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ระยะเวลาการรอดชีวิตโดยรวมของมะเร็งไตในโรงพยาบาลศรีนครินทร์: 2000-2010, ทะเบียนมะเร็งโรงพยาบาล

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Overall Median Survival Time of Kidney Cancer in Srinagarind Hospital: 2000-2010, Hospital Based Population

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หลักการและวัตถุประสงค์: มะเร็งไตเป็นมะเร็งที่พบบ่อยของโรคมะเร็งทางเดินปัสสาวะ วัตถุประสงค์ของการศึกษานี้เพื่อศึกษาแนวโน้มและลักษณะทางคลินิกของผู้ป่วยมะเร็งไตในโรงพยาบาลศรีนครินทร์ในระหว่างปี ค.ศ. 2000-2010 และวิเคราะห์ระยะเวลาการรอดชีวิตของผู้ป่วยในระยะของโรคต่างๆ

วิธีการศึกษา: ทำการศึกษาในผู้ป่วยมะเร็งไตรายใหม่ที่ได้ลงทะเบียนในโรงพยาบาลศรีนครินทร์ระหว่างวันที่ 1 มกราคม 2000 ถึงวันที่ 31 ธันวาคม 2010 ข้อมูลที่ศึกษานำมาจากระบบการลงทะเบียนผู้ป่วยมะเร็งของจังหวัดขอนแก่น ลักษณะทางคลินิกของผู้ป่วยและระยะเวลาการรอดชีวิตได้ถูกนำมาวิเคราะห์ทางสถิติ

ผลการศึกษา: แนวโน้มมะเร็งไตในโรงพยาบาลศรีนครินทร์เพิ่มขึ้นร้อยละ 10 ทั้งในเพศชายและหญิง โดยในเพศชายพบเพิ่มขึ้นร้อยละ 11 ในขณะที่เพศหญิงพบเพิ่มขึ้นร้อยละ 7 สัดส่วนของผู้ป่วยรายใหม่ต่อจำนวนผู้ป่วยโรคมะเร็งทั้งหมด คือ 1: 169.26 (294: 49,763) หรือ ร้อยละ 0.59 กลุ่ม ตัวอย่างมีค่ามัธยฐานของอายุเป็น 48 ปีในเพศชาย และ 42 ปี ในเพศหญิง ผู้ป่วยส่วนมากอยู่ในระยะที่ 4 (ร้อยละ 43.2) ระยะเวลาการรอดชีวิตโดยรวมของมะเร็งไต คือ 20.28 เดือน (ช่วงความเชื่อมั่น ร้อยละ 95, 12.24, 44.76; $p < 0.05$) นอกจากนี้ ระยะเวลาการรอดชีวิตของผู้ป่วยในระยะที่ 1-3 ยังไม่ถึงค่ามัธยฐานของระยะเวลาการรอดชีวิตในขณะที่ระยะที่ 4 มีระยะเวลาการรอดชีวิตเพียง 9 เดือน

Background and objectives: Kidney cancer is the malignant disease, which is commonly found in the urinary tract system. The aim of this study is to review trends and the characteristics of kidney cancer patients in Srinagarind Hospital during 2000-2010 and analyse the survival time of patients with different stages of disease.

Material and Method: All new kidney 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 overall increment rate of kidney cancer was 10% in both genders. Additionally, male had 11% of such incremental number while 7% increase was found in female. The proportion of new kidney cancer cases: total cancer cases was 1: 169.26 (294: 49,763) or 0.59%. The median age of patient presenting with kidney cancer was 48 years in male and 42 years in female. Patients commonly presented with stage IV at the first diagnosis (43.2%). Overall median survival time of kidney cancer patients were 20.28 months (95%

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สรุป: แนวโน้มผู้ป่วยมะเร็งไตเพิ่มสูงขึ้น โดยพบผู้ป่วยรายใหม่เพศชายสูงกว่าเพศหญิง ระยะเวลาการรอดชีวิตโดยรวมต่ำเพราะผู้ป่วยมะเร็งไตส่วนมากอยู่ในระยะของโรคที่ลุกลาม (ระยะที่ 4) ดังนั้น หากมีการตระหนักและสามารถตรวจพบมะเร็งไตได้ตั้งแต่ระยะเริ่มต้น น่าจะส่งผลให้ผู้ป่วยมีพยากรณ์โรคที่ดีขึ้นทำให้ผู้ป่วยมีระยะเวลาการรอดชีวิตยาวมากขึ้น

คำสำคัญ: มะเร็งไต, ระยะเวลาการรอดชีวิต, โรงพยาบาลศรีนครินทร์

confidence interval (CI), 12.24, 44.76; p < 0.05). In addition, overall median survival time of patients with stage I-III did not reach the analytical point whereas patients with stage IV had 9 months of overall survival time.

