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Erstveröffentlichung in / First published in:

Urologia Internationalis. 2016, 96 (3), S. 302 – 308 [Zugriff am: 19.05.2020]. Karger. ISSN 1423-0399.

DOI: <https://doi.org/10.1159/000440729>

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Is the Post-Radical Prostatectomy Gleason Score a Valid Predictor of Mortality after Neoadjuvant Hormonal Treatment?

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Key Words

Prostate cancer · Radical prostatectomy · Prognostic factors · Hormonal treatment · Neoadjuvant · Gleason score · Health outcomes research

Abstract

Purpose: To evaluate the validity of the Gleason score after neoadjuvant hormonal treatment as predictor of disease-specific mortality after radical prostatectomy. **Patients and Methods:** A total of 2,880 patients with a complete data set and a mean follow-up of 10.3 years were studied; 425 of them (15%) had a history of hormonal treatment prior to surgery. The cumulative incidence of deaths from prostate cancer was determined by univariate and multivariate competing risk analysis. Cox proportional hazard models for competing risks were used to study combined effects of the variables on prostate cancer-specific mortality. **Results:** A higher portion of specimens with a history of neoadjuvant hormonal treatment were assigned Gleason scores of 8–10 (28 vs. 17%, $p < 0.0001$). The mortality curves in the Gleason score strata <8 vs. 8–10 were at large congruent in patients with and without neoadjuvant hormonal treatment. In patients with neoadjuvant hormonal treatment, a Gleason score of 8–10 was an independent predictor of prostate cancer-specific mortality; the hazard ratio was, however, somewhat lower than in patients without neoadjuvant hormonal

treatment. **Conclusion:** This study suggests that the prognostic value of the post-radical prostatectomy Gleason score is not meaningfully jeopardized by heterogeneous neoadjuvant hormonal treatment in a routine clinical setting.

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Introduction

Neoadjuvant hormonal treatment of prostate cancer leads to cellular changes resulting in a tendency towards a more frequent assignment of higher Gleason scores and Gleason 5 pattern [1–3]. Therefore, the German S3 prostate cancer guidelines [4] and other authors [3, 5, 6] recommend not giving a Gleason score to radical prostatectomy specimens after neoadjuvant hormonal manipulations. Some authors, however, used the prostatectomy specimen Gleason score assigned after neoadjuvant hormonal treatment, nevertheless, for analysis purposes [7].

To our knowledge, there is little data on the actual consequences of the described cellular changes of neoadjuvant hormonal therapy on the capability of the Gleason score to predict outcome. Since the Gleason score is the most important prognostic parameter in patients with prostate cancer [4, 8–11], the absence of the prognostic information delivered by the Gleason score makes it difficult to counsel patients on their mortality risk and on

Table 1. Demographic data of the study population stratified by the use of neoadjuvant hormonal treatment

Parameter	No neoadjuvant hormonal treatment	Neoadjuvant hormonal treatment	p value
Sample size	2,455	425	
Median, mean, age, years	65 (64)	65 (64)	0.2521
Median, mean, follow-up, censored patients, years	9.6 (10.2)	10.4 (11.0)	<0.0001
Median, mean, PSA value, ng/ml	7.4 (11.0)	Not available	
Organ confined, lymph node-negative disease, %	1,662 (68)	258 (61)	0.0048
Positive lymph nodes, %	204 (8)	49 (12)	0.0304
Gleason score 8–10, %	425 (17)	121 (28)	<0.0001
ASA class 3, %	404 (16)	89 (21)	0.0234
Charlson score 2 or higher, %	364 (15)	84 (20)	0.0095
Deaths from prostate cancer	97	36	
Deaths from competing causes*	328	62	
Deaths from unknown causes	7	2	

* Deaths from non-cancer causes, second cancers or unknown causes.

adjuvant treatment options. Furthermore, retrospective series may contain patients with neoadjuvant hormonal treatment in whom the validity of postoperatively assigned Gleason score may be of concern. In this study, we evaluated the impact of neoadjuvant hormonal treatment on the validity of the Gleason score determined in the prostatectomy specimen as a predictor of prostate cancer-specific mortality in a large sample with long-term follow-up.

