Asian Journal of Andrology (2013) 15, 667–671

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ORIGINAL ARTICLE

Comorbidity and survival of patients selected for radical prostatectomy at an age of 75 years or older

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Radical prostatectomy in elderly patients is controversial. To identify very old candidates for radical prostatectomy with the highest probability of long-term survival, we studied 47 consecutive men who underwent radical prostatectomy between 1992 and 2005 at an age of 75 years or older. A heuristic approach was used to search for subgroups with particularly high long-term survival. Several two-sided comorbidity measures and combinations of these measures were investigated to find classifications best identifying healthy, long-living elderly candidates for radical prostatectomy. Four of the 25 two-sided comorbidity classifications or combinations reached the significance level with hazard ratios between 4.00 and 4.80. After 10 years, patients identified as healthy patients according to these comorbidity measurements had exhibited relative survival rates between 129% and 137% and overall survival rates between 86% and 95%, whereas those with comorbidities had exhibited relative survival rates of only 66%–84% and overall survival rates of 44%–58%. In conclusion, classifying comorbidity may identify a meaningful proportion of men selected for radical prostatectomy at an age of 75 years or older with an excellent long-term survival probability superseding that of the general population.
Asian Journal of Andrology (2013) **15,** 667–671; doi:10.1038/aja.2013.25; published online 3 June 2013

Keywords: comorbidity; old age; overall survival; prostate cancer; radical prostatectomy; relative survival

INTRODUCTION

Radical prostatectomy in elderly patients is controversial.[1,2] Neither prostate-specific antigen-based screening (in men aged 70 years or older[3]) nor radical prostatectomy (in men aged 65 years or older, compared with watchful waiting in clinically diagnosed disease[4]) has demonstrated numerable survival benefits in this population until now. Few data are available on the survival rates in of the oldest old candidates for radical prostatectomy.[1,5,6] The usefulness of comorbidity classifications in stratifying these men is largely unknown. Due to selection, in the mortality of patients undergoing radical prostatectomy, even competing mortality is unlikely to reach the 50% level within 10 years in the presence of serious comorbidity.[7] This high survival probability limits the clinical applicability of comorbidity classifications, particularly in younger men. In elderly patients, however, a particularly high survival probability may influence clinical decision making. In this study, we searched for comorbidity classifications able to identify subsets of elderly candidates for radical prostatectomy with a particularly high long-term survival probability having and the highest chance to of benefiting from curative treatment for early prostate cancer despite their advanced age.

MATERIALS AND METHODS

Patients

The population sample consisted of 47 consecutive patients aged 75 years or older (range: 75–79 years) out of a sample of 2205 men who underwent radical prostatectomy between 1992 and 2005. Approval by the institutional review board of the University Hospital Dresden was obtained. Demographic data are provided in **Table 1**.

Classification of comorbidity

Comorbidity data were obtained from the preoperative cardiopulmonary risk assessment and the discharge records and classified as previously described.[7] Preoperative cardiopulmonary risk assessment was performed by an anaesthesiologist and documented on the premedication record. The data were checked for plausibility and transferred into a database. The following conditions were recorded during this process: the American Society of Anesthesiologists (ASA) physical status classification,[8] the New York Heart Association (NYHA) classification of cardiac insufficiency,[9] the classification of angina pectoris of the Canadian Cardiovascular Society (CCS),[10] hypertension, and history of thromboembolism, lung disease and diabetes mellitus. For

Table 1 Demographic data of the patient sample

Parameter	
Mean follow-up in censored patients (year)	8.3
Mean PSA in men without neoadjuvant hormonal treatment (39/47) (ng ml^{-1})	10.5
Organ-confined node-negative disease	62% (29/47)
Gleason score 6 or less	43% (20/47)
Gleason score 7	38% (18/47)
Gleason score 8–10	19% (9/47)

Abbreviation: PSA, prostate-specific antigen.

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Received: 5 December 2012; Revised: 27 January 2013; Accepted: 5 March 2013; Published online: 3 June 2013

the assignment of the Charlson score,[11] besides these data, additional information was derived from the discharge records. Furthermore, a disease count was calculated by adding all the concomitant diseases recorded in the database (angina pectoris, hypertension, history of thromboembolism, body mass index 30 kg m^{-2} or higher, myocardial infarction, cardiac insufficiency, peripheral artery disease, cerebrovascular disease, lung disease, ulcer disease, mild liver disease, diabetes mellitus, connective tissue disease, hemiplegia, moderate or severe

Table 2 Ten-year survival rates, hazard ratios, 95% confidence intervals and *P* values of the 47 patients stratified by 25 comorbidity classifications. Three stratifications reached statistical significance as predictors of overall mortality

