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Health Related Quality of Life in Patients Treated With Multimodal Therapy for Prostate Cancer

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Purpose: Patients with prostate cancer and high risk disease characteristics may benefit from multimodal therapy. However, the effects of multimodal therapy on health related quality of life have not been comprehensively described. We further characterized health related quality of life in patients treated with multimodal therapy.

Materials and Methods: Patient data were obtained from the CaPSURE™ database, a national disease registry of men with prostate cancer. Included patients received active primary therapy (ie surgery or various forms of radiation) for prostate cancer with or without adjuvant or neoadjuvant therapy, and had complete clinical data, including health related quality of life assessments at baseline and through 2 years after treatment. The association between health related quality of life outcomes and different primary therapies with and without adjuvant or neoadjuvant therapy over time was analyzed using a repeated measures mixed model for each primary therapy.

Results: A total of 2,204 men met the study criteria. As primary therapy 1,427 patients received radical prostatectomy, 267 received external beam radiation therapy and 510 received brachytherapy. When androgen deprivation therapy was included with radical prostatectomy, brachytherapy or external beam radiation therapy, there was a transient loss of sexual function that improved within 9 months postoperatively. When external beam radiation therapy was given with brachytherapy there was continuous worsening of urinary function and bother through 21 months.

Conclusions: Multimodal therapy may lead to declines in health related quality of life especially in the domains of urinary function, urinary bother and sexual function. These effects must be considered and patients must be counseled appropriately before initiation of multimodal therapy.

Key Words: prostatic neoplasms, quality of life, combined modality therapy

Patients with prostate cancer and high risk disease characteristics face a high likelihood of disease recurrence and progression following monotherapy and, therefore, may benefit from multimodal therapy. Indeed, randomized controlled trials have confirmed that in select settings multimodal therapy confers a survival benefit. For example, adjuvant androgen deprivation therapy has been shown to improve overall survival in patients receiving external beam radiation therapy.[1] Additionally, patients found to have lymph node involvement on radical prostatectomy have a survival benefit from adjuvant ADT.[2]

Other supplemental therapies have not conferred such clear benefit. In patients with pT3 disease and those with positive surgical margins, adjuvant EBRT given with RP has to date been proven only to improve biochemical relapse rates, but not survival.[3] Neoadjuvant ADT before RP decreases the positive surgical margin rate but has not been confirmed to improve relapse rates or survival.[4] Among intermediate and high risk patients receiving brachytherapy, the addition of ADT might improve relapse rates, but not survival.[5] Combination EBRT with standard BT does not consistently improve biochemical relapse rates compared to BT alone.[6]

Current guidelines support the use of ADT with EBRT for intermediate and high risk disease.[7] However, clear guidelines on other combinations of therapy are not yet available, and the benefits of multimodal therapy must be considered within the context of their impacts on quality of life. While previous studies have examined the sexual and hormonal side effects of multimodal therapy, a comprehensive analysis of the HRQOL effects of multimodal therapy has not yet been reported.[8–11] Thus, we characterized the impact of multimodal therapy compared to monotherapy on quality of life.

METHODS

Patient Population

Patient data were obtained from CaPSURE, a national observational database of men with biopsy proven prostate adenocarcinoma initiated in 1995. Patients are recruited into the database through 31 community, academic and government urological practices, and are asked to complete an HRQOL survey at baseline and every 6 months after initiation of treatment. Further details regarding the database and data collection procedures have been reported previously.[12] Men were selected for the study population if they underwent primary therapy, including RP, EBRT, and BT

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TABLE 1. *Demographic and clinical data*

