RESEARCH ARTICLE

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Cost-Effectiveness Analysis of Ultrasound Surveillance for Cholangiocarcinoma in an Endemic Area of Thailand

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Abstract

Objective: This research aimed to analyze the cost-effectiveness of ultrasound surveillance for Cholangiocarcinoma (CCA) in a high-risk population residing in the northern region of Thailand and compare these results with the non-surveillance patients who presented with CCA. **Methods:** This was a retrospective descriptive study of two groups monitored and treated for CCA in the same institute, but differing as to whether ultrasound was included in the surveillance. The ultrasound surveillance group comprised those who participated in the cohort study of CCA at Chulabhorn Hospital from 2011 to 2017. Whereas, the non-ultrasound surveillance group consisted of patients treated for CCA at Chulabhorn Hospital from 2009 to 2015 (and not part of the first group). Historical data and societal perspectives were analyzed and interpreted using a decision tree model. The results of one-way sensitivity analyses of probability and cost parameters affecting the change in incremental cost-effectiveness ratio (ICER) were analyzed and presented using tornado diagrams. **Result:** The ultrasound surveillance group had the quality-adjusted life years gained (QALY gained) of 0.117 years, resulting in the incremental cost-effectiveness ratio (ICER) of 152,985 Thai Baht (THB) or equal to 4,222.6 US-dollars (USD) /QALY gained which is about when compared to the non-ultrasound surveillance group. Moreover, the ICER value was within the willingness to pay (WTP) calculated for Thailand of 4,416.2 USD (160,000 THB) /QALY gained. The probability of non-diagnostic CCA in non-ultrasound surveillance group and the cost of abdominal ultrasound were found to be major factors affecting the ICER. **Conclusion:** Ultrasound surveillance of CCA was cost-effective in Thailand. This information can be helpful for national policy planning in regard to Thai populations at high risk of CCA. Further study is recommended to assess cost-effectiveness in other areas with lower incidences of CCA.

Keywords: Cost-effectiveness analysis- ultrasound surveillance- cholangiocarcinoma

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Introduction

CCA is a common malignancy in northern and northeastern parts of Thailand. These two regions of Thailand are endemic because the population in both regions has a high incidence of liver fluke infestation due to consumption of raw foods such as fermented and pickled fish which are often contaminated with the parasite (Chaitheerakit, 2018). The main symptoms of CCA are fatigue, loss of appetite, weight loss, right upper quadrant pain, jaundice and, in some, ascites. CCA mortality in Thailand is estimated to be approximately 14,000 cases per year, extremely high compared with the other developed countries. Moreover, most patients carry a poor prognosis with a dismal survival rate since the majority of cases are in unresectable stage resulting in severe disability and decreases the ability to perform daily life.

Abdominal ultrasound surveillance for CCA is an imaging tool that can detect small cancerous lesions, and allow diagnosis and treatment early in disease progression. Ultrasound is generally harmless because there is no radiation, while having an accuracy of up to 84% in diagnosing CCA (Saengdidtha, 2015). It is an inexpensive surveillance tool for CCA when compared to other imaging methods and has proved to provide survival benefits.

From 2011-2017, the "Study and treatment project for CCA" was conducted by Chulabhorn Hospital in Ban Luang District, Nan Province, using abdominal ultrasound examination. The local population of Banluang District had the highest incidence of CCA recorded in the northern Thailand (2015). The risk factors in this population included the consumption of raw freshwater fish, agricultural chemical use, alcohol drinking, and smoking. Akkarachinorate and colleagues reported the data of this cohort on epidemiological study of CCA in

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a cohort of 4,225 adults (aged 30-60 years) who were at high risk for CCA, using ultrasound to diagnose CCA and identify premalignant lesions. The study found that CCA was the most common cancer in this population. The patients with CCA received surgical treatment where resulted in increased survival and longer disease-free periods (Akkarachinorate, 2018).

The following report of Banluang cohort have been published supporting the idea that ultrasound surveillance is helpful in the diagnosis of CCA. For example, Sungkasubun et al., (2016) compared upper abdominal ultrasound surveillance every 6 months with blood and stool test results. CCAs were found in patients with a mean age of 51.9 years and prevalence of 166 cases per 100,000 CCA at the premalignant stage was found in 11 subjects all of whom had good postoperative outcomes. Thus, ultrasound surveillance can help diagnose CCA at premalignant and early cancer stages (Sungkasubun et al., 2016). Also, in this long-term surveillance cohort, Siripongsakun et al, reported a survival benefit associated with using ultrasound for CCA surveillance (Siripongsakun et al., 2018), an increased median survival from 6.7 to 31.8 months.

