Title

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Permalink

https://escholarship.org/uc/item/1xs2426s

Journal

Prostate International, 7(2)

ISSN

2287-8882

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Publication Date

2019-06-01

DOI

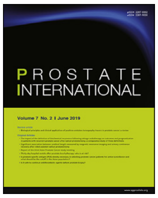
10.1016/j.prnil.2018.06.001

Prostate International 7 (2019) 60–67

Contents lists available at ScienceDirect

Prostate International

journal homepage: https://www.journals.elsevier.com/prostate-international



Original Article

Report of the third Asian Prostate Cancer study meeting

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ARTICLE INFO

Article history:
Received 24 January 2018
Received in revised form
6 June 2018
Accepted 7 June 2018
Available online 14 June 2018

ABSTRACT

The Asian Prostate Cancer (A-CaP) study is an Asia-wide initiative that was launched in December 2015 in Tokyo, Japan, with the objective of surveying information about patients who have received a histopathological diagnosis of prostate cancer (PCa) and are undergoing treatment and clarifying distribution of staging, the actual status of treatment choices, and treatment outcomes. The study aims to clarify the clinical situation for PCa in Asia and use the outcomes for the purposes of international comparison. Following the first meeting in Tokyo in December 2015, the second A-CaP meeting was held in Seoul, Korea, in September 2016. This, the third A-CaP meeting, was held on October 14, 2017, in

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https://doi.org/10.1016/j.prnil.2018.06.001

Keywords:
Asia
Cancer
Database
Prospective study
Prostate cancer
Registry

Chiang Mai, Thailand, with the participation of members and collaborators from 12 countries and regions. In the meeting, participating countries and regions presented the current status of data collection, and the A-CaP office presented a preliminary analysis of the registered cases received from each country and region. Participants discussed ongoing challenges relating to data input and collection, institutional, and legislative issues that may present barriers to data sharing, and the outlook for further patient registrations through to the end of the registration period in December 2018. In addition to A-CaP—specific discussions, a series of special lectures were also delivered on the situation for health insurance in the United States, the correlation between insurance coverage and PCa outcomes, and the outlook for robotic surgery in the Asia-Pacific region. Members also confirmed the principles of authorship in collaborative studies, with a view to publishing original articles based on A-CaP data in the future.

1. Introduction

The third meeting of the Asian Prostate Cancer (A-CaP) study was held on October 14, 2017, in Chiang Mai, Thailand, in conjunction with the seventh Congress of the Asian Pacific Prostate Society 2017. The meeting was attended by representatives of 10 countries and regions in Asia participating in the study (China, Hong Kong, Indonesia, Japan, Korea, Malaysia, Philippines, Singapore, Thailand, and Turkey) and collaborators from the United States and Australia. Following on from the A-CaP launch symposium in December 2015[1] and the second A-CaP meeting in Seoul, Korea, in September 2016[2], members discussed the current status of progress with patient registration, the outlook for further registrations and ways in which to utilize the database that is being accumulated through the A-CaP project. In the business meeting held before the scientific meeting, the A-CaP office also proposed the distribution of a tuned-up Excel-based input system for those countries that are collecting data in Excel-based format, as a measure to help ensure data consistency and minimize time required for data cleaning. Special lectures were provided by collaborators from the United States and Australia. The following is a summary of the proceedings of the symposium.

2. Year report from each A-CaP member country: part I

2.1. Japan

Mizuki Onozawa (Tokyo-Kita Medical Center) noted that patient registration started in July 2016 and the number of registered patients is increasing gradually. As of October 13, 2017, there are 6,300 patients registered, although this presentation would be based on 5,275 patients and compare data with previous database studies in Japan.

The median patient age is about 70 years, and there is no clear difference between studies. About 10% of patients have metastatic disease. In terms of PSA distribution, there was no remarkable difference between jpA-CaP2016 and J-CaP2010 data.

In terms of first line main treatment, the proportion of hormonal therapy is rapidly decreasing. In the JUA2000 data, more than half were treated with hormonal therapy; whereas, in jpA-CaP2016, this proportion had fallen to 34.0%.

In terms of radical prostatectomy, the proportion of robot-assisted prostatectomies has increased drastically since J-CaP2010 data. This is because robot-assisted surgery is now approved under the Japanese health insurance system.

The number of newly registered patients is steadily increasing. As of July 2017, there seems to be no remarkable differences in patient and tumor background factors during the past several years. However, clinical practice patterns are dramatically changing in Japan.

