Histopathology Analysis of Benign Colorectal Diseases and Colorectal Cancer in Hatyai Hospital, Songkhla, Thailand

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Abstract

**Background:** Colorectal cancer (CRC) is a major cause of morbidity and mortality in the western world and also ranks as the fifth-leading malignancy and death in Thailand. This study aimed to provide a present outlook of colorectal diseases among Thai patients with special emphasis on CRC in Hatyai, Songkhla, southern Thailand. **Materials and Methods:** This retrospective study covered ten year data of CRC, benign colorectal tumors and non-colorectal tumors from the Department of Pathology in Hatyai Hospital, Songkhla, Thailand, between years 2003-2012. Incidence rates based on age, gender, ten year incidence trends, and distribution of histopathological characteristics of patients were calculated and demonstrated. **Results:** Out of 730 biopsies, 100 cases were benign colorectal tumors, 336 were CRC and 294 were non-colorectal tumors. Colorectal tumors (both benign and CRC) (60.1%) were more common than non-colorectal tumors (39.9%). CRC (77.1%) were more common than benign colorectal tumors (32.9%). Colorectal tumors were mainly found in patients aged over sixty whereas non-colorectal and benign colorectal tumors were found in those under sixty (P=0.01). Among CRC, adenocarcinoma contributed about 97.3% of all cases with well differentiated tumors being the most frequent (56.9%). Both benign colorectal tumors and CRC were more commonly found in males (63%) than females (37%). The incidence trend of CRC demonstrated increase from 2003-2012. **Conclusions:** The incidence of CRC increased in Hatyai from 2003-2012. CRC tends to be more common in people older than sixty, thus, screening programs, cost-effective analysis of treatment modalities, and treatment protocols for the elderly should be examined. Proper implementation of preventive measures such as changing lifestyle factors might enhance control of colorectal disease.

Keywords: Colorectal cancer - benign colorectal disease - non-colorectal tumors - Hatyai, Thailand

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Introduction

Colorectal cancer (CRC) is the third most common cancer in men (663,000 cases, 10.0% of the total) and the second in women (571,000 cases, 9.4% of the total) worldwide. Almost 60% of the cases occur in developed regions of the world. About 608,000 deaths from CRC account for 8% of all cancer deaths and is fourth of the most common cause of death from cancer and also ranks as the fifth-leading malignancy and death in Thailand (Ferlay et al., 2008).

Factors associated with increasing risk of CRC include energy imbalance; a lower risk was found among moderately active and active participants with a BMI less than 25 g/m² compared to inactive participants with a BMI more than 30 g/m² (Friedenreich et al., 2006). The key signalling pathways linking weight and CRC is the PI3K/Akt/mTOR pathway which is a target of many of the obesity-associated factors and regulates cell proliferation and survival (Vucenik and Stains, 2012). A previous study reported that increasing length of activity was associated with a decreased risk of CRC among women who were moderately or vigorously active (Wolin et al., 2007) and the protection effect was found in persons who participated in vigorous activity over the past 20 years (Slattery et al., 2004). Nutritional factors such as consumption of red meat, fresh red meat and processed meat were associated with risk of CRC (Larsson et al., 2006; Chan et al., 2011). Low folate intake, high alcohol intake, and cigarette smoking were also found to be risk factors for CRC (Giovannucci et al., 2002; Tsong et al., 2007). Moreover, CRC can arise from mucosal colonic polyps (Tsai and Lu, 1995) which comprise the two most common histologic types, hyperplastic and adenomatous polyps (Bussey, 1975). The risk of CRC can increase with high numbers of adenomatous polyps and hyperplastic polyps (Cappell and Forde, 1989). However, polyps and adenomas prevalence can be protected by exercising one hour per week (Sanchez et al., 2012). The risk factor which can not be controlled is the genetic factor. Previous reports suggested that first-degree relatives of patients with newly diagnosed adenomas who are fifty years of age or younger...
at diagnosis, are at increased risk for CRC (Ahsan et al., 1998). Siblings and parents of patients with adenomatous polyps are at increased risk for CRC, particularly when the adenoma is diagnosed before the age of sixty (Zarchy and Ershoff, 1996). Changes in nucleotide sequence, single nucleotide polymorphism (SNP), such as insulin growth factor 1 (IGF1) could have an impact on developing CRC and is a high risk for colorectal polyps (Feik et al., 2010).