Category	*Events* / n	*10-year survival*	*95% CI*	*HR*	*95% CI*	P
All patients	11/47	72%	50%–86%			
CCS 0	4/29	90%	71%–96%	1		
CCS 1+	7/18	44%	12%–72%	4.09	1.14–14.61	0.0304
CCS 0 and Charlson score 0[a]	2/19	95%	68%–99%	1		
Other	9/28	54%	24%–77%	4.00	1.17–13.63	0.0269
ASA 1–2 and Charlson score 0 and CCS 0	1/17	94%	65%–99%	1		
Other	10/30	58%	28%–79%	4.80	1.41–16.41	0.0123
Disease count 0–1	3/24	86%	51%–97%	1		
Disease count 2+	8/23	56%	23%–79%	4.42	1.27–15.37	0.0193
Disease count 0	0/8	100%	NA			
Disease count 1+	11/39	65%	40%–82%	NA	NA	NA
CCS 0 and BMI <25	0/6	100%	NA			
Other	11/41	68%	45%–84%	NA	NA	NA
ASA 1	0/3	100%	NA			
ASA 2–3	11/44	68%	44%–84%	NA	NA	NA
ASA 1–2 and disease count 0	0/8	100%	NA			
Other	11/39	65%	40%–82%	NA	NA	NA
CCS 0 and BMI <25	0/6	100%	NA			
Other	11/41	68%	45%–84%	NA	NA	NA
NYHA 0 and CCS 0 and BMI <25	0/6	100%	NA			
Other	11/41	68%	45%–84%	NA	NA	NA
ASA 1–2	8/37	75%	52%–89%	1		
ASA 3	3/10	66%	16%–91%	1.47	0.33–6.45	0.61
NYHA 0	9/39	73%	49%–87%	1		
NYHA 1+	2/8	73%	28%–92%	1.79	0.28–11.34	0.54
CCS 0–1	8/40	79%	56%–91%	1		
CCS 2+	3/7	69%[b]	21%–91%	4.40	0.70–27.78	0.12
NYHA 0 and CCS 0	4/27	89%	69%–96%	1		
Other	7/20	51%	18%–76%	3.14	0.90–10.90	0.07
BMI <25	2/13	92%	57%–99%	1		
BMI 25+	9/34	67%	42%–83%	2.02	0.53–7.63	0.30
BMI <30	10/43	73%	50%–87%	1		
BMI 30+	1/4	67%	5%–94%	1.32	0.13–13.19	0.81
Charlson score 0	4/25	83%	51%–95%	1		
Charlson score 1+	7/22	59%	24%–82%	2.84	0.83–9.69	0.10
CCS 0–1 and Charlson score 0	4/25	83%	51%–95%	1		
Other	7/22	59%	24%–82%	2.84	0.83–9.69	0.10
Charlson score 0 and BMI <25	1/6	83%	27%–98%	1		
Other	10/41	70%	46%–85%	1.89	0.38–9.50	0.44
ASA 1–2 and Charlson score 0	3/23	81%	48%–94%	1		
Other	8/24	63%	30%–84%	3.24	0.97–10.83	0.06
ASA 1–2 and Charlson score 0 and BMI <25	1/6	83%	27%–98%	1		
Other	10/41	70%	46%–85%	1.89	0.38–9.50	0.44
Charlson score 0–1	11/40	68%	44%–83%	1		
Charlson score 2+	0/7	100%	NA	NA	NA	NA
CCS 0 and BMI <30	4/26	88%	68%–96%	1		
CCS 1+ or BMI 30+	7/21	51%	18%–77%	2.98	0.86–10.32	0.09
Charlson 0 and BMI <30	4/23	81%	48%–94%	1		
Charlson 1+ or BMI 30+	7/24	63%	30%–84%	2.36	0.70–7.95	0.17
ASA 1–2 and Charlson score 0 and BMI <30	3/22	79%	44%–94%	1		
Other	8/25	66%	35%–85%	2.86	0.86–9.53	0.09

Abbreviations: ASA: American Society of Anesthesiologists physical status classification; BMI, body mass index, kg m^{-2}; CI, confidence interval; HR, hazard ratio; NA, not available because of lack of events in the low-risk category.

[a] Or no cardiac insufficiency classified by the New York Heart Association (NYHA) and no angina pectoris classified by the Canadian Cardiovascular Society (CCS) and Charlson 0: because the Charlson score encompasses congestive heart failure, all patients with a Charlson score 0 were classified as NYHA 0.

[b] 9-year data.

