ONCOLOGY

Comorbidity Prevalence and Impact on Quality of Life in Gay and Bisexual Men Following Prostate Cancer Treatment

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ABSTRACT

Introduction: Studies have demonstrated worse health related quality of life (HRQOL) outcomes in gay and bisexual men (GBM) following prostate cancer treatment compared to heterosexual men potentially due to differences in comorbidity burden.

Aim: To establish the prevalence of comorbidities and their association with HRQOL metrics in GBM following prostate cancer treatment.

Methods: We evaluated HRQOL and prevalence of comorbidities in 193 GBM from the United States and Canada in a cross-sectional, online survey: the Masked for Review. HRQOL was measured with the Expanded Prostate Cancer Index Composite (EPIC) and the 12-Item Short Form Health Survey (SF-12).

Main Outcome Measures: Our outcomes included comorbidity prevalence, mean differences for HRQOL scores by comorbidity status, and mean differences for HRQOL by comorbidity count.

Results: GBM were found to have a higher prevalence of blood vessel disease and mental health disorders but lower prevalence of obesity and type 2 diabetes when compared to published data in general prostate cancer populations. Statistically significant reductions in HRQOL metrics were associated with mental health diagnoses, diabetes, and obesity. Increased number of comorbidities was also associated with reductions in HRQOL metrics in nearly all categories.

Conclusion: These results suggest that the worse QOL outcomes in GBM following prostate cancer treatment may be due to differences in comorbidity burden. This study is the first to evaluate the relationship between comorbidities and HRQOL outcomes in GBM. Limitations of this study include a small sample size and cross-sectional study design. If confirmed in larger, longitudinal, clinically confirmed studies, these findings indicate a need to intervene on and consider comorbidities in GBM diagnosed with prostate cancer. **Haggart R, Polter E, Ross M, et al. Comorbidity Prevalence and Impact on Quality of Life in Gay and Bisexual Men Following Prostate Cancer Treatment. Sex Med 2021;9:100439.**

Key Words: Prostate Cancer; Gay Men; Bisexual Men; Homosexual Men; Health Related Quality of Life; EPIC; SF12

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INTRODUCTION

Extrapolating from CDC data, between 124,839 and 174,774 gay and bisexual men (GBM) are living with a diagnosis of prostate cancer making it the most common invasive cancer in GBM and male couples.[1] Only 8 quantitative studies have examined sexual functioning in GBM following prostate cancer treatment, and most report disparities in quality of life outcomes for GBM compared to either heterosexual men or published norms.[2] Differences include worse urinary and hormonal function, and worse hormonal bother, but better sexual function and bother on health related quality of life metrics (HRQOL).[2-4] The explanation for these outcomes needs further study and is most likely multifactorial, but differences in baseline comorbidity is 1 hypothesis.[2,4-10]

Prostate cancer is primarily a disease of the elderly with a median age of diagnosis at.[11] Treatment for prostate cancer involves a shared decision-making process based on the cancer grade, extent of tumor involvement, and patient comorbidities to decide between continued surveillance, prostatectomy, radiation, androgen deprivation therapy, or a combination.[12] Many of these patients have significant comorbidity burden, and a growing body of research has been devoted to determining how comorbidity affects postsurgical outcomes.[13] HRQOL metrics have been studied extensively, typically using the 12-Item Short Form Surveys (SF-12) and Expanded Prostate Cancer Index (EPIC) surveys.[14,15] Having an increased number of comorbidities has been associated with lower sexual, urinary, physical, mental, and overall life satisfaction scores and increased 10 year mortality from both cancer related and other-cause mortality.[16-18] Following treatment in samples of the general population, diabetes has been associated with worse urinary and sexual function,[16,19-22] depression, anxiety, and/or distress with worse urinary and sexual function,[19] cardiovascular disease with worse physical, mental, and bowel scores and slower recovery of physical and sexual functioning,[22] and obesity with worse urinary function.[20]

It is well established that GBM in general have different degrees of comorbidity burden to heterosexual men. GBM are more likely to suffer from disorders of mental health, substance abuse including tobacco and alcohol usage, HIV, hypertension, and type II diabetes.[23-25] They are less likely to be obese than other men.[26] What role, if any, these comorbidities play in HRQOL differences in GBM has not been studied. The purpose of this paper is to report comorbidity prevalence data for GBM who have undergone prostate cancer treatment and to examine any association between comorbidity and HRQOL factors following prostate cancer treatment. Based on previously published prevalence data from the GBM population and HRQOL data on the general population, we hypothesized:

- Disorders of mental health, cardiovascular disease, and type II diabetes will have an increased prevalence and obesity a lower prevalence in GBM prostate cancer patients compared to the general population.
- Mental health disorders, cardiovascular disease, and diabetes will be associated with worse sexual and urinary outcomes and obesity with worse urinary outcomes in GBM following prostate cancer treatment.
- Increased comorbidity burden will be associated with worse HRQOL scores across categories.

