โรคมะเร็งในผู้สูงอายุจังหวัดชลบุรี 2541-2560

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บทคัดย่อ

บทนำและวัตถุประสงค์: ประเทศไทยกำลังก้าวเข้าสู่สังคมผู้สูงอายุ อีกทั้งผู้สูงอายุก็เป็นความเสี่ยงต่อการเกิดโรคมะเร็ง การศึกษานี้บรรยายถึงระบาดวิทยาโรคมะเร็งเฉพาะประชากรสูงอายุ

วิธีการ: ผู้ป่วยมะเว็งรายใหม่อายุ 60 ปีขึ้นไปจากฐานข้อมูลทะเบียนมะเว็งระดับประชากรจังหวัดชลบุรีปี 2541-2560 ใน การศึกษานี้ ได้รับการตรวจทาน และบันทึกลงในโปรแกรม Canreg5 รวมทั้งสถานะการมีชีพและสาเหตุการตายซึ่งติดตามจนถึง สิ้นปี 2564 จากนั้นคำนวณค่าสถิติ จำนวน อัตราอุบัติการณ์มาตรฐานตามอายุ ค่ามัธยฐานการรอดชีวิต อัตราการรอดชีวิตสัมพัทธ์ แนวโน้มการเปลี่ยนแปลงของอุบัติการณ์คำนวณด้วย จอยพ้อยท์โมเดล

ผลการศึกษา: ผู้ป่วยมะเร็งสูงอายุรายใหม่ 18092 ราย คิดเป็น ร้อยละ 48.9 ของผู้ป่วยมะเร็งรายใหม่ทั้งหมด และ จำนวนผู้ป่วยมะเร็งสูงอายุในสิบปีหลังมากกว่าสิบปีแรก ร้อยละ 48 โดยในปี 2556-2560 พบอัตราอุบัติการณ์มาตรฐานตาม อายุโรคมะเร็ง 585.4 และ 474.6 ต่อหนึ่งแสนประชากรในผู้สูงอายุชายหญิง ตามลำดับ มะเร็งที่พบบ่อย คือ มะเร็งตับท่อน้ำดี มะเร็งลำไส้ใหญ่ลำไส้ตรง มะเร็งเต้านม มะเร็งปอด และมะเร็งต่อมลูกหมาก แนวโน้มของอัตราอุบัติการณ์มาตรฐานตามอายุโรค มะเร็งเพิ่มขึ้นในช่วงสิบปีแรก จากนั้นมีแนวโน้มลดลงจนถึงปีล่าสุด ค่าเฉลี่ยการเปลี่ยนแปลงของอุบัติการณ์รายปีในหญิงลดลง ร้อยละ 0.3 แต่ไม่มีการเปลี่ยนแปลงของอุบัติการณ์ในชาย ค่าเฉลี่ยการเปลี่ยนแปลงรายปีของอุบัติการณ์ในมะเร็งลำไส้ใหญ่ลำไส้ ตรงชายหญิง มะเร็งตับท่อน้ำดีชายหญิง มะเร็งเม็ดเลือดขาวชาย มะเร็งเต้านมหญิง มะเร็งไทรอยด์หญิง เพิ่มขึ้นร้อยละ 2-4 และมี ค่าลดลง ร้อยละ 2 ในมะเร็งกระเพาะปัสสาวะชายหญิง มะเร็งปอดชาย มะเร็งเม็ดเลือดขาวหญิง อัตรารอดชีวิตโรคมะเร็งที่ 5 ปี ร้อยละ 18.4 และ 29.8 และค่ามัธยฐานการรอดชีวิตโรคมะเร็งเป็น 0.7 และ 1.6 ปี ในผู้สูงอายุชายหญิง ตามลำดับ

