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IMPACT OF COMORBIDITY ON HEALTH-RELATED QUALITY OF LIFE IN MEN UNDERGOING RADICAL PROSTATECTOMY: DATA FROM CaPSURE

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ABSTRACT

Objectives. Comorbidity is one of many factors that may affect health-related quality of life (HRQOL) in men with prostate cancer. We hypothesized that the number and type of comorbidities negatively affect HRQOL in men undergoing radical prostatectomy.

Methods. We reviewed HRQOL outcomes before and up to 2 years after radical prostatectomy for men with localized prostate cancer in the Cancer of the Prostate Strategic Urologic Research Endeavor (CaPSURE), a longitudinal disease registry. This analysis focused on 856 men who completed a pretreatment survey and at least one posttreatment survey. HRQOL was assessed using the University of California, Los Angeles, Prostate Cancer Index (six subscales) and the Medical Outcomes Study 36-Item Short Form questionnaire (eight subscales and two summary scales). The associations between HRQOL and the number and type of comorbidities were analyzed using repeated measures during a 2-year follow-up period.

Results. Preoperatively, men with no comorbidities had greater HRQOL scores than did men with comorbidities for physical health and disease-specific measures, but not for mental health measures. Only sexual function and the physical component summary scores showed a significant interaction between the number of comorbidities and time ($P < 0.01$ and $P = 0.03$, respectively). Significant interactions with time were observed for other urinary conditions, gastrointestinal disease, heart disease, and hypertension on at least one HRQOL domain.

Conclusions. Men with comorbidities had worse HRQOL scores than men without comorbidities, both before and after radical prostatectomy. However, with two exceptions, the scores declined at similar rates after surgery. Specific comorbidities also had an association with certain HRQOL domains. Therefore, during preoperative counseling, clinicians should consider a patient's number and type of comorbidities. UROLOGY **67:** 559–565, 2006. © 2006 Elsevier Inc.

Because men with prostate cancer are often elderly, they are likely to have other medical conditions, such as heart disease, hypertension, diabetes, and arthritis.[1] Patient comorbidity has been shown to predict for health-related quality of life (HRQOL) for those with prostate[2,3] and other cancers.[3–8] Comorbidity may be associated with worse HRQOL in specific domains, depending on the

The current CaPSURE Investigators are listed in the Appendix.

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cancer type.[6–8] Recently, Hu and colleagues[2] studied characteristics that might assist in predicting prostate cancer-specific domains of HRQOL 1 year after radical prostatectomy (RP) and found the presence of comorbidity to be one of those predictors. In addition, Schag and colleagues[3] showed that prostate cancer survivors experience HRQOL declines over time that were predicted by the presence of comorbidity.

However, these analyses of an association between comorbidity and HRQOL have been conducted mostly for patients with cancer other than prostate cancer.[4–8] We undertook this analysis to examine the impact of comorbidity on general and disease-specific HRQOL over time in men undergoing RP for prostate cancer. We hypothesized that men with more comorbid conditions at baseline would have worse HRQOL at baseline than men with no comorbidities. We also hypothesized that over time these HRQOL differences would persist.

MATERIAL AND METHODS

We drew subjects from the Cancer of the Prostate Strategic Urologic Research Endeavor (CaPSURE), a longitudinal, observational prostate cancer disease registry that includes patients with biopsy-proven adenocarcinoma from 40 urology practices nationwide. Subjects submit semiannual HRQOL questionnaires until death or withdrawal from the study. All participants provided informed consent before study enrollment. Additional details of the project method have been previously reported.[9]

All subjects included in this analysis underwent RP without neoadjuvant or adjuvant androgen deprivation or other treatment, all had clinically localized disease, baseline comorbidity information, and answered a preoperative HRQOL questionnaire and at least one postoperative HRQOL questionnaire. As of June 2003, 3391 men in the database had undergone RP. Of these, 2826 (83%) had provided comorbidity information. Of these, 856 completed preoperative and postoperative HRQOL questionnaires and constituted our sample. We analyzed HRQOL outcomes for 2 years after RP.