METHODS

Participants

Participants included in this study were: (i) gay, bisexual, or other men who have sex with men, (ii) treated for prostate cancer, and (iii) residing in a US zip code or Canadian postal code. The institutional review board of the Masked for Review approved the Masked for Review study protocol. Recruitment for the Masked for Review study survey was conducted online at Masked for Review, a large North American cancer support group and advocacy organization. Masked for Review users who responded to online advertisements were directed to an eligibility survey, followed by a consent process for eligible respondents. For consent, we adapted our published chunked online consent protocol.[27] After screening and consent, participants were immediately directed to the study survey. Screening, consent, and the main study survey were conducted using Qualtrics, a web-based survey service. A cross-validation and deduplication protocol[28] was used to flag and manually investigate suspect surveys. Data collection began October 21, 2015 and ended January 1, 2016 (72 days). Each participant received a $25 gift card as compensation.

In total, there were 502 respondents who began the eligibility survey. A total of 434 (86.5%) passed eligibility, and 417 (96.1%) consented to participate. Prior to analysis, 233 surveys were identified by our protocol as likely invalid or duplicative.[29] In addition, 1 incomplete survey was also removed leaving 193 (99.5%) surveys deemed to be from unique, valid participants.

Measures

The survey was in English and consisted of 15 sections with a total of about 150 items. To minimize participant burden, skip and branch patterns were used to administer only those questions that were relevant to each participant.

Demographics, Sexual Characteristics, and Medical Information. Demographic questions (age, gender, race, ethnicity, and education) were adapted from the US Census. Sexual characteristic questions (relationship status and HIV status) were based on prior research[30,31] Participants were asked to select their prostate cancer treatment from a list of 9.

To assess prevalence of comorbidities, participants were asked if they'd ever been diagnosed with each illness. Comorbidities assessed were: diabetes, excessive weight (eg, obesity), blood vessel diseases (eg, atherosclerosis, high blood pressure, or high

cholesterol), mental health (eg, depression, anxiety, or stress), stroke, neurological diseases (eg, multiple sclerosis, Alzheimer's, or Parkinson's), kidney disease, bladder cancer, hormonal imbalance (including low testosterone), injury to the pelvis, bladder, or spinal cord, or other condition(s) affecting sexual functioning.

Disease Specific Quality of Life. The Expanded Prostate Cancer Index Composite (EPIC) is a comprehensive assessment of prostate cancer-related quality of life. This 50-item scale measured frequency and perceived bother in 4 domains (urinary, bowel, sexual, and hormonal). Each domain and subscale are scored from 0 to 100, with higher scores indicating better health. The EPIC-50 scale has acceptable scale and subscale reliability ($r \geq 0.80$) and internal consistency ($\alpha \geq 0.82$).[3,15] A 5-point difference in each subscale between groups was considered clinically meaningful.[32]

Physical and Mental Quality of Life. The 12-item Short Form Survey (SF-12) is a generic measure of health functioning yielding 2 subscales (mental and physical functioning) which combine to estimate overall health-related quality of life. Each subscale is normed with a mean of 50, with higher scores indicating better health. Two week test−retest reliability for the physical subscale was r = 0.8, and for the mental subscale r =0 .76.[14] A 5-point difference in scores between groups was considered clinically meaningful.[33]

Analysis. Participant demographic, sexual, prostate cancer characteristics, and prevalence of each comorbidity were summarized using means and standard deviations (for continuous variables) or frequencies and percentages (for categorical variables). At analysis, prostate cancer treatment was collapsed into 3 groups (surgery only, radiation only, and other/combination). The normality of each outcome was assessed by visual inspection of histograms. *A priori*, we determined 4 comorbidities most likely to impact quality of life based on prior literature: blood vessel diseases, obesity, diabetes, and mental health.[16,19-22] For those 4 comorbidities, linear regression was used to estimate the bivariate association between each comorbidity and each EPIC overall domain (urinary, sexual, bowel, and hormonal) and SF-12 domain (physical and mental). We also conducted multiple linear regression to estimate the association between each comorbidity and each SF-12 or EPIC domain after adjustment for age, race, time since diagnosis, and prostate cancer treatment. Because obesity may be a confounder of the associations of blood vessel diseases, diabetes, and mental health with quality of life, all analyses for those 3 diagnoses adjusted for obesity.