สรุป: แนวโน้มจำนวนผู้ป่วยมะเร็งในผู้สูงอายุเพิ่มขึ้น โดยที่ค่าเฉลี่ยการเปลี่ยนแปลงของอุบัติการณ์รายปีไม่เปลี่ยนแปลง มะเร็งที่เป็นภาระสำคัญในสูงอายุจังหวัดชลบุรี คือมะเร็งลำไส้ใหญ่ลำไส้ตรง มะเร็งตับท่อน้ำดี และมะเร็งเต้านมหญิง ซึ่งจำเป็น ต้องมีมาตรฐานการดูแลรักษามะเร็งและการดูแลประคับประคองในผู้สูงอายุ

คำสำคัญ: มะเร็ง, ผู้สูงอายุ, อุบัติการณ์การเกิดโรค, แนวโน้มโรค, อัตราการรอดชีวิต

The Cancer Burden in Elderly, Chonburi, 1998-2017

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Abstracts

Background: Thailand is becoming an aging society. Aging is a significant risk factor for developing cancer. the study describes the epidemiology in cancer focusing on the elderly population.

Materials and Methods: New cancer cases, aged 60 years and older, derived from Chonburi population-based cancer registry during 1998 – 2017 were included in this study. All data were verified and entered into the Canreg5 software. The registered cases were followed up to assess vital status and cause of death until the end of 2021. The number, age-standardized incidence rates (ASR) median survival and relative survival rate were calculated. The joinpoint regression model was used to analysis the change in trend.

Received: Oct 25, 2022 Revised: Apr 28, 2023 Accepted: Dec 29, 2023

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Results: There were 18,092 new elderly cancer cases, accounted for 48.9% of all cancer patients and new elderly cancer cases increased 48% from the first to second decades. During 2013-2017, the ASR for all cancer sites were 585.4 and 474.6 per 100,000 in male and female, respectively. The leading cancers were liver & biliary tract, colorectum, breast, lung and prostate. Trend of ASR for cancer had increased in first decade and then declined in the latest years. The average annual percent change (AAPC) for twenty years was 0% and -0.3% among male and female, respectively. The incidence rate increased for cancer of colorectum and liver & biliary tract in both sexes, male leukemia, female breast cancer and female thyroid cancer, with annual increase 2-4 percent. The incidences were decrease about 2 percent per year for bladder cancer in both sexes, male lung cancer and female leukemia. The five-year relative survival rate was 18.4%, 29.8% and median survival was 0.7 years, 1.6 years for elderly male and female, respectively.

Conclusions: The number of elderly cancer cases have been increasing, while no change of AAPC. The cancer of colorectum, liver & biliary tract and female breast is the burden in Chonburi. Treatment modalities and palliative care for elderly population are needed.

Keywords: cancer, elderly, incidence rate, trend, survival rate

Introduction

Aging is a biological process in all living being. Nowadays, the developments in therapeutic medicine, and improvements in the quality of life, that affect to increase older adults. The proportion of elderly will increase from 18.8 percent in 2020 to 31.4 percent by 2040.1 It is well known that aging is the significant risk factor for developing cancer.² As people get older, more will suffer from cancer. Since Thailand is moving toward an aging society, the number of cancer cases diagnosed in elderly patients is expected to increase. So, we need to know the cancer informatics in elderly age group, this study presents cancer incidence, incidence trends and survival rate. Findings should help us understand and better prepare for the increasing number of elderly cancer cases that our health care system will face in the near future.

Materials and Methods

This retrospective descriptive study is based on all new cancer case aged 60 years and older who diagnosed between January 1st, 1998 and December 31st, 2017 from the Chonburi Population based-cancer registry. All cancer case were classified according to the International Classification of Disease for Oncology third edition,³ while multiple primaries were handled using the International Agency for Research on Cancer International Association of Cancer Registries (IARC-IACR) rules. ⁴ The data were checked and entered into CanReg5 software. Mortality data from death certificates mentioning cancer as the cause of death were matched against the registered case in databases file. The registered cases were followed up to assess vital status and cause of death until the end of 2021.

