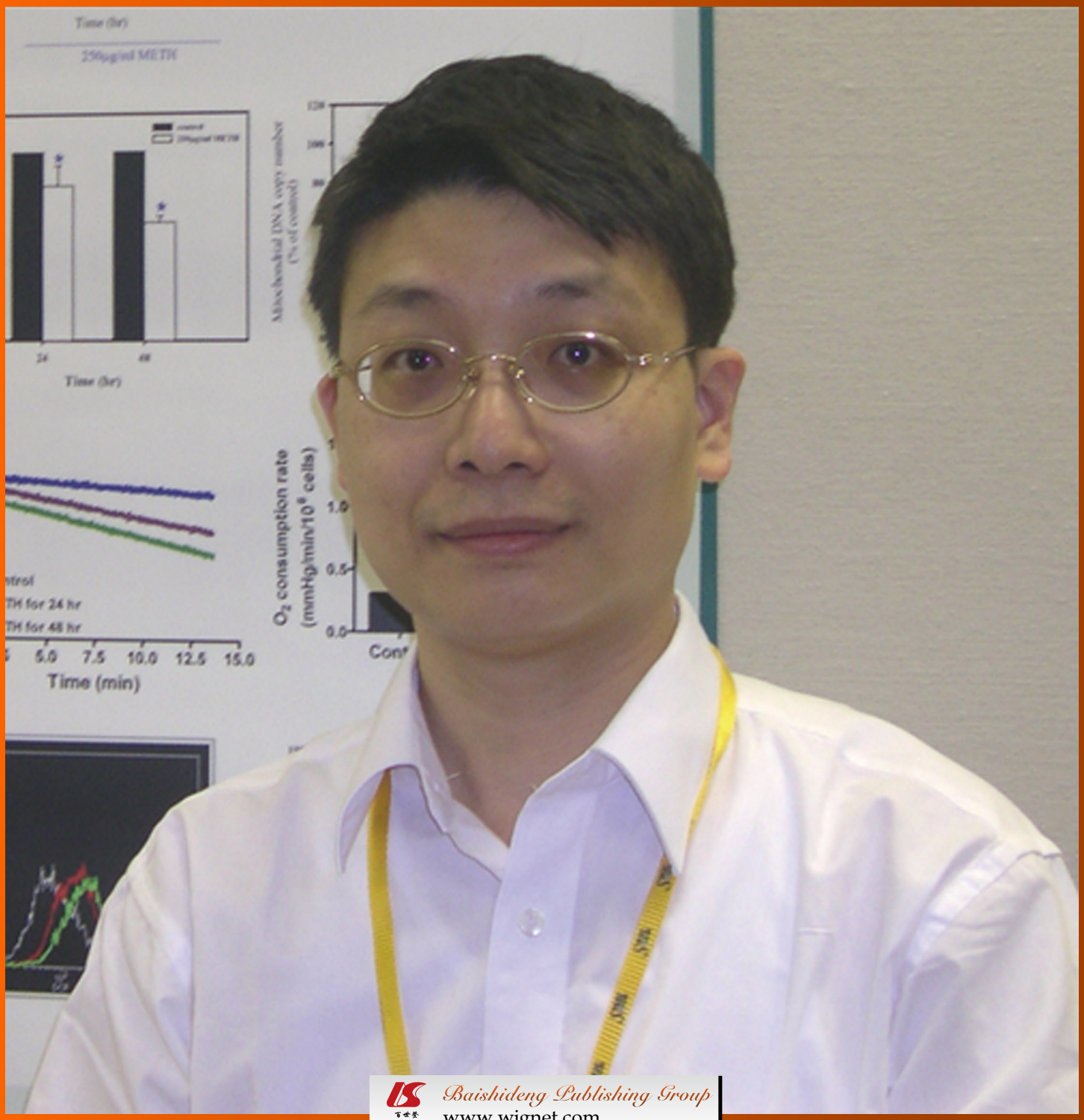
ISSN 1948-5204 (online)

World Journal of *Gastrointestinal Oncology*

World J Gastrointest Oncol 2012 April 15; 4(4): 68-93



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WJGO World Journal of Gastrointestinal Oncology

A peer-reviewed, online, open-access journal of gastrointestinal oncology

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WJGO
World Journal of Gastrointestinal Oncology

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Monthly Volume 4 Number 4 April 15, 2012

World Journal of Gastrointestinal Oncology
Volume 4 Number 4 April 15, 2012

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NAME OF JOURNAL
World Journal of Gastrointestinal Oncology

ISSN
ISSN 1948-5204 (online)

LAUNCH DATE
October 15, 2009

FREQUENCY
Monthly

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PUBLICATION DATE
April 15, 2012

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World Journal of Gastrointestinal Oncology

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doi:10.4251/wjgo.v4.i4.68

World J Gastrointest Oncol 2012 April 15; 4(4): 68-70
ISSN 1948-5204 (online)

EDITORIAL

Increased burden of colorectal cancer in Asia

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Received: May 18, 2011 Revised: March 3, 2012
Accepted: March 10, 2012
Published online: April 15, 2012

Abstract

The incidence and mortality of colorectal cancer (CRC) is rising rapidly in Asia. It seems that ethnicity has an important etiological role in CRC in Asia. However the incidence, anatomical distribution and mortality of CRC among Asian populations are not different from those in Western countries. There is little support by health authorities for CRC screening and very low public awareness of this emerging epidemic in Asia. The increasing rate of CRC in Asia means that we need to take action immediately to prevent CRC and to diagnose the disease at the early stages by introducing CRC screening in countries at high risk of an increasing burden of CRC.

Key words: Colorectal cancer; Burden; Asia

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Pourhoseingholi MA. Increased burden of colorectal cancer in Asia. *World J Gastrointest Oncol* 2012; 4(4): 68-70 Available from: URL: http://www.wjgnet.com/1948-5204/full/v4/i4/68.htm DOI: http://dx.doi.org/10.4251/wjgo.v4.i4.68

INTRODUCTION

With its high incidence and mortality, colorectal cancer (CRC) constitutes a public health burden in most industrialized countries[1]. CRC is the third most common cause of cancer-related deaths globally[2].

Given the high incidence and mortality in Western populations, CRC has been extensively studied in these countries. The highest rates are in developed countries, including the United States, Canada, Australia, and northwestern Europe. A comparatively low rate is observed in Asian, African, and South American countries although incidence rates are increasing in countries that were previously considered low incidence[3].

Asia is the most populous continent with approximately 4 billion people: 60% of the world's current population. CRC rates are rising rapidly in Asia[4]. In this editorial, we discuss briefly the burden of CRC in Asia. In this issue, there are three topic highlights regarding CRC in Asian countries: first written by Moghimi-Dehkordi *et al*[5] gives an overview of CRC survival rates and prognosis in Asia; the second by Maserat *et al*[6] concerns endoscopic electronic medical record and information systems as a new approach for improving information management in CRC prevention; the third paper by Pourhoseingholi *et al*[7] concerns the necessity of CRC screening in the Iranian population.

INCIDENCE

CRC is now the third most common malignant disease in both men and women in Asia[8]. Data from the Cancer Base of the International Agency for Research on Cancer show that the incidence in many affluent Asian countries is similar to that in the West[9]. In Eastern Asia, countries such as China, Japan, South Korea and Singapore have experienced a two- to four-fold increase in incidence in recent decades[8]. Among ethnic groups in Asia, the incidence of CRC is significantly higher among the Chinese[10]. According to the Chinese National Cancer Database of 2003, CRC was one of three cancers with the most rapidly increasing incidence (together with lung

cancer and female breast cancer) in the country between 1991 and 2005[11]. In Japan, the incidence of CRC may have exceeded that of gastric cancer[12]. A rapid increase in incidence of CRC has also been reported in Taiwan[13]. In the Middle East, the incidence of CRC has increased in Iran in recent years[14,15] and Iranian data suggest a younger age distribution compared to Western reports[15-17].

While the overall age-standardized rate (ASR) has increased in most Asian countries in last two decades, there have been recent decreases in ASR in some countries, especially in the younger population[18-20]. However, data are lacking in countries such as India, Indonesia, and other countries located in the Middle East. These findings indicate a rapid increase of CRC incidence in Asia and a changing epidemiology which is as worrying as the rising incidence.

MORTALITY

The 5-year mortality for people diagnosed with CRC is approximately 40% although survival improves substantially if the cancer is diagnosed while it is still localized[21]. The mortality of CRC has been increasing in the last decade in Asian countries, with the exception of Japan and Singapore[8]. The WHO Mortality Database indicates that colorectal-cancer mortality in Singapore has doubled in both men and women over the past three decades[22]. The National Cancer Center of Korea reported a declining trend in mortality from stomach and liver cancers but a 35% increase in colorectal-cancer mortality in both men and women[23]. According to data from the national mortality routine reporting system in China, mortality from CRC has increased through recent decades[24]. National death statistics of Iran reported a slight increasing trend for CRC mortality from 1995 to 2003, and CRC mortality was higher in older age and males[25,26].

EPIDEMIOLOGY

It seems that ethnicity has an important etiological role in CRC in Asia. In Singapore, where different ethnic groups live in the same environment, the incidence of CRC is lower among the Indian and Malay populations than among the Chinese[10,27]. Similarly, Chinese people who live in Malaysia, have a significantly higher incidence of colon and rectal cancers than others[28].

According to the Asia Pacific Cohort Studies Collaboration (involving over half a million subjects from 33 cohort studies in the region), smoking, body mass index and lack of physical activity increase the risk of CRC[29].

The incidence, anatomical distribution and mortality of CRC among Asian populations are not different from those in Western countries. There is a trend for proximal migration of colonic polyps and flat or depressed lesions are not uncommon[30].

SCREENING

Facilitating access to CRC screening is an important key to reducing the burden of CRC. The first guidelines for CRC screening were issued in 1989 by the US Preventive Services Task Force[31]. These guidelines were updated in 1996 after randomized controlled trials[32-34].

There are three frequently used screening modalities, namely fecal occult blood tests (FOBT), flexible sigmoidoscopy (FS) and total colonoscopy, each with their advantages and disadvantages. Among these three, biennial guaiac-based FOBT is the only method shown in large randomized studies to decrease mortality[4].

The Japan Public Health Center-based Prospective Study group in a cohort study (with a 13-year follow-up involving 42 000 subjects) showed a risk reduction in advanced CRC of almost 60% and in mortality of 30%[35].

A study to evaluate the cost-effectiveness of FOBT, FS and colonoscopy in Asian countries indicated that FOBT is cost-effective compared to FS or colonoscopy for CRC screening in average-risk individuals aged from 50 to 80 years[36].

In most Asian countries, national healthcare systems and health insurance cover only a minority of people. So, access to healthcare facilities is limited in many rural areas and communities of low socio-economic status[8].

There is little health authority support for CRC screening and very low public awareness of this emerging epidemic in Asia. Therefore Sequential FOBT to select high-risk individuals for further investigation is probably the only viable option for most Asian countries[4].

The increasing rate of CRC in Asia means that we need to take action immediately to prevent CRC and to diagnose the disease at the early stages. The cost-effectiveness of screening programs must be assessed in each individual country and research should be done to elucidate the epidemiology, genetic and environmental factors in the development of CRC.

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S- Editor Wang JL **L- Editor** Hughes D **E- Editor** Zheng XM

World Journal of Gastrointestinal Oncology

Online Submissions: http://www.wjgnet.com/1948-5204office
wjgo@wjgnet.com
doi:10.4251/wjgo.v4.i4.71

World J Gastrointest Oncol 2012 April 15; 4(4): 71-75
ISSN 1948-5204 (online)

TOPIC HIGHLIGHT

Mohamad Amin Pourhoseingholi, PhD, *Series Editor*

An overview of colorectal cancer survival rates and prognosis in Asia

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Received: May 18, 2011 Revised: March 3, 2012
Accepted: March 10, 2012
Published online: April 15, 2012

Abstract

Colorectal cancer is a rapidly rising trend in Asia. The incidence in many Asian countries is on par with the West. Several studies have provided data regarding the survival of patients with colorectal cancer. In Asia, the overall cure rate of colorectal cancer has not improved dramatically in the last decade, 5-year survival remaining at approximately 60%. Colorectal cancer survival time has increased in recent years, but mortality rate remains high. Although studies have determined a number of factors that can predict survival of patients after diagnosis, life expectancy has not been increased dramatically. It seems that among the prognostic factors explored so far, the most important are those that relate to early diagnosis of cancer. Primary detection is feasible since efficient screening modalities are available. Colonoscopic surveillance is needed, especially in subjects at higher risk.

