Screening and management of metabolic, cardiac, and bone health in prostate cancer patients on androgen deprivation therapy

A survey of specialized physicians

David-Dan Nguyen[1], Ahmad Mousa[1], Laurence Klotz[1,2], Tamim Niazi[3], Frédéric Pouliot[4], Andrea Kokorovic[5], Luke T. Lavallée[6], Melissa Huynh[7], Nathalie Lapointe[8], Michelle Di Risio[8], Christopher J.D. Wallis[1,9,10]

[1]Division of Urology, Department of Surgery, University of Toronto, Toronto, ON, Canada; [2]Division of Urology, Department of Surgery, Sunnybrook Health Sciences, University of Toronto, ON, Canada; [3]Department of Radiation Oncology, Jewish General Hospital, McGill University, Montreal, QC, Canada; [4]Division of Urology, Department of Surgery, Centre hospitalier de l'Université Laval, Quebec, QC, Canada; [5]Division of Urology, Department of Surgery, Centre hospitalier de l'Université de Montréal, Montreal, QC, Canada; [6]Division of Urology, Department of Surgery, The Ottawa Hospital, University of Ottawa, Ottawa, ON, Canada; [7]Division of Urology, Department of Surgery, Victoria Hospital, of Western University, London, ON, Canada; [8]Knight Therapeutics, Montreal, QC, Canada; [9]Division of Urology, Department of Surgery, Mount Sinai Hospital, Toronto, ON, Canada; [10]Department of Surgical Oncology, University Health Network, Toronto, ON, Canada

Cite as: Nguyen DD, Mousa A, Klotz L, et al. Screening and management of metabolic, cardiac, and bone health in prostate cancer patients on androgen deprivation therapy: A survey of specialized physicians. *Can Urol Assoc J* 2024;18(6):212-5. http://dx.doi.org/10.5489/cuaj.8687

Published online April 2, 2024

Appendix available at *cuaj.ca*

INTRODUCTION

Patients with prostate cancer (PCa) often require androgen deprivation therapy (ADT) in later stages of their disease. Although ADT is effective, it is associated with significant morbidity.[1] This is particularly relevant considering that for many stages of PCa, patients are more likely to die of their comorbidities than PCa itself.[2]

ADT use can induce metabolic syndrome and osteoporosis secondary to hypogonadism.[3,4] It increases the risk of cardiovascular diseases (CVD) and the loss of bone mineral density (BMD) is associated with an increase in the risk of fragility fractures. These effects are concerning, especially in older patients who are at increased risk of these conditions.

This study reports the findings from a survey investigating the perceptions and practices of specialists treating patients with PCa to cardiac, bone, and metabolic health issues in patients receiving ADT.

METHODS

Study design

This cross-sectional survey is part of the Prostate Cancer Practice Assessment (PCPA), an initiative designed to enhance the quality of care for PCa patients, with a particular focus on those receiving ADT. The primary objective of this initiative was to empower clinicians to assess their approaches to managing adverse events associated with ADT.

Physicians treating PCa patients were identified by purposeful sampling based on their clinical practice and relevant academic activities and invited to fill out an online survey between January 2021 and May 2021. After reviewing the program rationale, those who agreed to participate were prompted to complete the survey. Survey respondents were not reimbursed for completing the surveys. Monthly reminder emails were sent to study participants to fill out the surveys over 10 months.

The survey was designed by a study steering committee comprising two uro-oncologists (LK and FP) and a radiation oncologist (TN) in consultation with the sponsor's medical team (NL and MDR). It is composed of two main sections. The first section inquired about respondents' clinical experience, considerations for the use of ADT in patients with PCa, and the most common challenges faced by providers when treating PCa patients with ADT. The second section required that respondents answer using information based on 5–10 of their patients who had received their first prescription of ADT for the treatment of PCa within the last 12 months. Information provided included de-identified patient characteristics, as well as issues related to the loss of BMD, metabolic syndrome, and CVD. The relevant survey questions used for this report are presented in the Appendix (available online at *cuaj.ca*).

In the context of the quality improvement intent of this project, results were aggregated and presented descriptively.

