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มะเร็งลำไส้ตรงในโรงพยาบาลศรีนครินทร์: 2543-2553, ทะเบียนมะเร็งโรงพยาบาล

โกสินทร์ วิระษร[1,5], ภัคณัณท์ อุสันเทียะ[2], กฤษฎา เปานาเรียง[3,5], วิยะดา ปัญจรัก[*4,5*]
[1]หน่วยมะเร็ง, ภาควิชาอายุรกรรม, คณะแพทยศาสตร์, มหาวิทยาลัยขอนแก่น
[2]หน่วยมะเร็ง, โรงพยาบาลศรีนครินทร์
[3]หน่วยศัลยกรรมทั่วไป, ภาควิชาศัลยศาสตร์, คณะแพทยศาสตร์, มหาวิทยาลัยขอนแก่น
[4]ภาควิชาสรีรวิทยา, คณะแพทยศาสตร์, มหาวิทยาลัยขอนแก่น
[5]มหาวิทยาลัยขอนแก่น, กลุ่มวิจัยมะเร็งแบบองค์รวม

Rectal Cancer in Srinagarind Hospital: 2000-2010, Hospital Based Population

Kosin Wirasorn[1,5], Pakanant Usantia[2], Krisada Paonariang[3,5], Wiyada Punjaruk*[4,5,*]
[1]Division of Oncology, Department of Medicine, Faculty of Medicine, Khon Kaen University
[2]Cancer Unit, Srinagarind Hospital
[3]Division of General Surgery, Department of Surgery, Faculty of Medicine, Khon Kaen University
[4]Department of Physiology, Faculty of Medicine, Khon Kaen University
[5]Khon Kaen University, Comprehensive Cancer Research Group (KKU CCRG)

หลักการและวัตถุประสงค์: โรงพยาบาลศรีนครินทร์เป็นศูนย์กลางการดูแลสุขภาพซึ่งประกอบด้วยแพทย์ผู้เชี่ยวชาญหลากหลายสาขารวมทั้งสาขาโรคมะเร็ง ดังนั้นผู้ป่วยโรคมะเร็งรวมทั้งมะเร็งลำไส้ตรงในภูมิภาคตะวันออกเฉียงเหนือถูกส่งตัวมารับการรักษาต่อเนื่องที่โรงพยาบาลนี้เพื่อให้ได้รับการรักษาที่เหมาะสม ดังนั้นสถานการณ์ของโรคมะเร็งที่พบในโรงพยาบาลศรีนครินทร์อาจสะท้อนปัญหาโรคมะเร็งในภูมิภาคดังกล่าว

วิธีการศึกษา: ทำการศึกษาในผู้ป่วยมะเร็งลำไส้ตรงรายใหม่ที่ได้ลงทะเบียนในโรงพยาบาลศรีนครินทร์ระหว่างวันที่ 1 มกราคม 2543 ถึงวันที่ 31 ธันวาคม 2553 ข้อมูลที่นำมาศึกษาจากระบบการลงทะเบียนผู้ป่วยมะเร็งของจังหวัดขอนแก่น ลักษณะทางคลินิกของผู้ป่วยและระยะเวลาการรอดชีวิตได้ถูกนำมาวิเคราะห์ทางสถิติ

ผลการศึกษา: จำนวนผู้ป่วยโรคมะเร็งลำไส้ตรงมีแนวโน้มเพิ่มมากขึ้น โดยเพิ่มมากขึ้นเป็น 2 เท่าเมื่อเปรียบเทียบกับจำนวนผู้ป่วยในช่วงต้นของการศึกษา จำนวนผู้ป่วยทั้งหมดที่ทำการศึกษา 1,031 ราย โดยมีสัดส่วนผู้ป่วยเพศชายต่อหญิงคือ 1.28:1 กลุ่มตัวอย่างมีค่ามัธยฐานของอายุเป็น 58 และ 57 ปี ในเพศชายและหญิงตามลำดับ ผู้ป่วยจำนวนมากอยู่ในระยะของโรคที่ลุกลาม โดยพบระยะที่ 4 เป็นร้อยละ

Background and Objective: Srinagarind hospital is a tertiary health care center comprising many subspecialty physicians expertising on malignancy, hence, most cancer cases including rectal caner in the Northeast (NE) are referred to this hospital for proper management. Therefore, the cancer situation occurring in Srinagarind Hospital might reflect the situation of cancer in NE as a whole.

