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REVIEW ARTICLE

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Complex Epidemiology of Prostate Cancer in Asian Countries

Kagenori Ito, Takahiro Kimura

Department of Urology, The Jikei University School of Medicine, Tokyo, Japan

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Corresponding author:
Takahiro Kimura
Department of Urology, The Jikei University School of Medicine, Tokyo, Japan
Email: tkimura0809@gmail.com
https://orcid.org/0000-0002-5673-1553

The incidence of prostate cancer (PCa) has increased worldwide in recent years along with the recommendation for prostate-specific antigen testing, and mortality has been declining owing to advances in fragmented and simplified access to treatment care. However, GLOBOCAN (Global Cancer Observatory) data show that this result is not true for all countries. It has been reported that the degree of PCa progression at diagnosis and survival rates differ among racial groups. Based on various comparisons between Caucasians and Asians, it was inferred that survival rates were higher in Asians despite the higher degree of progression at diagnosis, suggesting a better prognosis for life compared with Caucasians. The survey among Asian countries did not reveal any obvious differences among Asian subregions; rather, it inferred that the impact of the level of development among the countries was significant. The development of healthcare systems and medical care could improve PCa survival in developing countries.

Key Words: Prostate cancer, Asia, Epidemiology

INCIDENCE AND MORTALITY OF PROSTATE CANCER IN ASIA

Prostate cancer (PCa) is one of the leading causes of death in humans, the second most common cancer, and the fifth leading cause of mortality worldwide [1]. Older men are more susceptible to PCa, and >80% of patients are diagnosed after 65 years of age. However, the mortality rate of PCa is lower than that of other cancers. The incidence of PCa is 7.3% of the total cancer incidence (developed countries: 3%–15%, developing countries: 3%–4%) [1, 2]. People who die from PCa account for 3.8% of all cancer deaths [1, 3]. In addition, latent PCa has been well identified by autopsy. According to a systematic study of autopsy studies, the prevalence of PCa is 5% in those under 30 years of age and increases to 59% in those over 79 years of age [4]. PCa is characterized by high morbidity and low mortality.

However, the incidence and mortality of PCa differ according to race and country of residence. The incidence of PCa has been increasing, especially in developed countries since the 1990s when prostate-specific antigen (PSA) testing was approved [5]. Oceania (specifically, Australia and New Zealand), North America, and Europe (specifically, Western and Northern Europe) have the highest incidence of PCa in the world. Asian countries have the lowest incidence of PCa in the world [1]. Prevalence of PSA testing and prostate biopsies and racial differences are the main sources of these differences between countries [6]. A Swedish study showed a continuous increase in the incidence of PCa over 30 years despite the low frequency of PSA testing, indicating that there are other influences besides PSA testing [7]. It is questionable whether the reported incidence rates in different countries are true. The reporting of incidence rates is influenced by factors such as ease of access to healthcare,

quality of care, and accuracy of registration. The incidence in African countries is low compared to that in Asian countries [8]. Global Cancer Observatory (GLOBOCAN) data for 2020 show that the incidence rate in African countries is increasing, while the incidence rate in Asian countries remains at a low level. This is because reliable data are available for African countries but not for Asian countries [1, 9]. Racial differences were highlighted in a migration study. Japanese immigration from Japan to the United States (US) increases the incidence of PCa among Japanese, but still only 50% of the white Americans and 25% of African Americans [10]. PCa has been associated with Western lifestyles, especially a diet high in fat, meat, and dairy products [11, 12]. Not only the country's development in PCa treatment but also racial differences and dietary habits have important roles in PCa incidence. The decline in the number of deaths from other causes may be one of the reasons for the relative increase in PCa mortality. Many factors affect PCa incidence and mortality in each country, which complicates our understanding.