KEY MESSAGES

- Specialized prostate cancer providers generally felt they were unlikely to screen and manage metabolic and cardiac health.
- They were more comfortable screening and managing bone health.
- There is a need for initiatives and policies bolstering the comprehensive management of patients on ADT.

RESULTS

Physician respondents

Among 55 physicians invited to participate, 33 (60%) completed the survey. Among the respondents, 18 (55%) reported their specialty as urology, eight (24%) urologic oncology, six (18%) radiation oncology, and one (3%) medical oncology/internal medicine. Seventeen (52%) practiced in teaching hospitals. Twenty-six (78%) had >10 years' experience. Twenty-five (75%) treated more than 25 PCa patients per month, on average. Additional respondent demographics are presented in Table 1.

Managing comorbidities and/or associated medications and managing the side effects of ADT were noted as the most common challenges for three (9%) and five (15%) respondents, respectively.

Table 1. Respondent demographics

	n	%
Primary specialty		
Medical oncology/internal medicine	1	3
Radiation oncology	6	18
Urologic oncology	8	24
Urology	18	55
Other	0	0
Practice setting		
Community health centre/hospital	8	24
Private practice	7	21
Teaching hospital/center of excellence	17	52
Other	1	3
Years in practice		
>5 years	2	6
5–10 years	5	15
11–20 years	11	33
21–30 years	13	39
>30 years	2	6
Number of patients with prostate cancer typically treated in a month		
1–10 patients	2	6
10–25 patients	6	18
25–50 patients	16	48
>50 patients	9	27

Physicians' likelihood to screen and manage metabolic, cardiac, and bone health

Of the physician respondents, nine (27%), 12 (36%), 12 (36%), and six (18%) felt that they were unlikely to screen for or manage diabetes, dyslipidemia, hypertension, and obesity, respectively. In contrast, two (6%), two (6%), two (6%), and four (12%) felt that they were extremely likely to screen and manage diabetes, dyslipidemia, hypertension, and obesity, respectively. Seven (21%) of the respondents felt they were unlikely to screen and manage CVD in their patients on ADT compared to six (18%) who indicated that this was extremely likely. For bone health, one (3%) felt they were unlikely to screen and manage osteopenia/osteoporosis in their patients on ADT, while 10 (30%) felt that this was extremely likely.

Patient profiles

Physician respondents completed 225 profiles of patients under their care. The mean patient age was 72.7 years. There were 34 (15%) patients with localized PCa; all others had either locally advanced, metastatic, non-metastatic castration-resistant prostate cancer (CRPC), or metastatic CRPC.

There were, respectively, 40 (18%), 50 (22%), 66 (29%), 25 (11%), 94 (42%), 27 (12%), and 12 (5%) patients with CVD, diabetes, hypercholesterolemia, hypertriglyceridemia, hypertension, obesity, and osteopenia/osteoporosis. Most patients (n=134, 80%) had at least one of diabetes, dyslipidemia, hypertension, or obesity. Additional patient clinical information is presented in Table 2.

Table 2. Patient characteristics

Clinical stage of prostate cancer	
Localized (T1 or T2, N0, M0), n (%)	34 (15)
Localized advanced (T3 or T4, N0, M0 or any T, N1, M0), n (%)	64 (28)
Metastatic (M1), n (%)	98 (44)
Non-metastatic CRPC, n (%)	7 (3)
Metastatic CRPC, n (%)	
Indications for current androgen-deprivation therapy regimen	
Adjuvant to radiation therapy, n (%)	76 (34)
Biochemical failure, n (%)	29 (13)
Metastatic disease, n (%)	120 (53)
Metabolic, cardiac, and bone health clinical parameters	
BMI, mean	26.9
BMD	
Above or equal to -1 (normal)	40 (18)
Between -1 and -2.5 (osteopenia)	16 (7)
Below or equal -2.5 (osteoporosis)	5 (2)
Unknown	164 (73)
A1C, mean	5.7
Blood pressure (mmHg), mean	131/80
HDL-C (mmol/L), mean	1.3
LDL-C (mmol/L), mean	2.3
Triglycerides (mmol/L), mean	1.6

BMD: bone mineral density; BMI: body mass index; CRPC: castration-resistant prostate cancer; HDL-C: high-density lipoprotein cholesterol; LDL-C: low-density lipoprotein cholesterol.