Patients and Methods

Between December 1, 1992, and December 31, 2007, 2,961 patients consecutively underwent radical prostatectomy at our institution. Among them, 2,880 had complete information on specimen tumour stage, Gleason score, and lymph node status and were analyzed in this study. The prostatectomy specimens of patients treated before the year 1999 were reevaluated to assign the histopathological tumour stage and the Gleason score to assure data completeness and uniformity. Later, the Gleason score was taken from the routine histopathological report without reevaluation. The following further variables were analyzed beside Gleason score, lymph node status and local tumour stage: history of neoadjuvant hormonal treatment, prostate specific antigen (PSA; only considered in patients without neoadjuvant hormonal treatment), age, American Society of Anesthesiologists physical status class and Charlson score. All this information was obtained by review of the patient charts. Institutional review board approval was obtained.

Deaths in the presence of uncontrolled prostate cancer were considered events concerning disease-specific mortality. The cumulative incidence of deaths from prostate cancer was determined by univariate and multivariable competing risk analysis. The univariate analyses were done using SAS macros and Pepe-Mori tests [12, 13]. Cox proportional hazard models for competing risks ac-

cording to Fine and Gray [14] were used to study the combined effects of the variables on prostate cancer-specific mortality. The analyses were performed with the Statistical Analysis Systems version 9.4 statistical package (SAS Institute, Cary, N.C., USA).

Results

Demographic data of the study sample are shown in table 1. A higher portion of specimens with a history of neoadjuvant hormonal treatment were assigned Gleason scores of 8–10 (table 1). A higher portion of patients who received neoadjuvant hormonal treatment had serious comorbidity, non-organ-confined disease and lymph node involvement (table 1). There was a trend towards higher prostate cancer-specific mortality that narrowly missed the significance level in patients with neoadjuvant hormonal treatment compared with patients without such treatment (fig. 1). When the patients were stratified by the Gleason score in the prostatectomy specimen, there was no detectable difference in prostate cancer-specific mortality between patients with and without neoadjuvant hormonal treatment (fig. 2). Stratifying the patients with and without neoadjuvant hormonal treatment by the Gleason score determined in the prostatectomy specimen resulted in clearly separated and largely similar cumulative mortality curves in both subgroups (fig. 3, 4). The relationship between the histopathological tumour stage and prostate cancer-specific mortality in patients with and without neoadjuvant hormonal treatment is shown in figure 5.

In the multivariable analysis, extraprostatic disease, positive lymph nodes and a prostatectomy specimen Glea-

Fig. 1. Cumulative prostate cancer-specific mortality in patients with and without neoadjuvant hormonal treatment.

Fig. 2. Cumulative prostate cancer-specific mortality stratified by the Gleason score in the prostatectomy specimen in patients with and without neoadjuvant hormonal treatment stratified by the Gleason score in the prostatectomy specimen.

Fig. 3. Impact of the Gleason score in the prostatectomy specimen on cumulative prostate cancer-specific mortality stratified by the application of neoadjuvant hormonal treatment using 2-sided stratifications.

Fig. 4. Impact of the Gleason score in the prostatectomy specimen on cumulative prostate cancer-specific mortality stratified by the application of neoadjuvant hormonal treatment using tree-

sided stratifications. All curves differed significantly from each other (Pepe Mori test p values ranging between 0.0323 and <0.0001).

Fig. 5. Impact of the histopathological tumour stage cumulative prostate cancer-specific mortality stratified by the application of neoadjuvant hormonal treatment. In patients without neoadjuvant hormonal treatment, all curves differed significantly from each other with Pepe Mori test p values <0.0001. In patients who received neoadjuvant hormonal treatment, the cumulative mortality curves of patients with extracapsular lymph node-negative dis-

ease and those with lymph node-positive disease did not differ significantly (Pepe Mori test p value 0.1023), whereas the comparison of the other cumulative mortality curves reached the significance level (organ confined versus extracapsular lymph node-negative disease: Pepe Mori test p value 0.0021; organ-confined lymph node-negative vs. lymph node-positive disease: Pepe Mori test p value 0.0006).