Table 3 Relative survival rates with 95% confidence intervals in all 47 patients aged 75 years or older

Year	*Relative survival (%)*
1	NA
2	NA
3	NA
4	104 (98–111)
5	108 (98–118)
6	107 (95–121)
7	114 (101–129)
8	116 (100–134)
9	121 (105–140)
10	111 (87–142)
11	115 (90–146)
12	110 (78–152)

NA: not available because of the lack of events at this time; in parentheses: 95% confidence intervals.

renal disease, solid tumour, leukaemia, lymphoma, moderate of or severe liver disease, dementia and metastatic solid tumour) without weighing according to the severity in an analogy of an approach described by Houterman and co-workers.[12]

Stratifications

A heuristic approach was used to search for subgroups with particularly high long-term survival. Several two-sided comorbidity classifications and combinations of these classifications separating healthy from non-healthy patients were investigated to identify classifications that best identified healthy, long-living elderly patients. In contrast to an earlier analysis focusing on worst-case scenarios,[7] we searched for strata with the lowest level comorbidity, representing high survival probability.

Statistical analysis

Overall survival was estimated with using the Kaplan–Meier method. Comparisons were made using Mantel–Haenszel hazard ratios and the log-rank test. Relative survival rates were determined with our own program derived from one of the Finnish Cancer Center[13] as previously described.[14] The mortality rates of the entire population of Saxony (source: Federal Government of Saxony, Ministry for Social Health and Family; http://www.sachsen.de) were used as reference population that was matched with the patients in terms of age, gender and time of surgery. The statistical analyses were performed using the Statistical Analysis Systems (SAS Institute, Cary, NC, USA) statistical package.

RESULTS

Of the 25 comorbidity classifications or combinations thereof dividing the 47 patients into two strata, four classifications with a relatively balanced distribution of the patients into the two risk groups reached the statistical significance level (**Table 2**). All four classifications—coronary heart disease classified by the classification of angina pectoris of the Canadian Cardiovascular Society; a combination of coronary heart disease and the Charlson score (which in its original form[10] does not contain this condition) with or without including the ASA classification; and a total disease count, respectively—were plausible measures of health status. In the entire patient sample, survival was slightly higher than in the general population in the region (**Table 3**). Healthy elderly patients but not those with moderate comorbid diseases exhibited a higher survival than the age-matched male population in the region, whereas in those with high-risk comorbidity, survival was similar to that in this population (**Table 4 and 5**).

DISCUSSION

In the study sample, classifying comorbidity identified a clinically meaningful subset of men selected for radical prostatectomy at an age of 75 years or older with very high probability to of surviving for longer than 10 years. Evaluating coronary heart disease might be a way to stratify these patients; however, counting comorbid diseases with (by including the Charlson score) or without weighing by disease severity could also be a useful stratification method (**Table 2**). In healthy elderly candidates for radical prostatectomy, overall survival superseded that of the age-matched male population in the region. In the presence of moderate comorbidity, however, this survival advantage, however, vanished (**Table 4 and 5**).

Considering the uncertain effect of early detection and curative treatment in the elderly population,[3,4] a critical appraisal of the health status is important. A benefit of radical prostatectomy may be expected only if there is a high probability of long-term survival probability. Current clinical guidelines cite a life expectancy of 10 or more years to be considered for radical prostatectomy, but the guidelines do not provide a formal age limit.[15,16] The National Comprehensive Cancer Network Prostate Cancer Guideline (version I.2013) considers a repeat prostate biopsy not indicated after 75 years of age.[16]

Comorbid conditions may be associated with meaningful competing mortality in unselected samples of patients with prostate cancer

Table 4 Relative survival rates (reference: age-matched male population in the region) with 95% confidence intervals in patients with low risk comorbidity of the four stratifications that achieved statistical significance predictors of overall mortality

Year	*CCS 0 and Charlson score 0 (%)*	*CCS 0 (%)*	*Disease count 0–1 (%)*	*ASA 1–2 and Charlson score 0 and CCS 0 (%)*
1	NA	NA	NA	NA
2	NA	NA	NA	NA
3	NA	NA	NA	NA
4	NA	102 (95–110)	NA	NA
5	NA	105 (95–117)	NA	NA
6	116 (101–123)	111 (96–123)	118 (105–123)	116 (99–123)
7	119 (104–126)	118 (103–132)	125 (112–130)	119 (102–126)
8	130 (112–137)	125 (109–140)	134 (119–139)	129 (110–137)
9	137 (119–145)	130 (114–146)	140 (125–146)	137 (117–145)
10	137 (119–145)	133 (116–148)	129 (119–141)	137 (117–145)
11	150 (130–159)	143 (125–160)	138 (107–160)	150 (128–160)
12	136 (95–167)	135 (99–172)	130 (90–172)	159 (136–169)

NA: not available because of the lack of events in this category at this time; in parentheses: 95% confidence intervals.

