Research Article

The Impact of COVID-19 Pandemic on The Selection of Prostate Cancer Treatment among Urologist in Indonesia: A Survey Analysis

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Abstract

Incidence of PCa in Indonesia placed in number 6th, the data from Globocan 2020 also showed that PCa lined up as the highest urological cancer cases in both sexes of the country. The cancer has broad spectrum treatments, the selection of which can be determined by risk classification. However, in the setting of the coronavirus disease 2019 (COVID-19) pandemic, health care, including urology services worldwide have been undergone changes particularly in terms of treatment protocol. This study seeks to determine how the COVID-19 pandemic influences the choice of treatment of PCa in Indonesia. This was a cross-sectional study through a questionnaire which was distributed via Survey Monkey (www.surveymonkey.com), a cloud-based online survey. A survey was delivered to all urologists in Indonesia. A total of 174 urologists completed the questionnaire. Amongst 117 respondents who performed prostate biopsy, 39.2% and 37.5% working in public and private hospital had more than 50% reduction or no prostate biopsy procedure during COVID-19 pandemic. However, only 27.0% deferred prostate biopsy due to COVID-19. During pandemic, 73 (42%) respondents who previously chose radical prostatectomy as their priority for localized PCa, shifted their choice into active surveillance and androgen deprivation therapy (ADT) evenly that made active surveillance as primary choice of treatment in localized cases. Moreover, only 12.1% and 10.3% chose ADT combination therapy (with docetaxel, abiraterone acetate, enzalutamide/apalutamide) as their primary choice of metastatic PCa treatment before and during COVID-19 pandemic. In conclusion, the impact of COVID-19 on PCa were prominent in diagnostic procedure and management of localized or low risk PCa.

Keywords*: COVID-19, prostate cancer, radical prostatectomy, active surveillance, radiation, androgen deprivation therapy, chemotherapy*

Dampak Pandemi COVID-19 Terhadap Pemilihan Terapi Kanker Prostat oleh Ahli Urologi di Indonesia: Analisis Survey

Abstrak

Di Indonesia insidens kanker prostat berada di peringkat ke-6 dan merupakan jenis kanker urologi terbanyak berdasarkan data Globocan 2020. Tersedia beragam terapi kanker prostat dan pemilihan terapi berdasarkan klasifikasi risiko tertentu. Pada situasi pandemi coronavirus disease 2019 (COVID-19), fasilitas pelayanan kesehatan di dunia, termasuk layanan urologi, mengalami perubahan terkait protokol tata laksana. Penelitian ini bertujuan untuk mengetahui pengaruh pandemi COVID-19 terhadap pilihan terapi kanker prostat di Indonesia. Penelitian ini menggunakan desain potong-lintang dan data diperoleh dari kuesioner yang didistribusikan melalui Survey Monkey (www.surveymonkey.com), sebuah survei daring berbasis cloud. Survei dikirim kepada seluruh ahli urologi di Indonesia.. Responden adalah 174 urolog yang telah melengkapi kuesioner. Di antara 117 responden yang mengerjakan biopsi prostat, 39,2% yang bekerja di rumah sakit umum dan 37,5% di rumah sakit swasta mengalami pengurangan jumlah prosedur biopsi prostat > 50% atau tidak melakukannya sama sekali. Hanya 27,0% yang menunda biopsi prostat akibat COVID-19. Sebelum pandemi, 73 responden (42%) memilih prostatektomi radikal sebagai prioritas utama untuk kanker prostat lokal, namun selama pandemi pilihan beralih ke surveilans aktif dan terapi deprivasi androgen secara merata, menjadikan surveilans aktif sebagai pilihan utama. Selain itu pada kasus kanker prostat metastasis jumlah responden yang memilih kombinasi terapi deprivasi androgen dengan dosetaksel, abirateron asetat, atau enzalutamid/apalutamid) sebagai pilihan utama hanya 12,1% sebelum dan 10,3% saat pandemi COVID-19. Disimpulkan dampak COVID-19 terlihat lebih nyata pada prosedur diagnostik dan manajemen kanker prostat lokal atau berisiko rendah.