More recent studies have shown another risk factor, H. pylori infection, confers an increased risk for colonic neoplasms (Sonnenberg et al., 2012). For race factors, the Chinese had a higher incidence of CRC than Malaysian but developed colorectal cancer at a later age in Brunei Darussalam (Chong et al., 2009). Young Cambodians (age less than 40) were 29.8% affected by CRC and ranked the second highest proportion in the world (Hav et al., 2011).

Songkhla is a southern province in Thailand. In contrast to most other provinces in Thailand, the capital Songkhla is not the largest city in the province but the much newer city of Hatyai, is considerably larger has twice the population of Songkhla. This study was conducted at Hatyai Hospital. Ten year data of CRC, benign colorectal tumor and non-colorectal tumor from the Department of Pathology at Hatyai Hospital, Songkhla Province, Thailand between 2003 and 2012 is presented. Incidence rates based on age, gender, ten year incidence trend and distribution of histopathological characteristics of patients are calculated and demonstrated.

Materials and Methods

This is a retrospective study based on the records obtained from the Department of Pathology of Hatyai Hospital between 2003 and 2012. The study was approved by the local ethics committee. All patients’ data were collected on the basis of age, gender, site and sub-site lesion of diseases, medical diagnosis and histopathological diagnosis (in case of CRC) such as type of cancer (adenocarcinoma, mucinous carcinoma, lymphoma, signet ring cell, diffuse type, adenocarcinoma in situ and lymphoma). Colonic duplication, colon perforation, colonic ectopia, imperforated anus, diverticulitis, intussusceptions with ischemia, ruptured colon, ruptured appendicitis and other diseases which were not tumor of the colon and rectum were defined as a “non-colorectal tumor”. Adenomatous polyp, juvenile polyp, villoglandular polyp, inflammatory polyp, hyperplastic polyp, tubular polyps, carcinoid tumor, villous adenoma were defined as a “benign colorectal tumor”. Incidence rate based on age at diagnosis, gender, site and sub-site of lesion, distribution of histological variants as well as year wise trend were determined. For age at diagnosis, the patients’ age were divided into two groups; patients younger than 60 years and those older than 60. Tumor grades were separated into three categories; well differentiated, moderately differentiated, and poorly differentiated tumor. Descriptive statistics and statistical analysis was performed using SPSS ver. 11.5 (SPSS Inc., Chicago, IL, USA) with P value less than 0.05 being different in each group.

Results

During 2003-2012, a total of 4,523 biopsies were submitted to the department of Pathology, Hatyai Hospital for histopathological examination. Of these 4,523 biopsies, 730 cases were colon and rectal site which can be divided into three groups; 438 cases were colorectal tumors (benign colorectal tumor=100 cases, CRC=338 cases) and 292 cases were non-colorectal tumors. Age distribution of benign colorectal tumors peaked at 51-60 years old but age distribution of CRC peaked at 61-70 years old. Non-colorectal tumors peaked at 61-70 years old as for CRC (Figure 1). Colorectal tumors occur in patient’s age older than sixty whereas non-colorectal tumor occur in patient’s age under sixty (P<0.01, OR=1.64, 95% CI=1.21-2.22, Table 1). CRC characteristics occur in patient’s age older than sixty whereas benign colorectal tumor occur in patients’ age under sixty (P=0.01, OR=1.81, 95% CI=1.14-2.85, Table 2). The trend in incidence of CRC, benign colorectal tumors and non-colorectal tumors increased over the past 10 years. Benign colorectal tumors increased from 2003-2009 becoming steady from 2009-2012. CRC increased from 2004-2005, became steady from 2005-2009, and decreased slightly in 2009-2010 before becoming steady from 2010-2012. Non-colorectal tumors increased from 2003-2005, were probably steady from 2005-2009, and decreased slightly in 2009-2010 and then steadied from 2010-2012 (Figure 2).