Population denominators used to calculate rates by sex, age group were estimated from the Chonburi population censuses surveyed in 2000 and 2010,5,6 and in 2005, 2015 was estimated and reported by the Office of the National Economic and Social Development Board. The age-standardized incidence rate (ASR) per 100,000 population was calculated by the direct method using age-specific rate for 5-year age interval and weights based on the age distribution of the standard world population. The average annual percent change in rates for trend analysis was quantified using the Joinpoint Regression Software. The survival time was defined as the time elapsed between diagnosis and death. To allow for death due to other disease, survival is expressed as relative rate. The relative survival rate is the ratio of the observed survival rate to the expected survival rate for a population similar to the cancer patients with respect to age, sex, race, and year of observation.8 Incidence rate take into account all primary cancer, including those diagnosed solely by death certificate or autopsy, but survival rate exclude case diagnosed by death certificate or autopsy.

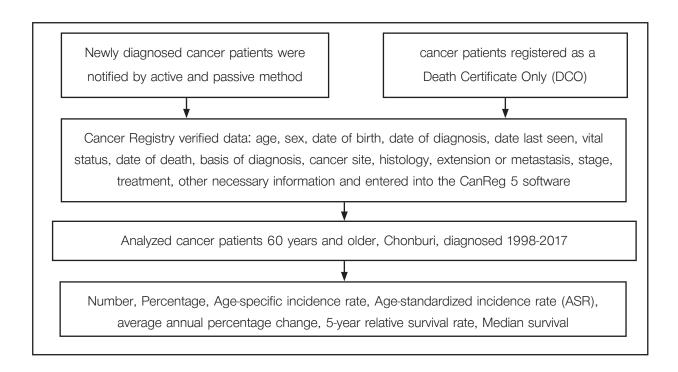


Figure 1 Study flow diagram and statistical analysis Results

Over the 20-year study period, a total of 18,092 new cancer cases were diagnosed in elderly (>60 years) accounted for 48.9% of all aged cancer cases in Chonburi. From the first to the second decade the mean age was comparable; 70.8 and 71.1 years. From the first to

the second, new elderly cancer cases increased by 48% and the absolute number of patients increased in all age group.

Table 1 Gender and age distribution of cancer case diagnosed during first and second decade

	1998-2007		2008-2017			
Characteristic	Number	%	Number	%		
Gender						
Male	4,087	56.0	5,787	53.6		
Female	3,209 44.0		5,009	46.4		
Age (year)						
60-64	1,791	24.5	2,675	24.8		
65-69	1,795	24.6	2,418	22.4		
70-74	1,508	20.7	2,174	20.1		
75-79	1,152	15.8	1,790	16.6		
≥80	1,050	14.4	1,739	16.1		
Mean(SD)	70.8(7.6)		71.1(7.9)			

Table 2 Number, ASR and Percent of all age cases by cancer sites and gender, 2013-2017