Conclusion: The trends of kidney cancers are accelerating increasing. Higher frequency of new kidney cancer cases was presented in male compared to female. The overall survival time was still very short because kidney cancer patients usually presented with advanced stages (stage IV). Therefore, if kidney cancer is intensively concerned and the early stages of disease can be detected, patients might have better prognosis resulting in longer survival time.

Key words: kidney cancer, Survival time, Srinagarind Hospital

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Introduction

The second commonest cancer of the urinary tract system is kidney cancer following urinary bladder cancer, which is the most common cancer presented in the urinary tract system[1]. The number of new kidney cancer cases worldwide was 273,518[2]. The number of kidney cancer cases in Thailand is low and the number could not climb into top 15 commonest cancers presenting in Thai patients[3]. Common clinical presentations of the patients are flank pain and painless hematuria. The most common type of kidney cancer is renal cell carcinoma and the most common subtype of renal cell carcinoma is clear cell subtype[4]. American Joint Committee on Cancer (AJCC)/International Union Against Cancer (UICC) staging system classifies the stages of kidney cancer principally based on TNM staging system. Basically, this staging system evaluates the stages of kidney cancer based on these essential factors including the sizes and extension of tumor (T), regional lymph node involvement (N) and distant metastasis (M). These 3 important factors (T, N and M) are essentially used to determine the staging of disease. Kidney cancer is classified into 4 stages (stage I-IV) based on the TNM system. Stage I is defined as tumor mass less than 7 cm and confining within kidney. If tumor mass larger than 7 cm but still confining within kidney, this is classified as stage II. When tumor mass metastasises to major renal veins, perinephric tissues or adjacent regional lymph nodes but does not invade ipsilateral adrenal gland or Gerota's fascia, this stage is designated as stage III. Stage IV is described as tumor mass invading beyond Gerota's fascia or having distant metastasis to other organs[5]. The most common site of distant metastasis for kidney cancer is lungs.

The optimal treatment of choice for renal cancer essentially depends on the stages of disease[6]. Surgery is a principal therapeutic choice for renal cancer patients with ranging from the early stage of disease to the locally advanced disease. For patients with metastatic disease, systemic treatment is the most optimal therapeutic choice because the nature of kidney cancer cells is highly resistant to chemotherapeutic agents. Additionally, the new highly effective treatment

of choice for kidney cancer is molecular targeted therapy such as sunitinib and pazopanib, which are appropriate for good and intermediate risk patients whilst patients with poor risk should receive temsirolimus as a main treatment of choice[7]. Kidney cancer is poor prognosis cancer and the majority of patients usually present with advanced or metastatic stage of disease at the first diagnosis. The previous study revealed that the median survival time of kidney cancer was 10 months (95% confidence interval [CI], 9 to 11 months) studied in New York[8]. However, the progression-free survival and overall survival of kidney cancer studied in Japan were 9.1 and 27.2 months, respectively[9]. Therefore, poor prognosis with short survival time of kidney cancer patients is still problematic worldwide and patients usually present with advanced stages of disease.

Srinagarind hospital is a tertiary health care center covering patients in the Northeast (NE) Thailand, receiving referrals from all over the region and thereby serving a population of around 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 is a major tertiary health care center comprising many subspecialty physicians expertising on malignancy, hence, most cancer cases in the NE have been referred to Srinagarind hospital to receive the proper management.

The data of kidney cancer in NE region in aspects of overall survival time, the characteristics of patients and trends of kidney cancer were still not revealed. Therefore, the aim of this study is to review the trends and characteristics of kidney cancer patients in Srinagarind Hospital during 2000-2010 and analyse the survival time of patients with different stages of disease.

Materials and methods

Case definition:

All new kidney 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, vital status at last follow-up and other necessary information. However, only relevant data were presented in this study. The diagnosis of kidney cancer was determined on the clinical presentation (flank pain and painless hematuria) and radio imaging showing renal mass. The definite diagnosis was confirmed by pathological findings from renal biopsy. However, renal biopsy could not be performed in all kidney cancer patients because the clinical symptoms of patients were not stable to undergo the process of biopsy or relatives of patients refused to perform renal biopsy. The follow up period was various and it depended on clinical symptoms of patients and the judgement of doctors. Hence, the progression-free or recurrence-free survival could not be analysed 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 r egression 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 complete for analysis in June 2014.

Results

The trends of new kidney cancer case number are obviously increased during 2000-2010. The rate of overall increase was approximately 10% in both genders (Figure 1). Additionally, male had 11% of increased such number while 7% increase was found in female. Male had higher number of new kidney cancer cases compared to female during the study period. In 2006 and 2008, the number of new kidney cancer cases in male obviously had increasing number of new cases compared to the trends during a whole period of study whereas the lowest number of new kidney cancer female cases was found in 2006.