Methods: All new rectal cancer cases registered in Srinagarind hospital between January 1st, 2000 and December 31st, 2010 were included in this study. Our data were obtained from the Khon Kaen Cancer Registry. The characteristics of patients and survival time were analysed.

Results: The trends of rectal cancer studied were obviously rising. The number of new rectal cancer cases at the end of study period was almost two folds higher than that at the beginning. There were 1,031 patients diagnosed as rectal cancer and the case number were almost comparable among males and females (1.28:1). The mean age at primary diagnosis was 58 years in

*Corresponding author: Wiyada Punjaruk, Department of Physiology, Faculty of Medicine, Khon Kaen University
E-mail : pwiyad@kku.ac.th

24.73 และระยะที่ 3 เป็นร้อยละ 15.23 อวัยวะที่พบการแพร่กระจายของโรคมะเร็งลำไส้ตรงมากที่สุด คือ ตับ (ร้อยละ 34.87) และปอด (ร้อยละ 15.97) ระยะเวลาการรอดชีวิตโดยรวมของผู้ป่วยทั้งหมดคือ 29.76 เดือน (ช่วงความเชื่อมั่นร้อยละ 95, 25.68, 33.84; p value < 0.05) นอกจากนี้ ระยะเวลาการรอดชีวิตโดยรวมของผู้ป่วยในระยะที่ 1 และ 2 ยังไม่ถึงค่ามัธยฐานในขณะที่ระยะที่ 3 และ 4 มีระยะเวลาการรอดชีวิตโดยรวมเป็น 73.92 และ 14.16 เดือน ตามลำดับ

สรุป: มะเร็งลำไส้ตรงมีแนวโน้มจำนวนเพิ่มขึ้นในช่วงที่ทำการศึกษา การพยากรณ์โรคและผลการรักษาโดยรวมไม่ดี เนื่องจากผู้ป่วยจำนวนมากอยู่ในระยะลุกลาม อย่างไรก็ตาม มะเร็งลำไส้ตรงมีพยากรณ์โรคที่ดีได้หากตรวจพบตั้งแต่ระยะเริ่มต้นและผู้ป่วยได้รับการรักษาที่เหมาะสม ดังนั้นการเฝ้าระวังอาการของมะเร็งลำไส้ตรงเป็นเรื่องที่ควรให้ความสำคัญ นอกจากนี้การตรวจคัดกรองมะเร็งลำไส้ตรงควรกระทำในระยะเริ่มต้น

คำสำคัญ: มะเร็งลำไส้ตรง, ระยะเวลาการรอดชีวิต, โรงพยาบาลศรีนครินทร์

males and 57 years in females. Patients commonly presented with advanced stages of disease, mostly stage IV (24.73%) and 15.23% was stage III. Liver was the most common site for distant metastasis of rectal cancer and the second common site was lungs. The average survival time of patients was 29.76 months (95% confidence interval (CI), 25.68-33.84; *p* value < 0.05). The median survival time of patients with stage I and II could not reach analytical point whereas the median survival time of stage III and IV were 73.92 and 14.16 months, respectively.

Conclusions: Rectal cancer trends had gradually increased during the period of study. Additionally, the prognosis and treatment outcome were poor. Most of patients were presented with advanced stages of disease. However, rectal cancer has fairly good prognosis if early stages can be detected and patients are treated earlier. Therefore, early awareness of rectal cancer symptom should be seriously concerned and the screening test for rectal cancer should be also performed earlier.