son score of 8–10 were independent predictors of prostate cancer-specific mortality in the whole study sample with the Gleason score having the highest hazard ratio (table 2). Neoadjuvant hormonal treatment narrowly missed the significance level as a predictor of adverse outcome in the multivariable analysis (table 2). Very similar models were obtained when the analysis was restricted to patients without neoadjuvant hormonal treatment (table 3). When the analysis was restricted to patients with neoadjuvant hormonal treatment, extraprostatic disease and a prostatectomy spec-

imen Gleason score of 8–10 were identified as independent predictors of prostate cancer-specific mortality, whereas the lymph node status narrowly missed the significance level in the multivariable analysis (table 4). In patients with neoadjuvant hormonal treatment, the hazard ratio of the prostatectomy specimen Gleason score was only second after that of the local disease stage (table 4). In patients without neoadjuvant hormonal treatment in whom prostate-specific antigen was analyzable, this variable was without detectable prognostic impact (table 3).

Table 2. Cox proportional hazard models for competing risks predicting prostate cancer-specific mortality in the whole study population (n = 2,880, 133 deaths from prostate cancer)

Parameter	Full model			Optimal model		
	hazard ratio	95% CI	p value	hazard ratio	95% CI	p value
Age (continuous variable, per year increase)	0.999	0.966–1.033	0.9316			
Charlson score (continuous variable)	1.118	0.936–1.335	0.2198			
ASA 3 (vs. 1–2)	0.933	0.574–1.518	0.7814			
Extraprostatic disease (vs. organ confined)	3.431	2.182–5.396	<0.0001	3.424	2.177–5.385	<0.0001
Positive lymph nodes (vs. negative nodes)	2.564	1.752–3.751	<0.0001	2.583	1.768–3.774	<0.0001
Gleason score 8–10 (vs. <8)	3.998	2.672–5.981	<0.0001	4.170	2.808–6.193	<0.0001
Neoadjuvant hormonal treatment (vs. none)	1.461	0.983–2.170	0.0608			

Table 3. Cox proportional hazard models for competing risks predicting prostate cancer-specific mortality in patients without neoadjuvant hormonal treatment (n = 2,455, 97 deaths from prostate cancer)

Parameter	Full model			Optimal model		
	hazard ratio	95% CI	p value	hazard ratio	95% CI	p value
Age (continuous variable, per year increase)	1.004	0.965–1.045	0.8429			
Charlson score (continuous variable)	1.168	0.950–1.436	0.1414			
ASA 3 (vs. 1–2)	0.838	0.478–1.470	0.5379			
Extraprostatic disease (vs. organ confined)	3.518	2.104–5.882	<0.0001	3.491	2.093–5.824	<0.0001
Positive lymph nodes (vs. negative nodes)	2.699	1.749–4.164	<0.0001	2.703	1.759–4.153	<0.0001
Gleason score 8–10 (vs. <8)	4.572	2.887–7.241	<0.0001	4.633	2.943–7.293	<0.0001

Adding prostate-specific antigen as a continuous variable to the analysis was without any detectable effect on the resulting models (hazard ratio 0.999 per ng/ml, 95% CI 0.978–1.010, p = 0.8225 in the proportional hazards model with all variables).

Table 4. Cox proportional hazard models for competing risks predicting prostate cancer-specific mortality in patients with neoadjuvant hormonal treatment (n = 425, 36 deaths from prostate cancer)

Parameter	Full model			Optimal model		
	hazard ratio	95% CI	p value	hazard ratio	95% CI	p value
Age (continuous variable, per year increase)	0.979	0.919–1.043	0.5199			
Charlson score (continuous variable)	0.972	0.693–1.364	0.8697			
ASA 3 (vs. 1–2)	1.300	0.482–3.508	0.6039			
Extraprostatic disease (vs. organ confined)	3.251	1.294–8.164	0.0121	3.682	1.555–8.719	0.0030
Positive lymph nodes (vs. negative nodes)	2.168	0.955–4.924	0.0644			
Gleason score 8–10 (vs. <8)	2.561	1.151–5.700	0.0212	3.037	1.416–6.513	0.0043