	No. (%)								
	RP Alone	RP + ADT	RP + EBRT	BT Alone	BT + ADT	BT + EBRT	BT + EBRT + ADT	EBRT Alone	EBRT + ADT
Age at diagnosis:									
Younger than 55	228 (18)	13 (11)	2 (13)	13 (5)	4 (3)	1 (2)	2 (3)	0 (0)	3 (2)
55–64	622 (48)	49 (41)	10 (63)	68 (28)	21 (15)	15 (25)	13 (22)	17 (20)	22 (12)
65–74	421 (33)	53 (44)	4 (25)	122 (50)	83 (58)	26 (43)	30 (51)	43 (52)	93 (51)
75+	19 (1)	6 (5)	0 (0)	43 (17)	36 (25)	19 (31)	14 (24)	23 (27)	66 (36)
PSA at diagnosis:									
Less than 4	255 (20)	10 (8)	0 (0)	49 (20)	16 (11)	8 (13)	5 (8)	9 (11)	18 (10)
4.1–10	882 (68)	74 (61)	13 (81)	181 (74)	104 (72)	37 (61)	28 (47)	52 (63)	84 (46)
10.1–20	128 (10)	25 (21)	3 (19)	12 (5)	22 (15)	12 (20)	22 (37)	17 (20)	56 (30)
Greater than 20	25 (2)	12 (10)	0 (0)	4 (2)	2 (1)	4 (7)	4 (7)	5 (6)	26 (14)
Gleason stage:									
2–4	16 (1)	1 (1)	0	3 (1)	4 (3)	1 (2)	0 (0)	2 (2)	5 (3)
5–6	916 (71)	58 (48)	10 (63)	212 (86)	109 (76)	20 (33)	19 (32)	59 (71)	72 (39)
7	304 (24)	44 (36)	4 (25)	25 (10)	27 (19)	34 (56)	33 (56)	18 (22)	77 (42)
8–10	54 (4)	18 (15)	2 (13)	6 (2)	4 (3)	6 (10)	6 (10)	4 (5)	30 (16)
T stage:									
T1	752 (58)	56 (46)	14 (88)	144 (58)	80 (56)	30 (49)	20 (34)	50 (60)	77 (42)
T2	526 (41)	63 (52)	2 (13)	102 (42)	62 (43)	30 (49)	39 (66)	33 (40)	95 (52)
T3/T4	12 (1)	2 (2)	0 (0)	0 (0)	2 (1)	1 (2)	0 (0)	0 (0)	12 (6)
Race/ethnicity:									
Asian	9 (1)	0 (0)	2 (1)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	2 (1)
Hispanic	15 (1)	0 (0)	5 (2)	4 (3)	1 (2)	3 (5)	3 (5)	0 (0)	0 (0)
Black	60 (5)	0 (0)	9 (4)	10 (7)	2 (3)	3 (5)	3 (5)	5 (6)	12 (7)
White	1,181 (92)	15 (94)	229 (93)	125 (87)	57 (93)	53 (90)	53 (90)	78 (94)	164 (89)
Other/mixed/unknown	25 (2)	1 (6)	1 (1)	5 (3)	1 (2)	0 (0)	0 (0)	0 (0)	6 (3)
Education level:									
Did not complete high school	91 (7)	15 (13)	2 (13)	32 (13)	24 (17)	13 (22)	12 (20)	10 (12)	26 (15)
High school diploma	272 (21)	30 (25)	3 (19)	63 (26)	44 (31)	18 (30)	18 (31)	24 (29)	53 (30)
Some college	242 (19)	24 (20)	3 (19)	53 (22)	30 (21)	8 (13)	9 (15)	14 (17)	28 (16)
College degree + beyond	677 (53)	49 (42)	8 (50)	94 (39)	42 (30)	21 (35)	20 (34)	35 (42)	70 (40)
Income:									
Less than $20,000	181 (14)	23 (19)	5 (31)	72 (29)	51 (35)	23 (38)	21 (36)	29 (35)	68 (37)
$30,000–$50,000	258 (20)	24 (20)	2 (13)	61 (25)	39 (27)	16 (26)	15 (25)	24 (29)	39 (21)
$50,000–$75,000	273 (22)	20 (17)	4 (25)	32 (13)	26 (18)	9 (15)	9 (15)	11 (13)	30 (16)
Greater than $75,000	496 (38)	36 (30)	5 (31)	48 (20)	11 (8)	7 (11)	10 (17)	10 (12)	24 (13)
Unknown	82 (6)	18 (15)	0 (0)	33 (13)	17 (12)	6 (10)	4 (7)	9 (11)	23 (13)
Relationship status:									
In relationship	1,208 (93)	111 (92)	12 (75)	219 (89)	128 (89)	51 (84)	52 (88)	73 (88)	153 (83)
Single	70 (5)	8 (7)	3 (19)	22 (9)	11 (8)	8 (13)	7 (12)	10 (12)	25 (14)
Unknown	12 (1)	2 (2)	1 (6)	5 (2)	5 (3)	2 (3)	0 (0)	0 (0)	6 (3)
Body mass index:									
Normal (less than 25.0)	313 (25)	27 (24)	3 (19)	73 (30)	31 (22)	14 (23)	15 (26)	22 (27)	57 (32)
Overwt (25.0–29.9)	701 (55)	59 (52)	10 (63)	116 (48)	72 (52)	28 (47)	29 (51)	39 (48)	88 (50)
Obese (30.0–34.9)	205 (16)	20 (18)	2 (13)	39 (16)	30 (22)	7 (12)	12 (21)	18 (22)	20 (11)
Very obese (35.0 or greater)	52 (4)	8 (7)	1 (6)	13 (5)	6 (4)	11 (18)	1 (2)	2 (2)	11 (6)
No. of comorbidities:									
None	252 (20)	26 (22)	2 (13)	29 (12)	9 (6)	3 (5)	5 (9)	5 (6)	18 (10)
1–2	407 (32)	34 (29)	5 (31)	64 (26)	33 (24)	8 (14)	13 (23)	18 (22)	47 (26)
3–5	335 (26)	32 (27)	7 (44)	65 (27)	47 (34)	17 (29)	20 (35)	29 (35)	47 (26)
6+	168 (13)	17 (15)	2 (13)	49 (20)	31 (22)	12 (20)	8 (14)	19 (23)	29 (16)

with or without neoadjuvant and/or adjuvant EBRT and/or ADT. In addition, to be included in the study population men were required to have complete clinical data available, including PSA, biopsy Gleason score and clinical T stage, and HRQOL assessment via surveys at baseline and during 2 years after treatment.

Treatment Technique

Patients were treated according to standard practices of individual physicians and institutions. ADT included treatment with luteinizing hormone-releasing hormone agonists and/or antiandrogens. EBRT included non-3-dimensional radiation therapy and 3-dimensional conformal planning techniques. BT was typically performed via a transperineal approach under transrectal ultrasound guidance. ^{103}Pd, ^{125}I and ^{192}Ir were all reported types of radioisotopes used. Nerve sparing RP and nonnerve sparing RP were performed.

Outcomes Assessment

Standard demographic data were obtained before the initiation of therapy. Clinical data provided by the enrolling urologist included medical history, pretreatment PSA, Gleason grade, staging and other laboratory data. Comorbidity data were collected from a 12-item medical history checklist based on the Charlson comorbidity rating scale.[15] General HRQOL data were obtained through the RAND Medical Outcomes Study Short Form-36, and the PCS and MCS were calculated.[13] Prostate specific HRQOL data were obtained using the UCLA-PCI, which includes the 6 domains of sexual function, sexual bother, bowel function, bowel bother,

TABLE 2. *Number of patients receiving each form of androgen deprivation therapy*

	RP + ADT	BT + ADT	EBRT + ADT
Adjuvant ADT:			
LHRH-a	17	1	5
Antiandrogen	3	0	1
Combined	12	0	0
Neoadjuvant ADT:			
LHRH-a	13	44	35
Antiandrogen	0	1	0
Combined	7	23	21
Adjuvant/neoadjuvant ADT:			
LHRH-a	25	28	61
Antiandrogen	2	29	3
Combined	16	32	44

urinary function and urinary bother.[14] All domains are scored from 0 to 100 with higher scores indicating better function and less bother. Differences of 5 to 10 points on the SF-36 and PCI scales are thought to represent clinically significant changes.[11] Among the analytic cohort HRQOL survey response rates were 100% at baseline, 84% at 3 months, 91% at 9 months, 85% at 15 months and 74% at 21 months.

