# Gleason score stratification according to age at diagnosis in 1028 men

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**Aim of the study:** Gleason score stratification according to age at diagnosis has been retrospectively evaluated in 1028 men with biopsy-proven prostate cancer (PCa).

**Material and methods:** From January 2006 to December 2014, 2435 Caucasian men aged between 37 and 92 years underwent transperineal prostate biopsy for suspicion of PCa. The indications were as follows: abnormal digital rectal examination (DRE), PSA values > 10 ng/ml or between 4.1–10 or 2.6–4 ng/ml, with free/total PSA < 25% and < 20%, respectively.

**Results:** In 1028 (42.2%) patients with median PSA of 9.6 ng/ml a PCa was found (median age 62.3 years; range: 42–92 years); 757 (73.7%) vs. 271 (26.3%) men had a T1c vs. T2 clinical stage, respectively. Median Gleason score was 7 (range: 6–10). The Gleason score progressively increased with the age of the patients at diagnosis, and a significantly correlation between Gleason score ≥ 8 and men older than 80 years was demonstrated ($p = 0.0001$).

**Conclusions:** The detection rate of aggressiveness of PCa progressively increased with the age at diagnosis; Gleason score ≥ 8 was more frequently diagnosed in men older than 80 years with PSA values > 10 ng/ml (about 80% of the cases) and abnormal DRE (about 60% of the cases).

**Key words:** prostate cancer, Gleason score and age, aggressiveness PCa in elderly.

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## Introduction

Prostate cancer (PCa) is the most frequent tumour diagnosed in men following screening and case-finding protocols for early diagnosis of cancer; however, the ERSPC (European Randomised Study of Screening for Prostate Cancer) reports a 20% reduction in mortality [1], nonetheless, today a high percentage of biopsies are predictive of indolent disease (about 50% of cases), so Active Surveillance protocols have been introduced in clinical practice to reduce the risk of overtreatment [2].

In older men with a life expectancy lower than 10 years, the screening is not recommended and PSA test should be stopped in the presence of values < 3 ng/ml [3–5]; moreover, also in the presence of biopsy-proven PCa initial watchful waiting and/or palliative treatment in case of clinical progression (i.e. acute urinary retention, bone metastases, hydronephrosis) should be encouraged. On the other hand, men older than 70 years have a higher proportion of poor pathological tumour stage and Gleason score in comparison with younger patients [6–8].

In this scenario, urologists are often called on to perform or avoid a prostate biopsy in elder men for suspicious PSA values following clinical indications suggested by other specialists; in addition, the decision making is not always easy because the difficulty to individualise the expectancy of life, the aggressiveness of the cancer [9], and the risk of legal trouble in case of disease progression. Nevertheless, in the majority of cases prostate biopsy remains the only procedure useful in the detection of the aggressiveness of PCa characterised by an high Gleason score, and which still constitutes the strongest pathologic predictor of poor prognosis, cancer-specific survival, and risk of metastasis development [10, 11].

In our study, Gleason score stratification according to age at diagnosis was retrospectively evaluated in 1028 men with biopsy proven PCa.

## Material and methods

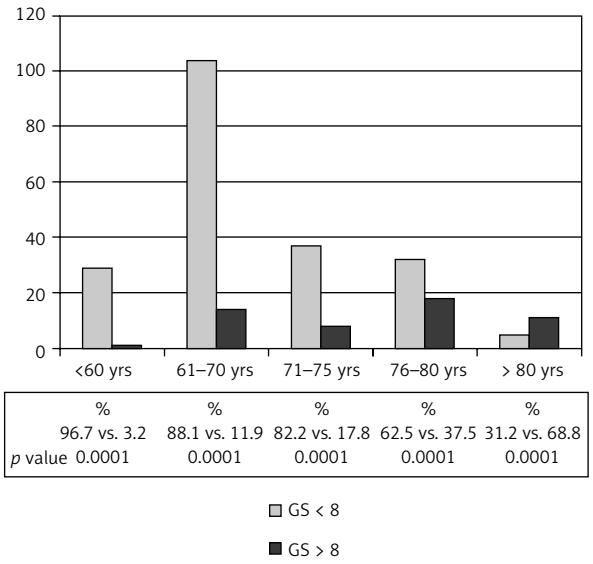
From January 2006 to December 2014, 2435 Caucasian men aged between 37 and 92 years (median 64.4 years) underwent prostate biopsy for suspicion of PCa. The indications were as follows [12]: abnormal digital rectal examination (DRE), PSA values greater than 10 ng/ml or between 4.1–10 or 2.6–4 ng/ml with free/total PSA < 25% and < 20%, respectively. The procedure was performed transperineally [13] using a Tru-Cut 18 gauge needle (Bard; Covington, GA), a GE Logiq 500 PRO echograph (General Electric; Milwaukee, WI), supplied with a biplanar transrectal probe (5–6.5 MHz), under sedation and antibiotic prophylaxis (one tablet of levofloxacin 500 daily for three days). The prostate biopsy protocol included a median of 18 (extended biopsy) and 28 (saturation biopsy) cores in case of initial and repeat procedure, respectively.

