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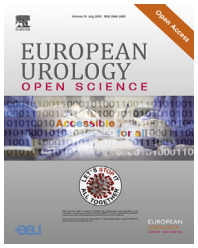

European Association of Urology

Prostate Cancer

Impact of Health-related Quality of Life and Prediagnosis Risk of Major Depressive Disorder on Treatment Choice in Low- and Intermediate-Risk Prostate Cancer

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Abstract

Background: Treatment for low-risk (LR), favorable intermediate-risk (FIR), and unfavorable intermediate-risk (UIR) prostate cancer (PC) is complicated by clinical equipoise between multiple options. It is unknown how prediagnosis health-related quality of life (HRQoL) and major depressive disorder (MDD) risk impact treatment decisions.

Objective: To analyze associations of patient-reported HRQoL and MDD risk with treatment for LR, FIR, and UIR PC patients.

Design, setting, and participants: Using the Surveillance, Epidemiology and End Results and Medicare Health Outcomes Survey–linked database, we identified 1678 PC patients (498 with LR, 685 with FIR, and 495 with UIR) aged ≥65 yr and diagnosed between 2004 and 2015, who completed the health outcomes survey ≤24 mo before diagnosis.

Outcome measurements and statistical analysis: HRQoL was measured by physical (PCS) and mental (MCS) component summaries of the Medical Outcomes Study Short Form 36 (SF-36) and Veterans RAND 12-item (VR-12) health survey instruments. MDD risk was derived from survey items screening for depressive symptoms. Associations with treatment choice were assessed by multivariable multinomial logistic regression.

Results and limitations: LR patients with higher PCS scores were more likely to receive radiation than surgery (adjusted odds ratio [AOR] 1.5 [95% confidence interval {CI}: 1.1–2.1; p = 0.02]). FIR patients with MDD risk were more likely to receive neither treatment than surgery or radiation (surgery: AOR 2.6 [95% CI: 1.1–6.2; p = 0.03]; radiation: AOR 2.2 [95% CI: 1.2–4.2; p = 0.01]). UIR patients with MDD risk were more likely to undergo radiation than surgery (AOR 2.3 [95% CI: 1.0–4.9; p =0.04]). Additionally, higher PCS scores were associated with receipt of surgery compared with neither treatment (AOR 1.5 [95% CI: 1.1–2.0; p =0.01]). This study is limited by its retrospective design.

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Conclusions: Older PC patients with MDD risk received less invasive treatments in the FIR and UIR groups. Higher PCS scores were associated with treatment modality in LR and UIR patients. HRQoL and MDD risk impact treatment choice, warranting additional study.

Patient summary: Treatment of prostate cancer requires thoughtful decision-making processes. This study shows that both pretreatment mental status and pretreatment physical status affect treatment decisions, and should be considered during counseling.

1. Introduction

Prostate cancer (PC) is the second most common malignancy diagnosed globally in men and accounts for more than one in 10 cancer diagnoses across genders. Seventy percent of PCs occur in men aged 65 yr and older [1]. More than three-quarters of patients present with either low-risk (LR) or intermediate-risk disease [2]. As such, there is a need to identify factors that aid in shared decision making for older patients.

There are many treatment options for LR and intermediate-risk PC with excellent survival outcomes. For LR and favorable intermediate-risk (FIR) PC, definitive treatment options include radical prostatectomy, external beam radiation therapy, or brachytherapy alone. Expectant management is also possible, including active surveillance or watchful waiting (usually reserved for patients with life expectancy $<$10 yr) [3]. For unfavorable intermediate-risk (UIR) PC, either prostatectomy or external beam radiation with or without brachytherapy boost is recommended. Expectant management is not recommended for patients with life expectancies $>$10 yr. There is significant variation among providers in treatment recommendations (eg, by specialty and by practice environment) [4]. This array of choices increases emphasis on patient preference in treatment decision making, which may reflect priorities related to healthcare-related quality of life (HRQoL), risk of disease progression, side effects, and convenience.

Depressive symptoms affect 10–25% of older adults [5]. After PC diagnosis, patients experience a reduction in HRQoL, and on average, a third of patients experience depression [6,7]. Depressive symptoms and HRQoL are associated with worse cancer outcomes across many cancers, including PC [8,9]. Nonetheless, the role of depressive symptoms and HRQoL in PC treatment decisions is not fully understood. This question is salient for older adults, among whom depression follows a unique course, characterized by increased chronicity, risk of relapse, and comorbid physical conditions [10]. Additionally, HRQoL is highly relevant to decision making in older adults who develop more comorbid physical conditions with age. We therefore sought to examine how prospectively assessed prediagnosis depressive symptoms and HRQoL affect decision making among older patients with LR, FIR, and UIR PC.