Statistical Analysis

The associations of different clinical and sociodemographic characteristics within each treatment type were evaluated by chi-square tests for categorical and 1-way ANOVA for continuous data. The association between HRQOL outcomes and different primary therapies with and without adjuvant or neoadjuvant therapy over time was analyzed using a repeated measures mixed model. Repeated measures analysis was used because it takes into account the correlation of the recurring outcome within patients. 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 comorbidities, risk stratification, baseline HRQOL score, nerve sparing status for RP, patient age, type of treatment, time period, and an interaction term between treatment type and time, included to determine whether patterns of HRQOL differ over time by type of treatment. Risk stratification was determined by pretreatment PSA, Gleason grade and clinical TNM staging. Each primary therapy (RP, EBRT and BT) was tested separately. All analyses were performed using SAS® version 8.

RESULTS

Patient Characteristics

A total of 13,124 men with prostate cancer were available in the CaPSURE database of whom 8,720 were treated with primary RP, EBRT or BT. Of the 8,720 men 2,204 who had complete clinical data and HRQOL surveys available at baseline and 2 years of followup constituted the analytic

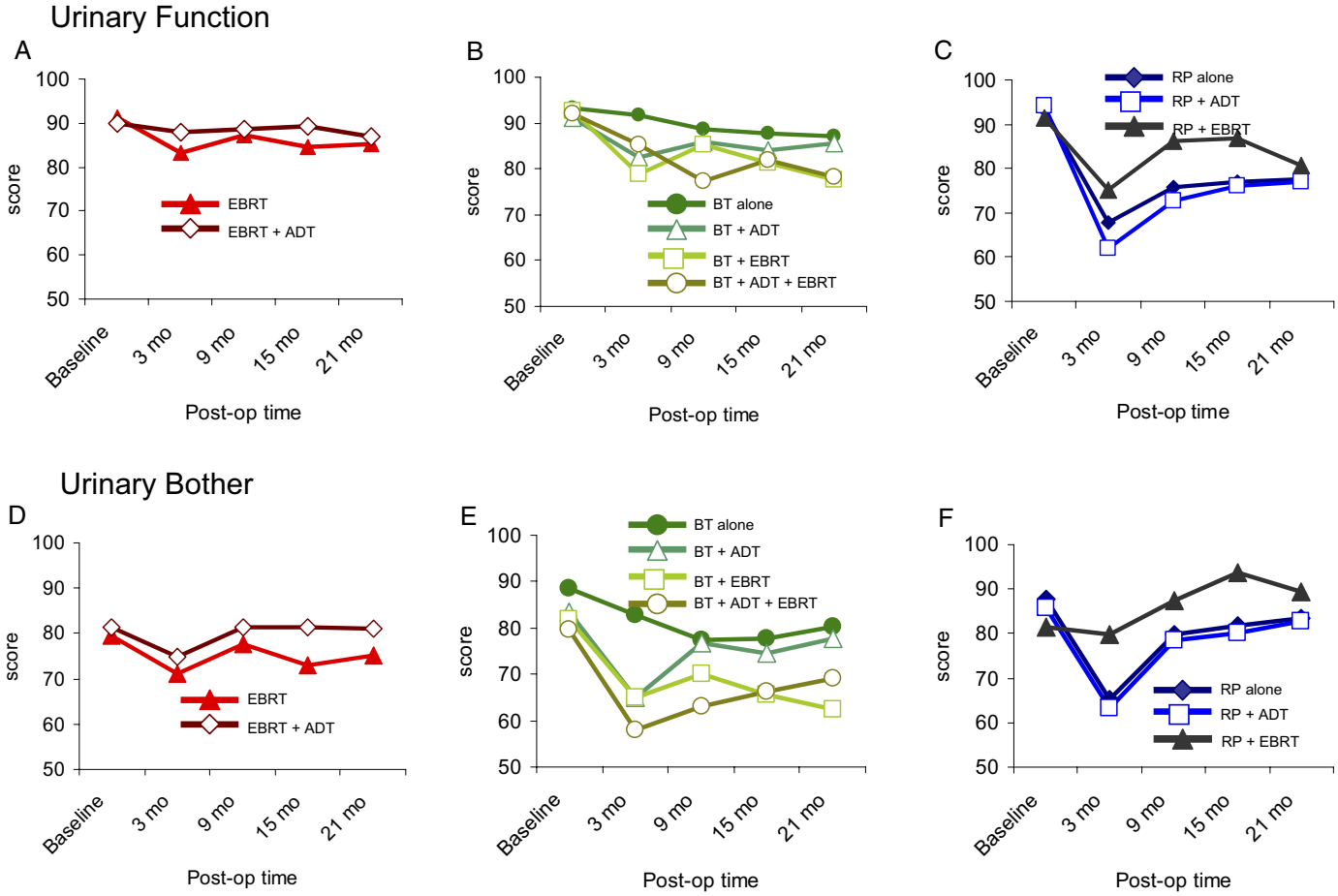

FIG. 1. Unadjusted means of urinary function scores for EBRT (*A*), BT (*B*) and RP (*C*). Unadjusted means of urinary bother scores for EBRT (*D*), BT (*E*) and RP (*F*).