The majority of the CCA patients are detected in the unresectable stage, resulting in limited treatment options including chemotherapy and procedure-related palliative treatments. These treatment options greatly decrease the quality of life (Wang et al., 2021). A study reported in 2015 evaluated the quality of life of CCA patients after one of four treatment interventions: surgery, endoscopic retrograde cholangiopancreatography (ERCP), percutaneous transhepatic biliary drainage (PTBD), and palliative care. They assessed quality of life in hepatic bile duct cancer patients before and after treatment. A Thai language version of the Health Quality of Life Questionnaire (EQ-5D) was used in evaluating 261 CCA patients likely to receive one of those treatments, with an assessment of 2-4 weeks before and again after treatment. The study found that the group with ERCP plus stent placement had significant improvement in quality of life. In the surgical and PTBD groups, there was also an improvement, but not statistically significant (Mairiang et al., 2015).

Currently, there are no published cost-effective analyses on CCA surveillance. However, there was such an analysis of hepatocellular carcinoma (HCC), a primary liver cancer, reported by Sangmala et al., (2014). Their cost-effectiveness and budgetary impact analyses of HCC in patients with chronic hepatitis B virus in Thailand used decision tree and Markov models to assess utility costs. They found that ultrasound surveillance [with or without alpha-fetoprotein (AFP) every half year] had an incremental cost-effectiveness ratio (ICER) gain of 3,279 USD (118,796 THB) /QALY gained. They also reported that willingness to pay (WTP) was 4,416 USD (160,000 THB)/QALY gained compared to a no surveillance program (Sangmala et al., 2014).

Thus, literature review revealed that ultrasound surveillance of HCC has a survival benefit and is cost-effective. However, there is little data available on the economics of CCA surveillance in Thailand. Therefore, this study aimed to determine the cost-effectiveness of ultrasound surveillance for CCA in a high-risk population residing in northern Thailand during 2011-2017. The results may provide valuable information on whether ultrasound surveillance of CCA is cost-effective, and thus should be expanded to other at risk populations in endemic areas of Thailand.

Materials and Methods

Study design

This was a retrospective descriptive study with data collected to compare two groups of CCA patients: current study group whose surveillance included abdominal US every 6 months, and a comparative group who were detected/diagnosed without ultrasound surveillance. This study has been approved by the Ethic Committee for Human Research of the Chulabhorn Research Institute and the inform consent was waived.

The ultrasound surveillance group comprised patients in the cohort of the “Study and treatment project for CCA” of Chulabhorn Hospital at Bangluang district, Nan province, during 2011-2017.(Siripongsakun et al., 2018) Whereas, the non-ultrasound surveillance group included patients with treatment of CCA at Chulabhorn Hospital during 2009-2015. (Siripongsakun et al., 2018) Both group of the patients received major investigations and treatment including Computorised Tomography (CT), Magnetic Resonance Imaging (MRI), Percuateneous Biliary Drainage (PTBD), Hepatic resection and Chemotherapy at Chulabhorn hospital.

Study population

The ultrasound surveillance group: CCA patients identified through US surveillance (Siripongsakun et al., 2019)

Inclusion criteria

- Population aged 30-60 years
- Living in Ban Luang District, Nan Province

Exclusion criteria

- Diagnosed with or undergoing treatment for another cancer
- Non compliant for US surveillance

The non-ultrasound surveillance group: CCA patients at Chulabhorn Hospital.

Inclusion criteria

- Patients diagnosed with CCA from Chulabhorn Hospital, 2009-2015
- Patients age between 30-60 years
- Follow-up and treatment for CCA at Chulabhorn Hospital

Exclusion criteria

- No pathological proved for CCA
- Diagnosed with or undergoing treatment for another cancer

Study procedures

Obtain historical data from "Study and treatment project for CCA" of Chulabhorn Hospital

Additional data sought from the Medical Records and Medical Statistics Department; images from Picture Archiving and Communication System (PACS) database of Chulabhorn Hospital

Analyze data for cost-effectiveness

Summarize and interpret results

Data collection

This study obtained data from two sources

Data from the Medical Records and Medical Statistics Department, Chulabhorn Hospital, during 2009-2015 for patients without ultrasound surveillance

Data on the cohort of "Study and treatment project for CCA" of Chulabhorn Hospital during 2011-2017

This study was based on ultrasound results from the upper abdomen of populations at high risk of CCA every 6 months in the northern area of Thailand to compare with the non-ultrasound surveillance group of patients with CCA in Chulabhorn Hospital.

Statistical analysis

Decision tree models were used to simulate the evaluation of outcomes and determine the consumption of resources according to the frequency of occurrence. The decision tree model paradigms were based on a cross-sectional observational period up to December 2020 in both the ultrasound surveillance group and the non-ultrasound surveillance group.

A cost-effectiveness analysis (CEA) was used to determine and compare cost-effectiveness in the two groups. CEA is a method of comparison between monetary costs and effectiveness. The results of all alternatives must be of the same type to measure the differences.