2. Patients and methods

2.1. SEER-MHOS dataset

The Surveillance, Epidemiology and End Results- Medicare Health Outcomes Survey (SEER-MHOS) database links clinical data from the SEER population-based cancer registry with HRQoL data from Medicare enrollees through the MHOS, providing a tool to study cancer-related treatment choices and patient-reported outcomes for adults aged $\geq$65 yr receiving Medicare benefits [11]. The SEER database comprises data collected from population-based registries covering approximately 30% of the US population [12]. The MHOS includes self-reported socioeconomic, demographic, comorbidity, health, and functional status information. It has been administered annually since 1998 to randomly selected Medicare managed care beneficiaries, with follow-up surveys every 2 yr for selected participants with a consistent managed care plan. Response rates for SEER-linked data are reported at 64.1–71.6% for baseline and at 76.3–84.9% for follow-up surveys [11]. This study was exempt from review by the UCLA Institutional Review Board.

2.2. Cohort assembly

The inclusion criteria were (1) age $\geq$65 yr, (2) pathologically confirmed PC diagnosed in 2004–2015, and (3) completion of the MHOS within 24 mo before diagnosis. This time interval was chosen to maximize the number of participants while reducing duplicate surveys. For the few participants with multiple responses to the survey in the 24 mo before diagnosis, the response closest to the date of diagnosis was chosen. Participants were excluded if they had a prior cancer diagnosis including PC.

Risk groups were defined as follows: LR patients had stage T1-T2a, Gleason score (GS) of 6, and prostate-specific antigen (PSA) $<$10; FIR patients had only one intermediate-risk feature of stage T2b-T2c, GS 7, or PSA 10–20; and UIR patients had two to three intermediate-risk features of stage T2b-T2c, GS 7, or PSA 10–20. Patients with stage labeled T2 NOS were stratified based on Gleason score and PSA (LR: GS 6 and PSA $<$ 10; FIR: GS 6 and PSA 10–20 or GS 7 and PSA $<$ 10; and UIR: GS 7 and PSA 10–20). All patients with T3, GS $>$ 7, or PSA $>$ 20 were excluded. Percent positive biopsy cores was excluded from risk stratification because it is available in the SEER data after 2010 only.

2.3. SEER-MHOS measures

As described previously, participants were categorized as having depressive symptoms, and therefore being at risk for major depressive disorder (MDD), if they met one of two criteria: (1) answered “yes” to the question “in the past year, have you had 2 weeks or more during which you felt sad, blue, or depressed; or when you lost interest or pleasure in things that you usually cared about or enjoyed?” or (2) answered “yes” to both “in the past year, have you felt depressed or sad much of the time?”

Table 1 – Patient characteristics by risk group.