Discussion

Cellular changes caused by neoadjuvant hormonal treatment may falsely upgrade good-risk patients into the unfavorable prognostic subgroups with a Gleason score of 8–10 [3]. The clinical significance of this upgrading in the Gleason score is not yet fully understood [5]. Such upgrading could result in an inflation of the higher risk

groups and a subsequent apparent decrease of mortality in all subgroups (Will Rogers phenomenon [15]). However, in the routine clinical setting of our study, neoadjuvant hormonal treatment did not discernibly compromise the prognostic value of the Gleason score. Although the higher portion of tumours classified as Gleason score 8–10 and the lower hazard ratio of the Gleason score after neoadjuvant hormonal treatment (table 4) actually sug-

gest some inflation of the Gleason score 8–10 subgroup, a Gleason score of 8–10 remained a powerful independent predictor of prostate cancer mortality (table 4). Furthermore, the cumulative mortality curves in the Gleason score subgroups were virtually identical in patients with and without neoadjuvant hormonal treatment (fig. 2). Since neoadjuvant hormonal treatment was simultaneously associated with a selection process (patients with poor prognostic features as for instance high PSA, clinically non-organ-confined disease or high tumour volume are more likely to receive such treatment, table 1) illustrated by a trend towards increased prostate cancer mortality in patients who had received neoadjuvant hormonal treatment in this study, figure 1, table 2, it is conceivable that the effect of Gleason score upgrading caused by neoadjuvant hormonal treatment (thus apparently decreasing mortality in high risk patients) was at least partially compensated by this selection-related enrichment of poor risks.

Neoadjuvant hormonal treatment failed to provide a survival benefit after radical prostatectomy [4, 8]. Whereas the guidelines of the European Association of Urology generally discourages neoadjuvant hormonal treatment prior to radical prostatectomy [8], the German S3 guidelines on diagnostics and treatment of prostate cancer [4] refers to the limited knowledge on neoadjuvant hormonal treatment in patients with locally advanced disease and does not completely rule out this option in this situation. The German S3 guidelines underline, however, the adverse impact of such treatment on the histopathological workup and prognostic stratification [5]. Currently, the prognostic evaluation of patients who received neoadjuvant hormonal treatment relies only on the anatomical tumour stage and the margin status, factors that may be influenced by neoadjuvant hormonal treatment as well as the Gleason score [8, 16, 17]. Neoadjuvant hormonal treatment is occasionally used in multimodality approaches for high-risk tumours [18, 19]. In such cases, the additional prognostic information provided by a Gleason score assignment might be of considerable clinical importance in order to tailor further treatment strategies after the removal of the prostate. Currently, counseling of patients who had received neoadjuvant hormonal treatment is hindered by the unavailability of the most important prognostic parameter and a reduced meaningfulness of the remaining factors. This study suggests that assigning the Gleason score regardless of neoadjuvant hormonal treatment might supplement the prognostic armamentarium in patients undergoing radical prostatectomy. It could be reasonable to add a ‘y’ sym-

bol to the Gleason score in order to indicate that it was assigned after neoadjuvant treatment in the analogy of the currently used tumour node metastasis classification after neoadjuvant treatment [20, 21].

Long-term neoadjuvant hormonal treatment may cause more pronounced effects on the cell architecture. In a controlled trial with a homogeneous long-term neoadjuvant treatment comparing 12 weeks of neoadjuvant cyproterone acetate versus no neoadjuvant treatment [3], there was a greater difference in the distribution of post-prostatectomy Gleason scores of 8–10 between patients with and without neoadjuvant hormonal treatment (52 vs. 13%) than in our series (28 vs. 17%). Another randomized trial demonstrated that a prolonged neoadjuvant treatment (8 months) led to further histopathological disease regression [22]. It is likely that a consequent long-term treatment may produce more marked histopathological changes than a heterogeneous and partially short-term and/or low-dose treatment in the routine setting of our study.

We are aware of only one study in the literature addressing a similar question. Bentley and coworkers investigated the prognostic significance of the Gleason score in 116 patients treated with different types of neoadjuvant hormonal treatment followed by radical prostatectomy [2]. The authors suggested that the Gleason score remained a significant measure in terms of predicting PSA progression after neoadjuvant hormonal treatment but did not compare mortality outcomes [2].