Kata kunci: *COVID-19, kanker prostat, prostatektomi radikal, surveilans aktif, radiasi, terapi deprivasi androgen, kemoterapi.*

Introduction

Coronavirus disease (COVID-19) pandemic caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has become the greatest challenge to humanity in 2020. Firstly recognized in December 2019, it has affected more than 30 million people worldwide with one million death in less than one year.[1] The pandemic greatly affects health care service including urology services.[2] While some countries have succeeded in flattening the COVID-19 curve, Indonesia is still experiencing an increase in the number of cases.[3] Even though there is a high risk in the spread of COVID-19, a proper urology service is mandatory to be delivered. Therefore, careful patient selection and adjustment of appropriate patient management which could handle the disease optimally while minimizing the risk of COVID-19 transmission to patient and health care provider should be done. This applies to the management of prostate cancer (PCa) patients.

PCa is the fifth leading cause of cancer death in men worldwide. Based on Globocan 2020 report in male cancer category, incidence of PCa in Indonesia placed in number 6th, the data also showed that PCa lined up as the highest urological cancer cases in both sexes of the country.[4] The cancer has broad spectrum treatments, i.e. radical prostatectomy (RP), external beam radiation therapy (EBRT), androgen deprivation therapy (ADT), active surveillance, and the selection of which is determined by risk classification with the involvement of multidisciplinary team.[5–7] Since majority of PCa patients are older than 60 years which intensify the susceptibility of poor COVID-19 outcome, considerations in choosing PCa therapies are not based solely on risk classification or patient's preference, but also whether those treatments could place the patient or health care provider in a position that is invulnerable to being exposed by SARS-CoV-2.[8,9]

To overcome this particular situation, several recommendations were offered to manage PCa patient, such as delay in screening; defer diagnosing, staging, or surgery in low or intermediate risk disease; or shorten the radiotherapy regimen.[10–12] However, implementation of daily clinical practice recommendation could be influenced by many factors and barriers, such as patient characteristics, equipment availabilities, or facilities.[13,14] Current study showed a decrease in number of patients, both in outpatient service and procedural or surgical service as a response to COVID-19 pandemic.[2] However, how physicians adapt or respond specifically to current situation for PCa management is currently unknown especially in Indonesia. Therefore, this study aimed to explore how COVID-19 pandemic influenced the urologists to therapeutic decision-making in PCa management.

Methods

Study Design, Setting, and Participants

This was a cross-sectional study through a questionnaire which was distributed via SurveyMonkey® (www.surveymonkey.com), a cloud-based online survey. A survey was opened from July to October 2020 to all urologists in Indonesia.

Survey Construction and Data Collection

The questionnaire was constructed in Bahasa Indonesia and consists of four pages as follow: first page contained about respondent consent to participate in the study; second page consisted of questions about respondent demographic characteristic; third page only contained one question to assign respondent specialty; and fourth page was composed to explore respondent's choice of treatment in PCa management. The question about choice of treatment priority was constructed by ranking the treatment priority in each given patient's condition was designed to. The questionnaire required the respondents to complete all questions before continuing to the next page.

The questionnaires were distributed to all target participants using a SurveyMonkey® link via each association. Each association distributed the link using e-mail or WhatsApp Messenger application (WhatsApp Inc.) for at least five times within period of July to October 2020. To prevent data redundancy, the SurveyMonkey® was set to allow the questionnaire to be submitted once from the same device, in-order-that, the data collectors were able to exclude double-submission from same person. Furthermore, respondent's e-mail address was also checked to prevent duplication data by confirming to each association member databases.

Data Analysis and Reporting

Data from SurveyMonkey® was translated into SPSS version 20 (IBM Corp, Armonk, NY, USA) to be analyzed. Data was presented in descriptive fashion using table or graph. Numeric data was presented as mean if it had normal data distribution and as median if it had abnormal data distribution. For questions about choice of treatment priority, ranking of priority

was determined using average with the lowest mean value was considered as the top priority. This study was approved by dr. Cipto Mangunkusumo Hospital and Faculty of Medicine, Universitas Indonesia ethical committee (ethical approval number: KET-640/UN2.F1/ETIK/PPM.00.02/2020).

Results

Out of 201 responses from urologists, 174 completed the questionnaire. The demographic characteristics of respondents can be seen in Table 1.