![Image](https://via.placeholder.com/150)

**Figure 1. Age Distribution of Colorectal Disease**

| Table 1. Incidence of Colorectal Tumor and Non-Colorectal Tumor in Difference Age Groups |
|-----------------------------------------------|-----------------------------------------------|------------------------------|-----------------|-----------------|
| Colorectal diseases | Total | P-value | Odd’s ratio (95%CI) |
|------------------|-------|---------|---------------------|
| Age* | ≤60 | 217 | 179 | 396 | <0.01*** | 1.64 |
| >60 | 219 | 110 | 329 | (1.21-2.22) |
| Total | 436 | 289 | 725 |

*Five cases age were missing (CA 2, other disease 3), **p-value by Pearson Chi-Square

| Table 2. Incidence of Benign Colorectal Tumor and CRC in Difference Age Group |
|-----------------------------------------------|-----------------------------------------------|------------------------------|-----------------|-----------------|
| Tumor type | Benign tumor | Cancer | Total | P-value | Odd’s ratio (95%CI) |
|------------------|-----------------|-------|-------|---------|---------------------|
| Age* | ≤60 | 61 | 156 | 217 | 0.01** | 1.81 |
| >60 | 39 | 180 | 219 | (1.14-2.85) |
| Total | 100 | 336 | 436 |

*Two cases age were missing, **p-value by Pearson Chi-Square
Table 3. Site and Sub-site Lesion of Benign Colorectal Tumor and CRC

| Site of tumor lesion | Tumor type | Total |
|----------------------|------------|-------|
| Descending           | Benign     | 100   |
| Sigmoil colon        | 1 (1.0%)   | (100%)|
| Rectal               | 14 (14.0%) | (100%)|
| Colon (not specified)| 9 (9.0%)   | (100%)|
| Ascending and sigmoid| 1 (1.0%)   | (100%)|
| Rectal               | 0 (0%)     | (100%)|
| Sigmoid colon        | 2 (2.5%)   | (100%)|
| Transverse           | 2 (2.5%)   | (100%)|
| Caecum               | 0 (0%)     | (100%)|
| Total                | 100 (100%) | 100   |

Table 4. Type of CRC

| Type               | Male       | Female      | Total      |
|--------------------|------------|-------------|------------|
| Diffuse type       | 1 (0.5%)   | 0 (0%)      | 1 (0.3%)   |
| Siginet ring cell  | 1 (0.5%)   | 1 (0.7%)    | 2 (0.6%)   |
| Musinous           | 2 (1.1%)   | 1 (0.7%)    | 3 (0.9%)   |
| Adenocarcinoma in situ | 1 (0.5%) | 1 (0.7%) | 2 (0.6%) |
| Lymphoma           | 1 (0.5%)   | 0 (0.0%)    | 1 (0.3%)   |
| Adenocarcinoma     | 181 (96.8%)| 148 (98.0%) | 329 (97.3%)|
| Total              | 187 (100%) | 151 (100%)  | 338 (100%) |

Discussion

Colorectal biopsies submitted to the Department during the period of study increased which can be attributed to several reasons like an increased awareness of people, and increased accessibility to health facilities in these 10 years. In this study, the CRC trend increased in Hatyai district, Songkhla in line with a previous study’s expectation (Sriplung et al., 2006). A previous study reported CRC incidence in many provinces such as Songkhla, it is a leading cancer in men second only to lung cancer and third to cervix and breast cancers; in Prachuap Khiri Khan, it is the second most common cancer in men and third in women; in the north of Thailand such as Chiang Mai, CRC is the third most important cancer in men and fourth in woman; in Lampang, it is the fifth leading cancer in both sexes; in the capital of Thailand, Bangkok, CRC is the third most important cancer of both genders; in the east of Thailand, Rayong, CRC is the forth leading cancer in women (Khuhaprema and Srivatanakul, 2008); in the northeastern regions, the incidence of CRC is lower than other regions (Srriaphorn et al., 2007). The factor related to the increase of CRC in Hatay, Songkhla is still to be determined but for other provinces such in Bangkok; nitrite-treated meat can increase CRC risk, while dietary fibre can decrease risk. Moreover, there is an elevated risk in those who have a history of bowel polyps (Lothsoonthorn and Danvivat, 1995).
2002-2006 confirmed that meat consumption and family history are risk factors of CRC (Sriamporn et al., 2007).