Key words: Colorectal cancer; Survival rate; Prognosis; Asia

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Moghimi-Dehkordi B, Safaee A. An overview of colorectal cancer survival rates and prognosis in Asia. *World J Gastrointest Oncol* 2012; 4(4): 71-75 Available from: URL: http://www.wjgnet.com/1948-5204/full/v4/i4/71.htm DOI: http://dx.doi.org/10.4251/wjgo.v4.i4.71

INTRODUCTION

Colorectal cancer is the fourth most common cancer in men and the third most common in women worldwide. It accounts for an estimated 1.2 million new cancer cases and over 630 000 cancer deaths per year, almost 8% of all cancer deaths[1,2]. Colorectal cancer has become an important problem in Asian countries[3-7]. Reports from the World Health Organization (WHO) data set and from individual countries or cities in Asia show that the incidence of CRC is rising rapidly rising in regions within countries such as China, Japan, South Korea and Singapore[7-10]. These countries, have experienced a 2-4-fold increase in the incidence of colorectal cancer during the past few decades[11]. The overall prevalence of advanced colorectal neoplasm in asymptomatic Asians was also found to be comparable with other developed countries[12].

In recent decades, claims have been made of numerous variables being related to survival. The extent of bowel wall penetration, lymph node metastases, distant metastases, tumor differentiation and tumor stage have been regarded as factors of the utmost prognostic importance; and they have been the basis of most staging systems[13-27]. Despite numerous attempts to detect cancer at an early stage, the overall long-term outcome of patients curatively resected has not significantly changed in the last decade, the 5-year survival rate being approximately 60 percent. More than half of colorectal adenocarcino-

mas are still diagnosed only when the disease involves regional or distant structures[22].

Many studies have been performed, using univariate and multivariate methods to define the prognostic significance of various clinical and pathologic factors[13-21,23-33]. However, the accurate determination of prognostic factors for colorectal cancer remains a problem. The present study considered a number of clinical studies on significant factors that can predict patient outcome. We report the results of some previous studies focused on colorectal cancer and review the literature concerning estimation of survival rates and evaluation of clinical and pathologic prognostic parameters, with an emphasis on Asian countries. Relevant articles, in which univariate and multivariate analyses were used, were selected, and results are discussed.

SURVIVAL ANALYSIS

Several studies have provided data regarding the survival of patients with colorectal cancer. In Asia, the overall cure rate of colorectal cancer has not improved dramatically in the last decade in Asia, 5-year survival remaining at approximately 60%. While the highest survival rates were found in China, the lowest rate was reported in India (Figure 1)[21,24,34-40]. The 5-year survival for persons with colorectal cancer is 64% in the United States. If the disease is detected at an early stage, the 5-year survival rate increases to 90%. However, because of lack of screening programs in many countries, only 39% of colorectal cancers are diagnosed at this stage. From 1982 to 1992, relative survival rates for patients diagnosed with colorectal cancer in five developing countries, comprising China, Cuba, India, the Philippines, and Thailand, was estimated at between 28 to 42%[1]. A report from Korea indicated that the 5-year survival rates were 62.1%[41]. In China, the overall 5-year post-operative survival rate was 60.8% in colorectal cancer patients, 62.3% in colonic cancer and 59.3% in rectal cancer. Another Chinese study reported an overall 5-year survival rate of 66.3%[34]. Various research studies from Iran have indicated the 5-year survival rates of colorectal cancer were 47%[35], 41%[36] and 61%[21], respectively.

According to one Japanese study, the overall 5-year survival rate was 61.4%[42]. The overall 5-year survival rate for colorectal cancer patients was 34.3%, lower than in either other Asian or Western countries[24]. However, results from Bombay, India indicated the lowest overall 5-year survival rates for colon and rectal cancer (31.2%)[43,44]. Data on this issue are scant in countries including Indonesia, Malaysia, Taiwan, and in Arab countries. In total, it seems that 5-year overall survival rates of colorectal cancer patients differ between Eastern and Western Asia. While the overall survival rates for colorectal cancer in South-West Asia were relatively lower than in US and European countries, in East Asia, rates are similar to those of Western communities. The main reason for the lack of progress is that currently a significant proportion of patients are diagnosed at later stages of disease or patients with seemingly localized tumor already have undetectable metastasis, mostly in the liver. To improve survival rates, in addition to earlier detection, more aggressive (adjuvant) treatment of high risk patients would be a rational strategy. This requires development of new therapeutic procedures, as well as reliable stratification of patients according to high risk or low risk for recurrent disease. In recent years, many attempts have been made to improve the prediction of final outcome.

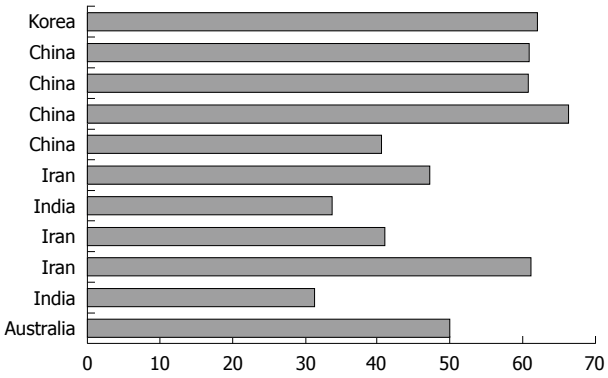

Figure 1 Overall 5-year survival of colorectal cancer in Asian countries[21,24,34-40].

PROGNOSTIC FACTORS

The prognostic factors for colorectal cancer were determined in various studies by both univariate (Kaplan-Meier) and multivariate (Cox proportional hazards model) methods. The most important independent prognostic factors related to survival of patients was determined by Cox models. Prognostic factors could be categorized as either demographic factors or pathological and clinical factors. In order to better compare the findings of various studies from different areas, the most important results are shown in Table 1[21,24,35,36,41-43,45,46].

Demographic factors

For a long time, prediction of patient outcome was attempted either by identification of patient attributes (age and sex) or from macroscopically evident tumor features. More recently, studies using multivariate analysis have clarified the prognostic role of clinical parameters. Patient gender has been extensively evaluated although in the majority of studies this was of no significance in predicting survival independently of other factors[14,19-21,24,25,35,38].

In the literature, results concerning patient age are even more diverse. In a number of studies[15,18,21,25,26], this parameter was not found to be an independent prognostic variable. However, in other reports[14,20,35,36], age did seem to play a role, predicting a poorer survival rate for older patients than younger ones.

Pathologic and clinical factors

Pathological evaluation is a critical component in the

Table 1 Comparison of the results from different countries

Study	Population	Year	Prognostic factors (indicated by univariate method)	Independent prognostic factors (indicated by multivariate method)
Mehrkhani *et al*[35]	Iran	1999-2002	Age, TNM stage, T-status, nodal status, distant metastasis, grade, lymphatic and vascular invasion, presurgery CEA level > 5 ng/mL	Age, TNM stage, grade
Shiono *et al*[42]	Japan	1999-2002	Aerogenous spread with floating cancer cell clusters (ASFC) vascular invasion, lymphatic invasion, pleural invasion	Vascular invasion, aerogenous spread with floating cancer cell clusters (ASFC)
Moghimi-Dehkordi *et al*[21]	Iran	2002-2007	Type of first treatment, body mass index, marital status, tumor grade, extent of wall penetration, distant metastasis, regional lymph nodes metastasis, and pathologic stage of tumor	Tumor size, metastasis of tumor, body mass index, marital status, and grade of tumor
Al-Shamsi *et al*[45]	United Arab Emirates	1985-1998	Age, Type of operation, Type of resection, lymph node status, peritoneal spread, liver metastasis, Dukes' staging, Lateral margins, Proximal and distal margins	Presence of lymph nodes and Duke staging
Moradi *et al*[36]	Iran	2000-2005	Age, sex, site of tumor, Type of tumor	-
Park *et al*[41]	Korea	1974-1993	Dukes' stage, extent of bowel wall invasion, lymph node metastasis and number of involved lymph nodes, preoperative CEA level, histologic grade, and gross morphology of the tumor	Dukes' stage, number of lymph node metastasis, CEA level, tumor location, gross morphology of tumor, depth of bowel wall invasion
Yeole *et al*[43]	India	1987–1991	Age, marital status, education, site (colon versus rectum), clinical extent of disease and treatment modality	Age group, site and clinical extent of disease emerged
Ghazali *et al*[24]	Malaysia	1996-2005	Age, sex, race, working status, smoking status, per rectal bleeding, liver metastasis, site of tumour, Dukes staging, preoperative CEA level and treatment modalities	Liver metastasis status, Dukes staging and treatment modalities
Goh *et al*[46]	Singapore	1987	Age, abdominal distension, Dukes' stage , tumour grade	Dukes' stage

management of patients with colorectal cancer. From initial diagnosis through definitive treatment, pathological assessment of a resected colorectal cancer is still considered the most accurate method of assessing the tumor-related features that determine postoperative outcome.

Different clinico-pathological prognostic factors have been proposed: location of the tumor[21,22,26,27,35,38], depth of tumor invasion[32,37,40], tumor stage[32,47], differentiation of tumor[20,21,48], surgical procedure[15,25], pathological type[25,48], tumor size[21,48-50], lymph node metastasis[21,51,52] and distant metastasis[15,25,48]. The site of the tumor has been investigated as a possible prognostic factor. Patients with colon cancer are considered to have a better survival than those with rectal cancer. In previous studies distal location and advanced stage of tumor were determined as independent prognostic factors for survival of patients with colorectal cancer. Several analyses confirmed the vital importance of tumor stage, as reflected in Dukes or TNM classification, in predicting survival. However, in the vast majority of studies documenting the prognostic power of tumor grade the number of grades has been reduced.

Although various studies have determined a number of factors that could predict survival of patients after diagnosis, life expectancy has not increased drastically. The review of the results from different reports shown in Table 1 supports the thesis that the pathological and clinical features of the disease may be better determinants for prognosis in colorectal cancer patients. It seems that among all the prognostic factors explored to date, the most important are those related to early diagnosis. Early detection or secondary prevention of cancer is increasingly important for the control of certain malignant diseases like colorectal cancer. CRC is more common in the elderly, although approximately 43 percent of colorectal cancer in Iran occurs before 50 years of age[53]. It is well established that colorectal cancer is one of those cancers that can largely be prevented by the early detection and removal of adenomatous polyps[54,55], and survival is therefore significantly better when colorectal cancer is diagnosed while still localized. Screening strategies are needed for early detection of colon adenomas and colorectal cancer.

CONCLUSION

In summary, colorectal cancer is a rapidly rising trend in Asia. The incidence in many Asian countries is in fact on a par with the West. Colorectal cancer survival time has increased in the past decades, but mortality rate remains high. Primary detection is feasible since efficient screening modalities are available. Colonoscopic surveillance is needed, especially in subjects at higher risk.

