REVIEW

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# Survival Rate and Prognostic Factors of Localised Prostate Cancer in Southeast Asian Countries: A Systematic Review with Meta-Analysis

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## Abstract

Prostate cancer (Pca) is one of the most prevalent health conditions affecting men, particularly older men, and cases have increased in recent years. **Objective:** This review examined the survival rate and prognostic factors of patients with Pca in Southeast Asia (SEA). **Methods:** We conducted a systematic search of three databases (PubMed, Scopus, Web of Science) and a manual search until April 1, 2022. The selected papers were evaluated using the Newcastle-Ottawa Quality Assessment Form for Cohort Studies. The review protocol was registered with PROSPERO (CRD42022326521). Pooled prevalence rates were calculated using the programme R version 4.2.1. Heterogeneity was assessed using the I2 statistic and p-value. A narrative approach was used to describe prognostic factors. Studies were selected and finalised based on the review question. The quality of the included studies was assessed. **Results:** A total of 11 studies were included in this review. The 1-, 3-, 5- and 10-year survival rates of SEA Pca cases were 80.8%, 51.9%, 66.1% (range 32.1–100) and 78% (range 55.9–100), respectively. Prognostic factors for Pca were discussed in terms of sociodemographic, disease-related and treatment-related aspects. The predictors of significantly lower survival were age more than 75 years, cancer detected during transurethral resection of the prostate, Gleason score more or equal to eight, high-risk group, metastases and no adjuvant radiotherapy. A meta-analysis on the pooled HR of prostate cancer could not be performed due to the heterogeneity of prognostic factors. The pooled prevalence of localised and metastatic prostate cancer in SEA countries was 39% 95% CI [20-62] and 40% 95% CI [28-53], respectively. **Conclusion:** The survival rate in SEA countries can be determined by prognostic factors, which can be divided into sociodemographic, disease-related and treatment-related factors. Therefore, further studies are needed to improve the understanding and treatment of Pca in the region SEA.

**Keywords:** Prostate cancer- survival- prognosis- Southeast Asia

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## Introduction

Prostate cancer (Pca) is the second most frequent male malignancy after lung cancer and the fifth cause of cancer mortality in 2020. According to GLOBOCAN 2020 estimates, 1,414,259 new cases of Pca were reported globally in 2020, representing 7.3% of all cancers in men and causing 375,304 deaths (3.8% of all deaths caused by cancer in men) (Sung et al., 2021). Pca is the most common cancer in more than half of the countries (112 of 185), with developed countries having a higher prevalence. The highest incidence rates were reported in Northern and Western Europe, the Caribbean, Australia/New Zealand, Northern America, and Southern Africa, while Asia and Northern Africa have the lowest rates. PCa incidence rates vary widely across the globe due to differences in detection practices, treatment, lifestyle, and genetic factors (Center et al., 2012; Zhou et al., 2016).

Most high-income countries (Northern America, Oceania, and Northern and Western Europe) have seen a decline in mortality rates (Bray and Piñeros, 2016; Center et al., 2012; Wong et al., 2016) due to improvements in early detection through targeted screening, diagnosing and cancer treatment (Etzioni et al., 2008; Tsodikov et al., 2017). Contrastingly, the Pca mortality rate increased in Central and Eastern Europe, Asia, Africa (Center et al., 2012), and some countries such as Thailand, Bulgaria, and Ukraine (Culp et al., 2020), which reflected an underlying increase in incidence trends, advanced disease at diagnosis, limited access to appropriate prostate-specific antigen (PSA) testing, and limited access to survival-prolonging treatments.

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Historically, Asia has substantially lower Pca incidence than Western countries, with 4.5, 10.5, and 11.2 cases per 100,000 people in South-Central Asia, Eastern Asia, and Southeast Asia (SEA), respectively (Center et al., 2012). However, the review by Chung et al., (2019) revealed that Pca incidence has generally increased in China, India, South Korea, Vietnam, Japan, and Singapore, reported from 1998 until 2009. Asian countries recorded an average mortality rate of PCa of 3.8 per 100,000 in year 2012 (Chen et al., 2014). According to the Malaysian National Cancer Registry 2012-2016, Pca is the third most common malignancy in men in Malaysia, with a 1 in 94 lifetime risk (Ministry of Health Malaysia, 2019a). Approximately 60% of Malaysian patients with Pca are diagnosed in the advanced stages (stages 3 and 4), resulting in a high burden of advanced Pca with a significant impact on the healthcare system (Ministry of Health Malaysia, 2019b). Substantial economic growth and sociocultural changes have increased life expectancy in several Asian countries, ultimately increasing Pca incidence and mortality in these countries (Gu et al., 2018; Hajjar et al., 2013). The rising Pca prevalence and mortality rate in SEA countries necessitates action, where proper planning, targeted screening programmes, and advanced treatment technology are required to improve survival (Cullen et al., 2012).

Survival rates are among the crucial indicators for evaluating the effectiveness of cancer prevention and treatment initiatives. Several studies on Pca survival in Asia yielded mixed results (Hassanipour et al. 2020). The estimated 5-year relative survival rate of Pca in China in 1992–2000 was 32.5% (Chen et al., 2011). In comparison, South Korea recorded higher survival rates of 67.2% and 93.3% in 1996 and 2010–2014, respectively (Chen et al., 2011; Jung et al., 2011, 2017). Prognostic variables such as the Gleason score (GS), capsular invasion, blood PSA, disease stage, and aneuploidy are the best progression markers to indicate the survival rate in organ-confined disease following radical prostatectomy.