2.1.1. Discussion

Matthew Cooperberg (UCSF) asked about trends in screening. Mizuki Onozawa responded that screening is gradually spreading in Japan. Screened patients account for only a small proportion of newly diagnosed patients.

Levent Türkeri (Acıbadem University) asked why 35% of patients still received only hormonal therapy. The main reason is that Japanese patients like to be treated conservatively and prefer to receive some kind of treatment, even for localized cancer. Hideyuki Akaza (University of Tokyo) noted that many Asian people choose hormonal therapy, even when cancer is localized. However, the proportion of hormonal treatment is gradually decreasing.

Kim Moretti (University of South Australia) noted that active surveillance has not increased a great deal and asked why the reason for the low rate of active surveillance is because patients prefer to have some kind of treatment.

Yoshihiko Hirao (Osaka Gyoumeikan Hospital) noted that Japanese people can receive the treatment they want, but only very low risk patients are accepting of active surveillance.

Mikio Namiki noted that patients that would normally be receiving active surveillance in the United States and elsewhere are generally receiving hormonal therapy in Japan.

2.2. Korea

Seung Hwan Lee (Yonsei University, Korea) noted that according to the trend of prostate cancer (PCa) incidence in Korea, about 10,000 people were newly diagnosed in 2014. The PCa survival rate was about 93.3% for the period 2011—2015, thanks to the effect of widespread use of PSA and early detection programs. In Korea, newly diagnosed PCa cases in 2016 amounted to 6,291 cases, and approximately 3,000 cases will be used for the purposes of A-CaP data.

2.2.1. Discussion

Zhu Gang (Beijing United Family Hospital and Clinics) asked about active surveillance in Korea. Seung Hwan Lee responded that in Korea it is the situation that many people who are diagnosed with cancer want to receive some kind of treatment. Therefore, active surveillance is not a popular option.

Zhu Gang noted that active surveillance is also very low in Japan and also China. It seems to be the philosophy of Asian people to seek to receive treatment that will help them to be rid of disease.

Hideyuki Akaza asked about the situation in Turkey. Levent Türkeri responded that the Turkish health-care system is based on payment for services, therefore active surveillance is not financially appealing to physicians. The Urooncological Society of Turkey is working to convince doctors that active surveillance should be a part of their treatment strategy. However, the rate is still very low. It is to be hoped that in the future the amount of active surveillance will rise.

Kim Moretti noted that active surveillance accounts for about 25% in South Australia. However, in the A-CaP database, this is only 15%. He suggested that it may be useful to look at the A-CaP data in this regard. He noted that active surveillance is sold in Australia as a way of avoiding nasty side-effects.

Matthew Cooperberg noted that the situation used to be the same in the United States, namely that doctors sought to treat low-risk disease. In a couple of years, however, after changing treatment guidelines, the active surveillance rate rose from 10% to 40%. It is important to educate the patients that cancer is not all the same and that active surveillance may be preferable.

Shigeo Horie (Juntendo University Graduate School of Medicine) noted that it is important to stress the difference between PCa in Asian and Caucasian populations.

Matthew Cooperberg noted that the question of low-risk disease management has been important in the West. Twenty-five percent of patients on active surveillance experience cancer progression, whereas 75% do not. There needs to be a better system for considering active surveillance.

2.3. China

Zhu Gang noted that PCa is the sixth most prevalent cancer among male cancers. PCa has been increasing over the years and mortality is also increasing. Five-year survival for PCa is 53.8% in China compared to 100% for the United States. The Chinese PCa database is a well-designed, ready-for-use database, and over 5,000 cases have been registered, although they are pending at the current moment. Data for 499 cases have been transferred to A-CaP, from hospitals around China. C-CaP is a collaborative body with A-CaP. In China the overwhelming majority of A-CaP patients have been treated with prostatectomy. So far, in 2017, 52 cases have been collected for A-CaP purposes.

2.3.1. Discussion

Rainy Umbas (University of Indonesia) asked about the clinical practice in examining PSA and asked if there are any PSA training programs for urologists. Zhu Gang responded that there is no national screening program in China, but at his hospital, a screening program has been introduced for the six most prevalent cancers in China.

Bannakij Lojanapiwat asked about modalities for staging, noting that not many people seem to have computed tomography (CT) or magnetic resonance imaging (MRI) scans. Zhu Gang noted that it is usually the case that patients have an MRI scan before having a biopsy.