Sensitivity analysis (SA) considered changes in point estimates. The results from the base case analysis were divided into two methods: 1) deterministic sensitivity analysis (DSA), a one-way sensitivity analysis of changes in outcomes when one of the data values changed (this method was widely used and logical as presented with Tornado diagrams); 2) probabilistic sensitivity analysis (PSA), a sensitivity analysis of simultaneous data changes. (Chaikledkaew and Teerawattanon, 2014)

There were two large cohorts in Thailand which participated in surveillance program for CCA: the Cholangiocarcinoma Screening and Care Program (CASCAP) cohort (Khuntikeo et al., 2015) and Banluang district cohort of Chulabhorn hospital. Both programs used 6-month intervals of ultrasound surveillance as a standard protocol. Therefore, our analysis was based on 6-month surveillance intervals to calculate the cost according to CASCAP program. After detecting CCA, the patient received a standard treatment depending on the cancer stage, including hepatic resection or chemotherapy, palliative treatment, or a combination of treatments. After treatment, patients received utilities or satisfaction evaluation according to different health conditions. The utilities evaluation of this study came from a literature review.

The cost parameters used in the analysis of both groups were as follows. 1) Direct medical costs: all diagnostic radiological [Ultrasound (US), Computed Tomography (CT), Magnetic Resonance Imaging (MRI), Positron Emission Tomography/Computed Tomography (PET/CT)] and pathological examinations. The costs included in this study were based on only definite standard treatment (including surgery and chemotherapy) And not palliative intervention costs which are adjunct to the standard treatment [such as endoscopic retrograde cholangiopancreatography (ERCP) and percutaneous transhepatic biliary drainage (PTBD)] since these have no impact on survival 2) Direct non-medical costs: travel expenses (to/from hospitals in Nan and Bangkok), food, and surplus expenses. 3) Indirect costs: loss of income or time (Permsuwan, 2020).

Results

The surveillance cohort includes 4,225 population (2,306 females and 1,919 males) who received continuous surveillance of CCA (Siripongsakun et al., 2019).

There were 63 and 121 CCA in surveillance and non-surveillance CCA groups, respectively. The mean ages of those with and without ultrasound surveillance were 59.6 years and 53.6 years, respectively ($P < 0.001$). Gender proportion was not significantly different in the two groups ($P = 0.438$). The demographic data of both groups are shown in Table 1.

This study divided the treatment of CCA into four types: surgery, surgery combined with chemotherapy, chemotherapy, and supportive treatment. Two cohorts which differed as to having or not having ultrasound surveillance were compared, as shown in Figure 1 and Figure 2 respectively.

For a one-way sensitivity analysis, the study used variables to analyze event sensitivity and likelihood, as shown in Table 2. Results of a one-way sensitivity analysis were presented as Tornado diagrams (Figures 3 and 4). The variables were divided into two groups: 1) probability and utility parameters (Table 3), including the top 3 factors or variables affecting ICER, such as the probability of non-diagnostic CCA of non-ultrasound surveillance, probability of diagnostic CCA from imaging positive of non-ultrasound surveillance and probability of ultrasound screening positive of ultrasound surveillance (Figure 3) and 2) the cost parameter (Table 4) group had the top 3 factors or variables affecting ICER, namely the ultrasound upper abdomen and ultrasound liver, travel expenses, and chemotherapy IPD cost of non-ultrasound surveillance (Figure 4).

The results revealed that the program without ultrasound surveillance had costs of 136.3 USD (5,046 THB), Life-years (LY) of 0.8728 years, and Quality-adjusted life years (QALY) of 0.8722 years while the program with ultrasound surveillance had costs of 633.9 USD (22,965 THB), LY of 0.9934 years and QALY of 0.9894 years. The group which received ultrasound surveillance for CCA had increased QALY gained of 0.1172 years with an incremental cost-effectiveness ratio (ICER) of 4,222.6 USD (152,985 THB)/QALY gained

Table 1. Demographic Data of Non-Ultrasound Surveillance and Ultrasound Surveillance CCA Patients

	Non-US surveillance (N=121)	US surveillance (N=63)	Total (N=184)	P value
Age	59.60±0.899	53.56±0.769	57.53±0.680	< 0.001
Gender				0.438
Female	48 (39.7%)	27 (42.9%)	75 (40.8%)	
Male	73 (60.3%)	36 (57.1%)	109 (59.2%)	
Treatment				
Surgical resection	7 (5.8%)	32 (50.8%)	39 (21.2%)	0.006
Surgical resection + chemotherapy	13 (10.7%)	15 (23.8%)	28 (15.2%)	< 0.001
Chemotherapy	63 (52.1%)	9 (14.3%)	72 (39.1%)	< 0.001
Palliative care	38 (31.4%)	7 (11.1%)	45 (24.5%)	< 0.001
Death				< 0.001
No	5 (4.1%)	30 (47.6%)	35 (19.0%)	
Yes	116 (95.9%)	33 (52.4%)	149 (81.0%)	
Median survival in months	9.3	80.27	14.17	< 0.001

