RESEARCH ARTICLE

Surveillance of Populations at Risk of Cholangiocarcinoma Development in Rural Communities of Thailand Using the Korat-CCA Verbal Screening Test

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Abstract

Cholangiocarcinoma (CCA) is a serious problem in Thailand, particularly in the northeastern region. Active surveillance in rural communities with an appropriate low-cost screening tool is required to facilitate early detection. Therefore, this study aimed to investigate the population at risk of CCA in Bua Yai district, Nakhon Ratchasima province, northeastern Thailand using the Korat-CCA verbal screening test (KCVST) during June to October 2015. Reliability of KCVST demonstrated a Cronbach alpha coefficient=0.75 Stepwise-multiple regression showed that alcohol consumption was important for CCA screened, followed by agriculture and pesticide use, under-cooked cyprinoid fish consumption, praziquantel use, naïve northeastern people, opisthorchiasis, family relatives with CCA, and cholangitis or cholecystitis or gallstones, respectively. Population at risk for CCA was classified to low risk (63.4%), moderate risk (33.7%), and high risk (1.3%) for CCA. When CCA was screened using ultrasonography, 4 of 32 high risk participants had an abnormal biliary tract with dilated bile ducts. This study indicates that KCVST is a potential useful tool which decrease the cost of large scale CCA screening.

Keywords: Cholangiocarcinoma - surveillance - Korat-CCA verbal screening test - Thailand

Introduction

Cholangiocarcinoma (CCA) is neoplasm that involves the epithelial cells of the bile duct. CCA is originated in the bile duct in which drained bile from the liver into the small intestine. It is also known to be one of the most common causes of cancer related to death in Thailand and it has been reported that Thailand is the highest incident of the world (Green et al., 1991; Sripa et al., 2007; Shin et al., 2010). It has an annual incidence rate of 1-2 cases per 100,000 in the Western world, but rates of CCA have been rising worldwide over the past several decades (Landis et al., 1998; Patel, 2002).

This disease is difficult to have early diagnosis, as most symptoms present late in the disease course. In addition, the specific anatomic position can cause periductal extension and result in a very low radical excision rate and a very poor prognosis. Furthermore, CCA is considered to be an incurable and rapidly lethal disease unless all the tumors can be fully resected. Three-year survival rates of 35% to 50% are achieved only in a subset of patients who have negative histological margins at the time of surgery (Akamatsu et al., 2011). Survival of CCA patients in northeastern Thailand after supportive treatment was reported and indicated that the stage of disease was an important prognosis factor affecting survival of CCA patients who had diagnosis in late stage. To encourage patients to see health personnel at early stage is very important (Thunyaharn et al., 2013). Palliative therapeutic approaches, consisting of percutaneous and endoscopic
biliary drainage, have usually been used for these patients because there is no effective chemotherapeutic treatment for this type of cancer.

Therefore, an active surveillance in the rural communities is needed and potential screening tool is useful for decreased a cost. This study aimed to investigate the population at risk for CCA in Bua Yai district, Nakhon Ratchasima province, Northeastern Thailand using Korat-CCA Verbal Screening Test (KCVST) during June to October 2015. Success data may useful for CCA screening in a large scale for CCA prevention and control.

**Materials and Methods**

A cross-sectional survey was a pilot project and conducted in Bua Yai district, Nakhon Ratchasima province, northeastern Thailand, between June and October 2015. Bua Yai is a district in the northern part of Nakhon Ratchasima, and neighboring districts are (from the north clockwise) Waeng Noi district of Khon Kaen province, Bua Lai, Sida, Non Daeng, Khong, Ban Lueam, and Kaeng Sanam Nang of Nakhon Ratchasima Province. Bua Yai district is subdivided into 10 sub-districts, and 121 villages. The district is subdivided into Bua Yai, Huai Yang, Sema Yai, Don Tanin, Nong Bua Sa-at, Non Thonglang, Kut Chk, Dan Chang, Khun Thong, and Nong Chaeng Yai. The town of Bua Yai covers part of the sub-district. This district is coverage areas 271.6 km² (104.9 sq mi), and has 84,133 populations.