Digital rectal examination was positive in 373 (15.3%) patients, and median PSA was 8.3 ng/ml (range: 1.2–712 ng/ml): 219 (9%), 1681 (69%), and

535 (22%) had a PSA included between 2.6 and 4 ng/ml, between 4.1 and 10 ng/ml, and greater than 10 ng/ml, respectively. A probability ($p$) level of less than 0.05 was considered statistically significant.

## Results

In 1028/2435 (42.2%) patients a PCa was found; median age was 62.3 years (range: 42–92 years), 757 (73.7%) vs. 271 (26.3%) men had a T1c vs. T2 clinical stage: median PSA was 9.6 ng/ml: 380 (36.9%), 549 (53.4%) and 99 (9.7%) had a PSA value > 10 ng/ml, included between 4.1 and 10 ng/ml and 2.6–4 ng/m, respectively (Table 1). Median Gleason score was 7 (range: 6–10); moreover, the Gleason score progressively increased with the age ($p$ = 0.0001) of the patients at diagnosis (Fig. 1). In detail, a significant correlation between Gleason score ≥ 8 and age older than 80 years was demonstrated ($p$ = 0.0001). None of the subjects developed sepsis, but haematuria, haematospermia, and acute retention of urine occurred in 326 (13.3%), 853 (35%), and 219 (9%) cases, respectively. Hospital admission occurred in 24 (1%) men, and 18 and 6 of them had a grade I and II on the Clavien-Dindo complication scale [14], respectively.




*GS – Gleason score*

**Fig. 1.** Gleason score stratification according to age at diagnosis in 1028 men with prostate cancer

## Discussion

Prostate cancer incidence increases significantly according to age and constitutes the third most common cause of cancer death among men aged > 80 years [15]; older men are diagnosed with higher grade and stage of prostate cancer than younger men and are less likely to receive curative therapy for their cancer [16]. The International Society of Geriatric Oncology recently recommended that older men with PCa should be managed according to their individual health status, and not according to age, suggesting that men older than 70 years, healthy or fit, should have the same treatment options as younger patients [17]. On the other hand, in men with a Charlson score of > 2, tumour aggressiveness had little impact on overall survival, suggesting that perhaps these patients could have been spared the biopsies and diagnosis of cancer.

In the ERSPC [2] randomised trial of screening there was no reduction in mortality among men aged 70 years or older [18]; in addition, the American Association of Urology guidelines [4] recommended that in men aged over 70 years, who wish to be screened, the prostate biopsy threshold should be increased for PSA values greater than 10 ng/ml [4].

Potential life-expectancy gains after curative therapy for prostate cancer depend on patient comorbidities and life expectancy. Although many older men who are diagnosed with PCa die of unrelated causes, some men may live long enough to derive a prostate cancer survival benefit from aggressive curative treatment sparing further diagnostic imaging and/or palliative treatment [19–21]. Merrick *et al.* [22] determined that 65% of men aged > 75 years, who they treated for prostate cancer, remained alive nine years after brachytherapy. Blood and Pickles [23] calculated that the median survival after prostate cancer treatment was greater than 10 years in men who were up to 80 years of age at the time of treatment.

In our series, in 1028 men with biopsy and histological diagnosis of PCa, the aggressiveness of the cancer was significantly correlated with the age at diagnosis ($p$ = = 0.0001); in detail, Gleason score ≥ 8 was more frequently

**Table 1.** Clinical parameters in the 1028 men with prostate cancer

| Age (years) | Overall N. pts | PSA > 10 ng/ml | PSA 4.1–10 ng/ml | PSA 2.6–4 ng/ml | Positive DRE N. pts | cT1c % |
|---|---|---|---|---|---|---|
| < 60 | 120 (11.6%) | 9 (7.5%) | 106 | 5 | 2 | 98.4 |
| 61–70 | 472 (46%) | 91 (19.2%) | 295 | 86 | 58 | 87.8 |
| 71–75 | 180 (17.5%) | 68 (37.8%) | 108 | 4 | 55 | 69.5 |
| 76–80 | 192 (18.7%) | 148 (77%) | 40 | 4 | 108 | 43.8 |
| > 80 | 64 (6.2%) | 64 (100%) | – | – | 48 | 25 |

*DRE – digital rectal examination; pts – patients; cT1c – clinical stage T1c; PSA – prostate specific antigen*

diagnosed in men older than 80 years with PSA values ≥ 10 ng/ml (about 80% of the cases) and abnormal DRE (about 60% of the cases).

In older men with a good performance status with aggressive cancers (i.e. Gleason score ≥ 8) early definitive treatment (i.e. external beam radiation therapy) could be suggested instead of palliative therapy at clinical progression to improve quality of life and to reduce the costs of metastatic disease management and side effects secondary to androgen deprivation.

Regarding our results, some considerations should be reported. Firstly, the higher percentage of older men with Gleason score ≥ 8 could be biased by the selection criteria for biopsy (i.e. higher PSA values, suspicious DRE); secondly, during the eight years of clinical evaluation, an increased number of elderly patients suspicious for PCa accepted criteria for watchful waiting, according to literature data.

In conclusion, Gleason score progressively increased with the age at diagnosis, and a significant correlation between Gleason score ≥ 8 and age above 80 years was demonstrated ($p = 0.0001$).

*The authors declare no conflict of interest.*

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