* CCA, Cholangiocarcinoma; US, ultrasound

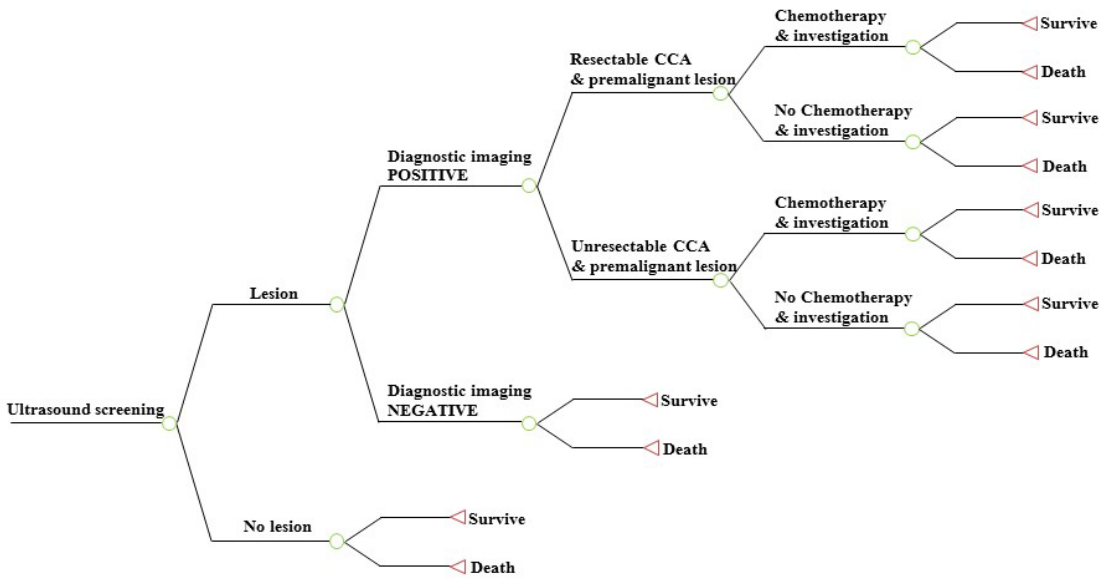

Figure 1. Decision Tree Model of Ultrasound Surveillance Cohort

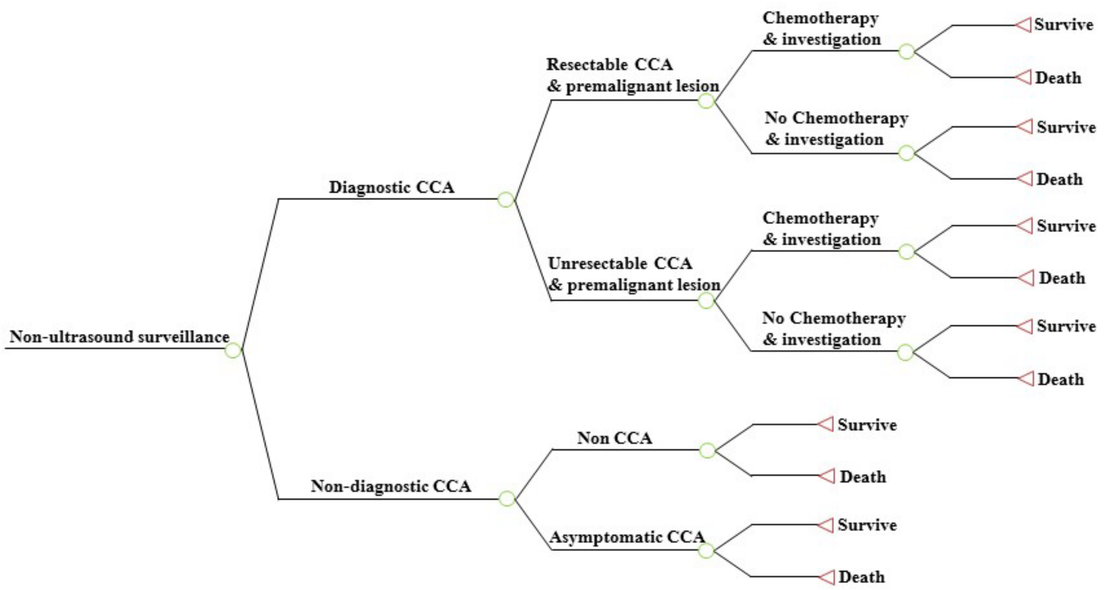

Figure 2. Decision Tree Model of Non-Ultrasound Surveillance Cohort

Table 2. Outcome Probability Parameter Description of Non-Surveillance and Surveillance Cohort