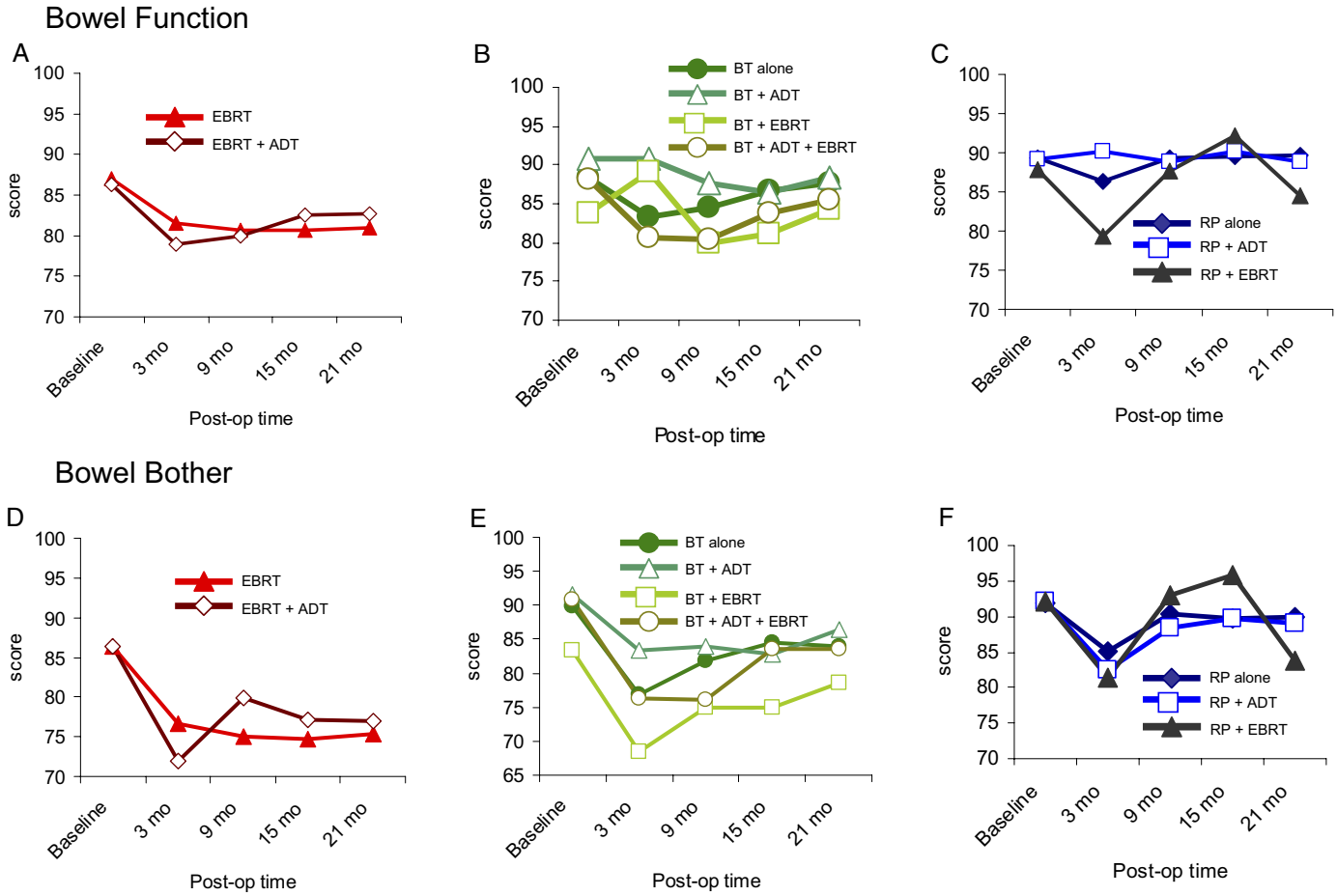

FIG. 2. Unadjusted means of bowel function scores for EBRT (*A*), BT (*B*) and RP (*C*). Unadjusted means of bowel bother scores for EBRT (*D*), BT (*E*) and RP (*F*).

data set. Distribution by type of treatment was RP alone (1,290), RP plus ADT (121), RP plus EBRT (16), EBRT alone (83), EBRT plus ADT (184), BT alone (246), BT plus EBRT (61), BT with ADT (144), BT plus EBRT and ADT (59). Patient demographic and clinical data are presented in table 1. The average length of ADT ± SD was 5 ± 3.7 months. The number of patients receiving each type of ADT is presented in table 2. Across these 3 groups patients differed significantly by age, PSA at diagnosis, Gleason stage, TNM stage, number of comorbidities, education level, income and relationship status. Patients treated with EBRT or BT were generally older with less income and education. Those treated with primary EBRT generally had higher grade lesions.

Patients treated with RP alone more often had Gleason grade less than 7 and PSA less than 10 compared to those who also received adjunctive ADT (72% vs 49% Gleason grade less than 7, 88% vs 69% PSA less than 10). Similarly those who received therapies adjunctive to primary BT and primary EBRT also tended to have higher PSAs and Gleason grades at diagnosis (table 1).

General HRQOL

There was a statistically significant difference in PCS between RP alone and RP with ADT (52.2 vs 50.0 at 3 months, $p < 0.05$), with the former having higher PCS scores. Also, patients receiving EBRT with ADT had statistically significantly higher MCS scores (53.7 vs 51.2 at 3 months, $p < 0.05$) but these differences were small and of questionable clinical significance. Other differences in PCS and MCS scores were not statistically significantly different among treatment groups.

