ORIGINAL RESEARCH

Impact of Race on Outcomes of High-Risk Patients With Prostate Cancer Treated With Moderately Hypofractionated Radiotherapy in an Equal Access Setting

David J. Carpenter, MD[a]; Divya Natesan, MD[a]; R. Warren Floyd[a]; Taofik Oyekunle, MS[a,b]; Donna Niedzwiecki, PhD[a]; Laura Waters[b]; Devon Godfrey, PhD[a,b]; Michael J. Moravan, MD[c]; Rhonda L. Bitting, MD[b,d]; Jeffrey R. Gingrich, MD[b,d]; W. Robert Lee, MD[a]; and Joseph K. Salama, MD[a,b]

Background: Moderately hypofractionated radiotherapy (MHRT) is an accepted treatment for localized prostate cancer; however, limited MHRT data address high-risk prostate cancer (HRPC) and/or African American patients. We report clinical outcomes and toxicity profiles for individuals with HRPC treated in an equal access system.

Methods: We identified patients with HRPC treated with MHRT at a US Department of Veterans Affairs referral center. Exclusion criteria included < 12 months follow-up and elective nodal irradiation. MHRT included 70 Gy over 28 fractions or 60 Gy over 20 fractions. Acute and late gastrointestinal (GI) and genitourinary (GU) toxicities were graded using Common Terminology Criteria for Adverse Events, version 5.0. Clinical endpoints, including biochemical recurrence-free survival (BRFS), distant metastases-free survival (DMFS), overall survival (OS), and prostate cancer–specific survival (PCSS) were estimated using Kaplan-Meier methods. Clinical outcomes, acute toxicity, and late toxicity-free survival were compared between African American and White patients with logistic regression and log-rank testing.

Results: Between November 2008 and August 2018, 143 patients with HRPC were treated with MHRT and followed for a median of 38.5 months; 82 (57%) were African American and 61 were White patients. Concurrent androgen deprivation therapy (ADT) was provided for 138 (97%) patients for a median duration of 24 months. No significant differences between African American and White patients were observed for 5-year OS (73% [95% CI, 58%-83%] vs 77% [95% CI, 60%-97%]; *P* = .55), PCSS (90% [95% CI, 79%-95%] vs 87% [95 % CI, 70%-95%]; *P* = .57), DMFS (91% [95% CI, 80%-96%] vs 81% [95% CI, 62%-91%]; *P* = .55), or BRFS (83% [95% CI, 70%-91%] vs 71% [95% CI, 53%-82%]; *P* = .57), respectively. Rates of acute grade 3+ GU and GI were low overall (4% and 1%, respectively). Late toxicities were similarly favorable with no significant differences by race.

Conclusions: Individuals with HRPC treated with MHRT in an equal access setting demonstrated favorable clinical outcomes that did not differ by race, alongside acceptable rates of acute and late toxicities.

Although moderately hypofractionated radiotherapy (MHRT) is an accepted treatment for localized prostate cancer, its adaptation remains limited in the United States.[1,2] MHRT theoretically exploits α/β ratio differences between the prostate (1.5 Gy), bladder (5-10 Gy), and rectum (3 Gy), thereby reducing late treatment-related adverse effects compared with those of conventional fractionation at biologically equivalent doses.[3-8] Multiple randomized noninferiority trials have demonstrated equivalent outcomes between MHRT and conventional fraction with no appreciable increase in patient-reported toxicity.[9-14] Although these studies have led to the acceptance of MHRT as a standard treatment, the majority of these trials involve individuals with low- and intermediate-risk disease.

There are less phase 3 data addressing MHRT for high-risk prostate cancer (HRPC).[10,12,14-17] Only 2 studies examined predominately high-risk populations, accounting for 83 and 292 patients, respectively.[15,16] Additional phase 3 trials with small proportions of high-risk patients (n = 126, 12%; n = 53, 35%) offer limited additional information regarding clinical outcomes and toxicity rates specific to high-risk disease.[10-12] Numerous phase 1 and 2 studies report various field designs and fractionation plans for MHRT in the context of high-risk disease, although the applicability of these data to off-trial populations remains limited.[18-20]

Furthermore, African American individuals are underrepresented in the trials establishing the role of MHRT despite higher rates of prostate cancer incidence, more advanced disease stage at diagnosis, and higher rates of prostate cancer–specific survival (PCSS) when compared with White patients.[21] Racial disparities across patients with prostate cancer and their management are multifactorial across health care literacy, education level, access to care (including transportation issues), and issues of adherence and distrust.[22-25] Correlation of

