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Patient-reported Outcomes in Metastatic Castration-sensitive Prostate Cancer in the Adjuvant Setting

Alicia K. Morgans^{a,*}, Martin R. Stockier^b

^aNorthwestern University, Chicago, IL, USA;

^bNHMRC Clinical Trials Centre, University of Sydney, Sydney, Australia

Abstract

We review the importance of quality of life (QOL) data from patient-reported outcome measures (PROMs) among men treated with androgen deprivation therapy (ADT) for metastatic castration-sensitive prostate cancer (mCSPC) or localized prostate cancer treated with adjuvant therapy. This information is important for patients as they make treatment choices and for regulatory agencies approving drug therapies. Studies of treatments for mCSPC suggest that the improvements in survival associated with more intensive systemic treatment are accompanied by improvements in QOL. ADT prolongs survival among men with intermediate- or high-risk localized disease in combination with radiation, but the optimal duration is still being defined. For men with biochemical recurrence, starting ADT earlier rather than later had minimal adverse effects on QOL but may not prolong survival. We conclude that rigorous assessment of QOL with validated PROMs must be a priority for clinical trials of novel and more intensive approaches to treatment with ADT.

Patient summary:

Data on quality of life that are collected using patient-reported outcome measures are important for patients with prostate cancer as they make treatment choices and for regulatory agencies approving drug therapies.

Keywords

prostate cancer; quality of life

In prostate cancer (PC) care, as across all of oncology, patient-centeredness is considered a component of the high quality of care that should be provided to all. In this context there is increasing interest in understanding the patient experience by asking men with PC about their quality of life (QOL) directly. Patient-reported QOL is assessed using patient-reported

*Corresponding author. Northwestern University, 676 N. St. Clair Street, Chicago, IL 60611, USA. Tel. +312-695-2381; Fax: +312-695-6189., alicia.morgans@northwestern.edu (A.K. Morgans).

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outcome measures (PROMs), which are validated instruments that evaluate aspects of the patient experience including symptoms, physical functioning, emotional wellbeing, social support, and global assessments. These standardized evaluations can detect symptoms that are underreported up to 50% of the time in routine clinical care [1]. Here we review the importance of considering PROMs in decision-making for men receiving androgen deprivation therapy (ADT) for metastatic castration-sensitive PC (mCSPC) and intermediate- or high-risk localized PC.

Decisions about treatment for men with PC require consideration of the effects of both the disease and its treatment on QOL, in addition to treatment efficacy. The median survival time for men with mCSPC has increased substantially over recent decades, with >50% of men living longer than 5 yr, and multiple treatment options of varying toxicity are available. Because of this, consideration of QOL is critical. In the population with intermediate- and high-risk localized PC, men who are asymptomatic or minimally symptomatic must consider the trade-offs between the potential for adjuvant therapy to lengthen survival and its possible detrimental effects on QOL. Making choices between treatments in these settings requires valid and reliable PROMs across clinical trials so that patients have the high-quality information needed to make patient-centered treatment decisions consistent with their personal preferences, although interpreting and using the data from these assessments in practice can prove challenging [2]. Even though multidisciplinary international teams of experts have worked to standardize PROMs and other disease-specific outcomes for localized and advanced PC, standard collection of these measurements is not universal [3,4].

Recent practice-defining clinical trials involving men with mCSPC have focused on both efficacy and QOL outcomes [5–7]. The CHAARTED trial demonstrated that adding early chemotherapy to ADT prolonged survival among men with recently diagnosed mCSPC, and was associated with significantly better QOL at 1 yr compared with ADT alone [7]. The LATITUDE study demonstrated that abiraterone acetate plus ADT was associated with both better survival and a longer time to deterioration in functional status when compared with ADT alone among men with recently diagnosed mCSPC [6]. Detailed effects of early chemotherapy with docetaxel and of early abiraterone on QOL have been assessed in the STAMPEDE trial, but are yet to be released.

In the localized PC and biochemical PC recurrence settings, men are often relatively asymptomatic from their PC, making trade-offs between impairments in QOL and improvements in survival time critical for decision-making. Multiple studies have demonstrated that concurrent ADT prolongs survival among men with intermediate- and high-risk localized PC receiving radiation therapy, but there are fewer data available on the QOL effects of ADT in this setting. A recently reported randomized trial of ADT given concurrently with radiation for high-risk PC did not demonstrate the hypothesized benefit of ADT continuation for 36 mo rather than 18 mo, and both global QOL and role functions were similar in the two groups. However, 36 mo of ADT was associated with significant detriments in physical, psychological, and social domains of QOL, as well as more severe fatigue, hormonal treatment effects, and sexual dysfunction [8]. Particularly for men with high-risk PC, an optimal ADT duration that balances prolongation of survival and maximization of QOL is still being defined.