Outcome parameter description non-ultrasound surveillance	Distribution	Probabilistic	Mean	SE
Probability of diagnostic CCA from imaging positive	beta	0.0723	0.1000	0.0300
Probability of resectable CCA or premalignant lesion from imaging positive	beta	0.1847	0.1653	0.0338
Probability of resectable CCA or premalignant lesion needed chemotherapy	beta	0.6291	0.6500	0.1067
Probability of unresectable CCA or premalignant lesion needed chemotherapy	beta	0.5991	0.6238	0.0482
Probability of survive of resectable CCA with treatment	beta	0.4023	0.2308	0.1169
Probability of survive of resectable CCA without treatment	beta	0.3682	0.4286	0.1870
Probability of survive of unresectable CCA with treatment	beta	0.0426	0.0317	0.0221
Probability of non-diagnostic CCA	beta	0.9031	0.8850	0.0391
Probability of survive of non-diagnostic CCA	beta	1.0000	1.0000	0.0000
Outcome parameter description ultrasound surveillance	**Distribution**	**Probabilistic**	**Mean**	**SE**
Probability of ultrasound surveillance positive	beta	0.0496	0.0473	0.0033
Probability of diagnostic surveillance positive	beta	0.2955	0.3150	0.0328
Probability of resectable CCA or premalignant lesion from imaging positive	beta	0.6681	0.7460	0.0548
Probability of resectable CCA or premalignant lesion needed chemotherapy	beta	0.2640	0.3191	0.0680
Probability of unresectable CCA or premalignant lesion needed chemotherapy	beta	0.4370	0.5625	0.1240
Probability of survive of resectable CCA with treatment	beta	0.4133	0.2667	0.1142
Probability of survive of resectable CCA without treatment	beta	0.8899	0.9063	0.0515
Probability of survive of unresectable CCA without treatment	beta	0.3251	0.2857	0.1707

as compared with non-ultrasound surveillance group (Table 5).

Overall, ultrasound surveillance of CCA was found to be cost-effective since the ICER was within the threshold of the Willingness to pay (WTP) in Thailand, that is, less than the 4,416.2 USD (160,000 THB)/QALY gained.

The relationship between incremental costs and QALY were explored with a probabilistic sensitivity analysis shown in Figure 5. From the randomization of cost variables, the uncertainty of most variables led to higher costs in the ultrasound surveillance group. To some extent, the cost was equal or lower in the ultrasound surveillance group as shown in Figure 5. In this study, the ultrasound surveillance group yielded higher efficacy but had a higher cost when compared to those without ultrasound surveillance. Following the cost-effectiveness plane, it was found that 578 points were lower than Thailand's WTP threshold of 4,416.2 USD (160,000 THB)/QALY

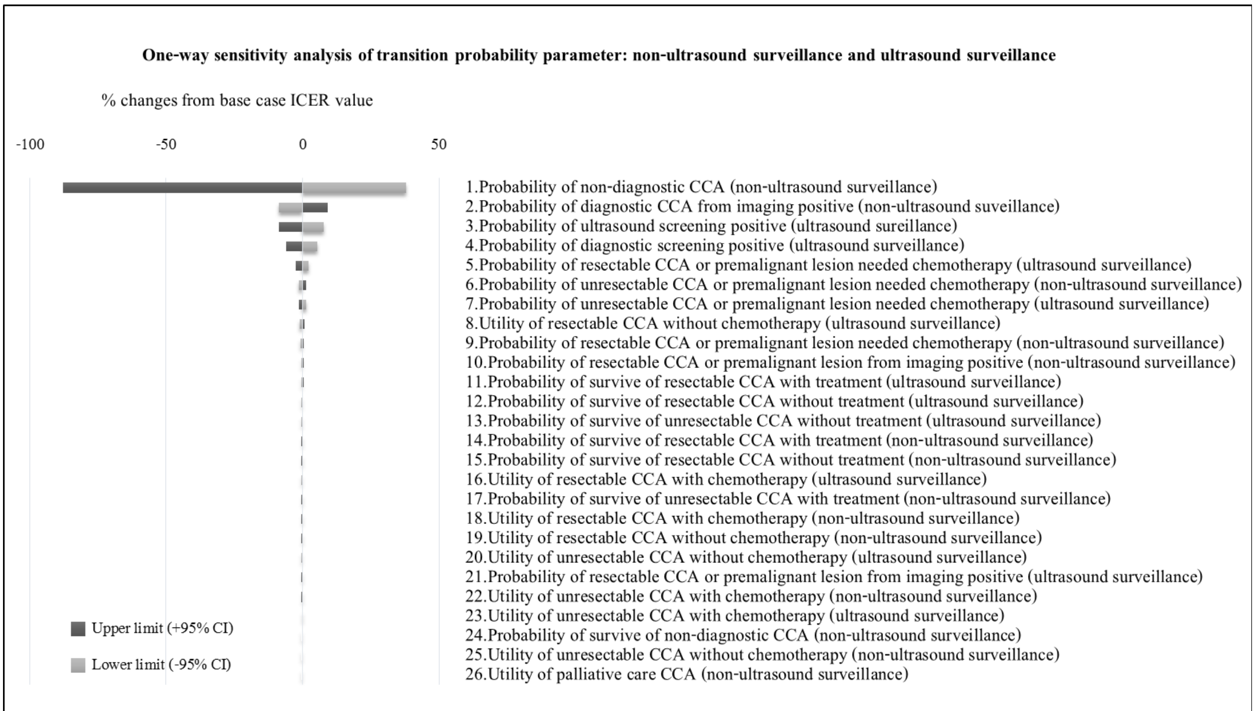

Figure 3. Deterministic Sensitivity Analysis Using Tornado Diagram, Representing Uncertainty of Probability and Utility Parameters.