Recently, we have reported Asian epidemiology features in PCa by analyzing GLOBOCAN 2012 database and the statistical information system mortality database of the World Health Organization [13]. According to the GLOBOCAN 2020 database, the incidence tends to be higher in Northern Europe (age-standardized rate [ASR], 83.4), Western Europe (ASR, 77.6), the Caribbean (ASR, 75.8), Australia and New Zealand (ASR, 75.8), and North America (ASR, 73.0) [14]. In contrast, the lowest regions were Asia including South-Central Asia (ASR, 6.3), Southeast Asia (ASR, 13.5), East Asia (ASR, 16.8), and Western Asia (ASR, 28.6) and Africa including Northern Africa (ASR, 16.6), East Africa (ASR, 27.9), and Western Africa (ASR, 33.1). The lowest region had approximately one-thirteenth the incidence of the highest region, which is a clear difference. Generally, developed countries tend to have a high incidence, while developing countries tend to have a low incidence. One can imagine that these findings reflect differences in the availability of medical care, such as testing and early detection, as well as the spread of national cancer registry systems in individual countries. Mortality tended to be higher in the Caribbean (ASR: 27.9) and African descents including those from Central Africa (ASR: 24.8), Southern Africa (ASR, 22.0), Western Africa (ASR, 20.2), Eastern Africa (ASR, 16.3), and Oceania including Polynesia (ASR, 20.5), Melanesia (ASR, 17.0), and Micronesia (ASR, 16.7). In contrast, mortality tended to be low in Asia including South-Central Asia (ASR, 3.1), South Eastern Asia (ASR, 5.4), East Asia (ASR, 4.6), and Western Asia (ASR, 8.4), Southern Europe (ASR, 7.8), Northern Africa (ASR, 8.2), North America (ASR, 8.3), Western Europe (ASR, 9.8), and Australia and New Zealand (ASR, 10.3). Developed countries tend to have low mortality rates, while developing countries tend to have high mortality rates. These results reflect the different environments in which people have access to medical care, including diagnosis, treatment methods, and technologies. Although many Asian countries are still underdeveloped, mortality rates are low, even lower than those in developed countries such as North America and Western Europe. Asian ethnic groups seem to have better survival rates for PCa than other ethnic groups. This result may be partially explained by the differences in dietary habits; however, racial differences remain unclear.

Almost 60% of people live in Asian countries. According to GLOBOCAN 2020 data, only 26.2% of estimated new cases and 32.1% of deaths from PCa worldwide occur in Asia [1]. Incidence and mortality rates vary not only between Asia and the rest of the world, but also between Asian countries. In Fig. 1A, the ASRs of PCa incidence and mortality in the Urological Association of Asia (UAA)-associated countries are shown [14]. The incidence was higher in Oceania including New Zealand (ASR, 92.9) and Australia (ASR, 72.5) than in other Asian countries in UAA (ASR, 3–56.1). Diet habits and racial differences were also associated. PSA testing popularization had the greatest influence in most countries [15]. Incident rates are high in Israel, Japan, Turkey, Singapore, and South Korea, followed by Oceanian countries. This probably reflects the widespread use of PSA testing and the maturity of the cancer registry system. On the other hand, the low incidence in other Asian countries does not seem to reflect the true low prevalence of PCa. This may be due to a variety of factors, including nutritional status, genetics, lifestyle, environmental factors, physical activity, smoking, race, and other characteristics such as registered cancer schemes [16-18]. The mortality-to-incidence rate was lower in Oceania including New Zealand (0.132) and Australia (0.138), Japan (0.087), Israel (0.119), South Korea (0.150),