Author affiliations can be found at the end of this article.
Correspondence: David Carpenter (david.j.carpenter@duke.edu)

Fed Pract. 2022;39(suppl 3). Published online August 15. doi:10.12788/fp.0305

TABLE 1 Patient Demographic Data by Race

Criteria	African American (n = 82)	White (n = 61)	Total (N = 143)	*P* value
Age, median (IQR), y	65 (62-69)	66 (63-70)	66 (62-70)	.42[a]
Clinical T stage, No. (%)				.37[b]
T1a/2a	55 (67)	34 (56)	89 (62)	
T2b/2c	14 (17)	13 (21)	27 (19)	
T3a/4	13 (16)	14 (23)	27 (19)	
Gleason grade group, No. (%)				.11[b]
1	2 (2)	4 (7)	6 (4)	
2	12 (15	3 (5)	15 (10)	
3	10 (12)	7 (11)	17 (12)	
4	41 (50)	26 (43)	67 (47)	
5	17 (21)	21 (34)	38 (27)	
Radiotherapy				
Duration, median (IQR), d	40.0 (37.0-42.0)	40.0 (38.0-42.0)	40.0 (38.0-42.0)	.34[a]
Total dose, No. (%)				.03[b]
60 Gy	16 (20)	4 (7)	20 (14)	
70 Gy	66 (80)	57 (93)	123 (86)	
High-risk subgroup, No. (%)				.98[b]
Favorable	16 (20)	12 (20)	28 (20)	
Unfavorable	66 (80)	49 (80)	115 (80)	
Before MHRT				
Prostate-specific antigen, median (IQR)	15.0 (8.2-32.6)	11.5 (7.0-22.8)	14.4 (7.8-28.6)	.11[a]
IPSS score, median (IQR)	11.0 (6.0-16.0)	14.0 (10.0-23.0)	12.0 (8.0-17.0)	.02[a]
Urinary medications, No. (%)				.97[b]
None	54 (66)	40 (66)	94 (66)	
≤ 1	28 (34)	21 (34)	49 (34)	
ADT use, No. (%)				.90[b]
Yes	79 (96)	59 (97)	138 (97)	
No	3 (4)	2 (3)	5 (3)	

Abbreviations: ADT, androgen deprivation therapy; MHRT, moderately hypofractionated radiotherapy.
[a]Wilcoxon rank sum test.
[b]χ^2 test.

patient race to prostate cancer outcomes varies greatly across health care systems, with the US Department of Veterans Affairs (VA) equal access system providing robust mental health services and transportation services for some patients, while demonstrating similar rates of stage-adjusted PCSS between African American and White patients across a broad range of treatment modalities.[26-28] Given the paucity of data exploring outcomes following MHRT for African American patients with HRPC, the present analysis provides long-term clinical outcomes and toxicity profiles for an off-trial majority African American population with HRPC treated with MHRT within the VA.

METHODS

Records were retrospectively reviewed under an institutional review board–approved protocol for all patients with HRPC treated with definitive MHRT at the Durham Veterans Affairs Healthcare System in North Carolina between November 2008 and August 2018. Exclusion criteria included < 12 months of follow-up or elective nodal irradiation. Demographic variables obtained included age at diagnosis, race, clinical T stage, pre-MHRT prostate-specific antigen (PSA), Gleason grade group at diagnosis, favorable vs unfavorable high-risk disease, pre-MHRT international prostate symptom score (IPSS), and pre-MHRT urinary medication usage (yes/no).[29]

Concurrent androgen deprivation therapy (ADT) was initiated 6 to 8 weeks before MHRT unless medically contraindicated per the discretion of the treating radiation oncologist. Patients generally received 18 to 24 months of ADT, with those with favorable HRPC (ie, T1c disease with either Gleason 4+4 and PSA < 10 mg/mL or Gleason 3+3 and PSA > 20 ng/mL) receiving 6 months after 2015.[29] Patients were simulated supine in either standard or custom immobilization with a full bladder and empty rectum. MHRT fractionation plans included 70 Gy at 2.5 Gy per fraction and 60 Gy at 3 Gy per fraction. Radiotherapy targets included the prostate and

seminal vesicles without elective nodal coverage per institutional practice. Treatments were delivered following image guidance, either prostate matching with cone beam computed tomography or fiducial matching with kilo voltage imaging. All patients received intensity-modulated radiotherapy. For plans delivering 70 Gy at 2.5 Gy per fraction, constraints included bladder V (volume receiving) 70 < 10 cc, V65 ≤ 15%, V40 ≤ 35%, rectum V70 < 10 cc, V65 ≤ 10%, V40 ≤ 35%, femoral heads maximum point dose ≤ 40 Gy, penile bulb mean dose ≤ 50 Gy, and small bowel V40 ≤ 1%. For plans delivering 60 Gy at 3 Gy per fraction, constraints included rectum V57 ≤ 15%, V46 ≤ 30%, V37 ≤ 50%, bladder V60 ≤ 5%, V46 ≤ 30%, V37 ≤ 50%, and femoral heads V43 ≤ 5%.

