COMPARISON OF THE AMERICAN SOCIETY OF ANESTHESIOLOGISTS PHYSICAL STATUS CLASSIFICATION WITH THE CHARLSON SCORE AS PREDICTORS OF SURVIVAL AFTER RADICAL PROSTATECTOMY

MICHAEL FROEHNER, RAINER KOCH, RAINER LITZ, AXEL HELLER, SVEN OEHLSCHLAEGER, AND MANFRED P. WIRTH

The treatment of early prostate cancer is a subject of controversy.[1] In a recently published randomized trial, it was estimated that 17 radical prostatectomies are needed to prevent one prostate cancer-associated death within the first 8 years of follow-up in men with clinically diagnosed, localized, well or moderately differentiated disease.[2] To facilitate the recommendation of a suitable treatment for individual patients, effort has been undertaken to investigate the prognostic significance of comorbidity in prostate cancer.[3–5] Although the Charlson score is probably most frequently used to classify comorbidity in cancer patients in general,[6,7] and also in prostate cancer,[3–5] a generally accepted oncologic comorbidity measure is still lacking.[8] The American Society of Anesthesiologists Physical Status (ASA) classification is a readily available and widely accepted way to stratify surgical patients according to their perioperative risk.[9] Compared with the Charlson score, one study demonstrated a similar, if not greater, prognostic value for the ASA classification, even beyond the perioperative period.[9] We observed that the ASA classification is capable of uncovering prognostic comorbidity in the radical prostatectomy setting as well.[10] This study compared the clinical usefulness of both comorbidity scores to predict survival during the first 8 years after radical prostatectomy.

From the Departments of Urology, Medical Statistics and Biometry, and Anesthesiology, University Hospital "Carl Gustav Carus," Technical University of Dresden, Dresden, Germany

Reprint requests: Michael Froehner, M.D., Department of Urology, University Hospital "Carl Gustav Carus," Technical University of Dresden, Fetscherstrasse 74, Dresden D-01307, Germany

MATERIAL AND METHODS

A total of 444 consecutive patients were enrolled in this study. All patients underwent radical prostatectomy for clinically localized prostate cancer between December 1, 1992 and December 31, 1998. We obtained institutional review board exemption. The mean age was 63.9 years (range 45 to 76). The ASA classification[11] (available at website http://www.asahq.org/Profinfo/PhysicalStatus.html) was obtained from the anesthesia chart. Additional comorbidity data relevant for anesthesia were collected from the anesthesia charts, patient records, and preoperative electrocardiograms and were entered into a database that included cardiac insufficiency (New York Heart Association classification), coronary heart disease (classification of angina pectoris of the Canadian Cardiovascular Society; both classifications available at website http://www.cochranfoundation.com/docs/nyha-class.htm), diabetes, hypertension, and history of thromboembolism, chronic obstructive disease, or restrictive pulmonary disease. The data were subject to a plausibility check and correction in cases of obvious false classification. This part of the chart review was performed under the surveillance of a senior anesthesiologist (R.L.).

The Charlson score was assigned by one urologist (M.F.) following the guidelines established by Charlson *et al.*[12] using the conditions available in the anesthesia database described above and any concomitant diseases mentioned on the discharge document of the Department of Urology. The discharge documents and anesthesia database were reviewed twice within a 4-week interval. The assigned Charlson scores were compared, and a third abstraction was performed in patients with differing results to reach consensus.

Follow-up data were obtained for all patients. All surviving patients had their last contact in 2002. The mean follow-up of the surviving patients was 5.9 years (range 3.3 to 9.7). Deaths in the absence of any uncontrolled cancer were considered events concerning comorbidity-specific survival (n = 24). One patient died in a car accident and was censored at the time of death concerning comorbidity-specific survival. Deaths in the presence of uncontrolled prostate cancer were considered deaths from prostate cancer (n = 18), and deaths in the presence of uncontrolled other malignancy were considered deaths from other cancer (n = 11). Kaplan-Meier time-event curves and Mantel-Haenszel hazard ratios were calculated for comorbidity-specific, prostate cancer-specific, second cancer-specific, and overall survival. Comparisons were made with the log-rank test. Statistical significance was accepted to be indicated at a limit of $P < 0.05$. The analyses were performed using the Statistical Analysis System and Statistical Package for Social Sciences statistical programs.