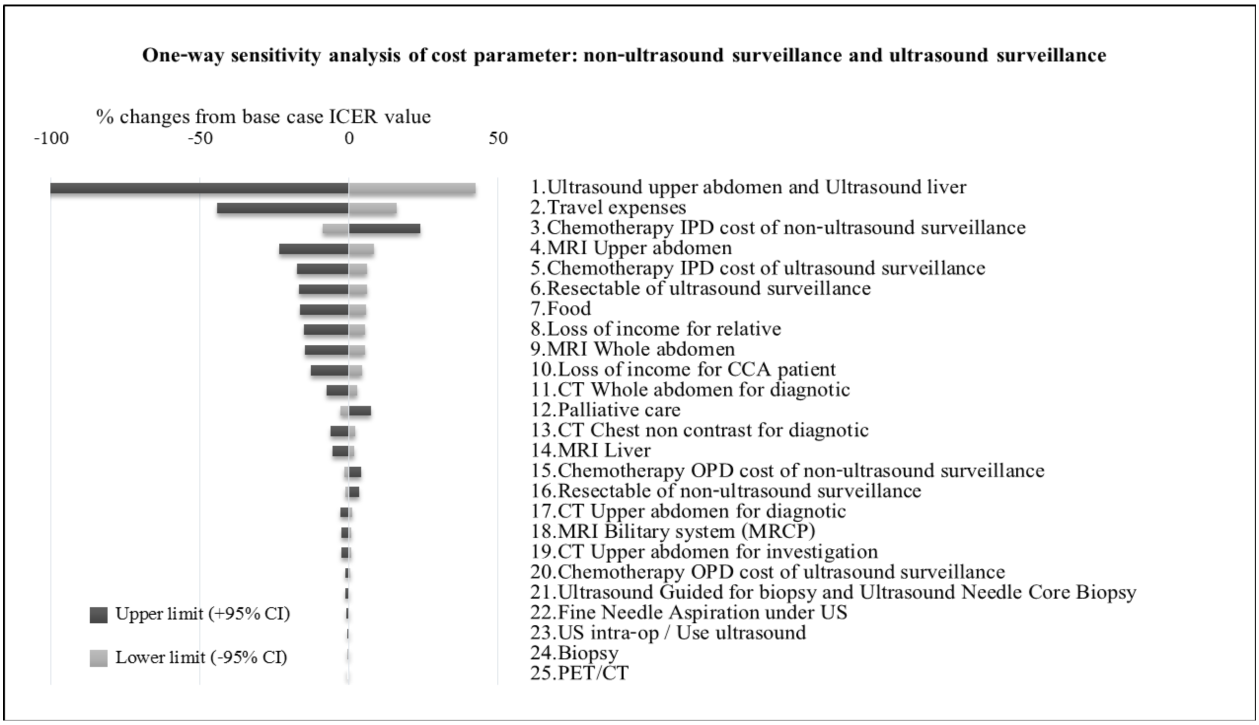

Figure 4. Deterministic Sensitivity Analysis Using Tornado Diagram, Representing Uncertainty of Cost Parameters.

Table 3. Treatment Utility Index Parameters of CCA

Utility index	Mean	Source
Utility of resectable CCA with chemotherapy	0.4500	Ref.[15, 16]
Utility of resectable CCA without chemotherapy	0.5300	Ref.[8]
Utility of unresectable CCA with chemotherapy	0.2600	Ref.[15, 16]
Utility of unresectable CCA without chemotherapy	0.4370	Ref.[17]
Utility of palliative care CCA	0.3540	Ref.[17]

* CCA, Cholangiocarcinoma

gained. Therefore, despite the uncertainty of variables, an incremental cost-effectiveness ratio of 57.8% was considered a cost-effective alternative.