Prostate Specific HRQOL

Unadjusted mean urinary function and bother scores over time for different therapies are shown in figure 1. For primary RP neither the addition of EBRT nor ADT significantly changed the trajectory ($p = 0.06$) or absolute values ($p = 0.3$) of urinary function. However, patients receiving adjunctive EBRT with RP seemed to experience declining urinary function at 21 months. In mixed model analysis when EBRT was given with BT, urinary function continued to decline through 21 months while after BT alone there was slight improvement in urinary function over this period ($p < 0.01$). Patients receiving BT with EBRT and ADT had significantly lower scores for urinary function relative to BT alone ($p < 0.05$). The addition of ADT to primary EBRT did not significantly impact urinary function values ($p = 0.2$) or trajectory over time ($p = 0.08$).

Urinary bother was not affected by the addition of ADT to primary RP ($p = 0.8$). However, the addition of EBRT to primary BT led to significantly worse bother ($p < 0.05$), which worsened through 21 months, although this difference in trajectory was not statistically significant ($p = 0.09$).

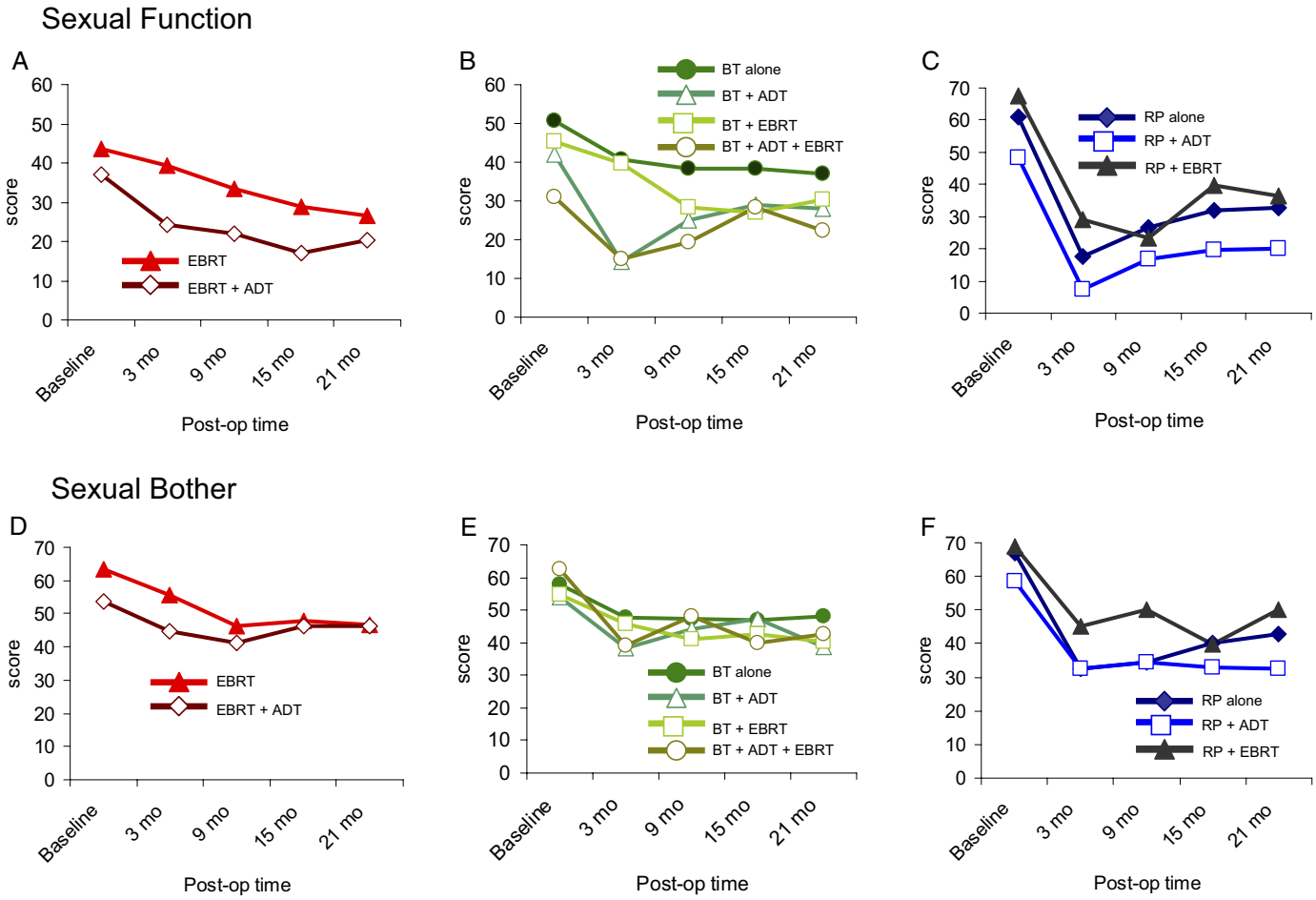

FIG. 3. Unadjusted means of sexual function scores for EBRT (*A*), BT (*B*) and RP (*C*). Unadjusted means of sexual bother scores for EBRT (*D*), BT (*E*) and RP (*F*).

Urinary bother was not affected by the addition of ADT to primary EBRT ($p = 0.6$).

Mean bowel function and bother scores over time for different therapies are shown in figure 2. RP alone and RP with EBRT or ADT did not differ significantly for bowel function ($p = 0.4$) or bowel bother ($p = 0.05$), but there was a trend for RP with ADT to have worse bowel bother in the early postoperative period. Neither bowel function nor bother was significantly altered by the addition of adjunctive therapies to BT or EBRT. Bowel bother scores 3 months postoperatively for BT combined with EBRT appeared to be lower than other BT therapies, and BT combined with EBRT and ADT did not show improvement in bowel bother until 15 months, but these differences were not significant ($p = 0.3$).

