TIME-DEPENDENT PREDICTIVE ACCURACY OF PROSTATE CANCER SPECIFIC MORTALITY OF THE CONTEMPORARY *vs.* ORIGINAL GLEASON SCORE

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Rationale and aim

- Prostate cancer is the most frequent male cancer in the US and Western Europe.
- The Gleason score (GS) is the most important prognostic indicator. A gradual upgrading in GS has occurred from the early 1990s to the early 2000s. In 2005, the International Society of Urological Pathology issued a revision of assignment criteria, causing a further upward shift of GS.
- A consequence of upgrading is an apparent but spurious improvement in grade-specific survival for more recent cases due to grade migration (Will Rogers phenomenon).
- Aim of the study: to assess, for the first time, the ability of the contemporary GS in predicting prostate cancer-specific mortality.

Methods

- Cohort of consecutive prostate cancer patients identified at a single pathology ward between 1993 and 1996.
- The GS assigned at diagnosis ("original GS") extracted from the pathology report; diagnostic slides blindly re-evaluated in 2010 by an experienced uropathologist (L.D.) according to current criteria ("contemporary GS").
- Patients followed-up until 15/01/2007 and death certificates obtained from the demographic offices.
- Effect of grade migration: assessed through cumulative probability of death from prostate cancer, taking into account competing risk events.
- Time-dependent measures for the accuracy of the original and contemporary GS in predicting the probability of prostate cancer death: ROC curves at different follow-up times, with censored survival and competing risks.
- AUCs compared through a Wilcoxon rank sum test for dependent samples.

Results

Table 1. Characteristics of prostate cancer patients included in the cohort. Turin, 1993-1996

Characteristics	Patients	
	N	%
Patients	243	
Person years	1591	
Mortality		
Overall	177	
Due to prostate cancer	76	42.9
Due to other causes	101	57.1
Range follow-up time (years)	0-14	
Median survival time (years)	6.3	(IQR: 2.6-14)
Mean age at diagnosis	70.6	(sd: 8.7)
Source of tumor tissue		
Biopsy	164	(sd: 67.5)
TURP	45	18.5
Radical prostatectomy	34	14.0

Figure 1. Cumulative probability of death due to prostate cancer by original and contemporary GS: the Will Rogers phenomenon.

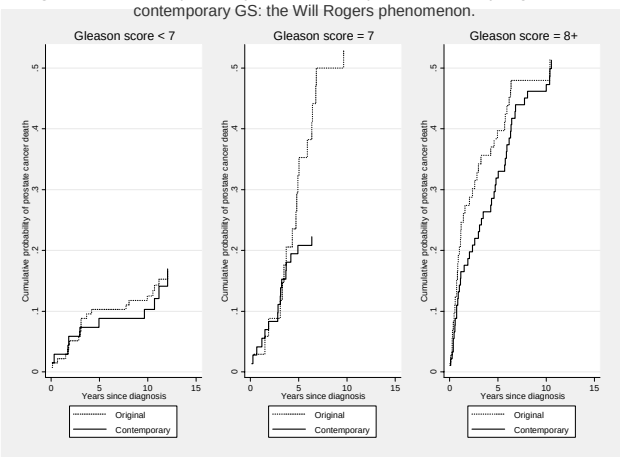
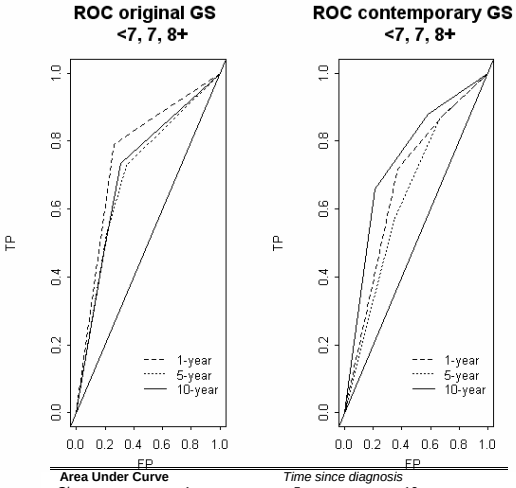


Table 2. Distribution of original and contemporary GS.

Original Gleason score (N)	Contemporary Gleason score (N) <7 (68)	7 (72)	8+ (91)
<7 *(131)*	59	52	20
7 *(32)*	3	9	20
8+ *(68)*	6	11	51

Figure 2. Time dependent predictive accuracy of original and contemporary GS (<7, 7, 8+) measured as the area under curve (AUC) of the receiver operating characteristics (ROC) curves at 1, 5 and 10 years after prostate cancer diagnosis.



Area Under Curve	Time since diagnosis		
Gleason score	1 year	5 years	10 years
Original	0.77 (0.67-0.86)	0.70 (0.63-0.78)	0.71 (0.62-0.80)
Contemporary	0.68 (0.56-0.78)	0.64 (0.56-0.72)	0.75 (0.68-0.82)

Discussion and conclusions

- Application of the contemporary GS criteria entails the artefactual improvement in clinical outcomes known as the Will Rogers phenomenon.
- Contemporary GS does not improve prediction of prostate cancer-specific mortality at least for the first 5 years of follow up.
- GS has been the strongest prognostic factor for prostate cancer since its introduction, is included in all prognostic models for prostate cancer, and is a critical factor in deciding on the choice of treatment. Although we did not evaluate the ability of the original and the contemporary GS to indicate the appropriate treatment for prostate cancer, we found that the contemporary GS is worse rather than better in predicting prostate cancer mortality, at least in the shorter term.