Limitations

The neoadjuvant hormonal treatment in this study was heterogeneous, partially short term and/or low dose and no details on the actual duration of treatment were available. No details on the biopsy Gleason scores prior to neoadjuvant hormonal treatment were available. It cannot be ruled out with certainty that some cases of neoadjuvant treatment have been overlooked due to incomplete documentation or ignorance of some patients as to the sort of tablets or injections given to them prior to surgery. Since information on neoadjuvant hormonal treatment may be found at different locations in the patient charts and a variety of drugs could be involved, this parameter is more prone to classification errors as other clinical data. It is likely that the pathologists who evaluated the prostatectomy specimens were in most cases not aware of the application of neoadjuvant hormonal treatment. It is conceivable that they would come to different judgements if they would have been aware of such treatment.

Conclusion

The Gleason score seems to be a powerful independent predictor of prostate cancer mortality despite neoadjuvant hormonal treatment in a routine clinical setting. Using the Gleason score despite neoadjuvant hormonal treatment as a predictor of mortality taking possible limitations into consideration appears to be reasonable rather than the currently recommended general dispense from giving a Gleason score after neoadjuvant hormonal treatment.

References

- 1 Vailancourt L, Ttu B, Fradet Y, Dupont A, Gomez J, Cusan L, Suburu ER, Diamond P, Candas B, Labrie F: Effect of neoadjuvant endocrine therapy (combined androgen blockade) on normal prostate and prostatic carcinoma. A randomized study. *Am J Surg Pathol* 1996;20:86–93.
- 2 Bentley G, Dey J, Sakr WA, Wood DP Jr, Pontes JE, Grignon DJ: Significance of the Gleason scoring system after neoadjuvant hormonal therapy. *Mol Urol* 2000;4:125; discussion 131.
- 3 Bullock MJ, Srigley JR, Klotz LH, Goldenberg SL: Pathologic effects of neoadjuvant cyproterone acetate on nonneoplastic prostate, prostatic intraepithelial neoplasia, and adenocarcinoma: a detailed analysis of radical prostatectomy specimens from a randomized trial. *Am J Surg Pathol* 2002;26:1400–1413.
- 4 Deutsche Gesellschaft für Urologie e. V.: Konsultationsfassung. Interdisziplinäre Leitlinie der Qualität S3 zur Früherkennung, Diagnose und Therapie der Verschiedenen Stadien des Prostatakarzinoms. AWMF-Register-Nummer (034/022OL) Version 2.2–2. Aktualisierung, 2014. <http://www.dgu.de/fileadmin/MDB/PDF/konsultationsfassung-leitlinie-prostatakarzinom.pdf> (visited August 22, 2015).
- 5 Soloway MS, Pareek K, Sharifi R, Wajzman Z, McLeod D, Wood DP Jr, Puras-Baez A; Lupron Depot Neoadjuvant Prostate Cancer Study Group: Neoadjuvant androgen ablation before radical prostatectomy in cT2bNxm prostate cancer: 5-year results. *J Urol* 2002; 167:112–116.
- 6 Efstathiou E, Abrahams NA, Tibbs RF, Wang X, Pettaway CA, Pisters LL, Mathew PF, Do KA, Logothetis CJ, Troncoso P: Morphologic characterization of preoperatively treated prostate cancer: toward a post-therapy histologic classification. *Eur Urol* 2010;57:1030–1038.
- 7 Berglund RK, Tangen CM, Powell IJ, Lowe BA, Haas GP, Carroll PR, Canby-Hagino ED, deVere White R, Hemstreet GP 3rd, Crawford ED, Thompson IM Jr, Klein EA: Ten-year follow-up of neoadjuvant therapy with goserelin acetate and flutamide before radical prostatectomy for clinical T3 and T4 prostate cancer: update on Southwest oncology group study 9109. *Urology* 2012;79:633–637.