Randomized trials assessing health-related QOL among men with castration-sensitive biochemical PC recurrence after local treatment are also relevant for men with either high-risk localized disease or asymptomatic metastatic PC. The TOAD trial randomly allocated 293 men to immediate or delayed ADT, of whom 261 had biochemical relapse after local treatment [9]. No differences were evident between the treatment groups in global QOL, physical, role, or emotional functioning, or feeling less masculine over 5 yr of follow-up. However, sexual activity, hot flushes, and sore or enlarged nipples or breasts were worse with immediate ADT than with delayed ADT over the first 2 yr, but not subsequently. Feeling less masculine and disturbed sleep were reported equally frequently with immediate and delayed ADT (40–50% in both groups), whereas the immediate ADT group were more likely to report hot flashes (31% vs 55%; $p < 0.001$), soreness or enlargement of nipples or breasts (14% vs 6%; $p < 0.001$), and shortness of breath (48% vs 39%; $p = 0.03$).

Regulatory bodies are also keen to include QOL assessments when they consider approval applications for new agents and expanded indications for existing ones [10]. Use of a standardized approach for PRO collection and analysis, as proposed by the Setting International Standards in Analyzing Patient-Reported Outcomes and Quality of Life End-points Data initiative, can help to ensure that methods are robust and that data can be compared across studies, enabling patients to make well-informed decisions that are consistent with their preferences. As we strive to standardize the measures used for men with mCSPC and for men with high-risk localized PC considering adjuvant treatment, consideration should also be given to eliciting the views of partners and/or caregivers to better understand their experiences.

Advances in our treatment armamentarium have improved metastatic prostate cancer outcomes by incorporating the use of more intensive therapies in earlier stages of the disease. As we continue down this path to improving survival with ADT and other systemic therapies, it remains imperative that we also gather comprehensive and unbiased information about the patient experience via validated PROMs that better characterize their experience than clinicians' assessments recorded using the Common Terminology Criteria for Adverse Events. By doing so, we can provide patients, clinicians, and regulators with information about efficacy, toxicity, and effects on QOL that is needed to make high-quality decisions consistent with the goals and preferences of those affected. Only then can we say that we are truly providing the patient-centered care we strive to achieve.

References

- [1]. Pakhomov SV, Jacobsen SJ, Chute CG, Roger VL. Agreement between patient-reported symptoms and their documentation in the medical record. *Am J Manage Care* 2008;14:530–9.
- [2]. Dowrick AS, Wootten AC, Murphy DG, Costello AJ. We used a validated questionnaire: what does this mean and is it an accurate statement in urologic research? *Urology* 2015;85:1304–10. [PubMed: 25881867]
- [3]. Martin NE, Massey L, Stowell C, et al. Defining a standard set of patient-centered outcomes for men with localized prostate cancer. *Eur Urol* 2015;67:460–7. [PubMed: 25234359]
- [4]. Morgans AK, van Bommel AC, Stowell C, et al. Development of a standardized set of patient-centered outcomes for advanced prostate cancer: an international effort for a unified approach. *Eur Urol* 2015;68:891–8. [PubMed: 26129856]

- [5]. Marino P, Sfumato P, Joly F, et al. Q-TWiST analysis of patients with metastatic castrate naive prostate cancer treated by androgen deprivation therapy with or without docetaxel in the randomised phase III GETUG-AFU 15 trial. *Eur J Cancer* 2017;84:27–33. [PubMed: 28780479]
- [6]. Chi KN, Protheroe A, Rodriguez-Antolin A, et al. Patient-reported outcomes following abiraterone acetate plus prednisone added to androgen deprivation therapy in patients with newly diagnosed metastatic castration-naïve prostate cancer (LATITUDE): an international, randomised phase 3 trial. *Lancet Oncol* 2018;19:194–206. [PubMed: 29326030]
- [7]. Morgans AK, Chen YH, Sweeney CJ, et al. Quality of life during treatment with chemohormonal therapy: analysis of E3805 chemohormonal androgen ablation randomized trial in prostate cancer. *J Clin Oncol* 2018;36:1088–95. [PubMed: 29522362]
- [8]. Nabid A, Carrier N, Martin AG, et al. Duration of androgen deprivation therapy in high-risk prostate cancer: a randomized phase III trial. *Eur Urol* 2018;74:432–41. [PubMed: 29980331]
- [9]. Duchesne GM, Woo HH, King M, et al. Health-related quality of life for immediate versus delayed androgen-deprivation therapy in patients with asymptomatic, non-curable prostate cancer (TROG 03. 06 and VCOG PR 01–03 [TOAD]): a randomised, multicentre, non-blinded, phase 3 trial. *Lancet Oncol* 2017;18:1192–201. [PubMed: 28760403]
- [10]. Kluetz PG, O'Connor DJ, Soltys K. Incorporating the patient experience into regulatory decision making in the USA, Europe, and Canada. *Lancet Oncol* 2018;19:e267–74. [PubMed: 29726391]