A summary count of physical comorbidities was created to estimate total comorbidity burden for each participant. Mental health diagnoses were excluded from the comorbidity burden estimate in order to account for potential similarities in participant perceptions of "Mental health diagnoses" vs SF-12 mental health scores. Simple and multiple linear regression models were fit to estimate the crude and adjusted (for age, race, treatment, and time since diagnosis) association between the total number of reported comorbidities and each HRQOL outcome. All analyses were conducted using Stata, version 16 (StataCorp. 2019. *Stata Statistical Software: Release 16*. College Station, TX, USA: StataCorp LLC.).

RESULTS

Participant characteristics are shown in Table 1. Participant ages ranged from 42 to 83, with a median of 63. The average

Table 1. Characteristics of participants

	Mean (SD) or frequency (%)
Age	63.4 (8.2)
Sexual orientation	
Gay/ Homosexual	174 (90.2)
Bisexual	15 (7.7)
Other	4 (2.1)
Relationship status	
Single	58 (30.1)
Dating	13 (6.7)
Married or in long-term relationship	103 (53.4)
Widowed, divorced, no longer n a relationship	14 (7.3)
Education level	
Less than bachelor's degree	9 (4.7)
Bachelor's degree	68 (35.2)
Graduate degree	80 (41.5)
White, non-Hispanic Race and Ethnicity	167 (86.5)
Geographic region	
United States West	68 (35.2)
United States Southeast	41 (2.1)
United States Midwest	28 (14.5)
United States Northeast	45 (23.3)
Canada	11 (5.7)
Years since prostate cancer diagnosis	5.6 (4.6)
Prostate cancer treatment	
Surgery/radical prostatectomy only	99 (51.3)
Radiation only	35 (18.1)
Advanced or systemic treatment	54 (28.0)
Gleason score (N = 161)	
2	2 (1.2)
3	11 (6.8)
4	5 (3.1)
5	5 (3.1)
6	48 (29.8
7	61 (37.9)
8	16 (9.9)
9	11 (6.8)
10	2 (1.2)
PSA (N = 150)	7.58 (6.52)
HIV prevalence	24 (12.4)

Table 2. Prevalence of comorbidities

Comorbidities	N	Prevalence
	193	
Diabetes	24	12.4
Excessive weight (obesity)	39	20.2
Blood vessel diseases (eg, Atherosclerosis, high blood pressure, high cholesterol)	102	52.9
Mental Health (eg, depression, anxiety, or stress)	90	46.6
Stroke	13	6.7
Neurological diseases	4	2.1
Kidney disease	13	6.7
Bladder cancer	6	3.1
Hormonal imbalance	37	19.2
Pelvis, bladder, spinal cord injury	9	4.7
Other	35	18.1

participant was white and non-Hispanic, gay or homosexual identified, and had at least a bachelor's degree. Participants on average had 5.6 years since prostate treatment. 51.3 percent were treated with surgery only, 18.1 percent received only brachytherapy or external beam radiation, and the remaining received combined or systemic treatments. The most prevalent comorbidities were blood vessel diseases (52.9%), mental health (46.6%), and obesity (20.2%) (Table 2).

In bivariate analyses, nearly all HRQOL scores were lower for participants with each comorbidity compared to those without. Clinically meaningful reductions in some HRQOL scales persisted for participants with mental health diagnoses, diabetes, and obesity following adjustment for covariates. Participants reporting mental health diagnoses had lower scores on the SF-12 Mental (Adjusted Mean Difference [AMD]: 7.84, 95% Confidence Interval [CI]: -10.93, -4.74) and EPIC Hormonal (AMD -12.29, -16.83, -7.74) Scales. Increased comorbidity burden was associated with significantly lower HRQOL scores following adjustment in all categories except for SF-12 mental and EPIC sexual (Tables 3 and 4).