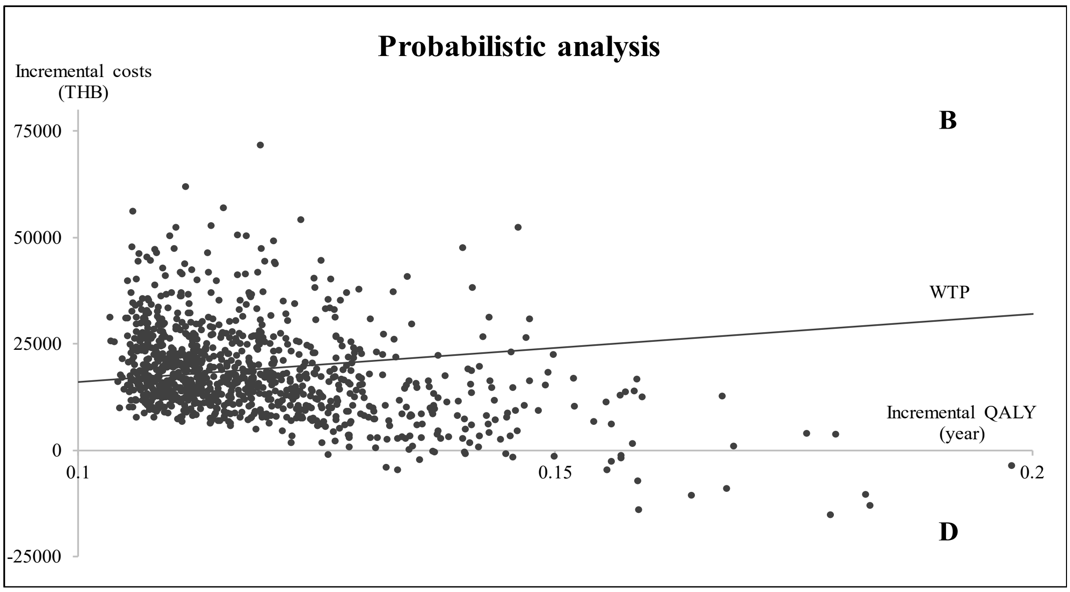

Figure 5. Probabilistic Sensitivity Analysis Achieving the Proportion of the QALY Benefit at a Cost Benefit Gained with a Defined WTP Threshold. QALY = Quality Adjusted Life Year, WTP = Willingness To Pay

Table 4. Medical and Non-Medical Costs Related to CCA from Thai Ministry of Health Prospective

Cost Parameter Description	Distribution	Value (USD)	Source
US upper abdomen and US liver	gamma	22.1 (800 THB)	GFPrice (CGD)
US Guided for biopsy and US Needle Core Biopsy"	gamma	63.5 (2300 THB)	GFPrice (CGD)
Fine Needle Aspiration under US	gamma	55.2 (2000 THB)	GFPrice (CGD)
US intraoperative / Use US	gamma	22.1 (800 THB)	GFPrice (CGD)
CT Upper abdomen for diagnostic	gamma	165.6 (6000 THB)	GFPrice (CGD)
CT Whole abdomen for diagnostic	gamma	276.0 (10000 THB)	GFPrice (CGD)
CT Chest non contrast for diagnostic	gamma	110.4 (4000 THB)	GFPrice (CGD)
CT Upper abdomen for investigation	gamma	165.6 (6000 THB)	GFPrice (CGD)
PET/CT	gamma	552.0 (20000 THB)	Chulabhorn hospital
MRI Upper abdomen	gamma	220.8 (8000 THB)	GFPrice (CGD)
MRI Liver	gamma	220.8 (8000 THB)	GFPrice (CGD)
MRI Bilitary system (MRCP)	gamma	110.4 (4000 THB)	GFPrice (CGD)
MRI Whole abdomen	gamma	441.6 (16000 THB)	GFPrice (CGD)
Resectable of non-US surveillance	gamma	2765.3 (100186 THB)	Chulabhorn DRG
Resectable of US surveillance	gamma	2518.8 (91256 THB)	Chulabhorn DRG
Biopsy	gamma	13.8 (500 THB)	GFPrice (CGD)
Chemotherapy OPD cost of non-US surveillance	gamma	90.6 (3281 THB)	Chulabhorn hospital
Chemotherapy OPD cost of US surveillance	gamma	119.9 (4344 THB)	Chulabhorn hospital
Chemotherapy IPD cost of non-US surveillance	gamma	834.2 (30224 THB)	Chulabhorn DRG
Chemotherapy IPD cost of US surveillance	gamma	836.5 (30306 THB)	Chulabhorn DRG
Palliative care	gamma	121.5 (4403 THB)	Ref.[17]
Travel expenses	gamma	3.9 (142 THB)	Ref.[18]
Food	gamma	1.5 (52 THB)	Ref.[18]
Loss of income for CCA patient	gamma	2.2 (80 THB)	Ref.[18]
Loss of income for relative	gamma	2.6 (95.5 THB)	Ref.[18]

CGD, The Comptroller General's Department; DRG, Diagnosis Related Group; OPD, Out-Patient Department and; IPD, In-Patient Department; THB, Thai Baht; US, ultrasound; USD, United-States Dollar; *Conversion rate of THB to USD at 36.23 THB to 1 USD, according to Bank of Thailand official exchange rate on 27 October 2023

Table 5. Incremental Cost-Effective Ratio (ICER) per Quality-adjust Life Year (QALY) Gain Calculation

	Non-ultrasound surveillance	Ultrasound surveillance
Costs	136.3 USD*, 5,046 THB	633.9 USD*, 22,965 THB
Life-years (LY)	0.8728	0.9934
Quality-adjusted life year (QALY)	0.8722	0.9894
Incremental costs	494.6 USD*, 17,919 THB	
Incremental LY	0.1206	
Incremental QALY	0.1172	
ICER per QALY gained	4,222.6 USD*, 152,985 THB	

THB, Thai baht; USD, United States dollar; *Conversion rate of THB to USD at 36.23 THB to 1 USD, according to Bank of Thailand official exchange rate on 27 October 2023