On their baseline questionnaires, subjects completed a checklist that included 11 categories of common comorbidity: arthritis, rheumatic diseases, and musculoskeletal conditions (collectively termed arthritis); hypertension; stomach, intestinal, and gastrointestinal (GI) diseases (GI diseases); urinary conditions; heart disease; cancer (other than prostate); lung disease; diabetes; kidney disease; stroke and neurologic conditions; and blood diseases. Space was also provided to write in other comorbid conditions. Recoding of common responses in the "other condition" text fields led to the creation of five additional categories: mental illness; ear, nose, and throat conditions; chronic infectious diseases (including human immunodeficiency virus/acquired immunodeficiency syndrome); and disease of the internal organs (eg, liver, pancreas, spleen).

The number of comorbidities reported was then summed and, because of its skewed distribution, analyzed as a categorical variable with three levels (none, one to two, and three or more). Information regarding illness severity was not collected. Because summing the number of comorbidities treated each comorbidity as equally important, the more common comorbidities were also analyzed individually (ie, arthritis, hypertension, GI diseases, urinary conditions, heart disease, other cancers, and lung disease).

The Medical Outcomes Study Short Form 36-Item (SF-36)[10] and University of California, Los Angeles, Prostate Cancer Index[11] (UCLA-PCI) health surveys were used to measure general and prostate-cancer specific HRQOL, respectively. The SF-36 consists of eight individual domains and two summary scores measuring physical and mental HRQOL. The UCLA-PCI quantifies sexual, urinary, and bowel function and bother in men with prostate cancer. Each domain is scored from 0 to 100, with higher scores representing better outcomes (better function and less bother). The mental and physical component summaries of the SF-36 are standardized to a population mean of 50 and standard deviation of 10. Minimally detectable and meaningful differences are considered to be three points (one-third of a standard deviation) for the SF-36 component summary scales and 5 to 10 points for the other SF-36 scales and the UCLA-PCI.[10,12] Because questionnaires were sent to the study participants biannually, 6-month time windows (ie, time from surgery to date of questionnaire) were used to analyze the longitudinal data.

The association of the number of comorbidities with HRQOL outcomes was analyzed using a repeated measures model. This analytic method accounted for the likelihood that an individual's scores on a given outcome measure would correlate over time. In addition, it handles missing values and truncation in an optimal way, by taking into account the time patterns of the available data. The repeated measures model included the number of comorbidities, 6-month period, and an interaction between comorbidities and time. This interaction term indicated whether patterns of HRQOL differed by the number of comorbidities. The model also included age at treatment, education, income, body mass index, relationship status, and race/ethnicity. Clinical risk (baseline serum prostate-specific antigen, cancer grade, and T stage) at diagnosis was not related to any HRQOL outcome in the preliminary models, and therefore was dropped from additional analysis. Individual comorbidities were analyzed in separate repeated measures models. No formal adjustment was made for multiple HRQOL outcomes, and $P < 0.05$ was used to report statistical significance. Analyses were performed using Statistical Analysis Systems, version 8.2 (SAS Institute, Cary, NC).

RESULTS

The 856 men included in this analysis were of similar age and marital status as other men receiving RP who were not included in the analysis. However, the men in this analysis were more educated, had higher incomes, were more likely to be white, and had a lower risk of disease than other men undergoing RP.

These 856 men contributed 3140 questionnaires (or 3.7 per person) permitting us to examine longitudinal changes in HRQOL. The median follow-up time after surgery was 16 months (range 3 to 30). During the observation period, 23 men underwent a second prostate cancer treatment and 6 died. The demographic and clinical characteristics of the men who met the study criteria are reported in Table I. Men with more comorbidities were older, more obese, and had lower incomes.