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S- Editor Wang JL **L- Editor** Hughes D **E- Editor** Zheng XM

World Journal of Gastrointestinal Oncology

Online Submissions: http://www.wjgnet.com/1948-5204office
wjgo@wjgnet.com
doi:10.4251/wjgo.v4.i4.76

World J Gastrointest Oncol 2012 April 15; 4(4): 76-81
ISSN 1948-5204 (online)

TOPIC HIGHLIGHT

Mohamad Amin Pourhoseingholi, PhD, *Series Editor*

Endoscopic electronic record: A new approach for improving management of colorectal cancer prevention

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Received: May 18, 2011 Revised: March 1, 2012
Accepted: March 10, 2012
Published online: April 15, 2012

Key words: Endoscopic electronic medical record; Minimum datasets; Information management; Reporting; Colorectal cancer prevention

Peer reviewers: Angelo Zullo, MD, Department of Gastroenterology and Digestive Endoscopy, "Nuovo Regina Margherita" Hospital, Via E. Morosini 30, Rome 00153, Italy; Antonio Russo, MD, PhD, Associate Professor, Genetic and Molecular Oncology Unit, Interdepartmental Center of Research in Clinical Oncology, School of Medicine, University of Palermo, Via del Vespro 127-90127 Palermo, Italy

Maserat E, Safdari R, Maserat E, Zali MR. Endoscopic electronic record: A new approach for improving management of colorectal cancer prevention. *World J Gastrointest Oncol* 2012; 4(4): 76-81 Available from: URL: http://www.wjgnet.com/1948-5204/full/v4/i4/76.htm DOI: http://dx.doi.org/10.4251/wjgo.v4.i4.76

Abstract

Digestive endoscopy is currently the main diagnostic procedure for investigation of the digestive tract when a digestive disease is suspected. The use of computers and electronic medical records for the management of endoscopic data are an important key to improving endoscopy unit efficiency and productivity. This technology supports optimal program operation, monitoring and evaluation colorectal cancer screening. This article is a comprehensive survey of endoscopic electronic medical records and information systems. Computerized clinical records have the capability of identifying patients due for screening and to calculate baseline rates of colorectal cancer screening by patient characteristics and by primary care physician and practice group. This paper describes data flow in the endoscopy unit, the minimum data set of colorectal cancer and key features of endoscopic electronic medical record. In addition, the researchers state standards in different aspects, especially terminology standards and interoperability standards for image and text.

INTRODUCTION

The concept of the computerized endoscopic medical record (CEMR) or endoscopic electronic medical record systems (EEMR) has existed since the development of the endoscope[1,2] and a substantial amount of work has been done for more than a decade in the design and development of endoscopic databases and application software[3-13]. Electronic medical records have been developed to modernize procedural information management in the endoscopy unit[14]. The advantage of the CEMR is that it is possible to search any database created, perform statistical analysis and avoid the need for hand-written or typed reports[11]. There is a growing recognition of the need to base cancer control policies on accurate, detailed and timely information on cancer management and outcomes. With the development of the National Cancer Control program, it is obvious that an integrated cancer information system, incorporating a national cancer dataset, is needed to provide detailed timely and consistent information across the country. This would ensure that

the care received by cancer patients is consistent and conforms to national guidelines, that information on trends in incidence, survival and mortality is readily available for planning and evaluation and that inequality in the delivery or outcome of services is quickly identified. EEMR not only have great potential to contribute to advantages such as better quality and safety in endoscopy and increased productivity due to automated data entry and report generation, but also aid in clinical research and education by recording complete and accurate data. It has repeatedly been reported in studies that structured reports are superior to free-text reports in endoscopy as they offer a built-in quality control into the report by specifying the terms to be used together unambiguously with their attributes and values[13-19].

APPLICABLE FEATURE OF THE EEMR SYSTEM

In the last decade, the introduction of electronic endoscopes in the daily practice of digestive endoscopy has dramatically increased the possibilities of documenting endoscopic procedures with high quality pictures. Combined with computers, the electronic endoscopes constitute actual "endoscopic workstations"[11]. Available features of CEMR include: (1) patient scheduling: multi-user configurable; (2) patient monitoring: vital signs, pulse oximetry; (3) procedural coding: pre-procedural diagnosis, current procedure terminology (CPT) and ICD; (4) report generation: endoscopic record with images; (5) pathology interface and tracking; (6) discharge planning; (7) correspondence and networkable; (8) billing: automated billing for insurance; (9) quality assurance; (10) instrument tracking, usage and maintenance; (11) inventory control for pharmaceutical and supplies; (12) practice management; (13) clinical investigations; (14) risk management: completeness of documentation; (15) image management; (16) video clip management; (17) remote access internet; (18) patient education material; (19) searchable fields; (20) nursing note module; and (21) office note module[1,14].

Patient scheduling systems normally allow the user to enter essential information. The user may customize lists of frequently used descriptors (e.g., procedure types, referring physicians and performing physicians).

Patient monitoring may be entered into the endoscopic record manually or in an automated process. The ability to generate a natural language report diminishes with increasing complexity of the report. All report generators are capable of generating standardized negative examinations. Procedure related medications may be entered using a menu, "default" or free text.

Procedural findings are usually taken from a customizable list. Free text entries are usually allowed but weaken the utility of the database.

Some systems use a graphical display of the GI tract to input and/or report the findings. CEMR systems are capable of generating discharge instructions, physician recommendations and correspondence that may be printed or distributed electronically (e.g., fax and e-mail).

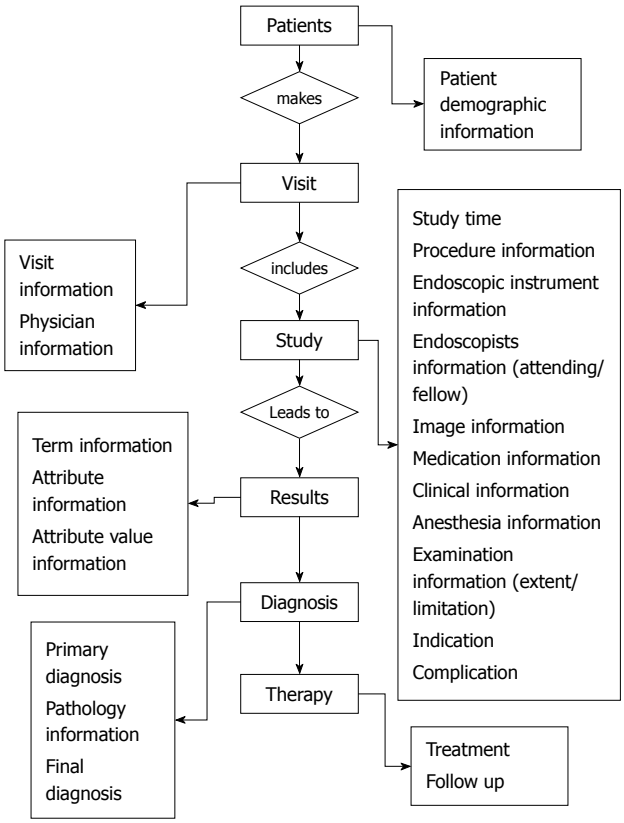

Figure 1 Standard endoscopy record flow.

Most CEMR systems can report CPT codes. However, certain systems may be unable to adjust the CPT code if the actual procedure performed differs from the planned procedure. Diagnostic ICD code may be generated automatically or manually selected.

Quality assurance can be performed using CEMR by identifying immediate complications and sentinel events (e.g., oxygen desaturation, use of supplemental oxygen or use of reversal agents). However, data regarding delayed complications and procedural outcomes may be limited by the lack of follow-up information. CEMR can monitor instrument usage and endoscopy unit inventory[14]. Other features, such as automated follow-up and endoscopy unit statistics, may streamline practice management[20].

REQUIREMENTS OF STANDARD EEMR

Minimum standard terminology and standard data flow

Although modern computing and communication technology holds great promise, its role in medicine has been limited by the absence of lexical and data exchange standards[18]. Furthermore, endoscopy reports have suffered from a lack of uniform terminology and content. The CEMR has evolved an increasing need for documentation of gastrointestinal procedures[14]. Standard endoscopy record flow is illustrated in Figure 1. The Minimal standard terminology (MST) is the result of a global effort to establish a common structure and vocabulary for electronic endoscopic reports[18]. Hierarchy of minimum standard terminology and examples of general data element in

Table 1 Examples of general data element in endoscopy

Elements	Example
Headings: Type of observation	Excavated Lesion
Term: Observation	Ulcer
Attribute: Characteristics of the term that expands the observation	Size
Attribute value: Defined characteristics	Size in mm
Anatomical concept: region + site + epicenter + locus	Regions (e.g., stomach, colon), sites (e.g., antrum, fundus), epicenters (e.g., extrinsic, intralumenal, wall), and loci (e.g., lumen, contents, mucosa)
Findings	Normal: Should be used if the organ has been examined entirely and everything is normal in it Lumen: Contains all terms regarding an abnormality of the size of the organ, any deformity, compression and the evidence of previous surgery Contents: Terms describing the presence of various materials within the organ Mucosa: Terms describing patterns of the mucosa that are mainly diffuse and which may involve all the mucosa of one limited area. These terms are not applicable to individual lesions Flat lesions: Terms to be used for individual lesions which remain in the plane of the mucosa Protruding lesions: Terms to be applied to lesions growing above the plane of the mucosa Excavated lesions: Terms to be applied to lesions where the surface is beneath the plane of mucosa
Therapy: intervention related to observation (coding from SNOMED or Clinical LOINC or ICD databases)	Biopsy

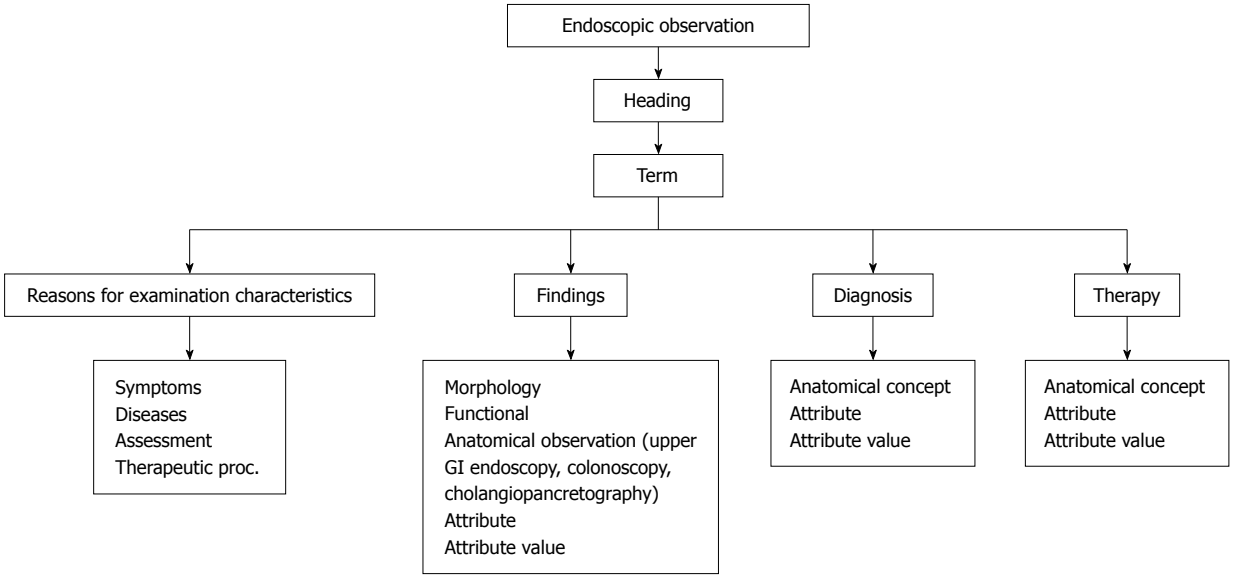

Figure 2 Hierarchy of minimum standard terminology.

endoscopy are illustrated in Figure 2 and Table 1. This flow data contain elements to describe: (1) reasons for performing an endoscopy, although a list of "Indications" is available in many countries and is intended as a means of assessing the relevance and necessity for an endoscopic examination. This list was devised on the basis of the appropriateness of an individual examination. While appreciating the reasons behind this decision, the committee felt that it was more important to record why a particular examination had been undertaken rather than instruct users when an examination was acceptable. "Reasons for" have, therefore, been divided into: (a) symptoms: to allow a user to record the symptoms for which an endoscopic examination is required. This is particularly important when a disease is difficult to define; (b) diseases: this lists the common diseases for which an endoscopic examination may be required. These can be qualified by "Suspected …", "For exclusion of …", "For follow-up of …" or "For therapy of …"; (c) assessment of: this category was introduced in the "Reasons for" list in order to allow the recording of examinations performed to evaluate the status of a part of the GI tract before or after a surgical procedure; and (d) diagnostic sampling: this was included as a "Reason for" as it was recognized that some examinations may be performed only to collect a sample; (2) endoscopic findings; and (3) endoscopic diagnosis: at the end of the list of terms for each examination, a diagnostic list appears. This indicates a diagnosis that the endoscopist feels is most likely on the basis of macroscopic findings. This is not necessarily the final diagnosis, which takes into account the findings of any additional procedures performed, such as biopsy/cytology. The diagnostic list has

been split into two parts: (a) main diagnoses ordered by expected prevalence; and (b) other (rarer) diagnoses listed alphabetically. The decision as to which list a particular diagnosis appears is based on the expected frequency of this finding in a European context. This "diagnosis" could be used to implement a "conclusion" field within any report generated based on a synthesis of all of the findings recorded. This is particularly true when a number of different lesions are described, such as in inflammatory bowel diseases at colonoscopy. It is also recommended that it should be possible to record a "negative conclusion" as well as a positive one. It is often just as important to record when a feature is not present as it is to describe it, e.g., failure to find any sign of bleeding when a patient presents with an apparent gastrointestinal bleed. It is suggested that it should be possible to qualify a diagnosis by "certain", "suspected", "probably not present" and "definitely excluded".

