World Journal of Urology (2019) 37:1085–1093
https://doi.org/10.1007/s00345-018-2495-0

ORIGINAL ARTICLE

New study suggests patients with advanced prostate cancer on androgen deprivation therapy need more dialogue with health care provider, especially around cardiovascular risk

Axel Merseburger[1] · Anne Bro Falkenberg[2] · Olga J. Kornilova[3]

Received: 26 February 2018 / Accepted: 14 September 2018 / Published online: 22 September 2018

Abstract

Purpose To study the current level of patients' awareness, and patient-health care provider (HCP) dialogue with respect to treatment-related risks, especially cardiovascular risk (CVR) associated with advanced prostate cancer (PCa) treatment.

Methods This 10-min online survey summarised data by treatment, region, and CVR (high or low).

Results Of the 411 patients, 83% were at high CVR while only 8% patients were aware of CVR associated with PCa treatment, majority of which (80%) were informed about this risk by HCPs. No significant difference in treatment approach was reported, regardless of patient's CVR status. Compared to other potential risks, patients were more likely to initiate discussion about heart problems with HCPs (38% patients). When prompted, 26% patients rated heart problems as the most concerning risk factor, and this concern was twice in patients with high CVR (28%) versus low CVR (14%). Lifestyle modifications were made by 64% patients, of which 45% patients reported an improvement in overall well-being. Improved diet was the most adopted lifestyle modification.

Conclusion There is a need to enhance a constant patient–HCP dialogue, and both groups need to make a conscious effort in that direction. This would help in increasing patients' awareness of risks, having better treatment choice and acceptance, and reducing side-effects.

Keywords Cardiovascular risk · Hormone therapy · Online survey · Patient–physician discussions · Prostate cancer

Introduction

Prostate cancer (PCa) is the second most common cancer among men in the United States of America (USA) and the second-leading cause of cancer-related deaths [1–3]. The goal of therapy in patients with advanced PCa is usually to delay the progression of the disease.

Androgen deprivation therapy (ADT) extends progression-free survival and has shown efficacy in patients with advanced PCa, and those with biochemical recurrence [4]. Health care providers (HCPs) have a number of modalities at their disposal for androgen deprivation, which includes surgical castration (orchiectomy) and medical castration (hormone therapy). While surgical castration, an irreversible procedure, can be a difficult treatment for patients to contemplate, hormone therapy seems to be a more viable option for the patients, allowing androgen restoration, and hence a better quality of life.

Gonadotropin-releasing hormone (GnRH) antagonists and luteinising hormone-releasing hormone (LHRH) agonists are approved hormone therapies for treating advanced PCa. These therapies, however, have their own benefits and risks [5]. Clinical studies have reported an increased risk of cardiovascular events, including high cholesterol, high blood pressure, stroke, heart attack, and even death [6, 7] with hormone therapy, particularly LHRH agonists.

Electronic supplementary material The online version of this article (https://doi.org/10.1007/s00345-018-2495-0) contains supplementary material, which is available to authorized users.

✉ Axel Merseburger
axel.merseburger@uksh.de

[1] University Hospital Schleswig-Holstein, Ratzeburger Allee 160, 23538 Lübeck, Germany

[2] Ferring Pharmaceuticals, Kay Fiskers Plads 11, Copenhagen, Denmark

[3] Ferring International Center, Chemin de la Vergognausaz 50, Saint-Prex, Switzerland

All these findings prompted AUA, ACS, and AHA to issue a joint statement warning physicians regarding the possibility of cardiovascular disorders (CVD) with ADT [8]. Also, the potential correlation between ADT and CV risk (CVR) prompted the inclusion of warnings in drug labels as well (FDA and EMA). Further, it was observed that patients undergoing ADT may be 2.6-times more likely to die of cardiovascular events than non-ADT controls [9]. This substantiates the need for an open dialogue between patients and HCPs and is important for two reasons. First, considering a late age onset of PCa, there is a strong possibility that these older patients have pre-existing comorbidities. This has been shown in a recent study where ADT was associated with greater risk of heart failure, arrhythmia, and conduction disorder in men with pre-existing CVD versus those without pre-existing CVD [10]. Data also show that about 25–30% of the patients report with an already existing cardiovascular disease at the time of PCa diagnosis [11]. Such comorbidities have a direct impact on the cardiovascular safety outcome in patients seeking ADT [12]. Second, ADT is independently associated with CVR factors like dyslipidaemia and hyperglycaemia [13], which may precipitate or exacerbate the cardiovascular events and mortality [14].

Despite the significant PCa treatment-related risks, there is a large gap in dialogue between the patient and HCP [15]. Data show that the treatment choice is largely based on the HCP's specialty and experience rather than the patient's preference [16]. As a result, some patients may regret HCP's decision of the choice of treatment [17]. Therefore, there is a need to bring forth a patient–HCP dialogue to increase the awareness regarding potential treatment risks [18], especially CVR associated with ADT. This might help patients to have a better perception and acceptance for the treatment, considering the risk–benefit ratio of the treatment(s) offered or available, and perhaps in some cases influence the treatment decisions.