Reliable survival rate data and prognostic factors for Pca are vital, as the information is used in various medical and diagnostic procedures. However, there is a gap in establishing a comprehensive estimate of the Pca survival rate and prognostic factors in SEA countries. Therefore, we used this systematic review to estimate the survival rate and prognostic factors of patients with Pca in SEA countries. This study was motivated by the need to understand the Pca survival rate and prognostic factors in hospital planning and the disparate findings between published articles.

## Materials and Methods

The review protocol is registered with PROSPERO (CRD42022326521). This systematic review was performed in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) updated guidelines (Page et al., 2021). The research question was formulated by utilising the population, prognostic factors (or models of interest), and outcome (PFO) framework (Munn et al., 2018). The three aspects included based on the PFO framework were patients with prostate cancer (population), prognosis factor (prognostic factor), and survival rate (outcome). The factors were used to frame the research question: "What are the survival rate and prognostic factors of patients with Pca in SEA countries?" The literature search was performed following the PRISMA flow shown in Figure 1.

*Search Strategy*

The literature search was conducted in April 2022. During the article identification process, one author (NM) searched for potentially relevant studies using relevant keywords in the form of medical subject heading (MeSH) terms. Specific search strings were developed using an advanced search of adjacency operators, truncation, and Boolean operators. We performed a comprehensive search of specific websites, organisations, and citations using the Web of Science, PubMed, and Scopus databases and manual search. The keywords used were:

("prostate carcinoma", "prostate Tumor", "Prostate Cancer", "prostate Neoplasms, "Cancer of prostate", "Neoplasms Of prostate", "Survival", "Survival Analysis", "Survival Rate", "Prognostic factor", "Outcome", "prediction", "Brunei", "Myanmar", "Cambodia", "Timor-Leste", "Indonesia", "Laos", "Malaysia", "the Philippines", "Singapore", "Thailand" and "Vietnam"). Three authors (R.O., N.M., T.K.) conducted the initial search and identified a total of 112 records. The three authors screened the titles and abstracts of all potentially eligible articles. Sixty-five articles were imported into the Mendeley library. Forty-three duplicate articles were deleted (Bramer et al., 2018).

*Screening*

The titles and abstracts of the articles were reviewed against the inclusion and exclusion criteria. Inclusion criteria were original studies investigating survival rate and prognostic factors of confirmed localised prostate cancer in Southeast Asian countries. Exclusion criteria were non-original articles such as conference proceedings, perspectives, commentaries, opinions, reports, systematic reviews, and meta-analyses. Suspected Pca, other cancers, and regional and metastatic Pca were also excluded. The review excluded 41 articles, leaving 24 articles.

*Eligibility Criteria*

Five of 24 articles that were not retrieved did not provide full-text access. Only 19 full-text research articles were reviewed for eligibility. During data confirmation, the articles reviewed were randomly assigned to two authors per article, who reviewed them independently and in exchange for each other. Disagreements were resolved through discussion and consensus between the two authors and occasionally by the research team leader. Eleven of 19 articles were excluded, with nine articles not answering the research question and two articles containing studies from the Southeast Asian region. A further four studies were identified through searching websites, organisations and citations. One article that did not meet the inclusion criteria was excluded. Thus, three more articles were included, bringing the total number of articles considered

for the final review to 11.

*Quality appraisal*

The risk of bias and quality of the studies were assessed with the Newcastle-Ottawa Quality Assessment Form for Cohort Studies. The assessment form comprised three parts: selection (four questions), comparability (one question), and outcome (three questions). The final scores were divided into three categories: good (selection domain, three or four stars; comparability domain, one or two stars; outcome/exposure domain, two or three stars), fair (selection domain, two stars; comparability domain, one or two stars; outcome/exposure domain, two or three stars), and poor (selection domain, zero or one star; or comparability domain, zero stars; or outcome/exposure domain, zero or one star). The article was selected if both assigned reviewers agreed on the quality of the article. In case of disagreement, the reviewers consulted a third independent reviewer. Table 1 shows the quality assessment.

*Data extraction*

The relevant information was extracted from each included article into a data extraction sheet and included the authors' name, publication year, study period, country of origin, survival rate by year for each survival period, and prognostic factors.

*Data analysis*

The studies were subjected to preliminary descriptive analysis. The heterogeneity of the studies was assessed using the I2 statistic. High heterogeneity is indicated by an I2 value of more than 75%. Not all included studies could be used for the meta-analysis because the reported results were so varied. If the reviewers conclude that a study does not contribute enough to the evidence, it is excluded. The statistical package "dosresmeta" by Robert Gentleman and Ross Ihaka from the Department of Statistics, University of Auckland, New Zealand, was used to generate pool estimates for prevalence and their 95% confidence interval.

## Results

*Study Selection*

Scopus, PubMed, and Web of Science yielded 108 articles. After removing 43 duplicates, 65 articles remained for screening. Nineteen full-text articles were assessed for eligibility, with eleven studies were excluded because they did not answer the research questions and were not from Southeast Asian countries. The remaining eight articles were included in the analysis. A further three articles from external resources (websites, organisations, citations) were accepted after discussion with team members. In total, 11 studies were included in this review which are summarised in Table 2.