Populations at risk for CCA, were screened by using mini-verbal screening questionnaire name; Korat-CCA Verbal Screening Test: KCVST, contained general information (name, gender, age, address, and health catchment area), and the question (yes/no choices) of the history with (1) opisthorchiasis; definitive diagnosed by medical doctor or related officers, (2) cholangitis or cholecystitis or gallstones; definitive diagnosed by medical doctor or related officers, (3) relative family with CCA, (4) under-cooked cyprinoid fish consumption, (5) praziquantel used, (6) alcohol consumption, (7) agriculture and pesticide used, and (8) naïve northeastern people. All questions were literature reviewed and designed from that possible risk data and strongly associated to CCA, according Table 1. Eight questions using yes/no choices.

The KCVST was tested before the study, we had tryout in 8 sub-districts of Bua Yai district, Nakhon Ratchasima (5 questionnaires/sub-district), Cronbach alpha coefficient was 0.75.

Before the study, permission and collaboration of the head of the public health center and/or head of the sub-district were obtained. Multi-stage sampling was used to select the participants in this studied. Briefly, total of 66,163 targets from 194,152 populations was selected with criteria of aged ≥30 years old. The interviewers received an interview training of 1 d. The study was conducted at weekends to increase the possibility of meeting people at home. The staff comprised 10 interview teams each.

### Table 1. Designing of Korat-CCA Verbal Screening Test: KCVST, Based on Possible Risk Associated to Cholangiocarcinoma

<table>
<thead>
<tr>
<th>Question</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>Opisthorchiasis</td>
<td>Viranuvatti and Mettiyawongse (1953); Bhamarapratavati and Viranuvatti (1966); Koompairocharana et al (1978); Sonakul et al (1978); Boonpucknavig et al (1986), cholangitis, cholecystitis, gallstones; Yeo et al (1990); Sripa et al (2014),</td>
</tr>
<tr>
<td>Relative family with cholangiocarcinoma</td>
<td>Manwong et al (2013); Miwa et al (2014)</td>
</tr>
<tr>
<td>Under-cooked cyprinoid fish consumption</td>
<td>Sithithaworn et al (1997); Liu et al (2010); Songserm et al. (2012)</td>
</tr>
<tr>
<td>Alcohol consumption</td>
<td>Songserm et al (2012; 2014)</td>
</tr>
<tr>
<td>Naïve northeastern people with the bases of habitat in the risk area and has a relative genetic risk to CCA</td>
<td>Subrungruanga et al (2013); Miwa et al (2014); Songserm et al (2014)</td>
</tr>
</tbody>
</table>

### Table 2. Numbers of Answers Classified by Item of the Korat-CCA Verbal Screening Test

<table>
<thead>
<tr>
<th>Histories</th>
<th>Participant (n)</th>
<th>Answer</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Opisthorchiasis; definitive diagnosed by medical doctor or related officers</td>
<td>11,719</td>
<td>423</td>
<td>3.61</td>
</tr>
<tr>
<td>Praziquantel used; given by medical doctor or related officers</td>
<td>11,719</td>
<td>793</td>
<td>6.77</td>
</tr>
<tr>
<td>Cholangitis or cholecystitis or gallstones</td>
<td>11,719</td>
<td>154</td>
<td>1.31</td>
</tr>
<tr>
<td>Under-cooked cyprinoid fish consumption</td>
<td>11,719</td>
<td>9,535</td>
<td>81.36</td>
</tr>
<tr>
<td>Alcohol consumption</td>
<td>11,719</td>
<td>5,488</td>
<td>46.83</td>
</tr>
<tr>
<td>Agriculture and pesticide used</td>
<td>11,719</td>
<td>6,648</td>
<td>56.73</td>
</tr>
<tr>
<td>Relative family with cholangiocarcinoma</td>
<td>11,719</td>
<td>272</td>
<td>2.32</td>
</tr>
<tr>
<td>Naïve northeastern people</td>
<td>11,719</td>
<td>11,221</td>
<td>95.75</td>
</tr>
</tbody>
</table>
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Results

A total of 11,719 participants was included in this study. The majorities of participants were female (56.5%), age group 51-60 years old (29.2%) and 41-50 years old (27.9%), Bua Yai sub-district (19.4%) and Non Thonglang subdistrict (12.2%). The majorities of number of answer were the question of naïve northeastern people and followed by under-cooked cyprinoid fish consumption, alcohol consumption, and agriculture and pesticide used (Table 2).