2.4. Malaysia

Teng Aik Ong (University of Malaya) noted that the Malaysian National Cancer Registry Report 2016 covers the 5-year period from 2007–2011. For males, PCa is the third most common cancer. On average, there are approximately 600 new cases a year.

In terms of the PCa cases in all participating centers ($n = 5$), the total number of new cases recruited in 2016 amounted to 371. In terms of ethnic profile, Malays and Chinese account for the majority. For the Malay population, the average age at presentation is 68.8 years, which is lower than the Chinese ethnic population, and the Malay population have a median PSA of 58.8 ng/ml at presentation, which is higher than Chinese (25.0 ng/mL) and Indian (31.0 ng/mL) ethnicities.

Modalities for staging include bone scan (50%), MRI (29%), and CT (20%).

In Malaysia active surveillance accounts for 10.8% of primary treatment cases, with ADT + chemotherapy accounting for 48.9% of primary treatment depending on the stages of the disease. The majority of cases (53.4%) present with Stage IV cancer at diagnosis. Common comorbidities include hypertension, hyperlipidemia, and diabetes.

The budget from A-CaP (38,145 RM) has been used for the study, in addition to which a grant from NIH Malaysia was also received (50,780 RM). Efforts will continue in 2017.

2.4.1. Discussion

Jasmine Lim (University of Malaya) suggested that it would be useful to prepare a concept form for utilizing the data from the A-CaP database.

Ji Youl Lee (The Catholic University of Korea) noted that the fact that grant money had been procured from NIH Malaysia was a very good example.

Jun Miyazaki (International University of Health and Welfare) asked about screening in Malaysia. Teng Aik Ong responded that there is no screening program in Malaysia.

Jason Letran (Cardinal Santos Medical Center) asked if there is any correlation between outcomes and diagnosis and the patient's financial means. Jasmine Lim noted that perhaps one of the reasons why Malay present later is due to an issue of awareness. During health awareness campaigns, it is generally ethnic Chinese who attend clinics.

Yoshihiko Hirao asked about the number of urologists in Malaysia. Teng Aik Ong responded that there are 111 urologists, which is a low number.

2.5. Indonesia

Lukman Hakim (Airlangga University) reported that the A-CaP study in Indonesia started in April 2016, with a meeting in Jakarta involving eight teaching hospitals. A board of advisors was appointed, and a simple web-based application system was announced, which was changed to MS Access. Enrollment started on April 1, 2016.

Currently there are nine hospitals participating, and a total of 189 new patients have been registered between April 2016 and October 12, 2017. A dictionary has been distributed to enable doctors to fill in the input system. In terms of the modalities for staging, CT and MRI were only used if imaging would change the definitive treatment. Despite the fact that bone scans were rarely used due to limited facilities particularly in the peripheral hospitals, bone survey was performed in the majority of cases.

In terms of initial PSA, the majority of patients have a PSA in excess of 20.

In terms of initial treatment, ADT without chemotherapy with radiotherapy is the predominant therapy (55%).

In terms of constraints, there is a risk of patients being lost in follow-up. There is also a difference in diagnostic facilities between hospitals. Another challenge is inconsistency in the standardized pathological reports between hospitals. There are differences of perception between study coordinators in under the study protocol. The “transition period” of the newly launched Indonesia University Health Coverage system is also presenting constraints as there are maximum budgetary limitations being imposed.

In terms of next plans, the hope is to involve more satellite hospitals and launch a web-based application very soon, which will help to facilitate data submission. A workshop is also being planned that will enable pathologists to build a uniform perception about standardized reporting of specimens. It is also important to emphasize the study protocol among principle investigators.

2.5.1. Discussion

Hideyuki Akaza referred to the transition period to University Health Coverage in Indonesia. He asked how many patients do not come to hospital for treatment. Lukman Hakim responded that a population-based survey in Indonesia reported that 35% of sick people go to a traditional healer in the first case to seek cure. In terms of transportation and financial background, there are some regional areas that make it difficult for some patients to visit hospital. The ministry of health is considering the implementation of financial support for transportation to hospital, but it is still not known when it will be implemented.

Hideyuki Akaza asked about medical and surgical castration and which one the patients choose. Lukman Hakim noted that due to the asymmetrical health information, it is usually the urologists who decide for patients. It is generally the case that surgical castration is practiced for patients who live in rural areas. If it is felt that the patient can be followed up regularly, medical castration is used.