The articles were published from 2008 to 2021 and were performed in Thailand (n = 4), Malaysia (n = 3), Indonesia (n = 2), and Singapore (n = 2). All studies were cohort studies with good quality scores. The studies all involved patients with localised Pca, and the study

Table 1. Detailed Newcastle-Ottawa Scale of each Included Cohort Study

| Authors | Selection | | | | Comparability | | Outcome | | | Total score | Quality |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | Representativeness of exposed cohort | Selection of non-exposed cohort | Ascertainment of exposure | Demonstration that outcome of interest was not present at start of study | Adjust for the most important risk factors | Adjust for other risk factors | Assessment of outcome | Follow-up Length enough? | Loss to follow-up rate | | |
| Alvarez et al. | 1 | 0 | 1 | 1 | 1 | 0 | 1 | 1 | 1 | 7 | Good |
| Yuri et al. | 1 | 0 | 1 | 1 | 1 | 0 | 1 | 1 | 1 | 7 | Good |
| Woranisarakul et al. | 1 | 0 | 1 | 1 | 1 | 0 | 1 | 1 | 1 | 7 | Good |
| Supit et al. | 1 | 1 | 1 | 1 | 1 | 0 | 1 | 1 | 1 | 8 | Good |
| Nonsrijun et al. | 1 | 1 | 1 | 1 | 1 | 0 | 1 | 1 | 0 | 7 | Good |
| Chemay et al. | 1 | 0 | 1 | 1 | 1 | 0 | 1 | 1 | 1 | 8 | Good |
| Lim et al. | 1 | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 8 | Good |
| Shah et al. | 1 | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 8 | Good |
| Sriplung & Prechavittayakul | 1 | 0 | 1 | 1 | 1 | 0 | 1 | 1 | 1 | 7 | Good |
| Lu et al. | 1 | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 8 | Good |
| Li et al. | 1 | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 8 | Good |

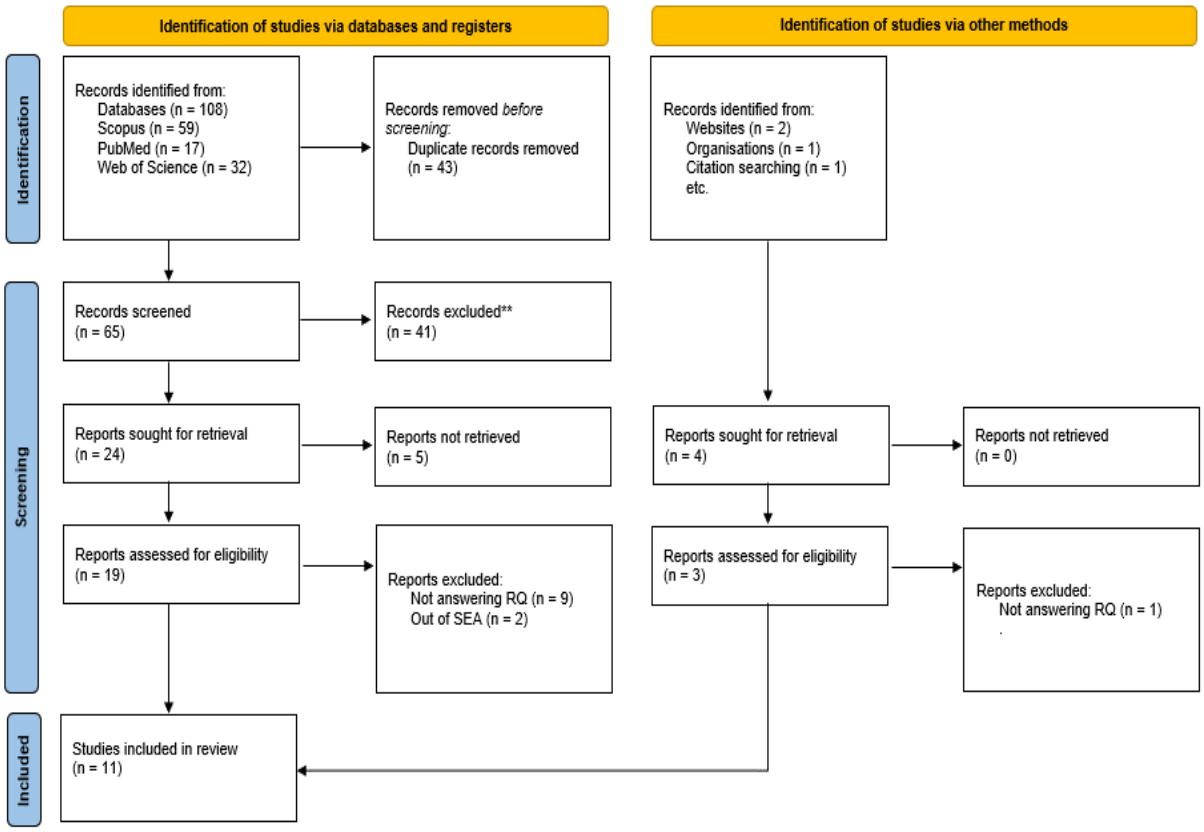


Figure 1. PRISMA Flow Diagram

duration was 50–240 months. The earliest study was in 2008 while the most recent was in 2021.