Men with more comorbidities had significantly worse HRQOL scores at baseline for all domains except mental health, role emotional, social function,

TABLE I. *Patient characteristics by number of comorbidities*

Characteristics	None (n = 168)	1–2 (n = 491)	3+ (n = 197)	*P* Value
Age (yr)				<0.0001
<55	41 (24)	76 (15)	19 (10)	
55–59	44 (26)	108 (22)	34 (17)	
60–64	35 (21)	122 (25)	42 (21)	
65–69	34 (20)	123 (25)	63 (32)	
70+	14 (8)	62 (13)	39 (20)	
Education				0.13
<High school	9 (5)	48 (10)	26 (13)	
High school graduate	39 (23)	121 (25)	41 (21)	
Some college	36 (22)	87 (18)	45 (23)	
College graduate	83 (50)	230 (47)	84 (43)	
Yearly income				0.01
<$30,000	19 (12)	83 (18)	41 (22)	
$30–50,000	37 (23)	100 (22)	58 (31)	
$50–75,000	33 (21)	93 (20)	32 (17)	
>$75,000	70 (44)	182 (40)	55 (30)	
Relationship status				0.11
Married/in relationship	160 (96)	458 (95)	179 (91)	
Single	7 (4)	24 (5)	17 (9)	
Race/ethnicity				0.73
African-American	7 (4)	20 (4)	12 (6)	
White, non-Hispanic	155 (92)	451 (92)	175 (89)	
Other	6 (4)	20 (4)	10 (5)	
Body mass index				<0.01
Normal	56 (34)	103 (21)	48 (25)	
Overweight	84 (51)	282 (59)	91 (47)	
Obese	26 (16)	96 (20)	56 (29)	
Clinical risk				0.12
Low	93 (57)	222 (46)	86 (45)	
Intermediate	54 (33)	192 (40)	75 (39)	
High	16 (10)	67 (14)	30 (16)	

Data presented as number, with percentages in parentheses.
Categories may not total to "n" because of missing values; percentages may not sum to 100 owing to rounding.

and the mental component summary (Table II). However, over time, all HRQOL domains, except for the SF-36 domain of role emotional, showed significant differences by the number of comorbidities.

Although their scores were consistently worse, in general, men with more comorbidities did not show a different pattern of HRQOL scores over time than men without comorbidities. Thus, although men with more comorbidities had lower absolute scores at all points, the slope, or rate of change, of their scores was similar to that of men without comorbidities. Two exceptions to this pattern were sexual function and the physical component summary.

For the physical component summary, changes over time differed, albeit by less than 3 points, for the three levels of comorbidity (interaction term, $P = 0.03$; Table II). For sexual function (Table II and Fig. 1), the changes in the scores for the three levels of comorbidity were significantly different (interaction term, $P < 0.001$). At baseline, men without comorbid conditions reported the best sexual functioning ($P < 0.0001$). However, by 24 months postoperatively, no significant differences were found in sexual functioning among the three groups ($P = 0.38$), indicating that the groups changed over time at different rates.

Specific comorbidities were also analyzed to determine their association with HRQOL during the 2 years after RP. For men with and without other urinary conditions, there was a 17-point difference in urinary bother scores before RP (73 versus 90, respectively, $P < 0.0001$). Two years after RP, the difference had narrowed to only 6 points (78 versus 84, $P = 0.07$). For men with GI conditions, urinary function ($P < 0.01$), urinary bother ($P < 0.01$), and sexual function ($P = 0.049$) differed significantly in their patterns over time compared with men without GI conditions.

The changes in scores for physical function ($P < 0.01$), role physical ($P < 0.01$), general health perceptions ($P < 0.01$), and the physical component summary ($P < 0.01$) were significantly differ-

TABLE II. *Adjusted* pretreatment HRQOL scores and changes at 1 and 2 years after treatment by number of comorbidities*