Key words: rectal cancer, survival time, Srinagarind hospital

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Introduction

Rectal cancer is the malignant tumor that locates approximately 12-15 cm above the anal verge. The most common cell type of rectal cancer is adenocarcinoma and the other cell types are neuroendocrine, gastrostromal tumor and lymphoma. The typical clinical presentations of rectal cancer are constipation, rectal bleeding, tenesmus and iron deficiency anemia resulting from chronic blood loss. The staging of disease is an important factor which significantly determines the prognosis and appropriate treatment for patients. American Joint Committee on Cancer (AJCC)/International Union Against Cancer (UICC) staging system classifies rectal cancer based on TNM staging system. Basically, this staging system requires all these 3 factors which are the invasion depth of rectal layers and the extension of tumor (T), regional lymph node involvement (N) and distant metastasis (M) for evaluation of stages of rectal cancer. These 3 factors (T, N and M) are used to determine the staging of disease. Four stages of rectal cancer are defined, stage I-IV. Rectal tumor invading only within the submucosal layer of rectum is classified as stage I. If tumor invades all layers of rectum throughout the perirectal tissues, this is defined as stage II. The stage III is patients presenting with regional lymph node metastasis. When rectal cancer distantly spreads to lung or liver, this is classified as stage IV. The optimal treatment for early stage of rectal cancer is surgery. However, it is difficult to perform complete radical resection of tumor mass because rectum situates in pelvic cavity which is a narrow cavity leading to inadequate approach for surgery. Consequently, high recurrent rate of rectal cancer is frequently occurred.

Therefore, the adjuvant treatment, concurrent chemotherapy (CCRT), has a significant role in preventing cancer recurrence in rectal cancer[1]. Rectal cancer patients receiving preoperative CCRT have an advantage on preserving anal sphincter function better than patients without this treatment [2]. Hence, preoperative CCRT is currently the standard treatment for patients with locally advanced disease. Postoperative chemotherapy has a significant role in patients with nodal metastasis. The principal treatment for metastatic rectal cancer is systemic treatment, which is either chemotherapy or combining with molecular targeted therapy.

Srinagarind hospital is a tertiary health care center covering patients in the Northeast (NE) region of Thailand. All advanced and complicated cancer cases from all over the region are referred to Srinagarind hospital. Therefore, this hospital provides health care service for approximately 22 million people within the NE. Malignant diseases are advanced and complicated conditions, which are required the tertiary health care center for appropriate treatment. Additionally, Srinagarind hospital comprises many subspecialty physicians expertising on malignancy, hence, most cancer cases in the NE are referred to Srinagarind hospital to receive the proper management. Therefore, various types of cancers including rectal cancer are coming to Srinagarind Hospital. Therefore, the cancer situation occurring in Srinagarind Hospital might reflect the situation of cancer in NE as a whole.

The aim of this study is to review the characteristics of rectal cancer patients who come to receive specific treatment in Srinagarind hospital during 2000-2010. Additionally, survival time of patients with different stages was analysed and presented in this study.

Materials and Methods

Case definition:

All new rectal cancer cases registered in Srinagarind Hospital between January 1st, 2000 and December 31st, 2010 were included in this study. This study is officially approved by the Khon Kaen University Ethics Committee for Human Research based on the Declaration of Helsinki and the ICH Good Clinical Practice Guidelines with HE571238 of reference number.

Sources of data:

Srinagarind hospital, Khon Kaen university (a thousand-bed university hospital), Khon Kaen, Thailand, is situated in the center of NE Thailand and accepts all referred cases from other health care centers in this region. Our data were obtained from the Khon Kaen Cancer Registry which has recorded data of all cancer cases treated in this hospital since 1987. All data were verified, checked for coding duplication and entered into the CANREG software (Version 4, available from http://www.iacr.com.fr/canreg4.htm). The data are normally collected from each cancer patient including age, sex, date of birth, date of diagnosis, method of diagnosis, primary site of cancer, extension or metastasis, histology of cancer, date of last visit, survival status at last follow-up and other necessary information. However, only relevant data were presented in this study.

Statistical analysis

The survival time was defined since the date of diagnosis to the date of last follow up or death from any causes. The data were analysed using Poisson regression to determine the trends of new case number throughout the studied period. Patients' characteristics were presented as mean and percentage. The cumulative survival rate is presented by the Kaplan Meier curve. Comparison of the median survival based on the stages of disease was analysed using Log-rank test. The statistical analyses were performed using statistical program R, version 3.1.1 (http://www.R-project.org/). A *p*-value less than 0.05 was considered statistical significance. The study was completed for analysis in June 2014.

Results

The trends of rectal cancer studied in Srinagarind hospital during 2000-2010 were obviously rising presented in Figure 1. The number of new rectal cancer cases at the end of study were almost 2 folds compared to the beginning of study (increased such number from 70 to 140 cases/year). Such number was detected at

slightly higher in male compared to female.