Table 4. Association of comorbidity "Count" with quality of life scores*

	Mean difference (crude)	Mean difference (adjusted)†
SF-12 Physical	-2.15 (-3.00, 1.29)	**-1.58 (-2.48, -0.68)**
SF-12 Mental	0.12 (-1.06, 1.31)	-0.25 (-1.49, 0.99)
EPIC Urinary	**-2.97 (-4.82, -1.12)**	**-2.87 (-4.90, -0.83)**
EPIC Sexual	**-3.16 (-5.39, -0.94)**	-2.20 (-4.54, 0.14)
EPIC Bowel	**-2.10 (-3.43, -0.76)**	**-2.03 (-3.40, -0.65)**
EPIC Hormonal	**-2.43 (-4.19, -0.66)**	**-2.06 (-3.89, -0.23)**

*Bold values are statistically significant at $P < .05$. Participants were compared using linear regression.
†Model adjusted for for age, race, time since diagnosis, and prostate cancer treatment. Because obesity may be a confounder of the associations of blood vessel diseases, diabetes, and mental health with quality of life, all analyses for those 3 diagnoses adjusted for obesity.

DISCUSSION

This is the first study to assess the association between comorbidities and HRQOL scores for GBM prostate cancer survivors. Our findings confirmed our overall hypothesis that different comorbidity burdens may partially explain disparities GBM experience in HRQOL after prostate cancer.

Table 3. Mean differences and 95% confidence intervals for quality of life scores by comorbidity status*

		Blood vessel diseases	Mental health	Diabetes	Obesity
		Mean difference (95% Confidence Interval)			
SF-12† Physical	Crude	**-4.18 (-6.61, -1.75)**	-1.55 (-4.06, 0.96)	**-4.20 (-7.93, -0.47)**	**-5.17 (-8.19, -2.16)**
	Adjusted§	-2.18 (-4.68, 0.31)	-1.68 (-4.11, 0.74)	-0.94 (-4.67, 2.78)	**-4.32 (-7.30, -1.34)**
SF-12† Mental	Crude	2.93 (-0.31, 6.17)	**-8.42 (-11.48, -5.37)**	4.54 (-0.34, 9.43)	-2.15 (-6.20, 1.89)
	Adjusted§	2.74 (-0.66, 6.14)	**-7.84 (-10.93, -4.74)**	1.40 (-2.07, 4.88)	-1.65 (-5.70, 2.40)
EPIC‡ Urinary	Crude	-3.21 (-8.39, 1.96)	-4.44 (-9.62, 0.74)	**-9.98 (-17.71, -2.26)**	-4.30 (-10.73, 2.12)
	Adjusted	-1.70 (-7.43, 4.03)	-4.60 (-10.12, 0.91)	-7.80 (-16.20, 0.60)	-4.04 (-10.83, 2.74)
EPIC‡ Sexual	Crude	-3.64 (-9.83, 2.55)	-3.15 (-9.36, 3.07)	-2.86 (-12.3, 6.54)	-5.87 (-13.55, 1.82)
	Adjusted§	0.79 (-5.73, 7.32)	-3.96 (-10.26, 2.33)	1.20 (-8.45, 10.86)	-4.63 (-12.35, 3.09)
EPIC‡ Bowel	Crude	-3.41 (-7.13, 0.30)	-3.54 (-7.27, 0.18)	-3.39 (-9.03, 2.26)	-3.38 (-8.01, 1.25)
	Adjusted§	-2.89 (-6.75, 0.98)	-2.92 (-6.66, 0.81)	-2.18 (-7.93, 3.57)	-2.84 (-7.44, 1.77)
EPIC‡ Hormonal	Crude	-1.26 (-6.27, 3.75)	**-11.98 (-16.72, -7.26)**	1.45 (-6.13, 9.04)	**-8.22 (-14.34, -2.10)**
	Adjusted§	2.07 (-2.99, 7.13)	**-12.29 (-16.83, -7.74)**	4.59 (-2.87, 12.06)	**-7.13 (-13.13, -1.13)**

*Bold values are statistically significant at $P < .05$. Participants were compared using t-tests.
†The 12-item Short-Form Health Survey (SF-12) is normed with a mean of 50, with higher scores indicating better quality of life
‡The Expanded Prostate Cancer Index Composite (EPIC) is scored from 0 to 100, with higher scores indicating better quality of life.
§Analyses of blood vessel disease, mental health, and diabetes are adjusted for age, race, years since prostate cancer diagnosis, prostate cancer treatment, and obesity. Analyses of obesity are adjusted for age, race, years since prostate cancer diagnosis, and prostate cancer treatment.