HRQOL Domain by No. Comorbidities	Before Treatment	Change in Score from Before Treatment to 1 yr After RP	Change in Score from Before Treatment to 2 yr After RP
Physical function			
No comorbidity	95.0 ± 1.2	−1.7 ± 1.2	−1.9 ± 1.6
1–2 Comorbidities	90.7 ± 0.7	−0.4 ± 0.7	−1.4 ± 1.0
3+ Comorbidities	85.0 ± 1.1	+2.0 ± 1.2	−2.1 ± 1.5
Role physical			
No comorbidity	92.8 ± 2.3	−1.0 ± 2.5	−2.6 ± 3.2
1–2 Comorbidities	85.7 ± 1.4	−1.1 ± 1.5	+1.3 ± 2.0
3+ Comorbidities	77.4 ± 2.2	+1.6 ± 2.5	+1.0 ± 2.9
Vitality			
No comorbidity	74.8 ± 1.4	+0.6 ± 1.3	−0.3 ± 1.9
1–2 Comorbidities	70.3 ± 0.8	−1.9 ± 0.8‡	−1.1 ± 1.2
3+ Comorbidities	63.1 ± 1.3	+0.9 ± 1.3	−1.3 ± 1.8
Bodily pain			
No comorbidity	92.9 ± 1.4	−0.6 ± 1.5	−6.1 ± 2.2‡
1–2 Comorbidities	87.3 ± 0.8	−2.5 ± 0.9‡	−2.5 ± 1.4
3+ Comorbidities	82.6 ± 1.3	−2.0 ± 1.5	−4.2 ± 2.1‡
Mental health			
No comorbidity	79.3 ± 1.3	+5.0 ± 1.2‡	+4.6 ± 1.6‡
1–2 Comorbidities	77.4 ± 0.8	+4.2 ± 0.7‡	+4.7 ± 1.0‡
3+ Comorbidities	76.0 ± 1.2	+4.0 ± 1.2‡	+2.0 ± 1.5
Role emotional			
No comorbidity	86.7 ± 2.5	+3.8 ± 2.8	+3.2 ± 3.7
1–2 Comorbidities	81.4 ± 1.5	+6.7 ± 1.7‡	+7.4 ± 2.3‡
3+ Comorbidities	81.7 ± 2.4	+6.2 ± 2.8‡	+4.8 ± 3.5
Social function			
No comorbidity	90.1 ± 1.5	+3.2 ± 1.6	+3.3 ± 2.2
1–2 Comorbidities	89.0 ± 0.9	+1.5 ± 1.0	+0.2 ± 1.4
3+ Comorbidities	87.5 ± 1.4	−1.0 ± 1.6	−6.8 ± 2.1‡
General health			
No comorbidity	84.2 ± 1.4	−0.5 ± 1.2	−2.3 ± 1.6
1–2 Comorbidities	76.3 ± 0.8	−0.4 ± 0.8	−2.2 ± 1.0‡
3+ Comorbidities	66.6 ± 1.3	+1.9 ± 1.2	−0.6 ± 1.5
Physical component summary†			
No comorbidity	56.3 ± 0.6	−1.4 ± 0.6‡	−2.7 ± 0.7‡
1–2 Comorbidities	53.6 ± 0.3	−1.7 ± 0.4‡	−1.8 ± 0.5‡
3+ Comorbidities	50.0 ± 0.5	−0.5 ± 0.6	−1.8 ± 0.7‡
Mental component summary			
No comorbidity	52.0 ± 0.8	+2.5 ± 0.7‡	+2.6 ± 0.9‡
1–2 Comorbidities	50.7 ± 0.7	+2.3 ± 0.5‡	+2.4 ± 0.6‡
3+ Comorbidities	51.0 ± 0.6	+1.8 ± 0.7‡	+0.8 ± 0.9
Urinary function			
No comorbidity	94.5 ± 1.0	−14.6 ± 1.9‡	−16.1 ± 2.1‡
1–2 Comorbidities	93.5 ± 0.6	−16.7 ± 1.1‡	−15.0 ± 1.3‡
3+ Comorbidities	90.6 ± 0.9	−18.1 ± 1.8‡	−18.1 ± 2.0‡
Urinary bother			
No comorbidity	91.2 ± 1.7	−4.4 ± 2.5	−6.2 ± 2.8‡
1–2 Comorbidities	87.4 ± 1.0	−6.1 ± 1.5‡	−3.9 ± 1.7‡
3+ Comorbidities	83.3 ± 1.6	−6.0 ± 2.4‡	−4.0 ± 2.6
Sexual function†			
No comorbidity	64.9 ± 2.0	−30.7 ± 2.1‡	−29.6 ± 2.4‡
1–2 Comorbidities	61.3 ± 1.2	−34.1 ± 1.3‡	−28.1 ± 1.5‡
3+ Comorbidities	53.1 ± 1.8	−27.4 ± 2.0‡	−22.2 ± 2.3‡
Sexual bother			
No comorbidity	74.5 ± 2.8	−29.9 ± 3.5‡	−24.4 ± 4.2‡
1–2 Comorbidities	66.8 ± 1.6	−32.0 ± 2.1‡	−24.2 ± 2.6‡
3+ Comorbidities	59.9 ± 2.6	−28.4 ± 3.4‡	−24.4 ± 4.0‡