2.6. Hong Kong

Ng Chi Fai (The Chinese University of Hong Kong) noted that data are being collected by three out of nine hospitals in Hong Kong, which covers more than 40% of the population. Ethical approval was received more than 2 years ago, and the hospitals are collecting data from Tuen Mun Hospital & North District Hospital, which regularly compiles lists of newly diagnosed cases. The Prince of Wales Hospital assists in data entry. In Hong Kong, there is a very good electronic hospital record system (Clinical Management System) for collecting data and other elements that are required for utilization in the A-CaP study.

In terms of current progress, a total of 295 cases have been collected in 2016.

In terms of major challenges, the cases collected from Hong Kong are from a public hospital system and there is delayed availability of data, including imaging, final plans and operation results, etc.

2.6.1. Discussion

Teng Aik Ong asked about the percentage of patients who are metastatic. Ng Chi Fai responded that about 25% are metastatic.

Jason Letran asked about waiting times for imaging and surgery. Ng Chi Fai responded that that the hospital system is public, and there can be considerable waiting times, up to a few months.

2.7. Turkey

Levent Türkeri noted that the Turkish database was already established ahead of the A-CaP study. This has created some problems because the Excel tables needed to be converted, which required manpower to create the necessary files.

In Turkey, the T category has changed in recent years, and the majority is localized disease, with only approximately 15% presenting with metastatic disease. This is thanks to PSA screening.

In terms of modalities for staging, PET scanning has started to be used, and it is also proving to be expensive.

In terms of information on initial treatment of patients in the Turkish database, 84.4% received treatment for local treatment. In 95% of cases of local treatment, the treatment was radical prostatectomy. A very small number received radiotherapy, hormonal therapy, or active surveillance.

In terms of the types of radical prostatectomy, open radical prostatectomy (ORP) is 57.5% and robot-assisted radical prostatectomy (RARP) is 41.6%, and the proportion of RARP is likely to increase in the future.

In terms of treatment for metastatic disease, the most used treatments are LHRH + flare protection and CAB. AA monotherapy is used in approximately 17% of cases.

The Urooncological Society of Turkey database has been subjected to a renovation. A meeting was held for quality control, and dedicated data managers have been hired to work for the society in Istanbul, Ankara, Izmir, and Adana.

As of September 2017, there are now 1,838 patients in the database, and it is expected that this number will increase to 3,000 patients by the end of 2018, thanks to the hiring of the dedicated data managers.

2.7.1. Discussion

Yoshihiko Hirao asked whether patients are from metropolitan areas or rural areas. Levent Türkeri responded that the majority of cases are from urban areas, as the majority of the population now lives in urban areas. The main information will be coming from cities, including public or teaching hospitals.

Bannakij Lojanapiwat noted that Turkey covers two continents and asked about the ethnicity of patients. Levent Türkeri responded that the population of Istanbul is 20 million, and one in four of the population of Turkey live in the city, and this population reflects the general population.

2.8. Thailand

Bannakij Lojanapiwat reported that 264 patients have been registered so far for the A-CaP study from three hospitals, one of which is in Chiang Mai. In the case of Chiang Mai, the PSA level on presentation is very high compared to the case of Bangkok, which reflects the lag in terms of screening in the Chiang Mai region. The staging of cancer is also higher in Chiang Mai, and metastatic disease is higher than in Bangkok.

In terms of initial treatment, in Chiang Mai, the majority of cases are treated with ADT as main treatment, and there is also a higher incidence of active surveillance, whereas hospitals in Bangkok offer more cases of radical prostatectomy.

2.8.1. Discussion

Hideyuki Akaza noted that Chiang Mai could provide a good model for treatment in rural areas. Bannakij Lojanapiwat noted that in urban areas patients live in closer proximity to hospitals, which makes it easier for patients to visit hospital. The situation in Chiang Mai reflects the situation in regional areas.

2.9. Singapore

Edmund Chiong (National University Health System) reported that the population of Singapore is 5.3 million, and PCa is the third most common cancer in Singapore men. It is the sixth leading cause of cancer death. When it comes to the national cancer registry, 30% of people present with Stage 4 cancer.

With regard to the S-CaP study, the three participating hospitals in the cluster system maintain their PCa databases in individual hospitals and academic institutions. However, there have been various regulatory changes to the system in Singapore in the past year. It is hoped that the clustering system that has been established this year will help in the collection of data.

In terms of progress, the official platform for data collection is REDCap, which will help to harmonize data fields and central subject identification. All hospitals have REDCap training. Single multiinstitutional IRB applications for all hospitals for prospective patient have been completed, and informed consent has also been gained. Each hospital retains its own database autonomy, and data sharing agreement contracts are required between hospitals, which is why data have not yet been shared with A-CaP.