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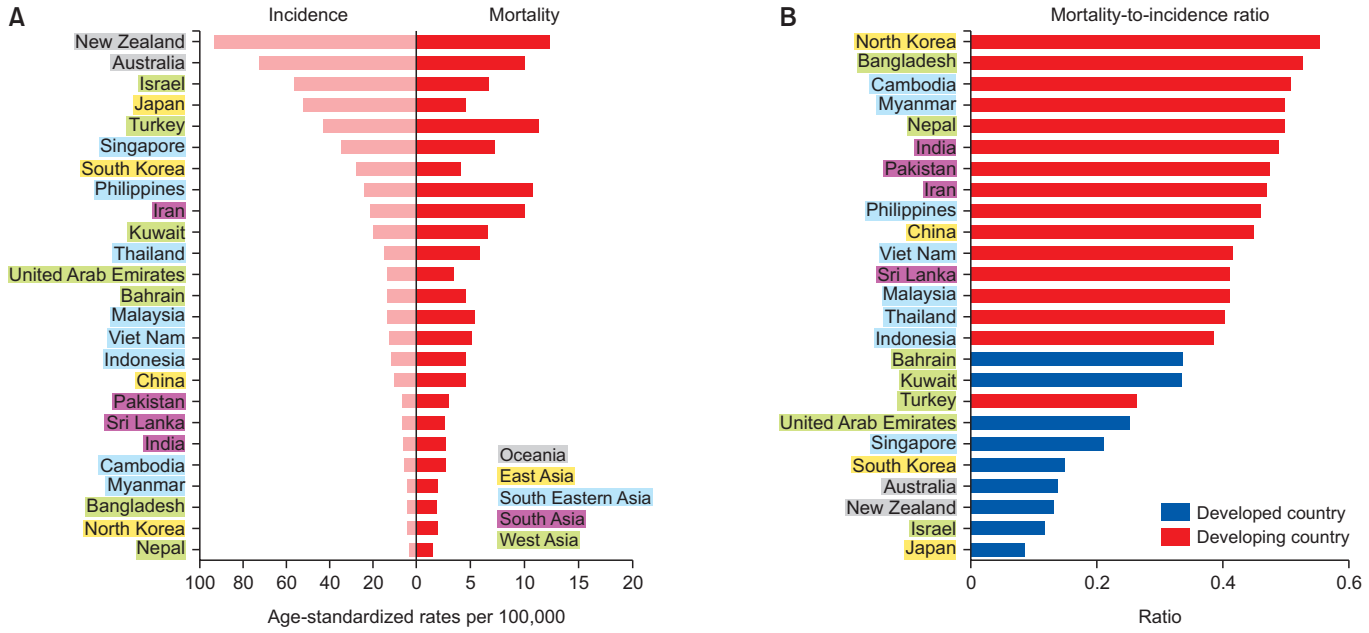

Fig. 1. Incidence and mortality of prostate cancer in Urological Association of Asia (UAA)-associated countries from 2020 GLOBOCAN (Global Cancer Observatory). (A) Age-standardized rates of incidence and mortality in UAA-associated countries are listed in descending order. (B) Mortality-to-incidence ratios are listed in descending order. Developing countries are listed in the Development Assistance Committee list of official development assistance recipients [41].

and Singapore (0.213) than in other Asian countries (0.254–0.556) (Fig. 1B). No significant difference in incidence, mortality, or mortality-to-incidence rate was found by Asian province classification, but it differed between countries. Moreover, developed countries have a lower mortality-to-incidence ratio than developing countries (Fig. 1B). These results indicate that the clinical level is more important than racial differences among Asian countries.

Mortality-to-incidence ratios are practical indicators for assessing the long-term success of cancer surveillance and the effectiveness of cancer control programs, particularly cancer testing [19]. Mortality-to-incidence ratios indicate survival but do not reveal real survival, which needs to be checked and compared.