Gastrointestinal (GI) and genitourinary (GU) toxicities were graded using Common Terminology Criteria for Adverse Events (CTCAE), version 5.0, with acute toxicity defined as on-treatment < 3 months following completion of MHRT. Late toxicity was defined as ≥ 3 months following completion of MHRT. Individuals were seen in follow-up at 6 weeks and 3 months with PSA and testosterone after MHRT completion, then every 6 to 12 months for 5 years and annually thereafter. Each follow-up visit included history, physical examination, IPSS, and CTCAE grading for GI and GU toxicity.

The Wilcoxon rank sum test and χ^2 test were used to compare differences in demographic data, dosimetric parameters, and frequency of toxicity events with respect to patient race. Clinical endpoints including biochemical recurrence-free survival (BRFS; defined by Phoenix criteria as 2.0 above PSA nadir), distant metastases-free survival (DMFS), PCSS, and overall survival (OS) were estimated from time of radiotherapy completion by the Kaplan-Meier method and compared between African American and White race by log-rank testing.[30] Late GI and GU toxicity-free survival were estimated by Kaplan-Meier plots and compared between African American and White patients by the log-rank test. Statistical analysis was performed using SAS 9.4.

RESULTS

We identified 143 patients with HRPC treated with definitive MHRT between November 2008 and August 2018 (Table 1). Mean age was 65 years (range, 36-80 years); 57% were African American men. Eighty percent of individuals had unfavorable high-risk disease. Median (IQR) PSA was 14.4 (7.8-28.6). Twenty-six percent had grade group 1-3 disease, 47% had grade group 4 disease, and 27% had grade group 5 disease. African American patients had significantly lower pre-MHRT IPSS scores than White patients (mean IPSS, 11 vs 14, respectively; $P = .02$) despite similar rates of preradiotherapy urinary medication usage (66% and 66%, respectively).

TABLE 2 Frequency of Acute Toxicity Events

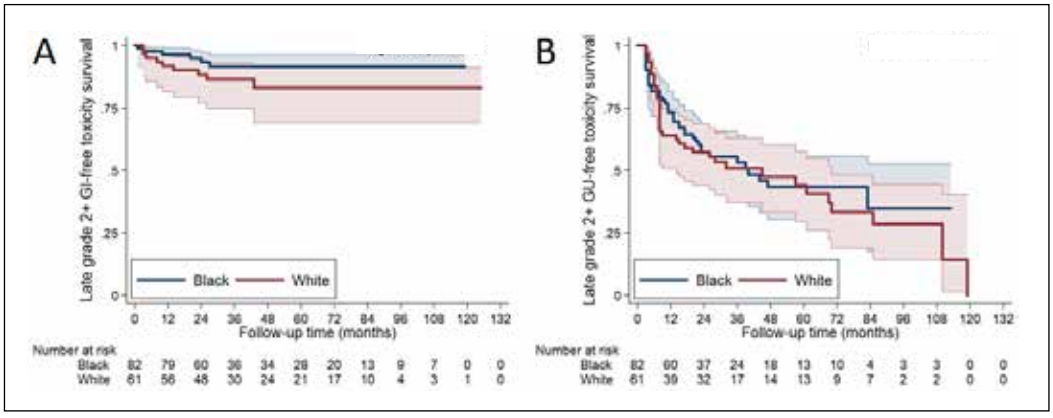
Acute toxicity grades	African American (n = 82)	White (n = 61)	Total (N = 143)	*P* value
Genitourinary, No. (%)				.31
0	19 (23)	18 (30)	37 (26)	
1	22 (27)	11 (18)	33 (23)	
2	36 (44)	31 (51)	67 (47)	
3	5 (6)	1 (2)	6 (4)	
Gastrointestinal, No. (%)				.52
0	70 (85)	48 (79)	118 (83)	
1	6 (7)	9 (15)	15 (10)	
2	5 (6)	3 (5)	8 (6)	
3	1 (1)	1 (2)	2 (1)	

Eighty-six percent received 70 Gy over 28 fractions, with institutional protocol shifting to 60 Gy over 20 fractions (14%) in June 2017. The median (IQR) duration of radiotherapy was 39 (38-42) days, with 97% of individuals undergoing ADT for a median (IQR) duration of 24 (24-36) months. The median follow-up time was 38 months, with 57 (40%) patients followed for at least 60 months.