RESULTS

Overall survival curves according to age group, ASA class, and Charlson score are shown in Figures 1 to 3, respectively. Mantel-Haenszel hazard ratios concerning comorbidity-specific and overall mortality are given in Table I. Age-related Mantel-Haenszel hazard ratios are shown in Table II. Dose-response patterns (increasing hazard ratios with increasing degree of severity) were present in all three methods of stratification (Table I). Statistical significance was reached for both comorbidity classifications, but not for age group (Table I). Compared with an earlier analysis,[10] the impact of the ASA classification tended to increase with longer follow-up regarding hazard ratios and

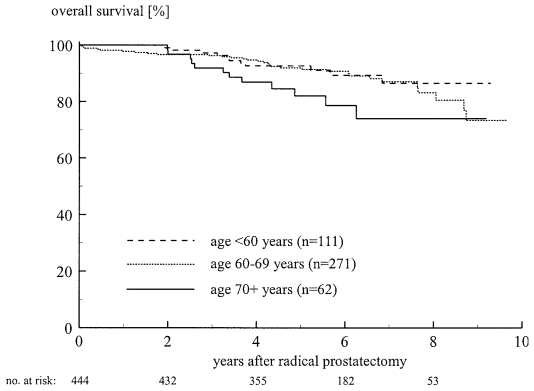

FIGURE 1. *Overall survival according to age group.*

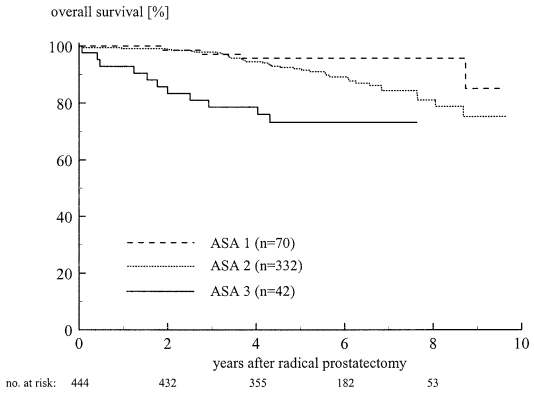

FIGURE 2. *Overall survival according to ASA class.*

P values. The prostate cancer-specific mortality did not differ significantly among age group, ASA class, and Charlson score. Concerning the mortality from a second cancer, only one comparison revealed a statistically significant difference (increased mortality in age group 70 years or older compared with patients aged 60 to 69 years, hazard ratio 11.54, 95% confidence interval 1.78 to 74.95, $P = 0.01$).

COMMENT

This study establishes the ASA classification assigned by experienced anesthesiologists as an alternative to the currently most commonly used Charlson score as a comorbidity measure in the radical prostatectomy setting. Considering hazard ratios and *P* values as the measures for the discrimination of the survival curves, an advantage was found for the ASA classification (Table I). The prognostic value of age alone was clearly inferior to that of the two comorbidity classifications (Figs. 1 to 3 and Table I).

To enable a valid comparison, one must ascertain that no appreciable comorbidity data have been lost because of incomplete documentation, which

TABLE I. *Hazard ratios with confidence intervals for comorbid and overall mortality, Mantel-Haenszel estimation*

	Comorbid Mortality				Overall Mortality			
Category	Proportion of Events	Hazard Ratio	95% CI	*P* Value	Proportion of Events	Hazard Ratio	95% CI	*P* Value
Age (yr)								
<60	2/111	1			11/111	1		
60–69	18/271	2.51	0.95–6.61	0.06	31/271	1.13	0.58–2.20	0.73
70+	4/62	4.56	0.83–25.02	0.08	12/62	2.19	0.96–5.44	0.06
ASA								
1	0/70	1			4/70	1		
2	16/332	3.59	1.07–12.02	0.04	39/332	2.05	0.98–4.28	0.06
3	8/42	17.68	4.13–75.80	<0.01	11/42	7.21	2.39–21.76	<0.01
Charlson score								
0	10/298	1			31/298	1		
1	4/85	1.83	0.48–6.93	0.37	12/85	1.72	0.81–3.68	0.15
2+	10/61	17.68	5.08–61.52	<0.01	11/61	2.83	1.18–6.82	0.02
ASA 1–2	16/402	1			43/402	1		
ASA 3	8/42	51.37	10.86–243.0	<0.01	11/42	9.21	3.14–26.98	<0.01
Charlson score 0	10/298	1			31/298	1		
Charlson score 1+	14/146	4.03	1.67–9.71	<0.01	23/146	1.95	1.08–3.52	0.03