Item analysis of Korat-CCA verbal screening test, was weighting and found that alcohol consumption had an important weight for CCA screened (β=0.427, t=409.892, p=0001), and partial correlation = 0.967, followed by agriculture and pesticide used, under-cooked cyprinoid fish consumption, praziquantel used, naïve northeastern people, opisthorchiasis, relative family with CCA, and cholangitis or cholecystitis or gallstones, respectively (Table 3).

Population at risk for CCA was classified to risk group and found that the majorities of answer had a low risk (63.4%), followed by moderate risk (33.7%). While, the high risk for CCA was 1.32%, and no risk group was 1.56% (Table 4). Ultrasonography was used for CCA screened, purposive selected of 32 participants who had a high risk scores, and found that 4 patients had dilated bile ducts (Figure 1).

Discussion

Based on published data in PubMed about the risk factor of CCA, here we designed and experience with a CCA verbal screening test as a name of Korat CCA verbal screening test; KCVST. KCVST had a reliability with Cronbach alpha coefficient = 0.75 and found that alcohol consumption had an important weight for CCA screened (β=0.427, t=409.892, p=0001), and partial correlation = 0.967, followed by agriculture and pesticide used, under-cooked cyprinoid fish consumption, praziquantel used, naïve northeastern people, opisthorchiasis, relative family with CCA, and cholangitis or cholecystitis or gallstones, respectively (Table 3). Population at risk for CCA was classified to risk group and found that the majorities of answer had a low risk (63.4%), followed by moderate risk (33.7%). While, the high risk for CCA was 1.32%, and no risk group was 1.56% (Table 4). Ultrasonography was used for CCA screened, purposive selected of 32 participants who had a high risk scores, and found that 4 patients had dilated bile ducts (Figure 1).
respectively. Previously reported that the patients who had histories with alcohol consumption, had a strongly associated to CCA (Songserm et al., 2012; 2014). In addition, there are many recent publications reporting on the high nitrogen species in the water reservoirs (Konda and Pásztor, 2001; Rabalai, 2002; Pilati et al., 2009). This is confirmed for the correlation to the contaminated pesticide in the water reservoirs (Gardner et al., 1998; Gammon et al., 2005). While, patient with opisthorchiasis (Viranuvatti and Mettiyawongse (1953); Bhamarapravati and Viranuvatti (1966); Kooompairochana et al. (1978); Sonakul et al. (1978); Boonpucknavig et al. (1986), cholangitis, cholecystitis, gallstones; Yeo et al (1990); Sripa et al. (2014) and repeated praziquantel used are strongly associated to CCA Mairiang et al. (1992); Mairiang et al. (1993); Kamsa-Ard et al. (2015).

A total of 11,719 participants, the majorities of number of answer were the question of naïve northeastern people and followed by under-cooked cyprinoid fish consumption, alcohol consumption, and agriculture and pesticide used. Population at risk for CCA was classified to risk group and found that the majorities of answer had a low risk (63.42%), followed by moderate risk (33.69%). While, the high risk for CCA was 1.32%, and no risk group was 1.56%. Ultrasonograpy was used for CCA screened, purposive selected of 32 participants who had a high risk scores, and found that 4 patients had a dilated bile ducts. This figure indicates that using of KCVST for screening CCA, is very simplified for answer and fastest analyzed by themselves. Participant took a time for answer approximately 2 minute/person and calculated their risk in the test.

In conclusion, KCVST is simplify, fast screen, decrease of cost, this tool may useful for CCA screening in a large scale for CCA prevention and control. Further study, Opisthorchis viverrini detection and CCA investigate with ultrasound in each risk group, are need to compare and analyze the correlation.

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