Only five studies reported the median survival time (range, 40.1–73.6 months) (Alvarez et al., 2018a; Chemay et al., 2008; Lim et al., 2021a; Nonsrijun et al., 2013a; Shah et al., 2021a; Supit et al., 2013a). The overall 5-year OS rate was 40.6–81.2% (Alvarez et al., 2018b; Li et al., 2021a; Lu et al., 2020a; Nonsrijun et al., 2013b; Shah et al., 2021b; Sriplung and Prechavittayakul, 2011a; Supit et al., 2013b). One study each reported the 1-year (Sriplung and Prechavittayakul, 2011b) and 3-year survival rate (Sriplung and Prechavittayakul, 2011b), while three studies reported the 10-year survival rate (Li et al., 2021b; Lu et al., 2020b; Shah et al., 2021b). Three studies reported biochemical recurrence (BCR)-free survival (BRFS) (Li et al., 2021b; Supit et al., 2013b; Woranisarakul et al., 2017a) and one reported metastasis-free survival (MFS) (Woranisarakul et al., 2017b). One study did not report the survival rate or median survival time but was included because it reported on predictors (Yuri et al., 2020). Two studies reported the survival rates but did not report on predictors (Lim et al., 2021b; Sriplung and Prechavittayakul, 2011b). Table 3 lists the characteristics of the median survival time and overall survival (OS) rate.

The prognostic factor findings were divided into better or poorer survival rates. Seven studies reported the factors indicating poor survival rates (Table 4) and two studies reported prognostic factors associated with a better survival rate (Table 5). The prognostic factors with a significant hazard ratio for the overall 5-year OS rate were categorised into sociodemographic, disease-related,

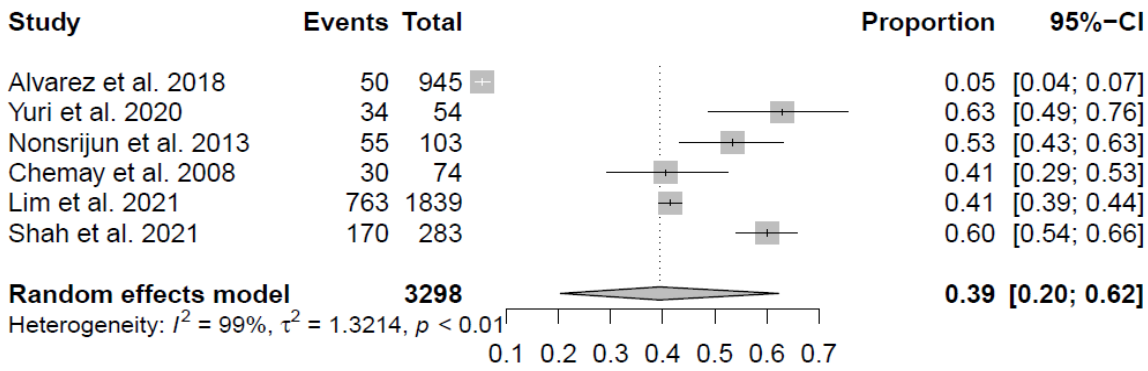


Figure 2. Forest Plot for Localized Prostate Cancer

Table 2. Characteristic of Included Studies and the Survival Rate

| Author | Year | Country | Study design | Sample size | Study population | Period | Duration of study (months) |
|---|---|---|---|---|---|---|---|
| Alvarez et al. | 2018 | Thailand | Retrospective cohort | 945 | Pca | 1990-2014 | Up to 240 |
| Yuri et al. | 2020 | Indonesia | Cohort | 54 | Pca | 2009-2011 | 60 to 70 |
| Woranisarakul et al. | 2017 | Thailand | Retrospective cohort | 151 | local advanced Pca | 2006-2014 | 120 |
| Supit et al. | 2013 | Indonesia | Retrospective cohort | 96 | localised or locally advanced Pca | 1995-2009 | 60 |
| Nonsrijun et al. | 2013 | Thailand | Cohort | 103 | Prostatic adenocarcinoma | 2003-2008 | 90 |
| Chemay et al. | 2008 | Malaysia | Retrospective cohort study | 73 | Pca | 1983- 2004 | up to 120 |
| Lim et al. | 2021 | Malaysia | Cohort | 1839 | Newly diagnosed Pca | 2016 - 2018 | 50 |
| Shah et al. | 2021 | Malaysia | Retrospective cohort study | 283 | Pca | 2008 - 2017 | 140 |
| Sriplung & Prechavittayakul | 2011 | Thailand | Cohort | 144 | Not mentioned | 1990- 1999 | Up to 156 |
| Lu et al. | 2020 | Singapore | Cohort | 1120 | Localised Pca | 1998- 2016 | Up to 144 |
| Li et al. | 2021 | Singapore | Cohort | 657 | Localised Pca | 2000 - 2019 | 127 |

NR. not reported ; Pca, Prostate cancer; BRFS, biochemical recurrence-free survival; OSR overall survival rate; MFS, metastasis-free survival; PFS, progression-free survival; LDR-BT, low-dose-rate brachytherapy; EBRT, external beam radiation therap

and treatment-related factors (Table 6). The prognostic factors significant for a shorter OS rate were age > 75 years, detection during prostate transurethral resection, GS ≥ 8, high-risk status, metastasis, higher MMP11 expression, and not undergoing adjuvant radiotherapy. The GS predicted the most extended 5-year OS survival rate while MMP11 expression predicted the shortest 5-year OS rate. The highest hazard ratio was for age > 75 years while the lowest hazard ratio was for radiotherapy status.