A multisite IRB was approved in August 2017. Two sites have already been initiated, with a third site making preparations. All patients have been histologically diagnosed with PCa from January 1, 2016 onwards. Informed consent has been obtained from all patients. Thus far data for 71 patients have been registered.

The median age is 69 years, and the median PSA was 13.8 μg/L, and specimens are largely taken by biopsy. In terms of stage distribution, most patients are T1 and T2. The use of CT scans is fairly common, and MRI is also increasing. Bone scanning is not generally implemented for low-risk disease.

In terms of initial treatment, the most used is ADT ± chemotherapy, followed by active surveillance/ watchful waiting (AS/WW) and prostatectomy.

The major challenge is the passage of the Human Biomedical Research Act, which is a complex piece of legislation that will have a significant impact on the way human biomedical research is conducted. Specific issues include the requirement for informed consent and implications for data-sharing agreements.

The challenges that need to be resolved are the funding of research assistants, accurate follow-up data and oversights, the time needed for contractual agreements between institutions and with A-Cap on data-sharing, and participation of other institutions, which is still pending due to resource limitations.

2.9.1. Discussion

Shiro Hinotsu noted that using the REDCap system each institution must have a server and a mainframe. He asked whether each hospital maintains its own server and mainframe. Edmund Chiong responded that all hospitals in Singapore are now electronic, but unfortunately, they all use different systems. The new law also stipulates that each hospital is in its own legal entity, which is why contracts need to be concluded.

Yoshiyuki Hirao referred to IRB and asked whether A-CaP was opt-out or opt-in. Edmund Chiong responded that in Singapore, the system is more like an opt-in, in that it is compulsory to acquire informed consent from patients to share their data with A-CaP. The consent form for informed consent will be the same for all institutions.

2.10. Philippines

Jason Letran reported that the Philippines had collected a total of 197 patients in 2016 and a total of 43 in 2017. For the patients who report their age, the average age is in excess of 65 years. Most patients have a college education and are from urban areas. With regard to initial PSA levels, 61.3% patients have a level less than 20.

Forty percent of patients are T3; 21.7% of patients received a CT scan and 22.9% received an MRI scan. A bone scan for staging was performed on 57.9% of patients.

In terms of initial treatment, 25.8% received RP, 17.9% received radiotherapy, and 8.75% received ADT. Active surveillance accounts for only 1.25% of initial treatment. Treatment was not specified for 41.3% of patients.

In terms of active surveillance, I would like to present a comparison between our data and that of a study in Toronto. The median PSA of active surveillance patients in the Philippines is 13.9 compared to 6.2 in Canada. 115 of 168 patients had clinical T1 upstaged to T3.

I think that more than cultural differences with regard to active surveillance, these results show scientific differences, and this is where the importance of the Asian focus of A-CaP comes to the fore. I would like to propose a joint study as a means of supporting the relative lesser usage of active surveillance. We hope to contribute more patients to the study in the future.

2.10.1. Discussion

Bannakij Lojanapiwat noted that many items of data are missing from Philippine patients, and this is a problem that was also encountered in Thailand. He suggested that more efforts be made to explain the kind of data that are needed.

Hideyuki Akaza noted that Jason Letran had made a very important proposal about the comparison of Asian and Western patients who undergo active surveillance and the need to check histological differences among patients. He noted that he would like to consider the possibility of engaging in such a study.

Yoshiyuki Hirao noted that the in Philippines there are many islands, and perhaps the 371 urologists are living in urban areas. He asked about the situation for rural areas. Jason Letran responded that half the urologists are located in metro Manila, serving only 15% of the population. With regard to screening campaigns, he noted that on the Saturday before Fathers' Day, a campaign is also implemented to raise awareness about PCa.

3. Special lectures: toward realization of universal health coverage for prostate cancer treatment

3.1. US health care: the current controversy

Matthew Cooperberg noted that the US healthcare system is costly because of high premiums and a high co-pay structure, but this does not necessarily translate to better care. The United States spends more than twice on health-care than other industrial nations, but this is not reflected in life expectancy. One of the reasons for this is inequality.

For PCa, the total cost of care was US$12 billion in 2010. Lifetime costs exceed US$110,520 per patient. 62% are insured by Medicare and 32% by commercial or private payers. There are also an increasing number of patients receiving more than one treatment. The costs are increasing due to new therapy and use of multiple therapies.