Using these standards can overcome a lack of interoperability between colorectal cancer databanks at national and international level. Standard data elements can be used in their databases. Core datasets for colorectal cancer are: (1) macroscopic; (2) site of tumor; (3) maximum tumor diameter; (4) distance to the near nearer end resection margin; (5) tumor perforation; (6) relationship of rectal tumors to the potential reflection; (7) microscopic; (8) histological type; (9) histological differentiation; (10) maximum extent of local invasion (pT stage); (11) lymph node status; (12) extramural venous invasion; (13) evidence of regression following therapy; (14) histologically confirmed distant metastases; (15) background abnormalities; (16) other; (17) TNM stage; (18) Dukes stage; (19) completeness; and (20) SNOMED (Systematized nomenclature of medicine clinical terms) codes[21].

Standard reporting

The widespread use of gastrointestinal endoscopy for diagnosis and treatment requires effective, standardized report systems[22]. Standardization of the endoscopic report is a key issue for future research in the field of digestive endoscopy[11]. Report generators should provide essential information, including patient identifier, physician identifier, date of procedure, relevant medical history, procedure type, medications, indication for procedure, extent of procedure, limitations of examination, findings, tissue acquired, adverse events, final diagnosis, results of therapeutic interventions, notation if images were acquired, complications and disposition[14]. The central role of the EEMR continues to be generation of the endoscopy procedure report[1]. Standard endoscopy report data element is illustrated in Table 2.

Table 2 Elements of an endoscopic report

Patient name
Address
Date of birth
Sex
SSN
Patient ID (internal)
Telephone No. (home)
Telephone No. (work)
Study date (date of procedure)
Study time
Study type (type of procedure)
Referring physician
Endoscopist (procedure MD)
Endoscopic instrument
Anesthesia status
Medication
Reason for examination
Indication
Anatomic extent of examination
Limitation of examination
Complication
Finding
Site
Term
Attribute
Attribute value
Therapeutic procedure
Diagnostic impression
Diagnostic impression IC9 code
Pathologic result
Final diagnosis
Final diagnosis ICD9 code
Recommendation

Standard for telecommunications (Nomenclature, coding, data and image interchange standard)

Nomenclature standard: Vague and insignificant forms of speech and abuse of language have passed for mysteries of science for so long, and hard and misapplied words with little or no meaning have, by prescription, been be taken for deep learning and height of speculation, that it will not be easy to persuade either those who speak them or those who hear them, that they are but the covers of ignorance and hindrance of true knowledge. The importance of precise language in medicine cannot be overestimated. All medical activity arises from the ability to observe and communicate intelligibly. Endoscopists view the GI tract and create text and images that reflect their observations and transmit this information to others who are also involved in the care of the patient. The increasing fragmentation of care, pressure for increased productivity and lack of rapid access to the patients' clinical reports make effective automation crucial to the future of medicine[18]. SNOMED is a system of standardized medical terminology. SNOMED Clinical Terms® or SNOMED CT is a comprehensive computerized clinical terminology covering clinical data for diseases, clinical findings and procedures. It is a "comprehensive and precise clinical reference terminology that provides unsurpassed clinical content and expressivity for clinical documentation and reporting". It allows a consistent way to index, store, retrieve and aggregate clinical data across specialties and sites of care. It also helps structure and computerizes the medical record, reducing the variability in the way data is captured, encoded and used for clinical care of patients and research. SNOMED created a common clinical language that is a necessary element of a health care information infrastructure[23]. The goal of SNOMED is to create a comprehensive nomenclature for indexing the

Table 3 Different fields that need a specific code in endoscopic information systems

Reason for endoscopy
Medication use
Sedation and medication during endoscopy
Preparation
Procedure for investigation
Endoscopic diagnosis/findings
Therapeutic and diagnostic interventions
Histology results
Therapy started
Advice to referring doctor
Complications

entire medical record, including signs, symptoms, diagnosis and procedures. SNOMED contains 156 602 unique concepts that, when linked to the MST, would permit endoscopic records to be automatically cross-indexed to other parts of the medical record[18].

Coding standard (ICD, CPT, logical observation identifier names and codes): In the course of creating an endoscopic report and submitting a claim for reimbursement, practitioners are required to classify the endoscopy according to coding systems: CPT and ICD. At the end of each procedure, the endoscopist must select a CPT code that indicates what was done and an ICD code that defines the indication for the procedure and what was found. Automation of these processes would improve the accuracy of the codes[18]. Different fields that need a specific code in endoscopic information systems are illustrated in Table 3.

Logical observation identifier names and codes (LOINC) is one of therapy coding in EEMR[24]. The LOINC database provides a set of universal names and ID codes for identifying laboratory and clinical observations[25]. They are mainly intended to identify the test results. LOINC was developed to facilitate the electronic transmission of laboratory results to hospital, physician, third party payers and other users of laboratory data. Each record in the LOINC database identifies a clinical observation and contains a formal six-part name and identifying code with a check digit, synonyms and other useful information[26].

Standard of interface of data and image (health level 7, Digital Imaging and Communications in Medicine): EEMRs can also be configured to interface promptly with a hospital electronic medical record systems (EMR), usually *via* standard technical compatibilities, such as health level 7 (HL7)[1]. HL7 is one of several American National Standards Institute-accredited Standards Developing Organizations (SDOs) operating in the health care arena. Most SDOs produce standards (sometimes called specifications or protocols) for a particular health care domain such as pharmacy, medical devices, imaging or insurance (claims processing) transactions. The HL7 domain is clinical and administrative data. HL7 develops specifications; the most widely used is a messaging standard that enables disparate health care applications to exchange key sets of clinical and administrative data (California Office of HIPPA implementation, 2008).

The advent of the video endoscope has revolutionized the practice of gastrointestinal endoscopy[27]. Images are critical components of the clinical record. Since the 1970s, when digital images first became widely used in clinical practice (with routine use of computerized tomography), there has been an ever-increasing need for a generic image-file format and exchange protocol to enable interchange of diagnostic images and related information in electronic form. The Digital Imaging and Communications in Medicine (DICOM) standard was developed by the American College of Radiology and the National Electrical Manufacturers Association to meet this need. DICOM is a set of engineering specifications for a generic image file format, a network image-interchange protocol and an explicit semantic data model for images and related information. The DICOM standard has been very favorably received by industry and professional organizations. Since publication of DICOM in 1993, digital image management systems enabled by DICOM interfaces have been widely implemented in radiology. Images from a variety of sources (video, fluoroscopy and US) should be DICOM compatible and can often be stored in the EEMR with easy export to other sources[28].

NETWORKABILITY EEMR WITH OTHER INFORMATION SYSTEM

Network connectivity (e.g., LAN, WAN) is available with many of these endoscopic medical record systems, allowing sharing of information with other health care systems. The ability to table interface with other clinical systems may enhance exchange of endoscopic information[14]. Newer functions include interfaces with hospital-wide EMR and pathology databases, improved communication with referring physicians through automated faxes or e-mail, and internet access to allow clinicians secure remote connections[20]. During the procedure, some systems allow automatic transfer of data from the patient's vital sign monitor to the EEMR[14].

COLORECTAL CANCER PREVENTION AND ELECTRONIC RECORD

Colorectal cancer is over 90% preventable. Screening of this disease is key for detecting and preventing colorectal cancer. New technologies enhance colorectal cancer screening. Electronic technology can effectively reduce mortality and increase successful treatment by evidence - based screening. Applications of this technology were developed to handle data entry, reporting, telecommunications and data sharing. Furthermore, health informatics is cost efficient for patient management and facilitates data access in any time and any place[29].

CONCLUSION

EEMR has the key role to greatly increase the efficiency of both the endoscopist and the entire endoscopy unit. It decreases duplication of procedures and increases the utility of databases for clinical research and education purposes. Current features of EEMR can improve patient care and reduce the cost of procedures. Capabilities of this innovation in information management of preprocedure, intraprocedure and postprocedure data can reduce duplication of documentation and reduce total patient time in the endoscopy center. Standard EEMR has the capability of sharing and integrating information among the many stakeholders involved in EEMR, such as participant, family physician, specialist, hospitals, laboratories and pharmacist. Application of endoscopic standard in this technology can be used to improve the quality of endoscopic reporting by integrating images and text, creating large image bases and facilitating clinical research by use of a common lexicon. The minimum datasets for reporting tumors are used in the system of standard setting, data collection, audit and feedback for those involving in caring for these patients. This technology provides minimum datasets for reporting colorectal cancer status and other gastrointestinal cancers. This tool facilitates data access and applications of this technology are cost efficient for patient management, health care organization management, documentation management and material management in the field of colorectal cancer. Electronic technology decreases errors of reporting and duplication in endoscopy activities and health care provider access to comprehensive information for decision making.

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S- Editor Wang JL **L- Editor** Roemmele A **E- Editor** Zheng XM

World Journal of Gastrointestinal Oncology

Online Submissions: http://www.wjgnet.com/1948-5204office
wjgo@wjgnet.com
doi:10.4251/wjgo.v4.i4.82

World J Gastrointest Oncol 2012 April 15; 4(4): 82-83
ISSN 1948-5204 (online)

TOPIC HIGHLIGHT

Mohamad Amin Pourhoseingholi, PhD, *Series Editor*

Colorectal cancer screening: Time for action in Iran

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Received: May 18, 2011 Revised: March 3, 2012
Accepted: March 10, 2012
Published online: April 15, 2012

Abstract

Colorectal cancer (CRC) is now the third most common cause of cancer-related deaths in the world. According to the Iranian Annual National Cancer Registration Report, CRC is the third most common cancer in Iranian women and fifth in men. The incidence of CRC has increased during the last 25 years. CRC screening is an efficient way to reduce the burden of CRC through detection of precursor lesions of cancer or early stage cancer. Iran may benefit even more from screening programs. According to recent studies, the prevalence of colorectal adenoma in first degree relatives of patients diagnosed with CRC is significantly higher than in the average risk population. So, appropriate screening strategies, especially in relatives of patients, should be considered as the first step of CRC screening in Iran.

Key words: Colorectal cancer; Screening; Prevention; Relatives; Iran

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Pourhoseingholi MA, Zali MR. Colorectal cancer screening: Time for action in Iran. *World J Gastrointest Oncol* 2012; 4(4): 82-83 Available from: URL: http://www.wjgnet.com/1948-5204/full/v4/i4/82.htm DOI: http://dx.doi.org/10.4251/wjgo.v4.i4.82

Cancer is the third most common cause of death in Iran[1]. Gastrointestinal cancers are the most frequent cancer among Iranian males and second to breast cancer among females[2].

Colorectal cancer (CRC) is a public health burden in most industrialized countries[3] and is now the third most common cause of cancer-related deaths in the world[4]. According to the Iranian annual national Cancer Registration Report, CRC is the third most common cancer in Iranain women and fifth in men. The incidence of CRC has increased during the last 25 years[5]. Iranian data suggest a younger age distribution for CRC compared to Western reports[5-7].