		Male	e	Female			
Cancer sites	Number	ASR	Percent of all aged cases	Number	ASR	Percent of all aged cases	
All sites	2,825	585.4	68.9	2,563	474.6	54.4	
Oral cavity(lip+tongue+mouth)	82	20.1	51.6	62	8.7	62.0	
Salivary gland	12	1.8	50.0	4	0.1	19.0	
Pharynx, tonsil	118	35.8	44.5	17	2.8	36.2	
Esophagus	82	21.5	58.6	33	4.7	82.5	
Stomach	59	11.3	66.3	54	8	73.0	
Small intestine	11	3.3	73.3	6	1.3	75.0	
Colon	275	61.4	73.9	245	38.9	74.5	
Rectum	186	42.7	67.9	123	22.2	68.7	
Anus	4	0.8	44.4	8	0.7	72.7	
Liver, biliary tract	381	110.3	72.2	215	34.7	82.7	
Gall bladder	31	3.1	72.1	37	4.8	88.1	
Pancreas	38	9.2	73.1	49	6.9	83.1	
Nose, sinus, middle ear	7	1.7	63.6	5	0.7	100.0	
Larynx	71	18.3	78.0	6	1.3	75.0	
Lung and bronchus	526	97.1	75.3	265	50.0	74.0	
Bone and joints	4	0.1	28.6	4	0.7	22.2	
Skin (melanoma+other)	78	7.2	78.0	112	10.2	82.4	
Connective tissue	39	7.0	61.9	27	2.8	51.9	
Breast	8	2.4	47.1	450	110.2	35.9	
Vulvar	-	-	-	7	0.1	63.6	
Vagina	-	-	-	3	0.6	27.3	
Cervix	-	-	-	215	49.8	39.0	
Uterus	-	-	-	115	29.2	56.1	
Ovary	-	-	-	78	19.7	47.6	
Penis	11	0.3	55.0	-	-	-	
Prostate	284	33.5	90.4	-	-	-	
Testis	2	0.8	28.6	-	- 0.0	- EE G	
Kidney Renal pelvis	22 7	2.8 0.3	66.7 100.0	20 3	3.3 0.1	55.6 60.0	
Ureter	3	0.3	75.0	5	1.8	100.0	
Urinary bladder	127	20.4	84.1	42	4.9	87.5	
Eye	2	0.8	25.0	0	0	0.0	
Brain, nervous system	21	3.6	38.9	23	2.8	46.9	
Thyroid gland	20	4.3	50.0	51	10.9	29.5	
Adrenal gland	1	0	33.3	1	0.6	50.0	
Hodgkin disease	1	0	12.5	4	0.1	36.4	
Non-Hodgkin lymphoma	94	22.6	60.6	79	13.3	52.3	
Multiple myeloma	23	6.5	63.9	27	4.1	73.0	
Leukemia	72	14.5	53.7	40	6.1	44.9	
Myelodysplasia	21	3.6	67.7	26	1.1	83.9	
Other and unspecified	101	15.3	77.3	102	16.6	80.3	
omer and unspecificu	101	10.0	11.0	102	10.0		

ASR: Age-standardized incidence rates

Table 2 shows the ASR per 100,000 was 585.4 for males and 474.6 for females during 2013-2017. The five leading primary cancer sites in males were liver & biliary tract, colorectum, lung, prostate and non-Hodgkin lymphoma; with the leading site among females, cancer of the Breast, colorectum, lung, uterine cervix and liver & biliary tract. The five most common cancers accounted for 61.6%, 59% of all elderly cancer cases among males, females, respectively. For male, the ASRs were higher than female rates for every cancer site common to both sexes, except gallbladder, skin, bone, thyroid gland and breast. The liver & biliary tract cancer ASR for male was about threefold increase than females, fourfold for cancer of esophagus and urinary bladder, and 15 times higher for head & neck cancer (lip, tongue, mouth, salivary gland, pharynx, tonsil, larynx). Female thyroid cancer incidence rate was 2.5 times greater than male, and 1.5 times higher for cancer of gall bladder and skin.

The elderly male for prostate cancer accounted for 90% of all aged male cancer cases and 84% for urinary bladder cancer. About three quarters of all male patients with the cancer of small intestine, colorectum, liver & biliary tract, pancreas, larynx, lung and skin were 60 years and older. The elderly female for cancer of digestive organs, respiratory organs, skin and urinary bladder accounted for 70-85% of all aged female cancer cases and somewhat less than 50% for cancer of breast, uterine cervix, ovary, thyroid gland and leukemia.

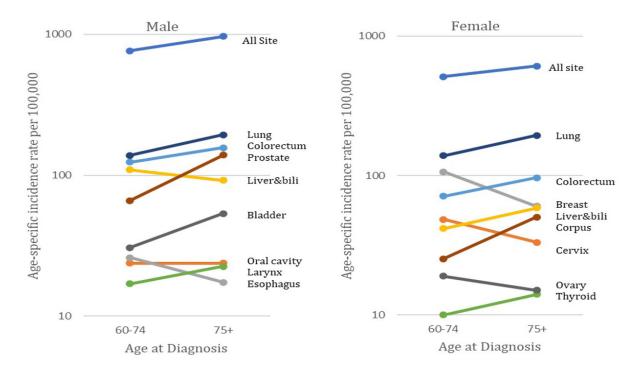


Figure 2 Age-specific incidence rate of the leading cancer sites by age-group and gender, 2013-2017

The figure 2 shows the difference in age-specific incidence rate by age for the most common cancer. For males, the incidence rate for ages 75 and over were, in general, 1.3 to 1.5 times those for the 60-74 age group, and twofold for prostate cancer. A notable exception were the cancer of oral cavity, esophagus and liver &

biliary tract, for which the ratios were 1, 0.7, 0.8, respectively. For female, the differences in incidence by age were similar to those for male, and twofold for uterine corpus cancer, with the exception for cancer of breast, uterine cervix and ovary, for which the age-incidence ratio were 0.6,0.7,0.8, respectively.