TRENDS OF INCIDENCE AND MORTALITY FROM PROSTATE CANCER IN ASIA

PCa is now easily detected by the serum PSA test and prostate imaging using multiparametric MRI [20]. PSA is a prostate-specific protein whose serum concentration is increased by prostate diseases such as PCa. PSA was discovered in 1979 and has been widely applied to PCa since its U.S. Food and Drug Administration approval in 1986 because it can detect PCa better than other methods [21]. In New Zealand, Australia, and Israel, the incidence of PCa increased rapidly around 1990 and has generally leveled off since 2000 (Fig. 2A). The incidence of PCa began to increase around 2000 in Turkey, Japan, South Korea, Kuwait, and China and is still increasing. In India and Thailand, the incidence of PCa is increasing slightly. These data are partially explained by the popularization of PSA testing. PSA testing has been highly popularized in Australia, New Zealand, and North America [10, 14]. However, PSA testing remains unpopular in India and Thailand. Although the PSA test rate in South Korea is lower than that in the US and Japan, the incidence of PCa continues to rise, becoming the most common cancer in 2022 [22]. PCa mortality rates in New Zealand, Australia, Israel, and Japan began to rise around 1990, but are now declining (Fig. 2B). In South Korea, PCa mortality began to rise around 2000, but is now declining. In Singapore, PCa mortality increased slightly until approximately 2000, but has generally leveled off since then. Detection of PCa by PSA testing temporarily increased mortality; however, in recent years, mortality has decreased due to improved PCa treatment and possibly the influence of early detection by PSA testing.

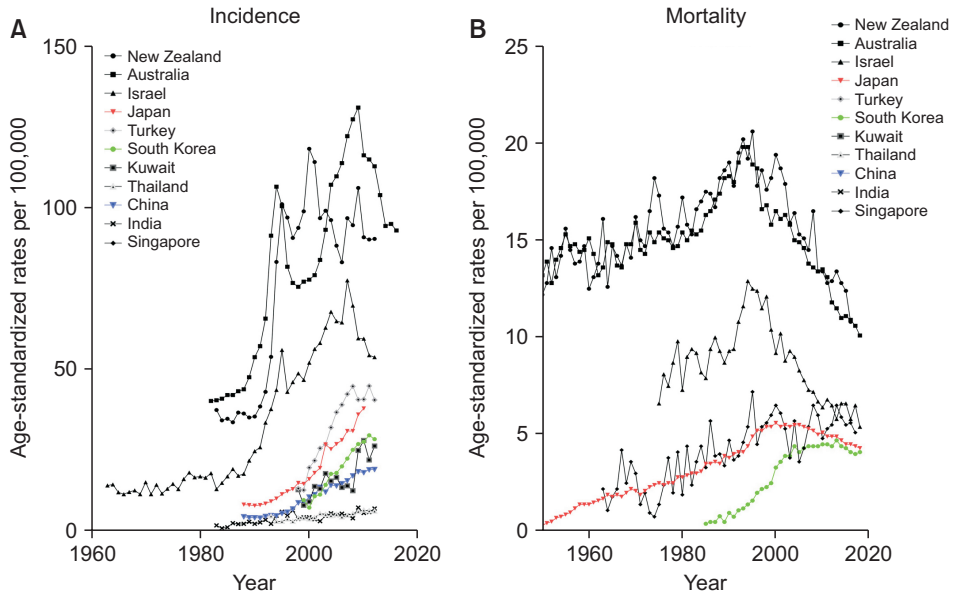

Fig. 2. Incidence and mortality trends in Urological Association of Asia-associated countries. (A) Annual incidence per 100,000 population in the World Health Organization (WHO) Statistical Information System Mortality Database. (B) Annual mortality per 100,000 population in the WHO Statistical Information System Mortality Database.

The incidence rates in Oceanian countries and Israel increased around the 1990s due to the popularization of PSA testing. PSA testing also increases the risk of overdiagnosis and overtreatment of low-risk PCa. Based on this result, the current guidelines in the US, the United Kingdom (UK), Canada, Australia, and Israel do not recommend PSA testing for healthy or asymptomatic men in the 2000s [23-27]. This decision led to the decreased incidence in Oceania and Israel from the 2010s to the 2020s (Fig. 2B). However, from the analysis of the Surveillance, Epidemiology, and End Results (SEER) 18 registry incidence data, a significant increase in the incidence of metastatic PCa was found in men aged 45–74 years (2010–2018) [28]. This phenomenon is related to the decrease in PSA testing recommendations by the US Preventive Services Task Force (USPSTF) [29]. In 2018, the USPSTF changed the PSA testing recommendation from D recommendation (no recommendation) to C recommendation (should not screen men who do not express a preference for testing) for men aged 55–69 years. This may increase the incidence rate in the US, the UK, Canada, Australia, Israel, and other countries. In Japan, PSA testing is strongly recommended, resulting in a continued increase in the incidence [30]. In South Korea and China, PSA testing is not performed in periodic medical check-ups; the incidence declined in South Korea and slightly increased in China [31, 32]. The incidence in Asian countries differs by country: it increased in India, but decreased in the Philippines and Bahrain between 2007–2016 [33].