Characteristics		Total sample, *n* (%)	LR, *n* (%)	FIR, *n* (%)	UIR, *n* (%)	*p* value*
No. of participants		1678	498	685	495	
Age (yr)	65–69	405 (24.1)	135 (27.1)	159 (23.2)	111 (22.4)	**0.02**
	70–74	684 (40.8)	209 (42.9)	283 (41.3)	192 (38.8)	
	75–79	438 (26.1)	116 (23.3)	192 (28.0)	130 (26.3)	
	80+	151 (9.0)	38 (7.6)	51 (7.4)	62 (12.5)	
Race	Black	243 (14.5)	79 (15.9)	104 (15.2)	60 (12.1)	0.4
	White	1269 (75.6)	370 (74.3)	519 (75.8)	380 (76.8)	
	Other	166 (9.9)	49 (9.8)	62 (9.1)	55 (11.1)	
Smoking status	Yes	159 (9.5)	47 (9.4)	60 (8.8)	52 (10.5)	09
	No	1446 (86.2)	429 (86.1)	596 (87.0)	421 (85.1)	
	Unknown	73 (4.4)	22 (4.4)	29 (4.2)	22 (4.4)	
Marital status	Married	1101 (65.6)	327 (65.7)	447 (65.3)	327 (66.1)	0.4
	Not married	345 (20.6)	112 (22.5)	132 (19.3)	101 (20.4)	
	Other	232 (13.8)	59 (11.8)	106 (15.5)	67 (13.5)	
Education	<High school	389 (23.2)	118 (23.7)	152 (22.2)	119 (24.0)	1.0
	High school	433 (25.8)	134 (26.9)	174 (25.4)	125 (25.3)	
	College	812 (48.4)	233 (46.8)	340 (49.6)	239 (48.3)	
	Unknown	44 (2.6)	13 (2.6)	19 (2.8)	12 (2.4)	
Income ($)	<20 000	465 (27.71)	95 (19.1)	152 (22.2)	116 (23.4)	**0.04**
	20 000–39 999	363 (21.63)	164 (32.9)	170 (24.8)	131 (26.5)	
	40 000–79 999	180 (10.73)	103 (20.7)	141 (20.6)	107 (21.6)	
	>80 000	351 (20.92)	45 (9)	90 (13.1)	45 (9.1)	
	Unknown	319 (19.01)	91 (18.3)	132 (19.3)	96 (19.4)	
Survey by proxy	Proxy	149 (8.9)	44 (8.8)	65 (9.5)	40 (8.1)	0.8
	Self	1438 (85.7)	423 (84.9)	585 (85.4)	430 (86.9)	
	Unknown	91 (5.4)	31 (6.2)	35 (5.1)	25 (5.1)	
Comorbidities	0–1	882 (52.7)	267 (53.9)	339 (49.6)	276 (55.8)	0.2
	2	318 (19.0)	92 (18.6)	133 (19.5)	93 (18.8)	
	3+	473 (28.3)	136 (27.5)	211 (30.9)	126 (25.5)	
Region	Midwest	173 (10.3)	41 (8.2)	77 (11.3)	55 (11.1)	**0.001**
	Northeast	291 (17.4)	107 (21.5)	122 (17.8)	62 (12.6)	
	South	387 (23.1)	124 (24.9)	159 (23.2)	104 (21.1)	
	West	825 (49.2)	226 (45.4)	326 (47.7)	273 (55.3)	
Diagnosis year	2004–2006	300 (17.9)	91 (18.3)	119 (17.4)	90 (18.2)	0.2
	2007–2009	418 (24.9)	123 (24.7)	182 (26.6)	113 (22.8)	
	2010–2013	699 (41.7)	222 (44.6)	269 (39.3)	208 (42)	
	2014–2015	261 (15.6)	62 (12.4)	115 (16.8)	84 (17)	
MDD risk	No	1472 (87.7)	426 (85.5)	607 (88.6)	439 (88.7)	0.2
	Yes	206 (12.2)	72 (14.5)	78 (11.4)	56 (11.3)	
Treatment	Neither	452 (26.9)	153 (30.7)	179 (26.1)	120 (24.2)	<**0.001**
	Radiation	877 (52.3)	279 (56.0)	391 (57.1)	207 (41.8)	
	Surgery	349 (20.8)	66 (13.3)	115 (16.8)	168 (33.9)	

FIR = favorable intermediate risk; LR = low risk; MDD = major depressive disorder; UIR = unfavorable intermediate risk.
* Differences of patient characteristics across risk groups were assessed using chi-square tests. Boldface indicates $p < 0.05$.

and to "have you ever had two years or more in your life when you felt depressed or sad most days, even if you felt okay sometimes?" and also responded at least "some of the time" to the question "how much of the time during the past 4 weeks have you felt downhearted and blue?" [13–15].

HRQoL was derived from physical (PCS) and mental (MCS) component summary scores of the Medical Outcomes Study Short-Form 36 Health Status Survey (SF-36; administered before 2005) and Veterans RAND 12-item Health survey (VR-12; administered after 2005). PCS and MCS data have been rescored to make data from before and after 2005 equivalent, with imputed scores available within the dataset. Higher scores reflect better HRQoL, and ≥5 points represent a clinically meaningful difference. All predictor variables were extracted from MHOS responses completed within 24 mo before diagnosis.

2.4. Statistical analysis

Patient characteristics and study variables were summarized using frequency (%) or mean and standard deviation, unless otherwise noted. MDD risk was modeled as binary. PCS and MCS were modeled as continuous, with odds ratios and adjusted odds ratios (AORs) presented per 10-point increase. Associations between patient characteristics and MDD risk were analyzed using chi-square tests, while analysis of variance was used for the associations with mean PCS or MCS scores.