Table 3	Trend of A	SR and	AAPC of	cancer sites	hy gender	1008-2017
Table 3	Helia of A	ion aliu .	AAFU UI	Cancer Sites	by genuer,	1990-2017

					AAPC					AAPC
Cancer sites	1998-	2003-	2008-	2013-	(Male)	1998-	2003-	2008-	2013-	(Female)
	2002	2007	2012	2017	(%)	2002	2007	2012	2017	(%)
All sites	619.9	740.3	771.5	585.4	0	502.8	559.9	521.6	474.6	-0.3
Oral cavity	29.3	33.5	36.9	20.1	-1.4	9.0	11.9	10.2	8.7	+0.2
Esophagus	28.9	35.5	40.6	21.5	-0.7	6.5	5.4	8.5	4.7	-0.3
Colorectum	57.1	78.8	86.2	104.1	+4.5	44.3	47.1	72.2	61.1	+2.9
Liver&biliary	83.6	88.4	102.4	110.3	+2.0	32	22.1	34	34.7	+1.7
Lung	161.4	192.6	148.8	97.1	-2.5	55.7	75.6	56.3	50.0	-0.1
Skin	16.2	25.3	34.2	7.2	+0.8	9.4	16.4	12.7	10.2	+2.1
Female Breast	-	-	-	-	-	77.7	106.5	102.1	110.2	+2.7
Cervix	-	-	-	-	-	93.3	92.4	56.9	49.3	-3.5
Uterus	-	-	-	-	-	23.3	23.9	25.6	29.2	+1.6
Ovary	-	-	-	-	-	16.3	15.7	16.1	19.7	+1.4
Prostate	32.4	40.1	45.2	33.5	+0.7	-	-	-	-	-
Bladder	38.9	29.4	33.5	20.4	-3.3	6.8	5.9	5.9	4.9	-2.0
Thyroid	6.8	4.2	4.5	4.3	-2.4	8.6	10.4	16.1	10.9	+2.9
NHL	22.2	19.1	23.8	22.6	+0.4	15.6	25.2	15.6	13.3	+0.6
Leukemia	10.1	10.6	13.6	14.5	+2.7	9.4	8.6	8.2	6.1	-2.6

ASR:Age-standardized incidence rates; AAPC:average annual percent change; NHL:non-Hodgkin lymphoma

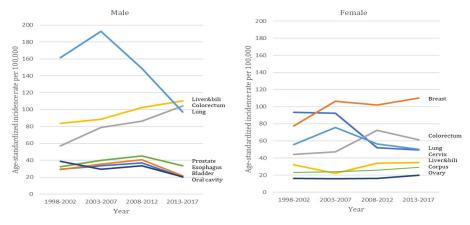


Figure 3 Time trends of the leading cancer sites in elderly by gender, 1998-2017

Trends over time in cancer incidence are indicated by comparing the average annual incidence rate from 1998-2002, 2003-2007, 2008-2012 with those for the latest years, 2012-2017 as showed in table 3 and figure 3. For males, the incidence rate increased for cancer of colorectum and liver & biliary tract with annual increase of 4.5% and 2.0%, respectively. There were decrease of about 2-3% per year for cancer of lung and bladder. For Females, there were

increase of about 2% per year or greater for cancer of the colorectum, thyroid and breast. There were striking decrease in incidence for cervical cancer (3.5% per year). For many of the sites common to both sexes, there was a consistent change over time in incidence. For lung cancer, the annual percent change of incidence for males decreased more rapidly than that observed for females. The incidence for leukemia is increase in male but decrease in female.

