also suggest that relative risks may be further improved in the RP group by a longer follow-up

mportant message from the study

The subgroup analysis suggest that the reduction in disease-specific mortality was greatest among patients aged <65 years

younger patients would benefit more from intervention rather than watchful waiting.

mportant message from the study

causes of death after observation in the
suggested that younger patients, with higher
Gleason sum carcinoma of the prostate,
=greater likelihood of prostate cancer
mortality with conservative management

watchful waiting

10-year follow-up of 223 patients,

cause-specific survival from prostate cancer was excellent-earlier study

20-year follow-up, the mortality from prostate cancer increased dramatically, indicating the pitfall of a shorter follow-up in a disease such as prostate cancer.