Discussion

Thailand is one of the most endemic countries for cholangiocarcinoma which has about 8.7% Opisthorchis Viverini infestation rate (Sripa et al., 2012) in the population of North and Northeastern region, accounting for about 6 million population at risk for CCA. Unfortunately, there is no sensitive serum tumor markers or laboratory test for CCA screening (Tshering et al., 2018). Therefore, abdominal ultrasound is currently the most effective method to detect early-stage cancer. Thai National Cancer Institute recommends CCA screening in the population who live in CCA endemic areas with the age starting from 40 years according to the age peak of the cancer (Chanwas et al., 2016). Our results showed that the probability parameter reflecting cost effectiveness is the probability of CCA in non-surveillance group which is related to the prevalence of CCA in the area; therefore, prevalence of CCA in the area should be the main consideration of the strategic planning.

The major challenge to implement a massive CCA surveillance in the endemic area is the work burden of ultrasound surveillance to cover 6 million population at risk in every 6 months. Manpower supporting the surveillance is one of the most challenging since the abdominal ultrasound scanning is mainly provided by radiologists and general physicians which number outweighs this huge workload. Therefore, a sonographer system, which allows other healthcare professionals to perform sonography, for screening is probably a good solution to expand the availability and accessibility of ultrasound examinations.

The cost-benefit of CCA surveillance is probably related to the detection of the CCA patients at the resectable stage. Data from Khantikeo and colleagues (Khuntikeo et al., 2015) reveal that surgery is the most effective treatment for CCA at present. If CCA is detected at an early stage and treated with surgery, the average treatment cost is within 2,760 USD (100,000 THB)/case and can be curative in up to 90% of patients. For advanced CCA, treatment and care will be complicated. Patients may lose their opportunity for curative treatment with 2-3 times higher costs for treatment. This study revealed that ultrasound surveillance can result in more QALY gained and ICER lower than the Thai WTP threshold. Therefore, we consider this to be an alternative worthy of support with government policy.

In the past, the cost-utility of surgical treatment for metastatic hepatic cholangiocarcinoma was analyzed. A comparative study of surgical treatment approaches and surgery combined with chemotherapy showed that surgical treatment was more cost-effective than chemotherapy in large intrahepatic CCA which is invasive into blood vessels (Cillo et al., 2015). For multiple intrahepatic CCA tumors, chemotherapy was preferable to surgery. This study was conducted based on the data of CCA patients, some with premalignant lesions, without determination of lesion size nor severity of CCA. The decision-making model for cost-effectiveness analysis in this study was designed to be similar to that of the cohort study at Chulabhorn Hospital and referred to data from literature reviews.

According to Chulabhorn Hospital experience with a reported study by Sungkasubun and colleagues, ultrasound screening could help diagnose CCA as well as premalignant lesions. Based on the results of this study, we concluded that the ultrasound surveillance was a cost-effective approach. Therefore, if patients receive screening and surveillance for CCA at an early stage, they will have more years of health with cheaper treatment costs and higher chances of receiving curative treatment.

The study had some limitations. The group with ultrasound surveillance included a population aged 30-60 years. However, the national guideline recommends that ultrasound surveillance of CCA should start at 40 years of age based on age of peak incidence of cancer. (Khuntikeo et al., 2015; Chanwas et al., 2016) Starting surveillance in a younger age may overestimate the cost of the surveillance group. However, this is a positive effect upon the surveillance group. If the surveillance started at 40 years of age, the ICER would probably be even less.

Further study is needed in the case of CCA patients who have disease recurrence or undergo resection since they will have greater costs. This study was conducted in a population at high risk of CCA, coming from the northern and northeastern regions of Thailand where CCA is the most common endemic cancer. Thus, in areas with a low risk of CCA and lower prevalence our approach will not be cost-effective. So, it would be advisable to consider alternative approaches.

In conclusion, ultrasound surveillance for CCA in an endemic area of Thailand was cost-effective. This information may be useful for considering a policy of such surveillance in the endemic areas of the country.

Author Contribution Statement

Study concept and design : Pavinee Laopachee, Surachate Siripongsakun, Pannapa Sangmala. Acquisition of data: Pavinee Laopachee, Surachate Siripongsakun, Phetcharaphon Chanree. Analysis and interpretation of data: Pavinee Laopachee, Surachate Siripongsakun, Pannapa Sangmala, Phetcharaphon Chanree. Drafting the manuscript: Pavinee Laopachee, Surachate Siripongsakun, Pantajaree Hiranrat. Critical revision of the manuscript: Surachate Siripongsakun, Pannapa Sangmala, Pantajaree Hiranrat, Songpon Srisittimongkon.

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Ethics, consent and permissions

The project was approved by the Ethics Committee for Human Research of Chulabhorn Research Institute (certificate no.102/2564). All individual participants' consents have been waived.

Data availability

The data that support the findings of this study are available from the corresponding author, S.S., surachate@yahoo.com upon reasonable request. The data are not publicly available due to privacy or ethical restrictions.

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