Table 4 Five-year relative survival rates and median survival of cancer sites by gender, 1998-2017

Cancer sites		Male		Female			
Cancer sites	Number	RS (%)	MS (year)	Number	RS (%)	MS (year)	
All sites	9,317	18.4	0.7	7,873	29.8	1.6	
Oral cavity	370	14.9	0.9	295	25.4	1.2	
Esophagus	340	2.4	0.3	94	8.5	0.3	
Colorectum	1,203	28.6	0.3	1,030	31.7	2.1	
Liver& biliary	1,031	4.8	0.2	562	6.6	0.2	
Lung	2,100	5.8	0.3	1,007	9.1	0.4	
Skin	497	36.1	2.9	436	58.5	6.2	
Female Breast	-	-	-	1,163	52.8	5.3	
Cervix	-	-	-	863	33.3	2.2	
Uterus	-	-	-	288	43.8	4.4	
Ovary	-	-	-	230	28.7	1.9	
Prostate	821	36.8	3.5	-	-	-	
Bladder	513	32.7	2.7	123	26.8	2.1	
Thyroid	61	37.7	1.1	191	52.9	0.5	
NHL	180	20.6	0.8	145	20.0	0.7	
Leukemia	206	9.7	0.2	156	10.3	0.2	

RS: 5-year relative survival rate; MS: median survival; NHL: non-Hodgkin Lymphoma

The length of survival after diagnosis of cancer is the impact of cancer on an elderly population. The 5-year relative survival rate for all cancer sites were 18.4% and 29.8% in male, female, respectively as showed in table 4. This overall female-to-male difference was due to difference in distribution in cancer site, because for many sites, female had a survival advantage. The relative survival rates for cancer of thyroid gland, oral cavity, esophagus and skin, in females was much higher than males. The relative survival rate in female bladder cancer was lower than male.

Dicussion

This study found that although 10% of local population is age 60 years or older in Chonburi, almost half of the cancer load occurs in this age group. The number of new cancer cases increased with a little change of the average annual percent change of ASR, that could be due to an expanded population size, demographic shift toward aging society in Thailand, better screening

program or diagnostic tools, and easier access to healthcare system from the policy of universal coverage since 2001. The late effects of a long history of smoking, obesity, dietary, lack of exercise, and modernization of lifestyle may be important contributing factors of cancer in elderly.

In the last five years, liver and biliary tract cancer was the first and the fifth leading cancer in elderly cancer cases among male and female, respectively. The main risk factors for liver cancer (hepatocellular carcinoma) are chronic infection with hepatitis B virus or hepatitis C virus, aflatoxin-contaminated foodstuffs, heavy alcohol intake, obesity, smoking and type 2 diabetes,9 while biliary tract cancer (cholangiocarcinoma) is associated with Opisthorchis viverrine infestation caused by consumption of uncooked fish.¹⁰ The trend in incidence rate has been increasing substantially despite the effort in promoting healthier and safer lifestyle. Therefore, ultrasound screening program for early diagnosis was established in 2016.¹¹ Surgery and chemotherapy(CMT) is the therapy for the disease however, most of the elderly patients may not be able to tolerate surgery and CMT, thus the survival for was quite bad.

Among the top five most common cancer, colorectal cancer (CRC) is becoming an increasing public health problem. The revised World Cancer Research Fund/American Institute for Cancer research report notes convincing evidence that processed meat, alcohol drinks and body fatness increase risk, whereas physical activity is protective for colon cancer only, but not rectal cancer.¹² In Japan, trend of CRC incidence, mortality in elderly was decline after promote the consumption of vegetable, cancer screening, removing premalignant polyps endoscopically or surgically.¹³ In Thailand, the fecal immunochemical test (FIT) has been as a tool for screening in 50-70 years old, at 5-year interval since 2018 and colonoscope in case of FIT positive results.¹⁴ The 5-year relative survival rate (RS) of CRC in this study was about 30%, while in developing country such as Germany, RS was about 60% in 55-74 years of age, during 1999-2003, because the elderly can tolerate with surgery and adjuvant CMT.¹⁵

