Prostate cancer profile in Dr. Sardjito General Yogyakarta

Yurisal Akhmad Dany, Ahmad Zulfan Hendri, Indrawarman Soerohardjo*
Division of Urology, Department of Internal Medicine, Faculty of Medicine, Public Health and Nursing, Universitas Gadjah Mada/Dr. Sardjito General Hospital, Yogyakarta, Indonesia

ABSTRACT

Prostate cancer is the fourth most common type of non-skin malignancy in male malignancies. In Indonesia, the definitive data are unreported, however, Globocan reported prostate cancer in 5th place in 2018. The aim of this study is to provide in updating database of prostate cancer profile in tertiary hospital in Indonesia. A retrospective study involving a total of 90 prostate cancer patients who underwent follow-up care at Dr. Sardjito General Hospital, Yogyakarta in the period of 2015 to 2020 was conducted. Data of the patients from their medical records consisted of age, gender, prostate volume, PSA level, testosterone level, hydronephrosis, TURP history. From a total 90 subjects, showed an average age of 67 years (SD=10.4). The level of prostate volume (TAUS), most subjects were >30 cm³ with 73 subjects (81.4%). Of the total subjects, the median of total PSA value for diagnosis is 234.4 (94.4 – 1720.3) ng/mL with the median of total testosterone value at diagnosis is 317 (10 – 384) ng/dL. An equal between biopsy and TURP were used in method of diagnosis and histologic finding consisting of Adenocarcinoma were found in 88 subjects (97.8%) with Gleason score > 7 in 69 subject (69.6%) and ISUP Grade 5 in 59 subject (65.6%). The staging T1c was found in 43 subjects (47.8%) and M staging with metastasis stage was found in 55 subjects (61.1%). In conclusion, most patients with prostate cancer are identified as adenocarcinoma with metastatic stage. In general, the prostate cancer patients age more than 61 years old with prostate volume (TAUS) > 30 cm³. In addition, prostate volume and testosterone level can be routinely used as initial screening and periodic assessment to evaluate prognosis and disease progression.

Keywords: Prostate Cancer; Serum PSA; TNM Staging;
INTRODUCTION

Prostate cancer is currently the most commonly diagnosed cancer in 105 countries. It is the fourth most common type of non-skin malignancy (7.1%) in male malignancies, the second most common malignancy in males worldwide. In 2018, 1.3 million new cases of prostate cancer and 359,000 related deaths worldwide were reported. With rapid population growth and aging worldwide, this cancer is the 5th leading cause of death in men. Early diagnosis and early treatment of prostate cancer have been associated with reduced mortality rates in many countries, including the United States, North America, Oceania, Northern, and Western Europe as well as in developing countries in Asia.

The incidence and mortality of cancer are increasing rapidly throughout the world as diagnostic tools advance. As one of the diagnostic methods of choice, the prostate-specific antigen (PSA) is a member of the kallikrein gene family. It is also known as the androgen-dependent hK3 (human kallikrein 3). Screening for PSA in prostate cancer cases has reduced the death rate of prostate cancer by more than 40%, as well as the 75% decrease in the number of advanced cases since diagnosis in the United States.

In Indonesia, there are no definite data, let alone in testosterone level or tumor burden data although Globocan reported that prostate cancer in the 5th place in Indonesia in 2018. Based on 2011 data from the Indonesian Urological Oncology Society (ISUO) during the 2006-2010 period, 971 patients were diagnosed with prostate cancer. The mean age was 68.3 years, mostly (37.6%) at 70-79 years of age. The diagnostic method used was primarily biopsied in 563 cases (57.9%). The majority cases were patients with stage 4 (50.5%), followed by stage 2 (271 cases or 27.9%), stage 1 (83 cases or 8.5%), and stage 3 (28 cases or 2.9%). Orchidectomy was the most widely used initial therapy (307 cases or 31%), followed by hormonal drugs (182 or 18%), radical prostatectomy (89 cases or 9%), radiotherapy (63 cases or 6%) and the rest was active monitoring, chemotherapy, and combinations. In this study, we reported the profile of the prostate cancer in Dr. Sardjito General, Yogyakarta for a period of 5 years.