Mortality rates were once very high in Oceanian countries and Israel in 1990 and have continued to decrease until now. This could be explained by the improvement in treatment care and early-stage detection by PSA testing. Additionally, mortality rates in Singapore, Japan, and South Korea increased slightly in the 2000s but have now slightly decreased, which could be explained by the same reasons. Mortality rates are currently increasing in some Asian countries. The mortality in Uzbekistan, Georgia, Thailand, Kyrgyzstan, and Kuwait increased between 2007–2016 [33]. The recent rise in mortality in many Asian countries may be related to the increased prevalence of risk factors associated with economic development, such as obesity, increased dietary fat consumption, and decreased physical activity, or may reflect improved data collection mechanisms [34].

SURVIVAL RATE TREND IN ASIAN COUNTRIES

PCa has a better survival rate than other cancer types [35]. Even so, survival rates vary between countries, with some countries having poor survival rates. According to data from the CONCORD-3 study, which surveyed cancer survivors worldwide (62 countries) during 1995–2014, although the timing is different, the 5-year survival of PCa is 70%–100% in most countries [35]. In Japan and South Korea, PCa survival

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increased by an average of 12% every 5 years, approaching 90% from 2010 to 2014. Survival was less than 70% in 4 African countries (Algeria, Mauritius, Nigeria, and South Africa), 3 Asian countries (China, India, and Thailand), and 2 European countries (Bulgaria and Gibraltar). India also saw a significant improvement in survival but remained the lowest among Asian countries with 44.3% during 2010–2014.

Asian populations have been reported to be different from the American or African populations in PCa malignancy. Many conflicting reports on PCa malignancy differences in Asia and the US are unclear. PSA level, Gleason score, and clinical TNM (tumor, node, metastasis) stage were reported to be worse in the Asian population than in the American population. The percentage of Caucasians with a Gleason score of 8–10 was 22.9%, whereas the percentages of South Korean, Chinese, and Japanese men in California were 34.5%, 30.9%, and 28.6%, respectively [36]. Among the Asians surveyed, South Koreans had the highest rates of poorly differentiated cancer, high Gleason scores, and advanced stages. Data from the SEER study showed that Asians living in the US had more distant metastases at diagnosis than Caucasians during 1988–1994 [37]. Data from the SEER database also revealed that PSA (median: 7.2 ng/mL vs. 6.7 ng/mL), Gleason score (8–10: 19.1% vs. 18.7%), and disease stage (cT3–4: 2.7% vs. 2.3%) were significantly higher in Asian men compared with US Caucasians [38]. Several other studies have reported that Asians living in North America have more aggressive cancers than Caucasians and African Americans [37]. However, some reports found no racial differences in Gleason scores among Asian US residents compared with Caucasians and African Americans, although Asians accounted for a minority of patients (approximately 5%) [39]. No conclusions have been reached, but the Asian population seems to have more aggressive PCa at the time of diagnosis than Caucasians. Surprisingly, it has been reported that the prognosis of Asian populations is even better than that of Caucasians, even with highly malignant cancers. Chinese, Filipino, Japanese, and South Korean men, except South Asians and Vietnamese men, had significantly better survival than Caucasians [36]. SEER data show that Asians in the US have higher survival rates than other races, such as Caucasians, African Americans, and Hispanics. Caucasian mortality was 22.4 per 100,000 population, whereas Asian mortality was 10.5 per 100,000 population [40]. From these reports, it was speculated that Asian populations have a better survival rate than Caucasians, despite their higher malignancy at diagnosis. This could be explained by the difference in PSA testing popularity between Asian countries and the US. PSA testing is less prevalent in Asian countries than in the US, and it is speculated that PCa is diagnosed at a more advanced stage in Asia. Asians have a good survival rate despite the advanced stage at the time of diagnosis, suggesting a good response to treatment or a slow progression.