With this objective in mind, and to understand the current level of patients' awareness regarding PCa treatment-related risks, Ferring Pharmaceuticals sponsored an online 'ManAging Survey' and questioned over 400 men with PCa from the USA and European Union. The survey also captured patient-reported treatment side-effects and lifestyle changes made. Here, we present the main findings from this survey.

Methods

Study population

Respondents were recruited from a panel of patients who identified themselves as having PCa from a blinded list of medical conditions. Upon entering the survey, respondents were re-screened to ensure that they met the recruitment criteria. Inclusion and exclusion criteria were kept to a minimum to ensure sufficient enrolment. Patients who were not employed as a primary-care physician or hospital physician, not affiliated in any way with a pharmaceutical company, and those who had not participated in a related market research in the previous 3 months were included.

Study design

This online survey was conducted by a third party "Healthcare Market Research agency" from May to July 2014. The agency conducted this unbiased survey to ensure that all questions were asked objectively and in a non-leading way. The participation time for each patient was approximately 10 min. The survey consisted of questions aiming at three main objectives. First, to understand the current level of patients' awareness of CVRs associated with PCa treatment; second, to understand whether relevant discussions take place between patients and HCPs regarding these CVRs, and whether the risk is being considered for treatment decision-making; and third, to understand what preventative measures (if any) were taken by patients, to reduce the CVR apart from treatment choice. A simplified stratification tool was used in the survey that examined body mass index (BMI), smoking and concomitant disease. The patients with BMI ≥ 30 kg/m^2, and/or smoking > 15 cigarettes/day, and/or diagnosed with cardiovascular problems, hypertension, diabetes or hypercholesterolemia, were labelled as 'High CVR' and were compared to a mutually exclusive sub-group labelled as 'Low CVR'.

Survey questions and data quality

The survey questions collected data on patient demographics, PCa history, comorbidities, and treatment approaches. Patients were also questioned about the awareness of risks associated with PCa treatment [erectile dysfunction, loss of libido, lower urinary tract symptoms, fatigue, mood change, bowel irritation, weight gain, hot flashes, decrease in muscle mass, high cholesterol, increased health-risk (if smoker), diabetes, loss of bone density, heart problems or any other]. Information on how frequently patients connected with their HCPs for the evaluation/discussion of potential risks associated with PCa treatment; patient-ranking/rating of most concerning risk factors; and impact of lifestyle modification on PCa management was also collected.

To ensure the collection of high-quality data, the following checks were carried out: verbatim, timestamp, straight-line checks, respondent verification, and patient verification. Respondents giving nonsensical answers to 'other-specify' questions and taking less time to complete the survey (identified as 'speeders') were removed from the data set. Respondents giving the same score for all factors

were further scrutinized and removed wherever appropriate. Digital fingerprinting was used to ensure that there was no duplication of respondents.

Statistical analysis

The sample size of 400 participants was agreed for this unbiased survey. The data collected were summarised by type of treatment, region, and CVR (high or low). Values were presented descriptively as percentages against either total patients or the corresponding country. A standard *T* test was used to establish the statistical significance within the data between the subgroup of respondents. Differences were considered significant at confidence interval levels of 95% or greater and a two-sided *p* value of 0.05.

Results

Demographics and clinical characteristics of the study population

A total of 411 patients participated in the online survey from four countries, i.e. the USA, France, Germany, and Italy (250, 52, 56, and 53 patients, respectively). The majority of patients were over 60 years (80%), were non-smokers (79%), and were either overweight (46% patients with BMI 25–29.9 kg/m^2) or obese (31% patients with BMI ≥ 30 kg/m^2). The mean time since PCa diagnosis was 5.1 years (median: 4 years). High blood pressure (56%), high cholesterol (45%), diabetes (25%), arthritis (24%), and heart problems (20%) were the most commonly diagnosed concurrent conditions in these patients. The total and country-wise demographic and clinical characteristics of patients are summarised in Table 1. It is important to mention here that 14% of the patients were on ADT (Hormone therapy: 13% and surgical castration: 1%) (Online Resource 1).