KEY: CI = confidence interval; ASA = American Society of Anesthesiologists.
When three strata were analyzed, comparisons were made versus age <60 yr, ASA 1, and Charlson score 0, respectively; P *values are raw values.*

TABLE II. *Hazard ratios and* P *values for comorbid and overall mortality in different age groups, Mantel-Haenszel estimation*

	Comorbid Mortality			Overall Mortality		
Class	<60 yr	60–69 yr	70+ yr	<60 yr	60–69 yr	70+ yr
ASA 1	No events	1	1	1	1	1
ASA 2	No events	3.63 (0.08)	3.03 (0.60)	0.98 (0.40)	2.87 (0.04)	2.93 (0.60)
ASA 3	No events	13.07 (<0.01)	4.48 (0.48)	0.29 (0.44)	13.49 (<0.01)	4.27 (0.90)
Charlson score 0	1	1	1	1	1	1
Charlson score 1	0.29 (0.63)	1.07 (0.93)	9.57 (0.09)	1.18 (0.84)	1.27 (0.66)	2.98 (0.12)
Charlson score 2+	15.75 (0.16)	18.06 (<0.01)	536.8 (0.02)	0.76 (0.77)	4.93 (<0.01)	3.97 (0.22)

Data presented as the hazard ratio, with the P *value in parentheses.*
Comparisons were made versus ASA 1 and Charlson score 0, respectively; P *values are raw values.*

would put the Charlson score at a disadvantage. When documented on the anesthesia chart before surgery, the ASA classification may be less sensitive to such information loss. Compared with other radical prostatectomy series,[4,5] the distribution of the Charlson classes was fairly similar, indicating that a comparable amount of comorbidity data was available for analysis in this study. We are aware of one study[4] that presented overall survival curves comparable with those shown in Figure 3. In our study, all three Charlson score strata had slightly greater overall survival within the first 8 years after radical prostatectomy. This difference may be explained by the probably more favorable risk profile in our prostate-specific antigen era series and by the exclusion of patients in whom the intended radical prostatectomy was not performed because of pelvic lymph node metastases. The survival curves in our series were, however, largely parallel to those in the cited study,[4] suggesting that the quality of the Charlson score was not meaningfully compromised.

Because the ASA class is likely to be documented in most charts of surgically treated cancer patients, it may be used as a readily available comorbidity measure in other malignancies also. Reid *et al.*[9] compared the ASA classification with the Charlson score in a head-and-neck cancer population and found a slight advantage for the ASA classification using two risk groups (ASA 1 to 2 versus ASA 3 to 4 and Charlson score 0 versus Charlson score greater than 1). Adopting this method of stratification, we observed a clear superiority of the ASA classification as a predictor of both comorbid and overall mortality (Table I).

From a clinical viewpoint, stratifying candidates for radical prostatectomy by high, intermediate, and low risk may be of interest. Patients at a high