Table 1. Respondent Demographic Characteristics

Characteristics		Urologist (n=174)
Age, median (min-max)		39 (30 – 72)
Gender, n (%)		
Male		164 (94.3)
Female		10 (5.7)
Work at, n (%)		
Public hospital only		6 (3.4)
Private hospital only		33 (18.9)
Both hospitals		135 (77.5)
Hospital accepting COVID-19 patient, n (%)		
Public hospital		135/141 (95.7)
Private hospital		116/168 (69)
Decrease in treated PCa patient before and during pandemic (%)		
Public hospital	No decrease	90/141 (63.8)
	<50% decrease	10/141 (42.9)
	>50% decrease	37/141 (26.2)
	Closing outpatient clinic	4/141 (2.8)
Private hospital	No decrease	115/168 (68.5)
	<50% decrease	4/168 (2.4)
	>50% decrease	37/168 (22)
	Closing outpatient clinic	12/168 (7.1)

Prostate Biopsy

Of 174 urologist respondents, there were only 120 (69.0%) urologists performing prostate biopsy procedures. Amongst them, 47 (39.2%) and 45 (37.5%) urologists who practiced in the public and private hospital, respectively, experienced a decrease of more than 50% in prostate biopsy and did not perform prostate biopsy during pandemic (Table 2). However, the decrease caused by procedural delay due to COVID-19 occurred in only 27.0% respondents.

Table 2. Decrease in Prostate Biopsy Procedure Before and During Pandemic

Hospital	Indicator	Decrease in Prostate n (%)
Public (n = 82)	No decrease	11 (13.4)
	<50% decrease	24 (29.3)
	>50% decrease	28 (34.1)
	No procedure	19 (23.2)
Private (n=80)	No decrease	8 (10.0)
	<50% decrease	27 (33.8)
	>50% decrease	22 (27.5)
	No procedure	23 (28.7)

Choice of PCa Treatment

The adjustment of localized, locally advanced, and metastatic PCa treatment during COVID-19 can be seen in Table 3. Before COVID-19, RP (42%) became the first priority for localized PCa, with active surveillance (34.5%) ranked in the second place. However, during COVID-19 respondents shifted their priority to active surveillance (39.7%) and from 73 (42%) respondents who chose RP as their priority treatment for localized PCa before COVID-19 pandemic, both 18 (24.7%) respondents shifted their priority to active surveillance and ADT, respectively. (Table 3) Moreover, hormonal ADT constantly was chosen as the priority for metastatic PCa treatment before and during COVID-19. A small portion of urologists (3.4%) provided home service for ADT administration (Table 4). Meanwhile, chemotherapy procedure given to the PCa patients with high susceptibility of COVID-19 was still performed by 62 (35.6%) respondents. Common comorbidities considered by urologists for delaying chemotherapy during COVID-19 is depicted in Figure 2.

Teleconsultation

The Teleconsultation method was used by 51 out of 174 (29.3%) respondents as their part of PCa management. Among them, the teleconsultation facility and system was provided by 20 public hospitals and 38 private hospitals where they work. Apart from that, respondents used their own gadget to facilitate teleconsultation. Post-procedural aftercare and follow up after systemic therapy are the conditions when 16 (31.4%) and 28 (54.9%) respondents utilized teleconsultation, respectively.

Table 3. PCa Choice of Treatment Priority in Localized and Locally Advanced PCa

Localized PCa			Locally Advanced PCa		
Rank	**Before COVID-19, Treatment (%)**	**During COVID-19, Treatment (%)**	**Rank**	**Before COVID-19, Treatment (%)**	**During COVID-19, Treatment (%)**
1st	Radical prostatectomy (42.0)	Active surveillance (39.7)	1st	ADT (44.8)	ADT (51.7)
2nd	Active surveillance (34.5)	ADT (24.1)	2nd	Radical prostatectomy (28.2)	Radiation therapy + ADT (22.4)
3rd	ADT (19.0)	Radical prostatectomy (18.4)	3rd	Radiation therapy + ADT (27.0)	Radical prostatectomy (17.2)
4th	Radiation therapy (4.6)	Delay all treatments (9.8)	4th	-	Delay all treatments (8.6)
5th	-	Radiation therapy (8.0)			

n = 174, ADT = Androgen deprivation therapy.
Rank order was determined based on the mean value
1 = highest priority, 4 or 5 = lowest priority

Table 4. PCa Choice of Treatment Priority in Metastatic PCa

Metastatic PCa		
Rank	**Before COVID-19, Treatment (%)**	**During COVID-19, Treatment (%)**
1st	Hormonal ADT (46.0)	Hormonal ADT (45.4)
2nd	Surgical ADT (42.0)	Surgical ADT (36.2)
3rd	ADT + Docetaxel (6.9)	Delay all treatments (8.0)
4th	ADT + Abiraterone (2.9)	ADT + Docetaxel (5.7)
5th	ADT + Enzalutamide/Apalutamide (2.3)	ADT + Abiraterone (2.9)
6th	-	ADT + Enzalutamide/Apalutamide (1.7)