Table 1 Patient demographics and clinical characteristics

	Total ($n=411$)	USA ($n=250$)	European Union ($n=161$)
Age ≥ 60 years, %	327 (80)	212 (85)	115 (71)
Age groups, *n* (%)			
<50 years	22 (5)	9 (4)	13 (8)
50–59 years	62 (15)	29 (12)	33 (20)
60–64 years	65 (16)	41 (16)	24 (15)
65–69 years	110 (27)	64 (26)	46 (29)
70–74 years	87 (21)	57 (23)	30 (19)
75–79 years	42 (10)	33 (13)	9 (6)
80–85 years	18 (4)	14 (6)	4 (2)
>85 years	5 (1)	3 (1)	2 (1)
Non-smokers, *n* (%)	323 (79)	214 (86)	109 (68)
BMI, kg/m^2			
Mean	28.7	29.2	27.9
Median	27.7	27.8	27.7
BMI groups, *n* (%)			
Normal	91 (22)	55 (22)	36 (22)
Overweight	191 (46)	111 (44)	80 (50)
Obese	129 (31)	84 (34)	45 (28)
Time since diagnosis, years			
Mean	5.1	5.5	4.4
Median	4.0	4.0	3.0
Medical history, %			
High blood pressure	230 (56)	150 (60)	80 (50)
High cholesterol	186 (45)	137 (55)	49 (30)
Diabetes	101 (25)	55 (22)	46 (29)
Heart problems	83 (20)	57 (23)	26 (16)
Arthritis	100 (24)	81 (32)	19 (12)
Asthma	38 (9)	18 (7)	20 (12)
Colorectal cancer	19 (5)	7 (3)	12 (7)
Urinary bladder cancer	19 (5)	11 (4)	8 (5)
Lung cancer	11 (3)	3 (1)	8 (5)
Others	30 (7)	24 (10)	6 (4)
High cardiovascular risk, %	341 (83)	212 (85)	129 (80)

BMI (Body mass index) Group: Normal 18.5–24.9 kg/m^2, Overweight 25–29.9 kg/m^2, Obese ≥ 30 kg/m^2

Prevalence and awareness of CVR associated with PCa treatment

Of the total survey population, 83% patients were considered to be at a high CVR as per the criteria defined for this survey (Table 1). The high CVR was defined as: BMI of 30 or above; or smoker with more than 15 cigarettes a day; or diagnosed with CVD (cardiovascular problems, e.g. heart attack/failure, stroke, angina, heart surgery or vascular disease), hypertension, diabetes or hypercholesterolemia). This number was based on "natural fall" in the random sample, where patients were selected and recruited, as long as they meet the recruitment criteria (men, diagnosed with PCa, have not been employed as HCP or working in pharmaceutical company or participated in the PCa-related survey in the past 3 months). Patients' awareness regarding the potential risk of heart problems associated with PCa treatment was low (8%). This was similar with the high CVR group, where awareness was only marginally higher (9%) (Fig. 1a, b). Similarly, in patients receiving hormone therapy the level of awareness for the associated CVR was 7%. Awareness regarding high cholesterol was greater in patients who were at a high CVR versus those at a low CVR (14% versus 3% patients, respectively) (Fig. 1b). On the other hand, a majority of patients