To understand the survival difference between Asian countries, we examined the 5-year survival rate of patients with PCa in UAA-associated countries (Fig. 3). No significant difference in the 5-year survival rate was found by Asian province classification, but it differed between countries. All developed countries (Japan, Australia, South Korea, New Zealand, Singapore, Kuwait, and Taiwan) have a survival rate of over 80%. Although no data are available for Israel, the United Arab Emirates, and Bahrain, since the mortality-to-incidence ratio is similar to that in other developed countries, the 5-year survival rate is predicted to be over 80% (Fig. 1B). The Whole Population Cancer Registry was adopted in Australia, New Zealand, Singapore, Hong Kong, and Macao, which made it easy to evaluate 5-year survival chronologically. The 5-year survival rate in Oceania (Australia and New Zealand) increased in the 1990s. In the 2000s, some Asian countries (South Korea, Singapore, and Hong Kong) had increased 5-year survival rates. This may be explained by the early detection of PCa by PSA testing and improvements in PCa treatment. Apart from Hong Kong, all developing countries (Macao, China, Malaysia, Thailand, India, and the Philippines) have a survival rate below 80%. Because of the lack of population-based studies in most developing countries and that of unification in the observation period between countries, it is difficult to simply compare survival rates between countries. However, developing countries with worse survival rates than developed countries can be easily predicted. These results also indicate that the clinical level is more important than racial differences among Asian countries.