Table 1 Demographic data of kidney cancer patients in Srinagarind Hospital.

Variables	Number (%)
Sex = male: female	193:101
	Male: 65.6%
	Female: 34.4%
Age (yr): Mean (SD)	Male: 48.7 (±20.5)
	Female: 42.4(±25.7)
Basis of diagnosis	Endoscopy & Radiology = 21 (7.14%)
	Surgery without histology = 3 (1.02%)
	Histology of Metastasis = 9 (3.06%)
	Histology of primary = 261 (88.78%)
Staging	Stage 1 = 13 (4.42%)
	Stage 2 = 14 (4.76%)
	Stage 3 = 27 (9.18%)
	Stage 4 = 127 (43.2%)
	NA = 113 (38.44%)
Metastatic sites	Lymph nodes: 46 (15.6%)
	Bone: 35 (11.93%)
	Liver: 54 (18.35%)
	Lung or pleura: 54 (18.35%)
	Brain: 13 (4.59%)
	Peritoneum: 16 (5.5%)
	Others: 46 (15.6%)
	Multiple: 27 (10.09%)
Treatment	Surgery: 192 (65.4%)
	Chemotherapy: 52 (17.9%)
	Radiation: 49 (16.7%)

NA: Not available

The characteristics of patients are presented in Table 1. The proportion of new kidney cancer cases: total cancer cases was 1: 169.26 (294 of new kidney cancer cases: 49,763 of total cancer cases) or 0.59% of total cancer cases. Kidney cancer was presented at a higher frequency in male compared to female (1.91:1). The median of patient age presenting with kidney cancer was 48 years in male and 42 years in female. Most of kidney cancer patients (88.78%) had pathological findings for the final diagnosis. A small proportion of kidney cancer patients was confirmed the diagnosis based on endoscopy and radio imaging (7.14%), surgery without histology (1.02%) and histologic findings of metastatic mass (3.06%). Patients with kidney cancer commonly presented with the stage IV of disease at the first diagnosis (43.2%) and the stage I, II and III of disease were found 4.42%, 4.76% and 9.18%, respectively. However, the stages of disease were not defined in 38.44% of all kidney cancer patients. The commonest sites of distant metastasis were liver (18.35%) and lung or pleura (18.35%); additionally, lymph nodes (15.6%) were also frequently found as distant metastatic site for kidney cancer. Surgery is the principal treatment for kidney cancer patients (65.4%) and the rest of kidney cancer patients received chemotherapy (17.9%) and radiation (16.7%).

Overall median survival time of kidney cancer patients treated in Srinagarind Hospital was 20.28 month (95% confidence interval (CI), 12.24, 44.76; $p < 0.05$) (Figure 2). In addition, overall median survival time of patients with stage I-III did not reached the analytical point whereas patients with stage IV had 9 months of overall median survival time. More than half of kidney cancer patients with stage I-III were still alive within 5 years after the diagnosis whilst almost 80% of stage IV kidney cancer patients were death within 1 years after the diagnosis.

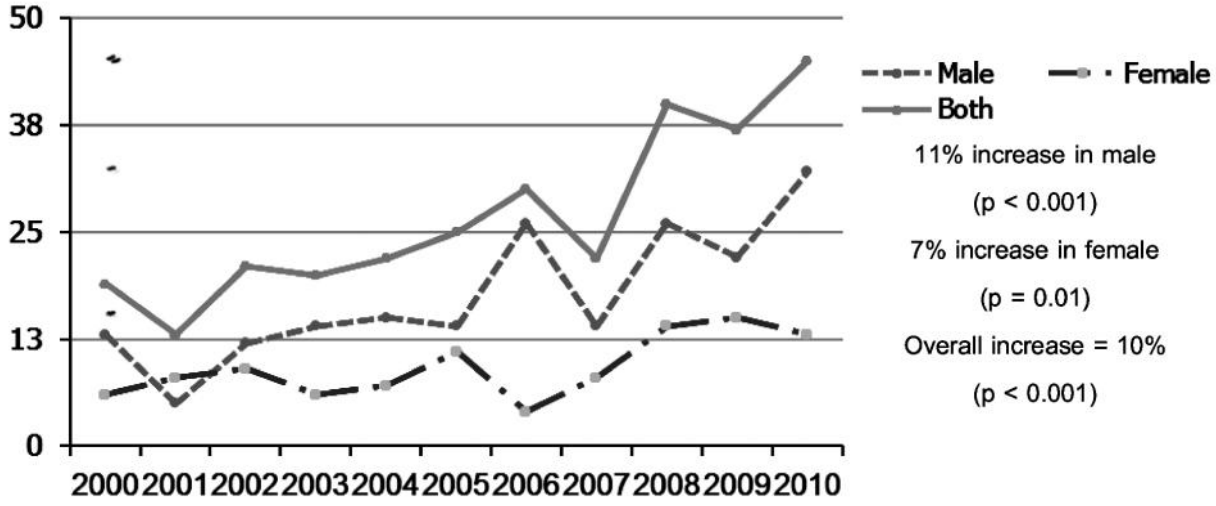

Figure 1 Trend of new kidney cancer cases studied in Srinagarind Hospital during 2000-2010