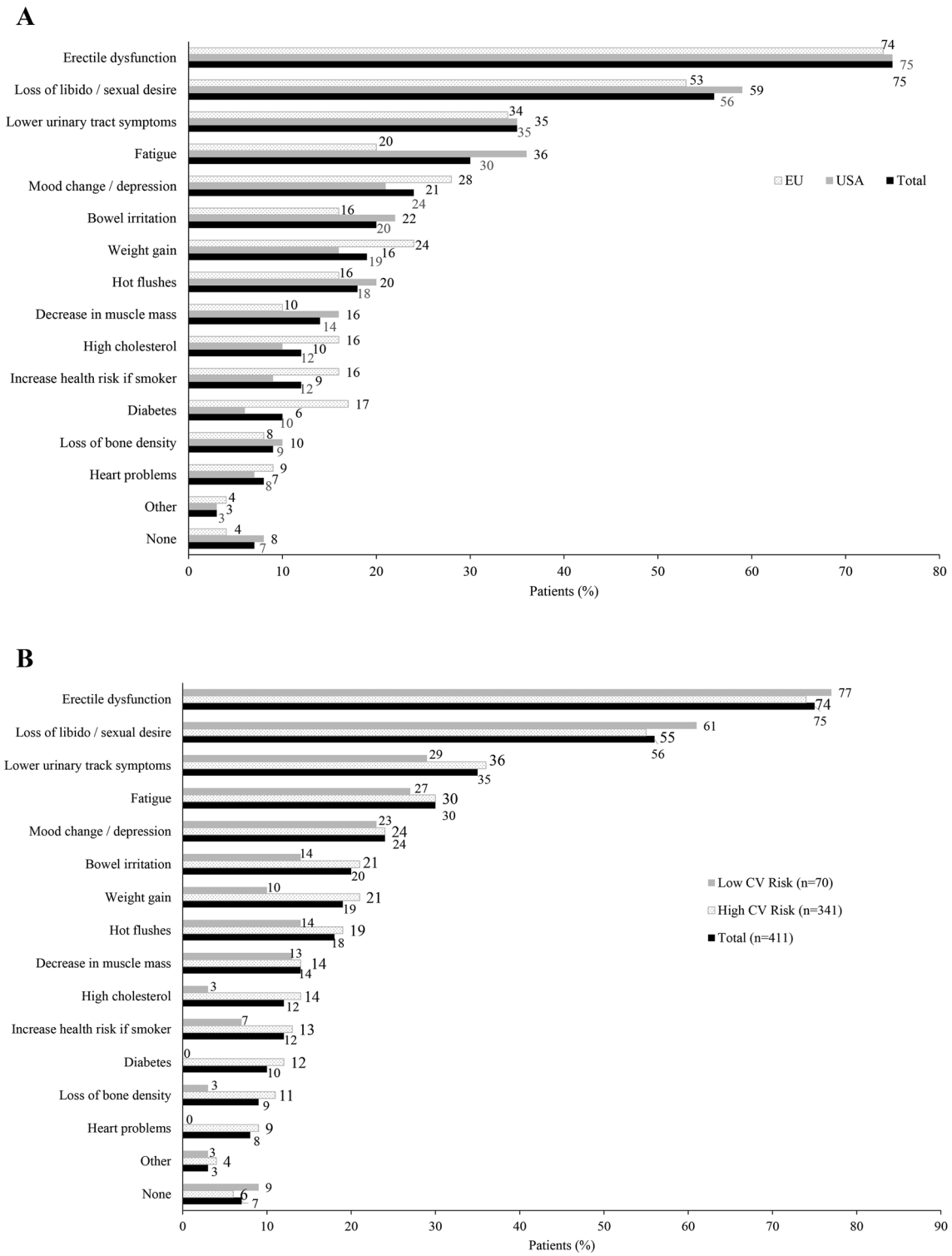

Fig. 1 **a** Awareness of prostate cancer treatment risks—country-wise data. *EU* European Union. **b** Awareness of prostate cancer treatment risks—as per cardiovascular risk category. *CV* cardiovascular

(75%) were aware of erectile dysfunction (Fig. 1a), and this awareness was similar in patients with high and low CVR (74 and 77% patients, respectively) (Fig. 1b).

Impact of CVR on PCa treatment approach

Though a majority of patients were at a high CVR, treatment approach did not differ between the patients with high

and low risk. LHRH agonists were the most commonly used hormone therapy (67%) for PCa treatment, with 31 (66%) patients with a high CVR and 6 (75%) patients with a low CVR receiving LHRH agonist therapy. The details of hormone therapy received by patients, with respect to CVR category, are presented in Online Resource 1.

Patient–HCP interaction regarding side-effects of PCa treatment

Out of 411 patients, only 32 patients were aware of CVR associated with the treatment, of which 26 (81%) patients were informed about this risk by their HCPs. Where discussed, patients were more likely to initiate discussions on heart problems versus other risks associated with PCa treatment (Fig. 2). The other sources of awareness regarding CVR included the internet, patient associations, word of mouth, and from prior experience. A similar pattern was noted for other side-effects as well, where the discussions were mainly HCP-initiated.

Upon prompting, 26% patients rated heart problems as the most concerning risk factor as compared to other risk factors associated with PCa treatment (Fig. 3a). This concern was twice as likely in patients at a high CVR versus those at a low CVR (28% versus 14% patients, respectively) (Fig. 3b).

Lifestyle modification for management of PCa treatment-related risks

On the whole 64% patients made changes in their lifestyles in order to alleviate the symptoms of PCa treatment. Of these, nearly half of the patients reported an improved overall well-being. Lifestyle modification also helped to reduce cholesterol level and fatigue, besides improving mood and maintaining optimal weight and blood sugar levels (Online Resource 2). Improvement in the diet was considered to be the most adopted lifestyle modification (44% patients), more so in patients at a high CVR versus patients at a low CVR (46% versus 31% patients, respectively). Other lifestyle modifications included frequent exercise, and reduced alcohol and smoking (Online Resource 3a, 3b).

Discussion

The results of this survey showed that the majority of the patients with advanced PCa were at a high CVR. Additionally, the CV mortality, which is the most common cause of death in PCa patients, even exceeds the PCa mortality [19]. In a large population study, increased relative risks of nonfatal and fatal CVD were found among all men with PCa, especially those treated with hormonal treatment [20,