Univariable and multivariable multinomial logistic regression models were used to assess the associations between individual predictors of interest (MDD risk, PCS, and MCS) and treatment received (radiation, surgery, or neither). Multivariable models were adjusted for all prespecified covariates regardless of statistical significance on univariable analyses. Statistical analysis was performed using SPSS version 25 (IBM Corp., Armonk, NY, USA), and an alpha level of 0.05 was used for all tests.

3. Results

3.1. Participant characteristics

We identified 1678 patients who had completed MHOS surveys within 24 mo before diagnosis. Of these patients,

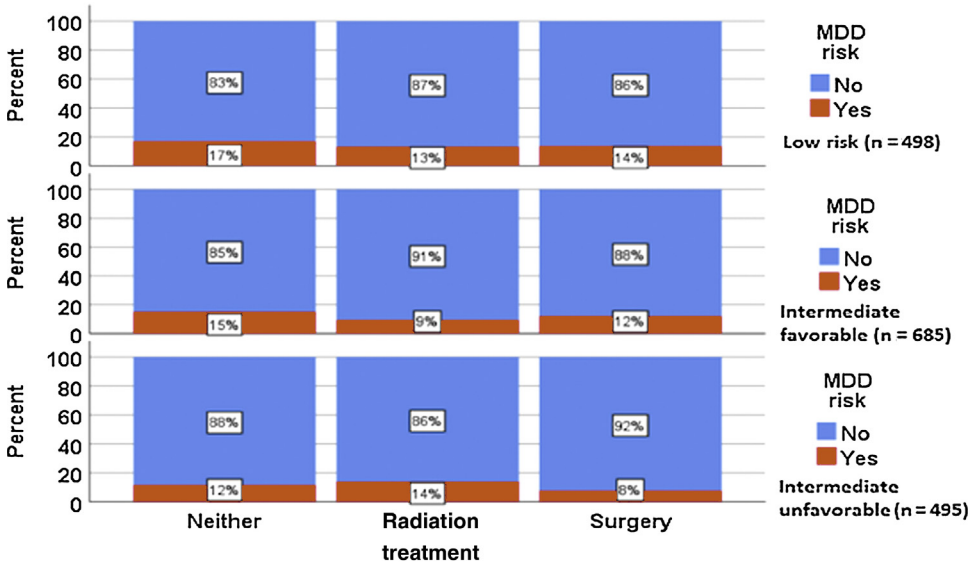

Fig. 1 – Distribution of treatment received by participants with low-risk, favorable intermediate-risk, and unfavorable intermediate-risk prostate cancer among those at risk for major depressive disorder (MDD) versus those not at risk for MDD within 24 mo before diagnosis.

498 were LR, 685 were FIR, and 495 were UIR patients. See Table 1 for distribution of patient characteristics by risk group and Fig. 1 for distribution of MDD risk by risk group.

Overall, 12.3% were at risk for MDD prediagnosis. MCS and PCS scores were 53.5 (standard deviation [SD] = 9.7) and 43.8 (SD = 10.6), respectively. MDD risk, MCS, and PCS differed significantly based on age, race, marital status, level of education, income, completion of survey by proxy, and number of comorbidities. PCS score additionally differed based on smoking status and geographic region, whereas MDD risk additionally differed based on diagnosis year (Table 2).

3.2. Associations between prediagnosis MDD risk, MCS and PCS scores, and treatment received for LR PC

Among older men with LR PC, 14.5% (n = 72) had MDD risk. There was no significant association between MDD risk and treatment choice (Table 3).

The mean prediagnosis MCS score among LR patients was 53.0 (SD = 9.6). Unadjusted multivariable analysis showed a significant association for increased MCS with a higher likelihood of radiation than surgery (AOR 1.3 [95% confidence interval {CI}: 1.0–1.7; p = 0.03]; Table 3). However, after adjustment for prespecified covariates, this association was not significant.

The mean prediagnosis PCS score among LR patients was 44.0 (SD = 10.6). Those with higher PCS scores were more likely to receive radiation than surgery (AOR 1.5 [95% CI: 1.1–2.1; p = 0.02]; Table 3).