Table 5 Relative survival rates (reference: age-matched male population in the region) with 95% confidence intervals in patients with high risk comorbidity of the four stratifications that achieved statistical significance predictors of overall mortality

Year	*CCS 1+ or Charlson score 1+ (%)*	*CCS 1+ (%)*	*Disease count 2+ (%)*	*ASA 3 or Charlson score 1+ or CCS 1+ (%)*
1	NA	NA	NA	NA
2	NA	NA	NA	NA
3	NA	NA	NA	NA
4	103 (96–111)	NA	101 (92–111)	104 (96–111)
5	105 (91–118)	110 (95–116)	102 (86–117)	106 (93–118)
6	100 (85–117)	98 (82–118)	94 (77–114)	101 (87–117)
7	107 (88–129)	98 (82–118)	101 (79–127)	108 (90–129)
8	105 (82–133)	100 (72–137)	96 (71–130)	107 (85–133)
9	110 (86–139)	105 (75–144)	101 (74–135)	112 (89–139)
10	83 (50–135)	66 (32–134)	84 (50–139)	88 (56–136)
11	85 (51–140)	68 (32–138)	87 (52–143)	91 (58–141)
12	92 (55–151)	68 (32–138)	87 (52–143)	65 (28–146)

NA: not available because of the lack of events in this category at this time; in parentheses: 95% confidence intervals.

(10-year competing mortality in patients with a Charlson score of 2 or higher: 74%[17]), but no longer do so when patients selected for radical prostatectomy are considered (10-year competing mortality in patients with a Charlson score of 2 or higher: 27%[7]). This study suggests that this finding is particularly true in men of the oldest ages who may still be considered suitable for curative treatment. The average life expectancy of a 75-year-old male in Eastern Germany in between 2007 and 2009 was 10.0 years.[18] In this sample, patients selected for radical prostatectomy at an age of 75 or more years survived considerably longer. When no meaningful comorbidity was present, 10-year survival rates of up to 100% were possible (**Table 2**). In the presence of moderate comorbidity (severe comorbidity was undoubtedly eliminated by selection in this very old population), the 10-year survival rates fell to approximately 50%, a rate that is similar to that expected in men at of this age range (**Tables 2 and 5**). Only one subgroup of patients with comorbidities fell below the 50% survival rate (**Table 2**), indicating that even with comorbid diseases, at least half of patients selected for radical prostatectomy at an age of 75 years or older will survive for more than 10 years. In patients selected for radical prostatectomy in general, the small survival differences attributable to comorbid diseases make incorporating comorbidity considerations into clinical decision making difficult. In the oldest men considered fit for this procedure, the comorbidity classifications could be of greater clinical value. Whereas the excellent long-term survival rates in those patients without (or with minor) comorbidity support active treatment despite advanced age, the impaired survival in those patients with moderate comorbidity suggests critical individual counselling or dispensation from immediate curative treatment.

The reported 10-year overall survival rates in patients selected for radical prostatectomy at an age of 70 years or older varying between 59%[5] and 82%.[6] Carefully selected men older than 80 years may also achieve high 10-year survival rates (79% in one study[1]). In this study, the 72% 10-year overall survival rate was in a similar range to that reported in the literature. Consulting a nomogram based on age and Charlson score,[19] the predicted 10-year overall survival rate in our sample was with 67% similar to the observed 72% (one-sample Wald test: $P=0.54$). Healthy elderly patients identified by the classifications shown in **Table 2**, however, exhibited 10-year survival rates 17%–24% higher than those predicted by this nomogram[19] (3/4 comparisons reached the statistical significance level with $P<0.001$). In contrast, the 10-year survival rates in the patients with comorbid diseases were 7%–21% lower than those predicted by nomogram,[19] but the differences did not reach statistical reaching the significance level ($P=0.25$–0.58). These observations were consistent with those of an earlier analysis in patients aged 70 years or older.[20]

This study has several limitations. Our study was a unicentric study with a limited sample size. Therefore, the results should be validated in a larger, preferably multicentric population. Several comorbidity classifications and combinations thereof have been tested; it is, however, possible that some meaningful parameters were not recorded in our database. The limited sample size did not allow meaningful analyses with more than two strata which could, however, also be of clinical interest.

In conclusion, comorbidity classifications may identify particularly healthy very old candidates for radical prostatectomy with a high long-term survival probability superseding that of the age-matched male population in the region. The excellent survival rates in these subgroups support radical prostatectomy as a treatment option. In the presence of moderate comorbidity, the 10-year survival rates are close to 50% and require a critical consideration of the possible treatment alternatives in this age group.

AUTHOR CONTRIBUTIONS

MF, RK and MW were responsible for the concept and framework of the paper. MF, RK and MW participated in collecting and evaluating the data. MF wrote the paper. MF, RK and MW were largely responsible for the drafting and final editing. All authors read and approved the final manuscript.

COMPETING FINANCIAL INTERESTS

The authors declare no potential conflicts of interest related to the matter discussed in this submission.

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