Sexual function and bother over time for different therapies are shown in figure 3. After adjusting for baseline sexual function, the addition of ADT to RP significantly decreased sexual function scores early ($p < 0.05$) but both showed continuous improvement through 21 months ($p = 0.5$). The addition of EBRT to RP did not appear to significantly alter sexual function. In mixed model analysis BT alone and BT with EBRT showed modest declines in sexual function during the entire postoperative period, while both BT therapies that included ADT (BT with ADT, BT with ADT and EBRT) showed significantly worse 3-month postoperative sexual function, and then showed continued improvements in function through 15 months and eventually matched BT therapies that did not include ADT ($p < 0.01$). Similar results were seen when comparing EBRT alone and EBRT with ADT ($p < 0.001$).

Sexual bother following RP did not differ significantly from RP with ADT ($p = 0.9$) as both showed continuous improvement during the course of 21 months. Similarly there was no significant difference in sexual bother between BT alone and multimodal BT therapies ($p = 0.7$) or between EBRT alone and EBRT with ADT ($p = 0.6$).

Since sexual function was quite low at 3 months in some categories, there is risk of a floor effect with patient surveys. Thus, a subgroup analysis was performed on the patients with the top 20% of sexual function scores at baseline. As seen in figure 4 the addition of ADT in this group seemed to result in a transient decrease in sexual function and bother relative to monotherapy, and sexual function and bother scores were similar by 15 and 21 months. In patients with high baseline sexual function receiving BT the addition of ADT resulted in worse sexual function that appears sustained ($p < 0.001$). Cases treated with RP and ADT approached statistically significantly worse sexual function compared to RP alone ($p = 0.06$).

DISCUSSION

In this study the use of neoadjuvant/adjuvant EBRT combined with BT resulted in worse urinary function and bother

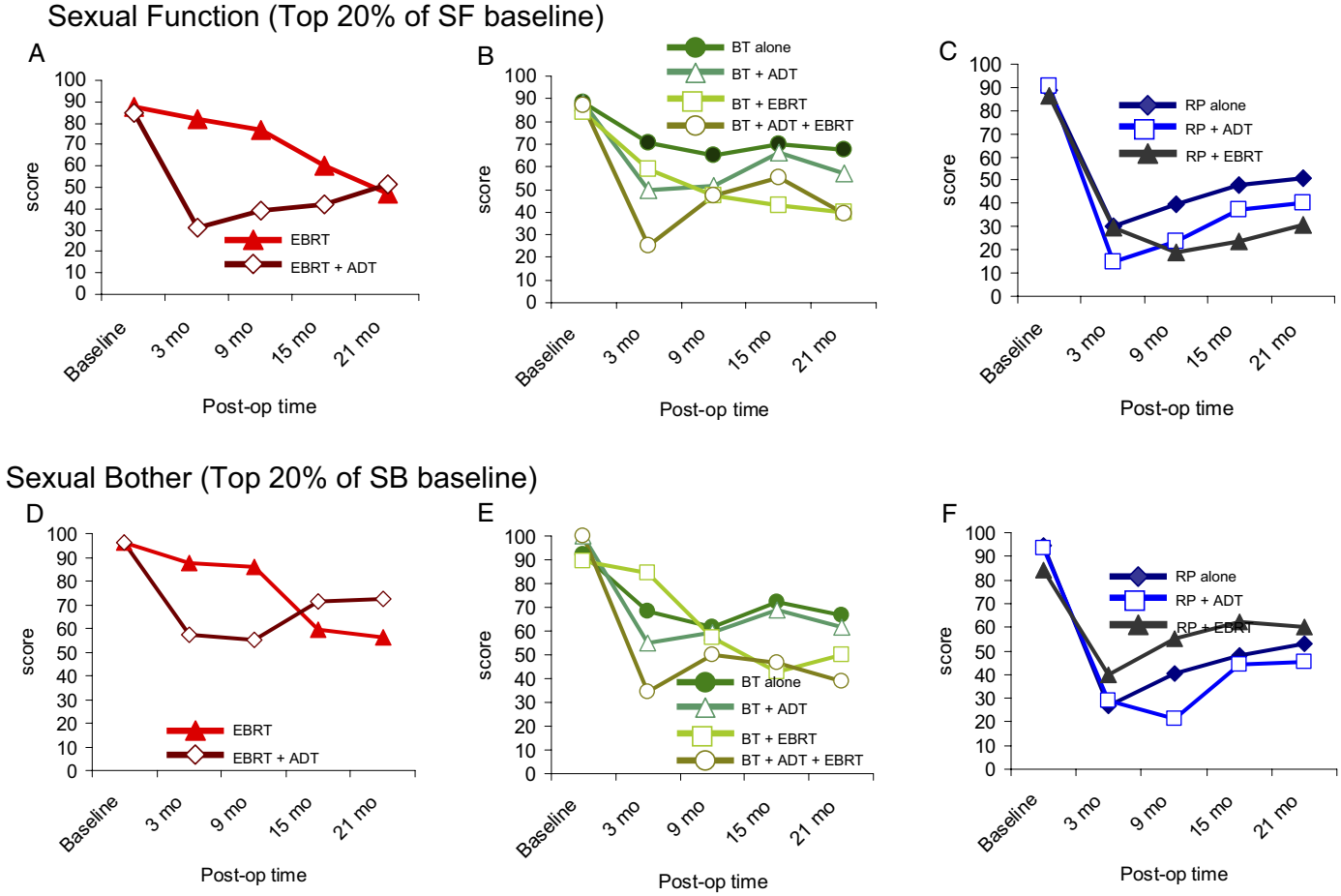

FIG. 4. Subgroup analysis of patients with top 20% of sexual function scores. Unadjusted means of sexual function scores for EBRT (*A*), BT (*B*) and RP (*C*). Unadjusted means of sexual bother scores for EBRT (*D*), BT (*E*) and RP (*F*).