CRC screening is an efficient way to reduce the burden of CRC through detection of precursor lesions of cancer or early stage cancer. The 5-year survival rate of CRC diagnosed early was reported to be around 90%[8,9]. The overall mortality rate of CRC was reduced by 16%, 12 to 18 years after the beginning of cancer screening[10], and the mortality rate of persons aged 50 to 75 years was also found to be reduced[11].

Screening guidelines recommend that average risk individuals initiate CRC screening at age 50 years[12,13], while high-risk individuals should obtain screening earlier[8,12].

Most cases of CRC (around 80%) are probably caused by environmental factors although in up to 5% of all CRCs, genetic factors play a dominant role[14,15]. The most common hereditary syndromes are Lynch syndrome (hereditary nonpolyposis CRC), familial adenomatous polyposis and MUTYH-associated polyposis[16]. So, individuals with a personal or family history of CRC[12], history of polyps[8,12], Crohn's disease or ulcerative colitis[17] are at high risk.

Iran, because of its demographic characteristics, may benefit even more from screening programs. The distribution of CRC has shifted towards lower age groups and, half of Iranian CRC patients are currently aged less than 50 years of age[7].

Although the facts mentioned above, suggest that implementation of screening and surveillance programs should be highly beneficial, the necessity of conducting such programs and the exact methods for performing them should be more thoroughly investigated.

Initially, the epidemiology of CRC and adenomatous polyps can be determined according to data banks, registry systems and research studies. Then, measures should be taken to determine the high risk groups for CRC in order to promote early diagnosis. However, actions should not be confined to determining vulnerable groups and all groups of people who might benefit from screening should be included in programs and the cost-benefit estimated[18].

In an unmatched case control study conducted in our research center, a significant positive correlation was found between the number of affected relatives per family and the risk of CRC, which increased nearly threefold[19]. Another study based on colonoscopy screening showed that the prevalence of colorectal adenoma and precancerous lesions in first degree relatives of patients diagnosed with CRC is significantly higher than in the average risk population[20].

It remains to be determined which method of screening yields a better outcome. Randomized and non-randomized studies are needed to assess the efficacy of screening programs. However, reaching a consensus in this regard may take a long time. So, in the meantime, implementation of CRC screening programs will be a matter of moral decision-making instead of being based on current data.

The prevalence of disease, its hygienic burden, applicability of screening programs and the possibility of early diagnosis, demographic characteristics of the population, availability of treatment modalities for patients with positive screening tests and finally, the cost-benefit of the whole procedure will determine whether or not a program should be conducted.

In conclusion, appropriate screening strategies especially in relatives of patients should be considered as the first step in CRC screening in Iran.

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S- Editor Wang JL **L- Editor** Hughes D **E- Editor** Zheng XM

World Journal of Gastrointestinal Oncology

Online Submissions: http://www.wjgnet.com/1948-5204office
wjgo@wjgnet.com
doi:10.4251/wjgo.v4.i4.84

World J Gastrointest Oncol 2012 April 15; 4(4): 84-88
ISSN 1948-5204 (online)

BRIEF ARTICLE

Oncological outcomes of transanal local excision for high risk T1 rectal cancers

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Received: December 11, 2011 Revised: March 4, 2012
Accepted: March 10, 2012
Published online: April 15, 2012

Abstract

AIM: To evaluate the oncological outcomes of transanal local excision and the need for immediate conventional reoperation in the treatment of patients with high risk T1 rectal cancers.

METHODS: Twenty five high risk T1 rectal cancers treated by transanal local excision at the Guangdong General Hospital were analyzed retrospectively. Twelve patients received transanal local excision and 13 patients underwent subsequent immediate surgical rescue after transanal local excision within 4 wk. Differences in the local recurrence rates and 5-year overall survival rates between the two groups were analyzed. The prognostic value of immediate conventional reoperation for high risk T1 rectal cancers was also evaluated.

RESULTS: The median follow-up period was 62 mo. The local recurrence rates after transanal local excision for high risk T1 rectal cancer were 50%. By immediate conventional reoperation, the local recurrence rates were significantly reduced to 7.7%. The difference between these two groups was statistically significant (P = 0.030). Kaplan-Meier survival analysis showed a trend for decreased 5-year overall survival rates for patients treated by transanal local excision compared with immediate conventional reoperation (63% *vs* 89%).

CONCLUSION: Transanal local excision cannot be considered sufficient treatment for patients with high risk T1 rectal cancers. Immediate conventional reoperation should be performed if the pathology of the local excision is high risk.

Key words: Rectal cancer; Transanal local excision; Immediate reoperation; Local recurrence; Overall survival

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Wu ZY, Zhao G, Chen Z, Du JL, Wan J, Lin F, Peng L. Oncological outcomes of transanal local excision for high risk T1 rectal cancers. *World J Gastrointest Oncol* 2012; 4(4): 84-88 Available from: URL: http://www.wjgnet.com/1948-5204/full/v4/i4/84.htm DOI: http://dx.doi.org/10.4251/wjgo.v4.i4.84

INTRODUCTION

With *en bloc* excision of the primary tumor and mesorectal lymph nodes, the abdominoperineal resection and low anterior resection have been considered as the gold standard treatments for rectal cancers because these operations led

to excellent oncological outcomes with a significant decrease in local recurrence and a trend for improved overall survival[1-4]. However, the main disadvantages of these radical procedures include significant mortality and morbidity, as well as the necessity of permanent colostomy that may not be warranted for early rectal cancers which may be treated with local excision[5,6]. With less intraoperative blood loss[7], shorter length of hospital stay[8,9], lower postoperative mortality and morbidity[10,11], excellent maintenance of function[12,13] and avoidance of permanent colostomy[14,15], the benefits of local excision compared to radical surgery are significant. However, local excision carries the unavoidable risk of leaving untreated potential disease in the mesorectum and cannot provide adequate nodal staging because mesorectal lymph nodes are not removed and are therefore not pathologically assessed.

Selecting appropriate patients who can be treated by local excision without compromising oncological outcomes is a prerequisite for accepting local excision as a curative therapy. However, specific patient selection criteria remain incompletely defined. The role of local excision as a curative therapy in the treatment of patients with T_1 rectal cancers is still controversial[16-18]. There is increasing evidence to suggest that local excision should be restricted to patients with low risk T_1 rectal cancers[5,6,11,19]. In these strictly selected patients, local excision may be an acceptable alternative with equivalent oncological outcomes to radical surgery. In the treatment of patients with high risk T_1 rectal cancers, the oncological adequacy of local excision has not been universally accepted and the efficacy of immediate conventional reoperation after local excision remains unclear. Therefore, the main objectives of this study were to evaluate the oncological outcomes of transanal local excision and the need for immediate surgical rescue in the treatment of patients with high risk T_1 rectal cancers.

MATERIALS AND METHODS

Data of 25 patients with high risk T_1 rectal cancers treated by transanal local excision were analyzed retrospectively. There were 14 men and 11 women, ranging in age from 43 to 87 years, with a median age of 63 years. The lesions were located 2-7 cm from the anal verge, with a median distance of 4 cm. The median tumor diameter was 3 (1-5) cm (Table 1). Immediate conventional reoperation (abdominoperineal resection or low anterior resection) was recommended for patients with high risk T_1 rectal cancers. Therefore, 13 patients underwent subsequent surgical rescue after transanal local excision within 4 wk. However, 5 patients (4 patients were classified ASA score Ⅳ and 1 patient ASA score Ⅴ) were unable to tolerate radical resection due to medical comorbidities and 7 patients would have required abdominoperineal resection but were opposed to permanent colostomy. These 12 patients only received transanal local excision. Thus, patients were divided into two groups: Group A (immediate conventional reoperation after transanal local excision) and Group B (transanal local excision). There were no significant differences according to age, gender, tumor location and tumor diameter between the two groups.

Table 1 Clinical characteristics of the study group

Clinical characteristics	
Surgical procedure	
Transanal local excision alone	12
Immediate reoperation	13
Gender	
Male	14
Female	11
Age (yr)	
Median	63
Range	43-87
Tumor location (cm)	
Median distance from the anal verge	4
Range	2-7
Tumor size (cm)	
Median	3
Range	1-5

In this study, preoperative assessment included digital rectal examination, proctoscopy, chest X-ray, abdominal computed tomography (CT) scan, endorectal ultrasound (ERUS) and measurement of serum carcinoembryonic antigen (CEA) levels. ERUS was performed preoperatively in all the patients to assess the invasion depth and lymph node status. Abdominal CT scan was used to exclude distant metastases. The clinical stage of the tumors was I stage ($T_1N_0M_0$). None of these patients received preoperative chemotherapy or radiotherapy. In Group A, two patients were identified with lymph node metastases after radical resection. These two patients were up-staged (ⅢA stage, $T_1N_1M_0$) and received postoperative adjuvant chemotherapy. In Group B, all patients received postoperative adjuvant chemoradiation because of these high risk features.

Transanal local excision was performed under general anesthesia using either the dorsal lithotomy or prone jackknife position. The lesions were removed using electrocautery to perform a full-thickness excision in all cases. The excised tumor specimens were pinned and oriented before submitting it to the pathologist. Histopathological observations, including depth of tumor invasion, margin status, histological grade and presence or absence of lymphovascular invasion, were performed whenever possible. In this study, histopathological examination confirmed that there were 18 poorly differentiated tumors. The surgical margin was positive in 11 cases and lymphovascular invasion was detected in 7 cases (Table 2). Tumors with poor differentiation or positive margin or lymphovascular invasion were defined as high risk tumors.

Patients were followed at 3 mo intervals during the first postoperative year, biannually the second postoperative year and annually thereafter. Digital rectal examination, chest X-ray, abdominal ultrasound and measurement of serum CEA levels were performed at each patient visit. Additional postoperative surveillance, including abdomi-

Table 2 Histopathological characteristics of the patients between two groups

Histopathological characteristics	Group A	Group B
Poorly differentiated	1	6
Poorly differentiated + positive margin	5	2
Positive margin	3	1
Lymphovascular invasion	1	2
Poorly differentiated + lymphovascular invasion	3	1

Group A: Immediate conventional reoperation after transanal local excision; Group B: Transanal local excision alone.

nopelvic CT scan and colonoscopy, was performed annually. Local recurrence was defined as any tumor recurrence within the true pelvis.

The difference of local recurrence rates between the two groups was tested by the Fishers Exact Test. Mean survival time and 5-year overall survival rates were evaluated by Kaplan-Meier survival analysis and log-rank test was used to assess the statistical significance. A value of $P < 0.05$ was considered statistically significant.

RESULTS

In total, 25 patients with high risk T1 rectal cancers were treated by transanal local excision. In Group A, 8 patients underwent low anterior resection and 5 patients were offered abdominoperineal resection. Immediate surgical rescue was performed within 4 wk. Two patients were identified with lymph node metastases after radical resection. These two patients were up-staged (from I stage to ⅢA stage). There was no postoperative mortality or severe complications in both groups.

The median follow-up period was 62 (14-140) mo. In Group A, 1 patient was found with local recurrence and unresectable lung metastases at 42 mo post-surgery. The patient received chemoradiotherapy only and died of the disease 10 mo later. In Group B, 6 patients had disease recurrence, of which 3 were local recurrence only, 2 local recurrence and hepatic metastases, and 1 local recurrence and lung metastases. Among the 3 patients who developed local recurrence only, 2 patients were able to have a successful salvage surgery to complete resection of their disease recurrence and were alive with no evidence of disease at the last follow up. The other patient underwent colostomy due to obstruction at 30 mo post-surgery and died of the disease 16 mo later. Three patients who developed local recurrence and distant recurrence died at 28, 35 and 38 mo post-surgery, respectively (Table 3). In total, local recurrence rates after transanal local excision alone for patients with high risk T1 rectal cancer were 50% (6 of 12 cases). By immediate conventional reoperation, the local recurrence rates were significantly reduced to 7.7% (1 of 13 cases). The difference between these two groups was statistically significant ($P = 0.030$).