ADT = Androgen deprivation therapy
Rank order was determined based on the mean value
1 = highest priority, 5/6 = lowest priority

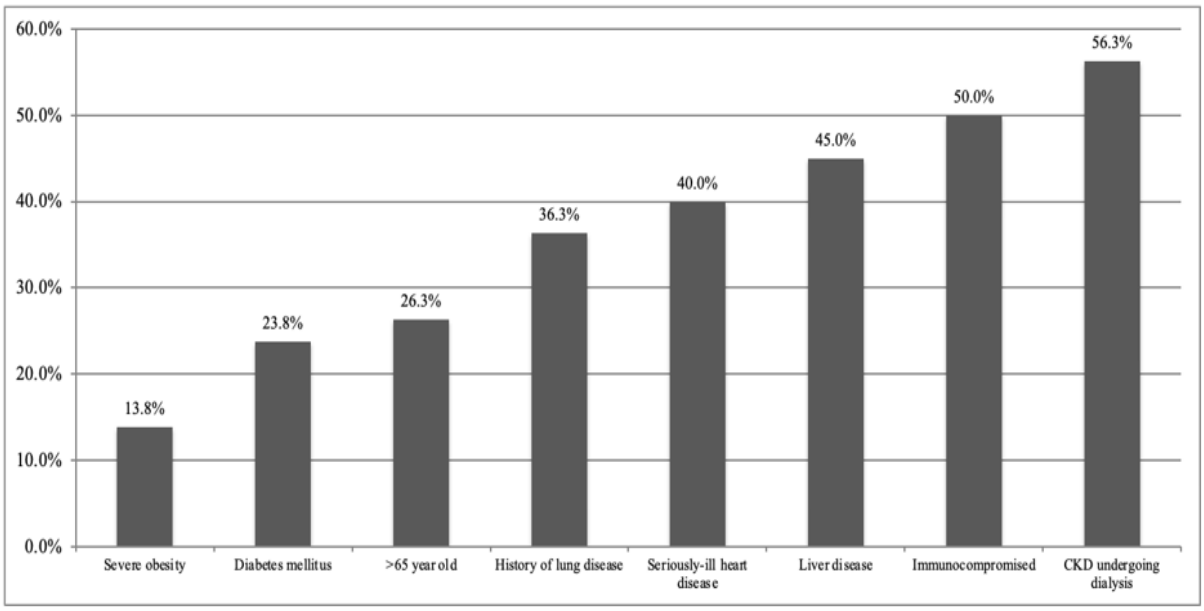

Figure 1. Comorbidities Considered for Delay of Chemotherapy among PCa Patients during COVID-19

Discussion

Management of PCa which has a broad range of treatment have been affected by current situation of COVID-19. The changes might be due to protocol establishment to prevent COVID-19 cross-infection within hospital and careful patient selection in outpatient clinic or surgery cases to conserve resource and prevent burnout of health care provider.[15] Even though a decrease in the number of outpatient clinic patient was seen during earlier time of COVID-19 pandemic, this study showed that more than 60% respondents felt similar number of PCa patient treated currently compared to before COVID-19 pandemic.[2] This finding could mean that hospital has been trying to restore its health care service into pre-pandemic level. However, more than 60% urologists who performed prostate biopsy, either in public or private hospital, felt more than 50% decrease in prostate biopsy procedure currently, but the decrease was mostly not due to urologist decision to defer in relation with COVID-19 situation. Therefore, this might happen due to a limitation and prioritization of elective surgery procedure. Current guideline recommends to defer prostate biopsy until pandemic is over, except for high risk PCa which should only delay for 3 month, or potentially lethal PCa.[12] Moreover, current reference also recommends to avoid transrectal prostate biopsy due to finding of SARS-CoV-2 in feces, though conclusive evidence is not yet demonstrated of COVID-19 dissemination by feces, the chance of fecal transmission should be minimized.[12,16]

Apart from COVID-19 situation, highlights should also be given to the fact that more than 30% of urologists did not perform prostate biopsy in their practice. Beside prostate specific antigen (PSA) which is used as screening and determining risk classification, prostate biopsy has an important role in PCa diagnosis and determination of further PCa management. Therefore, this situation should be addressed by identifying and treating the reason behind the insufficient number of biopsies performed. In line with this, the National Comprehensive Cancer Network (NCCN), European Association of Urology (EAU), and the Canadian Framework have advised urologists to suspend biopsies until after the pandemic, with exceptions for special circumstances such as the suspicion of a potentially lethal PCa, or when PSA levels are ≥ 10 ng/mL in which case a biopsy may be performed within 3-4 months.[17,18]