through 21 months. Similarly Krupski et al, using the International Prostate Symptom Scale, found increases in irritative and obstructive symptoms following BT with EBRT compared to BT alone.[16] Although combination EBRT with BT has been shown in other studies to result in greater bowel dysfunction compared to BT alone,[17] this was not seen in the current study. Given that combination EBRT and BT resulted in continued worsening of urinary function and bother through 21 months, and that past studies show significant morbidity[16,17] and in some cases limited efficacy,[6] the application of combination EBRT and BT should be considered judiciously, and the relative risks and benefits should be discussed with patients.

Data from the current study also suggest that ADT results in transient effects on sexual function when combined with EBRT, BT or RP. In a subgroup of patients with high baseline sexual function scores the effects of ADT on patients receiving RP or BT did not appear to resolve as completely. Speight et al, also analyzing CaPSURE data, showed that neoadjuvant short-term ADT resulted in transiently lower sexual function in patients receiving EBRT or BT during the first postoperative year.[11] Black et al likewise found that in patients receiving RP adjuvant ADT resulted in only a transient worsening of sexual function.[10] Thus, when ADT is given as adjunctive therapy to BT or EBRT, there is a transient decrease in sexual function that appears to be short-lived. However, in patients with baseline high sexual function scores undergoing RP or BT the HRQOL effects of ADT may be more pronounced and prolonged.

These findings should be measured against the established benefit of ADT in combination with EBRT or RP when counseling selected patients with advanced or high risk disease.[1,2] However, there is no evidence that the practice of giving neoadjuvant ADT before BT for volume reduction improves survival or decreases morbidity.[5,18] Given that patients with baseline high sexual function receiving BT and ADT may endure sustained decreases in sexual function, this practice should be applied with caution and patients advised to take cytoreductive therapy to facilitate brachytherapy should be advised of the potential adverse effect on sexual function.

Several limitations of this study should be considered. The analysis of patients receiving EBRT as adjuvant therapy to RP is significantly limited due to the small sample size. Previous studies have more thoroughly addressed the HRQOL effects of adjuvant EBRT following RP.[19] With regard to HRQOL assessments, the UCLA PCI is relatively insensitive to urinary irritative symptoms often seen after radiotherapy and does not assess hormonal symptoms.[21] Other HRQOL surveys, such as the EPIC, may have provided more information, but in terms of sexual and urinary domains the EPIC and the UCLA PCI have been shown to correlate well.[20] This study also showed no differences in bowel function or bother between multimodal therapy and

monotherapy. This also could be a consequence of the PCI questionnaire as it has been shown to not correlate well with the EPIC in terms of bowel function.[20]

We cannot rule out definitely that baseline HRQOL surveys were taken while the patient was being treated with neoadjuvant ADT but we have no reason to believe this is common. Furthermore, CaPSURE reflects community practice over time in a wide range of settings, and we were unable to control entirely for the heterogeneity of type and duration of ADT and/or EBRT. It is unlikely that doses of ADT were any different from recommended doses but the mean duration of therapy is shorter than the duration measured in other studies. It may be expected that more prolonged treatment would be associated with more adverse symptoms.

CONCLUSIONS

As multimodal therapy is applied in prostate cancer, a clear understanding of how these therapies interact in terms of adverse effects is important. These data demonstrate that multimodal therapy does not substantially affect general HRQOL. However, combination EBRT and BT appeared to result in continued worsening of urinary function and bother, and as such must be administered with adequate counseling to properly selected patients. Adjunctive ADT exerts a mostly transient negative effect on sexual function. Given its utility in improving disease specific and overall survival when combined with EBRT, these transient effects may be a tolerable side effect in this setting.

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Abbreviations and Acronyms

ADT	=	androgen deprivation therapy
BT	=	brachytherapy
CaPSURE	=	Cancer of the Prostate Strategic Urologic Research Endeavor
EBRT	=	external beam radiation therapy
EPIC	=	Expanded Prostate Cancer Index Composite
HRQOL	=	health related quality of life
LHRH-a	=	luteinizing hormone-releasing hormone-a
MCS	=	mental component score
PCI	=	Prostate Cancer Index
PCS	=	physical component score
PSA	=	prostate specific antigen
RP	=	radical prostatectomy
SF-36	=	RAND Medical Outcomes Study Short Form-36

