Comment on 'Validation of a contemporary prostate cancer grading system using prostate cancer death as outcome'

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Sir,

We read with great interest the article by Berney and colleagues (Berney et al, 2016) who validated the new prostate cancer (PCa) grading system (Pierorazio et al, 2013) in a biopsy series of 988 conservatively treated PCa patients identified between 1990 and 2003. The authors (Berney et al, 2016) provided evidence that there is a strong correlation between the new PCa grading system and PCa death, relying on pre-treatment models (Gleason score-GS at biopsy). Furthermore, they observed that the 'worst' GS has similar prognostic ability to the 'overall' GS in predicting PCa death. Berney and colleagues should be commended for their effort in validating the new PCa grading system using a stronger outcome, namely PCa mortality, compared with previous available studies (Epstein et al, 2015; Loeb et al, 2015; Spratt et al, 2016). Moreover, they tried to clarify a debated topic whether an 'overall' or 'worst' GS should be used in routine clinical practice. However, some points of the manuscript warrant discussion.

First, despite this being the first report that tested the new PCa grading system on the strongest available outcome, a discerning reader might argue that the findings of Berney and colleagues are fairly expected, given the fact that the GS is a known good predictor of PCa mortality (Bolton et al, 2015). In consequence, the authors do not provide any added advantage of the new PCa grading system that was not already known. The real unmet need that this report should have filled is: does the new PCa grading system improve the prediction of PCa death relative to the standard Gleason grading system? This comparison is mandatory to definitely prove the added value of the introduction of the new PCa grading system into daily clinical practice. Under this light, previous authors assessed the predictive ability of the new PCa grading system relative to the standard Gleason grading system on biochemical recurrence in patients treated with radical prostatectomy-RP (Epstein et al, 2015; Loeb et al, 2015; Spratt et al, 2016). For example, Epstein and colleagues (Epstein et al, 2015) were the first to validate the new PCa grading system in a multi-institutional series and to provide evidence that this new grading system is more accurate relative to the standard Gleason grading system. However, they were able to demonstrate only a limited increment in the predictive accuracy. Thereafter, Loeb and colleagues (Loeb et al, 2015) failed to observe higher predictive accuracy of the new PCa grading system relative to the standard Gleason grading system in a population-based setting.

Second, the accuracy of the new PCa grading system to predict PCa death was assessed exclusively relying on pretreatment models (i.e., GS at biopsy). Generally, GS at RP is more accurate to predict oncological outcomes relative to GS at biopsy, as proved by previous investigators that demonstrated higher predictive accuracy of the GS at RP relative to the GS at biopsy in predicting BCR (Epstein et al, 2015; Loeb et al, 2015).

Third, strict selection criteria were used to enroll patients in the current study, which might have biased its findings. For example, the investigators excluded patients older than 76 years. Currently, given the aging of the population and the increasing life expectancy worldwide (Tuljapurkar et al, 2000; United Nations, Department of Economic and Social Affairs, Population Division, 2015), the proportion of elderly is increasing. Consequently, it is mandatory to have evidence based that consider also elderly patients, which generally harboured worse disease characteristics (Shao et al, 2009; Dell'Oglio et al, 2016).

Fourth, the authors should be acclaimed to reassign GS of histological specimens from sextant biopsies performed between 1990 and 2003, according to a contemporary Gleason scoring system (Epstein, 2010). Certainly, this allowed to assess a hard outcome as PCa death, given the longer follow-up of non-contemporary patients. However, to date it should be more reasonable to evaluate less stronger outcome, namely clinical recurrence, relying on a cohort of patients that is treated with contemporary practice.

Last but not least, the authors did not assess the net benefit (Vickers and Elkin, 2006) of the new PCa grading system relative to the standard Gleason grading system for clinical decision-making, which is mandatory in a validation study. However, to the best of our knowledge, to date no studies overcome this issue.

In conclusion, the dilemma whether the new PCa grading system has higher predictive ability and superior clinical benefit relative to the standard Gleason grading system to predict PCa death, or it is only a user-friendly instrument to help patient counselling still persists. Future studies are needed to assess the discrimination and the net benefit of the new PCa grading system compared with the standard Gleason grading system on harder endpoint than BCR.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

REFERENCES

Berney DM, Beltran L, Fisher G, North BV, Greenberg D, Møller H, Soosay G, Scardino P, Cuzick J (2016) Validation of a contemporary prostate cancer grading system using prostate cancer death as outcome. Br J Cancer 114(10): 1078–1083.

Bolton DM, Papa N, Ta AD, Millar J, Davidson AJ, Pedersen J, Syme R, Patel MI, Giles GG (2015) Predictors of prostate cancer specific mortality after radical prostatectomy: 10 year oncologic outcomes from the Victorian Radical Prostatectomy Registry. BJU Int 116(Suppl 3): 66–72.

Dell'Oglio P, Suardi N, Boorjian SA, Fossati N, Gandaglia G, Tian Z, Moschini M, Capitanio U, Karakiewicz PI, Montorsi F, Karnes RJ, Briganti A (2016) Predicting survival of men with recurrent prostate cancer after radical prostatectomy. Eur J Cancer 54: 27–34.

Epstein JI (2010) An update of the Gleason grading system. J Urol 183(2): 433–440.

Epstein JI, Zelefsky MJ, Sjoberg DD, Nelson JB, Egevad L, Magi-Galluzzi C, Vickers AJ, Parwani AV, Reuter VE, Fine SW, Eastham JA, Wiklund P, Han M, Reddy CA, Ciezki JP, Nyberg T, Klein EA (2015) A contemporary prostate cancer grading system: a validated alternative to the gleason Score. Eur Urol 69(3): 428–435.

Loeb S, Folkvaljon Y, Robinson D, Lissbrant IF, Egevad L, Stattin P (2015) Evaluation of the 2015 gleason grade groups in a nationwide population-based cohort. Eur Urol 69(6): 1–7.

Pierorazio PM, Walsh PC, Partin AW, Epstein JI (2013) Prognostic Gleason grade grouping: data based on the modified Gleason scoring system. BJU Int 48(Suppl 2): 1–6.

Shao Y, Demissie K, Shih W, Mehta AR, Stein N, Roberts CB, Dipaola RS, Lu-yao GL (2009) Contemporary risk profile of prostate cancer in the United States. J Natl Cancer Inst 101(18): 1280–1283.

Spratt DE, Cole AI, Palapattu GS, Weizer AZ, Jackson WC, Montgomery JS, Dess RT, Zhao SG, Lee JY, Wu A, Kunju LP, Talmich E, Miller DC, Hollenbeck BK, Tomlins SA, Feng FY, Mehra R, Morgan TM (2016) Independent surgical validation of the new prostate cancer grade-grouping system. BJU Int. e-pub ahead of print 24 March 2016; doi:10.1111/bju.13488.

Tuljapurkar S, Li N, Boe C (2000) A universal pattern of mortality decline in the G7 countries. Nature 405(6788): 789–792.

United Nations, Department of Economic and Social Affairs, Population Division (2015) World Population Ageing. United Nations, New York, NY, USA. Available at: www.unpopulation.org.

Vickers AJ, Elkin EB (2006) Decision curve analysis: a novel method for evaluating prediction models. Med Decis Making 26(6): 565–574.

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