Patient management of metabolic, cardiac, and bone health

Among patients with these conditions at baseline, physicians reported that they initiated preventative or therapeutic interventions for 25 (64%) patients with CVD, 10 (26%) patients with diabetes, 20 (51%) patients with metabolic syndrome, and 26 (67%) patients with decreased BMD/osteoporosis. Overall, respondents felt that 39 (17%) patients would benefit from the initiation of preventative or therapeutic interventions and 84 (37%) patients would benefit from involving primary care or another specialist following the review of their chart in the context of this survey.

Many patients did not have any intervention to reduce the risk of metabolic syndrome and/or CVD (n=69, 31%). For those that did receive an intervention, these are detailed in Table 3. The most common intervention used to prevent the loss of BMD was dietary supplementation of vitamin D and calcium (n=167, 74%). Additional interventions used to manage bone health are detailed in Table 4.

Table 3. Interventions used to reduce the risk of metabolic syndrome and cardiovascular diseases among 225 patient profiles

Intervention	n (%)
Recommended education or counselling	56 (25)
Letter to the family physician advising on the management of ADT	29 (52)
Nutritional counseling	27 (48)
Patient education on cardiovascular health and risks	35 (63)
Psychosocial or behavioural counseling	5 (9)
Initiated therapy	11 (5)
Acetylsalicylic acid	6 (55)
Anti-hyperglycemic therapy	5 (45)
Anti-hypertensive therapy	6 (55)
Lipid-lowering therapy	7 (64)
Selection of intermittent ADT instead of continuous ADT	0 (0)
Dietary modifications	8 (73)
Physical exercise	9 (82)
Smoking cessation	1 (9)
Referral to a specialist	2 (18)
Used other interventions	5 (2)
Used no interventions	69 (31)

ADT: androgen deprivation therapy.

DISCUSSION

In this survey, specialized PCa providers generally felt that they were unlikely to screen and manage metabolic and cardiac health, while they were more comfortable screening and managing bone health. Physicians reported that very few of their patients were either being screened or managed for metabolic, cardiac, and bone health problems.

Appropriate management of and concomitant use of therapies for metabolic, cardiac, and bone health are associated with improved oncologic outcomes, including overall survival.[5,6] As such, there is a need for comprehensive management of patients on ADT. Comprehensive management can be bolstered by using simple validated screening tools to readily identify the patients that would most benefit from multidisciplinary management.[7] Broader systemic changes, including programmatic support and policies incentivizing holistic care to PCa patients across disciplines, may further enhance the quality of PCa survivorship care.[8] Ultimately, there is a need for multidisciplinary care spanning primary care providers to medical specialists.

Table 4. Interventions used to address bone health

Interventions	n (%)
Pre-treatment BMD scan using DXA	61 (27)
Pre-treatment assessment of fracture risk	22 (10)
Dietary supplementation of vitamin D and calcium	167 (74)
Letter to the family physician advising on the management of ADT	43 (19)
Lifestyle modifications	66 (29)
Oral bisphosphonates	25 (11)
Patient education on bone health and risk of loss of BMD	72 (32)
Physical exercise	97 (43)
Other interventions	5 (2)
No interventions	19 (8)

ADT: androgen deprivation therapy; BMD: bone mineral density; DXA: dual-energy X-ray absorptiometry.

Limitations

This study has several limitations. It relied on convenience sampling. The small sample size limits external generalizability. This survey relies on self-reporting, which may suffer from response bias. It is possible that respondents characterized how they screened and managed the risk of metabolic, cardiac, and bone health too favorably. The survey design precluded any comparison between PCa specialists' attitudes and beliefs on screening as opposed to the management of metabolic, cardiac, and bone health in PCa patients on ADT. It is plausible that PCa specialists are more likely to screen their patients for these conditions rather than manage them without a multidisciplinary team. Our findings further suggest that this may differ between cardiometabolic and bone-related side effects; however, this requires additional investigation.