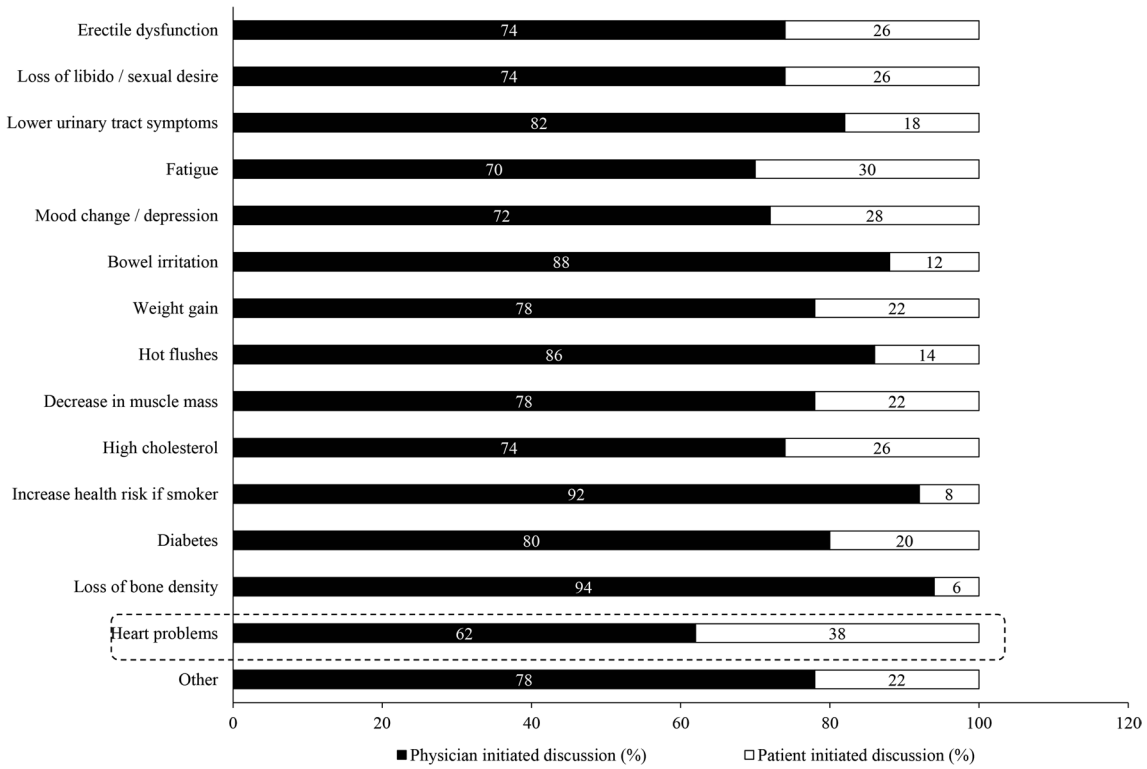

Fig. 2 Initiation of discussion on risks associated with prostate cancer treatment