Something needed to be done to address the health-care system in order to make sure that all Americans are able to get health insurance. The Patient Protection and Affordable Care Act (ACA) or “Obamacare” was signed into law on 2010. ACA requires individuals who do not receive health insurance benefits through their employees to purchase coverage or pay a penalty. It puts certain limits on what insurers may or may not do with respect to eligibility and coverage. One disadvantage was that ACA was not formulated in consultation with doctors.

The key provisions of ACA are dependents may be covered by their parents' insurance plans until they turn 26; insurers may not cancel polices when policy holders become sick; state health insurance exchanges allow businesses and individuals to compare plans and enroll for coverage; insurers may not place a lifetime monetary limit on hospital stays or other benefits deemed “essential” in new policies; and insurers may not deny coverage to individuals for preexisting conditions.

ACA also imposes an individual mandate, requiring all individuals to carry insurance or pay a tax penalty. Subsidies will help low-income people comply with this mandate. Larger employers will be charged a US$2,000 penalty per full-time employee who lacks health coverage.

Insurers are required to provide individuals with a standardized, plain-language summary of benefits and any rate increases of more than 10% must be publicly justified. Certain types of preventive care must be covered at no additional cost to the patient, and patients are granted the right to appeal whenever an insurer denies payment for health-care services.

The most controversial components are the requirement that nearly every individual in the United States have health-care coverage. Young, relatively healthy people who pay regular insurance premiums ultimately help cover the costs of older and less-healthy individuals. Since insurance companies may not refuse to cover those with preexisting conditions, the mandate will discourage people from simply waiting until they have a health-care emergency.

The primary mission of ACA was to get more insurance for Americans, and it was quite successful, cutting the rate of uninsured people by half and ensuring better access to care as a result. Now the biggest excuse for not receiving care is that people do not have a primary care physician.

The negative aspects of ACA are that many businesses have found it cheaper to pay the penalty rather than pay for insurance policies for their employees and that insurance companies have canceled some plans that did not cover essential benefits.

In addition, in terms of medical expense deductions, the level increased to 10% from 7.5% of income. Another issue is that ACA does not address out of pocket expenses for prescription drugs.

The public perception of health care is that ACA may not have much of an impact beyond those covered by Medicaid expansion and the marketplace. Thirty-one percent of Americans aged 18–64 years report they or a family member face problems paying health-care bills. Out of pocket costs are also increasing, and the average deductible for employee-provided health-care coverage rose from $303 to $1,505 between 2006 and 2007.

With regard to ACA and cancer care, there are subsidies for those with low incomes. People cannot be denied coverage or dropped from coverage because of having cancer. There are concerns that narrow networks are being formed to control costs and limit access, and cancer centers are being excluded from private networks.

Although ACA does not address all issues in the US health-care system, the proposal by the Trump administration to repeal the ACA failed, suggesting that it has broad overall support. There are current moves toward amending ACA, and there is a possibility that any revisions could negatively impact cancer care[3].

3.1.1. *Discussion*

Levent Türkeri noted that he would like to learn about the opinion of urologists with regard to the ACA. Matthew Cooperberg responded that hospitals have done a very good job of pitting primary care doctors against specialists. If you look at academic medical centers, academics are very much in favor of ACA. Physicians have been very shortsighted, and because they do not work as a group, they have not had a place at the negotiating table to formulate the ACA.

Hideyuki Akaza noted that the Japanese insurance system is very different to the ACA and is available to all people. There is no private insurance system in Japan for cancer care.

3.2. *Insurance and prostate cancer outcomes: a perspective from the US health-care "System"*

Matthew Cooperberg noted that the US health-care system is highly fragmented, including private, public, employer-based, and Medicare for people aged above 65 years. There are no centralized data covering all populations, and patients with no insurance do not make it into most databases. Insurance prices are opaque, and consumers bear a variable portion of the cost. Centers of excellence tend to treat patients with the best and the worst insurance. The ACA really only tried to resolve coverage issues, rather than quality and cost issues.

Individual costs for US citizens include their share of the premium, deductibles, and co-pay portions. The federal system will pay for people aged above 65 years (Medicare), people on low incomes (Medicaid), veterans (Veterans Affairs), and through the Indian Health Service. In terms of private insurance policies, medical loss ratios sustained by insurance companies have improved since the ACA, but the question remains as to whether quality is better. For-profit insurance costs more, but does not necessarily provide the best health care.

In terms of insurance distribution in CaPSURE, those persons without insurance were basically not able to register in the CaPSURE database. In the CaPSURE database, overall approximately 15% of patients had only Medicare insurance, while 35% had Medicare with extra insurance. Forty-two percent of patients had private insurance, and 3% had Veterans Affairs insurance.