3.3. Associations between prediagnosis MDD risk, MCS and PCS scores, and treatment received for FIR PC

Among older men with FIR PC, 11.4% (n = 78) were at risk for MDD. Those with MDD risk had an increased likelihood of neither treatment compared with surgery or radiation (surgery: AOR 2.6 [95% CI: 1.1–6.2; p = 0.03]; radiation: AOR 2.2 [95% CI: 1.2–4.2; p = 0.01]; Table 3).

The mean prediagnosis MCS and PCS scores among FIR patients were 53.7 (SD = 9.9) and 43.9 (SD = 10.3), respectively. There were no significant association between MCS or PCS scores and treatment choice (Table 3).

3.4. Associations between prediagnosis MDD risk, MCS and PCS scores, and treatment received for UIR PC

Among older men with UIR PC, 11.3% (n = 56) were at risk for MDD. Those with MDD risk had a significantly increased likelihood of receiving radiation compared with surgery (AOR 2.3 [95% CI: 1.0–5.0; p = 0.04]; Table 3).

The mean prediagnosis MCS score among UIR patients was 53.7 (SD = 9.4). Unadjusted multivariable analysis showed a significant association for increased MCS with a lower likelihood of surgery than radiation (AOR 0.8 [95 CI: 0.6–1.0; p = 0.03]; Table 3). However, after adjustment for prespecified covariates, this association was not significant.

The mean prediagnosis PCS score among UIR patients was 43.5 (SD = 10.9). Unadjusted multivariable analysis showed a significant association for increased PCS with a higher likelihood of surgery than radiation (AOR 1.4 [95% CI: 1.1–1.7; p = 0.003]; Table 3). However, after adjustment for prespecified covariates, this association was not significant. Adjusted multivariable analysis showed that PCS scores were significantly associated with a higher likelihood of surgery than neither treatment (AOR 1.5 [95% CI: 1.1–2.0; p = 0.01]; Table 3).

4. Discussion

Our results show that among older patients with PC, MDD risk is associated with receipt of no treatment compared with either surgery or radiation in the FIR group and receipt

Table 2 – Associations of PCS, MCS, and MDD risk with patient characteristics.

Patient characteristics		PCS, mean (SD)	*p* value*	MCS, mean (SD)	*p* value*	MDD risk, *n* (%)	*p* value*
Age (yr)	65–69	43.9 (10.7)	<**0.001**	52.7 (9.9)	**0.006**	74 (18.3)	<**0.001**
	70–74	44.7 (10.4)		54.2 (9.0)		70 (10.2)	
	75–79	43.6 (10.4)		53.7 (9.7)		41 (9.4)	
	80+	40.0 (11.0)		51.6 (11.2)		21 (13.9	
Race	Black	40.9 (10.4)	<**0.001**	51.5 (10.1)	**0.001**	42 (17.3)	**0.04**
	White	44.2 (10.5)		53.7 (9.6)		146 (11.5)	
	Other	45.0 (11.0)		54.6 (9.4)		18 (10.8)	
Smoking status	Yes	41.8 (10.9)	**0.04**	53.6 (9.8)	0.1	22 (13.8)	0.2
	No	44.0 (10.4)		53.4 (9.6)		180 (12.4)	
	Unknown	43.6 (12.7)		55.8 (10.8)		4 (5.5)	
Marital status	Married	44.5 (10.3)	**0.001**	54.3 (9.1)	<**0.001**	121 (11.0)	**0.02**
	Not married	42.5 (11.1)		51.4 (10.9)		58 (16.8)	
	Other	42.6 (10.8)		52.9 (10.0)		27 (11.6)	
Education	<High school	40.6 (10.9)	<**0.001**	50.8 (11.5)	<**0.001**	71 (18.3)	<**0.001**
	High school	42.9 (10.4)		53.7 (9.9)		54 (12.5)	
	College	45.8 (10.0)		54.7 (8.2)		74 (9.1)	
	Unknown	43.2 (11.2)		53.3 (9.7)		7 (15.9)	
Income ($)	<20 000	38.9 (11.3)	<**0.001**	49.7 (11.5)	<**0.001**	77 (21.2)	<**0.001**
	20 000–39 999	43.2 (10.3)		53.6 (8.9)		71 (15.3)	
	40 000–79 999	46.4 (9.5)		55.6 (7.7)		28 (8.0)	
	>80 000	48.2 (9.0)		55.8 (7.6)		10 (5.6)	
	Unknown	45.1 (9.9)		54.1 (10.3)		20 (6.3)	
Survey by proxy	Proxy	41.2 (11.5)	**0.007**	50.0 (12.9)	<**0.001**	32 (21.5)	**0.001**
	Self	44.0 (10.4)		53.9 (9.2)		161 (11.2)	
	Unknown	44.2 (10.5)		52.3 (9.7)		13 (14.3)	
Comorbidities	0–1	47.9 (8.4)	<**0.001**	55.5 (8.0)	<**0.001**	64 (7.3)	<**0.001**
	2	42.3 (9.7)		53.7 (9.1)		40 (12.6)	
	3+	37.0 (10.9)		49.6 (11.5)		102 (21.6)	
Region	Midwest	44.7 (10.9)	**0.002**	53.9 (10.4)	0.2	18 (10.4)	0.5
	Northeast	44.0 (10.1)		53.4 (9.7)		38 (13.1)	
	South	42.1 (11.0)		52.7 (9.9)		55 (14.2)	
	West	44.4 (10.4)		53.9 (9.3)		95 (11.5)	
Year of diagnosis	2004–2006	43.9 (10.8)	0.2	54.0 (9.4)	0.6	30 (10.0)	<**0.001**
	2007–2009	44.5 (9.9)		53.7 (10.1)		57 (13.6)	
	2010–2013	43.2 (10.8)		53.1 (9.5)		110 (15.7)	
	2014–2015	44.3 (10.7)		53.7 (9.9)		9 (3.4)	