Continued

TABLE II. *Continued*

HRQOL Domain by No. Comorbidities	Before Treatment	Change in Score from Before Treatment to 1 yr After RP	Change in Score from Before Treatment to 2 yr After RP
Bowel function			
No comorbidity	91.3 ± 1.1	+0.04 ± 1.1	−1.6 ± 1.5
1–2 Comorbidities	88.6 ± 0.6	+0.6 ± 0.7	−0.2 ± 1.0
3+ Comorbidities	85.9 ± 1.0	+1.9 ± 1.1	+0.8 ± 1.4
Bowel bother			
No comorbidity	94.4 ± 1.6	−2.5 ± 1.9	−2.7 ± 2.2
1–2 Comorbidities	90.7 ± 0.9	−1.6 ± 1.1	−1.4 ± 1.4
3+ Comorbidities	87.7 ± 1.5	−0.4 ± 1.9	−1.7 ± 2.1

KEY: HRQOL = health-related quality of life; RP = radical prostatectomy.
Data presented as mean ± standard error.
** All scores and change scores derived from repeated measures model that included age at treatment, education, income, body mass index, marital status, and race/ethnicity.*
† P <0.05 for interaction term between number of comorbidities and time period (ie, change over time differed by comorbidity group).
‡ P <0.05 represents change in score that deviates from 0.

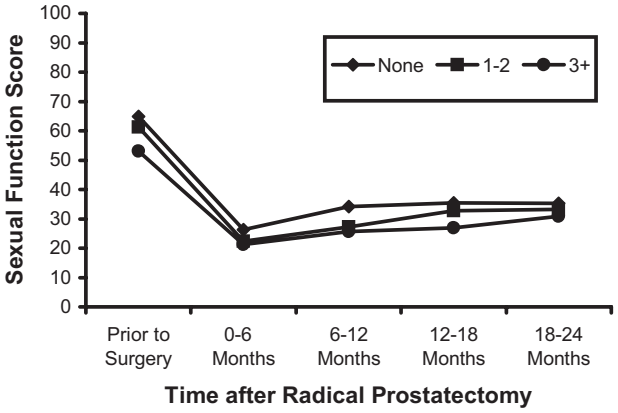

FIGURE 1. *UCLA-PCI sexual function by number of comorbidities showing adjusted mean sexual function scores for each period after RP. Scores were adjusted for age, education, income, body mass index, relationship status, and race/ethnicity. Interaction between period and number of comorbidities,* P *<0.001.*

ent for men with and without heart disease. In addition, men with hypertension had significantly different patterns over time for role emotional ($P = 0.01$), social function ($P < 0.01$), and the mental component summary ($P < 0.01$) compared with men without hypertension. No significant HRQOL differences were found for lung disease, other cancer, or arthritis during the 2-year period.

COMMENT

We began the study with two hypotheses. First, we hypothesized that men with more comorbid conditions would have worse HRQOL than men without comorbidities at baseline, and we found this to be true. Our second hypothesis was that these differences would be maintained over time; here our findings were mixed. In almost all cases, the HRQOL scores for men with comorbidities were worse at each point, and this difference was constant over time.