Grade 3 GI and GU acute toxicity events were observed in 1% and 4% of all individuals, respectively (Table 2). No acute GI or GU grade 4+ events were observed. No significant differences in acute GU or GI toxicity were observed between African American and White patients.

No significant differences between African American and White patients were observed for late grade 2+ GI ($P = .19$) or GU ($P = .55$) toxicity. Late grade 2+ GI toxicity was observed in 17 (12%) patients overall (Figure 1A). One grade 3 and 1 grade 4 late GI event were observed following MHRT completion: The latter involved hospitalization for bleeding secondary to radiation proctitis in the context of cirrhosis predating MHRT. Late grade 2+ GU toxicity was observed in 80 (56%) patients, with late grade 2 events steadily increasing over time (Figure 1B). Nine late grade 3 GU toxicity events were observed at a median

FIGURE 1 Toxicity-Free Survival for African American and White Patients



Abbreviations: GI, gastrointestinal; GU, genitourinary.
The log-rank test did not determine any significant between-group difference (A, *P* = .19; B, *P* = .56).

of 13 months following completion of MHRT, 2 of which occurred more than 24 months after MHRT completion. No late grade 4 or 5 GU events were observed. IPSS values both before MHRT and at time of last follow-up were available for 65 (40%) patients, with a median (IQR) IPSS of 10 (6-16) before MHRT and 12 (8-16) at last follow-up at a median (IQR) interval of 36 months (26-76) from radiation completion.

No significant differences were observed between African American and White patients with respect to BRFS, DMFS, PCSS, or OS (Figure 2). Overall, 21 of 143 (15%) patients experienced biochemical recurrence: 5-year BRFS was 77% (95% CI, 67%-85%) for all patients, 83% (95% CI, 70%-91%) for African American patients, and 71% (95% CI, 53%-82%) for White patients. Five-year DMFS was 87% (95% CI, 77%-92%) for all individuals, 91% (95% CI, 80%-96%) for African American patients, and 81% (95% CI, 62%-91%) for White patients. Five-year PCSS was 89% (95% CI, 80%-94%) for all patients, with 5-year PCSS rates of 90% (95% CI, 79%-95%) for African American patients and 87% (95% CI, 70%-95%) for White patients. Five-year OS was 75% overall (95% CI, 64%-82%), with 5-year OS rates of 73% (95% CI, 58%-83%) for African American patients and 77% (95% CI, 60%-87%) for White patients.

DISCUSSION

In this study, we reported acute and late GI and GU toxicity rates as well as clinical outcomes for a majority African American population with predominately unfavorable HRPC treated with MHRT in an equal access health care environment. We found that MHRT was well tolerated with high rates of biochemical control, PCSS, and OS. Additionally, outcomes were not significantly different across patient race. To our knowledge, this is the first report of MHRT for HRPC in a majority African American population.

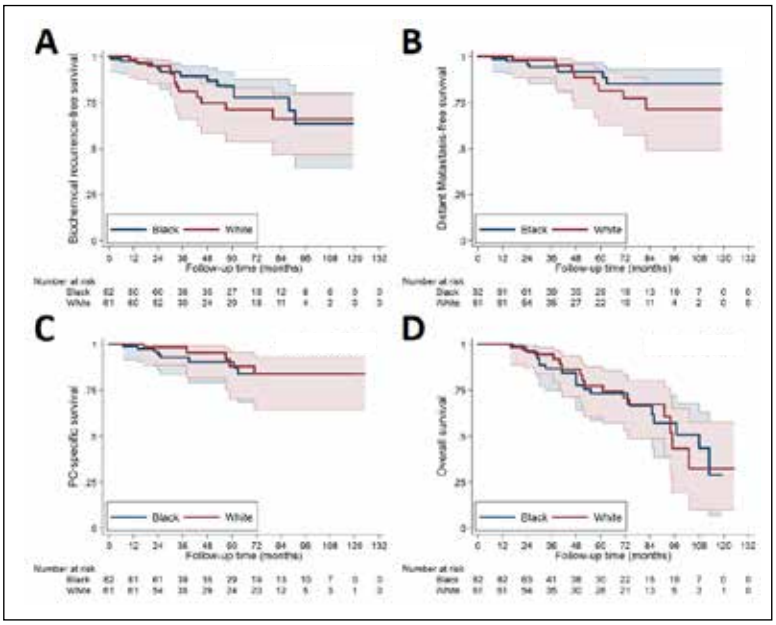
We found that MHRT was an effective treatment for patients with HRPC, in particular those with unfavorable high-risk disease. While prior prospective and randomized studies have investigated the use of MHRT, our series was larger than most and had a predominately unfavorable high-risk population.[12,15-17] Our biochemical and PCSS rates compare favorably with those of HRPC trial populations, particularly given the high proportion of unfavorable high-risk disease.[12,15,16] Despite similar rates of biochemical control, OS was lower in the present cohort than in HRPC trial populations, even with a younger median age at diagnosis. The similarly high rates of non–HRPC-related death across race may reflect differences in baseline comorbidities compared with trial populations as well as reported differences between individuals in the VA and the private sector.[31] This suggests that MHRT can be an effective treatment for patients with unfavorable HRPC.