With regard to the question of whether insurance affects outcomes, in a univariate analysis of insurance and prostate cancer specific mortality (PCSM), there are some differences. Patients with private insurance rather than Medicare (Ref value 1.0) had an approximately 50% reduction in mortality (0.55), whereas those patients with no insurance had an increased mortality rate (1.75).

However, in figures adjusted for age that compare insurance and PCSM, the difference between patients on Medicare (1.0) and those with private insurance (0.93) decreases, although the PCSM for those with no insurance is still higher (2.68).

In figures adjusted for age and SES, the difference between Medicare (1.0) and private insurance (0.95) remains small, but the PCSM for those without insurance remains high (2.10), although less than the model adjusted only for age.

However, in figures adjusted for age, with SES and risk, insurance is no longer predictive: Medicare (1.0), private insurance (0.82), and no insurance (1.35). The only aspect that is predictive is risk, meaning that if you have no insurance you tend to have higher risk of disease at presentation.

In figures adjusted for age, SES, risk and treatment type, and the type of insurance become even less predictive: Medicare (1.0), private insurance (0.79), and no insurance (1.20).

Regarding question of whether treatment variation explains disparity in insurance coverage, although patients with private insurance are more likely to get surgery, treatment is more driven by age than anything else. Broken down by age category, there is very little difference. A previous CaPSURE study showed that there can be regional differences in the choice of treatment, but this is not related to insurance coverage.

The Surveillance, Epidemiology, and End Results (SEER) Program has some data, but it does not have a great deal of granularity, lacking data about risk. It is, however, one of the greatest sources of information about uninsured patients. It shows that uninsured patients tend to present with high-risk disease (30.7%) rather than insured patients (21.1%). The likelihood of metastatic disease is also greater in uninsured patients (11.9%) than insured patients (2.6%). Insurance therefore can be said to drive outcomes in terms of screening and early diagnosis. In a multivariable analysis of the SEER data, the likelihood of metastatic disease is five times greater in uninsured patients at time of diagnosis than insured patients. The likelihood of being treated for high-risk non-metastatic disease is two-fold higher in insured patients. The SEER data also show a 40% survival advantage for patients with insurance, but data on risk is not comprehensive. The AQUA registry is expected to complement SEER data in the future. 60,000 patients from the first 100 practices have been registered on AQUA since 2014, and this registry provides much richer data than SEER. However, until more "safety-net" hospitals join, capturing data on uninsured patients will remain challenging.

In conclusion, the health effects of insurance are difficult to disentangle from other sociodemographic factors, including race, diet, lifestyle, and access to care. A lack of insurance predicts not only delayed diagnosis and undertreatment but also less overtreatment. A previous CaPSURE study has shown that PCa might be the first condition in the US where rich white men got worse care because they were more likely to be overtreated for low-risk disease. The effects of underinsurance are more difficult to discern. The US health-care system is a mess and unlikely to be fixed in the near future without political campaign finance reform and more influence by physicians[3].

3.2.1. Discussion

Hideyuki Akaza noted that the results of the data presented suggest that there is little difference in outcomes. Matthew Cooperberg noted that for low income men, their outcomes are okay if they make it into the system, but the question is whether they can actually make their way into the system in the first place.

Shiro Hinotsu asked whether patient payment data are recorded on the CaPSURE or SEER databases. Matthew Cooperberg responded that there are no data, as only Medicare tracks what it pays, but there is no tracking of self-pay components.

3.3. From robotic surgery to CRPC: How do we demonstrate value in the Asia-Pacific region?

Declan Murphy (Peter MacCallum Cancer Centre) noted that he would be assessing the value of robotic surgery in a public hospital setting and discuss a precision approach in metastatic PCa.

Compared to other countries, the United States spends more than double on health care as a percentage of GDP. This suggests that there needs to be massive reform in the US Robotic surgery, is an example of an expensive intervention that is impacting the Asia-Pacific region. In a article published year titled, “Patterns-of-care and health economic analysis of robot-assisted radical prostatectomy in the Australian public health system,” it has been shown that RARP performs better than ORP, but there is higher cost due to longer operating times. Once the number of cases reaches a certain level at a medical institution, the costs will, however, decrease.

In this study, the aim was to evaluate RARP in a public health system, comparing outcomes to current standards and conduct a health-economic analysis within an activity-based funding system.