In this study, 4 patients with lymphovascular invasion developed tumor recurrences and all these recurrences were UICC IV. All these patients died of the disease within 4 years postoperatively. In Group B, 3 patients with positive margins were detected with disease recurrence. About 66.7% (2 of 3 cases) of these patients were able to have a successful salvage surgery and acquire acceptable oncological results (Table 3).

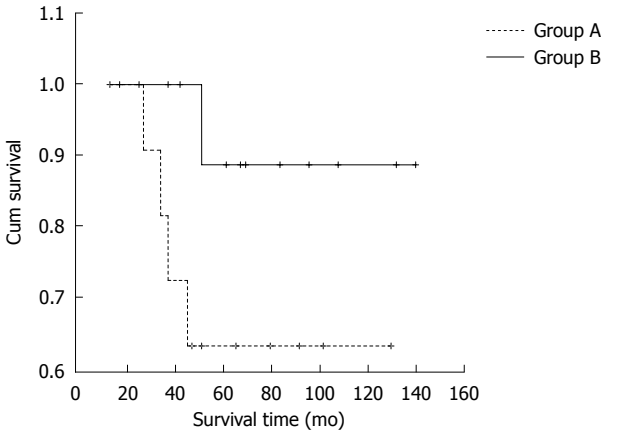

Figure 1 Survival time and overall survival rates for high risk T1 rectal cancers. Group A: Patients treated by transanal local excision alone; Group B: Patients underwent immediate conventional reoperation after transanal local excision.

Kaplan-Meier survival analysis showed a trend for improvement in mean survival time (130.22 ± 9.22 mo, 95% CI: 112.15-148.29 mo *vs* 96.09 ± 13.58 mo, 95% CI: 69.48-122.70 mo) of the patients following immediate reoperation after transanal local excision over the patients treated by transanal local excision alone. Five-year overall survival rates of the patients in Group A were as high as 89%, while that of the patients in Group B were only 63%. However, the differences between these two groups were not statistically significant (log-rank, $P = 0.126$) (Figure 1).

DISCUSSION

The challenge in treating rectal cancers is selecting the proper approach for the appropriate patient. With excellent oncological outcomes, the anterior resection and abdominoperineal resection have been regarded as curative therapies for rectal cancers until now. However, as stated above, these operations are accompanied by significant mortality and morbidity, as well as the risk of permanent colostomy, which have led surgeons to search for less invasive, safer alternatives that yield similar oncological outcomes[20]. Compared to radical surgery, the benefits of local excision are clear. Postoperative complications are low, maintenance of function is excellent and permanent colostomy is avoided. Over the past three decades, the use of local excision for T1 rectal cancers has dramatically increased[21]. However, controversy also exists about whether local excision compromises the oncological outcomes of patients with T1 rectal cancers. Although limited available prospective trials revealed that oncological outcomes of the patients with T1 rectal cancers treated by local excision were comparable to that observed after radical

Table 3 Histopathological characteristics of patients with tumor recurrence

Tumor differentiation	Margin status	Lymphovascular invasion	Group	Type of recurrence	Salvage therapy	Follow up (mo)	Remarks
Poor	Negative	Positive	A	Rectum lung	Chemoradiotherapy[1]	52	Dead
Poor	Positive	Negative	B	Rectum liver	Chemotherapy[1]	38	Dead
Poor	Positive	Negative	B	Rectum	APR	52	Alive
Poor	Negative	Positive	B	Rectum lung	Chemoradiotherapy[1]	28	Dead
Moderate	Positive	Negative	B	Rectum	LAR	48	Alive
Moderate	Negative	Positive	B	Rectum liver	Chemotherapy[1]	35	Dead
Well	Negative	Positive	B	Rectum	Colostomy[1]	46	Dead

[1]Palliative. Group A: Immediate conventional reoperation after transanal local excision; Group B: Transanal local excision alone. APR: Abdominoperineal resection; LAR: Low anterior resection.

surgery[22-24], multiple retrospective studies demonstrated that relatively high local recurrence rates were observed in the patients who underwent local excision for T1 rectal cancers[25]. Much of the apparent discrepancy is due to patient selection, which is far more rigid in prospective trials. It has been universally accepted that optimal candidates for local excision alone include mobile, low-lying, node negative on ERUS, occupying 40% or less of the rectal circumference, low risk (well to moderately differentiated, without lymphovascular invasion or microscopic involvement of the surgical margin) T1 rectal cancers. However, the oncological adequacy of local excision in the treatment of patients with high risk T1 rectal cancers lacks consensus and the efficacy of immediate surgical rescue after local excision remains unclear. Therefore, the main purpose of our study was to evaluate the oncological outcomes of transanal local excision for the patients with high risk T1 rectal cancers. The prognostic value of immediate conventional reoperation after transanal local excision was also evaluated.

In our study, local recurrence rates of patients with high risk T1 rectal cancers treated by transanal local excision alone were 50% (6 of 12 cases), considerably higher than those previously reported for radical surgery. What is the reason for the high local recurrence rates in our study? Firstly, unfavorable histopathological features may be a possible explanation for the high local recurrence rates. Gopaul *et al*[26] reported that the incidence of local recurrence was significantly associated with histological grade of differentiation and margin status. It should be noted that clear margins are critical for transanal local excision. In our study, patients with positive margins after transanal local excision developed disease recurrence. However, clear margins cannot be wholly obtained by transanal local excision. Secondly, the presence of unresected regional lymph node metastases may be another major cause of local recurrence after transanal local excision. The operation cannot provide adequate nodal staging since it does not remove mesorectal lymph nodes, which will be positive in up to 18% of unselected T1 rectal cancers[27,28]. Among thirteen patients who underwent radical resection after transanal local excision in our study, two patients (15.4%) were identified with lymph node metastases. These two patients were up-staged. Thirdly, the possible reason is the shedding and implantation of tumor cells into the surgical excision site that may contribute to local recurrence[29]. Therefore, irrigation of the surgical field prior to closure is recommended in order to improve local control after local excision.

Borschitz *et al*[19] reported that immediate reoperation after local excision of T1 rectal cancers with unfavorable histological finding could avoid local recurrences. However, awaiting recurrences would lead to bad oncological outcomes with high local recurrences and low survival rates. In our study, we found the local recurrence rates were significantly decreased to 7.7% (1 of 13 cases, $P = 0.030$) by immediate conventional reoperation. We also found a trend for decreased 5-year overall survival rates for patients treated by transanal local excision compared with immediate conventional reoperation (63% *vs* 89%). The results showed that the significant increase in local recurrence and the trend for decreased overall survival were insufficient to accept transanal local excision as curative therapy for patients with high risk T1 rectal cancers. By immediate conventional reoperation, the local recurrence rates could be significantly reduced and overall survival rates could be improved to a level similar to initial radical surgery. Therefore, we conclude that transanal local excision could not be considered sufficient treatment for patients with high risk T1 rectal cancers. Immediate conventional reoperation should be performed if the pathology of the local excision is high risk. For patients who are unable to undergo radical surgery or decline a permanent colostomy, transanal local excision is also an acceptable alternative. However, patients should be preoperatively informed of the increased risk of local recurrence and possible need for further salvage surgery.

COMMENTS

Background

The challenge in treating rectal cancers is selecting the proper approach for the appropriate patient. With excellent oncological outcomes, the anterior resection and abdominoperineal resection have been regarded as curative therapies for rectal cancers until now. However, these operations are accompanied by significant mortality and morbidity, as well as the risk of permanent colostomy, which have led surgeons to search for less invasive, safer alternatives that yield similar oncological outcomes. Compared to radical surgery, the benefits of local excision are clear. Postoperative complications are low, maintenance of function is excellent and permanent colostomy is avoided. Over the past three decades, the use of local excision for T1 rectal cancers has dramatically increased. How-

ever, controversy also exists about whether local excision compromises the oncological outcomes of patients with T_1 rectal cancers.

Research frontiers

There is increasing evidence to suggest that local excision should be restricted to patients with low risk T_1 rectal cancers. In these strictly selected patients, local excision may be an acceptable alternative, with equivalent oncological outcomes to radical surgery.

Innovations and breakthroughs

The oncological adequacy of local excision in the treatment of patients with high risk T_1 rectal cancers lacks consensus and the efficacy of immediate surgical rescue after local excision remains unclear. Therefore, the main purpose of our study was to evaluate the oncological outcomes of transanal local excision for the patients with high risk T_1 rectal cancers. The prognostic value of immediate conventional reoperation after transanal local excision was also evaluated.

Applications

In this study, the authors conclude that transanal local excision cannot be considered sufficient treatment for patients with high risk T_1 rectal cancers. Immediate conventional reoperation should be performed if the pathology of the local excision is high risk.

Terminology

Tumors with poor differentiation or positive margin or lymphovascular invasion were defined as high risk tumors.

Peer review

The authors evaluated the oncological outcomes of transanal local excision and the need for immediate conventional reoperation in the treatment of patients with high risk T_1 rectal cancers. This manuscript will be interesting for the readers.

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S- Editor Wang JL **L- Editor** Roemmele A **E- Editor** Zheng XM

World Journal of Gastrointestinal Oncology

Online Submissions: http://www.wjgnet.com/1948-5204office
wjgo@wjgnet.com
doi:10.4251/wjgo.v4.i4.89

World J Gastrointest Oncol 2012 April 15; 4(4): 89-93
ISSN 1948-5204 (online)

CASE REPORT

Simultaneous occurrence of colonic adenocarcinoma and MALT lymphoma: A series of three cases

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Received: November 16, 2011 Revised: January 14, 2012
Accepted: January 25, 2012
Published online: April 15, 2012

Abstract

Simultaneous development of adenocarcinoma and primary B cell lymphoma of mucosa-associated lymphoid tissue (MALT) lymphoma of the colon is rare; only one case has so far been reported out of 13 cases with the coexistence of colonic adenocarcinoma with involvement of the colon by lymphoma. We hereby present three more cases, two females (aged 75 and 71 years) and a male (aged 72 years). All three underwent colectomy based on a preoperative biopsy revealing colonic carcinoma. Histological examination of the resection specimens disclosed a colonic adenocarcinoma in two cases, whereas a tubulovillous adenoma with superficial foci of intraepithelial adenocarcinoma was seen in the third case. Moreover, in all three cases, a coexisting MALT lymphoma was diagnosed in the colon (1 case), in both colon and adjacent lymph nodes (1 case) or in colonic lymph nodes and omentum (1 case). In the last case, a post-operative bone marrow biopsy revealed extensive infiltration of the bone marrow, due to which the patient received postoperative chemotherapy. Diagnostic and treatment issues are briefly discussed.

Key words: Colon; Adenocarcinoma; B cell lymphoma of mucosa-associated lymphoid tissue lymphoma

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Argyropoulos T, Foukas P, Kefala M, Xylardistos P, Papageorgiou S, Machairas N, Boltetsou E, Machairas A, Panayiotides IG. Simultaneous occurrence of colonic adenocarcinoma and MALT lymphoma: A series of three cases. *World J Gastrointest Oncol* 2012; 4(4): 89-93 Available from: URL: http://www.wjgnet.com/1948-5204/full/v4/i4/89.htm DOI: http://dx.doi.org/10.4251/wjgo.v4.i4.89

INTRODUCTION

Colonic adenocarcinoma is the third most commonly diagnosed cancer worldwide[1]. In contrast, extranodal marginal zone B-cell lymphoma [lymphoma of the mucosa-associated lymphoid tissue (MALT) type] is rare, constituting 6%-8% of non Hodgkin lymphomas. The colon is a rare location for the aforementioned lymphoma[2]. Only one case of simultaneous occurrence of adenocarcinoma and MALT lymphoma of the colon has so far been reported[3] out of 13 cases with the coexistence of colonic adenocarcinoma and involvement of the colon by lymphoma[3-13]. We hereby report three more cases.