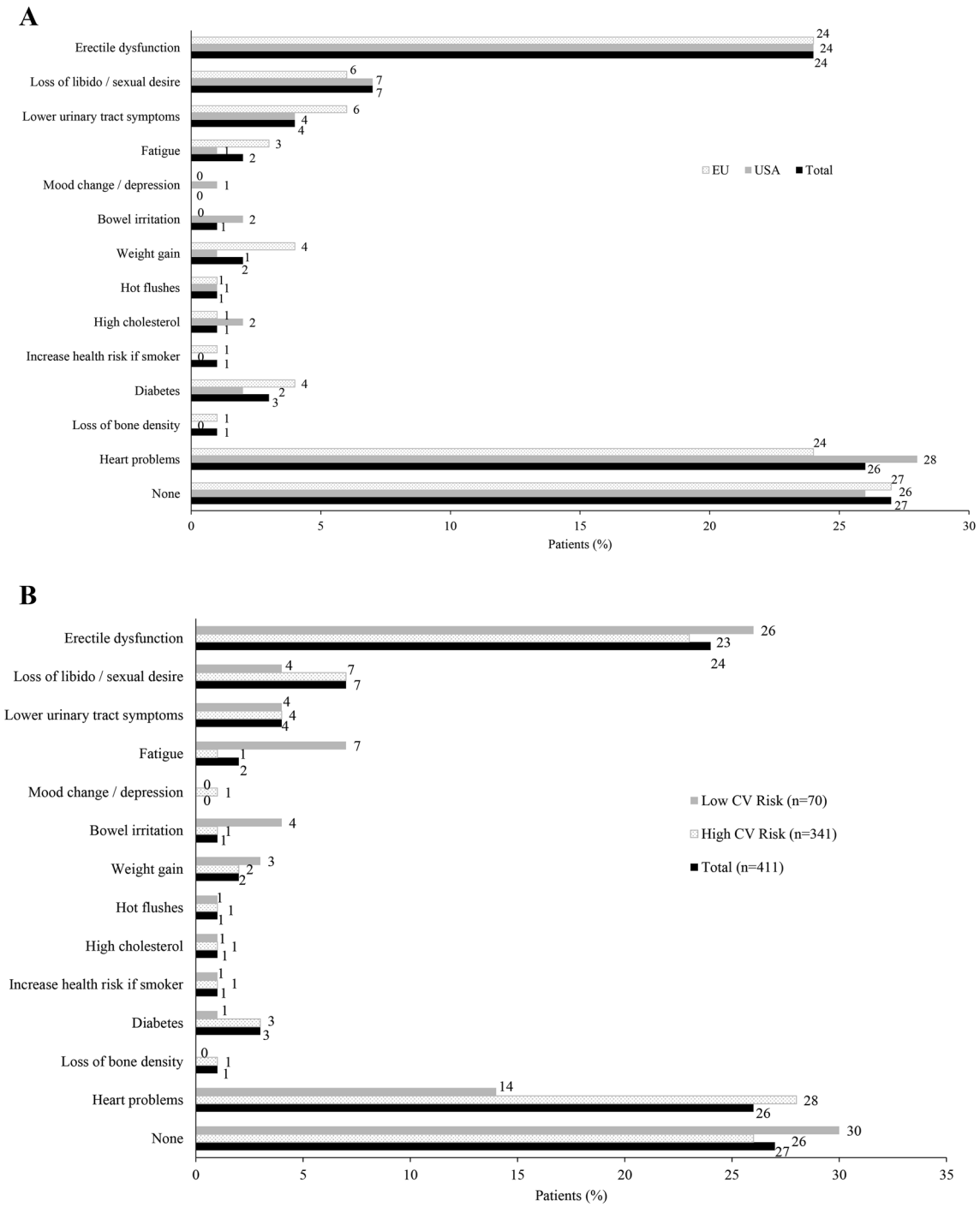

Fig. 3 **a** Most concerning potential risk factor associated with prostate cancer treatment—country-wise data. *EU* European Union. **b** Most concerning potential risk factor associated with prostate cancer treatment—as per cardiovascular risk category. *CV* cardiovascular

21]. ADT, especially hormone therapy in patients with PCa, is associated with increased CVR [16]. However, not only hormone therapy, but surgical castration is also associated with high CVR [22, 23]. Men with a recent CVD history are most at risk [24]. Moreover, advanced, metastatic, castration resistant, and chemo-resistant prostate cancer has triggered the change in the drug development landscape against prostate cancer [25]. However, despite numerous studies stating the risk of CVR with hormone therapy, none of these have established the risk associated with the use of hormone therapy in PCa [26, 27] and this needs to be proved in rigorous studies.

This study draws attention towards high CVR associated with PCa treatment; clinicians should carefully consider a range of CVR factors before prescribing ADT to patients based on the patient's cardiac history and identify high-risk men who might benefit from better patient–physician interaction, thus encouraging them for regular cardiac monitoring and lifestyle modifications. Cardiotoxicity of ADT is an area of intense ongoing investigation and clinical studies assessing the potential mechanisms by which any such risk could be mediated, are currently being conducted.

Despite this, the patients' awareness regarding CVR was at an alarmingly low rate versus awareness regarding sexual dysfunction and other side-effects. The awareness regarding CVR was even low in patients undergoing hormone therapy. This is in-line with a previous study, where the fear of compromised sexual functioning outweighed the concern for CVR associated with treatment [28]. Similar results have been shown in another study where patients were more aware and worried about urinary, bowel, and sexual functioning rather than cardiovascular or metabolic risks associated with PCa treatment [29]. Importantly, regardless of patients' CVR status, there were no changes in the treatment reported.

The results also showed that a majority of patients were informed of the CVR by their HCP. Per se, patients were less likely to initiate such discussions with their HCPs, even when they were at a high CVR. However, this did not mean that patients were not concerned about their CVRs, but it meant that there was a lack of awareness. This is apparent from the fact that where discussed, patients were more likely to initiate discussions on heart problems than the other risks associated with PCa treatment. Furthermore, a majority of patients made suitable lifestyle modifications to mitigate such risks, especially for those patients who were at a high CVR.

These findings are pertinent since PCa is a late-onset disease, and data show that by the time of diagnosis and initiation of treatment, many of these patients may already have a co-existing morbidity, such as cardiovascular disease [11], which may precipitate or exacerbate the existing condition. Furthermore, with an array of treatment-related side-effects, patients may feel anxious, depressed, and confused, which can be substantially improved by a better patient–HCP dialogue [30]. In this scenario, patient–HCP dialogue plays an important role in anchoring the patient's unmet needs [31, 32]. Similar findings were noted in this survey where patients were willing to make deliberate choices with respect to their treatment and lifestyle, once they were informed of the benefits and risks. This clearly substantiates the role of HCPs in spreading awareness regarding side-effects associated with PCa as observed in previous studies [33, 34], especially when it is pertaining to potentially life-threatening side-effects such as cardiovascular events.

In summary, there is a need to enhance medical dialogue between HCPs and patients. While certainly in some progressive clinics such conversations may happen, they are not taking place routinely everywhere in the US, EU and other parts of the world. In many countries the time for regular visit is simply insufficient for in-depth discussions.

Thus, the onus is on the HCP, the trusted advisor, to find the time and space to engage patients in dialogue around these topics. This will help patients to better understand treatment-related risks, make deliberate treatment choices to reduce such risks by adopting a healthier lifestyle. It is an equal responsibility of the patients to be aware of risk factors by accessing various sources, primarily the physician/HCP, patient groups, and the internet.

Conclusion

The outcome of PCa treatment is severely affected by comorbidities and certain types of hormone therapies are associated with treatment-related risks, such as increased cardiovascular events. For a better understanding and coping with treatment-related side-effects, HCPs and patients need to be in constant dialogue and exchange information regularly. HCPs need to integrate the patients' understanding and preference while making treatment decisions and impart the best suitable treatment options.

Acknowledgements The authors would like to thank Double Helix, Baker Street, London, for supporting the survey. Medical writing support was provided by Tania Peshin and Payal Bhardwaj (Tata Consultancy Services), both funded by Ferring.