*Meta-analysis of prostate cancer*

Of the eleven studies, 6 studies have sufficient data to perform a meta-analysis on the pooled prevalence of localised and metastatic prostate cancer. A meta-analysis on the pooled HR of prostate cancer could not be performed due to the heterogeneity of prognostic factors. A random effects model was used to calculate the combined prostate cancer metastasis. The pooled prevalence of localised and metastatic prostate cancer in Southeast Asian countries was 39% 95% CI [20-62] and 40% 95% CI [28-53], respectively. Heterogeneity was assessed using the I2 statistic compared to the p-value. A p-value of ≤0.05 and I2 ≥ 50% were considered high heterogeneity. The heterogeneity generated was high at 99% for localised prostate cancer, as shown in Figure 2, and 98% for metastatic prostate cancer, as shown in Figure 3, with a p-value of less than 0.01 indicating that the test was significant.

## Discussion

Pca causes significant morbidity and mortality in men globally, highlighting the necessity of conducting studies in developing countries such as those in SEA to identify prognostic factors and improve survival rates. In this review, the 1-, 3-, 5-, and 10-year survival rates for Pca in SEA countries were 80.8%, 51.9%, 66.1% (32.1–100), and 78% (55.9–100), respectively. The highest 1- and 3-year survival rates were recorded in Thailand in a patient safety study by Yoelao et al., (2014), which indicated that Thailand has established a comprehensive national health management system that promotes positive health-seeking behaviour and ensures access to healthcare. The highest 5- and 10-year survival rates were reported in Singapore. The high rates could be attributed to healthcare accessibility and affordability accompanied by an extensive primary care polyclinic network and tertiary healthcare centres that include up-to-date diagnostic and research centres that promote better Pca survival compared to other SEA regions (Singapore MOH, 2020).

The median survival rate we detected (57 months; range, 40–74 months) was generally higher than that reported in other studies. This could be attributed to the fact that we only reported localised Pca. Contrastingly,

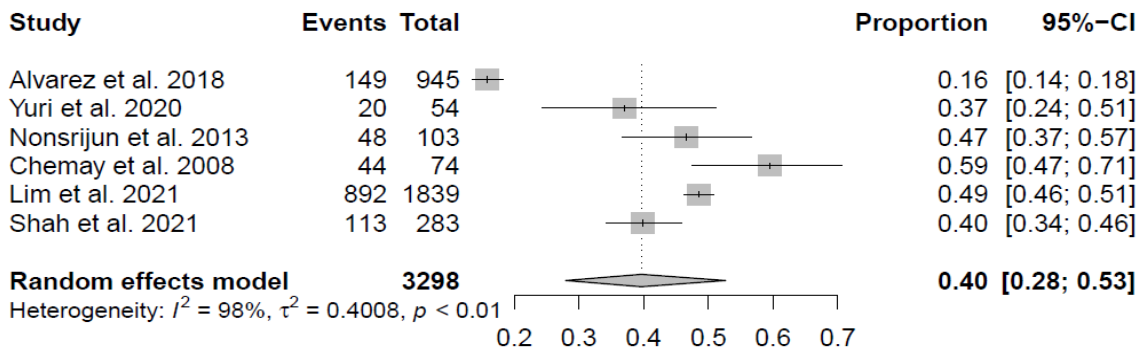


Figure 3. Forest Plot for Metastasized Prostate Cancer

Table 3. Characteristic of the Median Survival Time and Overall Survival Rate

| Author | Median Survival (month) | Group | 1yr | 3yr | 5y SR (%) | 10y SR | Group | 5y BRFS (%) | 5y MFS (%) |
|---|---|---|---|---|---|---|---|---|---|
| Alvarez et al. | 44 | OS | - | - | 40.6 | - | | - | -- |
| Yuri et al. | - | - | - | - | - | - | | - | - |
| Woranisarakul et al. | - | - | - | - | ** Because of the low mortality rate, the overall survival rate was not demonstrated. | - | Overall | 53.1 | 90.8 |
| | | | | | | | ART | 78.7 | 100 |
| | | | | | | | SRT | 69.1 | 90.6 |
| Supit et al. | 74 | OS | - | - | 74.8 | - | Overall | 68.3 | - |
| | | High risk | - | - | 67.9 | | High risk | 57.1 | - |
| | | Intermediate risk | - | - | 94.7 | | Intermediate risk | 94.1 | - |
| | | Low risk | - | - | 100 | | Low risk | 100 | |
| Nonsrijun et al. | 69 | MMP -High | - | - | 41.7 | - | | - | - |
| | | Low | - | - | 72.7 | | | - | - |
| Chemay et al. | 63 | - | - | - | - | - | | - | - |
| Lim et al. | 40 | - | - | - | - | - | | - | - |
| Shah et al. | - | OS | - | - | 77.8 | 65.5 | | - | - |
| | | Early | - | - | 81.2 | 68.9 | | - | - |
| | | Advanced | - | - | 71.7 | 55.9 | | - | - |
| Sriplung & Prechavittayakul | - | OS | 80.8 | 51.9 | 32.1 | - | | - | - |
| Lu et al. | - | Overall (OS) | | | | | | | |
| | | 45-54 | - | - | 100 | 99.1 | | - | - |
| | | 55-64 | - | - | 99.5 | 98.5 | | - | - |
| | | 65-74 | - | - | 97.5 | 95.5 | | - | - |
| | | Prostate cancer-specific survival | | | | | | | |
| | | 45-54 | | | 100 | 100 | | - | - |
| | | 55-64 | | | 99.8 | 99.5 | | - | - |
| | | 65-74 | | | 100 | 99.2 | | - | - |
| Li et al. | - | Low risk | | | | | | | |
| | | LDR | - | - | 96 | 91 | LDR | 92 | - |
| | | EBRT | - | - | 91 | 87 | EBRT | 87 | |
| | | Intermediate | | | | | | | |
| | | LDR | - | - | - | - | LDR | 96 | - |
| | | EBRT | - | | - | -- | EBRT | 89 | - |