In regards of PCa treatment during COVID-19 pandemic, choice of treatment recommended by current guideline was determined based on PCa risk classification or tumor extension.[10–12] The changes of treatment priority were only seen in localized PCa before and during COVID-19 period based on this study finding. Before pandemic, RP became top priority of treatment for 42.0% respondents. However, during pandemic, the choice of treatment shifted to active surveillance and ADT as first and second top priority, respectively. The choice of treatment to defer RP during COVID-19 pandemic is in line with current literatures and recommendations stated by NCCN, EAU, and the Canadian Framework.[12] EAU recommended to postpone the RP in intermediate and high risk PCa until after pandemic. If patients anxious to undergo treatment, combination of ADT and radiotherapy can be offered, but ADT alone as temporary substitute treatment while waiting the surgery is not recommended.[19] However, this study found that ADT alone was preferred by respondents rather than radiotherapy for localized PCa and even became top choice of treatment for locally advanced PCa before and during pandemic. Many trials showed oncological outcome benefit in combination of radiotherapy and ADT compared to ADT alone for locally advanced PCa.[18,20,21] This choice of treatment might be due to limited access or unequal radiotherapy service in Indonesia. This study did not explore further reasons behind the choice of ADT alone as choice of treatment, but this situation should be an input for stakeholders for better PCa management.

Combination ADT and other agent, such as docetaxel, abiraterone acetate, enzalutamide, or apalutamide has become a standard treatment for metastatic castration-naïve PCa.[5] However, in Indonesia, ADT alone, either hormonal or surgical, is still become the top priority choice of treatment for metastatic PCa before and during COVID-19 pandemic. This study showed that amongst combination therapies, ADT and docetaxel became top priority of choice for both urologist and medical oncologist, before and during COVID-19 pandemic, even though many guidelines recommended to avoid chemotherapy during COVID-19 pandemic due to risk of neutropenia and frequent hospital visit.[12] However, this is difficult to avoid since docetaxel is currently the only drug guaranteed by Indonesia's universal health coverage.

Telemedicine implementation during COVID-19 is set to prevent both patients and healthcare professionals from contracting COVID-19. EAU guideline recommended that the

in-visit patient should only be done to patients in need, that is, patients who require physical examination.[22] Our data showed that number of urologists who performed telemedicine were still low (29.3%). According to systematic review conducted by Novara et al., telemedicine has been widely applied and implemented successfully in a number of different clinical cases during COVID-19 pandemics, particularly in decision-making process and follow-up care of localized PCa patients who underwent curative therapies, as well as a significant preference from PCa patients.[22,23] Regardless, the successful telemedicine service can only be achieved if technology resources and staff adequate.[24]

The limitation of this study was due to data incompleteness that was further excluded from study analysis and could lead to result bias. Moreover, relatively long period to fill the questionnaire could also lead to different results due to COVID-19 pandemic situation differences. This study was performed in the middle of pandemic with no prediction when pandemic will end. Furthermore, COVID-19 is a dynamic and rapidly progressive disease, which in turn caused rapid practice changes in the span of one-year. Hence, the impact of COVID–19 to PCa management might be bigger if COVID-19 increases in spread and magnitude. As the world's fourth most populous country, Indonesia poses a significant danger of infection and viral transmission.[25] Despite of the significant drop in active cases of COVID-19 since March to May 2021, concerns must be raised to eradicate the new spike in cases due to the "triumphalism" over the vaccination and the new variants found in United Kingdom, South Africa, and India. The new variants might also change the previously established COVID-19 protocols.

The published guidelines are solely given the proper standard during practices. Still, patient management should be prioritized based on local resource availability (hospital regulation and restriction) rather than PCa grades consideration alone. The COVID-19 vaccination also brings a new hope to increase the volume of patient visits, so that the non-coronavirus services would not be sidelined.

Conclusion

The impact of COVID-19 on PCa in Indonesia was prominent in decreasing diagnostic procedure and delaying the management of localized or low-risk PCa. Thus, we might expect the increase of the new PCa cases in higher stages during or after pandemic time in Indonesia.

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