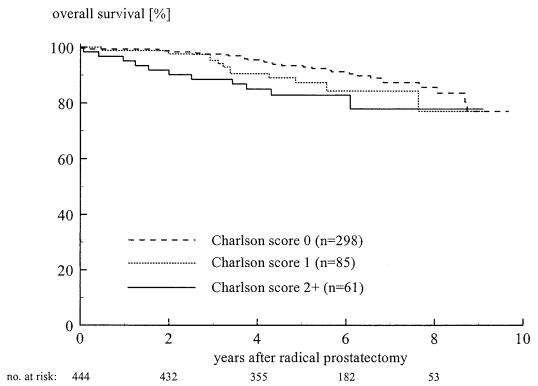

FIGURE 3. *Overall survival according to Charlson score.*

risk of a comorbid death are unlikely to benefit appreciably from radical prostatectomy and may be considered for alternative treatment options, such as external beam radiotherapy, interstitial brachytherapy, or watchful waiting. On the other hand, aggressive management may be recommended to low-risk patients. In this study, both the Charlson score and the ASA classification equally identified a group at high risk of comorbid death (Table I). Considering the discrimination of a low-risk group, an obvious advantage was noted for the ASA classification by defining a subgroup with an excellent long-term prognosis (no comorbid death among 70 ASA 1 patients, Table I). The difference for the intermediate-risk population (ASA 2) was significant concerning comorbid survival and narrowly failed the significance level concerning overall survival; no statistically detectable differences were found concerning comorbid and overall survival between Charlson class 0 and 1 in this study (Table I). Comparable data from published reports suggest that longer follow-up is needed to demonstrate this difference.[5]

Because radical prostatectomy is controversial for the age group of 70 years or older,[13] the applicability of comorbidity classifications to elderly patients is of interest. In our study, both classifications performed best in the age group of 60 to 69 years (Table II). Although the data were premature (too few events observed), a trend toward similar survival curves and hazard ratios (Table II) suggests an applicability of both comorbidity measures for patients older than 70 years of age. It is, however, conceivable that the association in this age group may be less strong. We observed increased mortality from second cancers in this age group, and one population-based study suggested a diminishing prognostic significance of comorbidity with increasing age.[14]

REFERENCES

1. Scardino PT: The Gordon Wilson Lecture: natural history and treatment of early stage prostate cancer. Trans Am Clin Climatol Assoc **111:** 201–241, 2000.

2. Holmberg L, Bill-Axelson A, Helgesen F, *et al:* A randomized trial comparing radical prostatectomy with watchful waiting in early prostate cancer. N Engl J Med **347:** 781–789, 2002.

3. Albertsen PC, Fryback DG, Storer BE, *et al:* The impact of co-morbidity on life expectancy among men with localized prostate cancer. J Urol **156:** 127–132, 1996.

4. Barry MJ, Albertsen PC, Bagshaw MA, *et al:* Outcomes for men with clinically nonmetastatic prostate carcinoma managed with radical prostatectomy, external beam radiotherapy, or expectant management: a retrospective analysis. Cancer **91:** 2302–2314, 2001.

5. Sweat SD, Bergstralh EJ, Slezak J, *et al:* Competing risk analysis after radical prostatectomy for clinically nonmetastatic prostate adenocarcinoma according to clinical Gleason score and patient age. J Urol **168:** 525–529, 2002.

6. Extermann M: Measurement and impact of comorbidity in older cancer patients. Crit Rev Oncol Hematol **35:** 181–200, 2000.

7. Klabunde CN, Warren JL, and Legler JM: Assessing comorbidity using claims data: an overview. Med Care **40**(suppl IV): 26–35, 2002.

8. Yancik R, Ganz PA, Varricchio CG, *et al:* Perspectives on comorbidity and cancer in older patients: approaches to expand the knowledge base. J Clin Oncol **19:** 1147–1151, 2001.

9. Reid BC, Alberg AJ, Klassen AC, *et al:* The American Society of Anesthesiologists' class as a comorbidity index in a cohort of head and neck cancer surgical patients. Head Neck **23:** 985–994, 2001.

10. Froehner M, Koch R, Litz R, *et al:* Preoperative cardiopulmonary risk assessment as predictor of early noncancer and overall mortality after radical prostatectomy. Urology **61:** 596–600, 2003.

11. Saklad M: Grading of patients for surgical procedures. Anesthesiology **2:** 281–284, 1941.

12. Charlson ME, Pompei P, Ales KL, *et al:* A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. J Chron Dis **40:** 373–383, 1987.

13. Catalona WJ, Ramos GR, and Carvalhal GF: Contemporary results of anatomic radical prostatectomy. CA Cancer J Clin **49:** 282–286, 1999.

14. Post PN, Hansen BE, Kil PJM, *et al:* The independent prognostic value of comorbidity among men aged <75 years with localized prostate cancer: a population-based study. BJU Int **87:** 821–826, 2001.