ANOVA = analysis of variance; MCS = mental component summary; MDD = major depressive disorder; PCS = physical component summary; SD = standard deviation.

* Comparisons were made using the one-way ANOVA for PCS and MCS, and the chi-square test for MDD. Boldface indicates $p < 0.05$.

of radiation compared with surgery in the UIR group. Additionally, higher pretreatment physical HRQoL is associated with receipt of radiation (vs surgery) in LR patients and surgery (vs no treatment) in UIR patients. These relationships of PCS and MDD risk with treatment choice were found to be independently associated after adjustment of several factors, including age at diagnosis, race and ethnicity, smoking status, marital status, level of education, income, survey completion by a proxy, number of comorbidities, geographic region, and year of diagnosis. The odds ratios are presented per 10-point increase in PCS or MCS, which is about one SD in both scores for the overall cohort and each risk group. Therefore, the odds ratios are readily interpretable for the clinical context. All statistically significant findings are associated with clinically significant effect sizes.

Although significant on unadjusted analyses in the LR and UIR groups, after adjustment for the above covariates, MCS scores prior to diagnosis were not found to be independently associated with treatment modality. A new diagnosis of PC can have profound effects on patients' sense of mental and physical well-being, which may confound the study of these factors not only on initial treatment choice [16], but also on overall quality of life after treatment. As such, measurement of HRQoL and MDD risk prior to diagnosis is an important strength of this study and constitutes an avenue that has not been explored previously.

Multiple treatment options exist for LR and intermediate-risk PC patients [17]. For LR and FIR, the ProtecT trial showed that prostatectomy, radiation, and active surveillance have comparable overall survival, but increased risk of progression and metastasis in the intermediate-risk group with active surveillance [18]. These findings have led to increased utilization of active surveillance as a primary treatment approach, and it is now the most common management strategy for LR PC [19]. The role of active surveillance in FIR is growing and is supported as an option but remains controversial [20]. For UIR, active surveillance is not recommended for patients with life expectancy of >10 yr and definitive treatment is preferred. Notably, the ProtecT trial was published in 2016, while the patients in our study were diagnosed between 2004 and 2015. Since the beginning of PSA testing in the late 1980s, there has

Table 3 – Associations among prediagnosis MDD risk, MCS and PCS scores, and treatment received.