MATERIALS AND METHODS

Subjects and design

This was an observational study with descriptive retrospective design involving 90 prostate cancer patients who underwent follow-up treatment at the Dr. Sardjito General Hospital, Yogyakarta, Indonesia from 2015 to 2020.

Protocol of study

The data from patients’ medical records in Dr. Sardjito General Hospital, Yogyakarta were collected by 2 observers to reduce bias. This study has been approved by the Medical and Health Research Ethics Committee, Faculty of Medicine, Public Health, and Nursing, Universitas Gadjah Mada, Yogyakarta (Ref. No. KE/FK/1059/EC/2020). Inclusion criteria were patients who have been diagnosed with prostate cancer from 2015 to 2020. Exclusion criteria were patients who were not registered in Dr. Sardjito General Hospital, Yogyakarta. The data of the patient’s age, gender, prostate volume, pre-treatment total PSA level, pre-treatment total testosterone level, hydronephrosis, TURP history, histopathology results, Gleason scores, ISUP grade, staging, and tumor burden were retrieved from the medical report.

Statistical analysis

Data were analyzed with cross tabulation table using the IBM SPSS 23.00 statistics and served in table form.
RESULTS

Ninety secondary data of prostate cancer inpatients visited and registered in Dr. Sardjito General Hospital, Yogyakarta from 2015 to 2020 were collected (TABLE 1). According to the patient age, among 90 patients, 22 patients (24.4%) were <60 y.o., 34 patients (37.8%) were 61-70 y.o. and 34 patients (37.8%) were >70 y.o. Average age of the patients were 67 ±10.4 y.o. Furthermore, according to the level of prostate volume (TAUS) showed most patients (48 patients or 53.3%) had prostate volume > 30 cm³ with median of 51 cm³ (38.3 – 104.4). Median of the PSA level for diagnosis was 234.4 (94.4 – 1720.3) ng/mL, whereas median of the testosterone level was 317 (10 - 384) ng/dL.

Based on the histological findings (TABLE 1), adenocarcinoma was found in most of all patients (88 patients or 97.8%) with most of patients had Gleason score > 7 (69 patients or 69.6%) and ISUP grade > 2 (75 patients or 83%). In addition, staging ≤ T2 was found in 74 patients (82.2%) and metastasis stage was found in 55 subjects (61.1%).

| Characteristics            | n (%) | Mean (SD)     | Median | Q1   | Q3   |
|----------------------------|-------|---------------|--------|------|------|
| Age (y.o)                  |       |               |        |      |      |
| • 60                       | 22 (24.4) | 67 ± 10.4     | 70     | 63.75| 75   |
| • 61 – 70                  | 34 (37.8) |               |        |      |      |
| • > 70                     | 34 (37.8) |               |        |      |      |
| Prostate volume (cm³)      |       |               |        |      |      |
| • ≤ 30                     | 17 (18.6) | 102 ± 117.5   | 51     | 38.3 | 104.4|
| • > 30                     | 48 (53.3) |               |        |      |      |
| • Unknown                  | 31 (34.4) |               |        |      |      |
| Total PSA (ng/mL)          |       |               |        |      |      |
| • ≤ 20                     | 8 (8.9)  | 710 ± 1334.5  | 234.4  | 94.4 | 1720.3|
| • > 20                     | 58 (64.4) |               |        |      |      |
| • Unknown                  | 24 (26.7) |               |        |      |      |
| Testosterone level (ng/dL) |       |               |        |      |      |
| • ≤ 300                    | 19 (21.1) | 280 ± 310     | 317    | 10   | 384  |
| • > 300                    | 19 (21.1) |               |        |      |      |
| • Unknown                  | 52 (47.8) |               |        |      |      |
| Hydronephrosis:            |       |               |        |      |      |
| • Unilateral               | 11 (12.2) |               |        |      |      |
| • Bilateral                | 26 (28.9) |               |        |      |      |
| • Without                  | 53 (58.9) |               |        |      |      |
| Method of Diagnosis        |       |               |        |      |      |
| • Biopsy                   | 45 (50)  |               |        |      |      |
| • Turp                     | 45 (50)  |               |        |      |      |
| Histopathologic finding    |       |               |        |      |      |
| • Adenocarcinoma           | 88 (97.8) |               |        |      |      |
| • Non-Adenocarcinoma       | 2 (2.2)  |               |        |      |      |
| Gleason Score              |       |               |        |      |      |
| • ≤ 7                      | 21 (23.3) |               |        |      |      |
| • > 7                      | 69 (69.6) |               |        |      |      |