We did not find any differences in outcomes between African American and White individuals with HRPC treated with MHRT. Furthermore, our study demonstrates long-term rates of BRFS and PCSS in a majority African American population with predominately

unfavorable HRPC that are comparable with those of prior randomized MHRT studies in high-risk, predominately White populations.[12,15,16] Prior reports have found that African American men with HRPC may be at increased risk for inferior clinical outcomes due to a number of socioeconomic, biologic, and cultural mediators.[26,27,32] Such individuals may disproportionally benefit from shorter treatment courses that improve access to radiotherapy, a well-documented disparity for African American men with localized prostate cancer.[33-36] The VA is an ideal system for studying racial disparities within prostate cancer, as accessibility of mental health and transportation services, income, and insurance status are not barriers to preventative or acute care.[37] Our results are concordant with those previously seen for African American patients with prostate cancer seen in the VA, which similarly demonstrate equal outcomes with those of other races.[28,36] Incorporation of the earlier mentioned VA services into oncologic care across other health care systems could better characterize determinants of racial disparities in prostate cancer, including the prognostic significance of shortening treatment duration and number of patient visits via MHRT.

Despite widespread acceptance in prostate cancer radiotherapy guidelines, routine use of MHRT seems limited across all stages of localized prostate cancer.[1,2] Late toxicity is a frequently noted concern regarding MHRT use. Higher rates of late grade 2+ GI toxicity were observed in the hypofractionation arm of the HYPRO trial.[17] While RTOG 0415 did not include patients with HRPC, significantly higher rates of physician-reported (but not patient-reported) late grade 2+ GI and GU toxicity were observed using the same MHRT fractionation regimen used for the majority of individuals in our cohort.[9] In our study, the steady increase in late grade 2 GU toxicity is consistent with what is seen following conventionally fractionated radiotherapy and is likely multifactorial.[38] The mean IPSS difference of 2/35 from pre-MHRT baseline to the time of last follow-up suggests minimal quality of life decline. The relatively stable IPSSs over time alongside the > 50% prevalence of late grade 2 GU toxicity per CTCAE grading seems consistent with the discrepancy noted in RTOG 0415 between increased physician-reported

FIGURE 2 Clinical Outcomes Across Patient Race



Abbreviation: PC, prostate cancer.
The log-rank test did not determine any significant between-group difference (A, $P = .57$; B, $P = .55$; C, $P = .57$; D, $P = .92$).

late toxicity and favorable patient-reported quality of life scores.[9] Moreover, significant variance exists in toxicity grading across scoring systems, revised editions of CTCAE, and physician-specific toxicity classification, particularly with regard to the use of adrenergic receptor blocker medications. In light of these factors, the high rate of late grade 2 GU toxicity in our study should be interpreted in the context of largely stable post-MHRT IPSSs and favorable rates of late GI grade 2+ and late GU grade 3+ toxicity.