CONCLUSIONS

Despite limitations, the information gathered from this survey provides valuable insights into the current state of clinical practice and identifies potential gaps or areas for improvement in the management of metabolic, cardiac, and bone health of PCa patients undergoing ADT. Future studies are needed to compare the rates of screening and management of comorbidities and side effects of ADT reported in our study, which may represent the upper bound of expectations, to that of real-world practice using administrative data. This can inform quality improvement initiatives to further the implementation of best practices.

COMPETING INTERESTS: Dr. Klotz has been a PCPA steering committee member and advisory board participant for Knight Therapeutics. Dr. Niazi has been a PCPA steering committee member and advisory board participant for Knight Therapeutics; and has received honoraria/travel funding from Knight Therapeutics. Dr. Pouliot has been a PCPA steering committee member and consult meeting participant for Knight Therapeutics; and advisory board member for Amgen, Astellas, AstraZeneca, Bayer, Janssen Novartis, Tersera, and Tolmar; and has received honoraria and/or research grants from Astellas and Merck. Dr. Kokorovic has been a consult meeting participant and chair for Knight. Dr. Lavallée has been an advisory board participant for Astellas, EMD, Knight Therapeutics, and Novartis; and has received research funding (to institution) from Knight Therapeutics and Tolmar. Dr. Huynh has been a speaker for Knight Therapeutics. Ms. Lapointe and Ms. Di Risio are employees of Knight Therapeutics. Dr. Wallis has received consulting fees from Janssen, Nanostics Inc, SESEN Bio, and Precision Point Specialty LLC; has received honoraria/travel funding from AbbVie, Astellas, Astra Zeneca, Bayer, EMD Serono, Haymarket Media, Healing and Cancer Foundation, Knight Therapeutics, Science & Medicine, TerSera, and Tolmar; and has received research funding from Bayer, Knight Therapeutics, and Tolmar. The remaining authors do not report any competing personal or financial interests related to this work.

FUNDING: This study was funded by Knight Therapeutics.

This paper has been peer-reviewed.

REFERENCES

1. Kokorovic A, So AI, Serag H, et al. UPDATE - Canadian Urological Association guideline on androgen deprivation therapy: Adverse events and management strategies. *Can Urol Assoc J* 2022;16:E416-31. https://doi.org/10.5489/cuaj.8054
2. Riihimäki M, Thomsen H, Brandt A, et al. What do prostate cancer patients die of? *Oncologist* 2011;16:175-81. https://doi.org/10.1634/theoncologist.2010-0338
3. Nguyen PL, Alibhai SMH, Basaria S, et al. Adverse effects of androgen deprivation therapy and strategies to mitigate them. *Eur Urol* 2015;67:825-36. https://doi.org/10.1016/j.eururo.2014.07.010
4. Wallis CJD, Mahar AL, Satkunasivam R, et al. Cardiovascular and skeletal-related events following localized prostate cancer treatment: Role of surgery, radiotherapy, and androgen deprivation. *Urology* 2016;97:145-52. https://doi.org/10.1016/j.urology.2016.08.002
5. Harshman LC, Wang X, Nakabayashi M, et al. Statin use at the time of initiation of androgen deprivation therapy and time to progression in patients with hormone-sensitive prostate cancer. *JAMA Oncol* 2015;1:495-504. https://doi.org/10.1001/jamaoncol.2015.0829
6. Margel D, Urbach DR, Lipscombe LL, et al. Metformin use and all-cause and prostate cancer-specific mortality among men with diabetes. *J Clin Oncol* 2013;31:3069-75. https://doi.org/10.1200/JCO.2012.46.7043
7. Kenk M, Grégoire JC, Coté MA, et al. Optimizing screening and management of cardiovascular health in prostate cancer: A review. *Can Urol Assoc J* 2020;14:E458-64. https://doi.org/10.5489/cuaj.6685
8. Nguyen DD, Wallis CJD, Fleshner NE, et al. Urologic oncology survivorship guidelines: An overview of the evidence and the current implementation gap. *Eur Urol Focus* 2023;9:431-4 https://doi.org/10.1016/j.euf.2023.02.006

CORRESPONDENCE Dr. Christopher J.D. Wallis, Division of Urology, Department of Surgery, Mount Sinai Hospital, University of Toronto, Toronto, ON, Canada; wallis.cjd@gmail.com