There were 1,031 patients diagnosed rectal cancer whereby the frequency of case number was almost comparable among male and female (1.28:1) as shown in Table 1. The mean age at primary diagnosis of patients diagnosed rectal cancer was 58 years in males and 57 years in females. The majority of rectal cancer patients (86%) provided pathological findings for the final diagnosis. Rectal cancer patients commonly presented with advanced stages of disease, mostly stage IV (24.73%) and 15.23% of rectal cancer patients presented with stage III. Liver was the most common site for distant metastasis of rectal cancer (34.87%) and the second common site for distant metastasis was lungs (15.97%). Surgery was the principal treatment for rectal cancer patients. Additionally, chemotherapy and radiotherapy were also combined with surgery.

Table 1 The demographic data of rectal cancer patient in Srinagarind Hospital during 2000-2010

Variables	Number (%)
Sex = male: female	580:451
	Male: 56.2%
	Female: 43.8%
Age (yr): Mean (SD)	Male: 58(12.1)
	Female: 57(12.6)
Basis of diagnosis	Clinical = 2.23%
	Endoscopy & Radiology = 5.63%
	Surgery without histology = 3.49%
	Specific biochem/Immuno test = 0.87%
	Cytology = 0.10%
	Histology of Metastasis = 1.16%
	Histology of primary = 86.52%
Staging	Stage 1 = 2.72%
	Stage 2 = 8.44%
	Stage 3 = 15.23%
	Stage 4 = 24.73%
	NA = 48.88%
Metastatic sites	Lymph nodes: 10.92%
	Bone: 2.52%
	Liver: 34.87%
	Lung or pleura: 15.97%
	Brain: 1.26%
	Peritoneum: 11.76%
	Others: 13.45%
	Multiple: 9.24%
Treatment	Surgery: 47.4%
	Chemotherapy: 30.2%
	Radiation: 22.4%

NA: Not available

This study revealed that the average survival time of rectal cancer patients was 29.76 months (95% confidence interval (CI), 25.68, 33.84; $p < 0.05$) as presented in Figure 2. The median survival time of rectal cancer patients with stage I, II could not be reached for analysing whereas the median survival time of stages III and IV rectal cancer patients were 73.92 and 14.16 months, respectively. The survival rate of patients with stages IV of disease was obviously worse compared to other stages. Additionally, the overall 1-, 3- and 5-year survival rates of rectal cancer were 75%, 43% and 32%, respectively.

Discussion

This study is the early pioneer rectal cancer study, which specifically revealed the descriptive data of rectal cancer in Srinagarind hospital. Rectal cancer presently has accelerating increasing trends and the number of new cases has gradually increased each year. The higher number of rectal cancer patients found in Srinagarind hospital might be because health care service system in official hospital is greatly improved and provide high standard of medical service. This improved system is comfortably available for all patients and they easily reach diagnoses and treatment. Additionally, the medical technologies relating to imaging system for early diagnosis of cancer are enormously improved and the health information is easily accessed. Therefore, patients have more awareness of health problems causing early coming for checking health. In addition, NE population acquires the Westernisation life style including consuming high fat diet and low fibers. The principal treatment for rectal cancer patients is surgery and Srinagarind hospital is one of the centre for radiation. Therefore, many cases of rectal cancer are referred to Srinagarind hospital resulting in high increasing number of new cases. This study showed that the proportion of rectal cancer patients in males are comparable with females. These data were contrast to