Our first finding is that compared to published samples of mainly heterosexual prostate cancer survivors, the prevalence of diabetes was similar (12% vs 13%),[21] obesity was lower (20% vs 32%),[22,34] blood vessel disease was higher (53% vs 45%),[22] and the percent with a diagnosed mental health disorder was higher (46.6% vs 15−27%).[35] These data support our first hypothesis that prevalence comorbidity differences between GBM and heterosexual men seen in the general population would also be seen in those undergoing prostate cancer treatment, although in our population type 2 diabetes prevalence was similar as opposed to higher as hypothesized.

Our second hypothesis was partially confirmed. Disorders of mental health and obesity were associated with lower adjusted sexual and urinary HRQOL scores as predicted. Blood vessel disease and diabetes were associated with lower adjusted sexual but not urinary HRQOL scores.

We did find statistically significant worse outcomes in those with mental health diagnoses for SF-12 Mental and EPIC Hormonal scores, diabetes for EPIC Urinary scores, and obesity for EPIC Hormonal scores. It should be noted that there are some similarities between the SF-12 Mental and EPIC Hormonal surveys (including overlapping items assessing feeling depressed and lack of energy). Total comorbidity burden was associated with worse HRQL scores in all categories except for SF-12 Mental and EPIC Sexual, partially confirming our third hypothesis.

Our findings suggest that differences in comorbidity burden may partially explain worse HRQOL outcomes in GBM following prostate cancer treatment. Higher prevalence of comorbidities in GBM has been attributed to increased prevalence of substance abuse and HIV in addition to factors associated with being a marginalized population such as increased distress and barriers to healthcare access.[24] Additional features to consider with our study population include 46 percent unmarried or non-long-term relationship status which is higher than studies report for heterosexual patients with numbers reported 22 percent .[36] Single relationship status has been associated with worse quality of life and mortality outcomes following prostate cancer treatment.[36-38] Additionally, 12% of our patients are HIV positive compared to the significantly lower prevalence in the general population of 0.335% per the CDC.[39] HIV is associated with worse prostate cancer mortality, comorbidity burden, and overall HRQOL.[40,41]

Further research with a larger sample size and cohort comparison between GBM and heterosexual men is needed to better elucidate how comorbidity impacts HRQOL differently between these 2 populations. Additional studies may consider evaluating comorbidity burden using validated risk scores such as the Charlson Comorbidity Index (CCI) which has shown promise clinically in predicting perioperative and 10-year post-prostatectomy mortality.[42,43]

There are several limitations to note when interpreting these results. Our small sample size *(N* = 193) limited our statistical power to examine rare but important comorbidities such as neurological disease and bladder cancer. These data are all patient reported which could lead to reporting inaccuracies; although, historically self-reporting of comorbidities has demonstrated similar accuracy to chart review in Urology clinics.[44] Survey questions were asked as broad questions to facilitate a wide range of health literacy. This resulted in comorbidity groupings such as "mental health disorders" which encompass multiple different diseases making it difficult to compare our data to published sources. It is also possible that within these broad categories there are specific conditions that exert more influence on HRQOL metrics than others. We attempted to address this when comparing our prevalence data to published sources by choosing studies with the most similar disease categories. Finally, because this is a cross-sectional survey collected after prostate cancer treatment, we are unable to define the temporal relationships between comorbidity incidence, prostate cancer treatment, and HRQOL.

CONCLUSION

GBM who have undergone prostate cancer treatment have an increased prevalence of blood vessel disease and mental health disorders but lower prevalence of obesity and type 2 diabetes compared to other prostate cancer survivors. Nearly all HRQOL scores were lower for participants with each comorbidity compared to those without, and several were clinically significant. These findings support the argument that the worse HRQOL outcomes in GBM following prostate cancer treatment may be due to differences in pre-existing comorbidity burden. Further research with a larger sample size and cohort comparison between GBM and heterosexual men is needed. These findings, if confirmed in larger, longitudinal, clinically-confirmed studies, may indicate a need to intervene on and consider comorbidities in GBM diagnosed with prostate cancer.

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Studies have demonstrated gay and bisexual men (GBM) following prostate cancer treatment have worse quality of life compared to heterosexual men. We hypothesized that differences in comorbidities could explain this, and our study provides evidence supporting this. If confirmed in larger studies, these findings indicate a need to intervene on and consider comorbidities in GBM diagnosed with prostate cancer.

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STATEMENT OF AUTHORSHIP

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