Limitations

This study has several inherent limitations. While the size of the current HRPC cohort is notably larger than similar populations within the majority of phase 3 MHRT trials, these data derive from a single VA hospital. It is unclear whether these outcomes would be representative in a similar high-risk population receiving care outside of the VA equal access system. Follow-up data beyond 5 years was available for less than half of patients, partially due to nonprostate cancer–related mortality at a higher rate than observed in HRPC trial populations.[12,15,16] Furthermore, all GI toxicity events were exclusively physician reported, and GU toxicity reporting was limited in the

off-trial setting with not all patients routinely completing IPSS questionnaires following MHRT completion. However, all patients were treated similarly, and radiation quality was verified over the treatment period with mandated accreditation, frequent standardized output checks, and systematic treatment review.[39]

CONCLUSIONS

Patients with HRPC treated with MHRT in an equal access, off-trial setting demonstrated favorable rates of biochemical control with acceptable rates of acute and late GI and GU toxicities. Clinical outcomes, including biochemical control, were not significantly different between African American and White patients, which may reflect equal access to care within the VA irrespective of income and insurance status. Incorporating VA services, such as access to primary care, mental health services, and transportation across other health care systems may aid in characterizing and mitigating racial and gender disparities in oncologic care.

Acknowledgments

Portions of this work were presented at the November 2020 ASTRO conference.[40]

Author affiliations

[a]Duke University School of Medicine, Durham, North Carolina
[b]Durham Veterans Affairs Health Care System, North Carolina
[c]St. Louis Veterans Affairs Health Care System, Missouri
[d]Duke Cancer Institute, Center for Prostate & Urologic Cancers, Duke University, Durham, North Carolina

Author disclosures

The authors report no actual or potential conflicts of interest or outside sources of funding with regard to this article.

Disclaimer

The opinions expressed herein are those of the authors and do not necessarily reflect those of *Federal Practitioner,* Frontline Medical Communications Inc., the US Government, or any of its agencies.

Ethics

The US Department of Veterans Affairs (VA) places legal restrictions on access to veteran's health care data, which includes both identifying data and sensitive patient information. The analytic data sets used for this study are not permitted to leave the VA firewall without a data use agreement. This limitation is consistent with other studies based on VA data. However, VA data are made freely available to researchers behind the VA firewall with an approved VA study protocol. For more information, please visit https://www.virec.research.va.gov or contact the VA Information Resource Center (VIReC) at vog.av@CeRIV.

References

1. Stokes WA, Kavanagh BD, Raben D, Pugh TJ. Implementation of hypofractionated prostate radiation therapy in the United States: a National Cancer Database analysis. *Pract Radiat Oncol.* 2017;7:270-278. doi:10.1016/j.prro.2017.03.011
2. Jaworski L, Dominello MM, Heimburger DK, et al. Contemporary practice patterns for intact and postoperative prostate cancer: results from a statewide collaborative. *Int J Radiat Oncol Biol Phys.* 2019;105(1):E282. doi:10.1016/j.ijrobp.2019.06.1915