Admission rates of CRC patients in Thailand showed an increase with age and the highest rate was observed in those sixty years and older (Chindaprasirt et al., 2012). This retrospective study, showed that if the patient’s age at diagnosis was more than sixty it they developed more colorectal tumor features compared to non-colorectal tumor phenotypes which might begin from changing of no dysplasia of the cell progressing to indefinite dysplasia, low-grade dysplasia, high-grade dysplasia and finally to invasive adenocarcinoma (Triantafillidis et al., 2009). In several epidemiological studies, many colorectal diseases were associated with CRC such as an ulcerative colitis (Ekbohm et al., 1990; Eaden et al., 2001; Withner et al., 2004), an inflammatory bowel disease (Sachar, 1994; IBD; Bernstein et al., 2001). Those diseases might be caused by an inflammation process which could promote colon tumorigenesis by various molecular mechanisms (Grivennikov, 2013). One review explained that CRC risk increases with longer duration of colitis, greater extent of colitis and the presence of inflammatory manifestations such as primary sclerosing cholangitis (Triantafillidis et al., 2009). Moreover, oxidative stress and oxidative cellular damage that occur in the process of inflammation were other important features that activate phagocytic activity of leukocytes resulting in enhanced production of pro-oxidant molecules which can pave the way for CRC (Roessner et al., 2008). Some cytokines and growth factors released during inflammation may influence the carcinogenesis process such as interleukin-6 and interleukin-23 (Atreya and Neurath, 2005; Fantini and Pallone, 2008). These ration might explain why the incidence of non-colorectal tumors increased along with the CRC incidence in the past 10 years.

Patient’s older than sixty years old developed more CRC features compared to benign colorectal tumors which is supported by several studies that CRC can arise from mucosal colonic polyps (Tsai and Lu, 1995) including two most common histological types, hyperplastic and adenomatous polyps (Bussey, 1976). A previous study reported that the risk of CRC markedly increases with increasing number of adenomatous and hyperplastic polyps (Cappell and Forde, 1989). More recently, there were evidences that serrated polyps characterized by a saw tooth appearance of the crypt epithelium resulting from failure of apoptosis and a build-up of aging colonocytes was the greatest risk factor for CRC (Hiraoka et al., 2010; Liang et al., 2012). Another finding suggested that colonocytes of ulcerative colitis patients showed premature shortening of telomeres, which might explain why older patients are at risk of CRC (Riques et al., 2008) and there was a study which supported that the oldest patients’ survival is associated long colonocyte telomeres (O’Sullivan et al., 2006).

In this study, the most common site lesion of CRC was in the colon which was commoner than rectal and recto-sigmoid site lesions similar to other studies where the highest incidence rate of CRC was found in the colon site (Ji et al., 1998; Liu et al., 2013). In terms of type of cancer, adenocarcinoma was the most common type of CRC found. It has a relatively better prognosis than other gastrointestinal malignancies such as a mucinous and signet-ring cell carcinoma types which have a poorer prognosis (Nozoe et al., 2000). Previous reports have indicated that when compared with non-mucinous adenocarcinoma, mucinous and signet-cell tumors present more peritoneal spread, infiltrating through all layers of the intestinal wall, more lymph node involvement, greater frequency of the advanced stage disease, a lower rate of curative resection, and lower overall 5-year survival rates (Kanemitsu et al., 2003; Longo et al., 2006). Well differentiated CRC was commoner in the colon site than moderately combined poorly differentiated CRC in contrast to “rectosigmoid and rectal” site in which moderately combined poorly differentiated CRC were commoner than well differentiated CRC. This could be supported by previous report where better survival of patients with lower tumor grades was found in the colon site compared to rectum (Ghabeljoo et al., 2011).

This is a single centre study and may have some limitations, but still provides a present outlook of CRC in this area, as there has been no previous report on CRC in the field of clinical and pathological characteristics. A screening program, cost-effective analysis of treatment modalities, and treatment protocol for the elderly (more than 60 years old) should be examined too.

In conclusions, the incidence trend of CRC increased from 2003-2012 and was commoner in people age older than sixty, thus screening programs, cost-effective analysis of treatment modalities, and treatment protocol for the elderly should be examined. This analysis can serve as a primary survey regarding colorectal spectrum for directing future population based or experimental studies as well as for planning prevention programs. Such specific prevention programs should aim to promote lifestyle modification and change in dietary habits such as increasing physical activity, reducing consumption of red meat, fresh red meat, limiting alcohol intake and cessation of cigarette smoking to promote better life for people.

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