However, for sexual function and the physical component summary, men without comorbidities had a greater decline in HRQOL than men with comorbidities. One explanation could be a floor effect, in that those men with more comorbidities had low sexual function scores at baseline and could not move much further down the scale. Certainly, those without comorbidities had more to lose in these domains after surgery. However, Hu *et al.*[2] demonstrated that men without comorbidities were more likely to return to baseline physical function 1 year after RP.

Notably, for most HRQOL domains, the patterns of decline after RP were similar in men with and without comorbidities. A study of women with breast cancer demonstrated similar results. Comorbidity was associated with a lower quality of well-being scores, but not the rate of change over time for breast cancer survivors.[8] In other cancer survivor studies, comorbidity has been associated with HRQOL declines over time.[3,5,7]

For the SF-36 scores that declined significantly after RP (ie, bodily pain, general health, and the physical component summary), the decline continued during the 2 years of the study. In contrast, the UCLA-PCI scores that were significantly lower after RP showed some improvement between years 1 and 2 (ie, sexual function) or a leveling between years 1 and 2 (ie, urinary function). The pattern for SF-36 scores might have been due to the effect of aging, whereas the specific bodily functions affected by prostatectomy might improve with recovery time.

The criteria of meaningful differences (3 points for the SF-36 component summary scales and 5 to 10 points for the other SF-36 scales and the UCLA-PCI) were met for statistically significant declines in sexual function, sexual bother, and urinary function after surgery. They were equivocal for the statistically significant changes in bodily pain, role

emotional, social function, and the physical and mental component summary scores.

In addition to the number of comorbidities, the individual comorbidities of heart disease, hypertension, other urinary conditions, and GI disease had an association with particular domains of HRQOL, although others did not (ie, arthritis, other cancers, and lung disease). Our findings might be consistent with the underlying pathophysiology of the specific comorbidities. Men without other urinary conditions showed greater declines than men with other urinary conditions in urinary bother scores 2 years after RP. It may be that these men developed outlet obstruction as a new condition after surgery and that the men with prior urinary conditions had learned to cope with these issues.

The association between hypertension and the emotional domains of the SF-36 is consistent with studies showing that hypertensive patients report a more depressed or anxious mood than those without hypertension.[13,14] Similarly, the association we found between heart disease and the physical domains of HRQOL may be related to the discomfort and limitation of daily activities seen with angina and dyspnea.[15] Our results are also consistent with a study showing that lung cancer survivors with known heart disease have lower physical component summary scores than those without heart disease.[7]

Our study had several limitations. This cohort of men was not a random sample and might not be representative of men who undergo RP in general or of all men in CaPSURE treated with surgery. Men who answered the study questionnaires and could be included in this analysis appeared to be of higher socioeconomic backgrounds. An important consideration is that we did not assess the severity of the comorbidities or the development of new comorbidities during the follow-up period. Many of the declines in HRQOL we noted during the 2-year observation period were statistically, but not clinically, significant. In addition, because comorbidity may predict the treatment received, these results may not be generalizable to men with prostate cancer who choose other management options.[16,17]

Nonetheless, the sample was drawn from practices across the United States, allowing geographic and clinical diversity. Most subjects were treated in community-based private practices. In addition, we were able to study a variety of specific comorbidities.

Therefore, our data support the hypothesis that comorbidity is associated with HRQOL in men undergoing RP. During preoperative counseling, clinicians should consider the number and type of a patient's comorbidities. Men without comorbidities should be told that their sexual function is more likely to decrease. In addition, men with other urinary conditions may find minimal differences in their urinary bother after surgery.

CONCLUSIONS

Men with more comorbidities have a worse quality of life before and after RP. However, with two exceptions, the HRQOL scores declined at similar rates in men with and without comorbidities. In addition, specific comorbidities, such as hypertension, heart disease, GI disease, and urinary conditions, were associated with declines in particular HRQOL domains.

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APPENDIX

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