the United States and Japan reported the median survival rate in metastasis Pca. For example, Kim et al., (2021) reported that the median survival of a patient with Pca in the United States was 28 months, while that for patients in Japan with bone metastatic Pca was 55.6 months (Miyoshi et al., 2015).

The 5- and 10-year survival rates we reported were higher than those in the review of Asian countries by Hassanipour et al., (2020), where the 5 year survival rate was 61.9% (95% CI 59.5–64.3) and the 10-year survival rate was 36.2% (95% CI 9.2–63.2). The lower 10 year-survival rate reported in the aforementioned study compared to our review could be attributed to different diets, lifestyles, and diagnostic facility accessibility. Furthermore, our review involved four SEA countries versus the 10 Asian countries reviewed by Hassanipour et al., (2020), which contributed to the variation in the reported survival rate values. However, Western countries such as the United States, which has the latest diagnostic and research facilities, revealed a much higher 5-year survival rate for Pca of 98% based on the Surveillance, Epidemiology, and End Results Program (SEER) database (The American Cancer Society, 2020).

*Sociodemographic Factors*

Consistent with the findings from other global studies, we determined that older age was a Pca prognostic factor, which could be attributed to the nature of Pca progression, as it occurs slowly with increasing age. This progression is inevitable and was highlighted by Merriel et al., (2018). Contrastingly, Da Cruz et al., (2017) examined 2,283 patients who underwent radical retropubic prostatectomy and determined that the different ages of patients with Pca were not an independent prognostic factor for Pca.

Table 4. Prognostic Factors Associated with the Poorer Survival Rate

| Authors | Analysis | Prognostic factor | Comparison | Univariate | | | Multivariate | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | | HR | 95% CI | P value | HR | 95% CI | P value |
| Alvarez et al. 2018 | CPHM | Muslims | Buddhists | 1.31 | 1.00, 1.72 | 0.04 | 1.27 | 0.97, 1.67 | 0.06 |
| Shah et al. 2021 | CPHM | Metastasis | No Metastasis | 6.97 | 3.89, 12.51 | - | 5.26 | 2.88, 9.63 | <0.001 |
| | | Age ≥75 years | <75 | 14.38 | 1.98, 104.39 | - | 8.49 | 1.16, 62.13 | 0.035 |
| | | Gleason score ≥8 | <8 | 4.39 | 2.24, 8.61 | - | 2.36 | 1.18, 4.73 | 0.015 |
| Nonsrijun et al. 2013 | CPHM | Expression of | | 0.343 | 0.183, 0.645 | 0.001 | 0.448 | 0.212, 0.946 | 0.035 |
| | | MMP-11 (cont) | | | | | | | |
| | | Pathological tumour classification (cont) | | 0.276 | 0.131, 0.583 | 0.001 | 0.333 | 0.15, 0.74 | 0.007 |
| | | Age (cont) | | 0.612 | 0.332-1.127 | | 0.936 | 0.443, 1.976 | 0.0861 |
| | | PSA(cont) | | 0.499 | 0.210-1.186 | 0.116 | 0.766 | 0.288, 2.039 | 0.593 |
| | | Gleason(cont) | | 0.161 | 0.490-0.526 | 0.002 | 0.301 | 0.080, 1.128 | 0.075 |
| | | Bone metastasis(cont) | | 0.304 | 0.162-0.573 | <0.001 | 0.487 | 0.235, 1.010 | 0.053 |
| Supit et al. 2013 | Multivariate Cox-regressions | High-risk group | Intermediate-risk group | - | - | - | 9.35 | 1.52, 57.60 | 0.016 |
| | | Detection method by TURP | Detection by prostate biopsy | - | - | - | 6.81 | 2.28, 20.33 | 0.001 |
| | | PSA>20 ng/mL | PSA≤20 ng/mL | - | - | - | 1.003 | 1.00, 1.01 | 0.039 |
| | | Adjuvant RT | No Adjuvant RT | - | - | - | 0.18 | 0.05, 0.58 | 0.005 |
| Chemay et al. 2008 | Multivariate Cox-regressions | Haemoglobin>11 | Hb≤11 | 0.39 | 0.14, 1.08 | 0.161 | 0.31 | 0.11, 0.91 | 0.022 |
| | | Metastasis | Localised | 2.35 | 0.78,7.09 | 0.103 | 2.37 | 0.71, 10.56 | 0.132 |
| | | Gleason ≥7 | Gleason<7 | 1.8 | 0.66, 4.90 | 0.137 | 1.1 | 0.33, 3.70 | 0.051 |
| Lu et al. 2020 | CPHM | OS | | | | | | | |
| | | 65-74 | ≤44 | 0.62 | 0.39,0.98 | 0.045 | 0.67 | 0.41, 1.11 | 0.123 |
| | | Gleason≥8 | Gleason ≤6 | 1.39 | 0.71,2.74 | 0.334 | 1.02 | 0.51, 2.04 | 0.955 |
| | | Stage T3/4 | T1/2 | 0.83 | 0.53,1.31 | 0.426 | 1.76 | 1.05, 2.96 | 0.034 |
| | | PSA at diagnosis | | 0.99 | 0.99–1.01 | 0.454 | 0.99 | 0.99, 1.01 | 0.234 |
| | | PcaSS | | | | | | | |
| | | 65-74 | ≤44 | 0.28 | 0.06, 1.32 | 0.1 | 1.87 | 0.77, 4.54 | 0.165 |
| | | Gleason≥8 | Gleason ≤6 | 5.38 | 1.83, 15.7 | 0.002 | 5.51 | 1.64, 18.5 | 0.006 |
| | | Stage T3/4 | T1/2 | 4.14 | 1.41, 12.1 | 0.01 | 2.25 | 0.71, 7.19 | 0.17 |
| | | PSA at diagnosis | | 1 | 0.99, 1.01 | 0.862 | 0.99 | 0.99, 1.01 | 0.579 |
| Li et al. 2021 | Log-rank | Age | | 1.02 | (0.9–1.1) | 0.3 | | | |
| | *this study provide univariate and multivariate analysis for predictors for BRFS in the intermediate-risk group only | PSA | | 1 | (0.9–1.1) | 0.6 | 1.02 | (0.9–1.1) | 0.4 |
| | | T2 | T1 | 1.3 | (0.8–2.2) | 0.3 | 1.4 | (0.8–2.4) | 0.3 |
| | | Gleason score ≥7 | ≤6 | 1.3 | (0.6–2.6) | 0.5 | 1.3 | (0.6–2.9) | 0.5 |
| | | Yes – hormonal therapy | No | 0.6 | (0.4–1.1) | 0.08 | 0.4 | (0.2–0.8) | 0.007 |
| | | EBRT | LDR | 2.8 | (1.1–6.9) | 0.03 | 3.1 | (1.2–8.0) | 0.02 |