REFERENCES

1. Bolla M, Collette L, Blank L, Warde P, Dubois JB, Mirimanoff RO et al: Long-term results with immediate androgen suppression and external irradiation in patients with locally advanced prostate cancer (an EORTC study): a phase III randomised trial. Lancet 2002; **360:** 103.
2. Messing EM, Manola J, Sarosdy M, Wilding G, Crawford ED and Trump D: Immediate hormonal therapy compared with observation after radical prostatectomy and pelvic lymphadenectomy in men with node-positive prostate cancer. N Engl J Med 1999; **341:** 1781.
3. Thompson IM Jr, Tangen CM, Paradelo J, Lucia MS, Miller G, Troyer D et al: Adjuvant radiotherapy for pathologically advanced prostate cancer: a randomized clinical trial. JAMA 2006; **296:** 2329.
4. Soloway MS, Pareek K, Sharifi R, Wajsman Z, McLeod D, Wood DP Jr et al: Neoadjuvant androgen ablation before radical prostatectomy in cT2bNxMo prostate cancer: 5-year results. J Urol 2002; **167:** 112.
5. Lee LN, Stock RG and Stone NN: Role of hormonal therapy in the management of intermediate- to high-risk prostate cancer treated with permanent radioactive seed implantation. Int J Radiat Oncol Biol Phys 2002; **52:** 444.
6. Merrick GS, Butler WM, Wallner KE, Galbreath RW, Lief JH, Allen Z et al: Impact of supplemental external beam radiotherapy and/or androgen deprivation therapy on biochemical outcome after permanent prostate brachytherapy. Int J Radiat Oncol Biol Phys 2005; **61:** 32.
7. Guideline for the management of clinically localized prostate cancer: 2007 update: American Urological Association Prostate Cancer Clinical Guidelines Panel, 2007.
8. Formenti SC, Lieskovsky G, Skinner D, Tsao-Wei DD, Groshen S and Petrovich Z: Update on impact of moderate dose of adjuvant radiation on urinary continence and sexual potency in prostate cancer patients treated with nerve-sparing prostatectomy. Urology 2000; **56:** 453.
9. Wei JT, Dunn RL, Sandler HM, McLaughlin PW, Montie JE, Litwin MS et al: Comprehensive comparison of health-related quality of life after contemporary therapies for localized prostate cancer. J Clin Oncol 2002; **20:** 557.
10. Black PC, Basen-Engquist K, Wang X, Swartz RJ, Eddings T, Matin SF et al: A randomized prospective trial evaluating testosterone, haemoglobin kinetics and quality of life, during and after 12 months of androgen deprivation after prostatectomy: results from the Postoperative Adjuvant Androgen Deprivation trial. BJU Int 2007; **100:** 63.
11. Speight JL, Elkin EP, Pasta DJ, Silva S, Lubeck DP, Carroll PR et al: Longitudinal assessment of changes in sexual function and bother in patients treated with external beam radiotherapy or brachytherapy, with and without neoadjuvant androgen ablation: data from CaPSURE. Int J Radiat Oncol Biol Phys 2004; **60:** 1066.
12. Cooperberg MR, Broering JM, Litwin MS, Lubeck DP, Mehta SS, Henning JM et al: The contemporary management of prostate cancer in the United States: lessons from the cancer of the prostate strategic urologic research endeavor (CapSURE), a national disease registry. J Urol 2004; **171:** 1393.
13. Ware JE Jr and Gandek B: Overview of the SF-36 Health Survey and the International Quality of Life Assessment (IQOLA) Project. J Clin Epidemiol 1998; **51:** 903.
14. Litwin MS, Hays RD, Fink A, Ganz PA, Leake B and Brook RH: The UCLA Prostate Cancer Index: development, reliability, and validity of a health-related quality of life measure. Med Care 1998; **36:** 1002.
15. Greenfield S, Apolone G, McNeil BJ and Cleary PD: The importance of co-existent disease in the occurrence of postoperative complications and one-year recovery in patients undergoing total hip replacement. Comorbidity and outcomes after hip replacement. Med Care 1993; **31:** 141.

16. Krupski T, Petroni GR, Bissonette EA and Theodorescu D: Quality-of-life comparison of radical prostatectomy and interstitial brachytherapy in the treatment of clinically localized prostate cancer. Urology 2000; **55:** 736.
17. Merrick GS, Butler WM, Wallner KE, Galbreath RW, Kurko B and Cleavinger S: Rectal function following brachytherapy with or without supplemental external beam radiation: results of two prospective randomized trials. Brachytherapy 2003; **2:** 147.
18. Petit JH, Gluck C, Kiger WS 3rd, Laury Henry D, Karasiewicz C, Talcott JA et al: Androgen deprivation-mediated cytoreduction before interstitial brachytherapy for prostate cancer does not abrogate the elevated risk of urinary morbidity associated with larger initial prostate volume. Brachytherapy 2007; **6:** 267.
19. Moinpour CM, Hayden KA, Unger JM, Thompson IM Jr, Redman MW, Canby-Hagino ED et al: Health-related quality of life results in pathologic stage C prostate cancer from a Southwest Oncology Group trial comparing radical prostatectomy alone with radical prostatectomy plus radiation therapy. J Clin Oncol 2008; **26:** 112.
20. Namiki S, Takegami M, Kakehi Y, Suzukamo Y, Fukuhara S and Arai Y: Analysis linking UCLA PCI with Expanded Prostate Cancer Index Composite: an evaluation of health related quality of life in Japanese men with localized prostate cancer. J Urol 2007; **178:** 473.
21. Wilt TJ, MacDonald R, Rutks I, Shamliyan TA, Taylor BC and Kane RL: Systematic review: comparative effectiveness and harms of treatments for clinically localized prostate cancer. Ann Intern Med 2008; **148:** 435.

EDITORIAL COMMENT

This article from the exceptionally well studied CaPSURE cohort insightfully evaluates HRQOL changes associated with multimodality treatment for early stage prostate cancer. Brachytherapy with external radiotherapy or ADT was associated with worse outcomes than brachytherapy monotherapy. This observation confirms previously reported findings from a consortium of academic medical centers and, importantly, extends the finding to the community practice setting.[1]

Because differences in sexual outcome between patients who received ADT and those who did not were worst early after ADT and decreased at later followup, the authors conclude that ADT effects are transient. However, an alternative explanation (equally supported by the reported data) is that sexual side effects of ADT are durable, but that differences between combination therapy and radiation monotherapy decrease with time because sexual dysfunction consequent to radiotherapy can eventually deteriorate to a level similar to that observed more immediately after adjuvant ADT.

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1. Sanda MG, Dunn RL, Michalski J, Sandler HM, Northouse L, Hembroff L et al: Quality of life and satisfaction with outcome among prostate-cancer survivors. N Engl J Med 2008; **358:** 1250.