3. Miralbell R, Roberts SA, Zubizarreta E, Hendry JH. Dose-fractionation sensitivity of prostate cancer deduced from radiotherapy outcomes of 5,969 patients in seven international institutional datasets: α/β = 1.4 (0.9-2.2) Gy. *Int J Radiat Oncol Biol Phys.* 2012;82(1):e17-e24. doi:10.1016/j.ijrobp.2010.10.075
4. Tree AC, Khoo VS, van As NJ, Partridge M. Is biochemical relapse-free survival after profoundly hypofractionated radiotherapy consistent with current radiobiological models? *Clin Oncol (R Coll Radiol).* 2014;26(4):216-229. doi:10.1016/j.clon.2014.01.008
5. Brenner DJ. Fractionation and late rectal toxicity. *Int J Radiat Oncol Biol Phys.* 2004;60(4):1013-1015. doi:10.1016/j.ijrobp.2004.04.014
6. Tucker SL, Thames HD, Michalski JM, et al. Estimation of α/β for late rectal toxicity based on RTOG 94-06. *Int J Radiat Oncol Biol Phys.* 2011;81(2):600-605. doi:10.1016/j.ijrobp.2010.11.080
7. Dasu A, Toma-Dasu I. Prostate alpha/beta revisited—an analysis of clinical results from 14 168 patients. *Acta Oncol.* 2012;51(8):963-974. doi:10.3109/0284186X.2012.719635 start
8. Proust-Lima C, Taylor JMG, Sécher S, et al. Confirmation of a Low α/β ratio for prostate cancer treated by external beam radiation therapy alone using a post-treatment repeated-measures model for PSA dynamics. *Int J Radiat Oncol Biol Phys.* 2011;79(1):195-201. doi:10.1016/j.ijrobp.2009.10.008
9. Lee WR, Dignam JJ, Amin MB, et al. Randomized phase III noninferiority study comparing two radiotherapy fractionation schedules in patients with low-risk prostate cancer. *J Clin Oncol.* 2016;34(20): 2325-2332. doi:10.1200/JCO.2016.67.0448
10. Dearnaley D, Syndikus I, Mossop H, et al. Conventional versus hypofractionated high-dose intensity-modulated radiotherapy for prostate cancer: 5-year outcomes of the randomised, non-inferiority, phase 3 CHHiP trial. *Lancet Oncol.* 2016;17(8):1047-1060. doi:10.1016/S1470-2045(16)30102-4
11. Catton CN, Lukka H, Gu C-S, et al. Randomized trial of a hypofractionated radiation regimen for the treatment of localized prostate cancer. *J Clin Oncol*. 2017;35(17):1884-1890. doi:10.1200/JCO.2016.71.7397
12. Pollack A, Walker G, Horwitz EM, et al. Randomized trial of hypofractionated external-beam radiotherapy for prostate cancer. *J Clin Oncol.* 2013;31(31):3860-3868. doi:10.1200/JCO.2013.51.1972
13. Hoffman KE, Voong KR, Levy LB, et al. Randomized trial of hypofractionated, dose-escalated, intensity-modulated radiation therapy (IMRT) versus conventionally fractionated IMRT for localized prostate cancer. *J Clin Oncol*. 2018;36(29):2943-2949. doi:10.1200/JCO.2018.77.9868
14. Wilkins A, Mossop H, Syndikus I, et al. Hypofractionated radiotherapy versus conventionally fractionated radiotherapy for patients with intermediate-risk localised prostate cancer: 2-year patient-reported outcomes of the randomised, non-inferiority, phase 3 CHHiP trial. *Lancet Oncol*. 2015;16(16):1605-1616. doi:10.1016/S1470-2045(15)00280-6
15. Incrocci L, Wortel RC, Alemayehu WG, et al. Hypofractionated versus conventionally fractionated radiotherapy for patients with localised prostate cancer (HYPRO): final efficacy results from a randomised, multicentre, open-label, phase 3 trial. *Lancet Oncol*. 2016;17(8):1061-1069. doi.10.1016/S1470-2045(16)30070-5
16. Arcangeli G, Saracino B, Arcangeli S, et al. Moderate hypofractionation in high-risk, organ-confined prostate cancer: final results of a phase III randomized trial. *J Clin Oncol*. 2017;35(17):1891-1897. doi:10.1200/JCO.2016.70.4189