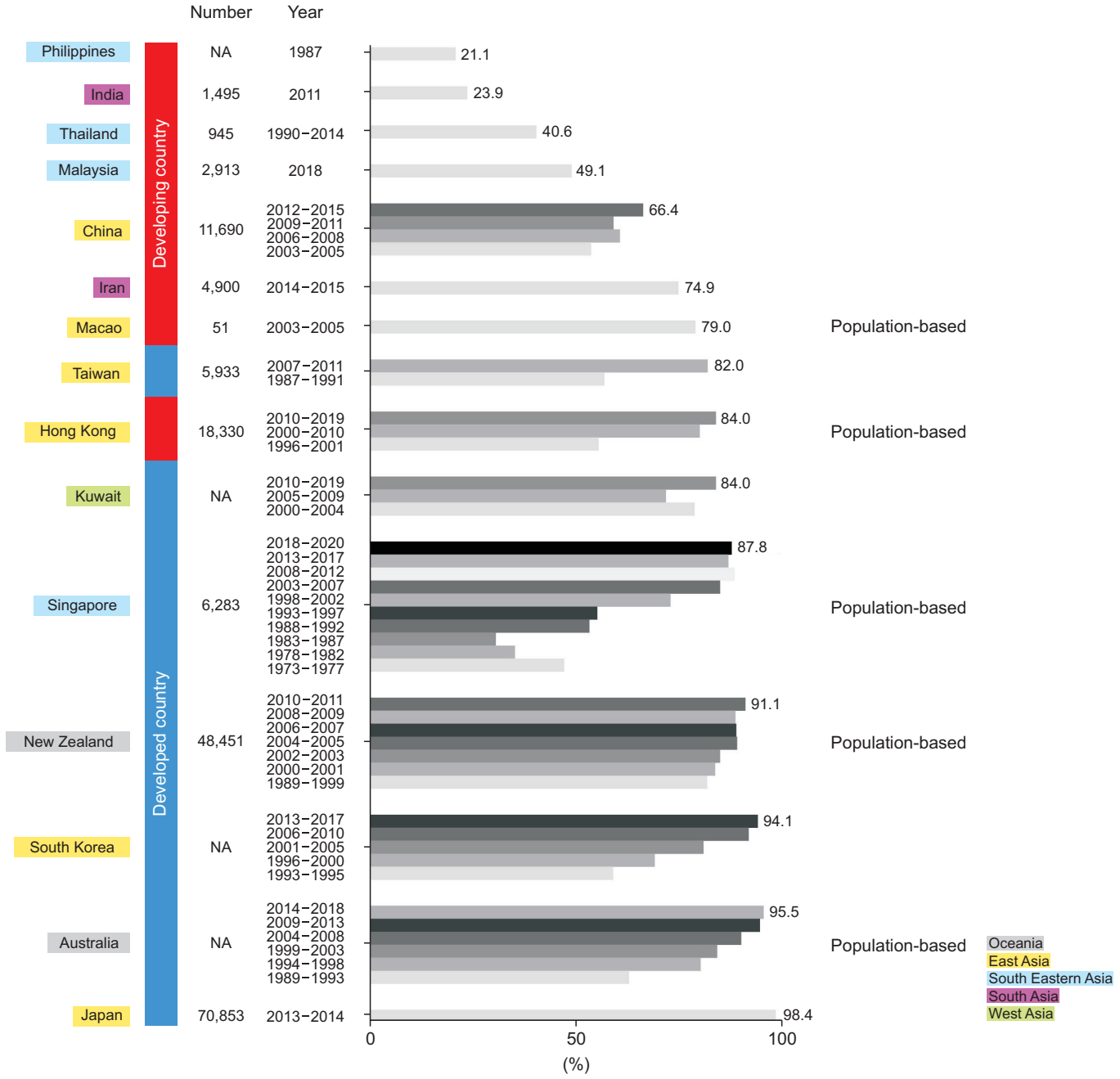

Fig. 3. Five-year overall survival of prostate cancer in Urological Association of Asia-associated countries. Data were selected from each paper or website (the Philippines [42], India [43], Thailand [44], Malaysia [45], China [46], Iran [47], Macao [48], Taiwan [49], Hong Kong [50], Kuwait [51], Singapore [52], New Zealand [53], South Korea [54], Australia [55], Japan [56]).

CONCLUSION

Asians are presumed to have a better prognosis for PCa than Caucasians, as they have lower mortality-to-incidence ratios and higher survival rates, despite being diagnosed with PCa in an advanced state. The situation of PCa in Asian countries was not distinctly different by region; rather, it varied widely between developed and developing countries. The widespread use of PSA testing has led to a temporary increase in PCa cases worldwide. Following the US and Oceania, the number of cases is also on the rise in most developed Asian countries. In the US and Oceania, the number of cases has been declining in recent years as PSA testing has become less recommended; however, in Asian

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countries, PSA testing has continued and has been on the rise. In some developed countries in Oceania and Asia, the number of deaths temporarily increased as the number of PCa diagnoses rose, but has been improving in recent years as medical technology and access to care have improved. Also, the 5-year survival rate is predominantly greater than 80%. On the other hand, some developing countries in Asia previously tended to have a low incidence, a high mortality-to-incidence ratio, and low 5-year survival rates. There are concerns regarding the negative effects of inadequate medical technology and access to medical care. The development of healthcare systems and medical care will likely improve PCa survival in developing countries.

NOTES

- Conflicts of Interest: Takahiro Kimura is a paid consultant/advisor of Astellas, Bayer, Janssen and Sanofi. The other author has nothing to disclose.
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- Author Contribution: Conceptualization: KI, TK; Data curation: KI; Formal analysis: KI; Methodology: KI, TK; Project administration: KI, TK; Visualization: KI, TK; Writing - original draft: KI, TK; Writing - review & editing: KI, TK.

- ORCID

Kagenori Ito: https://orcid.org/0000-0002-4970-1727

Takahiro Kimura: https://orcid.org/0000-0002-5673-1553

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