The results showed that patients had a shorter stay in hospital (1.4 days) for RARP than ORP (4.8 days). Length of stay was therefore greatly reduced through RARP. Positive surgical margins (PSMs) showed that patients undergoing RARP are significantly less likely to have a PSM compared with open or laparoscopic RP. Patients with a PSM are five times more likely to receive additional treatment within 12 months.

In a health-economic analysis, it was shown that RARP reduces hospital stay, blood transfusion rates, and positive surgical margins. However, it is expensive. If high-volume, high-quality cases are performed, it makes RARP cost-effective.

How are we going to make CRPC drugs more affordable in Asia? The question is whether it is possible to convince big pharma to dramatically increase access in the Asia-Pacific region. The answer to this question is “very unlikely.” Different strategies will be required to make drugs more affordable. For example, primary resistance to AR-targeted agents can be detected early, and this would help to reduce the use of androgen receptor (AR)-targeted agents.

Integrative landscape analysis of somatic and germline aberrations in mCRPC shows that 90% of mCRPC harbor clinically actionable molecular alterations, and 23% of mCRPC harbor DNA repair pathway aberrations. An editorial in European Urology titled, “The Evolving Narrative of DNA Repair Gene Defects: Distinguishing Indolent from Lethal Prostate Cancer,” makes four points, namely that DRG mutations, most notably BRCA2, are enriched in mCRPC, which are present in the germline or in somatic tumors in up to one in four patients. Secondly, these DRG aberrations are present in many more men with castration-sensitive metastatic PCa than previously expected, with 11.8% of such patients having germline DRG mutations. It is inevitable, and therefore that consideration will be given to screening these men. Thirdly, it is also now apparent that DRG mutations are more common in men with aggressive localized PCa than previously reported and that the presence of DRG mutations is predictive of death from PCa. Fourth, DRG mutations are a highly promising target for therapeutic options such as PARP inhibition and platinum, and perhaps as a neoadjuvant or adjuvant strategy for localized PCa[3,4].

In terms of practice, this means that biopsies will be performed more often to assess heterogeneity, including liquid biopsies. Genomics will also be more commonly used.

In conclusion, AR-targeted agents are very effective in mCRPC. Costs and access remain an issue, especially in the Asia-Pacific region. Biomarkers and patient selection will become more sophisticated, and a precision approach should help to increase value in the future. Efforts such as A-CaP will create opportunities to assess patterns of care and conduct research. It is important to approach big pharma for support for such initiatives.

3.3.1. Discussion

Hideyuki Akaza noted that pharmaceutical companies generate very large profits and asked about how to approach them. Declan Murphy noted that many pharmaceutical companies are looking for initiatives to support and that with Matthew Cooperberg's opinions and expertise as well, it could be very possible to find grant funding from pharmaceutical companies.

4. Publication rules

In the business meeting held prior to the main symposium, A-CaP members noted that following the collection of all A-CaP data, a prime objective will be to report on the work of A-CaP through scientific publications. Considering the multiinternational, multicenter nature of the A-CaP group, the matter of authorship is an important issue to consider ahead of proceeding with the project. A proposal was made concerning the Principles of Authorship in Collaborative Studies, which was adopted from the GAP3 Active Surveillance Project Guidelines. It was noted that all members would be forwarded details of these principles for future reference. It was further noted that if A-CaP members have ideas for articles based on A-CaP data and discussions, they are requested to provide their opinions to the A-CaP office. The A-CaP office will look into publishing a preliminary overview of the data accumulated to date.

Conflicts of interest

No conflicts of interest for all authors.

Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.prnil.2018.06.001.

References

1. Akaza H, Hirao Y, Kim CS, Oya M, Ozono S, Ye D, et al. Asia Prostate Cancer Study (A-CaP) launch symposium. Prostate Int 2016;4:88—96.
2. Kim CS, Lee JY, Chung BH, Kim WJ, Ng CF, Hakim L, et al. Report of the Second Asian Prostate Cancer (A-CaP) study meeting. Prostate Int 2017;5:95—103.
3. Basto M, Sathanathen N, Te Marvelde L, Ryern S, Goard J, Lawrentshuk N, et al. Patterns-of-care and health economic analysis of robot-assisted radical prostatectomy in the Australian public health system. BJU Int 2016 Jun;117(6):930—9.
4. Murphy DG, Risbridger GP, Sandhu S. The evolving narrative of DNA repair gene defects: distinguishing indolent from lethal prostate cancer. Eur Urol 2017 May;71(5):748—749c.