TABLE 1. Characteristic of subjects


| ISUP grade |       |
|-----------|-------|
| • 1       | 8 (8.9)|
| • 2       | 6 (6.1)|
| • 3       | 5 (5.6)|
| • 4       | 10 (11.1)|
| • 5       | 59 (59.6)|

| Staging     |       |
|-------------|-------|
| • ≤ T2      | 74 (82.2)|
| • > T2      | 13 (14.4)|
| • Unknown   | 3 (3.4)|

| Metastasis  |       |
|-------------|-------|
| • Yes       | 55 (61.1)|
| • No        | 14 (15.6)|
| • Unknown   | 21 (23.3)|

| Tumor burden: |       |
|---------------|-------|
| • High volume | 46 (51.1)|
| • Low volume  | 23 (25.6)|
| • Unknown     | 21 (23.3)|

**DISCUSSION**

The Indonesian Society of Urologic Oncology (ISUO) reported during the period of 2006 to 2010 971 patients were diagnosed with prostate cancer. The average age of the patients was 68.3 years. Demographics of prostate cancer patients at Dr. Sardjito General Hospital during the period of 2015 to 2020 showed 50% of cases were locally advanced prostate cancer, including high metastatic and high-volume Tumor Burden disease. This study also showed that the majority of patients with prostate cancers are only detected at an advanced stage or metastasis. Lack of knowledge of Indonesian people concerning prostate cancer and its screening test cause the delay in early diagnosis and not regularly performed. Metastatic tracking was mandatory based on the results of the data in this study. Cases of prostate cancer are of interest to researchers, where total serum testosterone levels may have reached castration levels at the time of initial diagnosis and without prior hormonal therapy.

PSA screening in cases of prostate cancer reduces the mortality rate and decreases in advanced cases based on the EAU Risk Group. The majority of patients visiting Dr. Sardjito General Hospital, Yogyakarta have been diagnosed with locally advanced prostate cancer early on. It is believed that early diagnosis of metastatic stage prostate cancer is very likely and that further screening efforts are required to take into account the cost-benefit of early-stage prostate cancer diagnostics.

Interestingly, according to the researchers, although the screening of testosterone levels in cases of prostate cancer at the time of initial diagnosis with serum total testosterone levels had low levels. Androgen is the main source of the prostate to grow. Higher consumption of androgen leads to the increase of prostate hyperplasia, which can be seen by measuring PSA. Two studies showed low level of serum total Testosterone correlated with advanced diseases. Researchers assume that further research involving total serum testosterone levels with a larger sample may be able to further explain the androgen-dependent pathway and the accuracy of the management options for prostate cancer. Researchers assume
that metastatic tracking is mandatory, considering the results of this study, it was found that the majority of the initial presence of PSA in prostate cancer patients with total serum PSA levels >20 ng/mL was due to cost-benefit considerations.

CONCLUSION

In contrast with developed country, this study shows that most Indonesian prostate cancer patients are diagnosed in metastatic stage with higher PSA level and ISUP grade. Further encouragement in prostate cancer screening for men with symptoms or risk factor should be considered to find more cases in lower stages for better prognosis and survival rate.

ACKNOWLEDGEMENT

Authors would like to thank staffs from the Medical Record Unit, Dr. Sardjito General Hospital, Yogyakarta for the valuable assistance during collecting the data of patients.