Table 1 Details of immunostains performed

	P/M (clone)	Company	Dilution	Treatment
CD3	M mouse (LN10)	Novocastra	1:200	PT
CD5	M rabbit (SP19)	DakoCytomation	1:50	PT
CD10	M mouse (56C6)	Novocastra	1:25	PT
CD20	M mouse (L26)	Novocastra	1:50	PT
CD21	M mouse (1F8)	DakoCytomation	r. t. u.	S1700
CD23	M rabbit (SP23)	DakoCytomation	1:50	PT
CD34	M mouse (QBEnd/10)	DakoCytomation	1:50	PT
CD35	M mouse (Ber-MAC-DRC)	DakoCytomation	1:30	S1700
CD43	M mouse (MT1)	Novocastra	1:50	PT
CD61	M mouse (Y2/51)	DakoCytomation	1:40	S1700
CD138	M mouse (MI15)	DakoCytomation	r. t. u.	ER1
cyclin D1	M rabbit (SP4)	DakoCytomation	r. t. u.	PT
Glycophorin A	M mouse (JC159)	DakoCytomation	1:100	PT
MPO	P rabbit	DakoCytomation	1:2500	PT
IgA	M mouse (6E2C1)	DakoCytomation	1:70	TR
IgG	M mouse (A57H)	DakoCytomation	1:70	TR
IgM	M mouse (R1/69)	DakoCytomation	1:100	TR
κ light chains	P rabbit	DakoCytomation	1:60.000	PT
λ light chains	P rabbit	DakoCytomation	1:60.000	PT
Bcl-2	M mouse (124)	DakoCytomation	1:40	PT

MPO: Myeloperoxidase; M: Monoclonal; P: Polyclonal; r. t. u.: Ready to use; PT: Dako Target Retrieval Solution, pH 9; S1700: Dako, Envision FLEX Target Retrieval Solution, low pH; ER1: Bond Epitope Retrieval Solution 1; TR: Trilogy, Cell Marque.

CASE REPORT

Case 1

A 75-year-old female was referred due to anemia, weakness, fatigue and presence of blood in the stools (positive Mayer test). Lower gastrointestinal endoscopy revealed a polypoid mass located about 4 cm proximal to the anal verge. An abdominoperineal resection was performed which showed a 7-cm polypoid tumor. Adjacent to the aforementioned tumor, a 1.5-cm large solid, whitish area was detected. A postsurgical work-up of upper endoscopy, abdominal computed tomography and bone marrow examination was negative for lymphoma involvement. The patient received no further treatment. Although she missed scheduled follow ups, she has since been readmitted due to intermittent incomplete intestinal obstruction. She is alive, 20 mo post-operatively.

Case 2

A 71-year-old female was admitted due to a fainting episode. She mentioned a loss of 20 kg over the past year and had anemia. Colonoscopy revealed a tumor of the ascending colon; a biopsy diagnosed it as adenocarcinoma. The patient underwent a right hemicolectomy which revealed an 8.5 cm large, constricting ulcerated tumor 12 cm from the ileocaecal valve. The patient received no adjuvant therapy. She has since been regularly followed up and is alive and well 4 years post-operatively.

Case 3

Colonoscopy of a 72-year-old male with anemia showed the presence of a polyp at the ascending colon, histologically shown to be a tubulovillous adenoma with superficial foci of intraepithelial adenocarcinoma. A subsequent right hemicolectomy specimen revealed a-4.5 cm large, fungating tumor at a distance of 7.6 cm from the ileocecal valve upon incision. He had no history of fever, loss of weight or night sweats. Clinical examination showed no peripheral lympadenopathy or hepatosplenomegaly. However, a post-operative bone marrow biopsy revealed infiltration (almost 80% of the total marrow area) by a CD20 (+), CD5 (-), CD10 (-), CD23 (-), CD43 (-), cyclin D1 (-) B cell lymphoid population, consistent with the MALT lymphoma previously diagnosed. Consequently, the patient was staged as IV A (Longano Staging system)[14] and was treated with six cycles of FCR [Fludarabine, Cyclophosphamide and Rituximab (monoclonal anti-CD20 antibody)]. He is alive and well 18 mo post-operatively.

Histological examination of the three cases

Surgical specimens were fixed in a 10% buffered formol solution and processed according to standard protocols. 4 μm thick, deparaffinised sections were stained with Haematoxylin-Eosin[15]. Moreover, immunostains with primary antibodies (Table 1) were performed.

Case 1: Histology showed the polypoid tumor to be a tubulovillous adenoma with superficial foci of high grade intraepithelial neoplasia (i.e., *in situ* adenocarcinoma), without invasion of muscularis mucosae or submucosa (Figure 1A). The whitish area had histological and immunohistochemical features of an extranodal marginal zone B-cell lymphoma (of MALT type) with prominent plasmacytic differentiation and cIgλ clonality (Figure 1B-F). Two out of twenty two colonic lymph nodes retrieved were involved by lymphoma. A postsurgical bone marrow biopsy revealed no involvement of the bone marrow.

Case 2: Histology showed the colonic tumor to be a moderately differentiated adenocarcinoma infiltrating the

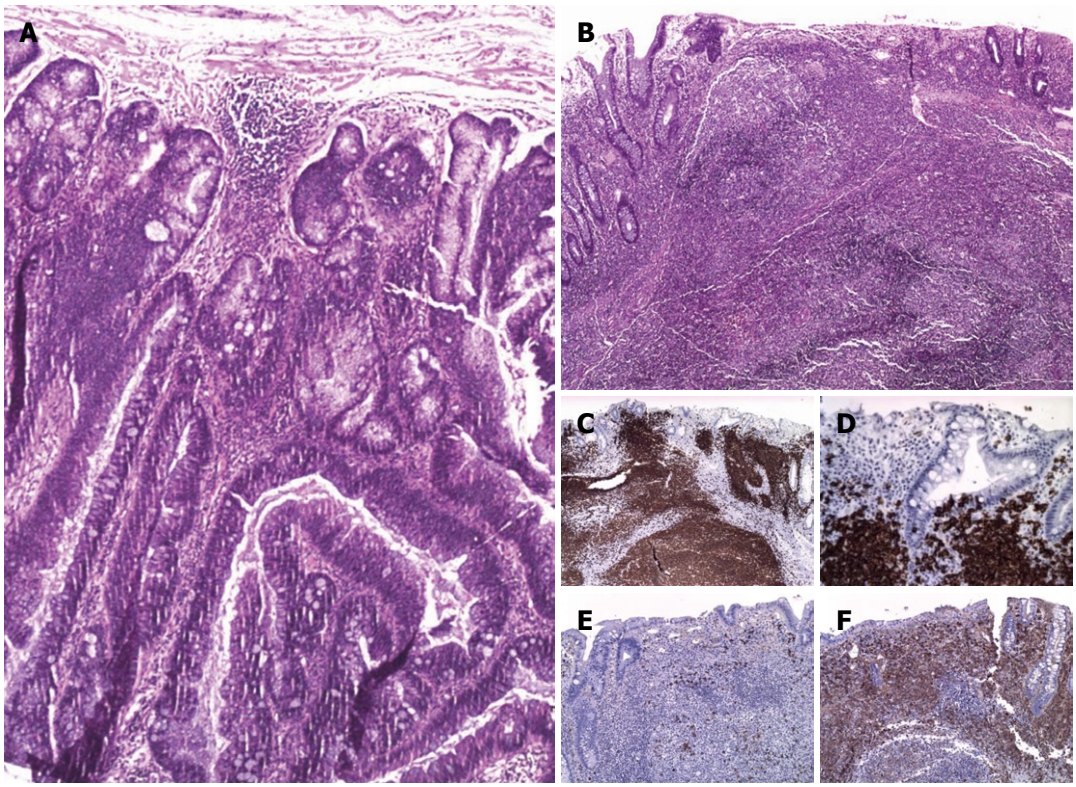

Figure 1 Histological examination of Case 1. Tubulovillous adenoma with superficial foci of high grade intraepithelial neoplasia (A: HE, × 4); coexisting colonic lymphoma of MALT type [B: HE, × 4; C: CD20, × 4; D: CD20, × 20 (lymphoepithelial lesions); E: κ light chain, × 4; F: λ light chain, × 4].

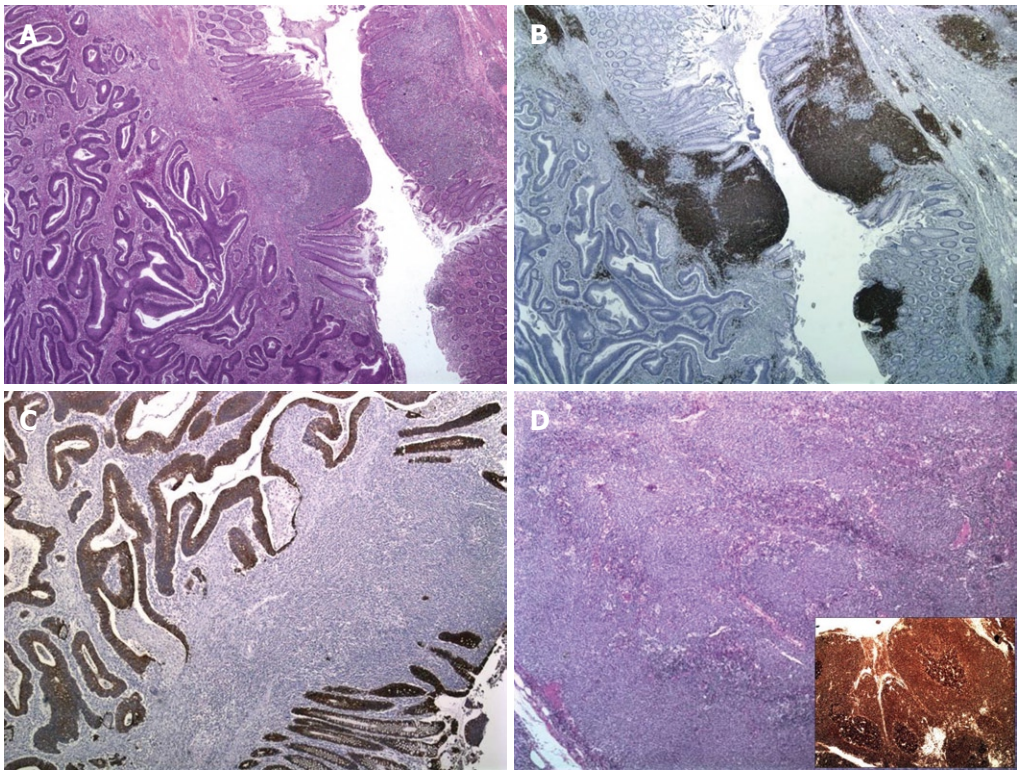

Figure 2 Histological examination of Case 2. Colonic lymphoma of MALT type adjacent to a moderately differentiated adenocarcinoma (A: HE, × 4; B: CD20, × 4; C: CKAE1/AE3, × 20). Colonic lymph node involved by lymphoma [D: HE, × 4; CD20, × 4 (inset)].

colonic wall and the surrounding adipose tissue, but not extending to or beyond the serosa. Adjacent to the carcinoma, areas of extranodal marginal zone B-cell lymphoma (of MALT type) were identified (Figure 2A-C), involving

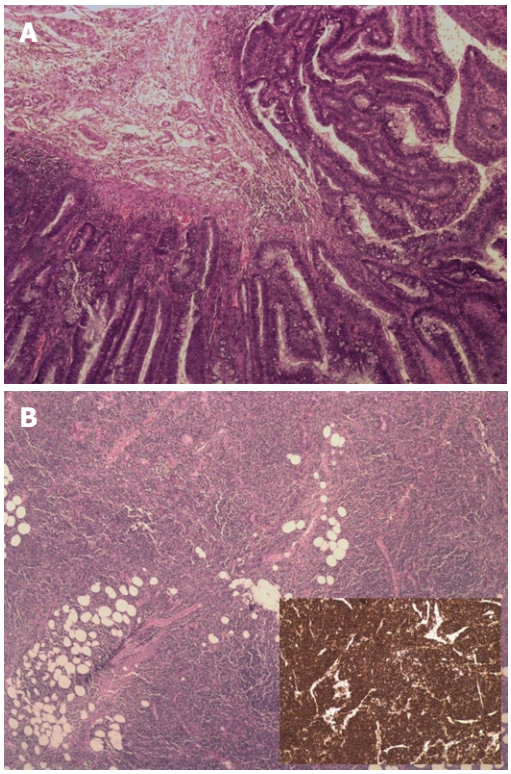

Figure 3 Histological examination of Case 3. Focus of *in situ* adenocarcinoma within a tubulovillous colonic adenoma (A: HE, × 4). Omentum involved by lymphoma of MALT type [B: HE, × 4; CD20, × 4 (inset)].