Risk group	Multinomial outcome	Prediagnosis predictor	Unadjusted		Adjusted[a]	
			OR (95% CI)	*p* value*	OR (95% CI)	*p* value*
LR (*n* = 498)	Neither vs surgery	At risk for MDD	1.3 (0.6–2.9)	0.5	1.8 (0.7–4.8)	0.2
		SF-12 MCS [b]	1.1 (0.9–1.5)	0.4	1.1 (0.8–1.6)	0.6
		SF-12 PCS [b]	1.2 (1.0–1.6)	0.1	1.2 (0.9–1.7)	0.3
	Radiation vs surgery	At risk for MDD	1.0 (0.4–2.1)	0.9	1.3 (0.5–3.2)	0.6
		SF-12 MCS [b]	1.3 (1.0–1.7)	**0.03**	1.4 (1.0–1.0)	0.08
		SF-12 PCS [b]	1.3 (1.0–1.7)	**0.03**	1.5 (1.1–2.1)	**0.02**
	Radiation vs neither	At risk for MDD	0.8 (0.4–1.3)	0.3	0.7 (0.4–1.3)	0.2
		SF-12 MCS [b]	1.2 (1.0–1.5)	0.1	1.3 (1.0–1.6)	0.1
		SF-12 PCS [b]	1.1 (0.9–1.3)	0.5	1.2 (1.0–1.6)	0.1
FIR (*n* = 685)	Neither vs surgery	At risk for MDD	1.3 (0.6–2.6)	0.6	2.6 (1.1–6.2)	**0.03**
		SF-12 MCS [b]	0.9 (0.7–1.2)	0.5	0.9 (0.7–1.2)	0.5
		SF-12 PCS [b]	1.0 (0.8–1.2)	0.7	1.1 (0.8–1.4)	0.7
	Radiation vs surgery	At risk for MDD	0.8 (0.4–1.5)	0.4	1.2 (0.5–2.6)	0.7
		SF-12 MCS [b]	1.0 (0.8–1.3)	0.7	1.0 (0.8–1.3)	0.9
		SF-12 PCS [b]	1.0 (0.8–1.2)	0.6	0.9 (0.7–1.2)	0.5
	Radiation vs neither	At risk for MDD	0.6 (0.3–1.0)	0.05	0.5 (0.2–0.9)	**0.01**
		SF-12 MCS [b]	1.1 (1.0–1.4)	0.1	1.1 (0.9–1.4)	0.3
		SF-12 PCS [b]	1.0 (0.8–1.2)	0.9	0.9 (0.7–1.1)	0.2
UIR (*n* = 495)	Neither vs surgery	At risk for MDD	1.6 (0.7–3.5)	0.3	1.4 (0.5–3.4)	0.5
		SF-12 MCS [b]	0.8 (0.6–1.1)	0.1	1.1 (0.8–1.5)	0.7
		SF-12 PCS [b]	0.6 (0.5–0.8)	**<0.001**	0.7 (0.5–0.9)	**0.01**
	Radiation vs surgery	At risk for MDD	1.9 (1.0–3.9)	0.06	2.3 (1.0–4.9)	**0.04**
		SF-12 MCS [b]	0.8 (0.6–1.0)	**0.03**	0.8 (0.6–1.1)	0.2
		SF-12 PCS [b]	0.7 (0.6–0.9)	**0.003**	0.8 (0.6–1.0)	0.08
	Radiation vs neither	At risk for MDD	1.2 (0.6–2.4)	0.5	1.6 (0.7–3.7)	0.3
		SF-12 MCS [b]	1.0 (0.8–1.2)	0.7	0.8 (0.6–1.0)	0.09
		SF-12 PCS [b]	1.2 (1.0–1.5)	0.06	1.2 (0.9–1.6)	0.2

CI = confidence interval; FIR = favorable intermediate risk; HRQoL = health-related quality of life; LR = low risk; MCS = mental component summary; MDD = major depressive disorder; OR = odds ratio; PCS = physical component summary; SF-36 = Medical Outcomes Study Short Form 36; VR-12 = Veterans RAND 12-Item Health Survey; UIR = unfavorable intermediate risk.

[a] Adjusted for age at diagnosis, race and ethnicity, smoking status, marital status, level of education, income, survey completion by a proxy, number of comorbidities, geographic region, and year of diagnosis.

[b] Per 10-point increase in MCS or PCS scores; higher MCS and PCS scores reflect better self-reported HRQoL.

* Separate multinomial logistic regression models were fit for each predictor of interest. Boldface indicates $p < 0.05$.

been a trend toward less invasive treatment options including active surveillance for LR PC; however, it was not as common as it is today [17,21].

Guidelines for risk stratification differ in whether to separate intermediate-risk patients into those with FIR and UIR. While this distinction is made in the National Comprehensive Cancer Network (NCCN) risk stratification, European Association of Urology (EAU) guidelines are based on a single intermediate-risk group. For the cohort studied here, the NCCN most likely reflects the guiding treatment principles.