Lung cancer ranks as the third leading cancer in both genders aged ≥60 years. Smoking has been consistently established as the main etiology factors for lung cancer and accounts for 80-90% of cases. As younger generations with lower smoking rates enter the older age group, lung cancer rates will likely continue to decline.¹³ The incidence rate of elderly lung cancer in Japan decreased in the past decade, similar to this study. The survival rate in lung cancer is poor, the treatment should be offered according to comorbidity and a geriatric assessment.

Majority (75%) of male patients diagnosed as prostate cancer are ≥65-years-old. The prostate-specific antigen (PSA) testing for early detection and diagnosis (1990) led the incidence rates rapidly increased in western countries.9 In the USA between the years 2006-2010 incidence of prostate cancer was decreased for elderly due to early PSA screening in age of 45-50.16 By the trend, the incidence rate of prostate cancer was slightly increase that may be associate with the PSA testing is currently not included in Thailand cancer screening program, although a clinical guideline exists. New surgical techniques for localized disease, antiandrogenic therapies and irradiation protocols could played an important role in survival improvement.¹³

Breast cancer is the most frequently malignancy among female in Chonburi similar in the vast majority of the countries. 9,17,18 The risked factors are related to menstruation (early age at menarche, later age at menopause), reproduction (nulliparity, late age at first birth, and fewer children), exogenous hormone intakes (oral contraception use and hormonal replacement therapy (HRT)), nutrition (alcohol intake), anthropometry (greater weight, weight gain during adult-hood and body fat distribution) and genetic factors (BRCA1, BRCA2); whereas breastfeeding and physical activity are known protective factors. 9,13 After publication of the Woman's Health Initiative trial linking postmenopausal hormone use to increased breast cancer risk, 19 the decline of HRT in postmenopausal woman and then the incidence rate is fall in the early 2000s in many western countries.9 However, the incidence rate of breast have been rising for most countries over the last decades, breast cancer screening and awareness are important. At present, Breast self-examination and clinical breast examination have national screening campaigns; together with voluntary mammographic examination in Thailand.¹⁴ Increased detection of early-stage cancer and improvement in treatment of advanced disease can result in improved breast cancer survival and reduction in mortality rate.¹³

Uterine cervical cancer ranks as the fourth most common in elderly female. The incidence rate for elderly appeared in decline similar in young adult age groups.^{18,20} There were various opportunistic screening campaigns, until an organized cervical screening program was established in 2002 with national coverage reaching 68% by 2009.²¹ In Thailand, Human papillomavirus (HPV) testing every 5 years in woman aged 30-60 years is currently cervical cancer screening program with treatment of precancerous lesions.¹⁴

The WHO recommends the vaccinations against HPV (2 doses) of girl aged 9-13 years that can reduce the long-term future burden of cervical cancer.9

The elderly cancer cases often had multiple chronic disease affecting their independence and making them more vulnerable to adverse outcomes. The clinical trial of older patients is limited, and data regarding the efficacy and safety of treatment regimens in elderly patients, mostly dose reduced, are lacking. International guidelines recommend that all elderly patients with cancer undergo geriatric assessment to better address all their needs to improve their functional status and possibly improve their survival.²²

In conclusion, by the trend, the cancer of colorectum, liver & biliary tract, female breast, female thyroid gland, corpus uteri, ovary and prostate may be the burden in Chonburi. In the future, an increase in cancer case caused by demographic change in Chonburi is expected, that will also lead to an increase in cancer-related health expenses. Cancer screening, treatment modalities and palliative care for elderly population are needed.

This Article does not contain any studies with human participants performed by the author and was approved by Ethic Committee of Chonburi Cancer Hospital.

No other potential conflicts of interest were reported.

Acknowledgements

The author feels grateful thanks to Cancer Registry Unit Staffs and Sinjai Santhong, statistician, for their help, assistance in providing data need to prepare and analyzed in this article.

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