- 8 Mottet N, Bellmunt J, Briers E, van den Bergh RCN, Bolla M, van Casteren NJ, Cornford P, Culine S, Joniau S, Lam T, Mason MD, Matveev V, van der Poel H, van der Kwast TH, Rouvière O, Wiegel T: EAU Guidelines on Prostate Cancer. http://uroweb.org/wp-content/uploads/09-Prostate-Cancer_LR.pdf (visited August 22, 2015).
- 9 Fumadó L, Cecchini L, Juanpere N, Ubré A, Lorente JA, Alcaraz A: Twelve core template prostate biopsy is an unreliable tool to select patients eligible for focal therapy. *Urol Int* 2015;95:197–202.
- 10 Servoll E, Vlatkovic L, Sæter T, Nesland JM, Axcróna U, Waaler G, Axcróna K: The length of a positive surgical margin is of prognostic significance in patients with clinically localized prostate cancer treated with radical prostatectomy. *Urol Int* 2014;93:289–295.
- 11 Winter A, Kneib T, Rohde M, Henke RP, Wawroschek F: First nomogram predicting the probability of lymph node involvement in prostate cancer patients undergoing radioisotope guided sentinel lymph node dissection. *Urol Int* 2015, Epub ahead of print.
- 12 Fine JP, Gray RJ: A proportional hazards model for the subdistribution of a competing risk. *J Am Stat Assoc* 1999;94:496–509.
- 13 Pintilie M: Competing Risks: A Practical Perspective. Chichester, England, Hoboken, John Wiley & Sons, 2006, pp 195–207.
- 14 Parmar MKB, Machin D: Survival Analysis. A Practical Approach. Chichester, England, John Wiley & Sons, 1996, pp 75–87.
- 15 Gofrit ON, Zorn KC, Steinberg GD, Zagaja GP, Shalhav AL: The will rogers phenomenon in urological oncology. *J Urol* 2008;179:28–33.
- 16 Goldenberg SL, LaBianca SE, Gleave ME: Neoadjuvant androgen withdrawal therapy before radical prostatectomy. *Curr Oncol* 2004;7(suppl 1):S5–S8.
- 17 Selli C, Montironi R, Bono A, Pagano F, Zattoni F, Manganelli A, Selvaggi FP, Comeri G, Fiaccavento G, Guazzieri S, Lembo A, Cosciani-Cunico S, Potenzoni D, Muto G, Mazzucchelli R, Santinelli A; PROSIT Study Group: Effects of complete androgen blockade for 12 and 24 weeks on the pathological stage and resection margin status of prostate cancer. *J Clin Pathol* 2002;55:508–513.
- 18 Hu J, Xu H, Zhu W, Wu F, Wang J, Ding Q, Jiang H: Neo-adjuvant hormone therapy for non-metastatic prostate cancer: a systematic review and meta-analysis of 5,194 patients. *World J Surg Oncol* 2015;13:73.
- 19 Bach C, Pisipati S, Daneshwar D, Wright M, Rowe E, Gillatt D, Persad R, Koupparis A: The status of surgery in the management of high-risk prostate cancer. *Nat Rev Urol* 2014;11: 342–351.
- 20 Brierley JD, Greene FL, Sobin LH, Wittekind C: The 'y' symbol: an important classification tool for neoadjuvant cancer treatment. *Cancer* 2006;106:2526–2527.
- 21 Sobin LH, Gospodarowicz MK, Wittekind C; International Union Against Cancer: TNM Classification of Malignant Tumours, ed 7, 2009. Chichester, West Sussex, UK, Hoboken, Wiley-Blackwell, 2010, pp 243–248.
- 22 Gleave ME, Goldenberg SL, Chin JL, Warner J, Saad F, Klotz LH, Jewett M, Kassabian V, Chetner M, Dupont C, Van Rensselaer S; Canadian Uro-Oncology Group: Randomized comparative study of 3 versus 8-month neoadjuvant hormonal therapy before radical prostatectomy: biochemical and pathological effects. *J Urol* 2001;166:500–506; discussion 506–507.

Disclosure Statement

The authors declare that they have no conflict of interest.

Author Contributions

M.F. was responsible for study design, data collection, data analysis and manuscript writing/editing. R.K. was responsible for data analysis and manuscript writing/editing. S.P., A.B., D.L., M.T., G.B.B. were responsible for data collection and manuscript writing/editing. M.P.W. was responsible for administrative support, supervision and manuscript writing/editing.