Therefore, further research is needed to explore the possible mechanism. Apart from age, the location of the prostate frequently causes clinicians difficulty in early screening as patients may have difficulty disclosing their symptoms. Furthermore, the digital rectal examination procedure is unpleasant, contributing to the delay in seeking treatment, especially in the elderly (Cui et al., 2016; Stevens et al., 2010).

*Disease-related Factors*

The PSA level, GS, high-risk status, biochemical level in terms of expression of MMP-11, and metastasis status were identified as Pca prognostic factors. These findings were similar to those of other worldwide studies

Table 5. Prognostic Factors Associated with the Better Survival Rate

| Authors | Analysis | Prognostic factor | Comparison | Univariate | | | Multivariate | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | | HR | 95% CI | P value | HR | 95% CI | P value |
| Woranisarakul et al. | Kaplan Meier analysis. (subgroup analysis) | Adjuvant RT (ART) after surgery | Surgery alone | 4.78 | 2.80, 8.09 | 0.001 | - | - | - |
| Yuri et al. | Log-rank test | Tumour-associated macrophages infiltration ≤28 | > 28 | 4.47 | 1.97, 10.15 | <0.001 | 3.51 | 1.49, 8.26 | 0.004 |
| | | No Metastasis | Metastasis | 2.29 | 0.14, 0.60 | 0.001 | 0.41 | 0.19, 0.89 | 0.023 |
| | | Prostate volume ≤45 | >45 | 2.19 | 1.27, 3.12 | 0.004 | - | - | - |
| | | PSA ≤50.7 | >50.7 | 2.46 | 0.94, 6.43 | 0.066 | - | - | - |
| | | Gleason ≤7 | >7 | 2.23 | 0.95, 5.2 | 0.065 | - | - | - |
| | | Age ≤ 68.9 | >68.9 | 1.11 | 0.54, 2.27 | 0.769 | - | - | - |

low-risk (T1c-T2a, GS <7 and PSA ≤10 ng/mL) intermediate-risk (T1b-T2b, GS 7, or PSA 11–20 ng/mL) high-risk (T2c–T3, GS >7, or PSA >20 ng/mL

Table 6. Predictors for Prostate Cancer Overall 5-Year Survival in SEA

| Theme | Categories | Prognostic factor | Comparison | 5y Survival rate | Multivariate | | |
|---|---|---|---|---|---|---|---|
| | | | | | HR | 95% CI | P value |
| Age | Age group | ≥75 years | <75 | 77.8 | 8.49 | 1.16, 62.13 | 0.035 |
| Diagnosis-related | Method | TURP (incidental finding) | prostate biopsy | 74.8 | 6.81 | 2.28, 20.33 | 0.001 |
| Disease-related | Gleason score | Gleason score ≥8 | <8 | 77.8 | 2.36 | 1.18, 4.73 | 0.015 |
| | | Gleason≥8 | Gleason ≤6 | 95.5- 99.1 | 5.51 | 1.64, 18.5 | 0.006 |
| | Risk group | High-risk | Intermediate risk | 74.8 | 9.35 | 1.52, 57.60 | 0.016 |
| | Biochemical level | Expression of MMP-11 (cont) | | 72.7 | 0.448 | 0.21, 0.95 | 0.035 |
| | Metastasis status | Yes | No | 77.8 | 5.26 | 2.88, 9.63 | <0.001 |
| Treatment-related | | ART | No ART | 74.8 | 0.18 | 0.05, 0.58 | 0.005 |

(Afriansyah et al., 2019; Kim et al., 2021; Miyoshi et al., 2015).