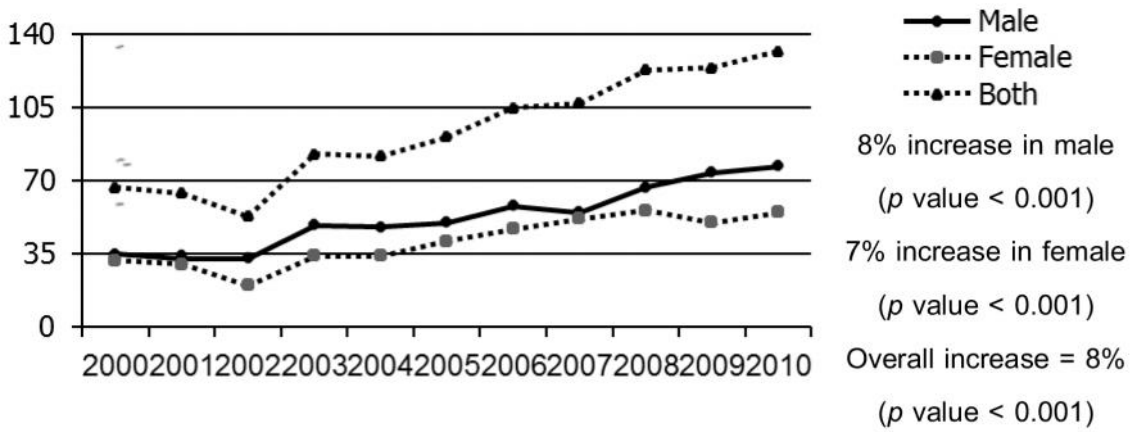

Figure 1 Trend of new rectal cancer cases during 2000-2010 in Srinagarind Hospital

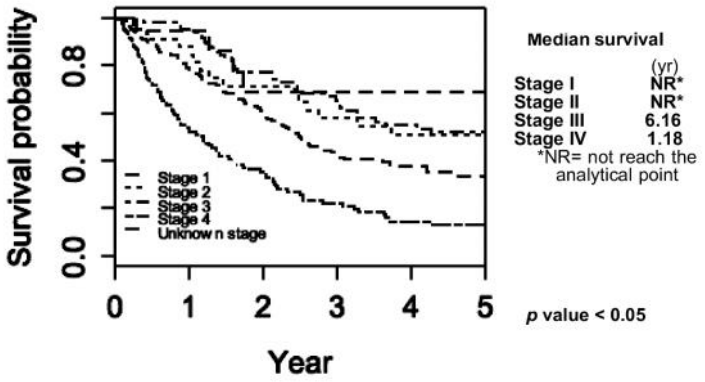

Figure 2 The overall survival rate of rectal cancer patients in Srinagarind Hospital during 2000-2010.

the previous studies showing that the incidence of rectal cancer in female was slightly higher than male[3]. Most of rectal cancer patients commonly presented with advanced stages of disease and distant metastasis because patients will normally seek for specific treatment only when worse symptoms are presented. Additionally, awareness of health promotion and prevention is still unconcerned in the majority of population. In addition, the cancer screening program of rectal cancer is still not available for local communities at this moment. Hence, the early stages of disease are hardly detected. It might also because Srinagarind hospital is the center for referral system in the NE, which is suitable for patients with advanced and complicated conditions that the primary and secondary health care center cannot effectively manage; therefore, most patients who come to treat at Srinagarind hospital, are usually presented with advanced stages of disease. The most common site for distant metastasis of rectal cancer was liver and lung was the second most common site for rectal cancer distant metastasis. Site of distant metastasis depends on the location of rectal cancer mass. If rectal cancer mass locating at the lower part of rectum, cancer is able to directly spread to lung. Conversely, the distant metastasis is presented in liver when the rectal cancer mass originates from the upper part of the rectum. This is consistent with the other previous studies[4,5].

The stages of rectal cancer are a significant prognostic factor, which can indicate survival time of patients[6]. Survival time of patients with stage I is longer than the others because the burden of tumor is smaller than the other stages and patients normally have better health status performance compared to advanced stages of disease. Additionally, these patients also have good tolerance to receive complete therapeutic options, which

is totally different from advanced stage or distant metastasis patients. These stages normally have cancer cells spreading into the blood circulation. Therefore, complete tumor resection is not effective enough to be the optimal treatment for these patients. Additionally, the survival rate analysed in this study is different from the results from other previous studies[4, 6-8]. This might be because most patients could not afford active chemotherapy agents such as oxaliplatin and irinotecan including molecular targeted therapy such as bevacizumab and cetuximab.

Limitation of study

This study is retrospective study; therefore, the registered cancer data might not be complete especially at the beginning of using cancer registration system. Additionally, essential data, which relate to the prognosis of rectal cancer patients, were not recorded such as the performance status of rectal cancer patients.

Conclusion

Rectal cancer trends had gradually increased during the period of study. Additionally, the prognosis and treatment outcome is poor. Most of patients presented with advanced stages of disease. However, rectal cancer has fairly good prognosis if early stages are able to be detected and patients are treated earlier. Therefore, early awareness of rectal cancer symptom should be seriously concerned and screening test for rectal cancer should be also performed earlier.

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