17. Aluwini S, Pos F, Schimmel E, et al. Hypofractionated versus conventionally fractionated radiotherapy for patients with prostate cancer (HYPRO): late toxicity results from a randomised, non-inferiority, phase 3 trial. *Lancet Oncol.* 2016;17(4):464-474. doi:10.1016/S1470-2045(15)00567-7
18. Pervez N, Small C, MacKenzie M, et al. Acute toxicity in high-risk prostate cancer patients treated with androgen suppression and hypofractionated intensity-modulated radiotherapy. *Int J Radiat Oncol Biol Phys.* 2010;76(1):57-64. doi:10.1016/j.ijrobp.2009.01.048
19. Magli A, Moretti E, Tullio A, Giannarini G. Hypofractionated simultaneous integrated boost (IMRT- cancer: results of a prospective phase II trial SIB) with pelvic nodal irradiation and concurrent androgen deprivation therapy for high-risk prostate cancer: results of a prospective phase II trial. *Prostate Cancer Prostatic Dis.* 2018;21(2):269-276. doi:10.1038/s41391-018-0034-0
20. Di Muzio NG, Fodor A, Noris Chiorda B, et al. Moderate hypofractionation with simultaneous integrated boost in prostate cancer: long-term results of a phase I–II study. *Clin Oncol (R Coll Radiol).* 2016;28(8):490-500. doi:10.1016/j.clon.2016.02.005
21. DeSantis CE, Miller KD, Goding Sauer A, Jemal A, Siegel RL. Cancer statistics for African Americans, 2019. *CA Cancer J Clin.* 2019;69(3):21-233. doi:10.3322/caac.21555
22. Wolf MS, Knight SJ, Lyons EA, et al. Literacy, race, and PSA level among low-income men newly diagnosed with prostate cancer. *Urology.* 2006(1);68:89-93. doi:10.1016/j.urology.2006.01.064
23. Rebbeck TR. Prostate cancer disparities by race and ethnicity: from nucleotide to neighborhood. *Cold Spring Harb Perspect Med.* 2018;8(9):a030387. doi:10.1101/cshperspect.a030387
24. Guidry JJ, Aday LA, Zhang D, Winn RJ. Transportation as a barrier to cancer treatment. *Cancer Pract.* 1997;5(6):361-366.
25. Friedman DB, Corwin SJ, Dominick GM, Rose ID. African American men's understanding and perceptions about prostate cancer: why multiple dimensions of health literacy are important in cancercommunication.*JCommunityHealth.*2009;34(5):449-460. doi:10.1007/s10900-009-9167-3
26. Connell PP, Ignacio L, Haraf D, et al. Equivalent racial outcome after conformal radiotherapy for prostate cancer: a single departmental experience. *J Clin Oncol.* 2001;19(1):54-61. doi:10.1200/JCO.2001.19.1.54
27. Dess RT, Hartman HE, Mahal BA, et al. Association of black race with prostate cancer-specific and other-cause mortality. *JAMA Oncol.* 2019;5(1):975-983. doi:10.1200/JCO.2001.19.1.54
28. McKay RR, Sarkar RR, Kumar A, et al. Outcomes of Black men with prostate cancer treated with radiation therapy in the Veterans Health Administration. *Cancer.* 2021;127(3):403-411. doi:10.1002/cncr.33224
29. Muralidhar V, Chen M-H, Reznor G, et al. Definition and validation of "favorable high-risk prostate cancer": implications for personalizing treatment of radiation-managed patients. *Int J Radiat Oncol Biol Phys*. 2015;93(4):828-835. doi:10.1016/j.ijrobp.2015.07.2281
30. Roach M 3rd, Hanks G, Thames H Jr, et al. Defining biochemical failure following radiotherapy with or without hormonal therapy in men with clinically localized prostate cancer: recommendations of the RTOG-ASTRO Phoenix Consensus Conference. *Int J Radiat Oncol Biol Phys*. 2006;65(4):965-974. doi:10.1016/j.ijrobp.2006.04.029
31. Freeman VL, Durazo-Arvizu R, Arozullah AM, Keys LC. Determinants of mortality following a diagnosis of prostate cancer in Veterans Affairs and private sector health care systems. *Am J Public Health*. 2003;93(100):1706-1712. doi:10.2105/ajph.93.10.1706
32. Ward E, Jemal A, Cokkinides V, et al. Cancer disparities by race/ethnicity and socioeconomic status. *CA Cancer J Clin*. 2004;54(2):78-93. doi:10.3322/canjclin.54.2.78
33. Zemplenyi AT, Kaló Z, Kovacs G, et al. Cost-effectiveness analysis of intensity-modulated radiation therapy with normal and hypofractionated schemes for the treatment of localised prostate cancer. *Eur J Cancer Care*. 2018;27(1):e12430. doi:10.1111/ecc.12430
34. Klabunde CN, Potosky AL, Harlan LC, Kramer BS. Trends and black/white differences in treatment for nonmetastatic prostate cancer. *Med Care*. 1998;36(9):1337-1348. doi:10.1097/00005650-199809000-00006
35. Harlan L, Brawley O, Pommerenke F, Wali P, Kramer B. Geographic, age, and racial variation in the treatment of local/regional carcinoma of the prostate. *J Clin Oncol*. 1995;13(1):93-100. doi:10.1200/JCO.1995.13.1.93
36. Riviere P, Luterstein E, Kumar A, et al. Racial equity among African-American and non-Hispanic white men diagnosed with prostate cancer in the veterans affairs healthcare system. *Int J Radiat Oncol Biol Phys*. 2019;105:E305.
37. Peterson K, Anderson J, Boundy E, Ferguson L, McCleery E, Waldrip K. Mortality disparities in racial/ethnic minority groups in the Veterans Health Administration: an evidence review and map. *Am J Public Health*. 2018;108(3):e1-e11. doi:10.2105/AJPH.2017.304246
38. Zietman AL, DeSilvio ML, Slater JD, et al. Comparison of conventional-dose vs high-dose conformal radiation therapy in clinically localized adenocarcinoma of the prostate: a randomized controlled trial. *JAMA*. 2005;294(10):1233-1239. doi:10.1001/jama.294.10.1233
39. Hagan M, Kapoor R, Michalski J, et al. VA-Radiation Oncology Quality Surveillance program. *Int J Radiat Oncol Biol Phys*. 2020;106(3):639-647. doi.10.1016/j.ijrobp.2019.08.064
40. Carpenter DJ, Natesan D, Floyd W, et al. Long-term experience in an equal access health care system using moderately hypofractionated radiotherapy for high risk prostate cancer in a predominately African American population with unfavorable disease. *Int J Radiat Oncol Biol Phys*. 2020;108(3):E417. https://www.redjournal.org/article/S0360-3016(20)33923-7/fulltext