PSA enables the detection of Pca during its treatable window and is a method for monitoring Pca treatment success and determining the extent of disease after diagnosis (Castelli et al., 2010). The usage of PSA as a prognostic factor was consistent with the findings of a study in Indonesia that linked higher PSA at the initial stage with poor prognosis (Afriansyah et al., 2019), while a study in China reported that PSA reduction of <90% of the pre-treatment PSA was associated with a higher OS rate (Kan et al., 2017). Utilising PSA as a predictor requires careful interpretation, as a Ugandan study reported a contradictory finding where the correlation between pre-treatment PSA and the 3-year OS rate was not statistically significant, as the ability of pre-treatment PSA to predict the OS rate in patients with Pca apparently differed in settings where Pca screening is uncommon (Yahaya et al., 2020).

The GS is a prognostic indicator that can accurately predict the OS of patients with Pca. The Ugandan study by Yahaya et al., (2020) revealed that patients in the GS ≥ 8 group had increased mortality risk compared to those with GS < 8. This finding was in line with a study that reported that increased GS was significantly associated with poorer outcomes (Yeong et al., 2017). Reliable prognostic indicators aid a person's understanding of their risk of developing Pca and provide clinicians more confidence to actively monitor low-risk Pca (Yeong et al., 2017). Further research involving long-term clinical results and larger, diversified geographic cohorts aid verification of the GS in predicting survival rates. Furthermore, an established grading system would enhance the classification of patients with Pca.

The disease stage (or extent and spread) at diagnosis is another main prognostic factor of Pca, where men diagnosed with localised disease have much higher survival outcomes than those with advanced disease. For example, the 5-year relative survival in Japan varied from near 100% for localised disease to 87% for regional disease (cancer that had grown beyond the original tumour to nearby lymph nodes or organs and tissues) and 40% in cases where cancer had spread to the distant lymph nodes or organs (Services, 2010). The result corresponded to the 5-year survival estimates from Singapore of 83%, 43%, and 23% for localised, regional, and distant Pca, respectively (Lim et al., 2009).

*Treatment-related Factors*

The role of adjuvant radiotherapy and better survival rate in Pca detected in this study were similar to that of other studies conducted worldwide. Trinh et al. (2019) examined the benefits of adjuvant radiotherapy and reported that patients who did not receive adjuvant

radiotherapy had the highest BCR risk. However, Bourbonne et al., (2022) demonstrated that adjuvant radiotherapy did not significantly affect the metastasis recurrence-free survival of Pca when compared to salvage radiotherapy. More studies are needed for a better understanding of the benefits of adjuvant radiotherapy in Pca management.

A study that explored the possible mechanism of the role of normal haemoglobin in better Pca prognosis (Dai et al., 2018) suggested that anaemia due to therapy modalities such as chemotherapy would cause hypoxia in the cancer cells. Although hypoxia can hinder the cell cycle, it causes the activation of oncogenes that lead to chemotherapy and radiotherapy resistance and eventually causes cancer progression.

*Limitations of the Study*

One study limitation is that there were few publications on the Pca survival rate and its prognostic factor in SEA. Of the 11 SEA countries, studies from only four countries were included in this study. The low publication number could have been due to a lack of studies or the fact that such studies were conducted in the local language and thus were not included in our study.

We recorded varying results for the predictors of the Pca survival rate due to differences in study context, population, diet, physical activity, and lifestyle, which may all affect the predictors of Pca survival. Furthermore, not all of the articles in this study reported the overall and median survival rates of Pca, limiting our ability to report and compare the results of SEA countries effectively. Therefore, a standardised reporting system for Pca survival is critical to obtain better comparison and understanding to ultimately reduce cancer morbidity and mortality.

Furthermore, only one article reported the 1-year survival rate while other studies did not report it due to a lack of data, which inevitably limited the exploration of possible mechanisms of Pca survival in SEA countries. Lastly, this review was restricted to localised Pca. Future studies could include the survival rate of patients with metastasis, which may make important contributions to clinical decision-making and treatment continuation.

In conclusion, survival rates of PCA in SEA countries are determined by prognostic factors, which can be divided into sociodemographic, disease-related and treatment-related factors. Survival rates are critical indicators for evaluating the effectiveness of cancer prevention and treatment initiatives. The prognostic factors identified in this study are consistent with those identified in other studies conducted worldwide. Further studies are needed to improve the understanding and treatment of Pca in the region SEA.

## Author Contribution Statement

Conceptualization, A.M.N, N.A.M., R.O., T.K.; methodology, N.A.M., R.O., T.K.; validation, A.M.N; Analysis, investigation, N.A.M., R.O., T.K.; writing-original draft preparation, N.A.M., R.O., T.K.; writing-review and editing, N.A.M., R.O., T.K., N.A., N.S.,; supervision, A.M.N., N.A., N.S. All authors have read and agreed to the published version of the manuscript.

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*Approval*

Not applicable.

*Study Registration*

The review protocol is registered with PROSPERO (CRD42022326521).

*Conflict of Interest*

The authors declare no conflict of interest.

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