Authors' contributions A Merseburger: scientific advisor; manuscript review. A Bro Falkenberg: project development including concept and design; manuscript review. O Kornilova: project development, data collection and management, data analysis, manuscript review.

Funding This online survey was conducted by Healthcare Market Research agency Double Helix and was funded by Ferring Pharmaceuticals.

Compliance with ethical standards

Conflict of interest Axel Merseburger is the associate editor of WJU and has contributed to pharmaceutical companies like Amgen, Apogepha, Astellas, Bayer, BMS, Clovis, Ferring, Hexal, Ipsen, Janssen, Merck, MSD, Novartis, Roche, Sanofi, Takeda, TEVA. Anne Bro Falkenberg was an employee of Ferring Pharmaceuticals at the time of conduct of this survey. Olga Kornilova is an employee of Ferring Pharmaceuticals.

Statement of human rights Patients participating in this anonymous online survey were asked for their agreement. Survey was conducted according to Market research industry code of conduct and privacy rights were respected in the analysis of results.

References

1. Prostate cancer statistics [Internet]: Centers for Disease Control and Prevention, CDC (US). Updated on 23 May 2017. https://www.cdc.gov/cancer/prostate/statistics/index.htm. Accessed 19 Jan 2018
2. Key statistics for Prostate cancer [Internet]. American Cancer Society. https://www.cancer.org/cancer/prostate-cancer/about/key-statistics.html. Accessed 19 Jan 2018
3. Tao ZQ, Shi AM, Wang KX, Zhang WD (2015) Epidemiology of prostate cancer: current status. Eur Rev Med Pharmacol Sci 19:805–812
4. Fu AZ, Tsai H-T, Haque R, Yood MU, Cassidy-Bushrow AE, Van Den Eeden SK, Keating NL, Smith MR, Zhou Y, Aaronson DS, Potosky AL (2017) Mortality and androgen deprivation therapy as salvage treatment for biochemical recurrence after primary therapy for clinically localized prostate cancer. J Urol 197:1448–1454
5. Greiman AK, Keane TE (2017) Approach to androgen deprivation in the prostate cancer patient with pre-existing cardiovascular disease. Curr Urol Rep 18:41
6. Keating NL, O'Malley AJ, Freedland SJ, Smith MR (2010) Diabetes and cardiovascular disease during androgen deprivation therapy: observational study of veterans with prostate cancer. J Natl Cancer Inst 102:39–46
7. Saigal CS, Gore JL, Krupski TL, Hanley J, Schonlau M, Litwin MS, Urologic Diseases in America Project (2007) Androgen deprivation therapy increases cardiovascular morbidity in men with prostate cancer. Cancer 110:1493–1500
8. Levine G, D'Amico AV, Berger P, Clark PE, Eckel RH, Keating NL, Milani RV, Sagalowsky AI, Smith MR, Zakai N (2010) Androgen deprivation therapy in prostate cancer and cardiovascular risk: a science advisory from the American Heart Association, American Cancer Society, and American Urologic Association: endorsed by the American Society for Radiation Oncology. Circulation 121:833–840
9. Tsai HK, D'Amico AV, Sadetsky N, Chen MH, Carroll PR (2007) Androgen deprivation therapy for localized prostate cancer and the risk of cardiovascular mortality. J Natl Cancer Inst 99:1516–1524
10. Haque R, UlcickasYood M, Xu X, Cassidy-Bushrow AE, Tsai HT, Keating NL, Van Den Eeden SK, Potosky AL (2017) Cardiovascular disease risk and androgen deprivation therapy in patients with localized prostate cancer: a prospective cohort study. Br J Cancer 117:1233–1240
11. Davis MK, Rajala JL, Tyldesley S, Pickles T, Virani SA (2015) The prevalence of cardiac risk factors in men with localized prostate cancer undergoing androgen deprivation therapy in British Columbia, Canada. J Oncol 2015:820403. https://doi.org/10.1155/2015/820403
12. Keating NL, O'Malley AJ, Freedland SJ, Smith MR (2013) Does comorbidity influence the risk of myocardial infarction or diabetes during androgen-deprivation therapy for prostate cancer? Eur Urol 64:159–166
13. Crawford ED, Moul JW (2015) ADT risks and side effects in advanced prostate cancer: cardiovascular and acute renal injury. Oncology 29(55–58):65–66
14. Gandaglia G, Sun M, Popa I, Schiffmann J, Trudeau V, Shariat SF, Trinh QD, Graefen M, Widmer H, Saad F, Briganti A, Montorsi F, Karakiewicz PI (2015) Cardiovascular mortality in patients with metastatic prostate cancer exposed to androgen deprivation therapy: a population-based study. Clin Genitourin Cancer 13:e123–e130