REFERENCES

1. Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin 2018; 68(6):394-424. https://doi.org/10.3322/caac.21492
2. Center MM, Jemal A, Lortet-Tieulent J, Ward E, Ferlay J, Brawley O, et al. International variation in prostate cancer incidence and mortality rates. Eur Urol 2012; 61(6):1079-92. https://doi.org/10.1016/j.eururo.2012.02.054
3. Bray F, Piñeros M. Cancer patterns, trends and projections in Latin America and the Caribbean: A global context. Salud Publica Mex 2016; 58(2):104-17.
4. Wong MCS, Goggins WB, Wang HHX, Fung FDH, Leung C, Wong SYS, et al. Global Incidence and mortality for prostate cancer: analysis of temporal patterns and trends in 36 countries. Eur Urol 2016; 70(5):862-74. https://doi.org/10.1016/j.eururo.2016.05.043
5. Brawley OW. Trends in prostate cancer in the United States. J Natl Cancer Inst Monogr 2012; (45):152-6. https://doi.org/10.1093/jncimonographs/lgs035
6. Diamandis EP, Yousef GM, Luo LY, Magklara A, Obiezu CV. The New human kallikrein gene family: implications in carcinogenesis. Trends Endocrinol Metab 2000; 11(2):54-60. https://doi.org/10.1186/1755-8794-4-76
7. Lundwall A, Lilja H. Molecular cloning of human prostate specific antigen cDNA. FEBS Lett 1987; 214(2):317-22. https://doi.org/10.1016/0014-5793(87)90054-X
8. Mccormack RT, Rittenhouse HG, Finaly JA, Sokoloff RL, Wang TJ, Wolfert RL, et al. Molecular forms of prostate-specific antigen and the human kallikrein gene family a new era. Urology 1995; 45(5):729-44. https://doi.org/10.1016/s0090-4295(99)80076-4
9. Henttu P, Liao S, Vihko P. Androgens up-regulate the human prostate-specific antigen messenger ribonucleic acid (mRNA), but down-regulate the prostatic acid phosphatase mRNA in the LNCaP cell line. Endocrinology 1992; 130(2):766-72. https://doi.org/10.1016/s0013-7227(17)30077-4
10. Etzioni R, Tsodikov A, Mariotto A, Szabo A, Falcon S, Wegelin J, et al. Quantifying the role of PSA screening in the US prostate cancer mortality decline. Cancer Causes Control 2008; 19(2):175-81. https://doi.org/10.1007/s10552-007-9083-8
11. World Health Organization.
Indonesia Source GLOBOCAN 2018. Int Agency Res Cancer. 2019; 256:1–2. https://gco.iarc.fr/today/data/factsheets/populations/360-indonesia-fact-sheets.pdf

12. Indonesian Society of Urologic Oncology (ISUO) meeting. 2011. Unpublished data.

13. Sweeney CJ, Chen YH, Carducci M, Liu G, Jarrard DF, Eisenberger M, et al. Chemohormonal therapy in metastatic hormone-sensitive prostate cancer. N Engl J Med 2015; 373(8):737-46. https://doi.org/10.1016/j.urolonc.2016.12.021

14. Broeck T, Van den. European Association of Urology 2020 EAU Guidelines. https://uroweb.org/guideline/prostate-cancer/

15. Oefelein MG, Feng A, Scolieri MJ, Ricchiuti D, Resnick MI. Reassessment of the definition of castrate levels of testosterone: implications for clinical decision making. Urology 2000; 56(6):1021-4. https://doi.org/10.1016/s0090-4295(00)00793-7

16. Tu H, Gu J, Meng QH, Kim J, Strom S, Davis JW, et al. Low serum testosterone is associated with tumor aggressiveness and poor prognosis in prostate cancer. Oncol Lett 2017; 13(3):1949-57. https://doi.org/10.3892/ol.2017.5616

17. Gyeong-Ju A. The relationship between levels of serum testosterone and prostate-specific antigen in healthy men: an integrative review. Journal of Korean Biological Nursing Science 2020; 22(2):71-80. https://doi.org/10.7586/jkbns.2020.22.2.71