Clinical equipoise between treatment approaches has led to significant interest in the factors affecting patient decision making [22–25]. Well-studied factors include provider recommendations, survival, recurrence, adverse effects of treatment, caregiver burden, costs, treatment specifics (duration, invasiveness, etc.), and level of health anxiety [25,26]. These results have been used to develop decision aids and tools that aim to guide patients through their treatment decisions [24,25].

Our study presents a novel finding that for older men with PC, better pretreatment physical status is associated with a higher likelihood of radiation treatment compared with surgery in LR patients and surgery compared with no treatment in UIR patients. One explanation for the preference of radiation over surgery in the low-risk setting is that older men with higher physical HRQoL attempt to preserve their physical status by undergoing a less invasive treatment. In the UIR group, guidelines recommend definitive treatment, explaining the finding that surgery is preferred to no treatment. Men with better physical status may feel able to follow this recommendation because they are more confident in their ability to recover from adverse effects and feel more prepared to tolerate the physical demands of treatment. Providers may feel more comfortable recommending surgery for men with better physical status. Additionally, studies of prediagnosis HRQoL in other cancers have found associations between higher HRQoL and receipt of more invasive treatment (eg, surgery for ovarian cancer [27] and early-stage lung cancer [15]).

Beyond physical status, our data additionally demonstrate that within the range of recommended treatment options, MDD risk is associated with receipt of less invasive modalities: no treatment for FIR patients and radiation rather than surgery in the UIR group. While depression in PC survivors has been studied extensively [7], the role of prediagnosis depression is less understood. In part, this stems from the logistical difficulties of assessing prediagnosis mental health. One study of the SEER-Medicare database analyzed the effect of pre–cancer diagnosis

depression (as measured by Medicare diagnostic codes) on PC treatment choice. Across risk categories, men with prediagnosis depression were more likely to choose expectant management than definitive treatment and, independent of treatment choice, had worse overall survival [28]. An important distinction between this study and the current report is the use of diagnostic codes, which, compared with MDD risk based on screening questions, is a more restrictive criterion. This is reflected in the reported prevalence rate of only 5% for MDD. Despite this difference, the finding that depressed men were more likely to undergo expectant management than definitive treatment is consistent with our results.

There are multiple possible explanations for the association between MDD risk and treatment. For patients, depression may affect motivation to undertake long or invasive treatments. Depressive symptoms may also occur in the context of limited social support. For providers, recognizing depressive symptoms in patients may influence perceptions of patient values, likelihood of adherence, and treatment tolerability.

Our study has several limitations. First, due to the retrospective observational nature of this study, we cannot exclude the possibility of unobserved confounders within these heterogeneous populations. Unmeasured factors, such as general health status, prediagnosis urinary symptoms, or measurement of exercise tolerance before surgery, may be strongly associated with self-reported HRQoL and may explain the differences in treatment. Provider recommendations and the specialty of the provider consulted have been shown to have significant effects on treatment choice, although this information is unavailable in the SEER-MHOS database. Second, the SF-36 and VR-12 are standardized tools that may not be sufficiently sensitive to detect clinically meaningful changes in individual mental status. This may partially explain why association between treatment choice and depressive symptoms did not translate into significant associations with prediagnosis MCS scores after adjustment for prespecified patient characteristics. Third, the SEER-MHOS database includes percent positive biopsy cores after 2010 only, and therefore this variable was not included in the risk stratification. Finally, future research is needed to expand on this study by investigating treatment decision making in PC for younger patients among whom depression is common.

5. Conclusions

MDD risk and HRQoL prior to the diagnosis of LR and intermediate-risk PC impact treatment choice. Additional study is warranted to explore the potential associations between mental health and treatment choice, as well as the mechanisms by which HRQoL affects decision making. Awareness of these effects may improve approaches to counseling and the creation of decision aids.

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Study concept and design: Raldow, Riskin-Jones.
Acquisition of data: Raldow.
Analysis and interpretation of data: Raldow, Riskin-Jones, Kishan, Grogan.
Drafting of the manuscript: Riskin-Jones, Raldow.
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CRediT authorship contribution statement

Hannah Riskin-Jones: Conceptualization, Writing - original draft, Writing - review & editing. **Tristan Grogan:** Formal analysis, Visualization, Data curation, Writing - review & editing. **Amar Kishan:** Writing - review & editing. **Ann Raldow:** Conceptualization, Writing - original draft, Writing - review & editing, Resources, Supervision, Project administration.

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