15. Snow SL, Panton RL, Butler LJ, Wilke DR, Rutledge RDH, Bell DG, Rendon RA (2007) Incomplete and inconsistent information provided to men making decisions for treatment of early-stage prostate cancer. Urology 69:941–945
16. Sommers BD, Beard CJ, D'Amico AV, Kaplan I, Richie JP, Zeckhauser RJ (2008) Predictors of patient preferences and treatment choices for localized prostate cancer. Cancer 113:2058–2067
17. Nguyen PL, Chen MH, Hoffman KE, Chen RC, Hu JC, Bennett CL, Kattan MW, Sartor O, Stein K, D'Amico AV (2012) Cardiovascular comorbidity and treatment regret in men with recurrent prostate cancer. BJU Int 110:201–205
18. Song L, Bensen JT, Zimmer C, Sleath B, Blackard B, Fontham E, Su LJ, Brennan CS, Mohler JL, Mishel M (2013) Patient-health care provider communication among patients with newly diagnosed prostate cancer: findings from a population-based survey. Patient Educ Couns 91:79–84
19. EAU Guidelines. Edn. presented at the EAU Annual Congress Copenhagen 2018
20. Van Hemelrijck M, Garmo H, Holmberg L, Ingelsson E, Bratt O, Bill-Axelson A, Lambe M, Stattin P, Adolfsson J (2010) Absolute and relative risk of cardiovascular disease in men with prostate cancer: results from the Population-Based PCBaSe Sweden. J Clin Oncol 28:3448–3456
21. Levine GN, D'Amico AV, Berger P, Clark PE, Eckel RH, Keating NL, Milani RV, Sagalowsky Zakai SN (2010) Androgen-deprivation therapy in prostate cancer and cardiovascular risk. Circulation 121:833–840
22. Teoh JY, Chan SY, Chiu PK, Poon DM, Cheung HY, Hou SS, Ng CF (2015) Risk of cardiovascular thrombotic events after surgical castration versus gonadotropin-releasing hormone agonists in Chinese men with prostate cancer. Asian J Androl 17:493–496
23. Chen DY, See LC, Liu JR, Chuang CK, Pang ST, Hsieh IC, Wen MS, Chen TH, Lin YC, Liaw CC, Hsu CL, Chang JW, Kuo CF, Huang WK (2017) Risk of cardiovascular ischemic events after surgical castration and gonadotropin-releasing hormone agonist therapy for prostate cancer: a nationwide cohort study. J Clin Oncol 35:3697–3705
24. O'Farrell S, Garmo H, Holmberg L, Adolfsson J, Stattin P, Van Hemelrijck M (2015) Risk and timing of cardiovascular disease after androgen-deprivation therapy in men with prostate cancer. J Clin Oncol 33:1243–1251
25. Iacovelli R, Ciccarese C, Bria E, Romano M, Fantinel E, Bimbatti D, Muraglia A, Porcaro AB, Siracusano S, Brunelli M, Mazzarotto R, Artibani W, Tortora G (2018) The Cardiovascular Toxicity of Abiraterone and Enzalutamide in Prostate Cancer. Clin Genitourin Cancer 16:e645–e653
26. Latorzeff I, Ploussard G, Guillotreau J, Jonca F, Labarthe P, Rollin G, Beauval JB, Pathak A (2016) Cardiovascular risks with prostate cancer hormonal treatment: rationale for a department of oncocardiology. Cancer Radiother 20:405–410
27. Bhatia N, Santos M, Jones LW, Beckman JA, Penson DF, Morgans AK, Moslehi J (2016) Cardiovascular effects of androgen deprivation therapy for the treatment of prostate cancer: ABCDE steps to reduce cardiovascular disease in patients with prostate cancer. Circulation 133:537–541
28. Knight SJ, Latini DM (2009) Sexual side effects and prostate cancer treatment decisions: patient information needs and preferences. Cancer J 15:41–44
29. Watson E, Shinkins B, Frith E, Neal D, Hamdy F, Walter F, Weller D, Wilkinson C, Faithfull S, Wolstenholme J, Sooriakumaran P, Kastner C, Campbell C, Neal R, Butcher H, Matthews M, Perera R, Rose P (2016) Symptoms, unmet needs, psychological well-being and health status in survivors of prostate cancer: implications for redesigning follow-up. BJU Int 117:E10–E19
30. Fourcade RO, Mensink P, Ernemo B, Ligensa C (2002) The value of patient–doctor dialog in the treatment of early prostate cancer. Prostate Cancer Prostatic Dis 5:S12–S14

31. Hardy C, Penn S, Morris T (2007) Attitudes of prostate cancer patients towards the diagnosis and treatment of their disease: findings from a multinational survey. Curr Med Res Opin 23:2107–2116
32. Basaria S (2012) Time to raise awareness regarding complications of androgen deprivation therapy. Asian J Androl 14:175–176
33. Schostak M, Wiegel T, Müller M, Hoecht S, Schrader M, Straub B, Bottke D, Hinkelbein W, Miller K (2004) Shared decision-making—results from an interdisciplinary consulting service for prostate cancer. World J Urol 22:441–448
34. Patel HR, Mirsadraee S, Emberton M (2003) The patient's dilemma: prostate cancer treatment choices. J Urol 169:828–833