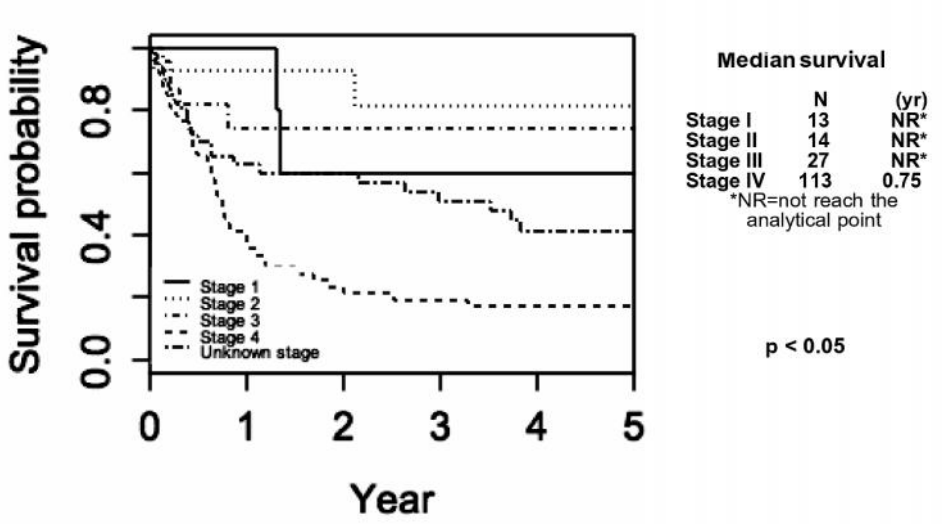

Figure 2 The overall survival rate of patients with different stages of kidney cancer in Srinagarind Hospital during 2000-2010.

Discussion

A number of new kidney cancer cases studied in Srinagarind Hospital during 2000-2010 had slightly higher frequency each year. It is possibly because Srinagarind Hospital is the tertiary health care, which receives all referral complicated cases especially advanced stages of cancer cases. These advanced kidney cancer cases were referred to Srinagarind hospital for highly effective surgery by expertise surgeons. In addition, medical referral system and coverage payment are improved; therefore, primary and secondary health care hospital conveniently refer complicated cases beyond their special potentiality to Srinagarind Hospital. Additionally, stage IV or metastatic kidney cancer patients should essentially receive systemic treatment by expertise oncologic physicians and Srinagarind Hospital is one of the tertiary health care centre, which can handle malignant complicated cases. The overall survival time of kidney cancer patients was low because the majority of kidney cancer patients treated in Srinagarind Hospital was stage IV or distant metastasis. The results are consistent with previous report studied in Japan[9], which has similar characteristics of

patients. Additionally, the overall survival time of patients with stage IV kidney cancer was shorter than that of previous studies[10,11]. Possibly, the optimal treatment for these patients is molecular targeted therapy, however, these drugs are presently still very expensive and the national overage insurance from government does not cover the cost of treatment for these patients. Therefore, only the government welfare insurance, which is a small proportion of total kidney cancer patients, is currently allowed to use the molecular targeted therapy. The rest of kidney cancer patients still could not afford this drug and received less effective therapeutic choice of treatment instead. Hence, this specific drugs is currently not available for all advanced kidney cancer patients in Thailand. Consequently, the median survival time of kidney cancer patients, who need molecular targeted therapy, is low.

The limitations of this study

This study is retrospective study, therefore, the quality of data recorded mainly depends on the system of cancer registration. The recorded data sometimes lack of some aspects of important factors including prognostic factors such as performance status of patients, levels of serum calcium and levels of serum LDH. Additionally, most of kidney cancer patients were confirmed diagnosis by the pathological findings but some kidney cancer patients could not be performed renal biopsy for the definite diagnosis because of unstable clinical symptoms and rejection of relatives. Therefore, these patients were diagnosed kidney cancer from the evidence of clinical symptoms and radio imaging findings.

Conclusion

The trends of kidney cancers are accelerating increasing. Higher frequency of new kidney cancer case number was present in male compared to female. The overall survival rate was still very low because kidney cancer patients usually presented with advanced stages (stage IV) of disease. Therefore, if kidney cancer is intensively concerned and the early stages of disease can be detected, patients might have better prognosis resulting in longer survival time.

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