22 out of 34 totally excised colonic lymph nodes as well (Figure 2D). No bone marrow involvement was detected.

Case 3: Histological examination revealed a tubulovillous adenoma containing superficial foci of well differentiated colonic adenocarcinoma infiltrating the submucosa (Figure 3A). No secondaries were found in the 12 colonic lymph nodes retrieved; nevertheless, both these lymph nodes and a 5-cm large fragment of omentum were involved by an extranodal marginal zone B-cell lymphoma (of MALT type) (Figure 3B).

DISCUSSION

Our cases are, to the best of our knowledge, the second ever reported concerning simultaneous occurrence of adenocarcinoma and MALT lymphoma of the colon. Out of 13 cases of coexisting adenocarcinoma and lymphoma of the colon[3-13], only one is a MALT type lymphoma[3]; the rest usually deal either with another type of primary colonic lymphoma, mostly mantle cell lymphoma[5,9,11], or with involvement of the colon by an extracolonic lymphoma.

Two issues are to be noted: (1) whereas the presence of lymphocytes in the vicinity of colonic carcinomas is common, these cells are not always reactive. The presence of a dense lymphocytic infiltrate should therefore alert the pathologist to carefully assess its morphology, immunophenotype and clonality in order to rule out a coexisting MALT lymphoma; and (2) in a case when such a lymphoma is diagnosed, it is important to closely scrutinize colonic lymph nodes for their eventual involvement.

In all three cases, MALT lymphoma was only diagnosed in the excision specimen, with no previous clinical symptoms attributable to it. The simultaneous diagnosis of a lymphoma in a colectomy specimen led to a different post-operative work-up, including a bone marrow biopsy, in order to exclude extracolonic extension of the lymphoma.

Since no etiological factor for primary colonic lymphomas has been determined until now, its coexistence with colonic adenocarcinoma might rather be attributed to the advanced age of the patient in all cases.

Treatment of colon MALT lymphoma is not standard. However, there is a general agreement that surgical treatment alone is effective for localized disease, while combined chemotherapy is the mainstay for disseminated disease[16]. The role of inclusion of Rituximab (monoclonal anti-CD20 antibody) to the chemotherapy has not yet been commented on in this rare entity. In our case series, surgical resection was the only treatment for two patients with local disease, whereas the third patient, due to disseminated disease with bone marrow involvement, also received post-operative combined chemo-immunotherapy.

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S- Editor Wang JL **L- Editor** Roemmele A **E- Editor** Zheng XM

World Journal of Gastrointestinal Oncology

Online Submissions: http://www.wjgnet.com/1948-5204office
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World J Gastrointest Oncol 2012 April 15; 4(4): I
ISSN 1948-5204 (online)

Acknowledgments to reviewers of *World Journal of Gastrointestinal Oncology*

Many reviewers have contributed their expertise and time to the peer review, a critical process to ensure the quality of *World Journal of Gastrointestinal Oncology*. The editors and authors of the articles submitted to the journal are grateful to the following reviewers for evaluating the articles (including those published in this issue and those rejected for this issue) during the last editing time period.

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World J Gastrointest Oncol 2012 April 15; 4(4): I
ISSN 1948-5204 (online)

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EASL Monothematic Conference: IMLI - Immune Mediated Liver Injury
Birmingham, United Kingdom

January 19-21, 2012
American Society of Clinical Oncology 2012 Gastrointestinal Cancers Symposium
San Francisco, CA, United States

January 19-21, 2012
2012 Gastrointestinal Cancers Symposium
San Francisco, CA, United States

January 20-21, 2012
American Gastroenterological Association Clinical Congress of Gastroenterology and Hepatology
Miami Beach, FL, United States

February 2-4, 2012
2012 Genitourinary Cancers Symposium
San Francisco, CA, United States

February 6-8, 2012
Pediatric Cancer Translational Genomics
Phoenix, AZ, United States

February 8–10, 2012
The 84th Annual Meeting of Japanese Gastric Cancer Association
Osaka, Japan

February 10-11, 2012
Cancer Survivorship for Clinicians
Seattle, WA, United States

February 14-17, 2012
ASCO Multidisciplinary Cancer Management Course
Eldoret, Kenya

February 20-24, 2012
Word Conference on Colorectal Cancer
FL, United States

February 22-23, 2012
National Cancer Institute Annual Biospecimen Research Network Symposium: "Advancing Cancer Research Through Biospecimen Science"
Bethesda, MD, United States

February 22-25, 2012
30th German Cancer Congress
Berlin, Germany

February 24, 2012
ASCO-German Cancer Society Joint Symposium, German Cancer Congress
Berlin, Germany

February 24-27, 2012
Canadian Digestive Diseases Week 2012
Montreal, Canada

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First International Gulf Joint Conference: Management of colon, breast, and lung cancer (Joint Symposium)
Dammam, Saudi Arabia

March 9-10, 2012
ESMO Conference on Sarcoma and GIST
Milan, Italy

March 10-11, 2012
Colorectal Polyps and Cancers: A Multidisciplinary Approach
Scottsdale, AZ, United States

March 17-21, 2012
Methods in Cancer Research Workshop (Advanced Cancer Course)
Al Asha, Saudi Arabia

March 22-24, 2012
The 1st St.Gallen EORTC Gastrointestinal Cancer Conference
St.Gallen, Switzerland

April 13-15, 2012
Asian Oncology Summit 2012
Singapore, Singapore

April 15-17, 2012
European Multidisciplinary Colorectal Cancer Congress 2012
Prague, Czech

April 18-20, 2012
The International Liver Congress 2012
Barcelona, Spain

April 19-21, 2012
Internal Medicine 2012
New Orleans, LA, United States

April 20–21, 2012
OOTR 8th Annual Conference - Organisation for Oncology and Translational Research
Kyoto, Japan

April 28, 2012
Issues in Pediatric Oncology
Kiev, Ukraine

May 19-22, 2012
Digestive Disease Week 2012
San Diego, CA, United States

June 18-21, 2012
Pancreatic Cancer: Progress and Challenges
Lake Tahoe, NV, United States

June 27-30, 2012
ESMO 14th World Congress on Gastrointestinal Cancer 2012
International Convention Center Of Barcelona,
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July 1–5, 2012
10th World Congress of the International Hepato-Pancreato-Biliary Association
Paris, France

July 5-7, 2012
International Research Conference on Liver Cancer
Heidelberg, Germany

July 6-8, 2012
The 3rd Asia – Pacific Primary Liver Cancer Expert Meeting "A Bridge to a Consensus on HCC Management"
Shanghai, China

September 1-4, 2012
OESO 11th World Conference
Como, Italy

September 14-16, 2012
ILCA 2012 - Sixth Annual Conference of the International Liver Cancer Association
Berlin, Germany

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Research Symposium, Inflammation and Cancer
Houston, TX, United States

October 15 - 17 2012
13th World Congress of the International Society for Diseases of the Esophagus
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World J Gastrointest Oncol 2012 April 15; 4(4): I-V
ISSN 1948-5204 (online)

GENERAL INFORMATION

World Journal of Gastrointestinal Oncology (*World J Gastrointest Oncol*, *WJGO*, ISSN 1948-5204, DOI: 10.4251), is a monthly, open-access (OA), peer-reviewed journal supported by an editorial board of 404 experts in gastrointestinal oncology from 41 countries.

The biggest advantage of the OA model is that it provides free, full-text articles in PDF and other formats for experts and the public without registration, which eliminates the obstacle that traditional journals possess and usually delays the speed of the propagation and communication of scientific research results. The open access model has been proven to be a true approach that may achieve the ultimate goal of the journals, i.e. the maximization of the value to the readers, authors and society.

Maximization of personal benefits

The role of academic journals is to exhibit the scientific levels of a country, a university, a center, a department, and even a scientist, and build an important bridge for communication between scientists and the public. As we all know, the significance of the publication of scientific articles lies not only in disseminating and communicating innovative scientific achievements and academic views, as well as promoting the application of scientific achievements, but also in formally recognizing the "priority" and "copyright" of innovative achievements published, as well as evaluating research performance and academic levels. So, to realize these desired attributes of *WJGO* and create a well-recognized journal, the following four types of personal benefits should be maximized. The maximization of personal benefits refers to the pursuit of the maximum personal benefits in a well-considered optimal manner without violation of the laws, ethical rules and the benefits of others. (1) Maximization of the benefits of editorial board members: The primary task of editorial board members is to give a peer review of an unpublished scientific article *via* online office system to evaluate its innovativeness, scientific and practical values and determine whether it should be published or not. During peer review, editorial board members can also obtain cutting-edge information in that field at first hand. As leaders in their field, they have priority to be invited to write articles and publish commentary articles. We will put peer reviewers' names and affiliations along with the article they reviewed in the journal to acknowledge their contribution; (2) Maximization of the benefits of authors: Since *WJGO* is an open-access journal, readers around the world can immediately download and read, free of charge, high-quality, peer-reviewed articles from *WJGO* official website, thereby realizing the goals and significance of the communication between authors and peers as well as public reading; (3) Maximization of the benefits of readers: Readers can read or use, free of charge, high-quality peer-reviewed articles without any limits, and cite the arguments, viewpoints, concepts, theories, methods, results, conclusion or facts and data of pertinent literature so as to validate the innovativeness, scientific and practical values of their own research achievements, thus ensuring that their articles have novel arguments or viewpoints, solid evidence and correct conclusion; and (4) Maximization of the benefits of employees: It is an iron law that a first-class journal is unable to exist without first-class editors, and only first-class editors can create a first-class academic journal. We insist on strengthening our team cultivation and construction so that every employee, in an open, fair and transparent environment, could contribute their wisdom to edit and publish high-quality articles, thereby realizing the maximization of the personal benefits of editorial board members, authors and readers, and yielding the greatest social and economic benefits.

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World Journal of Gastrointestinal Oncology

ISSN

ISSN 1948-5204 (online)

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World Journal of Gastrointestinal Oncology
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3 **Tian D**, Araki H, Stahl E, Bergelson J, Kreitman M. Signature of balancing selection in Arabidopsis. *Proc Natl Acad Sci USA* 2006; In press

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4 **Diabetes Prevention Program Research Group**. Hypertension, insulin, and proinsulin in participants with impaired glucose tolerance. *Hypertension* 2002; **40**: 679-686 [PMID: 12411462 PMCID:2516377 DOI:10.1161/01.HYP.0000035706.28494.09]

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5 **Vallancien G**, Emberton M, Harving N, van Moorselaar RJ; Alf-One Study Group. Sexual dysfunction in 1, 274 European men suffering from lower urinary tract symptoms. *J Urol* 2003; **169**: 2257-2261 [PMID: 12771764 DOI:10.1097/01.ju.0000067940.76090.73]

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6 21st century heart solution may have a sting in the tail. *BMJ* 2002; **325**: 184 [PMID: 12142303 DOI:10.1136/bmj.325.7357.184]

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9 Outreach: Bringing HIV-positive individuals into care. *HRSA Careaction* 2002; 1-6 [PMID: 12154804]

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10 **Sherlock S**, Dooley J. Diseases of the liver and billiary system. 9th ed. Oxford: Blackwell Sci Pub, 1993: 258-296

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12 **Breedlove GK**, Schorfheide AM. Adolescent pregnancy. 2nd ed. Wieczorek RR, editor. White Plains (NY): March of Dimes Education Services, 2001: 20-34

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15 Morse SS. Factors in the emergence of infectious diseases. Emerg Infect Dis serial online, 1995-01-03, cited 1996-06-05; 1(1): 24 screens. Available from: URL: http://www.cdc.gov/ncidod/eid/index.htm

Patent (list all authors)

16 **Pagedas AC**, inventor; Ancel Surgical R&D Inc., assignee. Flexible endoscopic grasping and cutting device and positioning tool assembly. United States patent US 20020103498. 2002 Aug 1

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